SECURITY
How to Survive Cyberwar

PSYCHOLOGY
The Power of Self-Control

BIOLOGY
Tricks for Extreme Evolution

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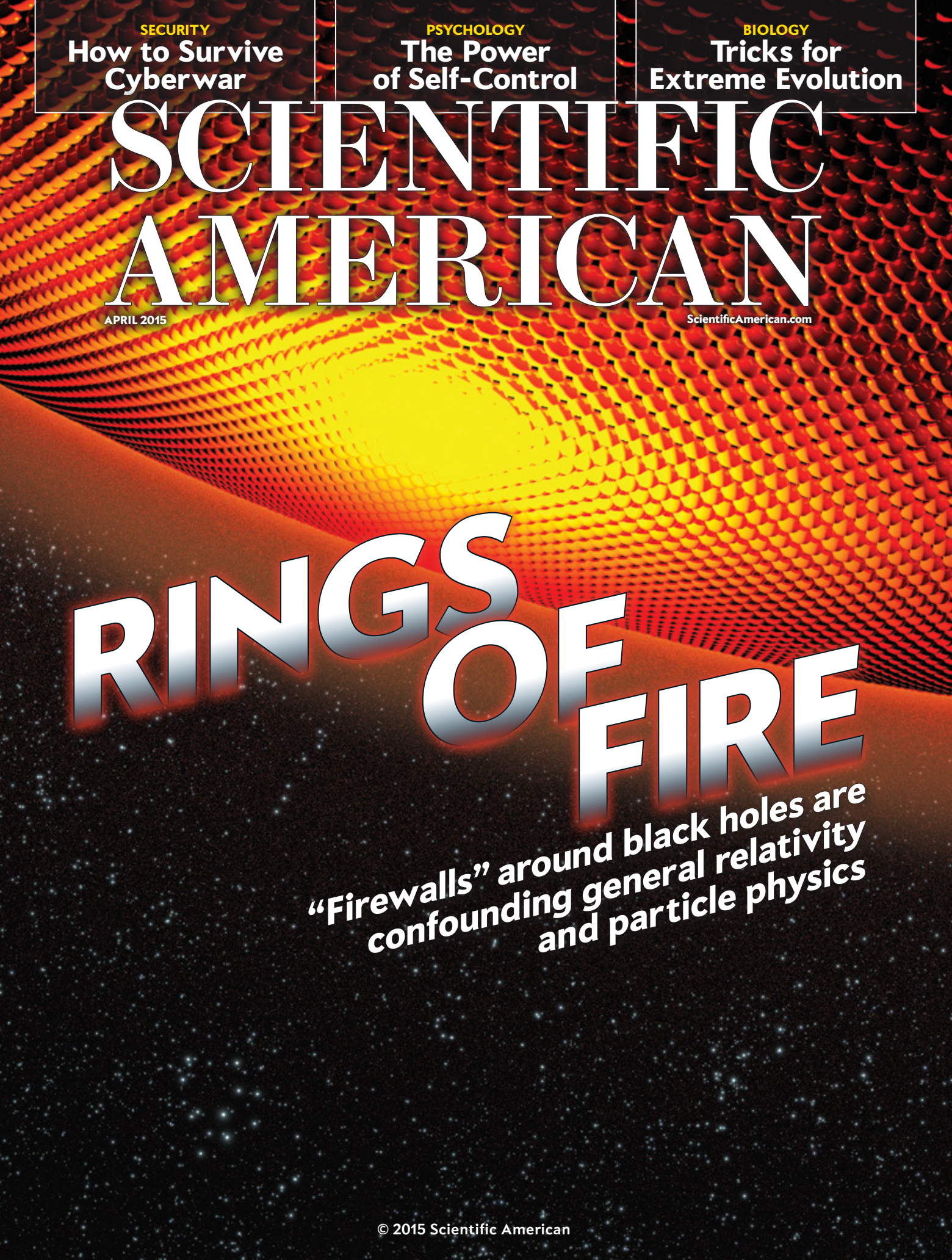

RINGS OF FIRE

"Firewalls" around black holes are confounding general relativity and particle physics


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ON THE COVER

The event horizon of a black hole—the point of no return—was once thought to be an unremarkable area of space. New considerations based on string theory, however, suggest this border is actually a wall of high-energy particles that would destroy any object that tried to pass through. These "firewalls" may even represent the end of spacetime altogether. Image by Kenn Brown, Mondolithic Studios.

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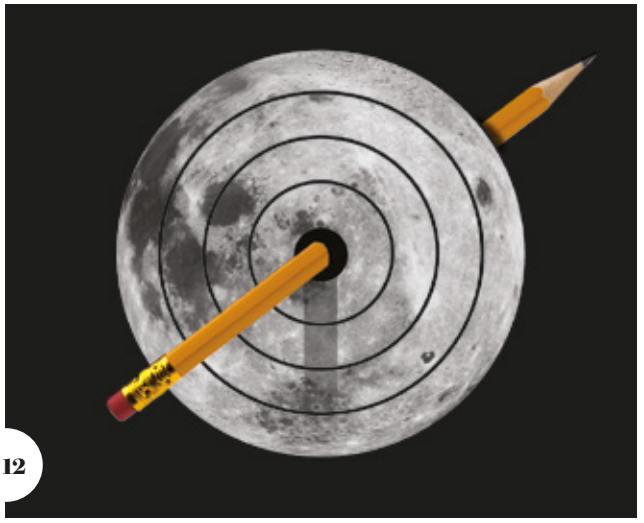
Photograph by Dominic Bracco II



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DEPARTMENTS

ON THE WEB

Dawn Arrives at Ceres
Follow our coverage of NASA's spacecraft Dawn, which recently rendezvoused with Ceres, the largest object in the asteroid belt between Mars and Jupiter.
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Mariette DiChristina is editor in chief of *Scientific American*. Follow her on Twitter @mdichristina

Dark and Stormy

WE'RE USED TO THINKING OF BLACK HOLES AS PLACES where gravity is so strong not even light can escape—where an unnoticed crossing by a hapless astronaut over an unseen and unfelt "event horizon" nonetheless means a point of no return. "According to Einstein's general theory of relativity, no signposts would mark the spot where the chance of escape dropped to zero," writes physicist Joseph Polchinski.

But in this issue's cover story, "Burning Rings of Fire," Polchinski paints a new picture, courtesy of his and others' work in a discipline that Albert Einstein found vexing: quantum mechanics. Replacing the unknowable border to an eternity of darkness is a stormy "firewall" of instantly lethal high-energy particles. "If quantum mechanics is to be trusted, firewalls are the consequence," Polchinski notes. The controversial finding arose from scientists' attempts to resolve apparent contradictions of physics that occur in extreme environments, a challenge highlighted by Stephen Hawking, among others. Turn to page 36.

Nanotechnology can be equally invisible to the eye but promises far more benign—in fact, salutary—encounters. In our special report on the "Future of Medicine," starting on page 42, we examine what benefits nanomedicine is bringing us already and how those will take shape in the future. We can look forward to improvements in cancer-fighting therapies, diagnostics, wound healing, delivery of drugs with nanomotors, and more.

NANOBOTS for future therapies

A different class of unseen actors is at work in the worrying trend of cyberattacks. Software vulnerabilities have led to hacked networks, servers, personal computers and online accounts—with theft of information from millions. Your own PC or corporate network can become enslaved to further the ends of cybercriminals.

"How to Survive Cyberwar," by Keren Elazari, takes an unsettling look at the growing problem. Taking a military point of view, Elazari argues, will ultimately not be the most successful approach—indeed, "it might just make things worse." Instead she suggests thinking of it as a public health issue. Government agencies are key players, "but they cannot stop the spread of [cyber]diseases on their own." Success will mean that all of us play important roles. See page 66 for how we can, as cybercitizens, do the equivalent of washing our hands and getting our vaccines. SA

Illustration by Harry Campbell (nanobots); Illustration by Nick Higgins (DiChristina)

editors@sciam.com

December 2014

CANCER TREATMENT IN SENIORS

As a bioethicist, a 67-year-old and a liberal, I find "Never Too Old for Chemo," by Claudia Wallis [The Science of Health], a welcome and long overdue antidote to the conventional wisdom that it is best for sick old people to bow out quickly, gracefully and inexpensively. (You bet I'll opt for aggressive treatment if I get cancer when I'm 100!)

Yet I'm uneasy about considering such factors as "social support" in determining which elderly patients should be eligible for chemotherapy. Doing so risks discriminating against patients who lack families—or whose families would prefer that their old folk be "allowed" to die even if they want to live.

Felicia Nimue Ackerman
Brown University

I would say that deciding whether to opt in to, or out of, aggressive therapies such as chemotherapy to treat cancer would greatly depend on what type of malignancy a person has. Wallis's father-in-law, whom she describes as deciding against treatment, had what most people would consider a "certain death sentence": advanced, metastatic pancreatic cancer. Two other elders described in the article, who decided to fight, respectively, bladder cancer and lymphoma, were, it is hoped, not coerced by family members or physicians.

"Considering 'social support' in determining which elderly patients should be eligible for chemotherapy risks discriminating against patients who lack families."

FELICIA NIMUE ACKERMAN *BROWN UNIVERSITY*

There are cancers that can be fought with chemotherapy, at any age, but many factors have to be weighed.

Gordon W. Reiter
Sedona, Ariz.

POLICE BODY CAMS

In "Caution: Cops with Cameras," the editors warn that further planning and research should precede more police departments adopting body cameras to record encounters between their officers and the public.

I think helpful information could be gleaned from the Federal Aviation Administration on the effects, bad and good, of workers and their charges being monitored. Airline pilots and air-traffic controllers may have their words recorded and stored for a while in the event that something happens. In addition, pilots have a "black box" watching their control inputs, and controllers may have their radar scopes recorded.

Because this approach seems to be fairly new to police departments, perhaps it would help for the FAA to share any information that might be useful.

Jeff Ottaway
Retired air-traffic controller
via e-mail

RESEARCH ETHICS

In discussing the new DNA-editing technique CRISPR in "The Gene Genie," Margaret Knox describes ethical concerns about the technology. These concerns can be extrapolated to a significant issue with research in general: that we must be mindful of ethical, legal and social implications.

Most scientific endeavors can have positive or negative applications but often just have ethically agnostic ones. Yet the typical ex post facto, knee-jerk, reactionary rules to regulate these endeavors—commonly based solely on fears of misuse—are at best misguided and are, in many instances, actually detrimental to the promotion of science.

As such, these issues should be brought up early in the course of basic science research and the development of new technologies. Any subsequent resulting restrictions on science and technology ought to always be balanced against the real possibility of impeding those innovations.

Dov Greenbaum
Yale University School of Medicine
Director, Zvi Meitar Institute for Legal Implications of Emerging Technologies, Interdisciplinary Center, Herzliya, Israel

CONFIRMED CONSPIRACY

The problem with Michael Shermer's Skeptic column "Conspiracy Central" is that it treats all "conspiracy theories" as roughly equal and implies that anybody who lends credence to even one such "theory" must have deep psychological problems. It certainly couldn't be because there might be actual evidence to support the conclusion that a conspiracy of some kind exists.

Regarding the events of 9/11, I would point out that the official version of what happened must be considered a "conspiracy theory." It has all four necessary elements that Shermer himself quotes from Joseph E. Uscinski and Joseph M. Parent's book on the subject: "(1) A group (2) acting in secret (3) to alter institutions … (4) at the expense of the common good."

Whether Shermer subscribes to the official 9/11 story or the "inside job" account, he must be a conspiracy theorist himself!

Yolanda DeByle
via e-mail

SHERMER REPLIES: Yes, the al Qaeda conspirators who plotted in secret to fly planes into buildings constitutes a conspiracy, but only one of the conspiracy theories about 9/11 is true, which is that Osama bin Laden and Khalid Sheik Mohammed acted without the knowledge of or assistance from the Bush administration.

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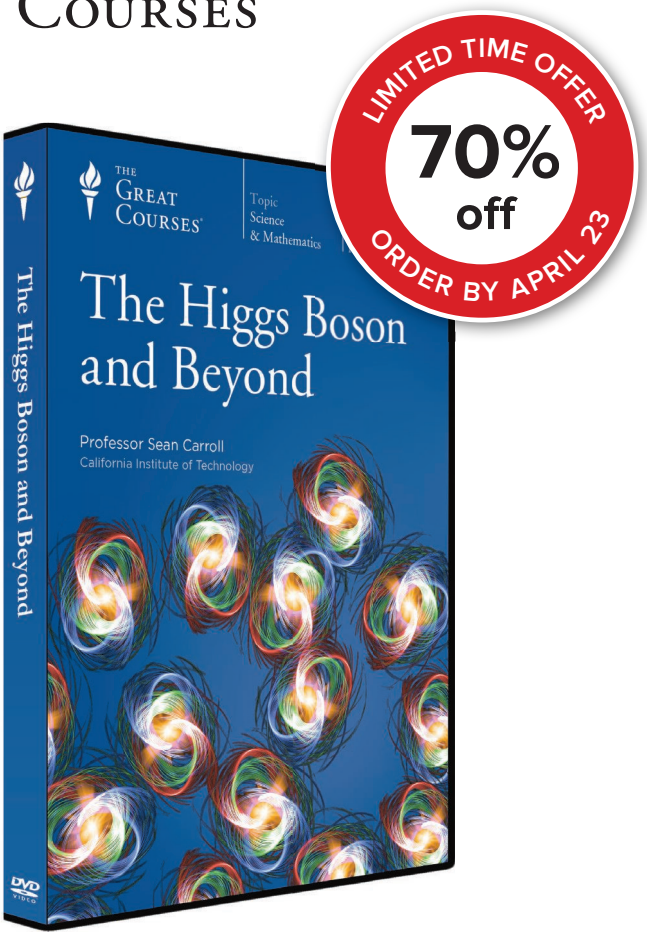

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The conspiracy theory that 9/11 was an inside job has been thoroughly debunked not only by Skeptic magazine (search "9/11" at Skeptic.com) but by al Qaeda itself, which boasted that it did it and that it would do it again elsewhere.

UNBEARABLE FRUIT

Stephani Sutherland's article on chronic "Pain That Won't Quit" reminded me of a problem I had 30 years ago. My feet were in constant pain. Doctors were not very helpful, and I thought that it was because I was running a mile or so every morning.

What I found out was that it was because of eating fruit: I drank a glass of orange juice every morning. When I went on a trip for a week and didn't drink juice, my feet quit hurting. When I tried drinking it again, the pain would come back. Other fruits such as strawberries cause problems for me, too. So the pain other people get might be from something they eat or drink.

PAUL HART
via e-mail

ERRATA

"Transparent Organisms," by Ryan Bradley [World Changing Ideas], incorrectly states that Viviana Gradinaru and her colleagues did work on replacing lipid molecules in tissues to make them transparent in the laboratory of the late neuroimmunologist Paul Patterson at the California Institute of Technology. The work was performed at neuroscientist Karl Deisseroth's lab at Stanford University.

"Taking the Sting Out of Pain," by Mark Peplow, which is an accompanying sidebar to "Pain That Won't Quit," by Stephani Sutherland, erroneously refers to the pain-killing drug ziconotide as based on a molecule from the venomous cone snail species *Conus victoriae*. It was from another cone snail, *Conus magus*. The new research described in the article involves painkillers derived from *C. victoriae*.

CLARIFICATION

"The Jet Stream Is Getting Weird," by Jeff Masters, refers to Rossby waves as bends in the jet stream that typically progress across the U.S. in three to five days. Rather smaller-scale bends called short waves are embedded in the larger Rossby waves and progress in that time frame.

LETTERS TO THE EDITOR

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Ban the Tan

Tanning beds can be seductive, addictive and a route to cancer—especially for teenagers

As spring begins, fun in the sun—even artificial sun—beckons teenagers. Many, especially girls, flock to tanning salons to acquire a base tan for the beach and get that "healthy glow" for a strapless prom dress. But whatever the reason or the season, minors should not be allowed to lie in tanning beds. These devices are skin cancer factories, and people younger than 18 have the highest risk.

One fifth of girls in grades 9 through 12 have bathed in ultraviolet (UV) rays from a tanning device in the past year, and one out of 10 girls reported popping into a tanning bed at least 10 times during that period, according to the Youth Risk Behavior Survey of 2013. (Only 5 percent of teen boys used beds at all.) The 14,000 tanning salons in the U.S. make that access easy. The quest for a tan contributes to frequent visits, but the behavior is also addictive. Basking under the bulbs releases opioid endorphins that increase relaxation and boost positive feelings that make patrons seek out the exposure again.

Their skin cells, however, are not happy. UV rays damage cellular DNA, which increases the chances those cells will become malignant. Radiation from indoor tanning devices is often more intense than the sun's natural rays. In a typical indoor tanning session, a person faces UV radiation at least as strong as midday sun in southern Europe. Concern over this intensity led the World Health Organization in 2009 to reclassify tanning devices as a high-level carcinogen—their most dangerous designation, which also includes cigarettes and plutonium. The number of skin cancer cases linked to tanning beds every year is two times the number of lung cancer cases associated with smoking.

The evidence of the danger continues to mount. Last year a systematic review and meta-analysis of 88 studies concluded that the beds lead to over 10,000 new cases of melanoma—the deadliest form of skin cancer—every year in the U.S., Australia and Europe and as many as 450,000 cases of other skin cancers.

The tanning habit is dangerous for anyone but especially risky for young users because the earlier UV damage begins, the more time it has to add up and get worse. People who begin tanning before the age of 35 have a melanoma risk that is at least 60 percent greater than those who start after that age. Melanoma is the second most common cancer among women in their 20s, and its incidence in those young women continues to rise, even as the rates of most other cancers have stabilized.

Because the hazards are so clear, Brazil outlawed artificial tanning for all its citizens—regardless of age—in 2011. Most of Australia's states and territories did the same as of this January. Nor can minors step foot in tanning salons in 11 European countries, including the U.K., France, Germany and Spain.

In the U.S., however, safety measures have been scattershot. Last year the Food and Drug Administration ordered that all tanning devices must carry a "black box" label warning that states indoor tanning is known to cause cancer and that minors should avoid it. Various states require parental consent, time limits and mandatory eye protection. Research shows, however, that these small-scale efforts are ineffective. Currently 10 states have absolute bans on the books for minors.

The U.S. needs a national ban so that all minors are protected immediately. Opponents, such as the Indoor Tanning Association, argue that such laws take away parenting rights and represent a slippery slope of growing government interference. But the health of our society's youngest members is paramount. The WHO, the U.S. Department of Health and Human Services, and leading medical societies support a ban for minors. We don't allow anyone younger than 18 to buy cigarettes. It is time to stop them from frying under bulbs. SA

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Commentary on science in the news from the experts

Russell Shilling is executive director of STEM at the U.S. Department of Education. A retired U.S. Navy captain and aerospace experimental psychologist, he has worked extensively with Sesame Workshop and has served as a program officer at both the Office of Naval Research and DARPA.

The Case for Education Moon Shots

Why the U.S. needs to establish a DARPA of pedagogy

In a recent study sponsored by the Business Roundtable and the nonprofit group Change the Equation, 97 percent of the CEOs of major American companies identified a lack of science, technology, engineering and math (STEM) skills among the national workforce as a problem for their businesses. Over the next five years these firms will need to hire approximately one million new employees with these skills and more than 600,000 with applied science backgrounds. The nation has been in this situation before. In 1944 President Franklin Delano Roosevelt commissioned Vannevar Bush, director of the wartime U.S. Office of Scientific Research and Development, to create a plan for sustaining the momentum of scientific achievement that had occurred during World War II, in part by responding to a looming skills shortage—the result of the large number of potential students who had been drafted into the military.

One of the biggest impacts of Bush's report was to create the separation of basic and applied research, a model that predominates in federally funded science today. Although this separation has been very effective in many fields, in education and the social sciences, basic research sometimes fails to translate successfully into applied settings. As we study ways to confront this new crisis, we should consider an alternative approach to research—one that the Defense Advanced Research Projects Agency has been demonstrating since 1958.

The DARPA process is reminiscent of the development cycles for radar and the atomic bomb during WWII: diverse teams of the brightest minds iterate continuously on basic research challenges aimed at solving enormously complex problems. Unlike traditional basic or applied research, the DARPA method resides in a category that the late science policy researcher Donald E. Stokes introduced in his 1997 book, *Pasteur's Quadrant*. In Stokes's classification, basic research resides in Bohr's quadrant: it is the quest for basic knowledge without regard for the final use of that knowledge. Applied research lies in Edison's quadrant, where producing a specific product is the top priority. In Pasteur's quadrant, named after Louis Pasteur, basic research is applied to solve specific and immediate problems.

As an agency, DARPA lives in Pasteur's quadrant. Every project is a moon shot. The final goal is clear, but the process for getting there remains flexible. In the U.S. Department of Education's Office of STEM, we have been proposing the use of Pasteur's quadrant as a means for creating so-called moon shots for education, especially at the intersections of science and technology. The possibilities for research are plentiful. Can customized digital tutors be created that adapt to the student over the course of their education, from preschool through college? Can these same educational technologies be developed in ways that encourage and enhance lifelong learning? Can we find new approaches to assessment that measure mastery in real time rather than at the end of a course? If solutions such as these are possible, they will be achieved only by bringing together the most innovative teams of researchers, professional developers and educators to tackle the problems as a whole. That is why President Barack Obama's 2016 budget proposes up to $50 million for an Advanced Research Projects Agency–Education (ARPA-ED) to allow the Department of Education to support rapid-cycle, high-impact technology development aimed at preparing students for the 21st-century workforce.

To determine where investment should be made, my colleagues and I are currently convening groups of innovators and educators to evolve a vision of STEM education in 2025. Once that vision is clear, we will deconstruct it and outline a plan for achieving it. Will that vision be the correct one? It is hard to say, but this initial vision does not have to be absolutely correct. As long as the basic target of improving educational outcomes remains in sight, the goal and the vision can be adjusted as we work toward them. Just as DARPA researchers could not have predicted what the Internet would become when they laid its foundation in 1968, today's innovators will not know how technology can transform education until they roll up their sleeves and do it. SA

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Illustration by Oliver Munday

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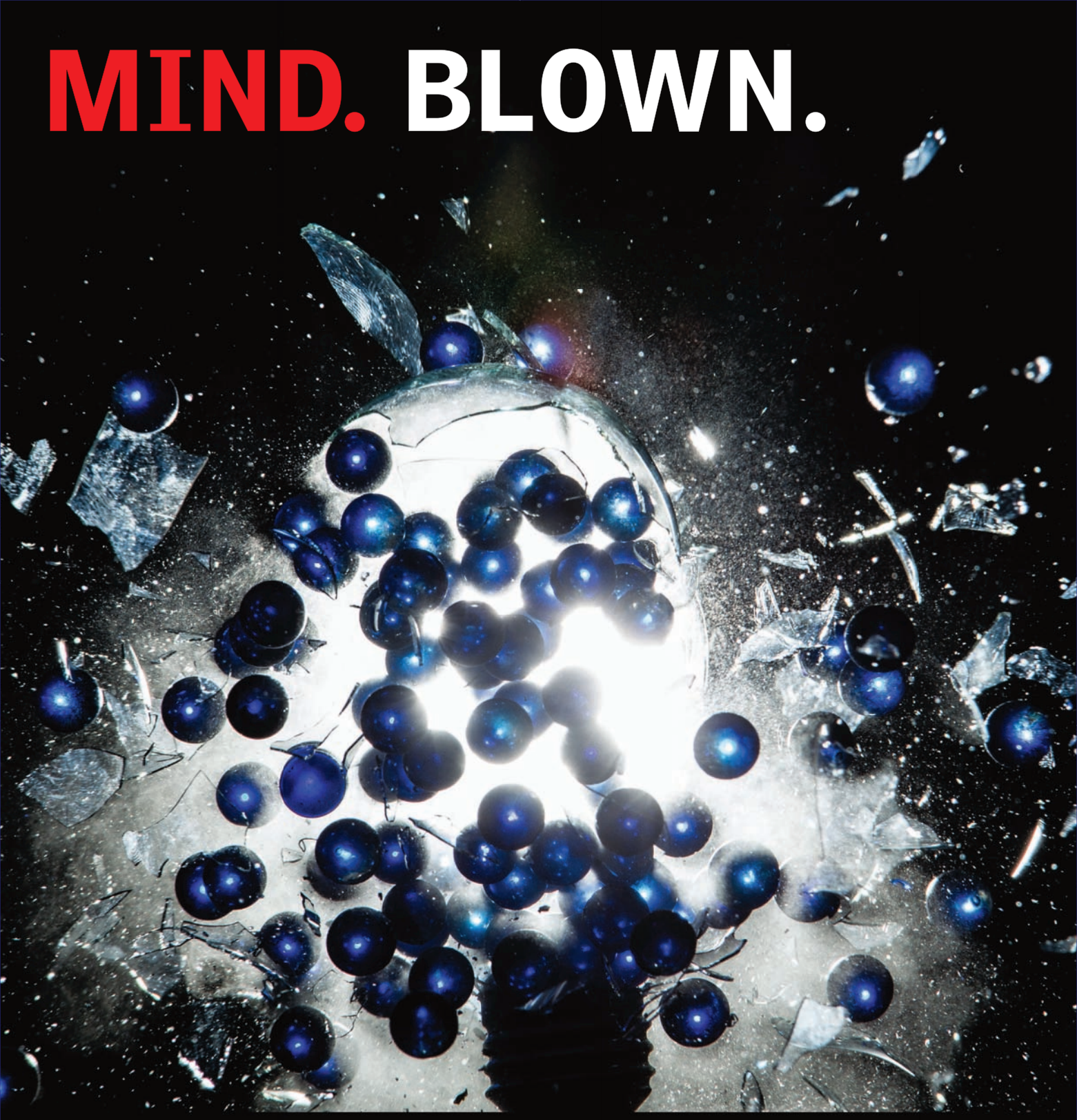

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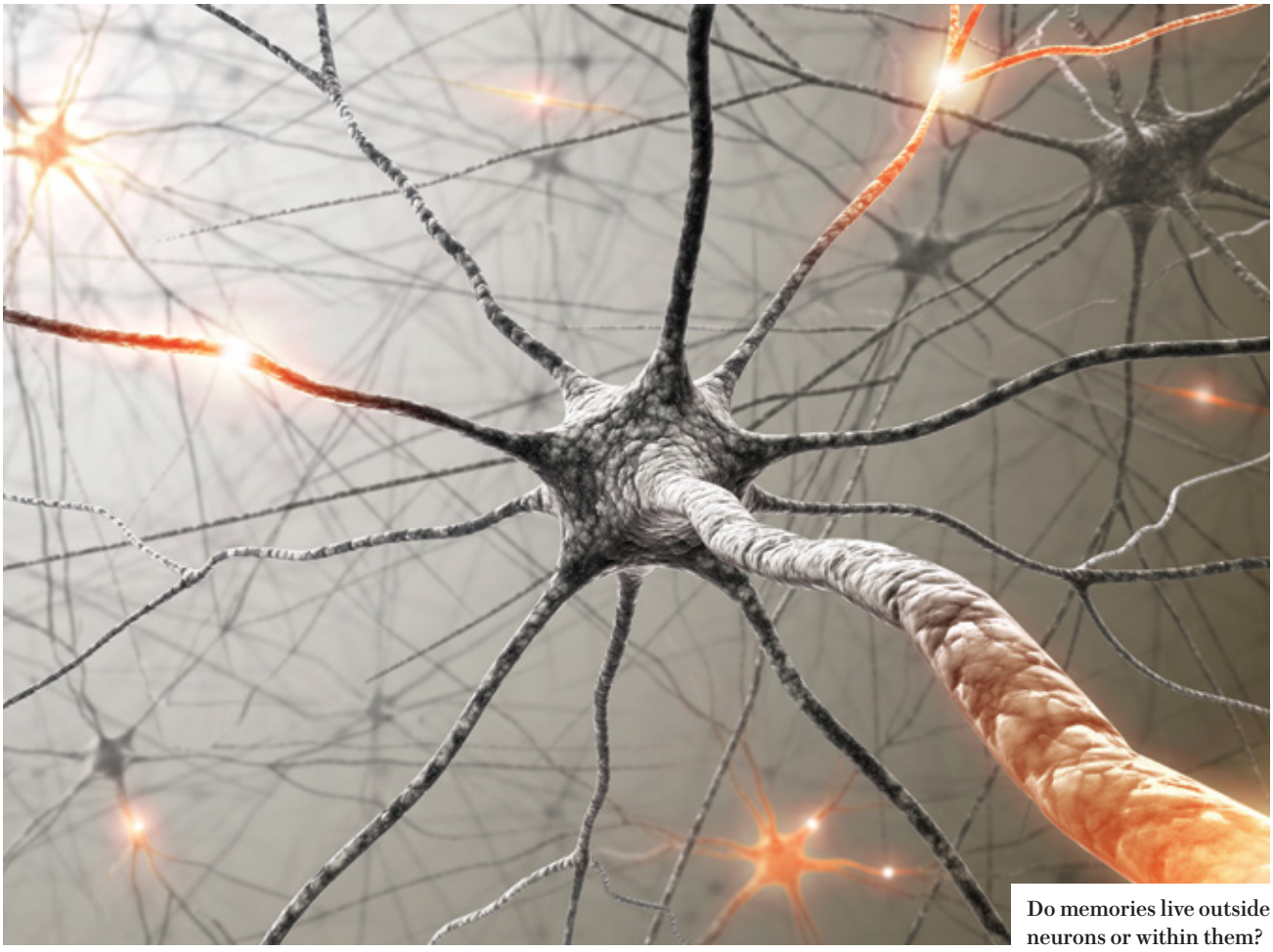

Do memories live outside neurons or within them?

NEUROSCIENCE

The Persistence of Memory

Recollections could be more enduring than recently thought

As intangible as they may seem, memories have a firm biological basis. According to textbook neuroscience, they form when neighboring brain cells send chemical communications across the synapses, or junctions, that connect them. Each time a memory is recalled, the connection is reactivated and strengthened. The idea that synapses store memories has dominated neuroscience for more than a century, but a new study by scientists at the University of California, Los Angeles, may fundamentally upend it: instead memories may reside *inside* brain cells.

If supported, the work could have major implications for the treatment of posttraumatic stress disorder (PTSD), a condition marked by painfully vivid and intrusive memories.

More than a decade ago scientists began investigating the drug propranolol for the treatment of PTSD. Propranolol was thought to prevent memories from forming by blocking production of proteins required for long-term storage. Unfortunately, the research quickly hit a snag. Unless administered immediately after the traumatic event, the treatment was ineffective. Lately researchers have been crafting a work-around: evidence suggests that when someone recalls a memory, the reactivated connection is not only strengthened but becomes temporarily susceptible to change, a process called memory reconsolidation. Administering propranolol (and perhaps also therapy, electrical stimulation and certain other drugs) during this window can enable scientists to block reconsolidation, wiping out the synapse on the spot.

The possibility of purging recollec-

Continued on page 16

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Innovations IN

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Continued from page 14

tions caught the eye of David Glanzman, a neurobiologist at U.C.L.A., who set out to study the process in *Aplysia,* a slug-like mollusk commonly used in neuroscience research. Glanzman and his team zapped *Aplysia* with mild electric shocks, creating a memory of the event expressed as new synapses in the brain. The scientists then transferred neurons from the mollusk into a petri dish and chemically triggered the memory of the shocks in them, quickly followed by a dose of propranolol.

Initially the drug appeared to confirm earlier research by wiping out the synaptic connection. But when cells were exposed to a reminder of the shocks, the memory came back at full strength within 48 hours. "It was totally reinstated," Glanzman says. "That implies to me that the memory wasn't stored in the synapse." The results were recently published in the online open-access journal eLife.

If memory is not located in the synapse, then where is it? When the neuroscientists took a closer look at the brain cells, they found that even when the synapse was erased, molecular and chemical changes persisted after the initial firing within the cell itself. The engram, or memory trace, could be preserved by these permanent changes. Alternatively, it could be encoded in modifications to the cell's DNA that alter how particular genes are expressed. Glanzman and others favor this reasoning.

Eric R. Kandel, a neuroscientist at Columbia University and recipient of the 2000 Nobel Prize in Physiology or Medicine for his work on memory, cautions that the study's results were observed in the first 48 hours after treatment, a time when consolidation is still sensitive.

Though preliminary, the results suggest that for people with PTSD, pill popping will most likely not eliminate painful memories. "If you had asked me two years ago if you could treat PTSD with medication blockade, I would have said yes, but now I don't think so," Glanzman says. On the bright side, he adds, the idea that memories persist deep within brain cells offers new hope for another disorder tied to memory: Alzheimer's.

—Roni Jacobson

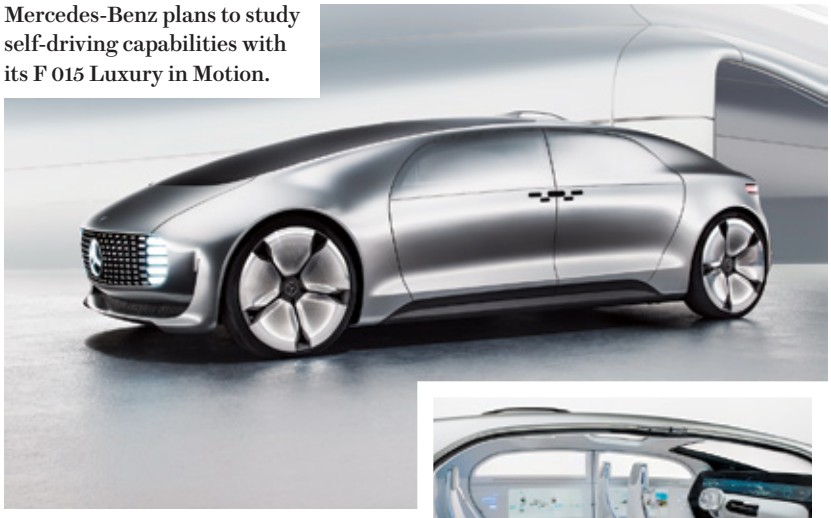
AUTOMOTIVE

Driverless Tech Inches Ahead

Today's safety features foreshadow the robotic cars of tomorrow

In the world of self-driving cars, all eyes are on Google. But major automakers are making moves toward autonomous driving, too. Although their advanced-safety and driver-assistance features may seem incremental in comparison, many are proofs of concept for technologies that could one day control driverless cars. At the same time, the National Highway Traffic Safety Administration (NHTSA), the arm of the Department of Transportation charged with establishing and enforcing car-safety standards and regulations, is studying and testing the road readiness of these control and machine-vision systems. In the short term, as buyers hold their breath for robotic cars, making automation features standard will save lives.

—Corinne Iozzio



Mercedes-Benz plans to study self-driving capabilities with its F 015 Luxury in Motion.

COURTESY OF MERCEDES-BENZ

4 AUTONOMOUS FEATURES GOING STANDARD

FORWARD COLLISION AVOIDANCE

In January the NHTSA announced that it would begin to factor crash-preventing braking systems into its car-safety ratings. The systems use forward-facing sensors—which can be radar-, camera- or laser-based—to detect imminent collisions and either apply or increase braking force to compensate for slow or insufficient driver reactions. Honda was first to introduce such a system in 2003; since then, nearly every automaker has rolled out similar features on high- and mid-range models.

BACKUP CAMERAS

Every new car sold after May 1, 2018, must have a backup camera, per a safety regulation issued by the NHTSA in 2014. The rear-facing cameras, available now on dozens of models, provide drivers with a full rear field of view and help to detect obstacles in blind spots. The NHTSA estimates that improving visibility in this way could save 69 lives every year.

VEHICLE-TO-VEHICLE COMMUNICATION

For self-driving cars to navigate roads en masse, each must have the position, speed and trajectory of nearby automobiles. Last summer the NHTSA announced that it would explore how to standardize such vehicle-to-vehicle communication. The feature could improve coordination for human and machine alike during accident-prone maneuvers, such as left-hand turns.

LANE DETECTION

In 2013 the NHTSA established how to test the effectiveness of camera systems that watch existing painted lane markers and alert drivers if they drift. Some cars, such as the Toyota Prius, now even take over steering if a driver does not respond quickly enough to warning signals. And new 2015 models from Mercedes-Benz and Volkswagen go further, using cameras and sensors to monitor surroundings and autonomously steer, change lanes and swerve to avoid accidents.

COMMENT AT ScientificAmerican.com/apr2015

INSTANT EGGHEAD

Itch, Scratch, Repeat

Why does scratching an itch make it itchier?

To scratch an itch is to scratch many itches: placing nails to skin brings sweet yet short-lived relief because it often instigates another bout of itchiness. The unexpected culprit behind this vicious cycle, new research reveals, is serotonin, the so-called happiness hormone.

Scientists thought itch was merely a mild form of pain until 2009, when Zhou-Feng Chen and his colleagues at the Center for the Study of Itch at Washington University in St. Louis discovered itch-specific neurons in mice. Though not identical, itch and pain are closely related; they share the same pathways in certain brain areas. Because of the doubling up, activating one suppresses the other, which is why scratching blocks the itch sensation momentarily. The act, however, also triggers the release of the chemical serotonin, which helps to alleviate pain. It is that burst that makes scratching feel good, but recent work by Chen's group showed that it exacerbates the itch-scratch cycle, too.

Itch-sensing neurons have a set of receptors that facilitates pain relief and another that induces itch. Serotonin can bind only to the pain-related receptor, but because the two sets sit close to each other and physically interact, the chemical's arrival indirectly enhances the itch pathway. When Chen and his colleagues activated both receptors simultaneously in mice, the rodents scratched much more than if the itch-inducing receptor was turned on alone. In another experiment, mice lacking the cells that produce serotonin scratched less than normal mice when exposed to a skin irritant. The findings were published in the journal *Neuron*.

Scientists have yet to locate itch-specific neurons in humans (macaques have them). For now it is safe to say: think twice before you twitch to the itch. —*Andrea Alfano*

Illustrations by Thomas Fuchs

ENGINEERING

Out-of-This-World Coffee

The space station gets an espresso maker

Fifteen years ago International Space Station crew members were eagerly awaiting their first functioning toilet. Now low-orbit life is so routine that astronauts will be sipping espresso like posh café-goers: the first coffee maker built to work in microgravity conditions arrives this month. ISSpresso is the product of a collaboration among the Italian Space Agency, Italian engineering company Argotec, and Lavazza, a 120-year-old, Turin-based coffee roaster. Astronauts will secure the microwave-size, aerospace-aluminum appliance to a station wall with adjustable tethers and then get to brewing (astronauts face days with 15 or 16 sunrises). The capsule-based system could eventually bring gourmet consommés, teas and soups to microgravity, Argotec's David Avino says. "It's a food laboratory." *—Bryan Lufkin*

BREW QUEUE
A piston pumps water from a pouch, through a heater and into a brewer (which is itself built to function in any position or orientation). Inside, hot water filters through an espresso capsule and then fills a second pouch with coffee, which doubles as the cup. The process takes about three minutes.

CLOSED-DOOR POLICY
A transparent door allows sky-high baristas to observe the foam-forming action but also serves as a safety measure. If it opens, brewing stops—protecting the crew from scalding floating java.

LAST STRAW
The coffee-filled pouch comes with a built-in straw, which engineers are now designing to aerate the liquid so the astronauts can appreciate its aroma. The caffeine is a nice perk, Avino says, but sipping on a cuppa joe is also about "relaxing in a very uncomfortable situation."

WITE-OUT
Each piece of onboard hardware must have the same coloration and reflective properties, per ISS standards, or else it distracts the crew. The machine is a sanctioned white.

PIPE DREAM
In terrestrial espresso makers, a plastic tube carries hot water, but ISSpresso swaps in a steel-and-Teflon pipe that can withstand orbital pressures of more than 400 bars. (Sea level is 1 bar.)

COURTESY OF LAVAZZA

COMMENT AT ScientificAmerican.com/apr2015

LINGUISTICS

Singing in the Rain

Humid locales foster more tonal languages

Opera singers and dry air don't get along. In fact, the best professional singers require humid settings to help them achieve the right pitch. "When your vocal cords are really dry, they're a little less elastic," says Caleb Everett, an anthropological linguist at the University of Miami. As a result, singers experience tiny variations in pitch, called jitter, as well as wavering volume—both of which contribute to rougher refrains.

If the amount of moisture in the air influences musical pitch, Everett wondered, has that translated into the development of fewer tonal languages in arid locations? Tonal languages, such as Mandarin Chinese and Cherokee, rely on variations in pitch to differentiate meaning: the same syllable spoken at a higher pitch can specify a different word if spoken at a lower pitch or in a rising or falling tone.

In a survey of more than 3,700 languages, Everett and his collaborators found that those with complex tones do indeed occur less frequently in dry areas than they do in humid ones, even after accounting for the clustering of related languages. For instance, more than half of the hundreds of languages spoken in tropical sub-Saharan locations feature complex tones, whereas none of the two dozen languages in the Sahara do. Overall, only one in 30 complex tonal languages flourished in dry areas; one in three nontonal languages cropped up in those same regions. The results appeared in February in the *Proceedings of the National Academy of Sciences USA*.

Those conclusions run counter to a traditional linguistic view that the structure of language is independent of its environment, says Robert Ladd, a linguistics researcher at the University of Edinburgh. To bolster the Miami group's findings, researchers in the field will need to prove that tonal languages require a precise control of pitch.

Along those lines, Everett and his team will next measure experimentally how well people voice complex tones in arid air. Although the evolution of tonal languages over the course of centuries cannot be observed, witnessing the physiological effect under controlled conditions could really make the hypothesis sing. —*Sarah Lewin*

ECOLOGY

Why Flowers Wear Shades

UV radiation may explain why plants and animals closer to the equator come in darker varieties

COURTESY OF MATTHEW KOSKI *University of Pittsburgh*

In 1833 a German researcher named Constantin Lambert Gloger noticed that birds from warmer habitats had darker feathers than those from cooler climes. His observations soon became known as Gloger's rule; ornithologists later verified that tropical plumage indeed darkens closer to the equator. Mammals seem to fit the pattern as well. But why would latitude influence animal coloration? More than 180 years later a possible answer has emerged from a surprising place: flowers.

University of Pittsburgh biologists Matthew Koski and Tia-Lynn Ashman recently looked at 34 different populations of silverweed cinquefoil, a widespread plant native in temperate zones on both sides of the equator, and found that its flowers were darker near the tropics. In this case, "darker" meant they displayed larger "bull's-eyes"—dark circles surrounded by lighter petals that are invisible to the human eye but show up under ultraviolet (UV) light (*above right*).

The bull's-eyes may act as beacons to pollinating insects, which can perceive UV. But Koski and Ashman found there is more to the dark spots than that. In a laboratory experiment, they discovered that pollen from darker flowers was more likely to germinate when grown under harmful UV light than pollen from flowers that

COMMENT AT ScientificAmerican.com/apr2015

Under UV light, silverweed cinquefoil flowers closer to the equator show larger areas of dark pigmentation (*above right*) than those farther away (*opposite page*).

were lighter, with smaller bull's-eyes. The pigmentation is protective, according to the study published online in January in the journal *Nature Plants:* the larger the bull's-eye, the more UV light is absorbed, rather than being reflected onto the pollen. Absorption is more important for plants in lower latitudes, which face more intense UV rays. (*Scientific American* is part of Nature Publishing Group.)

The role of bull's-eye size in UV protection does not necessarily discount other environmental factors correlated with latitude; for example, ornithologists have argued that Gloger's rule arises because darker pigmentation comes from a compound that protects feathers from bacteria in the wet, humid tropics. For mammals, researchers say that the overhead sunlight near the equator favors species with darker backs and lighter fronts because the combination offers camouflage in the shadowy rain forest.

Nevertheless, similar to rules, laws and theorems in chemistry or physics, general axioms exist for ecology that explain patterns. Because Koski's study established a link between UV radiation and the plants' reproductive potential, he thinks that UV protection will eventually emerge as a key mechanism behind pigmentation. "UV is universally damaging to DNA and protein structure in both plants and animals," Koski says, and darker pigmentation—visible or not—may be a strategy across species to avoid damage from the sun's harmful rays. —*Jason G. Goldman*

COURTESY OF NASA, ESA AND HUBBLE HERITAGE TEAM STSCI/AURA

ASTRONOMY

Galactic Ghosts

Thinly spread galaxies caught on camera

The word "galaxy" derives from the Greek for "milky," but some such celestial systems look more like extremely skim milk. A new array of small telescopes has serendipitously discovered 47 "ultra-diffuse" galaxies whose stars are so spread out from one another that they appear ghostly pale. Several of them are as large as our own, but each is much fainter, bearing roughly 1,000th as many stars as the Milky Way. No one knows how such odd galaxies originated.

The phantom galaxies materialized to astronomers after they deployed Dragonfly, an array in New Mexico composed of eight Canon telephoto lenses. "We just couldn't resist looking at Coma," says Roberto Abraham, an astronomer at the University of Toronto, referring to a rich galaxy cluster in the constellation Coma Berenices. The cluster houses thousands of galaxies 340 million light-years from Earth and has a storied legacy: in the 1930s astronomers first detected dark matter there.

COMMENT AT ScientificAmerican.com/apr2015

The Coma cluster (*left*) harbors galaxies so diffuse, they literally pale in comparison to spectacles such as the Sombrero galaxy (*above*).

Dragonfly's Coma image did not disappoint. On it, Abraham and his colleagues saw faint smudges indicative of large, diffuse galaxies. By luck, the Hubble Space Telescope had captured one of them during an unrelated observation, providing more detail. The galaxies, it reveals, look nothing like our own. Instead they are smooth, round and devoid of any gas to form new stars, and although the objects resemble diffuse galaxies known as dwarf spheroidals, they are anything but small. The discovery is described in a January issue of the *Astrophysical Journal Letters*.

How did such bizarre and difficult-to-detect galaxies arise? Team member Pieter van Dokkum, an astronomer at Yale University, suspects the galaxies may be failed Milky Ways—big galaxies that were headed for brilliance but lost their gas before forming many stars, perhaps because supernova explosions catapulted gas out of the galaxies and into the parent Coma cluster. They also must harbor lots of dark matter to hold together; otherwise the gravitational pull of other galaxies in the cluster would rip them apart.

Exactly how much dark matter they possess is unknown because no one has yet achieved the feat of measuring their mass. Nevertheless, "they're great dark matter labs," says Chris Impey, an astronomer at the University of Arizona. If dark matter emits radiation, these galaxies could be the place to see it.

—*Ken Croswell*

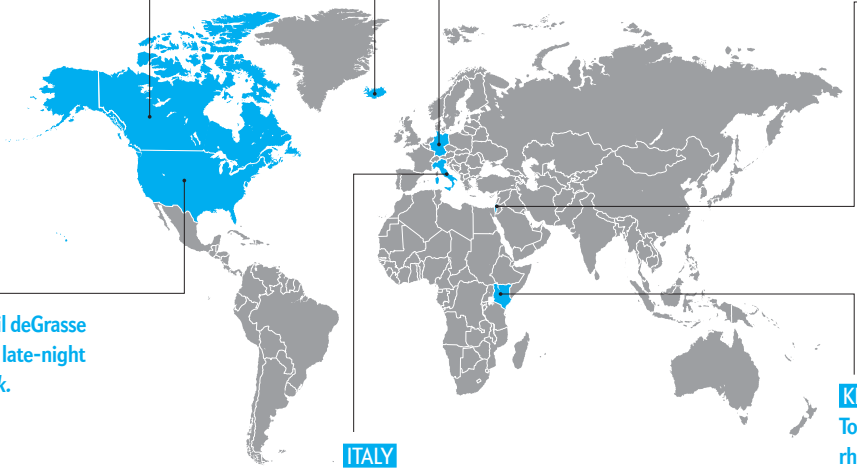
IN THE NEWS

Quick Hits

ICELAND
As it sheds ice—and weight—the island's land surface is rising 1.4 inches a year.

GERMANY
Spans of its high-speed autobahn system will open to self-driving cars in a pilot program, government officials say.

CANADA
Filled with nearly 8,000 pounds of liquid argon, a dark matter detector in Ontario begins operation.



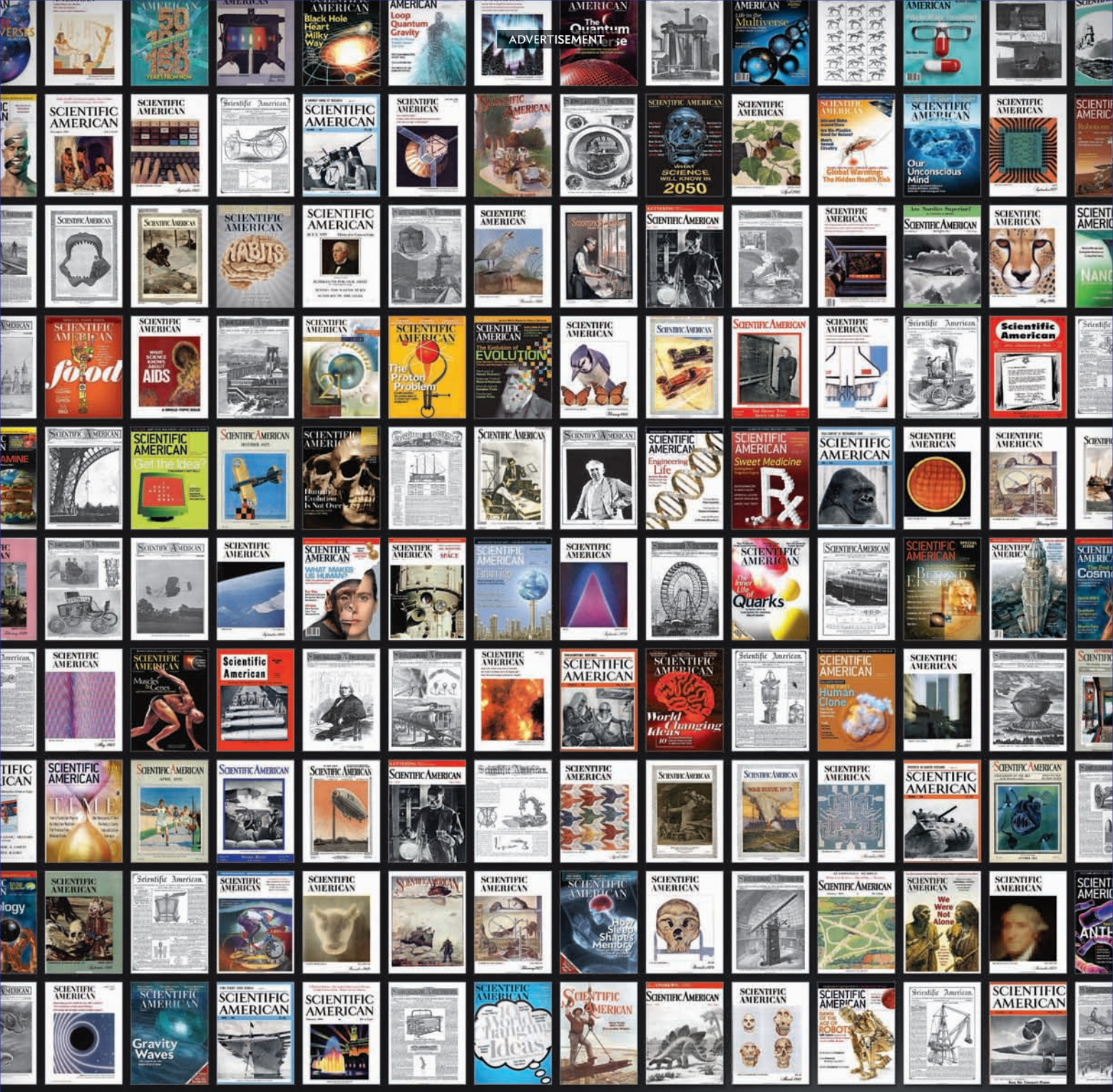
ISRAEL
In western Galilee, archaeologists found a 55,000-year-old partial human skull—making the area the most plausible for human and Neandertal interbreeding.

U.S.
Astrophysicist Neil deGrasse Tyson hosts a new late-night talk show, *Star Talk*.

KENYA
To save the northern white rhino, conservationists plan to collect eggs from the females for the first time. Only five rhinos remain.

ITALY
Seismologists concluded that thousands of mysterious rumbles across Italy, once thought to be caused by magma flow, originate from cement factory machinery.

For more details, visit www.ScientificAmerican.com/apr2015/advances



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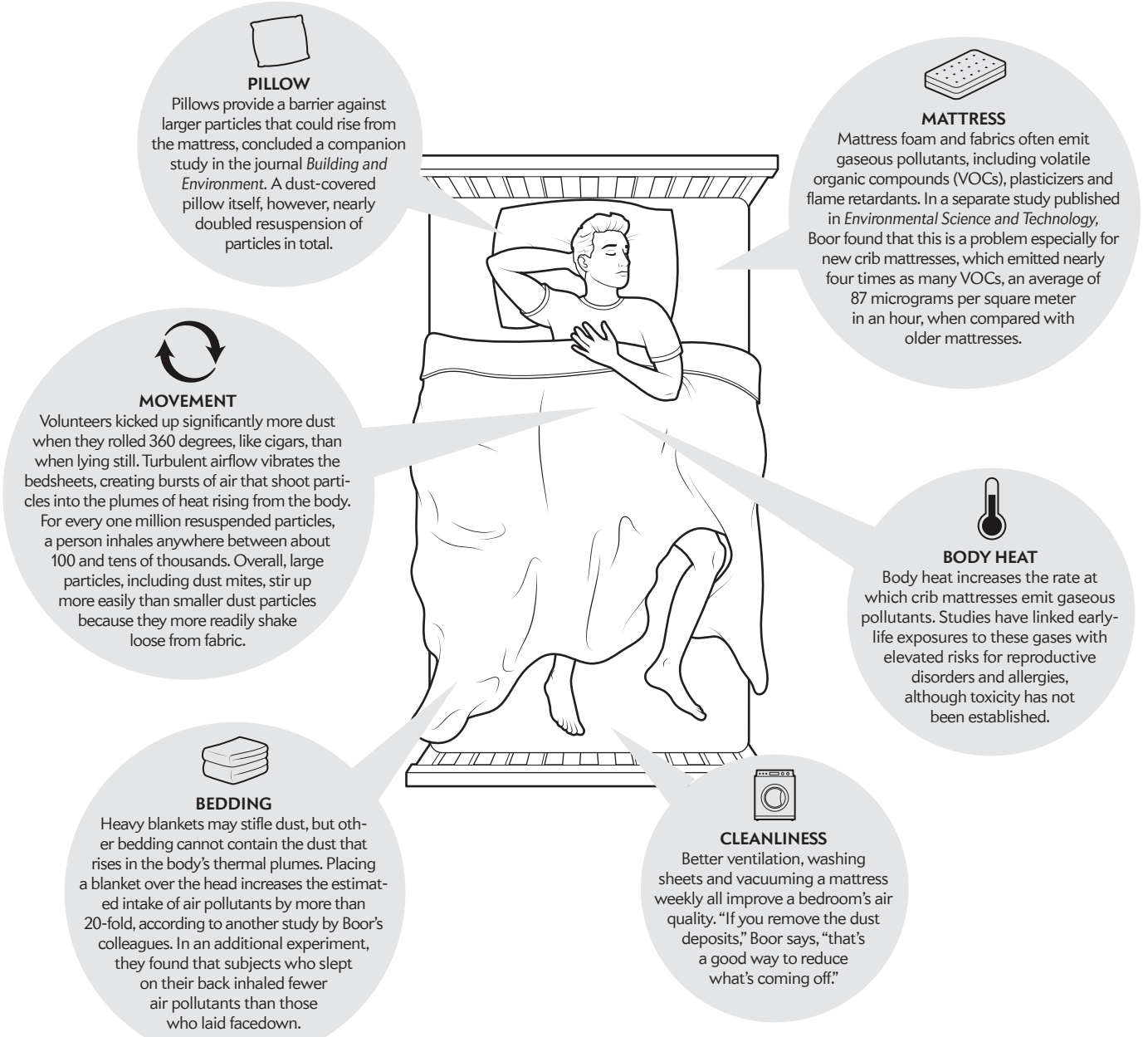
HEALTH

Dusty Dozing

Air quality in bed is a nightmare

If the average American lives to be 78 years old, roughly a third of those years are spent lying on a mattress. Brandon Boor, a doctoral student at the University of Texas at Austin, studies air pollutants in the sleep microenvironment. In his most recent study, detailed in the journal *Indoor Air,* Boor covered a twin mattress with 225-thread-count sheets and seeded the bed with artificial dust as a proxy for the microorganisms, fungal spores and skin cells that routinely collect there. Volunteers dressed in clean suits then sat and spun around on the bed—all inside a sealed chamber—while instruments measured the particles that were kicked up and could be inhaled by the subjects. The concentrations are minute, measured in parts per million, but could affect us because we spend eight hours every day in "uncustomary proximity" to bedding and mattresses. The time spent under roofs in general has led the Centers for Disease Control and Prevention to conclude that health risks such as asthma and chronic heart problems from exposure to indoor air pollution may be greater than the risks from outdoor pollution. When it comes to bedtime, blankets and sleeping behaviors, among other factors, determine the extent to which "we are such stuff as dreams are made on."

—Peter Andrey Smith



Illustrations by Brown Bird Design

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Mathematics

Speaker: Arthur Benjamin, Ph.D

The Secrets of Mental Math

Dr. Benjamin will demonstrate and explain how to perform amazing feats of mental calculation. You'll improve your ability to manipulate and memorize numbers, learn how to figure out the day of the week of any date in history, and other astounding feats of mind.

The Mathematics of Games and Gambling

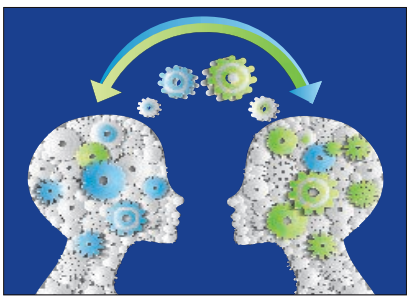
What are the best and worst games to play at the casino? When should you hit, split, or double down in blackjack? How much should you bet? Learn the answer to these questions, along with some games you can't lose, once you know the secret.

My Favorite Numbers

What makes the number 9 so magical? Explore the beauty of the Fibonacci Numbers 1, 2, 3, 5, 8, 13, 21, … and the golden ratio 1.618 … Is it irrational to be in love with Pi?

Discrete Mathematics

Learn the mathematics that underlie computer science and cryptography. Topics include combinatorics (the art of counting), number theory, and graph theory. But don't let the names of these topics scare you. You don't need much more than arithmetic and a logical mind to enjoy this lecture.



Psychology

Speaker: Jennifer Crocker, Ph.D.

Does Self-Esteem Matter?

Despite a huge volume of studies, researchers hotly debate whether self-esteem is actually important to well-being. We'll consider some of the major controversies in the field, such as whether high self-esteem people are happier, more successful, or more popular than low self-esteem people, and what factors actually affect our self-esteem.

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Pursuing Self-Esteem

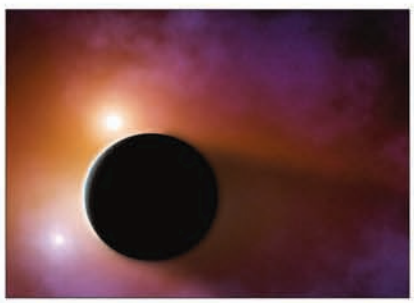
People tend to invest their self-esteem in just a few endeavors, such as academics, appearance or sports. Learn what research tells us about the benefits and pitfalls of pursing self-esteem by striving for success and avoiding failure in these domains, as well as successful strategies for avoiding the downsides of pursuing self-esteem.

Principles of Close Relationships

Many scientists assume that people in relationships are fundamentally self-interested, and aim to promote their own ends. Yet people can also transcend self-interest and care about relationship partners as much as themselves. Learn which relationships are likely to be governed by which set of principles, and what factors prompt these principles to shift.

The Key to Good Relationships

Learn how to create relationships that are good for your health and well-being through positive intentions. Evidence shows that when people strive to be supportive and constructive toward their partners, they tend to become so. Their partners notice and respond in kind, and the relationships tend to improve for everyone.



Astronomy

Speaker: Edwin L. Turner, Ph.D.

Exoplanets: Strange New Worlds

The first planet-sized body orbiting a star beyond the sun was discovered two decades ago. Since then, a torrent of new finds has come. Today we have catalogued and studied a few thousand exoplanets. Take a tour of these strange new worlds and learn about the future outlook for finding more.

The Quest for Earth's Twin

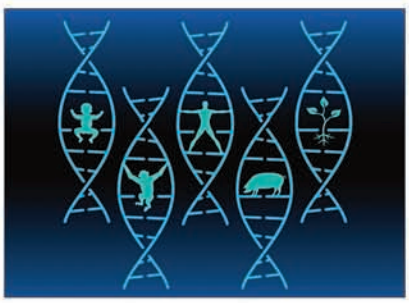
Is life on Earth unique in the universe? If not, our best hope for finding extraterrestrial organisms is to find a planet resembling our own, with the conditions and liquid water we think life probably requires. Learn how we search for Earth twins, and the prospects for detecting alien life from afar.

Life as We Don't Know It

Astrobiologists tend to search for extraterrestrial organisms resembling those found on Earth. But it's quite plausible that the universe contains life that is radically different from ours. Learn how scientists are beginning to study this topic, and how we might eventually hope to recognize life beyond our ability to imagine it.

Abiogenesis: Life's Origins

The biggest mystery about life is how it got started—that is, how it arose from a completely abiotic, or sterile, environment. Scientists have proposed radically different scenarios for this spark, and so far we have no way to discriminate between them. We'll discuss the latest thinking on the perplexing origins of life.



Evolution

Speaker: Spencer C.H. Barrett, Ph.D.

The Evolution Revolution

Evolution provides an explanation for all biodiversity on Earth, including human origins. Learn how and why evolution occurs, and why understanding the process of evolution is not only of profound biological importance but is also crucial for many contemporary issues affecting society.

Plant Sex for Grown-ups

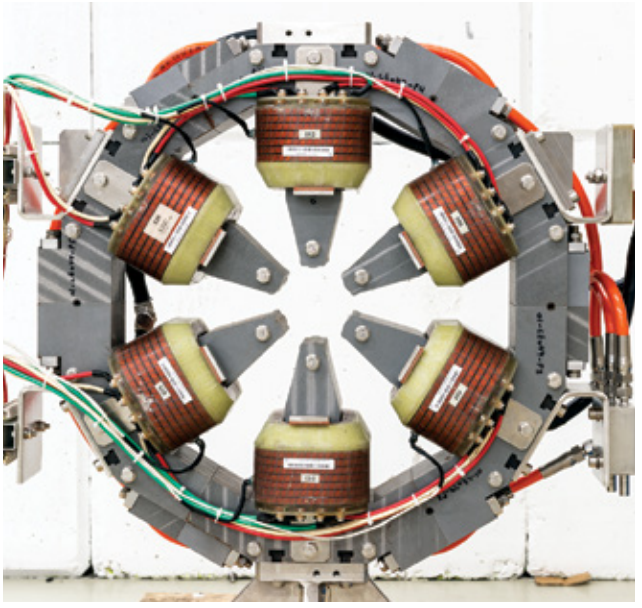
The reproductive strategies of plants exhibit greater variety than those of any other group of organisms. Why should this be so? We'll address a variety of fundamental questions about plant sex, highlight some of the bizarre floral adaptations associated with pollination, and discuss how experimental studies can yield insight.

Evolution On Islands

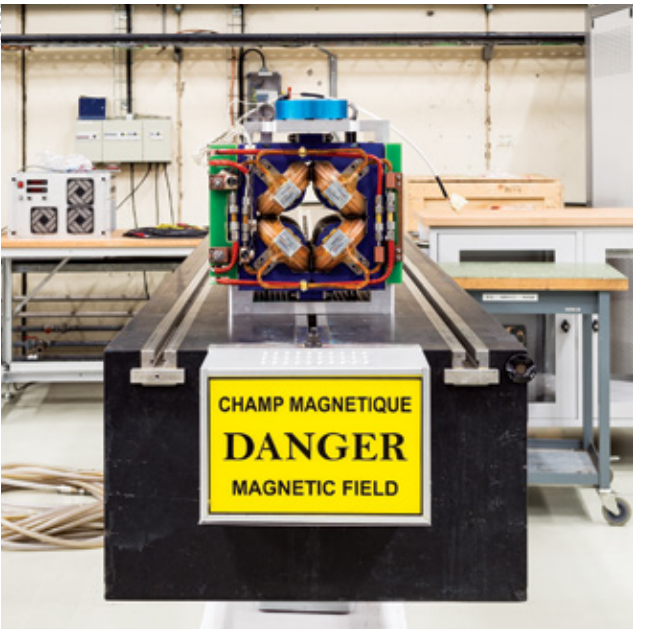
Islands can act as "evolutionary laboratories," providing some of the clearest evidence for natural selection. We'll contrast the case histories of Australia and New Zealand, highlighting the similarities and differences between the floras and faunas of the two regions, and discuss why islands provide such a rich source of biological novelty.

Biological Invaders

Invasive species can cause huge economic losses and threaten biodiversity and ecosystem function. We'll discuss the fascinating new field of applied science known as invasion biology. Learn why some invasive species have the capacity to evolve rapidly in response to local environmental conditions in their adopted homes, whereas others are characterized by genetic uniformity.



Resistive sextuple magnet



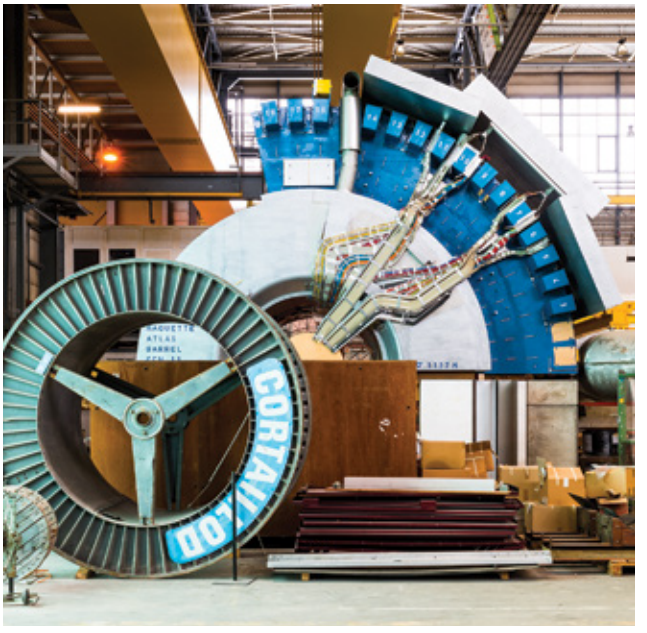
Resistive quadrupole lens for focusing particle beams

PHYSICS

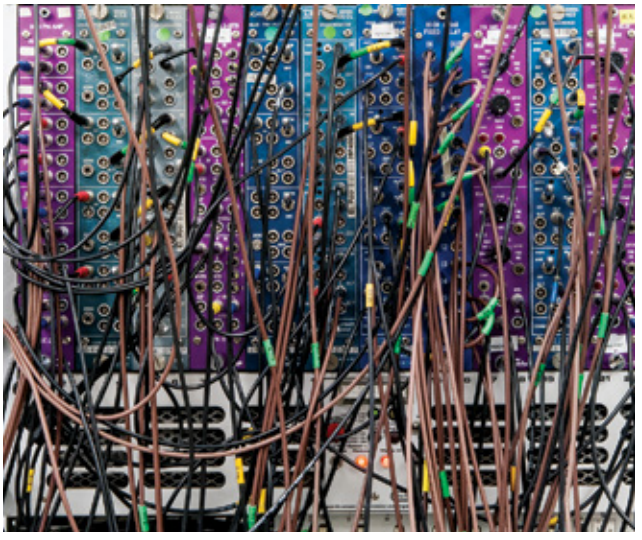
Atom Smasher Amps Up

The Large Hadron Collider's second run will break energy records

After a two-year shutdown for $163 million in upgrades, the world's largest particle accelerator is booting back up this spring. Among other improvements, the Large Hadron Collider near Geneva now has better connections between its magnets, which will support stronger fields and enable protons to crash together at the highest energies ever achieved. New particles could provide long-sought proof for theories such as supersymmetry that posit extra particles and dimensions in the universe. The collisions might even reveal new, heavier Higgs bosons to join the first Higgs discovery there in 2012. —*Clara Moskowitz*



Full-scale wiring test for ATLAS detector



Magnet protection electronics

BY THE NUMBERS

	RUN 1 (2009–2013)	RUN 2 (2015–2018)
ENERGY OF COLLISIONS (tera-electron volts)	8	13
CURRENT IN MAGNETS (amps)	6,000	11,000
MAGNETIC FIELD STRENGTH (teslas)	5.9	7.7

ALASTAIR PHILIP WIPER (*photographs*); SOURCE: FRÉDÉRICK BORDRY, DIRECTOR FOR ACCELERATORS AND TECHNOLOGY *CERN* (*By the Numbers figures*)

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MATHEMATICS

- The Five Elements of Effective Thinking
- To Infinity … and Beyond
- The Fourth Dimension
- Expect the Unexpected

ANTHROPOLOGY

- Human Evolution: the Big Picture
- The First Humans
- The Neanderthals: Another Kind of Human
- The Rise of Homo Sapiens

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SPEAKERS

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Monisha Pasupathi, Ph.D.
Chris Stringer, Ph.D.
Glenn Starkman, Ph.D.

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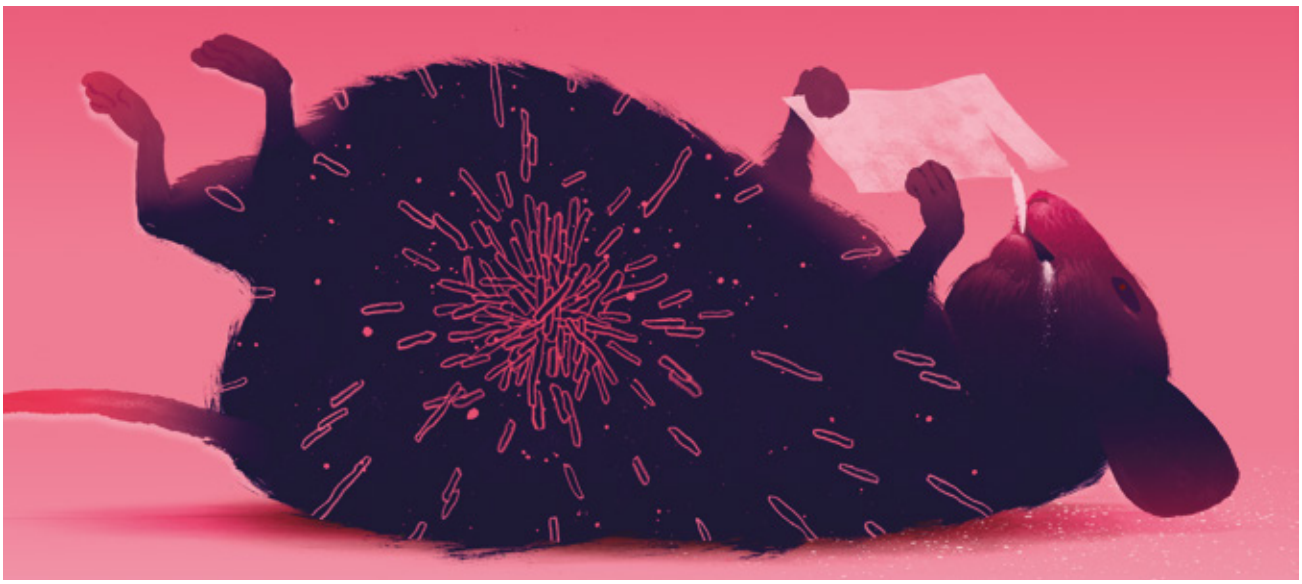

Artificial Sweeteners Get a Gut Check

The substances may change bacteria in our digestive systems in ways that lead to obesity

Many of us, particularly those who prefer to eat our cake and look like we have not done so, have a love-hate relationship with artificial sweeteners. These seemingly magical molecules deliver a dulcet taste without its customary caloric punch. We guzzle enormous quantities of these chemicals, mostly in the form of aspartame, sucralose and saccharin, which are used to enliven the flavor of everything from Diet Coke to toothpaste. Yet there are worries. Many suspect that all this sweetness comes at some hidden cost to our health, although science has only pointed at vague links to problems.

Last year, though, a team of Israeli scientists put together a stronger case. The researchers concluded from studies of mice that ingesting artificial sweeteners might lead to—of all things—obesity and related ailments such as diabetes. This study was not the first to note this link in animals, but it was the first to find evidence of a plausible cause: the sweeteners appear to change the population of intestinal bacteria that direct metabolism, the conversion of food to energy or stored fuel. And this result suggests the connection might also exist in humans.

In humans, as well as mice, the ability to digest and extract energy from our food is determined not only by our genes but also by the activity of the trillions of microbes that dwell within our digestive tract; collectively, these bacteria are known as the gut microbiome. The Israeli study suggests that artificial sweeteners enhance the populations of gut bacteria that are more efficient at pulling energy from our food and turning that energy into fat. In other words, artificial sweeteners may favor the growth of bacteria that make more calories available to us, calories that can then find their way to our hips, thighs and midriffs, says Peter Turnbaugh of the University of California, San Francisco, an expert on the interplay of bacteria and metabolism.

BACTERIAL GLUTTONS

IN THE ISRAELI EXPERIMENT, 10-week-old mice were fed a daily dose of aspartame, sucralose or saccharin. Another cluster of mice were given water laced with one of two natural sugars, glucose or sucrose. After 11 weeks, the mice receiving sugar were doing fine, whereas the mice fed artificial sweeteners had abnormally high blood sugar (glucose) levels, an indication that their tissues were having difficulty absorbing glucose from the blood. Left unchecked, this "glucose intolerance" can lead to a host of health problems, including diabetes and a heightened risk of liver and heart disease. But it is reversible: after the mice were treated with broad-spectrum antibiotics to kill all their gut bacteria, the microbial population eventually returned to its original makeup and balance, as did blood glucose control.

Illustration by Skip Sterling

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"These bacteria are not agnostic to artificial sweeteners," says computational biologist Eran Segal of the Weizmann Institute of Science in Rehovot, Israel, one of the two scientists leading the study. The investigators also found that the microbial populations that thrived on artificial sweeteners were the very same ones shown—by other researchers—to be particularly abundant in the guts of genetically obese mice.

Jeffrey Gordon, a physician and biologist at Washington University in St. Louis, has done research showing that this relation between bacteria and obesity is more than a coincidence. Gordon notes that more than 90 percent of the bacterial species in the gut come from just two subgroups—Bacteroidetes and Firmicutes. Gordon and his team found several years ago that genetically obese mice (the animals lacked the ability to make leptin, a hormone that limits appetite) had 50 percent fewer Bacteroidetes bacteria and 50 percent more Firmicutes bacteria than normal mice did. When they transferred a sample of the Firmicutes bacterial population from the obese mice into normal-weight ones, the normal mice became fatter. The reason for this response, Gordon says, was twofold: Firmicutes bacteria transplanted from the fat mice produced more of the enzymes that helped the animals extract more energy from their food, and the bacteria also manipulated the genes of the normal mice in ways that triggered the storage of fat rather than its breakdown for energy.

Gordon believes something similar occurs in obese humans. He found that the proportion of Bacteroidetes to Firmicutes bacteria increases as fat people lose weight through either a low-fat or low-carbohydrate diet. Stanford University microbiologist David Relman says this finding suggests that the bacteria in the human gut may not only influence our ability to extract calories and store energy from our diet but also have an impact on the balance of hormones, such as leptin, that shape our very eating behavior, leading some of us to eat more than others in any given situation.

The burning question, of course, is whether artificial sweeteners can truly make humans sick and fat. Segal thinks they probably do, at least in some cases. He and his team analyzed a database of 381 men and women and found that those who used artificial sweeteners were more likely than others to be overweight. They were also more likely to have impaired glucose tolerance. Obesity is, in fact, well known as a risk factor for the development of glucose intolerance as well as more severe glucose-related ailments, such as diabetes.

These patterns do not prove that the sweeteners caused the problems. Indeed, it is quite possible that overweight people are simply more likely than others to consume artificial sweeteners. But Segal's team went further, testing the association directly in a small group of lean and healthy human volunteers who normally eschewed artificial sweeteners. After consuming the U.S. Food and Drug Administration's maximum dose of saccharin over a period of five days, four of the seven subjects showed a reduced glucose response in addition to an abrupt change in their gut microbes. The three volunteers whose glucose tolerance did not dip showed no change in their gut microbes.

Although not everyone seems susceptible to this effect, the findings do warrant more research, the scientists say. The Israeli group concluded in its paper that artificial sweeteners "may have directly contributed to enhancing the exact epidemic that they themselves were intended to fight"—that is, the sweeteners may be making at least some of us heavier and more ill.

A cause-and-effect chain from sweeteners to microbes to obesity could explain some puzzles about obese people, says New York University gastroenterologist Ilseung Cho, who researches the role of gut bacteria in human disorders. He points out that in studies, most people who switch from sugar to low-calorie sweeteners in an effort to lose weight fail to do so at the expected rate. "We've suspected for years that changes in gut bacteria may play some role in obesity," he says, although it has been hard to pinpoint this effect. But Cho adds that it is clear that "whatever your normal diet is can have a huge impact on the bacterial population of your gut, an impact that is hard to overestimate. We know that we don't see the weight-loss benefit one would expect from these nonnutritive sweeteners, and a shift in the balance of gut bacteria may well be the reason, especially a shift that results in a change in hormonal balances. A hormone is like a force multiplier—and if a change in our gut microbes has an impact on hormones that control eating, well, that would explain a lot."

MICROBES VS. GENES

NATURALLY THERE ARE MANY QUESTIONS left to answer. Cathryn Nagler, a pathologist at the University of Chicago and an expert on gut bacteria and food allergies, says that the enormous genetic variations in humans make extrapolations from mice suspect. "Still, I found the data very compelling," she says of the Israeli artificial sweetener study. Relman agrees that rodent studies are not always reflective of what happens in humans. "Animal studies can point to a general phenomenon, but animals in these studies tend to be genetically identical, while in humans, lifestyle histories and genetic differences can play a very powerful role," he says. The constellation of microbes in a human body is a reflection of that body's particular history—both genetic and environmental.

"The microbiome is a component intertwined in a complex puzzle," Relman continues. "And sometimes the genetics is so strong that it will override and drive back the microbiota." Genetic variations might explain why only four of the seven saccharin-fed humans had a change in their gut bacteria, for instance, although genetics is only one of a number of possible factors. And if someone is genetically predisposed to obesity and consumes a diet that promotes that obesity, the microbes might change to take advantage of that diet, thereby amplifying the effect.

The Israeli researchers agree that it is far too soon to conclude that artificial sweeteners cause metabolic disorders, but they and other scientists are convinced that at least one—saccharin—has a significant effect on the balance of microbes in the human gut. "The evidence is very compelling," Turnbaugh says. "Something is definitely going on." Segal, for one, is taking no chances: he says that he has switched from using artificial to natural sweetener in his morning coffee. SA

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David Pogue is the anchor columnist for Yahoo Tech and host of several *NOVA* miniseries on PBS.

Unclear for Takeoff

Overly strict regulations could quash the drone revolution before it launches

How could anything as magical as drones be so controversial?

These hobby and commercial quadcopters are amazingly stable and simple to fly, thanks to incredible advances in sensors and electronics. Most can take off and land automatically—you just tap a button, and they can hover at eye level, motionless, even in a 30-mile-an-hour wind, awaiting your next command.

What makes these drones so powerful, and so contentious among the public, is also one of the things that makes them so enchanting: their cameras. As you fly a drone, you're treated to its point of view, thanks to a real-time feed to the screen of your phone or tablet. Suddenly, the world you've always known in roughly two dimensions becomes just as easy to explore in three. Inhabiting this third dimension becomes easy and affordable.

This freedom of vision is transforming industries. Filmmakers routinely employ drones to capture breathtaking chase sequences they could never film before. Engineers can inspect bridges and buildings without having to make risky climbs. Farmers monitor their crops from afar. Conservationists keep an eye on illegal poaching and dumping. Amazon is developing a program that would let you receive your orders in 30 minutes, thanks to drone-flown delivery of your packages.

It was all looking so promising—until the dimwits got involved.

People started abusing the privilege of having drones. They'd seek thrills by flying drones around airports, risking encounters with commercial airliners. They'd terrify privacy-sensitive neighbors by hovering near their windows. They'd fly on public beaches, zooming in on innocent bystanders.

The Federal Aviation Administration has taken its sweet time regulating the blossoming world of civilian drones. Now, however, it's stepping forward with proposed regulations so strict they could squash the entire field.

These rules would limit commercial drone flying to: daylight hours (sorry, moviemakers); 400 feet (sorry, aerial photographers); a line of sight between pilot and drone (sorry, crop inspectors); and those with an actual pilot's license. You'd have to learn to fly a plane before you could fly a $500 plastic quadcopter for a commercial undertaking. (Hobbyists can fly without FAA approval but are also required to comply with certain rules, such as maintaining a line of sight and avoiding manned aircraft.)

Now, the thing is, the FAA's job is tricky. It has to balance the popularity and promise of drones with issues of national security, radio-spectrum ranges, privacy and, above all, safety. One midair collision of a drone and an airplane would set the drone industry back much further than some FAA rules.

But the proposed rules have shocked drone fans and their representative groups (such as the Small Unmanned Aerial Vehicles Coalition and the Association for Unmanned Vehicle Systems International). These groups point out that the FAA seems to think that the new off-the-shelf, battery-powered drones such as the Parrot Bebop and the DJI Phantom (both under $1,000 and three pounds) are just as much a safety threat as huge, gas-powered military and industrial drones that weigh 40 pounds and stay aloft for 24 hours.

The line-of-sight rule, meanwhile, seems to ignore the fact that today's drones let you see where the drone is, by watching a phone or laptop screen in your hands, far from flying blind.

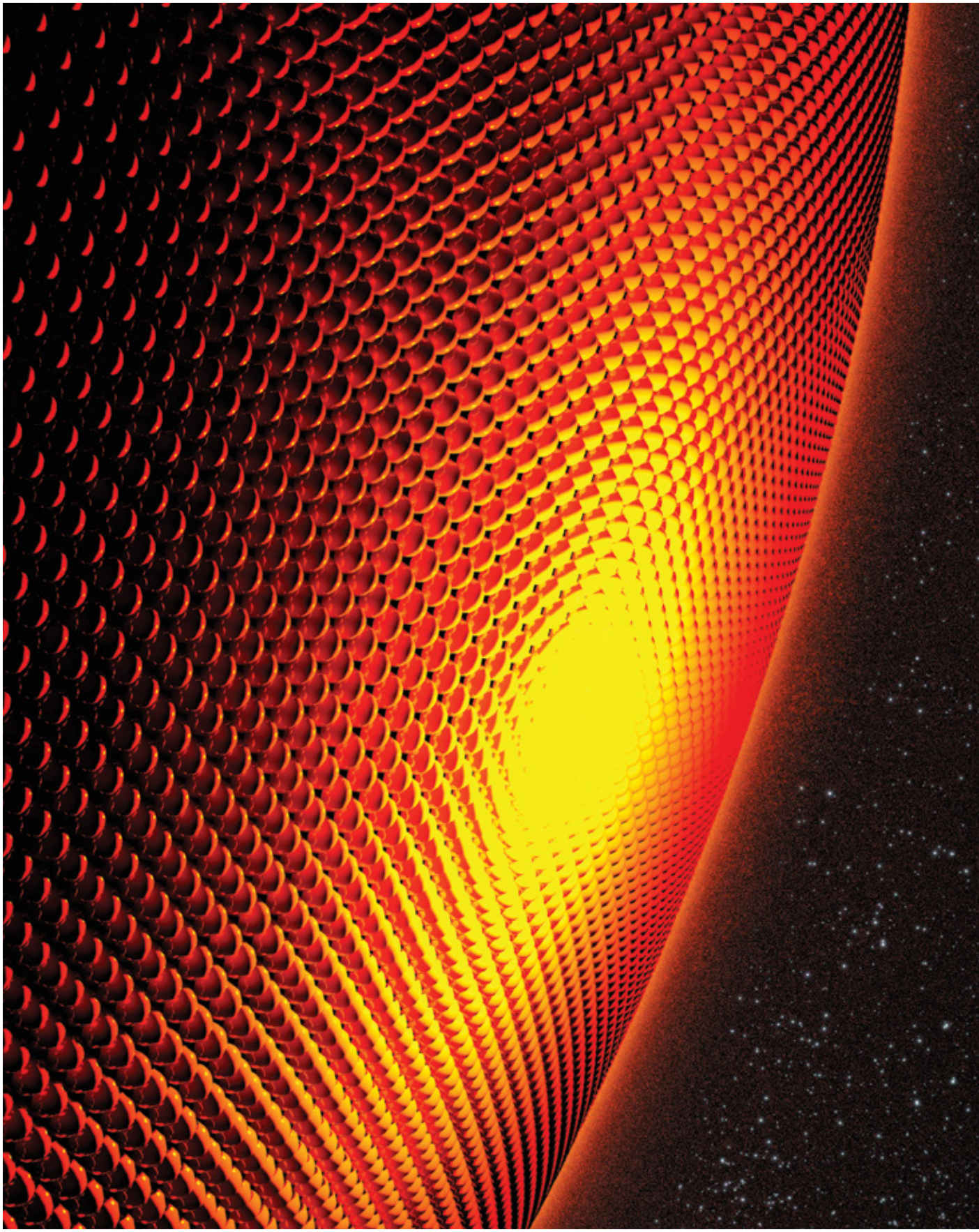
Critics of the proposed regulations note that the primary effect of these new rules would be to send the commercial drone industry into other countries, where the regulations are far less strict.

For many people, the biggest problem with today's drone popularity isn't safety of commercial operations—it's personal privacy. Their nightmares are haunted by hovering cameras. And the proposed FAA rules don't say anything at all about that problem.

The FAA's proposals are now in for a couple of years of public comment. Those who have become enchanted by the ability to explore the third dimension can now offer their two cents—and then hope that common sense prevails. SA

SCIENTIFIC AMERICAN ONLINE
Drone-flying misadventures: ScientificAmerican.com/apr2015/pogue

Illustration by Miko Maciaszek



PHYSICS

BURNING RINGS OF FIRE

"Firewalls" of particles may border black holes, confounding both general relativity and quantum mechanics

By Joseph Polchinski

FALLING INTO A BLACK HOLE WAS NEVER GOING TO be fun. As soon as physicists realized that black holes exist, we knew that getting too close to one spelled certain death. But we used to think that an astronaut falling past the point of no return—the so-called event horizon—would not feel anything special. According to Einstein's general theory of relativity, no signposts would mark the spot where the chance of escape dropped to zero. Anyone journeying past the horizon would just seem to fall down, down, down into a pit of blackness.

Recently, however, my colleagues and I have recast that picture in light of some new information about the effects of quantum mechanics on black holes. It now seems that our astronaut would have an experience very different from Albert Einstein's prediction. Rather than

Illustration by Kenn Brown, Mondolithic Studios

falling seamlessly into the interior, the astronaut would encounter a "firewall" of high-energy particles at the horizon that would be instantly lethal. The wall might even mark the end of space.

Three years ago four of us, all then at the University of California, Santa Barbara—my colleague Donald Marolf, then graduate students Ahmed Almheiri and James Sully, and I (now known by the acronym AMPS)—arrived at this conclusion after using ideas from string theory to take a closer look at the physics of black holes, particularly at an interesting argument put forward in the 1970s by Stephen Hawking. Hawking had identified a deep conflict between the predictions of quantum theory and relativity in these extreme environments. According to his reasoning, either quantum mechanics or Einstein's depiction of spacetime is flawed. The battle over which view is correct has swung back and forth ever since.

As with Hawking's original claim, our recent firewall proposal has raised a storm of disbelief, and no satisfactory alternative has yet emerged. If quantum mechanics is to be trusted, firewalls are the consequence. Yet their existence raises theoretical puzzles as well. It seems that physicists must give up one of our widely cherished beliefs, but we cannot agree on which one. We hope, however, that out of this confusion will come a more complete understanding of quantum mechanics and relativity—and, ideally, a way to finally resolve the apparent contradictions between these two reigning theories of physics.

THE SINGULARITY

GENERAL RELATIVITY, which gave birth to the very concept of black holes, derives its picture of these mysterious entities and their event horizons from an understanding of gravity's effect on space and time. According to the theory, if enough mass comes together, gravity's pull will cause it to start collapsing. Nothing can stop this process until all the mass is compressed into a single point where spacetime is infinitely dense and infinitely curved, called the singularity—in other words, a black hole.

Any space travelers who pass the black hole's event horizon boundary will be unable to escape the gravitational pull and will soon be drawn into the singularity. Even light, once it is past the horizon, cannot escape. The singularity is a very dramatic place, but the horizon itself is supposed to be unremarkable, according to what is called the equivalence principle of general relativity; individuals falling freely into a black hole will see the same physical laws as anywhere else as they cross the horizon. Theorists are fond of saying that the entire solar system could be falling into a giant black hole right now, and we would not experience anything out of the ordinary.

BLACK HOLE RADIATION

THE CHALLENGE HAWKING POSED to the traditional picture of black holes began in 1974, when he considered a strange prediction of quantum mechanics. According to this theory, pairs of particles and their antimatter counterparts constantly pop into existence and then disappear almost at once. If such fluctuations happen just outside the horizon of the black hole, Hawking showed, the pair could separate. One would fall into the singularity, and the other would escape from the black hole and carry away some of its mass. Eventually the black hole's entire mass could be depleted through this process, termed Hawking evaporation.

For black holes found in nature, evaporation is unimportant: these black holes add mass at a much more rapid rate from gas and dust falling in than they lose to radiation. But for theoretical purposes, we can investigate what would happen if a black hole were completely isolated and we had enough time to watch the full process of evaporation. By pursuing such a thought experiment, Hawking revealed two apparent contradictions between general relativity and quantum mechanics.

The entropy problem. In pondering the isolated black hole, Hawking noted that the light spectrum of the eponymous radiation streaming away from it would look the same as that of a radiating hot body, meaning that the black hole has a temperature. In general, temperature arises from the motion of atoms inside objects. The thermal nature of Hawking radiation, then, suggested that the black hole should have a microscopic structure made of some kind of discrete building blocks or bits. Physicist Jacob D. Bekenstein, now at the Hebrew University of Jerusalem, had also reached this conclusion two years earlier by engaging in thought experiments involving throwing things into black holes. The work of Bekenstein and Hawking gives a formula for the number of bits, a measure known as the black hole entropy. Entropy is a gauge of disorder, which becomes greater as the number of states that an object can have grows. The larger the number of bits in a black hole, the more possible arrangements they can have and the greater the entropy.

In contrast, general relativity describes a black hole as having a smooth geometry and indicates that every black hole of given mass, spin and charge should be exactly the same: in the words of the late physicist John Wheeler of Princeton University, "Black holes have no hair." So here is a contradiction: relativity says no

Joseph Polchinski is a professor of physics at the University of California, Santa Barbara, and a permanent member of the Kavli Institute for Theoretical Physics there. He works on many areas of theoretical physics, but he is guided by two big questions: How does duality work, and what is quantum gravity? In his spare time, he rides his bike in the hills of Santa Barbara.

IN BRIEF

Stephen Hawking's discovery that particles leak out of black holes revealed a fissure in scientists' understanding of physics. These escaped particles seem to imply that information is destroyed inside black holes—something quantum mechanics forbids.

An attempt to resolve this quandary using string theory looked promising, but recent calculations show that black holes are even more perplexing than was thought.

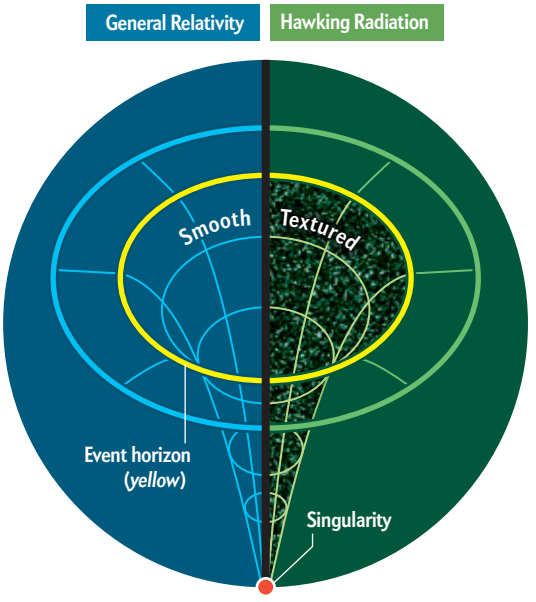
Barriers of high-energy particles called firewalls surround black holes, according to calculations by the author and his colleagues. Such firewalls may represent the end of space itself. Resolving the paradoxes of firewalls could offer a path toward unifying quantum mechanics and general relativity.

Resolving Black Hole Conundrums

In 1974 Stephen Hawking showed that a small amount of radiation leaks out of black holes. According to quantum mechanics, pairs of particles and their antimatter counterparts constantly spring into existence and then disappear moments later all over the universe. Hawking noted that when a pair shows up near the horizon of a black hole, one particle could fall in while the other escapes. This phenomenon, called Hawking radiation, raises some puzzles about the laws of physics inside black holes.

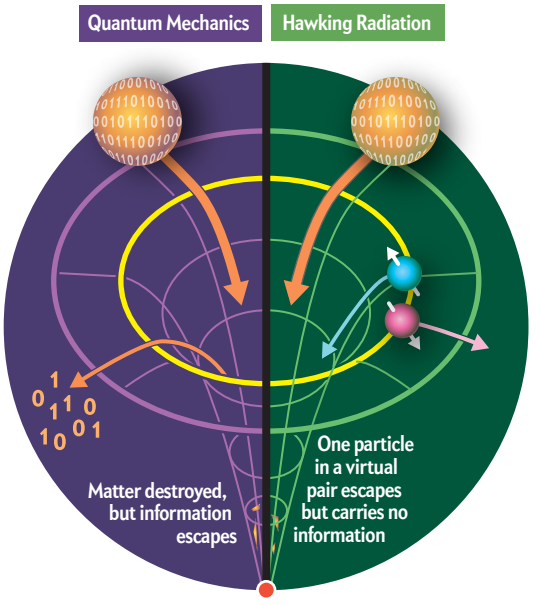
The Entropy Problem

The radiation spectrum of Hawking emission suggests that black holes have temperatures. Traditionally, heat arises from the motion of atoms within an object. The temperature of black holes implies that they have substructure—some type of internal building blocks that can rearrange themselves. The possibility of different arrangements gives black holes a measure of disorder, or "entropy," according to the quantum-mechanical picture of Hawking radiation. Entropy is forbidden to black holes by general relativity, however, because the theory requires them to be completely smooth, without substructure.



The Information Paradox

According to the standard picture of quantum mechanics, information can never be destroyed. Even when you burn a letter, for example, the original information encoded in the atoms of the letter is preserved in the ashes. Hawking radiation, however, implies that black holes destroy the information of the matter that falls into them because the particles that escape do not depend at all on the properties of the atoms that initially fell into the hole. Hawking suggested that quantum mechanics might have to be modified to allow for information loss.



Earlier Conjectures (*not shown*) …

In an effort to resolve these puzzles, physicists looked for new ways to combine general relativity and quantum mechanics into a coherent theory that could describe black holes. One breakthrough was string theory, which posits that particles are actually tiny loops of vibrating string. This theory appeared to solve elements of the information paradox and the entropy problem.

… Led to Firewalls

Yet the string theory solutions eventually led to a surprising conclusion: black holes might be surrounded by firewalls—walls of high-energy particles that would obliterate any object that encountered them. Firewalls seem to imply a drastic breakdown of the laws of physics at the boundary of black holes and could lead to extreme conclusions, such as the possibility that firewalls mark the end of space and time altogether.

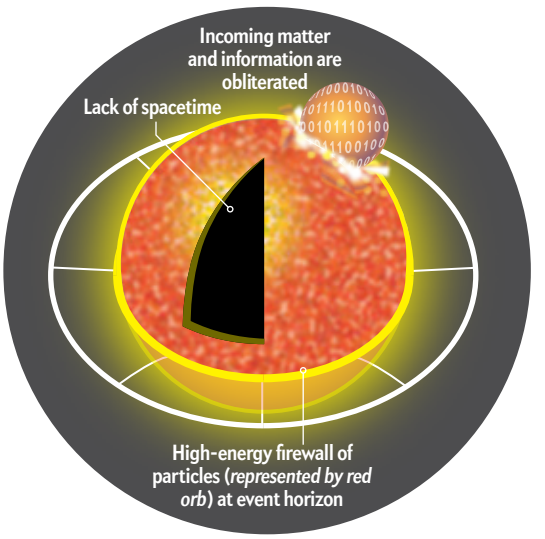


Illustration by Jen Christiansen

hair, whereas quantum mechanics says black holes have a large amount of entropy, meaning some microscopic structure, or hair.

The information paradox. Hawking evaporation also gives rise to a challenge to quantum theory. According to Hawking's calculation, the particles that escape from a black hole do not depend at all on the properties of the material that went into the hole—usually a massive star that collapsed. For example, we could send a note with a message into the black hole, and there would then be no way to reconstruct the message from the final particles that would emerge. Once the note passed through the horizon, it could not influence anything that came out later, because no information can escape from the interior. In quantum mechanics, every system is described by a formula called the wave function, which encodes the chances that the system will be in any particular state.

In Hawking's thought experiment, the loss of information means that we have no way to predict the wave function of Hawking radiation based on the properties of the mass that went into the black hole. Information loss is forbidden by quantum mechanics, so Hawking concluded that the laws of quantum physics had to be modified to allow for such loss in black holes.

You might be saying to yourself, "Of course, black holes destroy information—they destroy everything that enters them." But compare what happens if we simply burned the note. The message would certainly be scrambled, and it would be impractical to reconstruct it from the smoke. But the process of burning is described by ordinary quantum mechanics, applied to the atoms in the note, and the quantum description of the smoke would be a definite wave function that would depend on the original message. In theory, then, the message could be reconstructed through the wave function. In the case of black holes, however, there would be no definite wave function for the resulting radiation.

Based on this analogy, many theorists concluded that Hawking was wrong, that he had mistaken the scrambling of information for actual information loss. Further, some argued, if information can be lost, then it will not just happen in the exotic situation of black hole evaporation but everywhere and all the time—in quantum physics, anything that can happen will happen. If Hawking were right, we would see the signs in everyday physics, probably including severe violations of the law of conservation of energy.

Hawking's argument, though, stands up to simple objections. Unlike burning paper, black holes have horizons beyond which information cannot escape. Thus, we seem to have a sharp paradox: either modify quantum mechanics to allow information loss or modify relativity to allow information to escape from the black hole interior.

A third possibility also exists—that the black hole does not evaporate completely but ends up as a microscopic remnant containing all the information of the original star that created it. This "solution" has its own difficulties, however. For example, such a small object containing so much information would violate the Bekenstein-Hawking idea of entropy.

BLACK HOLES AND BRANES

STRING THEORY is one attempt to rectify some of the problems that arise when relativity and quantum mechanics collide, as in the case of black holes. This theory replaces the pointlike particles of previous theories with tiny loops or strands of string; these strings manage to eliminate some of the mathematical difficulties that arise when quantum mechanics and relativity are combined. Replacing points with strings does not, however, immediately change the black hole story.

A break came in 1995, when I was looking at another kind of thought experiment, studying strings in small spaces. Building on work that I and several others had done a few years earlier, I showed that string theory, as it was then understood, was not complete. Rather it required the existence of objects with more dimensions than the three of space and one of time we are familiar with. In black holes these higher-dimensional objects, called D-branes, would be tiny—wrapped up in hidden dimensions too small for us to detect. The next year Andrew Strominger and Cumrun Vafa, both now at Harvard University, showed that strings and D-branes together provide the precise number of bits to account for black hole entropy, at least for certain very symmetrical black holes. The entropy puzzle was partly solved.

The next question was, What about information loss? Then, in 1997, Juan Maldacena, now at the Institute for Advanced Study in Princeton, N.J., came up with a way around the information loss problem—a solution sometimes called the Maldacena duality. A duality is a surprising equivalence between two things that seem very different. Maldacena's duality shows that the mathematics of a theory combining quantum mechanics and gravity—a quantum theory of gravity—based on string theory are equivalent to the mathematics of an ordinary quantum theory under a special set of circumstances. In particular, the quantum physics of a black hole is equivalent to that of an ordinary gas of hot nuclear particles. It also means that spacetime is fundamentally different from what we perceive, more like a three-dimensional hologram projected from a more fundamental two-dimensional surface of a sphere.

Using Maldacena's duality, physicists also get a way to describe the quantum mechanics of black holes in the bargain. If Maldacena's assumptions are true, then ordinary quantum laws would apply to gravity as well, and information cannot be lost. By a less direct argument, evaporating black holes cannot leave behind any remnants, so it must be that the information gets out with the Hawking radiation.

Maldacena's duality is arguably the closest we have come to unifying general relativity and quantum mechanics, and Maldacena discovered it by chasing down the black hole puzzles of entropy and information loss. It is not yet proved to be true, but it is supported by much evidence—enough that in 2004 Hawking announced that he had changed his mind about the need for black holes to lose information and publicly paid off a bet with physicist John Preskill at the International Conference on General Relativity and Gravitation in Dublin.

Physicists widely believed that no single observer would see any violation of relativity or any other laws near a black hole that lived by Maldacena's rules, although his duality falls short in not giving a clear explanation for how information gets from the inside of a black hole to the outside.

About 20 years ago Leonard Susskind of Stanford University and Gerard 't Hooft of Utrecht University in the Netherlands proposed a solution to the original information problem that involves a kind of relativity principle called black hole complementarity. In essence, the argument holds that an observer who jumps into a black hole sees the information inside, whereas one who stays outside sees it come out. There is no contradiction because these two observers cannot communicate.

SCIENTIFIC AMERICAN ONLINE Watch a Google Hangout of Polchinski discussing black hole firewalls at ScientificAmerican.com/apr2015/firewall

THE FIREWALL

MALDACENA'S DUALITY and black hole complementarity seemed to dispel all the paradoxes, but many of the details had yet to be filled in. Three years ago my own AMPS collaboration tried to make a model of how the combined picture would work, building on ideas of physicists Samir D. Mathur of Ohio State University and Steven Giddings of U.C. Santa Barbara (and extending, unbeknownst to us, an earlier argument of Samuel Braunstein of the University of York in England). After failing repeatedly to make a successful model, we realized that the problem ran deeper than our mathematical shortcomings and that a contradiction remained.

This contradiction pops up when considering the phenomenon of quantum entanglement—the most unintuitive part of quantum theory and the one furthest from our experience. If particles were like dice, entangled particles would be two dice that always added to seven: if you roll the dice, and the first comes up as two, then the second will always come up as five, and so on. Similarly, when scientists measure the properties of one entangled particle, the measurement also determines the characteristics of its partner. It is a further consequence of quantum theory that a particle can be fully entangled only with one other: if particle B is entangled with particle A, then it cannot also be entangled with particle C. Entanglement is monogamous.

In the case of the black hole, think about a Hawking photon; call it "B," emitted after the black hole is at least halfway evaporated. The Hawking process implies that B is part of a pair; call its partner that falls into the black hole "A." A and B are entangled. Furthermore, the information that originally fell into the black hole has been encoded into all the Hawking radiation particles. Now, if information is not lost, and the outgoing Hawking photon B ends up in a definite quantum state, then B must be entangled with some combination, "C," of the other Hawking particles that already escaped (otherwise, the output would not preserve the information). But then we have a contradiction: polygamy!

The price of saving quantum mechanics, keeping the entanglement between B and C and not having anything else out of the ordinary on the outside of the black hole, is the loss of entanglement between A and B. The Hawking photons A and B began just inside and outside the horizon when they arose as an ephemeral particle-antiparticle pair. In quantum theory, the cost of breaking this entanglement, like the cost of breaking a chemical bond, is energy. Breaking the entanglement for all the Hawking pairs implies that the horizon is a wall of high-energy particles, which we termed a firewall. An infalling astronaut, rather than moving freely through the horizon, encounters something dramatic.

Finding such a large departure from general relativity—a wall of energy in a place where nothing unusual should be happening—was disturbing, but the argument was simple, and we could not find a flaw. In a sense, we had just run Hawking's original argument backward, assuming that information is not lost and seeing where that assumption would lead. We concluded that, rather than the subtle effects of complementarity, there was a drastic breakdown of general relativity. As we began to describe the argument to others, the common reaction was first skepticism and then the same puzzlement that we experienced.

Either these strange firewalls actually exist, or it seems we must again consider letting go of some of the deeply held doctrines of quantum theory. Information may not be destroyed, but perhaps some rewriting of quantum mechanics is in store. Unfortunately, observing real black holes will not decide the issue—any radiation from a firewall would be weakened by the gravitational pull of the black hole, making the firewall very hard to see.

THE END OF SPACE

FURTHERMORE, if the firewall exists, what is it? One idea is that the firewall is simply the end of space. Perhaps the conditions for spacetime to form do not exist inside the black hole. As Marolf once remarked, maybe the interior cannot form, because "the black hole's quantum memory is full." If spacetime cannot occur inside, then space ends at the horizon, and an infalling astronaut who hits it dissolves into quantum bits residing on this boundary.

To avoid such bizarre scenarios, physicists have attempted to circumvent the firewall conclusion. One idea is that because Hawking radiation particle B must be entangled with both A and C, then A must be part of C: the photon behind the horizon is somehow the same bit that is encoded in the earlier Hawking radiation, even though they are in very different places. This notion is something like the original idea of black hole complementarity, but to make a concrete model of this scenario, it seems, one ends up modifying quantum mechanics again. The most radical idea, from Maldacena and Susskind, is that every pair of entangled particles is connected by a microscopic spacetime wormhole, so that large regions of spacetime, such as the black hole interior, can be built up from large amounts of entanglement.

Hawking had proposed that general relativity works for black holes but that quantum mechanics breaks down. Maldacena concluded that quantum mechanics is unmodified but that spacetime is holographic. Perhaps the truth is somewhere in the middle.

Many other ideas have been proposed, most of which give up one long-standing principle or another, and there is no consensus as to the right direction to resolve the problems. A common question is, What do firewalls imply for real-life black holes, such as the one in the center of our Milky Way galaxy? It is too early to say.

For now investigators are excited that we have discovered a new contradiction between two of the central theories of physics. Our inability to say definitively whether or not the firewall is real exposes a limitation in our current formulations of quantum gravity, and theoretical physicists are rethinking their basic assumptions about the workings of the universe. Out of this may come a deeper understanding of the nature of space and time and of the principles underlying all the laws of physics. Ultimately, by unraveling the quandaries at the heart of black hole firewalls, we may finally get the break we need to unify quantum mechanics and general relativity into a single working theory. SA

MORE TO EXPLORE

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

Black Holes: Complementarity or Firewalls? Ahmed Almheiri, Donald Marolf, Joseph Polchinski and James Sully in *Journal of High Energy Physics*, Vol. 2013, No. 2, Article No. 62; February 2013. Preprint available at http://arxiv.org/abs/arXiv:1207.3123

FROM OUR ARCHIVES

Black Holes and the Information Paradox. Leonard Susskind; April 1997.

Information in the Holographic Universe. Jacob D. Bekenstein; August 2003.

The Illusion of Gravity. Juan Maldacena; November 2005.

scientificamerican.com/magazine/sa

FUTURE OF MEDICINE 2015

SMALL WONDERS

Nanomedicine is inventing new ways to fight cancer, heal wounds and pilot drugs into cells

By Josh Fischman

A molecule of DNA, holding its blueprint for life, is about 2.5 billionths of a meter in diameter. Scientists now have the ability to push and pull and build molecules of that size, as well as to create devices that sense them with unprecedented precision. These skills, gained through painstaking work during the past decade, are leading to new medicines and ways of diagnosing disease. In this special report, Scientific American examines what nanomedicine is bringing us now, what is coming soon and what the future will likely hold.

Right now chemotherapy is a major focus, and drugs that can slip into tumors because of their fine-grained construction are showing success where other medications fail patients [see "Cancer Drugs Hit Their Mark," on page 44]. Diagnostic tests are also taking advantage of the small sizes, using probes of unusually shaped DNA that can detect cancer with remarkable accuracy. Next, in the near future, patients should be able to use smart bandages made with nanosized molecules that enhance the healing of severe wounds—or that signal doctors when healing is not happening [see "A Smarter Bandage," on page 47]. Further out in time, researchers hope to attach tiny molecular motors to drugs, driving them through the bloodstream to their targets [see "Launch the Nanobots!" on page 50]. These are feats of nanoengineering, invisible to the eye, yet they could have an outsize effect on health.

***Josh Fischman** is a senior editor at* Scientific American.

Illustrations by Harry Campbell

Dina Fine Maron is an associate editor at *Scientific American*.

NANOMEDICINE NOW

CANCER DRUGS HIT THEIR MARK

Tiny vehicles deliver more medication to tumors and reduce side effects

By Dina Fine Maron

IN BRIEF

Chemotherapy drugs have trouble hitting their targets. The body attacks them, they do not penetrate tumors well, and they often mistake healthy cells for cancer cells.

By crafting drug shells on the nanoscale, scientists have created medicines that avoid these problems. Fine-grained control over the shell components lets researchers create drugs that slip past immune system alarms and home in on malignancies.

These medications are already in the final stages of clinical trials. Nanoparticles are also being developed that are more than shuttles but can shut down cancer-causing genes by themselves.

Cancer plays a deadly game of hide-and-seek in the body, and the drugs sent to treat it are often the losers—as is the cancer patient. The drugs have trouble distinguishing between tumor cells and healthy ones and may drop their payload on the normal cells, causing miserable side effects and leaving nearby cancer cells untouched. Malignancies may also get a helping hand from the body's own leading defense weapon, the immune system. It often mistakes anticancer drugs for harmful bacteria or other foreign invaders and breaks them down. The shattered pieces are conveyed to the body's trash receptacles in the liver, kidneys and spleen, again, before they reach their intended target. Even when the drugs do manage to arrive at a tumor, many of them become entangled in the dense undergrowth of the malignant mass—unable to penetrate it completely.

Recent advances in nanomedicine are now allowing drugs

SCIENTIFIC AMERICAN ONLINE Listen to a panel talk about nanomedicine advances at ScientificAmerican.com/apr2015/nanomed-advance

With its design and protective coating, the nanoscale drug is better poised to get to tumors without being destroyed by the body.

to better traverse this fraught landscape and hit tumors where they live. The key is a uniquely crafted drug vehicle, wrapped in a protective outer shell, that shuttles the chemotherapy drugs through the body. Fine-grained control over the components from which the vehicles are built, which can be just a few billionths of a meter across, has let scientists create a specialized architecture that, among other things, does not trip immune system alarms. Researchers such as Kazunori Kataoka of the University of Tokyo and his colleagues have tucked potent chemotherapy drugs inside sheaths the size of a hepatitis C virus—some 200 times as small as a red blood cell. On a molecular level, those drugs look a lot more like something the body makes. These compounds also have the advantage of being able to slip into tumors and steer clear of healthy cells.

Several versions of nanodrug vehicles from Kataoka's team, each holding different medications and aimed at different types of tumors, are now wending their way through the final stages of clinical trials in Asia. Drugs in these new carriers have slowed or reversed disease progression in people with breast or pancreatic cancer. Still another nanoparticle is in the second stage of clinical trials in the U.S. "With science like this, the initial stages take time, but I believe the field is starting to show promise," Kataoka says. "The development speed will be much faster in the coming five years."

DRUGS IN DISGUISE

EMPLOYING NANOTECHNOLOGY for chemotherapy drugs is not a brand-new idea. Medications such as Abraxane for metastatic breast cancer and Eligard for advanced prostate cancer, which are already on the market, are nanodrugs. But these pharmaceuticals attack only certain tumors, so more therapies are needed. Subsequent advances in engineering have allowed scientists to tweak the structure of nanocarriers so they work against a wider array of cancers with even greater precision. The nanotherapies now being tested—administered via an intravenous injection—seem to be more effective at eliminating tumors.

Most of these newer nanomedicines encase a drug-containing core in a soft sheath dotted with polyethylene glycol, a synthetic material that acts as a cloaking agent. That cloak is a covering of water molecules, which are attracted by the sheath material and thus surround it with a common body liquid. Water helps to block electrical charges from the particle that

TRACKING ILLNESS

A Flare for Cancer

Diagnostic spheres of DNA seek out and tag malignant cells

Cancer travels. Large tumors shed cells that move through the body and seed new malignancies. Now scientists are tinkering on the nanoscale to build unusual spheres made of DNA—a molecule that became famous as another shape, the double helix—that can find, tag and potentially kill off these tumor cells.

The spheres look a bit like toothpicks stuck in a small Styrofoam ball. The toothpicks are really a dense crowd of single DNA strands jutting out from a central core. The strands are chosen for their ability to bind to complementary DNA in cancer cells. When a bond happens, it displaces tiny light-emitting molecules stuck to the tips of the DNA in the sphere, essentially sending up a flare that indicates the presence of cancer. The brighter the flare, the more cancer DNA that is present, says Chad A. Mirkin, a chemist and director of the International Institute for Nanotechnology at Northwestern University, who has spearheaded the research.

These encounters occur in a sample of a patient's blood. When the spheres run into a cell, they move through pores in the cell membrane into the interior. Because spheres have more surface area than other shapes, the DNA that forms that outer rim has a much higher chance of encountering and latching on to cancer DNA than isolated strands would. Spherical nucleic acids "bind to other nucleic acids 100 times more strongly," Mirkin says.

Mirkin's spheres, also called Nanoflares, are already being used by hospitals for rapid cancer diagnosis. Other systems fish out dead tumor cells based on proteins on their outer surfaces, but because these spheres identify live cells, Mirkin says, scientists could test how the cells respond to different drugs and eventually develop personalized treatments based on the results. —*Joshua A. Krisch*

***Joshua A. Krisch** is a science writer based in New York City.*

would otherwise alert the immune system to the presence of a foreign substance.

The liquid buffer also covers the nanoparticle's edges, making it too smooth to provide purchase for any passing sentries from the immune system, such as antibodies. The size of the nanoparticle—somewhat larger than a traditional chemotherapy drug—also helps to ensure that it is not broken down too quickly by the body's enzymes. That resistance to degradation gives the drug more time to reach a tumor and do its job. For example, the first approved nanotherapy for cancer, called Doxil, has a half-life in the bloodstream that allows it to survive much longer than its conventional chemotherapy cousin, doxorubicin. (Both drugs are used to treat ovarian cancer.) With its design and protective coating, the nanoscale version is better poised to get to tumors without being destroyed by the body. The soft, flexible texture of the newest nanoshell-type drugs also allows them to skip through one of their final obstacles: the dense, irregular ecosystem of the malignant tissue that could snag something more rigid.

The final weapon of the new nanoparticles lies within their inner depths. The drug-containing core can be broken down by acid, so it will readily disintegrate and shed its drug cargo only after it leaves the neutral environment of the blood and arrives at its tumor destination, which has much higher acid levels.

To better steer the nanocarriers toward cancers and away from healthy cells, other scientists are trying to dot their exteriors with selected antibody molecules that are attracted to proteins that are particularly abundant on cancer cells. Proteins such as EGFR are one such example, and University of California, Los Angeles, bioengineer Dean Ho has done preliminary experiments, published in *Advanced Materials* in 2013, showing that nanoparticles can be layered with antibodies that link to those proteins.

Nanoparticles can also be built to serve as actual medicines, not just the delivery vehicles. Scientists at Northwestern University created nanoparticles made from bits of gold and laced with genetic material—RNA—selected for its ability to silence cancer-causing genes. Because of the particles' small size and other yet to be determined factors, gold nanoparticles studded with RNA can penetrate one of the hardest places to reach with a drug: the brain. In October 2013 researchers reported that, in animals, the nanoparticles can cross the blood-brain barrier—a tight mesh of small blood vessels—to help combat brain tumors. The approach caused overall tumor size to shrink in rodents, but ultimately the creatures still died from the cancer, says researcher Alexander Stegh of Northwestern. Exactly how this technique managed to clear the blood-brain barrier is still being explored, he notes. It is possible that the particles' structure binds to receptor molecules on the surfaces of blood vessel cells, and the receptors help to pull them in.

Still other types of nanoparticles made from nucleic acids are being studied as probes to detect cancer cells that circulate through human blood [*see box on this page*]. Chad A. Mirkin, a Northwestern chemist leading the project, says the research may lead to nanoparticles that carry both diagnostic chemicals and medicine—a formidable package that could eliminate hard-to-find cancerous cells before they spread to new places in the body. Devising that kind of tiny powerhouse would be no small feat.

MORE TO EXPLORE

Nanoparticle PEGylation for Imaging and Therapy. Jesse V. Jokerst et al. in *Nanomedicine*, Vol. 6, No. 4, pages 715–728; June 2011. www.ncbi.nlm.nih.gov/pmc/articles/PMC3217316

Nanomedicine: Towards Development of Patient-Friendly Drug-Delivery Systems for Oncological Applications. R. Ranganathan et al. in *International Journal of Nanomedicine*, Vol. 7, pages 1043–1060. Published online February 23, 2012. www.ncbi.nlm.nih.gov/pmc/articles/PMC3292417

Progress of Drug-Loaded Polymeric Micelles into Clinical Studies. Horacio Cabral and Kazunori Kataoka in *Journal of Controlled Release*, Vol. 190, pages 465–476; September 28, 2014.

FROM OUR ARCHIVES

Less Is More in Medicine A. Paul Alivisatos; September 2001.

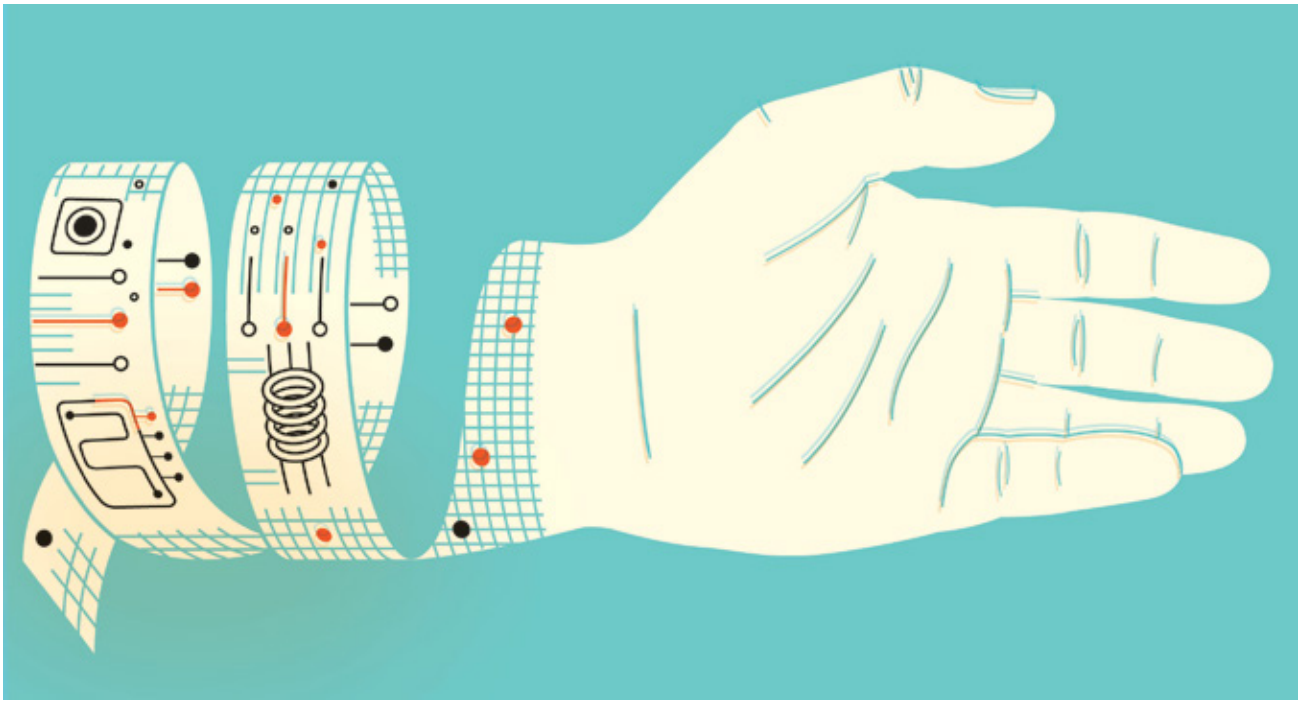
scientificamerican.com/magazine/sa

NANOMEDICINE SOON

A SMARTER BANDAGE

New materials will not simply cover wounds—they will alert doctors to problems and deliver drugs

By Mark Peplow



The injured soldiers had been treated well since their return from fighting in Afghanistan. At the San Antonio Military Medical Center in Texas, surgeons had carefully grafted healthy tissue over their burns and wounds, using microsurgery to connect their blood vessels to the new skin. But the patients still faced an uncertain recovery. The vessels might not supply enough oxygen for the transplants to thrive.

When Conor Evans visited San Antonio in 2010 and saw these soldiers, he realized that conventional techniques for monitoring oxygen levels did not work very well, and they often failed to give enough warning if the graft was failing. "What these physicians do is nothing short of amazing," says Evans, a chemist at Harvard Medical School and the Wellman Center for Photomedicine at Massachusetts General Hospital. "But the sensors they had just weren't cutting it."

So Evans built a better bandage. He and his colleagues started with dyes that react to different oxygen levels, added nanosized molecules that control the dye activity, and used them to

create a liquid bandage that indicates the health of the wound it covers. "The bandage changes color, just like a traffic light, from green through yellow and orange to red," depending on the amount of oxygen present, Evans says. After success in laboratory animals in 2014, human trials are set to begin this year.

By taking advantage of newfound abilities to manipulate materials as small as a few billionths of a meter, scientists such as Evans can not only improve rapid health assessments, they can also turn wound dressings into precise drug-delivery systems "Nanotechnology plays a large role in being able to control the amounts released and how well formulations get to the area of a wound that we need them to reach," says Paula Hammond, a chemist at the Massachusetts Institute of Technology. That precision has a major advantage over flooding body parts with drugs, only some of which find their targets.

Mark Peplow is a science journalist based in Cambridge, England.

COMING UP FOR AIR

POOR WOUND HEALING caused by a lack of oxygen affects more than six million people in the U.S. every year, and the medical costs are estimated to reach $25 billion. Typically physicians stick needle electrodes into injured tissue to measure tissue oxygenation, but the needles can be painful and give readings from only a single point in a large wound. Evans's bandage, in contrast, can provide an instant oxygen map of the entire injury.

It relies on two dyes mixed into a quick-drying liquid bandage that can be painted onto wounds. A brief burst of blue light energizes and illuminates both dyes: one glows bright red, the other green. Then oxygen molecules switch off the red dye's phosphorescence, so the bandage will appear green if the adjacent tissue is bathed in oxygen and is healthy. But if areas of the wound are oxygen-starved, patches of yellow, orange and, finally, an alarming red shine through.

The bandage will appear green if wound tissue is bathed in oxygen and healthy. But if areas of the wound are oxygen-starved, patches of yellow, orange and, finally, an alarming red shine through.

The key to the alert is a nanoscale addition to the red dye molecules. Evans coupled each of these molecules to a dendrimer, a treelike molecule with a branching structure up to two nanometers across. This molecular thicket prevents neighboring molecules from overlapping and quenching one another's phosphorescence. They also physically block some—but not all—of the oxygen molecules from reaching the dye; starting with lower levels makes any changes more obvious.

In a hospital, the warning red would prompt a nurse to photograph the bandage, and doctors would to try to improve the blood and oxygen circulation in the trouble spots. In principle, the bandage could work at home, Evans says: patients could take their own bandage snapshots and send them to a doctor for assessment.

Evans's team has also created alternative dyes that are much more efficient at converting blue light into red. "Our new bandage is so bright that it can be seen with very low dye loading, in a sunlit room," Evans says. In the future, the bandage might even be engineered to dispense therapeutic drugs into wounds, he adds.

DRUG-DELIVERY DRESSING

IN HAMMOND'S LAB, researchers have already loaded bandages with nanoengineered therapeutic substances. They have developed coatings that slowly release RNA or proteins, molecules that can shut down certain cell activities that might hamper wound recovery. Some RNA molecules, called small interfering RNAs, can hobble the ability of genes that give rise to problem-causing proteins, for example.

Her team encapsulated some of these RNAs within calcium phosphate shells, each about 200 nanometers wide, sandwiched the shells between two layers of a positively charged polymer made of biological molecules and then "buttered" one side of this sandwich with a negatively charged clay. (The opposite charges stick the layers to each other.) Stacking up 25 of these sandwiches formed a coating roughly half a micron thick, which Hammond placed on a conventional nylon bandage.

IN BRIEF

Wound dressings can be transformed into precise drug-delivery systems by manipulating materials sized at a few billionths of a meter (nanometers).

Nanotechnology enables researchers to sandwich drugs between the layers of a bandage and to control how much gets released.

Sensitive bandages can detect the conditions of serious wounds. They can also release molecules that hobble problem-causing proteins.

Small, layered devices can be placed in heart arteries, and dissolving layers release DNA for a protein that helps to reconstruct damaged blood vessels.

COMPUTER IMPLANTS

Gentle on the Heart

Soft electronic circuits that do not tear flesh enfold and monitor vital organs

The hardware in electronics has been a poor fit for the software of human flesh. Rigid circuits do not flex with pliable organs, and hard edges tear soft tissue. This problem has severely limited efforts to improve devices such as artery-clearing catheters by adding computerized control and finesse. Silicon may support the entire computer industry, but it is notoriously brittle.

Yet even the most stubborn materials become flexible if you make them thin enough, says John Rogers, a materials scientist at the University of Illinois at Urbana-Champaign. He is building stretchable electronic sheets, just 10 nanometers thick, for devices that could be placed within or around organs such as the heart and do their jobs without causing harm. Rogers calls them "soft electronics."

The circuits that Rogers builds must use high-fidelity conductors, such as silicon and gallium nitride, because they have to relay computer signals without a glitch. To get around silicon's tendency to break when bent, he has used nanoscale engineering to thin the material while maintaining its conductive ability. Shaved down to around 10 nanometers, silicon acts more like a rubber band and less like glass.

In animals, Rogers has already successfully tested a flexible membrane, with embedded electronics, that can be wrapped around a beating heart to watch for abnormal rhythms. If tests continue to show success, he imagines adding electronic monitors to artery-opening devices such as balloon catheters so they can sense narrow sections of blood vessels. "Dumb mechanical devices could become sophisticated surgical tools," Rogers says. —*J.A.K.*

As natural enzymes in the body break down the layers, the dressing discharges the RNA molecules into the wound over the course of a week. The slow, steady release could reduce side effects caused by a single, large dose of a conventional drug; this release method could also ensure that the wound is constantly treated.

Hammond has also used this so-called layer-by-layer coating to supply a therapeutic protein that aids wound healing in diabetic mice. The protein is already available as an ointment, but she says that the formulation is not very effective—after initially delivering a huge burst of protein, its activity fades away within 24 hours. Hammond's bandage, in contrast, sustains a steady flow over five to seven days to maintain the optimum dose of protein.

The layer-by-layer strategy could improve treatments for another ailment: coronary artery disease, which is caused by a buildup of plaque in vessels that carry blood through heart muscle. Treatment usually involves widening the artery with an inflatable balloon and keeping it open by inserting a small tube of stainless-steel mesh known as a stent. Some stents come loaded with therapeutic molecules to prevent the artery from narrowing again, but patients must then take more drugs to reduce the associated risks of blood clots that could break free from the area.

Treating the artery with doses of DNA, carefully delivered by devices with nanoscale coatings, could offer a better solution, according to David Lynn, a chemist at the University of Wisconsin–Madison. Inside the body, the DNA could make cells produce a protein that helps to stabilize and reconstruct blood vessel walls. To deliver such genetic therapies exactly when and where they are needed, Lynn has coated stents with successive layers of DNA and a biodegradable polymer, each several nanometers thick. By varying the number of layers, researchers can control the amount of DNA released into blood vessel walls. Experiments on pigs showed that the DNA gradually penetrated the surrounding tissue during the days after the stent was implanted. Fine-tuning the design of the coating, other tests show, can change the rate of release. "We now have reasonable control that allows us to time the release from seconds to months by modifying the structure of the polymer or how we put the film together," Lynn says.

The basic nanoengineering behind these inventions could be adapted for a wide range of other applications. Lynn is using polymer coatings to deliver biological molecules called peptides that interrupt the chemical conversations among bacteria. Cut off from one another, the bacteria cannot team up to form tough biofilms that resist breakup by antibiotics. Evans, for his part, is using his phosphorescent dyes in tissue samples to identify oxygen-poor tumor cells, which can be particularly resistant to chemotherapy, and he plans to test the technique in animals later this year. The same dye approach could also be used to detect the presence of infectious bacteria in wound tissue or reveal other kinds of molecules. "Really, the sky's the limit," Evans says.

MORE TO EXPLORE

Polyelectrolyte Multilayers Promote Stent-Mediated Delivery of DNA to Vascular Tissue. Eric M. Saurer et al. in *Biomacromolecules,* Vol. 14, No. 5, pages 1696–1704; May 13, 2013.

Nanolayered siRNA Dressing for Sustained Localized Knockdown. Steven Castleberry in *ACS Nano,* Vol. 7, No. 6, pages 5251–5261; June 25, 2013.

Surface Coatings That Promote Rapid Release of Peptide-Based AgrC Inhibitors for Attenuation of Quorum Sensing in *Staphylococcus aureus*. Adam H. Broderick et al. in *Advanced Healthcare Materials,* Vol. 3, No. 1, pages 97–105; January 2014.

Click-Assembled, Oxygen-Sensing Nanoconjugates for Depth-Resolved, Near-Infrared Imaging in a 3 D Cancer Model. Alexander J. Nichols in *Angewandte Chemie International Edition,* Vol. 53, No. 14, pages 3671–3674; April 1, 2014.

Non-Invasive Transdermal Two-Dimensional Mapping of Cutaneous Oxygenation with a Rapid-Drying Liquid Bandage. Zongxi Li in *Biomedical Optics Express,* Vol. 5, No. 11, pages 3748–3764; November 1, 2014.

FROM OUR ARCHIVES

Wound Healing. Russell Ross; June 1969.

Skin Deep. Ricki Rusting; September 1989.

scientificamerican.com/magazine/sa

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

NANOMEDICINE IN COMING DECADES

LAUNCH THE NANOBOTS!

> Overcoming all the technical challenges may take 20 years or more, but the first steps toward remote-controlled medicine have already been taken
>
> *By Larry Greenemeier*

The long-term future envisioned by nanomedicine researchers includes incredibly tiny therapeutic agents that smartly navigate under their own power to a specific target—and only that target—anywhere in the body. On arrival, these self-guided machines may act in any number of ways—from delivering a medicinal payload to providing real-time updates on the status of their disease-fighting progress. Then, having achieved their mission, they will safely biodegrade, leaving little or no trace behind. These so-called nanobots will be made of biocompatible materials, magnetic metals or even filaments of DNA: all materials carefully chosen for their useful properties at the atomic scale, as well as their ability to slip past the body's defenses undisturbed and without triggering any cellular damage.

Although this vision will likely take a decade or two to fulfill, medical researchers have already begun addressing some of the technical problems. One of the biggest challenges is making sure the nanodevices get to their target in the body.

WAVE POWER

MOST DRUGS on the market today readily float through the body in the bloodstream, either after being injected directly into the blood or, in the case of pills, getting absorbed into the bloodstream from the gastrointestinal tract. But they wind up traveling both to where they are needed and to where they can cause unwanted complications. Sophisticated nanomedicines, in contrast, are being designed to be guided to a tumor or other problem site, where their medicinal payload is released, reducing the chance of side effects.

Magnetic fields and ultrasound waves are the leading candidates for guiding nanomedicines in the near term, says Joseph Wang, chair of nanoengineering and a distinguished professor at the University of California, San Diego. In the magnetic approach, researchers embed nanoparticles of iron oxide or nickel, for example, within a particular medication. They then use an array of permanent magnets positioned outside a mouse or other subject and push or pull the metallic medicine through the

IN BRIEF

Some day a fleet of nanomedicines and devices will travel anywhere it needs to go in the body, under its own power, using biocompatible motors and fuels to get there.

Before that day arrives, however, researchers must learn how to design these compounds so that they can move without damaging or interfering with any normal biological functions.

In the near term, scientists are generating magnetic fields and ultrasound waves to propel nanoparticles to their target areas. But such approaches cannot penetrate deep into the body.

Nanobots made of DNA are another alternative. Some of these compounds are designed to work like boxes that open and release their cargo only under specific circumstances.

body to a selected site by manipulating various magnetic fields. In the ultrasound approach, researchers have directed sound waves at medicine-containing nanobubbles—causing them to burst with enough force that the bubble's cargo can penetrate deep within a targeted tissue or tumor.

Last year medical researchers at Keele University and the University of Nottingham, both in England, added a helpful twist to their magnetic approach in work aimed at healing broken bones. They attached iron oxide nanoparticles to individual stem cells and then injected the preparation into two different experimental environments: fetal chicken femurs and a synthetic bone scaffold made from tissue-engineered collagen hydrogels. Once the stem cells arrived at the break, the researchers used an oscillating external magnetic field to rapidly shift the mechanical stress on the nanoparticles, which in turn transferred the force to the stem cells. This kind of biomechanical stress helped the stem cells to differentiate more effectively into bone. New bone growth occurred in both cases—although overall healing was uneven. Eventually the researchers hope that adding various growth factors to the iron oxide–studded stem cells will make the repair process smoother, says James Henstock, a postdoctoral research associate at Keele's Institute for Science and Technology in Medicine.

AUTONOMOUS NANOMEDS

THE PRIMARY DRAWBACKS to the magnetic and acoustic approaches are the need for external guidance—which is cumbersome—and the fact that magnetic fields and ultrasound waves can penetrate only so far into the body. Developing autonomous "micro motors" for the delivery of therapeutic cargo could surmount those problems.

Such micro motors would rely on chemical reactions for propulsion, but toxicity is an issue. For example, oxidizing glucose, a sugar molecule found in the blood, would generate hydrogen peroxide, which could be used as a fuel. But researchers already know that this particular approach would not work in the long run. Hydrogen peroxide corrodes living tissue, and glucose in the body would not produce enough hydrogen peroxide to adequately power micro motors. More promising are efforts to use other naturally occurring substances, such as stomach acid (for applications in the stomach) or water (which is abundant in blood and tissues), as power sources.

Accurate navigation by these self-propelling devices may be an even greater hurdle, however. Just because nanoparticles can move anywhere does not mean that they will necessarily travel exactly where researchers want them to go. Autonomous steering is not yet an option, but a work-around would be to make sure that nanomedicines become active only when they find themselves in the right environment.

To accomplish this trick, researchers have begun creating nanomachines out of synthetic forms of DNA. By ordering the subunits of the molecule so that their electrostatic charges force it to fold in a particular configuration, scientists can engineer the constructs to perform various tasks. For example, some DNA segments may fold themselves into containers that will open and release their contents only when the package comes across a protein important to a disease process or encounters the acidic conditions inside a tumor, says University of Chicago chemistry professor Yamuna Krishnan.

Krishnan and her colleagues envision more advanced, modular entities made of DNA that could be programmed for different tasks, such as imaging or even assembling other nanobots. Yet synthetic DNA is expensive—costing about 100 times more than more traditional materials used to deliver drugs. For now, then, the price discourages drug companies from investing in it as a candidate for treatments, Krishnan says.

All of this may be a far cry from building a fleet of smart submarines reminiscent of *Proteus* in the 1966 film *Fantastic Voyage*. Still, nanobots are finally moving in that direction. SA

MORE TO EXPLORE

Motion Control at the Nanoscale. Joseph Wang and Kalayil Manian Manesh in *Small*, Vol. 6, No. 3, pages 338–345; February 5, 2010.

Designer Nucleic Acids to Probe and Program the Cell. Yamuna Krishnan and Mark Bathe in *Trends in Cell Biology*, Vol. 22, No. 12, pages 624–633; December 2012.

Remotely Activated Mechanotransduction via Magnetic Nanoparticles Promotes Mineralization Synergistically with Bone Morphogenetic Protein 2: Applications for Injectable Cell Therapy. James R. Henstock et al. in *Stem Cells Translational Medicine*, Vol. 3, No. 11, pages 1363–1374; November 2014.

FROM OUR ARCHIVES

Of Chemistry, Love and Nanobots. Richard E. Smalley; September 2001.

scientificamerican.com/magazine/sa

SUSTAINABILITY

How a small group of visionaries are trying to feed China—and save the world's oceans

By Erik Vance

Photographs by Dominic Bracco II

Fishing *for* Billions

NETTING partitions Liangzi Lake into zones cultivated by two companies. Greater productivity from freshwater fish farms is needed to ease overfishing at sea.

Erik Vance is a science writer based in Mexico City who focuses on the oceans and on brain science. He longs for the day he can eat seafood without guilt.

IN JANUARY 2007 NGUYÊN PHÚ WAS PREPPING HIS SMALL BOAT FOR WHAT APPEARED to be just another day of fishing for octopus off the Vietnamese coast. Soon after he headed out to sea, several Chinese boats appeared on the horizon. Phú thought momentarily about fleeing but knew he would not get far. When the gunships sidled up to his boat, he and his crew put up no resistance. "We don't mess with the Chinese," he says. "We just go into this position"—he crouches down with his hands above his head—"and we pray to God that we can suffer this."

He claims Chinese soldiers took him and his crew to a jail on a nearby island and confiscated his boat. Phú spent more than a month in a cramped cell and received daily beatings, he and his crew say. Then he was let go; no trial, no judge, no reason given. The military had caught him and released him, just like a fish.

Phú's story, which he told me through an interpreter in August 2014, fits a well-documented pattern of grandstanding by China in Pacific waters near Asia in recent years. Fijian tuna fishers say that Chinese captains refuse to acknowledge catch limits around their islands. Chinese poaching in Japan's marine parks has strained already tense relations between those countries. The Philippines is escalating its military presence near a few scattered shoals that Chinese fishing boats now patrol off its coast. China claims that the South China Sea has been part of its territory for hundreds of years.

What is not in dispute is the basic fact that China is hungry for fish. As the nation's standard of living rises, demand for seafood has soared. Per capita, the Chinese eat 50 percent more fish than Americans. The country's 1.4 billion citizens eat more fish than those of the next 10 biggest countries combined.

To meet the growing demand, China in 2012 produced 57 million metric tons (tonnes) of fish from wild fisheries and fish farms—one third of the world's total—according to the United Nations Food and Agriculture Organization. China currently has 700,000 fishing vessels that patrol waters around the globe. Its ships drag enormous cages along the ocean bottom and haul nets the size of football fields through the water. Other nations use similar techniques, but China surpasses even Japan and the U.S. as the country most responsible for emptying the world's fisheries.

As a result, many animals in popular dishes—sea cucumbers, sharks, abalone—are steadily declining around the world. Beyond symbolic gestures such as banning shark fin soup at official functions, the Chinese government has so far been reluctant to acknowledge the issue.

But some Chinese scientists and businesspeople, worried that modern fishing methods are depleting the world's oceans faster than they can replenish themselves, are starting to tackle the problem. A handful of these visionaries are trying to reverse the trend by reinventing China's aquaculture—from the thousands of small, freshwater farms still using ancient methods to massive industrial ocean farms.

Their goal is to transform the old, wasteful, polluting operations into a uniquely Chinese form of sustainable seafood while helping fish farmers, big and small, to prosper. They are hoping to appeal to the desire of Chinese consumers for fish that is clean and healthy to eat by presenting their aquaculture as a modern alternative to conventional practices. If the researchers and business leaders can find sustainable ways to fulfill demand for traditional favorites such as freshwater carp, they could go a long way to saving the world's fisheries from collapse.

MANAGING THE OCEAN LIKE A FARM

THE WATERS of the fish farm around Zhangzi Island, near Korea, are cold. The chilly water here is said to produce the best seafood in the world. The particular cove I am preparing to enter is

IN BRIEF

China produces one third of the world's seafood, and it consumes more than the next 10 countries combined. Whether it can reinvent its freshwater and saltwater fish farms to lessen its take from the sea will determine if the world's fisheries survive or collapse.

A handful of scientists and businesspeople are redesigning ocean aquaculture operations so that multiple species recycle one another's effluents, making the farms less polluting and more sustainable. They are trying to do the same with China's thousands of large and small freshwater farms, which supply 70 percent of the nation's fish.

So far seafood raised this way is expensive; costs will have to come down before Chinese consumers buy the products widely.

ZHANGZIDAO FARM relies on ocean currents to move nutrients among different species. Farmers sort juvenile scallops before placing them in the sea (*below*), dive (*left*) to check growing sea cucumbers (*above, left*) and prepare big blocks made from recycled scallop shells (*above*) used to direct the currents.

famous because in 1972 its abalone was chosen for the banquet honoring then president Richard Nixon's historic visit, which opened trade relations with China.

Today the air is warm, so my seven-millimeter-thick wet suit is stiflingly hot for the few minutes before I plop into the water, along with two guides and a photographer, like so many neoprene potatoes. My companions are fishers at Zhangzidao Group, a once traditional fish farming corporation that today is experimenting with a new idea. They are friendly enough but also seem a little suspicious. We are the first foreign journalists to tour the site.

As we descend into the dark water we see what looks like a common coastal ecosystem: grasses, kelp and wide, sandy stretches. Then I notice that the ocean floor is littered with sea cucumbers, bivalves and urchins—not hidden in nooks and crannies as one would expect but wandering out in the open. Immediately, the fishers begin plucking up sea creatures by hand like children on an Easter egg hunt.

This fish farm—if one can even call it that—uses a novel approach that replicates natural systems on a grand scale. Behind us, spanning this and every other cove, are endless lines of caged, baby scallops that will be dropped into the waters, where they will stay until they are big enough to be harvested by the men who are swimming next to me. Other than these, there are no cages or enclosures. There are also no fertilizers, artificial feeds or antibiotics.

"We use a model called IMTA," says Liang Jun, the company's chief scientist, "where the excrement from one species can be the nutrients for the other species."

Integrated multitrophic aquaculture, or IMTA, is a broad concept that has appeared in various forms in countries that include Canada, Scotland, the U.S. and Norway. The idea is that having multiple species recycle one another's excrement (or "nutrients") decreases water pollution. Most conventional IMTA approaches take the form of a series of neighboring cages,

in which the occupants of each cage feed off the nutrients of another. For example, the most well-known IMTA project is in Canada's Bay of Fundy, which uses lined-up cages to pass nutrients, down current, from salmon to bivalves and kelp.

Zhangzidao takes a totally different tack, however. In essence, Zhangzi and several other islands act as de facto cages. Jun's team has carefully studied the movement of nutrients along the shores, occasionally building artificial reefs to redirect the currents that move them. Then they seed nutrient-rich parts of the islands with young scallops bred to thrive here while carefully removing their predators.

Naturally the waters become rich with a few select species. The company monitors key markers such as temperature, but mostly the animals are left to fend for themselves until divers systematically collect them. There is no bycatch—the wasteful scooping up of unwanted species—as in wild fishing, and little pollution. The company recycles its shells into concrete blocks for future reefs.

What really sets this project apart is its scale. "When they decide to have aquaculture in a bay, they go massively—something that would be impossible in the Western world," says Thierry Chopin, a biologist at the University of New Brunswick, who is working on the Bay of Fundy project. "It's completely different."

FARMERS at Luhu Lake feed the mandarin fish they cultivate there, having given up on carp, which polluted the water.

The Bay of Fundy operation covers a few hectares and holds nine "mussel rafts" filtering effluent. In contrast, the Zhangzi Island ocean ranch is four times the size of Chicago. The Bay of Fundy produces around 200 tonnes of kelp every year and 300 to 400 tonnes of mussels. The islands around Zhangzi produce 60,000 tonnes of kelp, mostly as a by-product that is sold locally. The real money is in the 200 tonnes of sea urchins, 300 tonnes of oysters, 700 tonnes of sea snails, 2,000 tonnes of abalones and a whopping 50,000 tonnes of scallops raised a year. The operation is so productive that Zhangzidao recently created a fishing tourism business to catch the many fish that wander into the coves to snack on the thriving invertebrates.

Jun says this particular brand of aquaculture can only work at a very large size. "You have to have a system that is at least 100 square kilometers," about the area of a small town, he says, to be economically viable. "And to farm something like this, you need lots of research into ocean dynamics."

He spins his computer screen around to reveal a detailed map of the islands showing where nutrients concentrate and where yields are highest. Most of these factors are based on ocean currents, which Jun can fine-tune by dropping concrete blocks the size of refrigerators into the water to form the artificial reefs. He has lowered 20,000 such blocks into the sea.

Some Westerners argue that Zhangzidao is not truly using IMTA, because it does not grow or harvest finfish, whose excrement, in theory, would feed the invertebrates. They prefer a less technical term, such as "ocean ranch." Either way, Zhangzidao is stunning in size and efficiency. Yet it is by no means perfect. According to a spokesperson, more than half of the ranch is too deep to harvest by hand, so fishers still use trawls—heavy, stiff five-meter-wide nets that are dragged along the ocean bottom and generally damage the seafloor. And the products coming out of Zhangzidao are very expensive. Sea cucumbers—small, bumpy, sluglike relatives of sea stars—sell for as much as $250 apiece in China. As in the U.S. and Europe, Chinese sustainable seafood seems to be primarily for the wealthy.

BRINGING CONSUMERS ALONG

STILL, THE UNPRECEDENTED SCALE of the project hints at a potential solution for China's massive seafood demand. The trick is to make sustainable seafood work for consumers at all income levels. "Marketing sustainable products is a big challenge in China, at least at this moment," admits Yuming Feng, Zhangzidao's president. Consumers will have the final say, he says, adding, "Their question will be, 'What's in it for me?'"

For now Chinese consumers are not focused on the environment or willing to spend more to help save it, because they have a bigger concern in mind. "The Chinese government and the Chinese consumers are really looking for truthful products" related to food safety, says An Yan of the Marine Stewardship Council's Asia Pacific office.

Health scares over lead poisoning and melamine-laced milk have made Chinese consumers nervous about where their food comes from. But Yan argues that production changes aimed to improve food safety open the door to conservation. When Zhangzidao started its experiment, it exported most of its scallops to environmentally conscious buyers in the U.S., Australia and Europe. Today all its seafood stays in China, marketed as clean and healthy rather than environmentally friendly.

That pitch rings true in a market in nearby Dalian, where the desire for the product is obvious. I walk down aisles lined with sea cucumbers, crabs, scallops and conches, buffeted by calls in Chinese of "What do you want?!" Fresh clams squirt water onto my pants. Older women are scooping up prawns with dust-

pans under colorfully gaudy banners of grinning cartoon fish.

Almost every stall in the fish market claims its seafood comes from the Zhangzi ranch, which is unlikely because Zhangzidao mostly sells to big retailers and high-end restaurants. But it is telling that the Zhangzi brand is so coveted. "They have artificial reefs, and this is very healthy for the fish," says Meng Ni Ou Yang, a stall owner who sells "island" products for an extra 20 percent. Another seller, 35-year-old Hong Zhe Liang, simply says, "The water is cleaner there."

None of the fishmongers mention environmental concerns, and when asked, they say wildlife conservation is not that important to their customers. Yet other regions are experimenting with IMTA, too. Along the shores near Dalian and farther to the south in Sanggou Bay are endless expanses of kelp farms that incorporate elements of the technique on equally sprawling scales, though with decidedly less variety of life. To meet the massive demands of a hungry China, ocean aquaculturists will have to expand such models much further.

CLEANER LAKES AND PONDS

CHINA'S HUNDREDS OF THOUSANDS of seafaring boats may dominate the global market, but all that seafood does not dominate the country's own consumption. More than 70 percent of the fish China eats comes from its lakes and rivers. Recent scares over freshwater pollution have made some diners nervous about traditional fish, however. Thus, any attempt to curb China's impact on the sea will require restoring faith in freshwater fish farms. A network of scientists up and down China's most significant fish-growing region is trying to do just that.

The importance of aquaculture around the Yangtze River is obvious as soon as one lands in Wuhan, 500 kilometers upriver from Shanghai. It is the center of the largest fish-growing region of the world's biggest fish-growing country. Surrounding the airport, under freeway overpasses and along the roads as far as the eye can see, every square centimeter of unused land is dug out, filled with water and growing fish.

"Look off to the left," says Shouqi Xie, a researcher at the Chinese Academy of Sciences, as we pass seemingly unending lines of ponds. "This is why we call Hubei Province the land of 1,000 lakes."

About 18,400 square kilometers of China—roughly the area of New Jersey—are fishponds. Although it may be hard for Americans to imagine, Chinese experts say one fifth of the world's animal protein comes from freshwater fish, half of which come from here, in China's heartland along the Yangtze.

But these days headlines about rampant water pollution and contaminated foods have eroded consumer confidence in traditional pond fare such as carp and catfish. "This is ridiculous," Xie says. "We track fish through their entire lives. With wild fish, no one is tracking where they go or what pollutants they encounter."

Even so, traditional freshwater farms are not exactly sustainable. Chinese aquaculture traces back to Fan Li, who was a fifth-century B.C. philosopher, tactician and adviser to the powerful king Goujian of Yue. After a successful military career, Fan Li retired to the lakeside town of Wuxi, where he wrote the world's first aquaculture manual. The 400-character-long pamphlet includes such details as the number of carp to start with, the best growing season and a recommendation to raise turtles to ward off the "flood dragon."

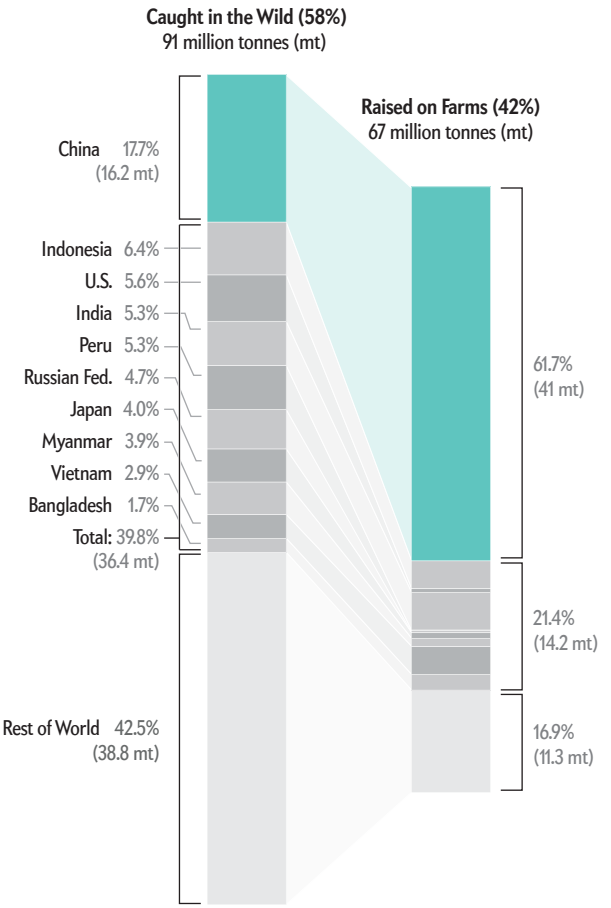
The ancient practices worked for thousands of years, with small ponds operating alongside terrestrial farms that maintained clean water and healthy fish. In the 1980s, however, the industry turned toward sprawling, industrial ponds. That shift, along with huge growth in other industries, caused heavy pollution. In 2007 the situation culminated in a fateful algal bloom in Tai Hu (*Hu* means "lake"), the legendary home of Fan Li. "Because most of the tap water in Wuxi comes from Tai Hu, citizens couldn't drink from their tap. The water ran black," Xie says. "If you took a shower with the water, it smelled really bad."

LEADER BOARD

The Biggest Fishmonger

China is by far the world's largest supplier of fish, crustaceans and mollusks—"seafood" from oceans, lakes and rivers. In 2012 (the latest data), China produced 17.7 percent of the seafood caught in the wild (*left column, below*), nearly three times as much as the next nation. Even more impressive, China raised 61.7 percent of the fish from saltwater and freshwater farms (*right column*). If wild fisheries, now disappearing, are to survive, countries will have to farm more fish, with China leading the way.

Seafood Production, Saltwater and Freshwater (2012)



SOURCE: *FAO YEARBOOK: FISHERY AND AQUACULTURE STATISTICS, 2012.* FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS, 2014

Graphic by Tiffany Farrant-Gonzalez

HUSBAND-AND-WIFE team fertilize a pond they manage near Wuhan. Scientists are trying to help thousands of families operate their ponds more sustainably, vital to supplying China's ever growing demand for fish.

The 2007 black tide was a wake-up call for China. People could no longer trust the water they drank or the fish they ate. And although the bloom was not primarily caused by fish farms, the event has helped push Chinese aquaculturists to focus on high productivity that preserves the environment. People such as Xie are working on keeping water clean while increasing yield.

BALANCING ACT

ALL FRESHWATER ECOSYSTEMS are in a constant balancing act between too many nutrients and too few. The Great Lakes, for example, have invasive species that sap the water of nutrition, leaving it clear and oxygen-rich but dead. In contrast, the Yangtze has too many nutrients, such as nitrogen and phosphorus, and too little oxygen. The result is murky green water inhabited by the only creatures that can thrive in an oxygen-poor aquatic environment: algae.

For centuries the nutrients coming into and out of many fish farms were in a natural balance. But in recent years that alignment has shifted. Part of the problem is pollution, but another part comes from aquaculture itself. The most popular type of fish in China is carp—a fast-growing family that happily feeds on anything from algae to sewage. Carp excrete nitrogen-rich waste that settles into the soil. That nutrient, along with fish fertilizers, feeds the algae that then block light from plants that could produce oxygen. The cycle continues until very little can live in a lake except carp and algae. During a decade of rapid development, algae increased almost 20-fold in one Hubei Province lake and the lake's visibility dropped by half.

I contemplate this as I step onto a small speedboat on the shores of Liangzi Lake. The lake is eerily silent, and I cannot tell if the blanket above us is low cloud cover or smog. The water is greenish and perfectly still, like a giant expanse of weak pea soup.

Ten years ago dozens of pens, each full of carp, would have been stacked along the lakeshore, their waste killing everything else in the water. The local government asked Wuhan University to help restructure the farming in the lake, the second largest in the province. Jiashou Liu, Xie's colleague at the Chinese Academy of Sciences, realized that the concentration of waste was feeding the algal blooms.

Today all the cages are gone. Fish farmers now manage the entire lake as one sort of cage, letting nature guide the fish. Also gone are most of the carp. Farmers and scientists focus on higher-value fish, such as crabs and mandarin fish, which pollute less but also decrease the number of fish in the lake. And they have added plants to the shoreline that put oxygen back into the water.

Once a year the farmers corral the fish into a corner of the lake and harvest them all together. As in Dalian, there is no need for fertilizers or expensive feed, which increase the nutrient load. And with more room to roam, the fish do not get sick as much. Amazingly, the lower volume does not affect the bottom line.

"The profit is better than what you would get from ponds," says Fu Jun Deng, a manager at one of the two companies that manage the lake. "It's very easy work. Normally all we do is patrol the lake and make sure nobody steals our fish."

Fewer fish, however, will not satisfy rising demand. And the lake is not pristine; it is murky, and a lot of algae still persist. But the water quality has improved. Oxygen is up, nitrogen is down, aquatic plants are flourishing along the shores, and the visibility is slowly getting better.

Similar projects are rehabilitating other large, natural lakes in the area, but they are still dwarfed by the many thousands of smaller ponds—each maybe the size of a football field—blanketing the countryside around them. These family ponds are truly feeding the nation, producing a great deal of food per hectare. Keeping the water clean and the fish healthy in these local operations is a challenge. Thus, in addition to bigger projects, scientists are innovating low-tech ways to raise a healthier, more sustainable product.

Congxin Xie (unrelated to Shouqi Xie), a professor at Huazhong Agricultural University, has been experimenting with so-called floating islands to purify water. Early one morning he drives me to a test pond near the small town of Gong'an. Sprinkled on the water are half a dozen white, plastic frames overflowing with water spinach. The frames look a little like giant,

SCIENTIFIC AMERICAN ONLINE For a slide show of China's fishing operations, see ScientificAmerican.com/apr2015/vance

floating window boxes. Xie has spent years studying how aquatic plants interact with their environment and eventually settled on this species because it grows fast and creates large root networks using massive amounts of nutrients. Xie says that with just a few floating planters in the past three months, the ammonia levels in the water have dropped by one third. (Too much ammonia kills fish.)

"The water quality has gotten better. Clearer," says Yung Chang Xu, one of the fish farmers who operate the ponds. There are "not as many dead fish as last year."

Chang's son takes us out in a wood boat to the pens, and Xie pulls off a few handfuls of spinach. The plastic frames, maybe the size of two or three bathtubs end to end, are not moored to the bottom but float around. The pens cost about $150 to build but pay for themselves in a year if a farmer can sell the spinach as organic produce. At a nearby restaurant, a chef steams the spinach leaves in some kind of salty dressing, adds nuts and serves them alongside several species of freshwater fish. I am still not used to the flavor of carp (or their tiny bones), but the spinach is delicious and is quickly gone.

This mix of products is key, Xie says. Reforms have to benefit both the environment and the farmer, and scientists have to work closely with the locals. The spinach boxes here have satisfied both criteria, and local farmers say they plan to cover at least 5 percent of the ponds with them. Workers along the shorelines are busily building more.

Aquatic plants and animals have become a centerpiece for China's efforts to clean its waters. After the 2007 Wuxi algal bloom, scientists ramped up efforts to incorporate wetlands into fish farming. The Chinese Academy of Sciences began funding multiple projects along the Yangtze using freshwater snails, lotus, and dozens of other plants and animals to battle water pollution.

Ge Hu, a lake just upstream from Tai Hu, for example, no longer hosts fish pens. It is now covered in 2.6 square kilometers of water hyacinths cultivated to fight pollution. Nearby, Wu Jing Aquaculture Farm—a sprawling complex of industrial ponds—dedicates 30 percent of its ponds to a similar form of wetland filtration.

Another series of ponds attached to Luhu Lake in Wuhan once raised heavily polluting carp on its cooperative farm. With an intense 12,000 kilograms of fish harvested annually, farmers could make thousands of dollars per hectare if everything went well. But everything rarely went well. At that density, disease and pollution were rampant. In 2008, with the help of the Chinese Academy of Sciences, the farm added wetlands to the outflow area connected to the main part of the lake. Meanwhile the farmers switched from tightly packed carp to the mandarin fish, which is 10 times less concentrated, more environmentally friendly and commands a higher price.

"It's an experiment every year. We'll [introduce] 50 or 100 of one species [of freshwater fish] and then 100 of another type of species," says Hui Shang Xia, a 50-year-old fish farmer who has worked here for decades. "I've never lost money on a pond, but sometimes I make less."

Other solutions require more creative tinkering. For instance, scientists at the Chinese Academy of Fishery Sciences' Fishery Machinery and Instrument Research Institute in Shanghai have developed a machine to fix a problem common in smaller fishponds. The issue is poor photosynthesis in plants that could filter the nutrients. A lack of phosphorus in the water when the sun is shining limits photosynthesis, yet there is ample phosphorus in sediment at the bottom, says Hao Xu, director of the institute, as he points out across a massive complex of pea-green test ponds. Engineers at the institution have developed a machine powered by solar panels that stirs up the mud along the pond floor. When the sun is bright, it kicks up phosphorus for the plants. When the clouds cover the sun, the machine stops.

A NEED TO SUCCEED

CHINA'S RECENT EXPLOSION of wealth has fueled an appetite for meat protein that might be unprecedented in world history. Conservation efforts in both freshwater and saltwater must, likewise, be massive. The Chinese Academy of Sciences is working with about 30,000 hectares of ponds up and down the Yangtze River Basin. Zhangzidao is the largest ocean farm of its kind in the world, and it and the nearby kelp farm dwarf any other IMTA projects on the planet.

The work borrows many ideas from the U.S. and Europe, but one would be foolish to expect the aquaculture here to look like its Western counterparts. The U.S. and Europe favor cold-water fish such as trout and salmon that require highly oxygenated water. China prefers low-oxygen carp and catfish. Chinese ideas about ecosystem health are also very different. "What we would consider a polluted lake, in the Chinese thinking, is considered efficient food production," says Trond Storebakken, a fisheries expert at Norwegian University of Life Sciences near Oslo. "But an overpolluted lake is a disaster. Managing to keep this good balance—that's what impresses me."

Storebakken has consulted widely with the Chinese Academy of Fishery Sciences. He has traveled around China and has been stunned at how scientists seamlessly replicate natural systems—making use of the roles of predators, herbivores and filter feeders together. He has faith that China, after thousands of years of evolving and shaping its relationship with seafood, is beginning yet another chapter. "It's a completely different thing than what we are doing" in the West, Storebakken says. "They are mastering these challenges. Not to perfection—no way—but much better than anywhere else." SA

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MORE TO EXPLORE

Sustainable Seafood and Integrated Fish Farming in China. Online video. World Wide Fund for Nature International. September 2, 2012. www.youtube.com/watch?v=18xyR8KWrgE#t=220

Rich Countries Pay Zombie Fishing Boats $5 Billion a Year to Plunder the Seas. Gwynn Guilford in Quartz. Published online June 25, 2014. http://qz.com/225432/rich-countries-pay-zombie-fishing-boats-5-billion-a-year-to-plunder-the-seas

Freshwater Aquaculture in PR China: Trends and Prospects. Qidong Wang et al. in *Reviews in Aquaculture.* Published online October 25, 2014.

Draft Intertek Fisheries Certification report on Zhangzidao scallop fishery: www.msc.org/track-a-fishery/fisheries-in-the-program/in-assessment/pacific/zhangzidao-scallop/assessment-downloads-½0141103_PCDR_SCA326.pdf

FROM OUR ARCHIVES

The Blue Food Revolution. Sarah Simpson; February 2011.

scientificamerican.com/magazine/sa

PSYCHOLOGY

conquer yourself, conquer the world

Self-control is not just a puritanical virtue. It is a key psychological trait that breeds success at work and play—and in overcoming life's hardships

By Roy F. Baumeister

The ability to regulate our impulses and desires is indispensable to success in living and working with others. People with good control over their thought processes, emotions and behaviors not only flourish in school and in their jobs but are also healthier, wealthier and more popular. And they have better intimate relationships (as their partners confirm) and are more trusted by others. What is more, they are less likely to go astray by getting arrested, becoming addicted to drugs or experiencing unplanned pregnancies. They even live longer. Brazilian writer Paulo Coelho summed up these benefits in one of his novels: "If you conquer yourself, then you will conquer the world."

IN BRIEF

Thirty years ago psychologists mistakenly regarded cultivation of self-esteem as a panacea for personal problems and social ills.

Self-control, not self-esteem, turned out to be the real deal. The ability to regulate impulses and desires is key to living and working with others.

The dynamics of self-control are, in fact, quite complex. Willpower can be depleted through overuse as if it were a repository of energy.

Research on self-control is now extending in new directions to provide insight into the roots of addiction and how to combat it.

Illustrations by Daniel Stolle

Self-control is another name for changing ourselves—and it is by far the most critical way we have of adapting to our environment. Indeed, the desire to control ourselves and our environment is deeply rooted in the psyche and underlies human engagement in science, politics, business and the arts. Given that most of us lack the kingly power to command others to do our bidding and that we need to enlist the cooperation of others to survive, the ability to restrain aggression, greed and sexual impulses becomes a necessity.

Social psychologists' appreciation of the importance of self-control reflects a shift in perspective. Thirty years ago many of them mistakenly regarded cultivation of self-esteem as a panacea for personal problems and social ills—an honest mistake. High self-esteem is associated with doing well in life, so it was reasonable to assume that a boost would improve people's lives.

When analyzed more closely, the data suggested that self-esteem does not itself lead to success. It is less a cause than an effect. When researchers tracked students over long periods, they found that getting good grades results in better self-esteem later. But having higher self-esteem does not produce stellar report cards. Self-control, however, is the real deal.

Experiments on self-control began in the 1960s with pioneering studies of delaying gratification conducted by Walter Mischel, now at Columbia University. Using a procedure that came to be dubbed the "marshmallow test," he offered children a choice between immediately getting the white, cylindrical candies (or another of their favorite treats) or else receiving a couple of those same sweets if they could only wait for a while. More than a decade after these early experiments were published, Mischel and his colleagues tracked down the children, by then young adults, and did so again as they entered middle age. The ones who had the most success at resisting temptation at age four went on to be the most successful as adults.

Recognizing the requirement of self-control for well-being, I and others have set about probing the psychological and biological processes underlying it. The findings indicate that the act of opting to not express anger or of choosing to forgo a marshmallow is akin to drawing on a store of energy that gets you through mile 26 of a marathon. As with any source of energy, it becomes depleted over time and needs replenishing. What psychologists have learned about self-control in recent studies may even provide new ideas for treating the seemingly intractable challenges of drug and alcohol addictions.

MENTAL MUSCLE BUILDING

I HAVE SPENT a quarter of a century doing laboratory studies on self-control with an endlessly fascinating stream of creative colleagues. Over that time, I have come to the conclusion that self-control, which might also be referred to as self-regulation or willpower, works something like a muscle does. In particular, it seems to "tire" after a workout. Several hundred studies in many labs have now replicated the basic finding that, after exerting willpower, people have less left over to complete a second chore. In one early study, we found that people who called on their self-control to resist chocolates and cookies later showed less fortitude on a difficult problem-solving exercise. They gave up much more easily than people who had not worked their willpower "muscle." In other studies, trying to suppress a forbidden thought—such as being told not to think of a white bear—made participants less able to control subsequent emotional reactions.

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We coined the term "ego depletion" to label the state of diminished willpower that follows from expending psychic energy on self-control, be it resisting temptation or forcing oneself to make tough decisions. The term was chosen as an homage to Sigmund Freud, who proposed that the self consists partly of a well of energy. His vague theories about how this energy worked are now mostly obsolete, but he did recognize that some form of psychic energy explains our behavior. Cast aside for decades, this idea reemerged when our experiments found that self-control operates as a mental muscle of sorts, a muscle in which energy stores get depleted with use.

Two other lines of research have extended the muscle analogy. Experiments by Mark Muraven of the University at Albany and his colleagues have shown that after exertion, willpower has not entirely vanished. Rather the body seems to be conserving energy; if an important challenge or opportunity arises, more self-control can be tapped. This finding parallels what happens with physical muscles. As muscles begin to tire, athletes cut back on exertion to conserve remaining energy and strength. But they can marshal concerted effort if needed, calling on reserves for a sprint to the finish.

Muscles do not just become fatigued; they increase in strength when used regularly. Self-control can also strengthen with practice, as shown when people go through an exercise program to enhance it. In several studies, volunteers were assigned for a two-week period to change how they speak—avoiding curse words, using complete sentences, and saying "yes" and "no" instead of "yeah" or "nope." In another program, subjects were simply asked to improve their posture—sitting or standing up straight. After the exercises were completed, we evaluated the subjects' self-control using lab tests, such as squeezing a handgrip for as long as possible, but without any altering of speech or posture patterns. Those who had practiced the earlier exercises performed significantly better than a control group that had not had to clean up their language or sit up straight.

It has occurred to us from these studies that the Victorian notion of "building character" seems to have some scientific validity. Exerting self-control on a regular basis appears to build up a person's capacity to call on more of this character trait in a pinch.

When we did these studies, we began to ask ourselves whether actual physical energy was getting used up—or whether the notion of energy consumption was just a psychological metaphor. An answer to this question came serendipitously when a failure in one experiment led to a new and useful insight.

Some scientists presumably march from one successful study to another, but I am not one of them. In this case, Matt Gailliot, then a graduate student, wondered whether we could extend the

observation that willpower becomes depleted when someone resists temptation. What about the opposite case? Would indulging in temptation actually strengthen willpower?

I had my doubts, but I encouraged Gailliot to pursue the question, which we informally called the "Mardi Gras theory," in reference to the Christian tradition of indulging in sinful impulses in preparation for a period of self-denial during Lent. First we sapped people's self-control by requiring them to mentally suppress the forbidden thought of a white bear. Then we randomly assigned some of the participants to drink a delicious ice cream milk shake before they took a disguised test of willpower that consisted of searching a matrix of numbers for a particular sequence. In fact, the sequence was not there, and the goal was to see how long people could keep trying before they gave up.

New findings suggest that any brain changes occurring in addicts do not lead to a loss of self-control. People can often choose whether to give in to a craving or resist.

The folks who drank the shake persevered longer on the test than those who got nothing. This apparent victory for the Mardi Gras theory was soon undercut by another result that involved an additional control group. One of the groups, as before, received nothing to drink before the test and, as expected, did badly on that test. The other group drank a milk shake that did not taste good; it contained unsweetened half-and-half rather than ice cream, so it was basically a large, unappetizing glass of dairy glop. Unfortunately for Gailliot's theory, the half-and-half group also did better than the unfed subjects. Gailliot was initially glum because the experiment seemed a bust. But as we talked, another thought occurred to us: If it was not the pleasure of indulgence that restored willpower, could it have been the calories?

We started reading up on glucose, the sugar in the bloodstream that provides energy to bodily tissues, including the brain, the seat of self-control. We ran a large series of studies and came up with two supportive findings that have stood the test of time. One showed that when blood glucose is low, self-control suffers, often substantially. This pattern, by the way, gives credence to the oft-heard complaint that a person is having difficulty functioning because of "low blood sugar"—a conclusion that also jibes with studies from nutritionists.

The other meaningful finding confirmed that a dose of glucose administered just before self-control is beginning to flag helps to restore the needed willpower to press ahead. These results strongly suggest that willpower is, indeed, more than a metaphor. Further, if exerting self-control diminishes willpower and the energy needed to sustain it, then the remaining energy can be conserved by cutting back on further demands for self-control.

A third result did not hold up. We found in one study that blood glucose levels drop during a task that requires self-control. Such a finding would be consistent with the idea that exerting willpower uses up glucose. But we could not replicate the pattern reliably in later tests. Some studies from other labs have shown, however, that the brain uses more glucose when exerting greater effort—which makes sense, after all, given that it is the brain that controls self-restraint.

A CHALLENGE TO OUR IDEAS

LIKE MANY SCIENTIFIC THEORIES, our muscle model of self-control has evolved as other researchers have gotten into the act. Some have tried to build on what we have done, and others have wanted to dismantle or challenge our work. These new findings—and the debates they have engendered—have helped flesh out our understanding of self-control.

One contentious issue has been whether the brain really runs out of fuel for willpower. Like us, other investigators have confirmed that self-control is impaired when blood glucose is low, a physiological state that affects both body and brain. Some researchers have argued that the human body has extensive reserves of glucose that could be drawn on if an amount allotted to willpower got used up.

Compounding the skepticism over our notion of energy depletion, the brain's glucose consumption does not fluctuate much—still, it does change some. In prehistory, people might have faced a threat of running low on glucose, but few in industrial societies need to worry—certainly not the well-fed college students in our experiments who showed signs of ego depletion or impaired self-regulation.

All these points are well taken. It is possible, though, that exercise of self-control does not necessarily lead directly to the exhaustion of glucose and that when the body senses that available glucose is running low, it makes adjustments to direct the sugar to where it is needed most. In that case, we would still be correct in thinking that willpower is a precious resource—one that needs to be conserved. The simplistic view that ego depletion means that the brain exhausts its fuel supplies is not tenable, but it does seem likely that the urge to conserve a partly depleted resource is powerful and pervasive.

Another critique suggests that any willpower deficit can be overcome by just putting people with declining reserves into circumstances that cause them to call up additional resolve. Studies have shown that assigning people to a position of power and leadership—or even paying them to try harder—makes them continue to show good self-control even in situations where their energy should be depleted by prior exertion of willpower.

This research raises the possibility that willpower is all in your head. No resource is actually depleted, but people simply lose motivation to work hard. It can also mean that when willpower declines, you can still exert effective self-control if doing so is critical. Think of the chief executive who feels the responsibilities and pressures of leadership during a corporate crisis.

In a related criticism of our view, Veronika Job, then at Stan-

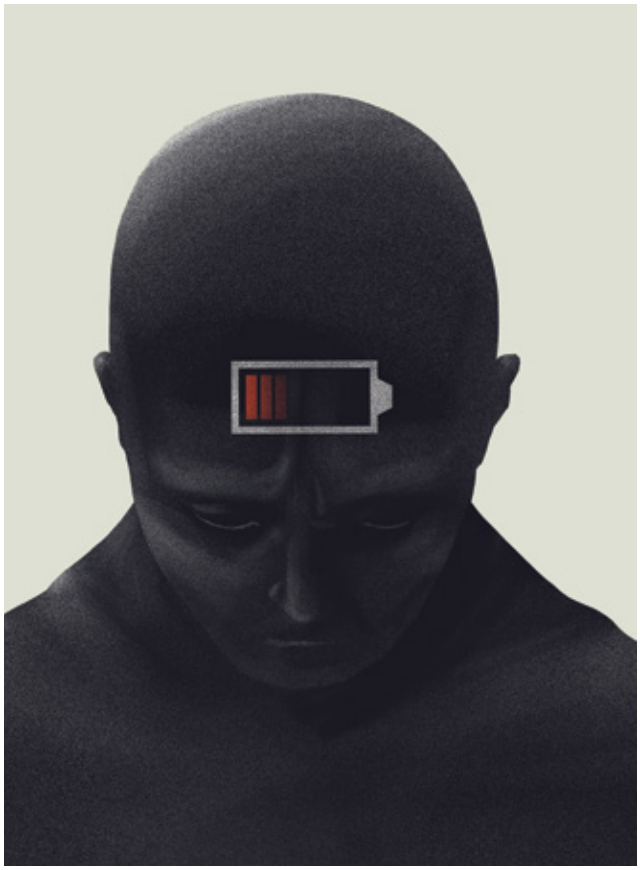
ford University, and her colleagues, including Carol Dweck of Stanford, whose innovative theories they built on, have proposed that willpower is limitless and that a person with sufficient motivation can simply keep going. For these researchers, the idea of ego depletion is an illusion based on a false belief.

Our energy-allocation theory does not entirely disagree with the view that people can draw on spare resources for a time. If your willpower is slightly depleted, your body may naturally seek to conserve what remains—but you can still suck it up and perform well if the situation warrants. Tired athletes conserve their energy for the winnable points and the crucial, decisive moments. Ego-depleted people do the same with willpower.

In our own studies, we have found that people who believe in unlimited willpower tap into existing reserves to increase blood glucose levels when the sugar should have otherwise been depleted. The story, though, grows a little more complicated when examined more closely.

A crucial test came when people were not just slightly depleted but continued exercising self-control until serious fatigue could no longer be ignored. Kathleen Vohs of the University of Minnesota, Sarah Ainsworth (one of my graduate students at Florida State University) and others had shown that cash incentives or leadership responsibilities enable people to sustain self-control even when their willpower is depleted. But these various studies then initiated a grueling series of exercises, which showed that depletion worsened, and self-control started to diminish. Crucially, those who had been led to believe in unlimited willpower actually did worse than others. That belief had been helpful at first, but in the long run it backfired.

Self-control, it seems, can be maintained—but not indefinitely. After all, you do not get an infusion of glucose because you think willpower is unlimited or because you have been promoted to a managerial role. You just become more willing to spend from your reserves. Eventually a limit is reached. The illusion of endless self-control is tantamount to believing that a bank account has infinite funds. At the beginning, you may spend freely, but ultimately you seriously risk running out of money.



CAN YOU WILL AWAY AN ADDICTION?

RECENT STUDIES HAVE REVEALED newly discovered areas in which self-control plays a pivotal role. Some of these findings overturn prevailing ideas about various forms of addiction. A widely held view suggests that cravings for drugs, alcohol or cigarettes take over an addict's life and that quitting is impossible without complex medical treatments or at least a firm commitment to a 12-step-like program. Alan I. Leshner, former director of the National Institute on Drug Abuse and now CEO of the American Association for the Advancement of Science, has asserted that addiction is a "brain disease." As he put it, a user may take a puff or inject a substance voluntarily, but at some point, a switch in the brain is thrown. Substance abuse becomes involuntary, and the compulsion lingers even when the addict earnestly desires to quit. Willpower and volition disappear once addiction takes hold.

New findings indicate, however, that any brain changes occurring in addicts do not lead to a loss of control over one's actions; often these people have the power to choose whether to give in to a craving or resist.

More specifically, addiction does not bring about changes in a brain area essential for self-control that governs movement—that is, the motor cortex, where actions, whether brushing one's teeth or reaching for a crack pipe, are initiated. As addiction grows, the decision to grab the pipe does not suddenly become involuntary. Instead addiction brings on a slow and insidious change in desire. Heroin or cigarettes evoke pleasant feelings that develop into a longing for these substances.

The addict can resist for a time but gives in at some point, perhaps sooner rather than later, and must thwart the desire again and again. The desire is not always overwhelming, however. In a study by Wilhelm Hofmann, now at the University of Cologne in Germany, people were contacted at random throughout the week and asked to report on any desires that came to mind. Yearnings for cigarettes or alcohol were rated as weaker than any others.

This and other findings indicate that the addict experiences an intermittent stream of one mild urge after another. The frequently recurring nature of these urges is what makes quitting a challenge. But the addict is not beset by the mythically insurmountable difficulty of resisting an overwhelming desire.

The controversy about whether addicts are still in control will likely persist. Arguments from politicians, drug counselors and others help to sustain the myth that addiction is rooted in overwhelming, uncontrollable urges. Many addicts themselves favor this viewpoint because it exonerates them from personal responsibility. The media often promulgate these arguments, perhaps because actors and other celebrities who develop an addiction want to retain the love and loyalty of their fan base, an easier task if they can attribute their drug use to external demons and uncontrollable psychological drives. Fans might not be so forgiv-

SCIENTIFIC AMERICAN ONLINE Watch a video of Baumeister discussing his work at ScientificAmerican.com/apr2015/willpower

ing if celebrities just admitted that they simply like taking drugs.

Psychologists differ as to whether self-control can be an effective antiaddiction medicine. A survey in the U.K. found that addiction-treatment counselors who worked as volunteers tended to think that addicts can regulate their impulses. But those who received compensation for their work preferred to think that addicts are helpless and cannot get better without expert help. This argument is not intended to suggest that clinicians are in it only for the money. But when a controversy arises, financial incentives probably make it easier for people to endorse evidence that goes along with their own interests and to spot flaws in counterarguments.

Another addiction myth holds that cravings grow more acute only when quitting an addictive substance. A clever study by Michael Sayette of the University of Pittsburgh and his colleagues demonstrated that smokers believed that their desire would increase steadily over time, especially if they were told they could not light up.

The study also showed that these beliefs were wrong. Some participants had to abstain for a time and report their desire to smoke as part of the study protocol. Instead of the desire for a cigarette rising steadily, it went up and down unpredictably. Other studies have found that when a smoker quits, the desire to smoke goes down immediately and mostly stays in abeyance. If the addict relapses, as happens frequently, it is not because of an overwhelmingly strong urge for a cigarette. Rather it stems from a rather weak urge to light up at a moment when the smoker's willpower happens to have reached a nadir.

ADDICTION IS FOR THE STRONG-WILLED

THE IDEA THAT QUITTING an addiction requires willpower makes sense to most people. But until recently, few have considered that starting a drug habit and staying addicted also require self-control. Most of us do not really like the first taste of beer or the first puff of a cigarette. Public health warnings about their dangers can also dissuade indulging for the first time. Willpower, in fact, is needed to overcome those negative influences and take the first steps on the path toward addiction. To sustain an addiction over a long period, a user must expend a substantial amount of energy to ensure that a habit does not interfere with work, family and relationships.

Consider smoking. So many restrictions exist today that smokers need to craft elaborate plans to sneak a cigarette. When my former university introduced rules prohibiting professors from smoking in their offices, one colleague struggled heroically to comply. I will not soon forget the sight of her heading out of the building into a Cleveland snowstorm, while holding her tiny baby in her arms, on the way to light up.

Just think about how much self-control she had to muster. First, she had to plan when she would find breaks between classes, appointments and meetings—and where she would go to not violate campus smoking restrictions. Then she had to dress herself and the baby warmly. She also had to remember her cigarette pack and lighter on the way out into the storm.

A study on smoking conducted in the Netherlands by Michael Daly of the University of Stirling in Scotland, myself and our colleagues lends some credence to the anecdotal observation that maintaining an addiction requires good self-control. Daly's group found that a Dutch workplace ban that began in 2004 reduced smoking but with a couple of important qualifications. The ban lowered smoking mainly among people who rated themselves lower on a survey of self-discipline, and this group returned to its old habits within a few years. There was no apparent effect on people scoring high in self-discipline.

Scientists who favor the view that addicts have little self-control might have expected a different initial outcome—high self-control types would alter their behavior in response to the ban, whereas poor self-regulators would keep right on smoking. And they might explain the fact that we found the opposite result by reasoning that people with low self-control needed the strong push from the law to get them over the hump—and interpret the subsequent relapse by suggesting that over time the threat of a legal cudgel somehow faded.

But the explanation for the results appears to be related to the addicts' need to draw on reserves of willpower to preserve their habit. For years people had comfortably smoked right at their desks. Suddenly, that option was gone. To continue their habit after the ban, smokers had to make elaborate adjustments. Each break had to be arranged carefully to plan where and when it could happen.

People with good self-control could handle these demands. But those with low self-control gave up and quit for a while. Over time, however, they noticed the coping strategies of the self-controlling smokers. They saw, for instance, that these diehards headed outside to a particular "smoker's spot" in the park. They then simply copied those strategies.

A number of studies have shown that addicts seem able to consistently plan and execute intricate strategies to maintain heroin or cigarette habits—habits that researchers, clinicians and even users themselves once thought to be unshakable. These findings provide a new perspective on addiction. The possibility exists that these groups may be able to redirect the same sustained willfulness they use to procure a drink or fix toward kicking their habits. But this idea also raises a new set of issues.

A therapist may have difficulty convincing an addict that he or she has taken the wrong path if that person sees nothing permanently damaging with having a few drinks or popping painkillers while continuing to fulfill responsibilities at home and work. This new insight into the nature of addiction provides further evidence of the extent that self-control can influence our behaviors in myriad ways—and how it may even, perhaps counterintuitively, enable us to persist in adhering to self-destructive habits. It demonstrates, once again, that our ability to control our emotions and desires lets us manage, for good or bad, the endless challenge of adapting to the world around us. SA

MORE TO EXPLORE

The Strength Model of Self Control. Roy F. Baumeister et. al. in *Current Directions in Psychological Science*, Vol. 16, No. 6, pages 351–355; December 2007.

Willpower: Rediscovering the Greatest Human Strength. Roy F. Baumeister and John Tierney. Penguin Press, 2011.

Uses of Self-Restraint to Facilitate and Restrain Addictive Behavior. Roy F. Baumeister and Andrew J. Vonasch in *Addictive Behaviors* (in press).

FROM OUR ARCHIVES

Exploding the Self-Esteem Myth. Roy F. Baumeister, Jennifer D. Campbell, Joachim I. Krueger and Kathleen D. Vohs; January 2005.

scientificamerican.com/magazine/sa

SECURITY

HOW TO SURVIVE CYBER

STEP ONE: Stop counting on others to protect you

By Keren Elazari

CYBERSECURITY PEOPLE LIKE TO SAY THAT THERE ARE TWO TYPES of organizations—those that have been hit and those that do not know it yet. Recent headlines should prove that this joke is largely true. Cybercriminals stole the credit-card information and personal data of millions of people from companies that included Target, Home Depot and JPMorgan Chase. Security researchers discovered fundamental flaws in Internet building blocks, such as the so-called Heartbleed vulnerability in the popular OpenSSL cryptographic software library. A massive data-destruction attack sent Sony Pictures Entertainment back to using pen and paper. Criminals accessed the data of more than 80 million customers of health insurance giant Anthem. And these are just the incidents we know about.

In the coming years, cyberattacks will almost certainly intensify, and that is a problem for all of us. Now that everyone is connected in some way to cyberspace—through our phones, our laptops, our corporate networks—we are all vulnerable. Hacked networks, servers, personal computers and online accounts are a basic resource for cybercriminals and government snoops alike. Your corporate network or personal gaming PC can easily become another tool in the arsenal of criminals—or taxpayer-sponsored cyberspies. Compromised computers can be used as stepping-stones for the next attack or become part of a "botnet," a malicious network of controlled zombie devices rented out by the hour to launch denial-of-service attacks or distribute spam.

In response to threats such as these, the natural reflex of

IN BRIEF

Cyberattacks will become more common in the years ahead. That is not just a problem for big companies and governments: every person who uses modern technology is a target.

At risk is not abstract data or "secrets." Cybersecurity is now about protecting things, infrastructures and processes—the technologies that underpin modern life.

Governments and tech companies cannot secure cyberspace alone. It will take a distributed immune system—one that includes hackers—to do the job.

Individuals also have a role to play. Every network-connected person needs to support the collective immune system by practicing the cyberequivalent of personal hygiene.

Keren Elazari, an Israeli cybersecurity expert, has worked with leading security firms, government organizations and Fortune 500 companies. Her TED talk on hackers has been viewed more than 1.2 million times, translated into 24 languages and selected for TED's list of "most powerful ideas."

governments in the U.S. and elsewhere is to militarize cyberspace, to attempt to police the digital world using centralized bureaucracies and secret agencies. But this approach will never work. In fact, for reasons we will get to shortly, it might just make things worse. Cybersecurity is like a public health problem. Government agencies such as the Centers for Disease Control and Prevention have important roles to play, but they cannot stop the spread of diseases on their own. They can only do their job if citizens do theirs.

THE VASTNESS OF CYBERSPACE

PART OF THE CHALLENGE of protecting cyberspace is that there is no single "cyberspace." It is a vast, interconnected system of systems, and it is changing and growing all the time. To appreciate this fact, we must go back half a century, to the work of Norbert Wiener, a professor of mathematics at the Massachusetts Institute of Technology. In 1948 Wiener borrowed from the ancient Greeks to describe a new scientific discipline he was developing: cybernetics, which he defined as the study of "control and communication in the animal and the machine." In the original Greek, *kybernētēs* was the title for the steersman or the pilot directing and controlling naval vessels sailing in the Mediterranean. By analogy, cyberspace should be understood as the collection of interconnected electronic and digital technologies that enable control and communications of all systems underpinning modern life. Cyberspace consists of a huge spectrum of remote control and communications technologies: from radio-enabled embedded insulin pumps to GPS satellites.

Cyberspace is not a public commons; it is not like international waters or the moon. It is not a collection of territories that governments or militaries could effectively control—even if we were to ask them to. Most of the technologies and networks that make up cyberspace are owned and maintained by multinational, for-profit conglomerates.

The number and variety of technologies included in this space are growing rapidly. Networking technology vendor Cisco Systems forecasts that by 2020, 50 billion devices will be connected to the Internet, including a large proportion of industrial-, military- and aerospace-related devices and systems. Each new thing that connects to cyberspace is a potential target for a cyberattack, and attackers are good at finding the weakest links in any network. The hackers who breached Target's point-of-sale system and stole millions of payment cards, for example, gained access to the retailer's network by first hacking into an easier target: Fazio Mechanical Services, the refrigeration maintenance company that runs Target's heating and cooling systems. The Chinese spies

who allegedly gained access to the networks of defense company Lockheed Martin in 2011 did so by first hacking into security company RSA, which provided Lockheed Martin with its security tokens. RSA itself was compromised only because an employee at its parent corporation, EMC, opened an innocuous-looking Excel file attachment in an e-mail.

The "things" of the Internet of Things are not just windows that attackers can sneak through: they are themselves targets for potential sabotage. As early as 2008, security researchers demonstrated that they could remotely hack into embedded pacemakers. Since then, hackers have shown that they can hijack implanted insulin pumps using radio signals, instructing the devices to dump insulin into patients' bloodstream, with potentially lethal results.

Physical infrastructure is also at risk of attack, as we learned in 2010, when the infamous computer virus Stuxnet was found to be responsible for widespread destruction of uranium-enrichment centrifuges inside a clandestine facility in Natanz, Iran. Stuxnet, allegedly the fruit of an intensive and costly collaboration between the U.S. and Israel, made a historic point: digital computer code can disrupt and destroy analog, physical systems. Other attacks have since reinforced the point. Last December, Germany's Federal Office for Information Security reported that hackers had disrupted systems in a steel mill, preventing the blast furnace from shutting down and causing "massive damage to the system." Three months earlier Chinese hackers attacked the U.S. National Oceanic and Atmospheric Administration Web sites that process data from satellites used for aviation, disaster response and other critical duties.

What this means is that cybersecurity is not just about securing computers, networks or Web servers. It is certainly not just about securing "secrets" (as if there is much Google and Facebook do not already know about us). The real battle in cyberspace is about protecting things, infrastructures and processes. The danger is the subversion and sabotage of the technologies we rely on every day. Our cars, ATMs and medical devices. Our electric grids, communications satellites and telephone networks. Cybersecurity is about protecting our way of life.

THE ROLE OF GOVERNMENT

GOVERNMENTS FACE DEEP CONFLICTS when it comes to securing cyberspace. Many federal agencies, including the Department of Homeland Security in the U.S., have an earnest interest in protecting national companies and citizens from cyberattacks. Yet other government entities can benefit from keeping the world's networks riddled with vulnerabilities. Clandestine groups such as the National Security Agency invest millions in finding and curating technical flaws that could allow an attacker to take control of a system.

One person's terrifying security vulnerability is another's secret weapon. Consider the Heartbleed bug. If you have used the Internet in the past five years, your information has probably been encrypted and decrypted by computers running OpenSSL software. SSL is the basic technology behind those "lock" icons we have grown to expect on secure Web sites. Heartbleed was the result of a basic software development error in one of OpenSSL's popular extensions, "Heartbeat," hence the name. When exploited, the bug gave eavesdroppers easy access to cryptographic keys, usernames and passwords, rendering moot any security offered by SSL encryption. OpenSSL was vulnerable for two years before two separate teams of security researchers (one headed by Neel Mehta, a security expert at Google, and the other at Codenomicon, headquartered in Finland) discovered the bug. A few days later *Bloomberg Businessweek* cited anonymous sources claiming the NSA had been using the flaw to conduct cyberespionage for years.

Many of the world's leading powers have devoted their best tech talent and millions of dollars to finding and exploiting vulnerabilities such as Heartbleed. Governments also buy bugs on the open market, helping to sustain the trade in security flaws. A growing number of companies such as Vupen Security, a French firm, and Austin-based Exodus Intelligence specialize in the discovery and packaging of these precious bugs. In fact, some governments spend more money on researching and developing offensive cybercapabilities than they do on defensive cyberresearch. The Pentagon employs legions of vulnerability researchers, and the NSA reportedly spends two and a half times more money on offensive cyberresearch than on defense.

Illustration by Justin Renteria

None of this is to say that governments are nefarious or that they are the enemies of cybersecurity. It is easy to see where agencies such as the NSA are coming from. Their job is to gather intelligence to prevent terrible acts; it makes sense that they would use any tool at their disposal to make that happen. Yet an important step in securing cyberspace is to honestly weigh the costs and benefits of government agencies cultivating vulnerabilities. Another key is to take full advantage of those things that governments can do and other organizations cannot. For example, they can enable or even compel companies and other organizations to share information about cyberattacks.

Banks in particular would benefit from sharing information about cyberattacks because attacks on financial institutions usually follow a predictable pattern: once criminals find something that works on one bank, they try it on another bank and then another. Yet banks traditionally avoid disclosing information about attacks because it raises questions about their security. They also avoid talking to competitors; in some cases, antitrust laws prohibit them from doing so. Governments, however, can facilitate information sharing among banks. This is already happening in the U.S. in the form of the Financial Services Information Sharing and Analysis Center (FS-ISAC), which also serves global financial organizations. And in February, President Barack Obama signed an executive order that urged other companies to share similar information with one another and the government.

HACKERS CAN HELP

AS LONG AS HUMANS WRITE CODE, vulnerabilities will exist. Driven by increasingly intense market pressures, technology companies push new products to market faster than ever before. These companies would be wise to tap into the vast human resource that is the global hacker community. In the past year, catalyzed by events such as the Edward Snowden NSA revelations, the technology industry and hacking community have become open to working together. Hundreds of companies now see the value of engaging hackers through so-called bug bounties and vulnerability reward programs, which offer incentives to independent researchers who report vulnerabilities and security problems. Netscape Communications created the first bug bounty program in 1995 as a way to find flaws in the Netscape Navigator Web browser. Today, 20 years later, research has shown that the strategy is one of the more cost-effective measures the organization and its successor, Mozilla, have taken to bolster security. Private and public communities of security professionals share information about malware, threats and vulnerabilities to create a kind of distributed immune system.

As cyberspace expands, car manufacturers, medical device companies, home-entertainment-system providers and other businesses will have to start thinking like cybersecurity firms. That involves baking security into the research and development process—investing in the security of products and services in the design phase, not as an afterthought or in response to government mandates. Here, too, the hacker community can help. In 2013, for example, security experts Joshua Corman and Nicholas Percoco launched a movement called "I Am the Cavalry," urging hackers to conduct responsible security research that makes a difference in the world, with an emphasis on critical areas such as public infrastructures and automotive, medical device and connected home technologies. Another initiative, started by prominent security researchers Mark Stanislav and Zach Lanier, is called "BuildItSecure.ly" and aims to create a platform for developing secure Internet of Things applications.

The good news is that this distributed immune system is growing stronger. In January, Google launched a new program that complements its bug bounty program, offering grants to encourage security researchers to scrutinize the company's products. The program is an admission that even companies with the best in-house tech talent on the planet could use the outside perspective of friendly hackers. Some governments are even onboard. For example, the Dutch National Cyber Security Center established its own responsible disclosure program, allowing hackers to report vulnerabilities with no risk of legal reprisals.

The bad news is that some elements of the cybersecurity approach the Obama administration is pursuing could effectively criminalize common vulnerability research practices and tools, weakening this developing immune system. Many in the security community fear that both the current version of the Computer Fraud and Abuse Act and proposed changes to the law define hacking so expansively that even clicking on a link to a Web site containing leaked or stolen information could be considered trafficking in stolen goods. Criminalizing the work of independent security researchers would harm us all and have little effect on criminals motivated by profit or ideology.

INDIVIDUAL RESPONSIBILITY

THE NEXT FEW YEARS could be messy. We will see more data breaches, and we will almost certainly see a vigorous debate about how much control over the digital realm we should cede to governments in return for security. The truth is that securing cyberspace will require solutions from many realms: technical, legal, economic and political. It is also up to us, the general public. As consumers, we should demand that companies make their products more secure. As citizens, we should hold our governments accountable when they intentionally weaken security. And as individual points of potential failure, we have a responsibility to secure our own stuff.

Defending ourselves involves simple steps such as keeping our software up-to-date, using secure Web browsers, and enabling two-factor authentication on our e-mail and social-media accounts. But it also involves being aware that each of our devices is a node in a much larger system and that the little choices we make can have wide-ranging effects. Again, cybersecurity is just like public health. Wash your hands and get vaccinated, and you can avoid spreading the disease further. SA

MORE TO EXPLORE

War and Anti-War: Survival at the Dawn of the 21st Century. Alvin and Heidi Toffler. Little, Brown, 1993.

A Fierce Domain: Conflict in Cyberspace, 1986 to 2012. Edited by Jason Healey. Cyber Conflict Studies Association, 2013.

Countdown to Zero Day: Stuxnet and the Launch of the World's First Digital Weapon. Kim Zetter. Crown, 2014.

TED's Who Are the Hackers? playlist: www.ted.com/playlists/10/who_are_the_hackers

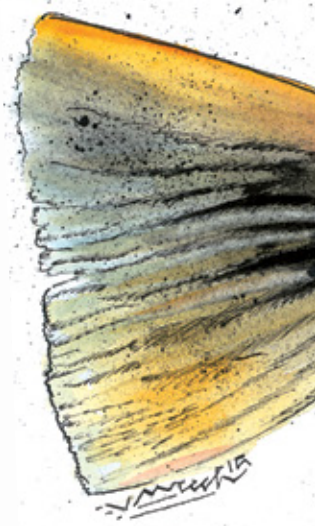
FROM OUR ARCHIVES

Industry Roundtable: Improving Online Security. September 2008.

scientificamerican.com/magazine/sa

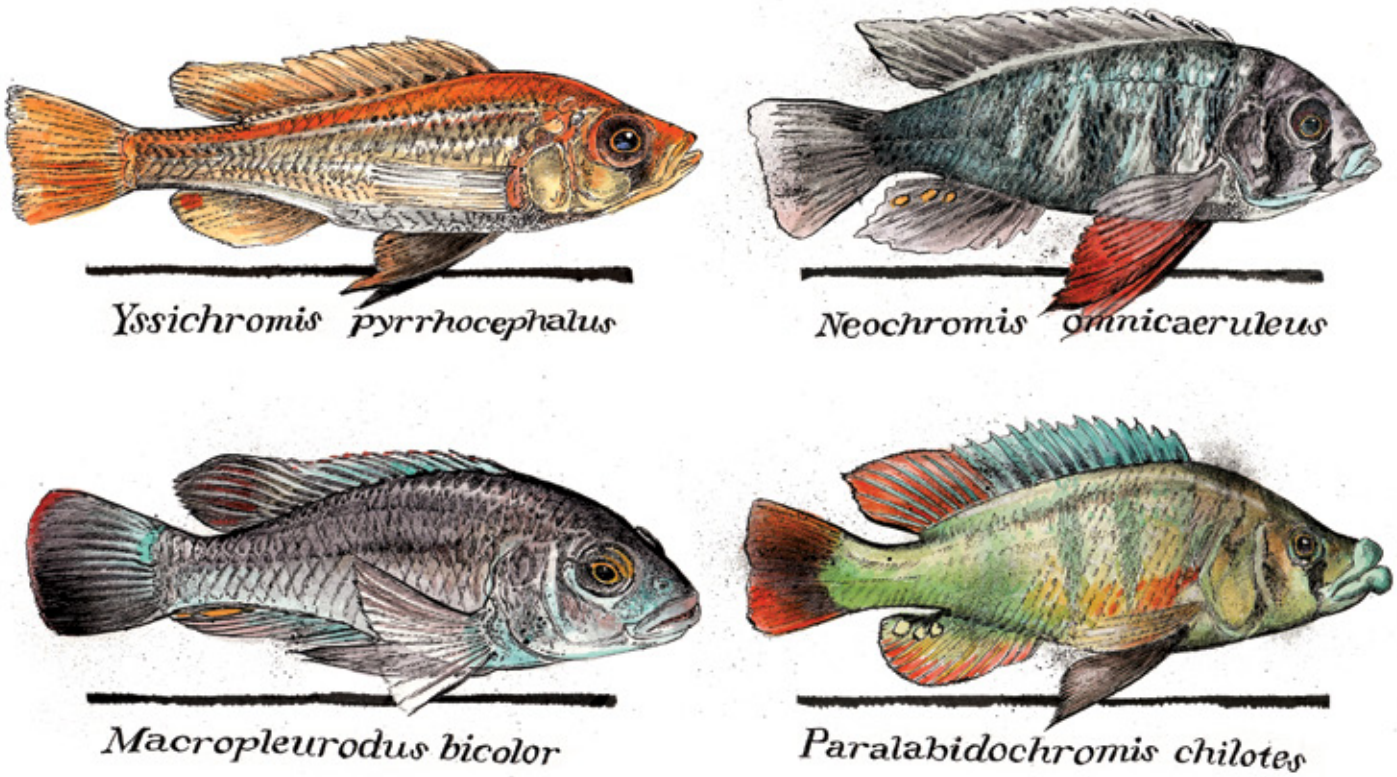
LIFE SCIENCE

EXTREME EVOLUTION



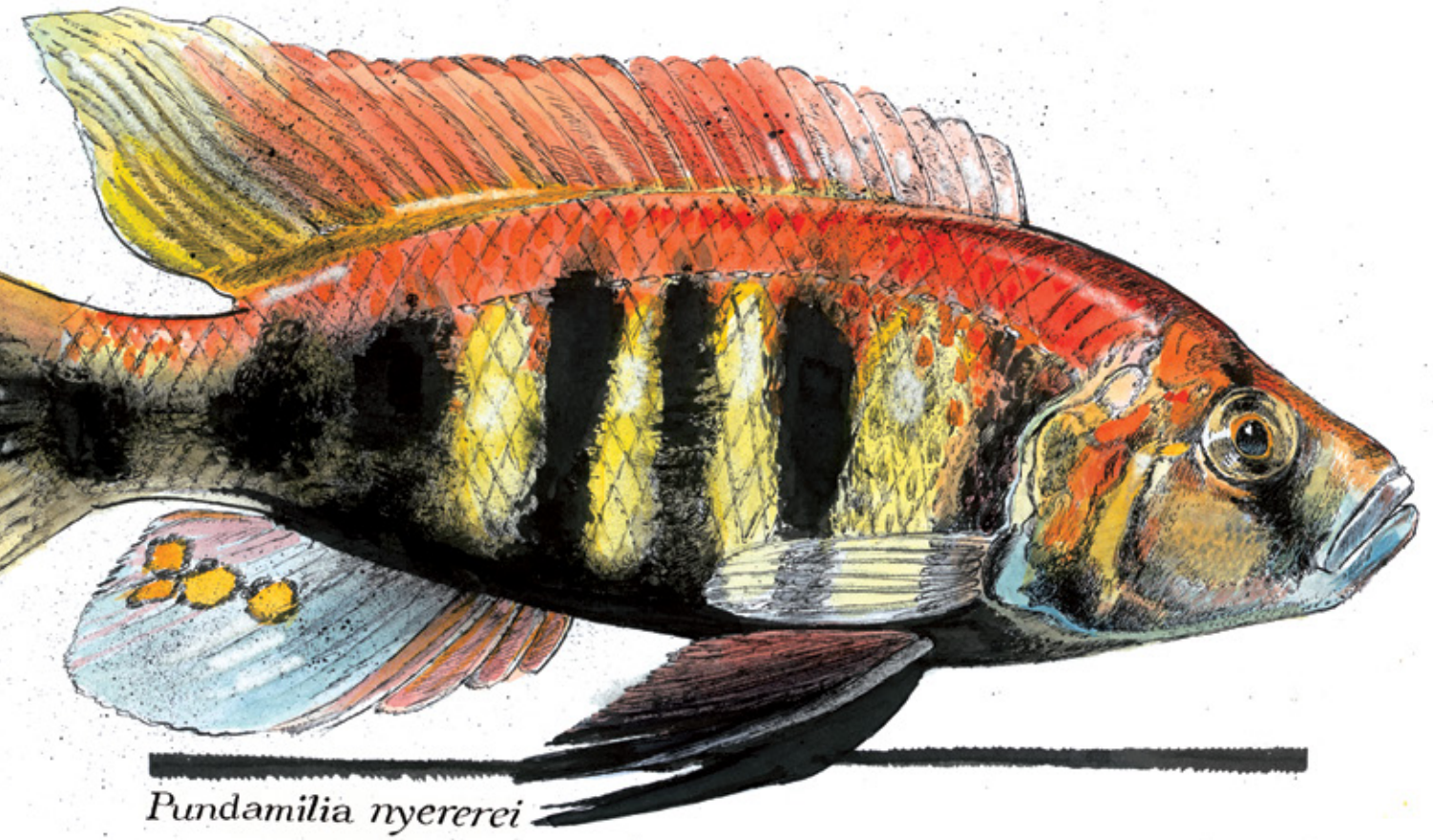
Cichlid fishes have undergone a mind-boggling degree of speciation. New research is revealing features of their genomes that primed them to diversify so spectacularly

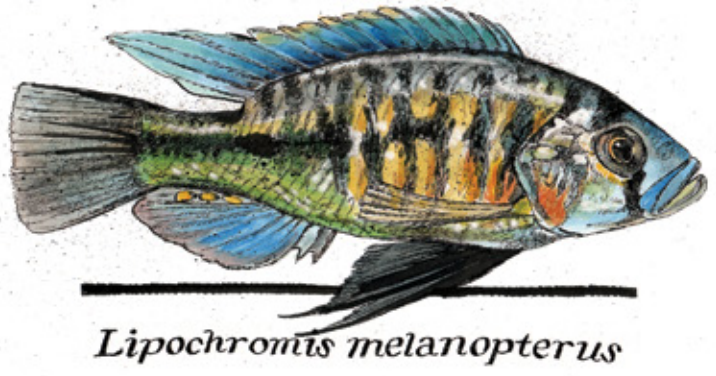
By Axel Meyer

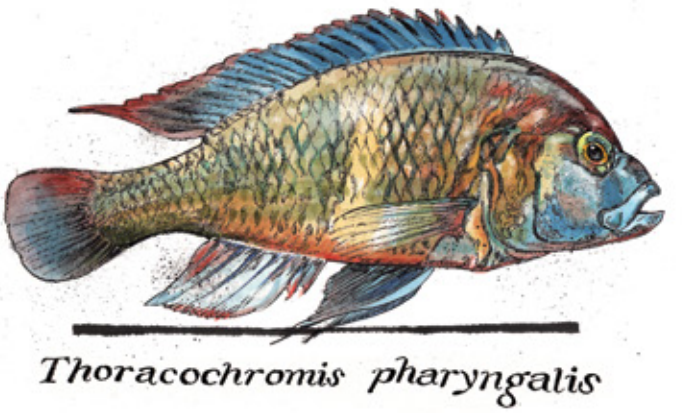


ASTONISHING VARIETY of cichlid fishes live in East Africa's Lake Victoria. The 500 or so species, representative examples of

Illustrations by Jack Unruh







which are shown here, are thought to have evolved within the past 15,000 years—a remarkably short period.

Axel Meyer is a professor of zoology and evolutionary biology at the University of Konstanz in Germany. His research focuses on the origins of adaptations and biodiversity at both the molecular and organismal levels. He was among the first scientists to use DNA sequences to study species differences and speciation.

AFRICA'S LAKE VICTORIA IS HOME TO ONE OF EVOLUTION'S GREATEST EXPERIMENTS. IN its waters, what began as a single lineage belonging to the cichlid family of fishes has since given rise to a dazzling array of forms. Like Charles Darwin's famous finches, which evolved a wide range of beak shapes and sizes to exploit the different foods available in the Galápagos Islands, these cichlids represent a textbook example of what biologists term an adaptive radiation—the phenomenon whereby one lineage spawns numerous species that evolve specializations to an array of ecological roles. But the Lake Victoria cichlids far surpass Darwin's finches in the astonishing speed with which they diversified: the more than 500 species that live there and only there today all evolved within the past 15,000 to 10,000 years—an eyeblink in geologic terms—compared with the 14 finch species that evolved over several million years.

Lake Victoria is not the only locale cichlids call home. Other tropical freshwater lakes and rivers in Africa, as well as the Americas and the tip of the Indian subcontinent, harbor their own cichlids. All told, the family is estimated to comprise more than 2,500 species. Some, such as the tilapias, are farmed for food and are among the most important aquaculture species in the world. Most, like the oscars and angelfish, are popular with aquarium enthusiasts because they are beautiful and have many interesting courtship and parenting behaviors. Many species have yet to be formally described. The cichlids share their lakes with other families of fishes, but only cichlids have managed to speciate so extensively and so fast. Indeed, no other group of vertebrate animals can rival the cichlids in terms of sheer number of species and variety of body shape, coloration and behavior. At the same time, however, evolution has often repeated itself in these fishes: a number of the same adaptations have evolved in parallel in the separate cichlid lineages—a curious trend.

I and other scientists have long marveled at the manifold forms of cichlids and wondered what factors allowed this group to differentiate in such spectacular fashion. Recent advances in genome-sequencing technology have allowed us to comb their DNA for clues to this evolutionary exuberance. We have not solved the full puzzle of cichlid diversity yet—far from it. But we have found some special characteristics of cichlid genomes that might have primed them to diversify with such speed yet also to evolve certain traits again and again. As we explore the genetic underpinnings of the extraordinary success of this group of fishes, we are glimpsing the very cogs and wheels of evolution—insights that will help researchers decode the origins of all manner of species.

DIFFERENT BUT THE SAME

TO GET A CLEARER PICTURE of just how amazingly diverse cichlids are, consider the forms in Lake Victoria and the two other lakes in which the major East African cichlid radiations occurred: Lake Malawi, which harbors perhaps 800 to 1,000 species, and Lake Tanganyika, with its roughly 250 species from older cichlid lineages, one of which colonized the other two younger lakes and spawned the radiations there. These cichlids display every rainbow hue and range from about an inch to three feet in length. And they have evolved adaptations to eating every conceivable food source in their environment. Algae scrapers have flat teeth like human incisors that allow them to nibble the nutritious growths on rock surfaces; insect eaters have long, pointy teeth that help them to get into rock crevices; ambush predators possess huge extendable jaws with which they can suck in their unsuspecting prey in a matter of milliseconds. Those are just some of the broader categories of specialization. Among the algae scrapers, for instance, some species are adapted to foraging in the wave-break zone, others to harvesting food from one particular pile of rocks and no other, and still others to feeding on certain angles from the rocks or only on specific types of algae.

And yet for all the variety seen in the East African cichlids, some highly specialized traits have evolved repeatedly—to a surprising degree. For instance, several species of cichlids in all three

IN BRIEF

Cichlid fishes are the most diverse family of vertebrate animals on record, with more than 2,500 species.

The recent sequencing of several cichlid genomes has begun to furnish clues to their astounding diversification.

Cichlid genomes exhibit a number of special features that may have accelerated the evolution of this group.

Other genome traits may explain cichlids' tendency to independently evolve the same adaptations repeatedly.

PAGE 70: ISTOCKPHOTO (tack and card)

lakes feed almost exclusively on the scales of other fishes. They have all developed the same distinctive rakelike teeth that allow them to hold on to the scales of their victims. But their teeth are not the only adaptation to this diet. Their jaws have evolved to be asymmetrical, opening either to the left or to the right, but not both, so as to better grab the scales from a given side of their targets. "Left-headed" cichlids rasp the scales from the right side of their victim; "right-headed" ones scrape from the left. (Natural selection has kept these asymmetrical forms in balance: about half of the scale eaters that my colleagues and I collected around Lake Tanganyika were right-headed, and the other half were left-headed.) The scale eaters have a very particular set of adaptations to their way of life, but somehow these same traits have arisen at least three separate times in these East African lakes.

Another distinctive adaptation that has emerged independently multiple times is enlarged lips in species that target prey found in rock crevices. My colleagues and I have shown that these "Angelina Jolie" lips act as seals and bumpers that help the fishes suck prey out from their hiding spots. (Cichlids lacking such lips cannot reach prey efficiently in narrow crevices.) Remarkably, species in all three African radiations, as well as two New World radiations, have developed this trait in parallel.

Similarly, distinctive coloration patterns have evolved independently in several separate cichlid lineages. Whereas the vast majority of cichlids sport dark, vertical stripes that presumably camouflage them from predators, a handful of species from each of the three East African lakes also evolved horizontal stripes. This strikingly different patterning occurs mostly in open-water species that tend to be fast swimmers and predators, possibly because the horizontal stripes help to obscure their body shapes from watchful prey.

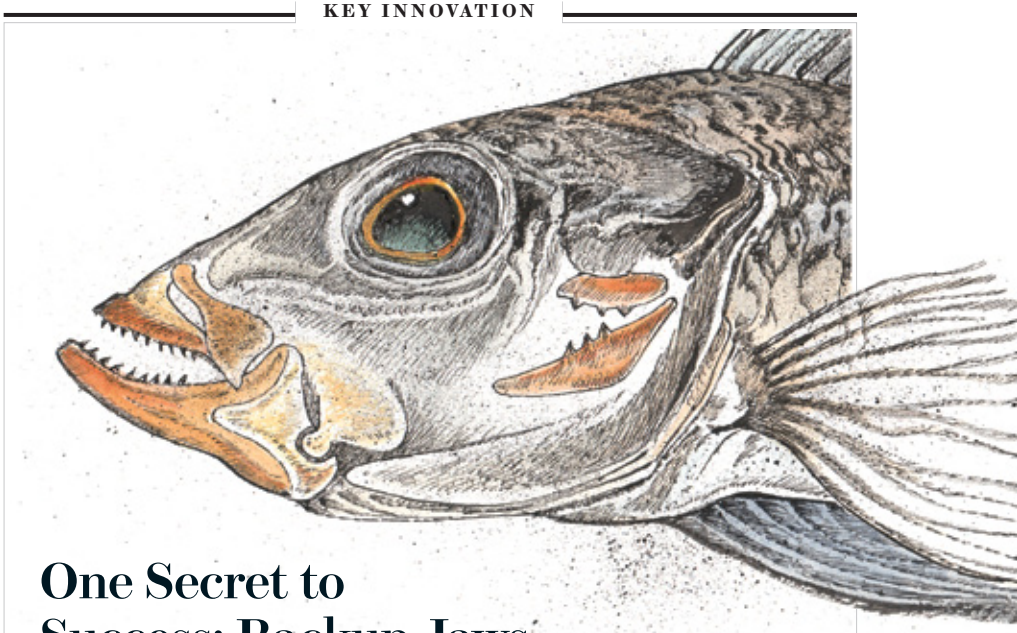
ENGINES OF INNOVATION

THE SEEMINGLY CONTRADICTORY THEMES of extreme diversification and repeated parallel evolution of ultraspecialized adaptations in cichlid evolution raise several key questions. One begins with the highly specialized eaters and the observation that, ordinarily, adapting to a narrow diet means that if something goes wrong with the needed food source, the specialist is in trouble. So how have the cichlids managed to avoid falling into that trap? One answer seems to be a strange anatomical feature that cichlids alone possess among freshwater fishes. All cichlids have a normal pair of mouth jaws and a second pair of jaws located in the throat, like the monster in the movie *Alien*. Any food they eat gets grabbed and processed first by the mouth jaws and second by the throat jaws. As a result, cichlids can have mouth jaws adapted to one kind of food, and their throat jaws can break down other stuff. In this novel way, many cichlids have become jacks-of-all-trades, masters-of-one. In other words, they can evolve a specialization but remain generalists at the same time in case their preferred food runs out or a better option becomes available.

The throat jaws explain how cichlids have been able to mitigate the risk of specializing, but what was the source of all the evolutionary novelty in these fishes? What were the factors that spurred the genes that encode their traits to change so rapidly, and how did the same adaptations keep turning up in separate lineages? Recently, thanks to the advent of fast genome-sequencing methods for health research, my colleagues and I—a consortium of more than 70 researchers from laboratories around the world, led by the Broad Institute in Cambridge, Mass.—have begun making inroads into answering these questions and solving the riddle of the cichlid family's stunning success. Last year, for the first time, we decoded the sequence of DNA code letters in cichlid genomes. We obtained complete sequences for five African species and partial sequences for 60 individuals representing six very closely related species from Lake Victoria alone. By comparing these genomes with one another and with those of the cichlids' relatives, the sticklebacks—a far less diverse family of fishes—we have been able to identify features of cichlid genomes that help to explain the group's diversity.

Among the first things the Cichlid Genome Consortium looked for in these genomes were mutations that have produced changes in the amino acids that make up proteins; proteins do much of the work in cells, and many genes specify the sequence of amino acids that get strung together to generate a given protein. An overabundance of proteins containing altered amino acids would suggest that the genes harboring the underlying mutations were

KEY INNOVATION



One Secret to Success: Backup Jaws

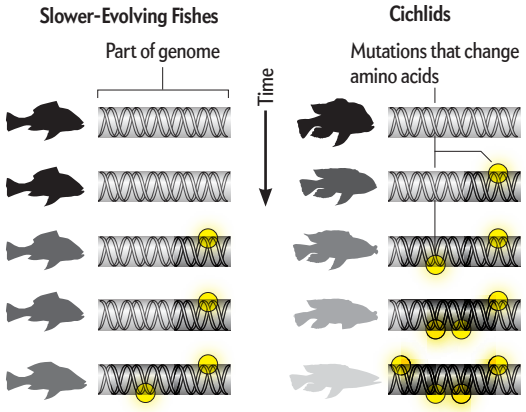
All cichlids have the usual mouth jaws, but they also possess a second set of jaws located in the throat. The food they eat gets broken down by both sets of jaws. This duplication leaves the mouth jaws free to evolve adaptations to particular kinds of sustenance—from algae to the scales of other fishes—without risk of a species becoming dangerously dependent on any given food source that could run out.

Genome Clues

The recent sequencing and analysis of genomes from African cichlids has revealed a number of mechanisms that may have spurred cichlids to quickly diversify into myriad forms. Some of these mechanisms could also help explain another mysterious aspect of this group of fishes: namely the extreme degree of parallel evolution, in which the same highly specialized traits emerged again and again.

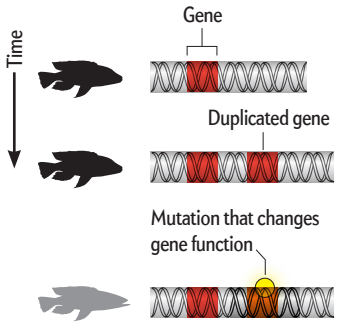
Abundant Mutations

A surfeit of mutations that produced changes in the amino acids that make up proteins suggests the genes harboring these mutations were under intense selection pressure to evolve quickly.



Gene Duplication

Cichlid genomes exhibit a high rate of gene duplication, in which errors in DNA replication produce multiple copies of genes. The extra copies can change in function without harming the fishes and can thus help them adapt to their environment.



under strong selection pressure to evolve quickly; that is, conditions were such that fishes that acquired certain amino acid changes thereby gained a strong survival or reproductive advantage. We found that even the tilapia species we sequenced, which is an evolutionarily unremarkable cichlid compared with its brethren, had more such mutations than the sticklebacks. And the cichlids from the hyperdiverse groups in Lake Malawi and Lake Victoria had mutation rates several times higher than the tilapia's. Many of the affected genes are known to be involved in jaw development, which makes sense, given the range of dietary adaptations seen in cichlids. Thus, one mechanism that has hastened cichlid speciation is intense selection pressure acting on many genes.

But individual genes can have great power, too. My laboratory has found evidence that a single gene determines the orientation of the stripes on the cichlids. Genes that on their own make a huge difference in an organism's appearance, as the stripe coders do, could help explain why there are so many kinds of cichlids.

We were also eager to survey the cichlid genomes for multiple copies of individual genes. Scientists have known for decades that duplication of genes—which arise from errors in DNA replication—is one of the most important mechanisms by which gene function can rapidly diversify. In essence, if a gene were duplicated, the new copy might be free to change without denying the animal any of the material encoded by the gene (because the other copy would still work), and the change could potentially help the creature to adapt to its environment. Typically genes are quite constrained in the mutations that can occur without harming the "host." Our genome analyses show that cichlids have rates of gene duplication that are up to five times higher than that of "normal" fishes such as the sticklebacks.

A third type of genomic mechanism we sought to analyze was the activity of so-called jumping genes. Around 16 to 19 percent of the genome of a typical fish is made up of such DNA sequences, which do not serve an obvious function but make copies of themselves and jump from one location in the genome to another. They can be a force of evolution if they insert themselves close enough to a protein-coding gene to change its function. In the cichlid genomes, we have found telltale signs of several periods in which jumping genes accumulated rapidly, including one that coincided with the Lake Victoria radiation. The timing suggests that jumping genes may have helped facilitate the diversification of cichlids during such events.

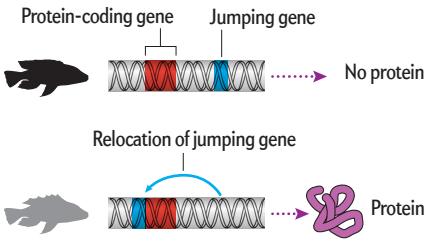
We also examined DNA sequences that ordinarily do not change much. Certain regions of the genome that do not specify amino acids in proteins tend to be highly conserved across large evolutionary time spans. These conserved noncoding elements (CNEs), as they are known, probably affect the functioning of genes. Otherwise, random mutations would accumulate, as they typically do over time in nonconserved regions, rendering these regions different from species to species. Cichlids share a number of CNEs with one another and with more distantly related species, such as sticklebacks. But when we took a closer look at the DNA, we found that although the cichlid CNEs are similar enough from species to species to spot them, they have changed more than one would expect for CNEs. Our cichlid genome comparisons found that about 60 percent of the CNEs had undergone significant changes in particular lineages of cichlids. This surprisingly high percentage suggested that the genes to which these CNEs are linked might have undergone a change in function. Subsequent experiments bore this hunch out: researchers assessed the function of conserved and altered cichlid CNEs by inserting this genetic material into the genomes of zebra fish and found that the altered CNEs switched on their associated genes differently than the unaltered CNEs did—a sure sign that evolution of the CNEs led to changes in gene function in cichlids.

Another kind of genetic material that tends to be highly conserved across species is microRNA. MicroRNAs are small molecules that act as switches for genes, telling them where and when they should do their work. We were surprised to find 40 that had never been seen before in other fishes. We then studied cichlid embryos to see where in the body some of these microRNAs were regulating gene activity. It turns out they work in a highly specific manner, influencing genes only in certain tissues, such as a particular region of the facial skeleton. The targeted activity of

SCIENTIFIC AMERICAN ONLINE Read more about cichlid throat jaws at ScientificAmerican.com/apr2015/cichlids

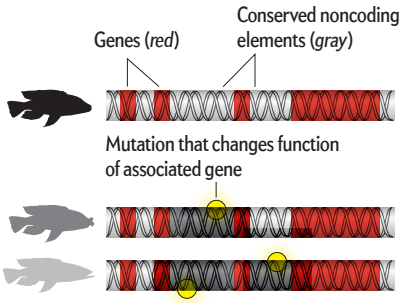
Jumping Genes

Sequences of DNA that make copies of themselves and jump to new positions in the genome are called transposable elements, or jumping genes. Depending on where the jumping gene lands, it may change the function of a nearby protein-coding gene. Cichlids underwent several periods in which jumping genes accrued rapidly, possibly hastening evolution.



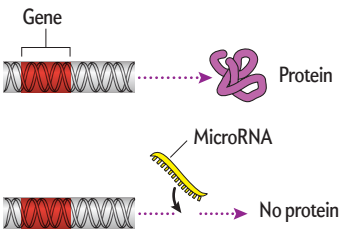
Mutations in DNA That Typically Does Not Change

Some genome regions that do not encode proteins tend to be highly conserved in evolution, probably because they affect gene function. Cichlids have significantly more mutations in some of these regions than expected, exhibiting a pattern that suggests the associated genes experienced a shift in function.



Novel microRNAs

Small pieces of genetic material called microRNAs, which can block genes from doing their job of making proteins, also tend to be conserved. Cichlids have more new microRNAs than other fishes have. With their ability to control genes in particular tissues, these microRNAs may have enabled the precise sculpting that gave rise to cichlid feeding specializations.



microRNAs hints that they could have enabled the kind of precision sculpting that gave rise to the various feeding specializations cichlids possess, among other traits.

We remain a long way from fully understanding if and how all the hundreds of microRNAs in cichlid genomes actually foster evolutionary change, but they are strong candidates for such a role. We hypothesize that by preventing genes from being switched on at the wrong place or time, microRNAs could encourage both more variation and more precision in orchestrating the intricate ballet of genes that interact to make slightly different teeth, jawbones, color patterns, courtship behaviors, and so on—variation that is the basis for adaptation and speciation.

WHAT'S OLD IS NEW

THIS INITIAL FORAY INTO CICHLID GENOMES suggests that new random mutations, such as those seen in the CNEs and those that give rise to novel microRNAs, have figured significantly in the extraordinary evolution of these fishes. But we suspect that relatively old genetic variation, including that from duplicated genes and jumping genes, may have done most of the work. These variants lurked quietly in the genome until new ecological opportunities—for instance, those that arose when ancestral river-dwelling cichlids colonized the Great Lakes of Africa—suddenly made them advantageous. By tapping into that ancient genetic variation, natural selection created species suited to the new habitats.

We think old variation is the key because when we look at the genomes of these cichlid species, we cannot find many fixed genetic differences between them. That is, there are very few examples of genes for which all members of a species carry the same variant. Instead the gene pool of a species retains old gene variants even after fish have branched off from their ancestors to form a new species. And not only does a young species retain old DNA from its ancestors, but it may still be similar enough to interbreed and hybridize with closely related species. Such mixing would allow new gene variants to flow across species boundaries—more potentially useful genetic material that can be recycled when needed. The retention of old genetic variation, in addition to fueling rapid diversification in cichlids, can also help explain how the same ultraspecific traits have evolved over and over in separate lineages: we suspect that traits such as asymmetrical jaws and Angelina Jolie lips may not have arisen anew each time; rather the same genes and gene switches were repeatedly recruited into service. This hypothesis awaits testing.

The genomic mechanisms described here were not the only drivers of cichlid evolution. Surely environmental factors had a crucial part in establishing the patterns and rates of diversification in this group. Differences in the extent of cichlid diversity in the various radiations of these fishes around the world support this surmise: in Africa and in Nicaragua, the radiations that occur in lakes with more complex habitats (and thus more ecological niches) have more species than the radiations in lakes with simpler habitats. In addition to the speciation that occurred as cichlids evolved feeding specializations to fill these niches, further diversification took place as skin color differences arose and females developed preferences for particular hues.

We still have much to learn. Now that we have complete genomes, as well as powerful new techniques for analyzing them, though, our knowledge will advance very quickly indeed. I expect that the mechanisms underlying the speed of cichlid speciation will continue to be an area of intense research. Soon we will have a far deeper understanding of the language of the genome and the DNA that connects all living things even as it drives them apart. SA

MORE TO EXPLORE

The Evolutionary Genomics of Cichlid Fishes: Explosive Speciation and Adaptation in the Postgenomic Era. Frederico Henning and Axel Meyer in *Annual Review of Genomics and Human Genetics*, Vol. 15, pages 417–441; August 2014.

The Genomic Substrate for Adaptive Radiation in African Cichlid Fish. David Brawand et al. in *Nature*, Vol. 513, pages 375–381; September 18, 2014.

FROM THE ARCHIVES

Cichlids of the Rift Lakes. Melanie L. J. Stiassny and Axel Meyer; February 1999.

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Illustration by Jen Christiansen

MORE TO EXPLORE For more recommendations and to watch a video of dragonfly metamorphosis, go to ScientificAmerican.com/apr2015/recommended

Dragonflies: Magnificent Creatures of Water, Air, and Land

by Pieter van Dokkum. Yale University Press, 2015 ($35)

Van Dokkum is an astronomer with a passion for dragonflies. When he is not imaging distant objects in the cosmos using some of the world's most powerful telescopes, he produces close-up photographs of one of the universe's smaller inhabitants: the dragonfly. In this large-format book, van Dokkum captures the exquisite colors and varied features of the insects, portraying the creatures' full life cycle, from the time a larval "nymph" metamorphoses into an adult dragonfly through mating and eventually death at the hands of bird predators, spider webs, cold weather or other mishaps. Captions and commentary fill out the pictures, tracing the short but curious lives of dragonflies.

Scientific Babel: How Science Was Done Before and After Global English

by Michael D. Gordin. University of Chicago Press, 2015 ($30)

More than 90 percent of scientific publications today are in English, but that was not always the case. Latin was once a near-universal language for scholarship in Western science; then Latin gave way to a "Scientific Babel," as historian Gordin calls it, where research came to light in a profusion of languages.

From 1880 to 1910 roughly equal numbers of publications appeared in German, French and English, and German overtook English by 1910. Scientists might still be communicating in German had it not been for the fallout from World War I, Gordin argues. His book investigates how English came to be the lingua franca for modern science and what it means that a single language dominates. "Today's situation raises obvious issues of fairness," Gordin writes, because non-English speakers have the extra burden of needing to learn a foreign language and translate their work to participate in science.

So You've Been Publicly Shamed

by Jon Ronson. Riverhead, 2015 ($27.95)

Social media has brought about "a great renaissance of public shaming," writes journalist Ronson, who tells of people whose mistakes have invited mass scorn. He interviews a woman, Justine Sacco, whose ill-considered joke about AIDS and Africa on Twitter temporarily made her the Internet's Public Enemy No. 1, as well as journalist Jonah Lehrer, who fabricated quotes and plagiarized himself—and was broadly lambasted when the truth was revealed.

Twitter, Facebook and their ilk allow a kind of "democratization of justice" with far-reaching consequences for its targets, Ronson writes. He probes why we seem to love heaping contempt on strangers and what happens to the shamed when the Internet's collective notice has moved on. In Sacco's case, for instance, she lost her job, traveled to Ethiopia for a time and is still trying to get back on her feet. The resulting book adds up to an intriguing look into the psychology of public shaming and the technology that enables it.

Infested: How the Bed Bug Infiltrated Our Bedrooms and Took Over the World

by Brooke Borel. University of Chicago Press, 2015 ($26)

They are many city dwellers' worst nightmare: the dark spots on the mattress and itchy blotches on arms and legs that indicate a bed bug infestation. Journalist Borel suffered through multiple invasions that set her on a quest to understand the history and biology of the bugs, as well as the psychology of why they drive us crazy.

Borel attends a bed bug conference and surveys the myriad products designed to combat the critters (self-heating suitcases are one example). She also describes the depression, insomnia and even suicide attempts that infestations have provoked. Yet this scourge is nothing new; it turns out that bed bugs have been feasting off human blood throughout our history and may date back to the Pleistocene. "In a way, we created the modern bed bug: it evolved to live on us and to follow us," Borel writes. "Understanding its path helps illuminate ours."

PIETER VAN DOKKUM

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Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com). His new book is *The Moral Arc* (Henry Holt, 2015). Follow him on Twitter @michaelshermer

Paleo Diets, GMOs and Food Taboos

What do we mean by "natural"?

In 1980 I subjected myself to a weeklong cleansing diet of water, cayenne pepper, lemon and honey, topped off with a 150-mile bicycle ride that left me puking on the side of the road. Neither this nor any of the other fad diets I tried in my bike-racing days to enhance performance seemed to work as well as the "see-food" diet one of my fellow cyclists was on: you see it, you eat it.

In its essence, the see-food diet was the first so-called Paleo diet, not today's popular fad, premised on the false idea that there is a single set of natural foods—and a correct ratio of them—that our Paleolithic ancestors ate. Anthropologists have documented a wide variety of foods consumed by traditional peoples, from the Masai diet of mostly meat, milk and blood to New Guineans' fare of yams, taro and sago. As for food ratios, according to a 2000 study entitled "Plant-Animal Subsistence Ratios and Macronutrient Energy Estimations in Worldwide Hunter-Gatherer Diets," published in the *American Journal of Clinical Nutrition,* the range for carbohydrates is 22 to 40 percent, for protein 19 to 56 percent, and for fat 23 to 58 percent.

And what constitutes "natural" anyway? Humans have been genetically modifying foods through selective breeding for more than 10,000 years. Were it not for these original genetically modified organisms—and today's more engineered GMOs designed for resistance to pathogens and herbicides and for better nutrient profiles—the planet could sustain only a tiny fraction of its current population. Golden rice, for example, was modified to enhance vitamin A levels, in part, to help Third World children with nutritional deficiencies that have caused millions to go blind. As for health and safety concerns, according to *A Decade of EU-Funded GMO Research,* a 2010 report published by the European Commission:

> The main conclusion to be drawn from the efforts of more than 130 research projects, covering a period of more than 25 years of research, and involving more than 500 independent research groups, is that biotechnology, and in particular GMOs, are not *per se* more risky than e.g. conventional plant breeding technologies.

So why are so many people in a near moral panic over GMOs? One explanation may be found in University of California, Los Angeles, anthropologist Alan Fiske's four-factor relational model theory of how people and objects interact: (1) communal sharing (equality among people); (2) authority ranking (between superiors and subordinates); (3) equality matching (one-to-one exchange); and (4) market pricing (from barter to money). Our Paleolithic ancestors lived in egalitarian bands in which food was mostly shared equally among members (communal sharing). As these bands and tribes coalesced into chiefdoms and states, unequal distribution of food and other resources became common (authority ranking) until the system shifted to market pricing.

Violations of these relations help to show how GMOs have come to be treated more like moral categories than biological entities. Roommates, for example, are expected to eat only their own food or to replace one another's consumed items (equality matching), whereas spouses share without keeping tabs (communal sharing). If you invite friends to dinner, it would be disconcerting if they offered to pay for the meal, but if you dine at a restaurant, you are required to pay the bill and not summon the owner to your home for a comparable cuisine. All four relational models are grounded in our natural desire for fairness and reciprocity, and when there is a perceived violation, it creates a sense of injustice.

Given the importance of food for survival and flourishing, I suspect GMOs—especially in light of their association with large corporations such as Monsanto that operate on the market-pricing model—feel like an infringement of communal sharing and equality matching. Moreover, the elevation of "natural foods" to near-mythic status, coupled with the taboo many genetic-modification technologies are burdened with—remember when in vitro fertilization was considered unnatural?—makes GMOs feel like a desecration. It need not be so. GMOs are scientifically sound, nutritionally valuable and morally noble in helping humanity during a period of rising population. Until then, eat, drink and be merry. SA

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Illustration by Izhar Cohen

TECHONOMY BIO

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The ongoing search for fundamental farces

Steve Mirsky has been writing the Anti Gravity column since a typical tectonic plate was about 34 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.

Immune Reaction

I've seen the needle and the damage avoided

As I write these words in early February, the nation is watching a measles outbreak caused by parents opting out of vaccines for their children. Meanwhile presidential hopefuls have been making news via their strong pro-choicey opinions, which are somehow about whether to get your kids vaccinated. I was going to pass on commenting, so weary did I become upon hearing the retrograde absurdities that came out of the mouths of Senator Rand Paul (R-KY), Governor Chris Christie (R-NJ) and Representative Sean Duffy (R-WI).

But then Senator Thom Tillis (R-NC) saw and raised them in this game of high-stakes public health poker by questioning whether we need regulations mandating that restaurant employees wash up after they defecate.

Just when I thought I was out, they pull me back in.

Speaking at the Bipartisan Policy Center, Tillis noted his sadness over the shackles that regulations put on businesses. And as an example, he cited the onerous hand-washing requirements. "I don't have any problem with Starbucks," he said, "if they choose to opt out of this policy as long as they post a sign that says we don't require our employees to wash their hands after leaving the restroom. The market will take care of that." I hope you don't die of *E. coli* before the market correction.

Now that I'm up to my waist, I'll dive in the rest of the way.

Appearing on MSNBC, Duffy said of vaccine mandates, "I know what morals and values are right for my children. I think we should not have an oppressive state telling us what to do ... I vaccinate my kids on most things, but then there are some things where I'm like, this may not work for me and my values." The word "values" makes me suspect Duffy might have an issue with keeping his kids safe from cancers caused by human papillomaviruses because they are spread by S-E-X.

On a recent visit to England, Christie said, "We vaccinate ours [kids], and so, you know, that's the best expression I can give you of my opinion. You know it's much more important what you think as a parent than what you think as a public official. And that's what we do. But I also understand that parents need to have some measure of choice in things as well, so that's the balance that the government has to decide." I can't really come up with a comment to this statement because, huh?

Dr. Rand Paul said on CNBC he'd heard of "many tragic cases of walking, talking, normal children who wound up with profound mental disorders after vaccines." He also claimed that vaccinations should not be required, because "the state doesn't own your children. Parents own the children. And it is an issue of freedom and public health."

After being criticized for his comments, Paul told a *New York Times* reporter, "It just annoys me that I'm being characterized as someone who's against vaccines.... That's not what I said. I said I've heard of people who've had vaccines, and they see a temporal association and they believe that." And I know guys who believe what chair they sit in affects whether their favorite sports team wins. For the record, the connection is harder to spot between the many, many happy cases of walking, talking, normal kids who wound up being healthy adults after vaccines because of the lack of any temporal association.

I was getting pretty depressed, but then I heard a man on the radio say to an antivaccine parent, "You're a danger to this country. Your children must be vaccinated, for the good of society and for your children's health. Stop with all this cockamamy fake science that you guys are making up." And radio personality Howard Stern, because that's the guy who was making all this sense, went on to say, "There are some things we do because they're proven. If your child had polio, if you had seen the ravages of polio and of mumps and measles—mumps and measles kill babies. If someone told you there's a cure, you would rush to get it—and there is one! And you guys are acting like there isn't. And then you're saying, 'Well, everyone else will get these vaccines.' It's not fair. We've got to immunize everyone. And there's nothing out there that says your child is going to be damaged by these vaccines, nothing!"

So that's the state of our national discourse: a notoriously foul-mouthed shock jock apparently has a better and more sensible understanding of immunology and public health than does a medical doctor in the U.S. Senate. Thank you, Mr. Stern, for the shot in the arm. SA

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Illustration by Matt Collins

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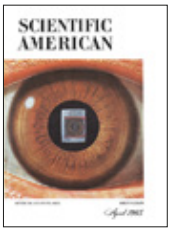


April 1965

An Economic Model

"Further development of input-output analysis and the realization of its potentialities for informed and rational decision-making at all levels of economic life call for detailed and more up-to-date tables. Comparison of the 1947 and 1958 input-output tables for the U.S. economy indicates significant changes in the input-output coefficients arising from technological innovation. Work has now begun on the preparation of an input-output table for the U.S. economy based on the data from the census of manufactures for 1963.—Wassily W. Leontief"

Leontief won the 1973 Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel for this work.

Heroin Antidote

"Vincent P. Dole of the Rockefeller Institute has reported promising results from experiments with a drug that simultaneously meets the physiological need of the addict and blocks any attendant euphoria. Dole has induced several heroin addicts hospitalized at the Institute to take methadone, a drug that reduces withdrawal distress. Methadone does not produce the 'high,' or euphoria, brought on by heroin; indeed, a strong enough dose of methadone makes the subsequent intake of heroin incapable of producing a 'high.' Thus the addict who has received methadone is deprived of his euphoria but does not suffer the agony usually associated with such deprivation. Methadone is a synthetic compound developed in Germany more than 25 years ago and used in Europe today as an ordinary analgesic."

April 1915

Aerodynamic Designs

"The remarkably shaped motorcar shown in the accompanying illustration has been built in Italy, it is reported, according to designs evolved by Count Marco Ricotti of Milan. It carries, as will readily be understood, the matter of streamline body design further toward its logical conclusion. The Ricotti car is fitted with a 50 horsepower four-cylinder motor, which enables this torpedo on wheels to cover ground at the high rate of 80 miles an hour. Removing the streamline body and letting the car go at top speed in 'stripped' shape, immediately reduced its speed to 65 miles an hour. When one considers the considerable weight which such a body has, it must be regarded as a remarkable demonstration of the importance of wind resistance at high speeds."

Take a spin through the technology of motor vehicles in 1915 at www.ScientificAmerican.com/apr2015/motor-vehicles

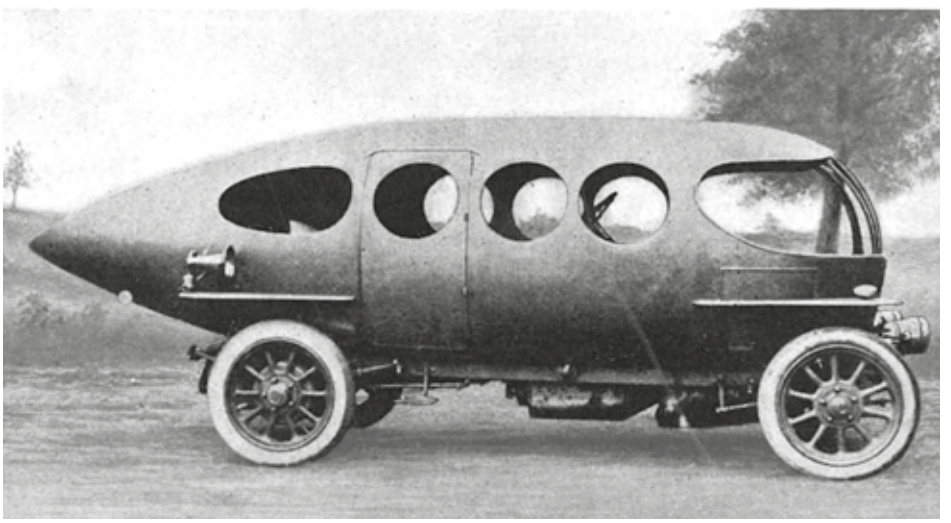
A City for Movies

"There is a wonderful city out in the heart of the San Fernando Valley in the State of California, which is probably the most unique city in the world. Its name is Universal City, and it is the only municipality in the universe devoted to the manufacture of moving-picture films. It was officially opened on March 15th, and all of its population of 1,500 people are employed in the art of making pictures. It is nothing more or less than a chameleon city, for the entire complexion and appearance of Universal City can be changed in three days to conform to any nationality, style of architecture, color scheme, or state of preservation which occasion requires."

April 1865

End of the War, Assassination of Lincoln

"An appalling and overwhelming calamity has befallen the nation. The Chief Magistrate has been stricken down by the hand of an assassin; and, as one man, the people are aghast at the magnitude of their loss. In the flood tide of victory, in the fullness of the joy which our successes in overthrowing the rebellion warranted, a pall drops upon the flag, ashes are strewn upon the laurel, the jubilant shouts are changed to cries of mourning.... The deep grief which sits upon the faces of the people, shows how dear to them was the simple, honest, upright man, who so lately guided us. Wise in judgment, inflexible in decision, magnanimous to his enemies, pure in private as in public life, history will record no brighter name upon its pages than that of ABRAHAM LINCOLN."



AERODYNAMIC PROTOTYPE: A streamlined road and race car from A.L.F.A. (later Alfa Romeo), 1915. Note how far back the steering wheel is.

SCIENTIFIC AMERICAN, VOL. CXII, NO. 15; APRIL 10, 1915

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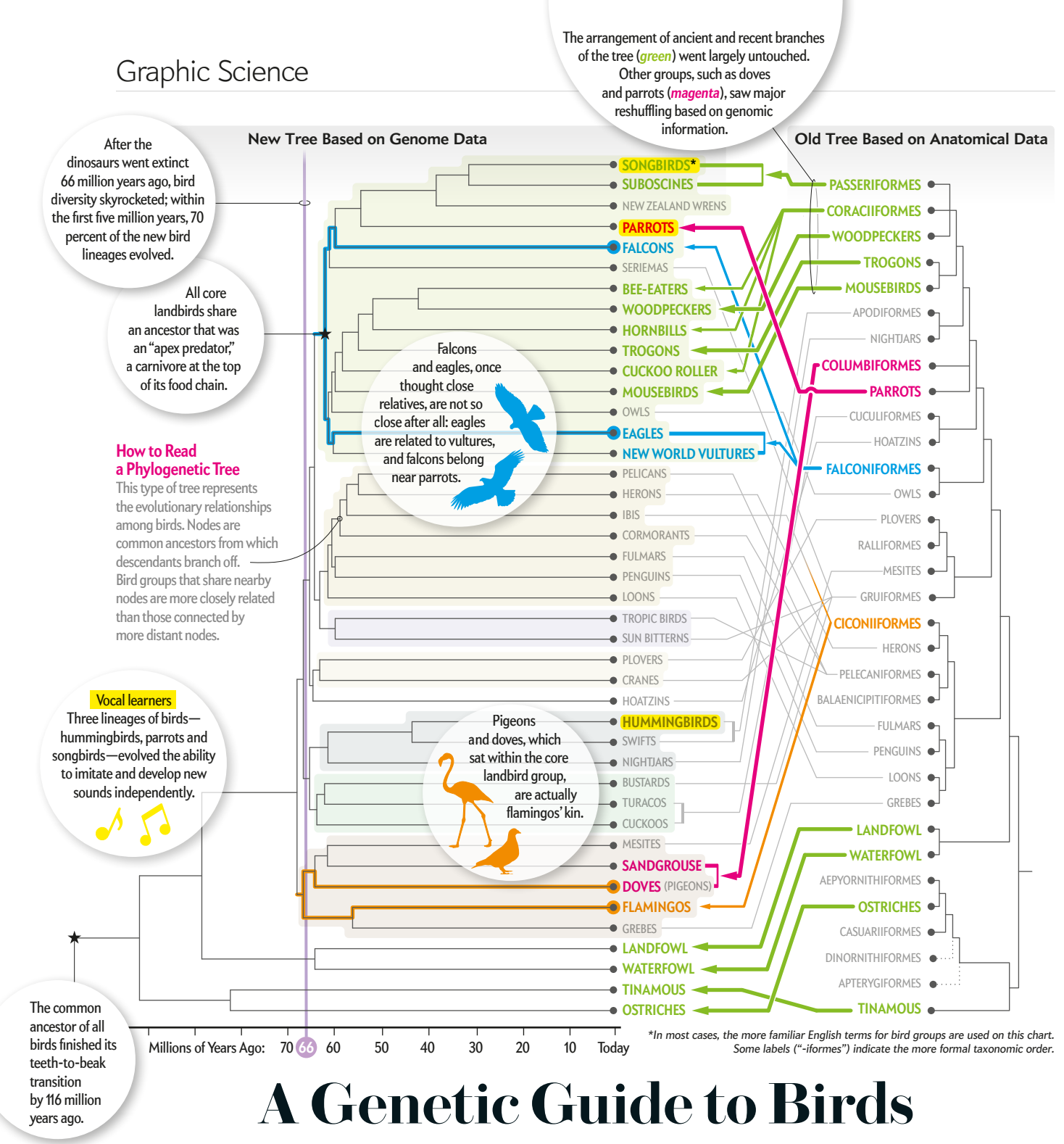

A Genetic Guide to Birds

The avian family tree gets a makeover

Classifying birds by plumage and other anatomical features served scientists well over the centuries, but genetic analyses have opened up a world of detail about avian family ties. An international group of researchers recently developed a tree based on the full genomes of 48 species, representing every major bird lineage—the most thorough genetic study of a large branch on the tree of life to date. The massive effort, with more than 200 collaborators, includes investigations of the emergence and disappearance of teeth, the origin of vocal learning, and the timing of the explosion of bird diversity.

The new tree confirms many past observations, such as the common ancestor of the core landbirds. It also resolves some controversial links. Who might have guessed, for instance, that pigeons and flamingos are close cousins? —*Sarah Lewin*

***Sarah Lewin** is a science writer based in New York City.*

SOURCES: "WHOLE-GENOME ANALYSES RESOLVE EARLY BRANCHES IN THE TREE OF LIFE OF MODERN BIRDS," BY ERICH D. JARVIS ET AL., IN *SCIENCE*, VOL. 346; DECEMBER 12, 2014 (*left tree*); "HIGHER-ORDER PHYLOGENY OF MODERN BIRDS (THEROPODA, AVES: NEORNITHES) BASED ON COMPARATIVE ANATOMY," PART II: "ANALYSIS AND DISCUSSION," BY BRADLEY C. LIVEZEY AND RICHARD L. ZUSI, IN *ZOOLOGICAL JOURNAL OF THE LINNEAN SOCIETY*, VOL. 149, NO. 1; JANUARY 2007 (*right tree*)

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Graphic by Jen Christiansen

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