UNCANNY VISION
What Some Blind People Perceive

WARMING ARCTIC
How Plants Are Changing

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New Eyes on the Skies
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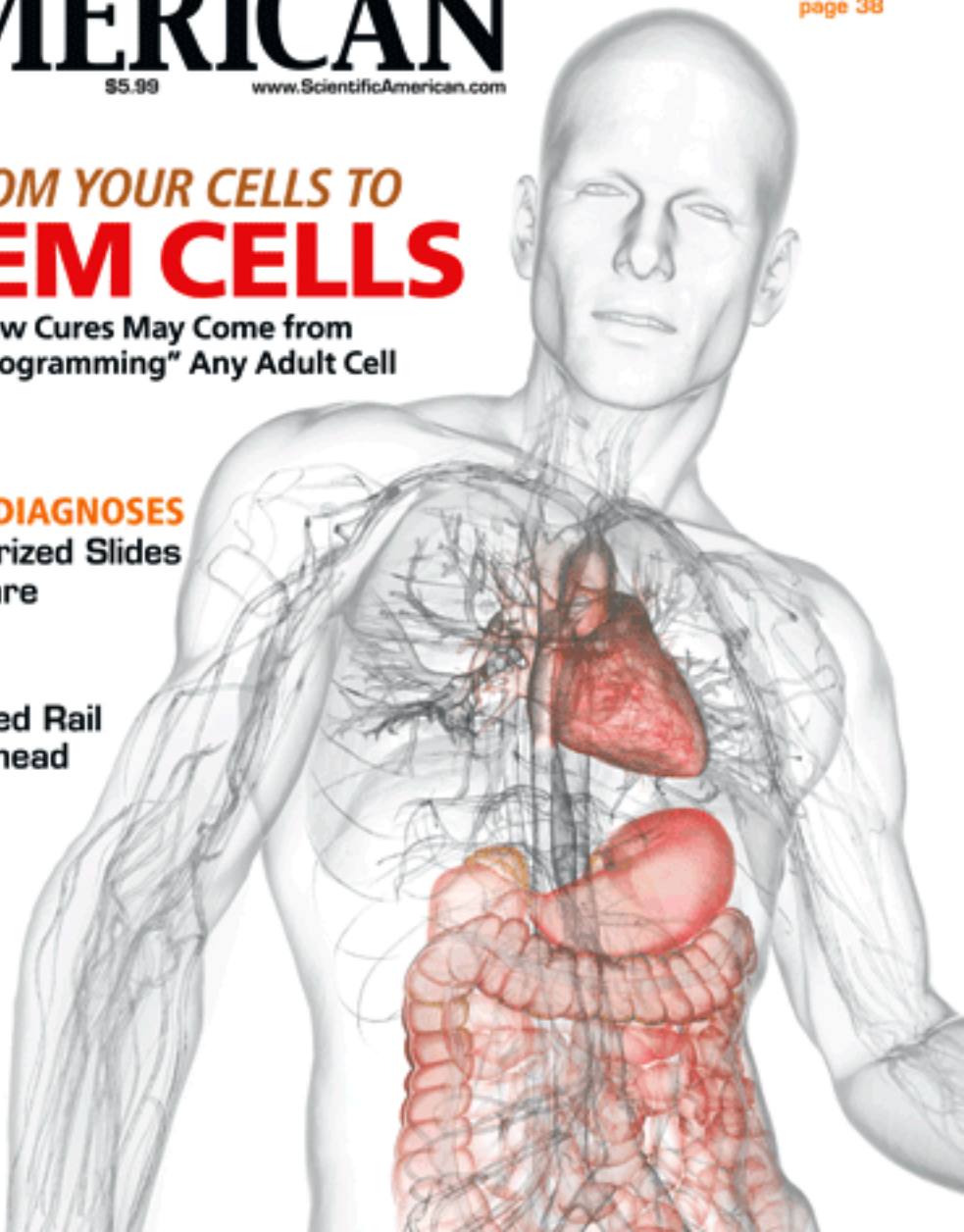
FROM YOUR CELLS TO
STEM CELLS
New Cures May Come from "Reprogramming" Any Adult Cell

DIGITAL DIAGNOSES
Computerized Slides Speed Care

PLUS:
High-Speed Rail Moves Ahead



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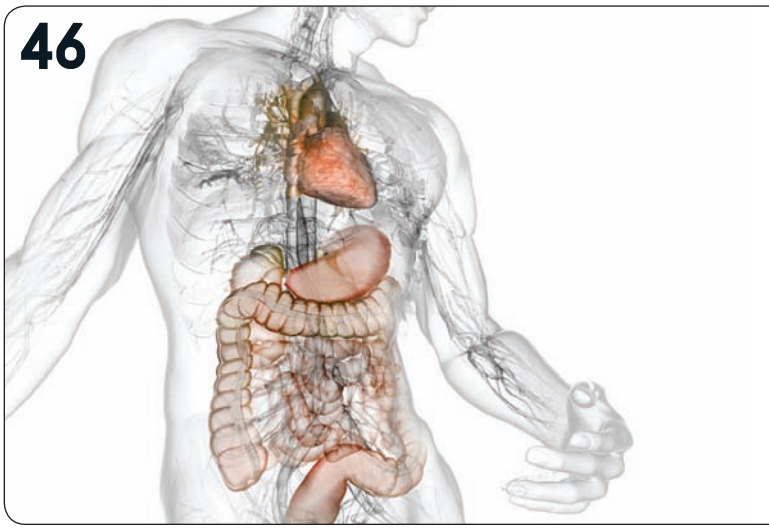

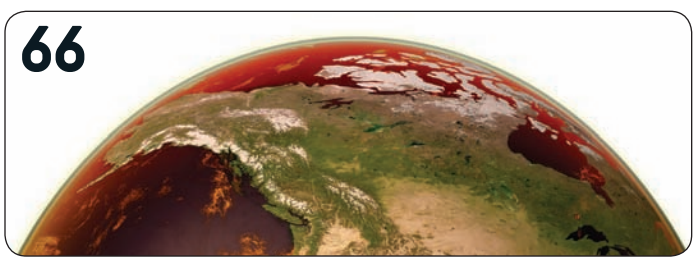

ON THE COVER

Stem cells potentially can be converted into any tissue needing repair. A newly invented type holds enormous promise for medicine. Illustration by Bryan Christie Design.

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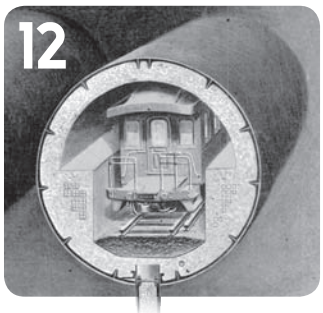

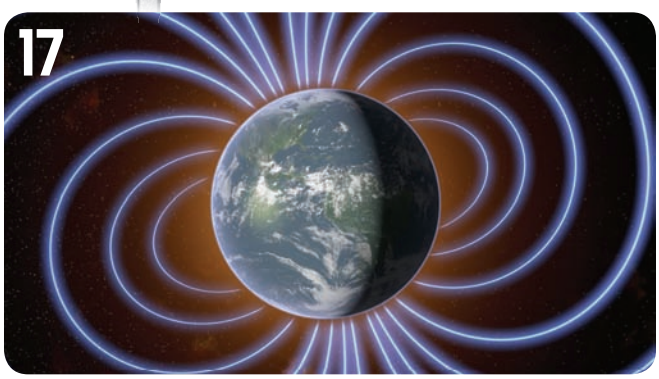

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Consumer Electronics: More Than Just Fun and Games

Video games, e-readers, smart phones and other gadgets have changed the way we interact with one another and with the world around us. What's next? (Hint: Get used to those 3-D glasses.)

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TIM PANNELL *Corbis*

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Society and Science

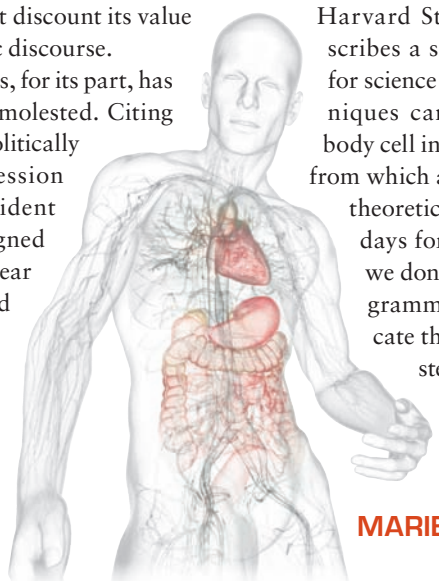
When you read hundreds of letters from readers every month, as I do, common patterns of argument emerge. I can't answer every note individually, so in this column I'd like to at least respond to one type of assertion. That is the idea, whenever the letter writer doesn't agree with an expert-informed point of view expressed in *Scientific American*, that science should not mention or touch on politically sensitive areas—that science is somehow apart from social concerns. I say: Wrong.

Science findings are not random opinions but the result of a rational, critical process. Science itself advances gradually through a preponderance of evidence toward a fuller understanding about how things work. And what we learn from that process is not just equivalent to statements made by any another political-interest group. It is evidence-based information that is subject to constant questioning and testing from within the scientific community. Thus, the science-informed point of view is a more authoritative and reliable source of guidance than uninformed opinions. We should not discount its value in informing public discourse.

Certainly politics, for its part, has not left science unmolested. Citing past instances of politically motivated suppression of findings, President Barack Obama signed a memorandum a year ago that directed John P. Holdren, the White House science and technology adviser, to explore ways to restore scientific integrity to government decision making. I salute the gesture, although at press time I still remain impatient for the actual delivery of that strategy.

One well-known area of research government stifled in the past is stem cells. Embryonic stem cells offer amazing potential for cures, because they can become any of the 220 types of cells in the human body. They could be used to replace diseased tissue or to develop therapies for ailments such as Parkinson's disease or cancer. Several years ago the Bush administration limited research to then existing stem cell lines, citing ethical concerns about procuring such cells by destroying early-stage—containing about 200 cells—embryos. (A quick aside: politicians seem to have less of a problem with in vitro fertilization techniques, in use for decades, which create thousands of frozen embryos that may be later destroyed.) The current administration later lifted those restrictions, but the topic remains fraught.

In this issue's cover story, "Your Inner Healers," starting on page 46, Konrad Hochedlinger, a Harvard University associate professor of stem cell and regenerative biology and a faculty member of the Harvard Stem Cell Institute, describes a solution that may work for science *and* politics. New techniques can convert any mature body cell into an embryonic state—from which any desired tissue could theoretically be grown. It is early days for this exciting advance; we don't know yet if the reprogrammed cells can truly duplicate the abilities of embryonic stem cells. But we do know that science, if we allow it to proceed, will strive to find out. ■



ETHAN HILL (*DiChristina*); BRYAN CHRISTIE DESIGN (*illustration*)

MARIETTE DiCHRISTINA
editor in chief

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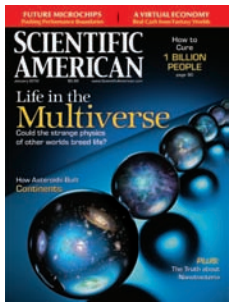
Antimatter ▪ Nanotech Safety ▪ Firestorms



JANUARY 2010

"Information about 'Life, the Universe, and Everything' can be found on none other than page 42."
—*William D. Brown* SEEKONK, MASS.

Life, the Multiverse and Everything

In "Looking for Life in the Multiverse," Alejandro Jenkins and Gilad Perez say that life would be possible in a universe without the weak nuclear force. But they fail to note that the weak force is unique in treating matter and antimatter asymmetrically. Only because of this asymmetry did matter slightly outweigh antimatter before nearly all antimatter annihilated with an equal amount of matter, within the first seconds after the big bang. Everything we see—including stars, which are essential to life—is composed of that slight excess of matter. A universe without the asymmetric weak force would have virtually no normal matter and hence no life in any form we might recognize.

Robert L. Piccioni
The writer is author of *Everyone's Guide to Atoms, Einstein, and the Universe*

THE AUTHORS REPLY: *By itself, the weak nuclear force cannot distinguish between matter and antimatter, because it preserves what physicists call charge-parity (CP) symmetry, meaning that it treats a particle in the same way as the mirror image of the corresponding antiparticle. As Piccioni points out, however, it is possible to combine the weak force with other interactions in such a way that this CP symmetry is broken.*

Today we know that CP asymmetry is way too small to account for the fact that our universe contains as much matter as it does, but no antimatter. Some new physical interactions at high energies, as yet undetected, are needed to resolve this fascinating puzzle. These other interactions could also produce an excess of matter over antimatter in a weakless universe. We did not cover this interesting point in our Scientific American *article because of space limitations.*

That information about "Life, the Universe, and Everything" could be found on none other than page 42 of this issue was ironic, given that this number had been specified in 1979 as the "Answer to the Ultimate Question" in Douglas Adams's classic text, *The Hitchhiker's Guide to the Galaxy*. For those of us who can barely get around the monoverse we find ourselves living in, it is a comfort to know that *Scientific American* has provided additional evidence that a convergence of multiverses arises from this locus, 42, as predicted by Adams.

William D. Brown
Seekonk, Mass.

Proceeding, with Care

In "Big Need for a Little Testing" [Perspectives], the editors write that "many companies are hesitant to invest in nanotechnology R&D, fearing the exposure to legal action that could result if one day a technology is deemed dangerous. Procter & Gamble, for example, is not pursuing nanotechnology because of the long-term risk of litigation."

Contrary to what was stated, P&G is interested in nanotechnology, and we are actively pursuing the benefits it can deliver. We believe it holds great potential to bring exciting new levels of performance to products people use everyday. Nanotechnology opens up many possibilities to boost performance, reduce environmental impact

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and improve sustainability in virtually every consumer product category. As with any new technology, however, the potential for adverse effects must be understood, and the technology should advance only as fast as our ability to thoroughly evaluate it. We are taking an appropriately cautious approach with nanotechnology. In addition to our own research programs, we are also working together with others in the industry, with university labs and with government scientists to ensure the right tools are in place for the responsible development of this promising technology.

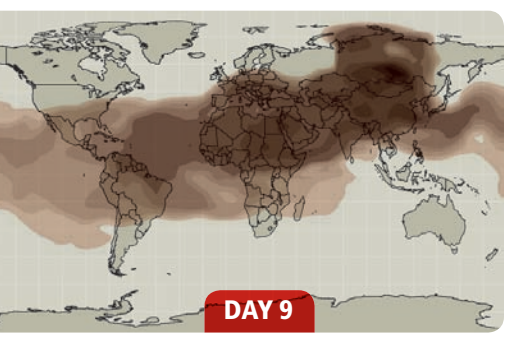
Mark Lafranconi
Section Head, Central Product Safety
Procter & Gamble

Nuclear Inferno

In "Local Nuclear War, Global Suffering," Alan Robock and Owen Brian Toon claim that a nuclear exchange of 100 Hiroshima-size weapons between India and Pakistan would cause a global catastrophe from smoke particles lofted into the stratosphere. How do the authors reconcile the massive amount of smoke pumped into the earth's atmosphere during World War II?

Toward the end of the war, more than 60 Japanese cities were firebombed. Other areas to consider, of course, are the British, German and Russian cities burned and destroyed during the war, as well as particularly "dirty" bombings like the oil refineries at Ploesti, Romania and numerous major battles. In my opinion, the authors have overstated the global damage from a nuclear war of the type they describe, and perhaps they did not consider thoroughly enough the environmental effects incurred during WWII.

Kevin A. Capps
Corona del Mar, Calif.



NUCLEAR CONFLICT between India and Pakistan would not only kill millions of people but also loft enough smoke into the stratosphere to cause a global winter.

THE AUTHORS REPLY: *There were indeed numerous fires in Japan and Europe during World War II, several of which occurred near the end of the war.*

The observational database from WWII is not adequate to tell if smoke from these fires reached the stratosphere. For the scenario discussed by Capps, over a period of four weeks, 155 square kilometers (60 square miles) of cities burned in Japan. Unless each fire was of a sufficient intensity to produce a firestorm, the smoke would not have been pumped into the stratosphere and would have remained in the troposphere, like the smoke from the oil well fires during the Gulf War in 1991. This means the smoke would have a lifetime in the atmosphere of only about a week, with only small, short-term local effects. Even if all the smoke did get into the stratosphere, the optical depth would have been much less than that from the regional nuclear conflict we studied: the burned area we considered was 1,300 km^2. The number of large firestorms in WW II was small compared with the 100 in our study.

Our models suggest that the small number of events in WWII would not have produced climate effects that would have been detectable against the background of natural weather and climate variability. We do not know if there was a small effect on climate from the smoke generated in WWII, because nobody has studied it. Thus, WWII does not give any evidence that our results are incorrect. In fact, the unfortunate example of cities burning supports our theory that large firestorms would follow atomic bombing. More recent studies of large forest and brush fires, such as in Australia during January 2003, do show that smoke can be injected into the lower stratosphere and may be lofted by sunlight to higher altitudes.

ERRATA An illustration on page 46 of "Looking for Life in the Multiverse," by Alejandro Jenkins and Gilad Perez, shows a reaction producing helium 4, two electrons and two antineutrinos. The reaction actually produces helium 4, two positrons and two neutrinos.

Because of an editing error, "The Rise and Fall of Nanobacteria," by John D. Young and Jan Martel, states that certain geologic beds dated back to the Paleozoic and Mesozoic periods and adds that those periods are "considered to have preceded the era of life on Earth," which is incorrect. The authors' manuscript read, instead, that some beds "dated back to the Paleozoic and Mesozoic periods and, in fact, to periods of geologic times that were deemed to have preceded any biological life."

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JEN CHRISTIANSEN

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Early Experience ▪ Aviators ▪ Home Chemistry

Compiled by Daniel C. Schlenoff

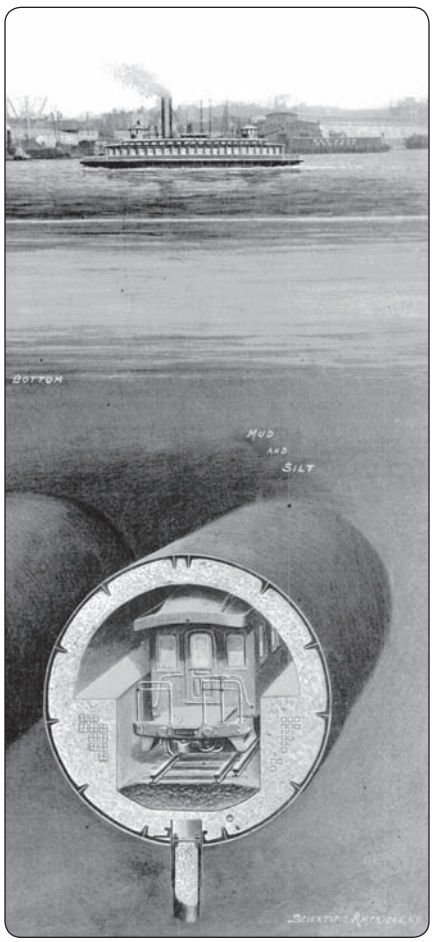
MAY 1960

DEVELOPING INFANTS—"We expected that the shocked rats would be affected by their experience, and we looked for signs of emotional disorder when they reached adulthood. To our surprise it was the second control group—the rats we had not handled at all—that behaved in a peculiar manner. The behavior of the shocked rats could not be distinguished from that of the control group which had experienced the same handling but no electric shock. Thus the results of our first experiment caused us to reframe our question. Our investigation at the Columbus Psychiatric Institute and Hospital of Ohio State University has since been concerned not so much with the effects of stressful experience—which after all is the more usual experience of infants—as with the effects of the absence of such experience in infancy. —Seymour Levine"

MAY 1910

AIR RACES— "Louis Paulhan, the most distinguished aviator of them all, has soared nearly a mile into the air, and finally has surpassed even that feat by flying from London to Manchester, covering a distance of 186 miles, with but one stop for fuel, at an average speed of over forty miles an hour. The significance of this really wonderful race between Paulhan, the Frenchman, and Claude Grahame-White, the Englishman, is apparent only when we consider some of the details which have been cabled to this side of the Atlantic. That Paulhan won the $50,000 prize in such superb style is a tribute both to his own skill in manipulation [piloting], and to the excellence of the Farman biplane with which the race was won."

SAND HOGS—"For the Pennsylvania Railroad Terminal in New York, the tunnels were bored for the most part by means of huge shields which burrowed their way through silt and sand seventy feet below the surface of the Hudson River [*see illustration*]. Men of all nationalities built the Pennsylvania tunnels, negroes doing a large part of the work. They say there must be something about the compressed air which generates energy and enthusiasm, for the 'muckers'—commonly known as 'sand hogs'—vied with one another to make the record progress. Coffee was the mainstay of the tunnel worker, and it was to be had at all times and at all places. The most important of the rules enforced while the Pennsylvania tunnels were being built was one requiring the men to go slowly through the air locks."



BOLD ENGINEERING: Railroad tunnels under the Hudson River, 1910

MAY 1860

ENDEMIC TUBERCULOSIS—"Henry B. Millard, M.D., estimates that nearly one-sixth of the deaths among the human race occur from consumption. In New York, from 1848 to 1859, mortality was one in 8.46. Consumption is not necessarily more prevalent in large than in small cities. Among the trades and professions, the greatest mortality was among tailors and shoemakers, the least, among lawyers."

ELECTRIC LIGHTHOUSE—"Professor Faraday, F.R.S., described the application of the Electric Light to the South Foreland lighthouse (England) by Professor Holmes: 'Two magneto-electric machines are employed at the South Foreland lighthouse, and each is operated by a two-horse-power steam engine. Excepting wear and tear of the apparatus, the whole of the material consumed to produce the light are coal and water for the boilers of the engines, and carbon points for the lamp in the lantern.' While it appears beyond a doubt that this light is wonderfully brilliant in comparison with others, yet its expense must be much greater than that obtained by the use of the Fresnel lens with the best oil in common mode."

CHEMIST AT HOME—"We would yet advise to set a room apart in mansions, with the title of 'laboratory,' or the more ancient one of 'still-room.' The amount of instruction that can be derived from a private laboratory is far more than at first sight can be conceived, and the entertainment, changeable as a kaleidoscope, is (intellectually considered) immeasurably superior either to crochet or Berlin work [embroidery]. The delicate manipulations of chemical experiments are well, even better, suited to their physical powers than to the sterner sex; and to the ladies, therefore, we commend the charge of becoming the *chefs* of the modern still-room.—Septimus Piesse's *Art of Perfumery*"

SCIENTIFIC AMERICAN SUPPLEMENT, VOL. LXIX, NO. 1793; MAY 14, 1910

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Research & Discovery

Portrait in DNA

Can forensic analysis yield police-style sketches of suspects? BY CHRISTINE SOARES

MALE, SHORT AND STOUT, WITH DARK SKIN, BROWN EYES, shovel-shaped teeth, type A+ blood and coarse, dark brown hair giving way to pattern baldness. He would have a high tolerance for alcohol and a higher-than-average risk of nicotine dependence—fortunately, he lived thousands of years before humans discovered smoking. The description of a Stone Age Greenland resident published in February paints an extraordinary portrait of a man who vanished more than 4,000 years ago, drawn almost solely from his DNA remains.

The analysis, led by Danish scientists, not only marks the first full sequencing of an ancient human genome but also offers a startling example of how much modern-day detectives can discern just from a suspect's genetic code. Far beyond using DNA "fingerprints" to link an individual to a crime scene, forensic profiling is edging toward the capability to create a police-artist-style sketch of an unknown person by reading traits inscribed in the genome. "The body interprets the DNA to determine the appearance of the face," says anthropologist Mark Shriver of Morehouse College, who hopes to duplicate that ability within a decade.

The scientists reconstructing the ancient Greenlander had only a few tufts of hair, preserved in permafrost, from which they extracted DNA. The hair itself is dark and thick and contains chemical traces indicating mainly a seafood diet. From the man's genes, the researchers resolved a long-standing debate about the origins of Greenland's paleo-Eskimos by showing he had a pattern of DNA variations most common in Siberian population groups. Having established his ancestral origins in northern Asia, the team could then interpret variations called single-nucleotide polymorphisms (SNPs) in four genes linked to brown eye color in modern Asians. The same method revealed SNPs associated with shovel-shaped front teeth and a dry type of earwax, both traits common in modern Asians and Native Americans. Four more SNPs suggest that he probably had dark skin. Another set of variations typical of populations adapted to cold climates indicates he had a compact body and ample body fat.

Together those traits might not make the ancient Greenlander stand out in a lineup, but they could dramatically narrow the search for suspects. A handful of high-profile criminal cases has already demonstrated the utility of even basic prospective information. In 2007 Christopher Phillips and his colleagues at the University of Santiago de Compostela in Spain used markers in a DNA sample obtained from a toothbrush to identify a suspect in the 2004 Madrid train bombing as being of North African descent. Police later confirmed that the terrorist was Algerian.

DNA PROFILING could take on new meaning as scientists discover how genes produce a specific trait. Such advances could allow law enforcement to sketch a description from clues in a suspect's genes.

PETER DAZELEY *Getty Images*

In an infamous Louisiana serial killer investigation, witness testimony had indicated a Caucasian culprit, but DNA evidence pointed to someone of significant African-American and Native American descent. Police widened their search and eventually caught the killer.

Having more to go on than ancestry, a generally poor indicator of appearance, is the goal of programs such as the DNA Initiative of the National Institute of Justice, which funds research into alternative genetic markers for forensic use. Daniele Podini of George Washington University is developing a forensic kit to determine, by analyzing 50 to 100 genetic markers, a suspect's eye and hair color, sex and probable ancestry. "The idea is just to provide another investigational tool," he says, "one that can help corroborate the testimony of a witness or reduce the number of suspects."

Getting more specific gets significantly more difficult, Podini adds. DNA alone offers few clues to age, for instance. With whole cells, researchers could examine telomeres, the chromosomal end caps that wear away with time, but individual health and other factors can influence their shrinkage. One recent study showed that dedicated athletes in their 50s might have the telomeres of a 25-year-old. Another important feature in profiling, height, has hereditary roots but also depends on environmental factors, such as nutrition during childhood.

Nevertheless, pinning down the effects of genes that influence

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RECONSTRUCTED: **Ancient DNA provided details about the looks of a man who lived in Greenland more than 4,000 years ago.**

FROM "ANCIENT HUMAN GENOME SEQUENCE OF AN EXTINCT PALAEO-ESKIMO," BY MORTEN RASMUSSEN ET AL., IN *NATURE*, VOL. 463; FEBRUARY 11, 2010 (*man*); PHOTO RESEARCHERS, INC. (*Earth's magnetic field*)

body development is the key to predicting a specific individual's looks. Shriver is studying populations in Europe and mixed-race groups elsewhere in the hope that correlating a Gallic nose or smiling Irish eyes with genes that influence their distinctive shapes may begin to crack the code the body uses to build a specific feature. He is even exposing inch-square patches of volunteers' skin to ultraviolet light to gauge the range of skin shades and tones possible for people with various racial and ethnic backgrounds.

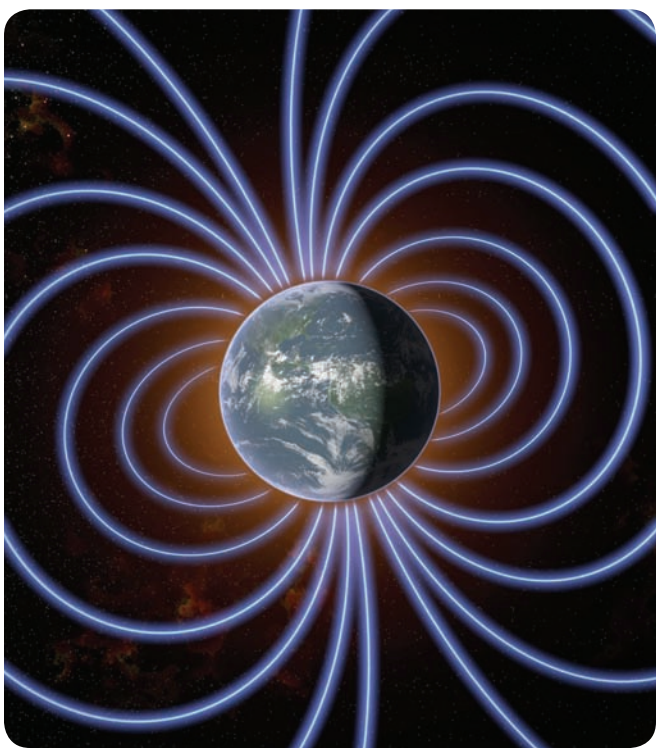
Skin-deep is as far as a DNA sketch should go, according to some bioethicists. The ancient Greenlander also had an elevated risk for hypertension and diabetes. A modern all-points bulletin could, in principle, describe a suspect's pigmentation, ancestry, and higher-than-average likelihood of being obese, a smoker, alcoholic or just depressed. "I think there are some valid ethical issues around this kind of work," Shriver remarks.

Practical considerations may be what delays deployment of any but the simplest forensic kits, though. "The forensic field is very, very conservative," Podini says, "so before you actually apply something to casework, it has to be proven beyond a reasonable doubt as something that works well, is reliable and is accepted by the scientific community."

Shields Up

Magnetized rock sets start of magnetic field closer to life's origin BY JOHN MATSON

EARTH'S ROBUST MAGNETIC FIELD PROTECTS THE PLANET AND its inhabitants from the full brunt of the solar wind, a torrent of charged particles that on less shielded planets such as Venus and Mars has over the ages stripped away water reserves and degraded their atmospheres. Unraveling the timeline for the emergence of that magnetic field and the mechanism that generates it—a dynamo of convective fluid in Earth's outer core—can help constrain the early history of the planet, including the interplay of geologic, atmospheric and astronomical processes that rendered the world habitable.



LINES OF DEFENSE: **New evidence suggests that Earth's magnetic field, which protects the planet from the full force of the solar wind, got going about 3.45 billion years ago, about when life began.**

University of Rochester geophysicist John A. Tarduno and his colleagues have attempted to do just that, presenting evidence that Earth had a dynamo-generated magnetic field as early as 3.45 billion years ago, just a billion or so years after the planet had formed. The new research, in the March 5 *Science*, pushes back the record of Earth's magnetic field by at least 200 million years; a related group had presented similar evidence from slightly younger rocks in 2007, arguing for a strong terrestrial magnetic field 3.2 billion years ago.

Tarduno and his team analyzed rocks from the Kaapvaal craton, a region near the southern tip of Africa that hosts relatively pristine early Archean crust. (The Archean eon began about 3.8 billion years ago and ended 2.5 billion years ago.) In 2009 they had found that some of the rocks were magnetized 3.45 billion years ago—roughly coinciding with the direct evidence for Earth's first life, at 3.5 billion years ago. But an external source for the magnetism—such as a blast from the solar wind—could not be ruled out. Venus, for instance, which lacks a strong internal magnetic field, does have a feeble external field induced by the impact of the solar wind into the planet's dense atmosphere.

The new study examines the magnetic field strength required to imprint magnetism on the Kaapvaal rocks; it concludes that the field was 50 to 70 percent of its present strength. That value is many times greater than would be expected for an external magnetic field, such as the weak Venusian field, supporting the presence of an inner-Earth dynamo at that time.

The researchers then extrapolated how well that field could keep the solar wind at bay and found that the early Archean magnetopause, the boundary in space where the magnetic field meets

the solar wind, was about 30,000 kilometers or less from Earth. The magnetopause is about twice that distance today but can shift in response to extreme energetic outbursts from the sun. "Those steady-state conditions 3.5 billion years ago are similar to what we see during severe solar storms today," Tarduno says. With the magnetopause so close, Earth would not have been totally shielded from the solar wind and may have lost much of its water early on.

As efforts accelerate to find Earth-like planets outside the solar system, Tarduno says the relation between stellar wind, atmospheres and magnetic fields should come into play when modeling a planet's potential habitability. He points out that a magnetic field's impact on a planet's water budget seems particularly important.

Peter A. Selkin, a geologist at the University of Washington Tacoma, finds the work engaging and the results plausible, although he notes that even the relatively pristine rocks of the Kaapvaal craton have undergone low-grade mineralogical and temperature changes over billions of years. "They're not exactly in the state they were in initially," Selkin says. "I think that there are still things that we need to know about the minerals that Tarduno and his co-authors used in this study to be able to completely buy the results."

David J. Dunlop, a geophysicist at the University of Toronto, is more convinced, calling the work a "very careful demonstration." The field strengths, he says, "can be assigned quite confidently" to the interval 3.4 billion to 3.45 billion years ago. "It would be exciting to push back the curtain shadowing [the] onset of the geodynamo still further, but this seems unlikely," Dunlop adds. Nowhere else in the world, he says, has nature been so kind in preserving nearly pristine carriers of ancient magnetism.

Cold Snap: A Secret of the Chameleon's Tongue Revealed

When the weather cools, cold-blooded animals slow down, which should be good news for their potential prey. But the colorful chameleon, which can unfurl a tongue twice its body length in 0.07 second, does not lose much speed in unleashing its weapon.

To find out why, Christopher Anderson and Stephen Deban of the University of South Florida tested chameleons under different conditions, discovering that if temperatures dropped 10 degrees Celsius, tongue snaps slowed only by about 10 to 19 percent. The secret lies in the collagen tissue of the tongue, which uncoils based on momentum, not muscle activity. In contrast, under the same chilly conditions, the tongue movements of ectotherms, which rely fully on a muscle-based system, slowed by 42 percent.

The lizards, however, were not quite as quick to reel in their prey; the recoiling action, which depends on muscle contraction, fell by 42 to 63 percent. Considering that some chameleons inhabit locations where temperatures dip below freezing, the findings, described online March 8 in the *Proceedings of the National Academy of Sciences USA*, explain how the lizards can maintain such an extensive feeding niche. *—Katherine Harmon*

STEPHEN DALTON *Photo Researchers, Inc.*

Carbs against Cardio

More data that refined carbohydrates, not fats, threaten the heart

BY MELINDA WENNER MOYER

EAT LESS SATURATED FAT: THAT HAS BEEN THE take-home message from the U.S. government for the past 30 years. But while Americans have dutifully reduced the percentage of daily calories from saturated fat since 1970, the obesity rate during that time has more than doubled, diabetes has tripled, and heart disease is still the country's biggest killer. Now a spate of new research, including a meta-analysis of nearly two dozen studies, suggests a reason why: investigators may have picked the wrong culprit. Processed carbohydrates, which many Americans eat today in place of fat, may increase the risk of obesity, diabetes and heart disease more than fat does—a finding that has serious implications for new dietary guidelines expected this year.

In March the *American Journal of Clinical Nutrition* published a meta-analysis—which combines data from several studies—that compared the reported daily food intake of nearly 350,000 people against their risk of developing cardiovascular disease over a period of five to 23 years. The analysis, overseen by Ronald M. Krauss, director of atherosclerosis research at the Children's Hospital Oakland Research Institute, found no association between the amount of saturated fat consumed and the risk of heart disease.

The finding joins other conclusions of the past few years that run counter to the

CHRISTOPHER STEVENSON *Getty Images*

STACKED ODDS: **This year U.S. dietary guidelines may target refined carbohydrates, which increase the risk for cardiovascular disease.**

conventional wisdom that saturated fat is bad for the heart because it increases total cholesterol levels. That idea is "based in large measure on extrapolations, which are not supported by the data," Krauss says.

One problem with the old logic is that "total cholesterol is not a great predictor of risk," says Meir Stampfer, a professor of nutrition and epidemiology at the Harvard School of Public Health. Although saturated fat boosts blood levels of "bad" LDL cholesterol, it also increases "good" HDL cholesterol. In 2008 Stampfer co-authored a study in the *New England Journal of Medicine* that followed 322 moderately obese individuals for two years as they adopted one of three diets: a low-fat, calorie-restricted diet based on American Heart Association guidelines; a Mediterranean, restricted-calorie diet rich in vegetables and low in red meat; and a low-carbohydrate, nonrestricted-calorie diet. Although the subjects on the low-carb diet ate the most saturated fat, they ended up with the healthiest ratio of HDL to LDL cholesterol and lost twice as much weight as their low-fat-eating counterparts.

Stampfer's findings do not merely sug-

One's Enough: Kidney Donors Live Just as Long as Nondonors

Every 30 minutes all the blood in our bodies is filtered through two kidneys. But diabetes can cause these fist-size organs to fail, leading to a buildup of chemicals in the blood that would be fatal without dialysis or a kidney transplant.

At least 6,000 healthy people every year in the U.S. donate a kidney to someone they know, and about 100 more come forward to anonymously give the gift of glomeruli (the basic filtration units of the kidney). It's true that you only need one kidney to live, but the operation required to remove its twin and the risk of disease developing in the remaining one later on make donation a serious decision.

Transplant surgeon Dorry Segev of the Johns Hopkins University School of Medicine studied mortality among 80,000 kidney donors during the past 15 years, comparing them with healthy people who have both kidneys. The study, published March 10 in the *Journal of the American Medical Association*—60 years after the first kidney transplant in the U.S.—found no increase in mortality among donors once they recover from the operation.

Although donors are carefully screened before the procedure, Segev emphasizes that there are risks: "It's still a major operation. You're still living with one kidney. People still need to think about it and be aware of the risks in taking on this heroic act." —*Katie Moisse*

DONATING A KIDNEY does not appear to shorten life span.

MICHELLE DEL GUERCIO *Photo Researchers, Inc.*

gest that saturated fats are not so bad; they indicate that carbohydrates could be worse. A 1997 study he co-authored in the *Journal of the American Medical Association* evaluated 65,000 women and found that the quintile of women who ate the most easily digestible and readily absorbed carbohydrates—that is, those with the highest glycemic index—were 47 percent more likely to acquire type 2 diabetes than those in the quintile with the lowest average glycemic-index score. (The amount of fat the women ate did not affect diabetes risk.) And a 2007 Dutch study of 15,000 women published in the *Journal of the American College of Cardiology* found that women who were overweight and in the quartile that consumed meals with the highest average glycemic load, a metric that incorporates portion size, were 79 percent more likely to develop coronary vascular disease than overweight women in the lowest quartile. These trends may be explained in part by the yo-yo effects that high glycemic-index carbohydrates have on blood glucose, which can stimulate fat production and inflammation, increase overall caloric intake and lower insulin sensitivity, says David Ludwig, director of the obesity program at Children's Hospital Boston.

Will the more recent thinking on fats and carbs be reflected in the 2010 federal Dietary Guidelines for Americans, updated once every five years? It depends on the strength of the evidence, explains Robert C. Post, deputy director of the U.S. Department of Agriculture's Center for Nutrition Policy and Promotion. Findings that "have less support are put on the list of things to do with regard to more research." Right now, Post explains, the agency's main message to Americans is to limit overall calorie intake, irrespective of the source. "We're finding that messages to consumers need to be short and simple and to the point," he says. Another issue facing regulatory agencies, notes Harvard's Stampfer, is that "the sugared beverage industry is lobbying very hard and trying to cast doubt on all these studies."

Nobody is advocating that people start gorging themselves on saturated fats, tempting as that may sound. Some monounsaturated and polyunsaturated fats, such as those found in fish and olive oil, can protect against heart disease. What is more, some high-fiber carbohydrates are unquestionably good for the body. But saturated fats may ultimately be neutral compared with processed carbs and sugars such as those found in cereals, breads, pasta and cookies.

"If you reduce saturated fat and replace it with high glycemic-index carbohydrates, you may not only *not* get benefits—you might actually produce harm," Ludwig argues. The next time you eat a piece of buttered toast, he says, consider that "butter is actually the more healthful component."

Melinda Wenner Moyer is based in New York City.

Genetics in the Gut

Intestinal census suggests how microbes can drive obesity and other metabolic ills BY KATHERINE HARMON

Outnumbering our human cells by about 10 to one, the many minuscule microbes that live in and on our bodies are a big part of crucial everyday functions. The lion's share live in the intestinal tract, where they help to fend off bad bacteria and aid in digestion. But as scientists determine what microbes are actually present and what they are doing, they are discovering that the bugs play an even larger role in human health than previously suspected—and perhaps at times exerting more influence than genes themselves.

A team that included Junjie Qin and Jun Wang of BGI-Shenzhen (formerly the Beijing Genomics Institute) completed a catalogue of some 3.3 million human gut microbe genes. The work, published in the March 4 *Nature,* adds to the expanding—but nowhere near complete—census of intestinal species. (*Scientific American* is part of Nature Publishing Group.)

The 3.3 million genes were a good deal "more than what we originally expected," Wang says. The number was especially surprising given that the microbiota tended to be very similar across the 124 individuals the scientists sampled in Denmark and Spain. The team sequenced 576 billion base pairs, much larger than past work that found three billion base pairs. "These bacteria have functions that are essential to our health: they synthesize vitamins, break down certain compounds—which cannot be assimilated by our body—[and] play an important role in our immune system," Wang points out.

Another group, led by Andrew Gewirtz of Emory University, turned its attention to a particular host gene that seems to affect these intestinal inhabitants. It found that in mice, a loss of one key gene led to a shift in microbiota communities and a rise in insulin resistance, obesity and other symptoms of so-called metabolic syndrome (a cluster of these conditions).

Gewirtz and his co-workers studied mice bred with the genetic deficiency: an absence of Toll-like receptor 5, or TLR5, which has a hand in immune response. They wanted to see how it might change microbial gut communities and metabolic health—and try to understand the order in which the changes were happening. "Obesity is associated with insulin resistance and type 2 diabetes," Gewirtz says. But "which comes first is not entirely clear."

As the researchers described in their paper published online March 4 by *Science,* they found that mice without the TLR5 gene—even when put on restricted diets—still showed insulin resistance, suggesting that the condition might lead to obesity rather than the other way around. But if these mice were allowed to eat as they pleased, they consumed 10 percent more than their peers and, by 20 weeks old, had body mass indexes that were 20 percent higher.

Many researchers and public health officials have blamed the availability (and content) of contemporary foods, increasingly sedentary lifestyles and human genetics for the increase in metabolic syndrome cases. But the mouse study suggests that there might be more to the picture. "The tendency to overeat may be underlain by changes that are more likely physiological," Gewirtz says.

Gewirtz and others propose that inflammation—in conjunction with changes in the gut microbiome—might be driving the cycle. Inflammation can change the character of the gut microbes, in some cases allowing more calories to be extracted from food. But, Gewirtz says, "we do not know which is coming first," if inflammation is changing the microbiota, or vice versa. He also believes that the findings will carry over to people and has already started an investigation comparing the genes and microbial profiles of individuals who have metabolic syndrome with those of healthy controls.

Although a fuller grasp of microbial genetics promises to boost wellness even fur-

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ther, plenty of big unknowns remain. Scientists are still unsure just how and when these communities of microbes establish themselves in each person's gut. "Everyone is born sterile," Gewirtz says, noting that colonization starts during birth, but when it reaches relative stability is not known. If gut microbiota strongly contribute to diseases, then a recent change in these communities might help explain the expansion of the patient populations—and waistlines—in developed countries.

Wang and his colleagues are already attempting to track the composition of human gut microbiota back in time. But they have their sights set on even bigger collections of genetic data. "Our dream is to build a library" of reference genomes, Wang says. And, he notes, as soon as more definitive data about these gut genetics emerge, microbial-targeted therapeutics will likely be quick to follow.

Energy & Environment

Sex-Changing Weed Killer

Widely used herbicide atrazine disrupts frogs' sexual development

BY DAVID BIELLO

The bountiful fields of the U.S. are awash in atrazine. About 36 million kilograms of the odorless, white powder are applied on farms to control grassy weeds. Every year some 225,000 kilograms of the herbicide become airborne and fall with the rain, up to 1,000 kilometers from the source. All that atrazine may have a sexual effect: turning male frogs female.

As described in the March 1 *Proceedings of the National Academy of Sciences USA*, biologist Tyrone Hayes of the University of California, Berkeley, and his colleagues exposed 40 African clawed frogs (*Xenopus laevis*) to 2.5 parts per billion (ppb) of atrazine continuously for three years—a level below the 3 ppb allowed in drinking water by the Environmental Protection Agency. As a result, 30 of the frogs were chemically castrated, incapable of reproducing, among other consequences. Also, four of the treated frogs actually turned female, going so far as to mate with other males and produce viable eggs despite being genetically male. Only six of the treated frogs resisted atrazine or at least showed normal sexual behavior.

To be sure of their results, the research-

SEXUAL BIAS: African clawed frogs may change sex when exposed to a herbicide.

TOM McHUGH *Photo Researchers, Inc.*

ers used males bearing only the ZZ sex chromosomes. In previous studies "if we got hermaphrodites, there was no way to know if they were males with ovaries or females with testes," Hayes says. "By using all ZZ males, we were assured that any hermaphrodites or females were indeed sex-reversed males." Frogs follow the ZZ (male), ZW (female) sex determination scheme, rather than the more familiar XX (female), XY (male) pattern of humans.

A key culprit in the sex change may be aromatase, a protein that spurs the production of the female hormone estrogen, causing originally male gonads to become ovaries. Atrazine may be boosting the production of aromatase.

Hayes has a long history of studying atrazine, starting in the 1990s with research funded by its maker, now known as Syngenta, which first raised the prospect that the herbicide might be interfering with the natural hormones of animals, including humans. A barrage of studies on

IPCC Errors Prompt a Review on Climate Science Data

HIMALAYAN GLACIERS will probably stay icy during the next few decades.

ALAN KEARNEY *Getty Images*

African crop yields wither, along with the Amazon rain forest; Himalayan glaciers disappear by 2035. These are the erroneous predictions ascribed to the most recent report from the United Nations Intergovernmental Panel on Climate Change (IPCC)—a document reviewed by some 2,500 scientists and other experts as well as vetted by officials from more than 190 countries. So do the few errors in a report exceeding 3,000 pages merit a revision of IPCC processes?

That question will face a panel to be assembled by the InterAcademy Council (IAC) in Amsterdam, a composite board of many of the world's national scientific bodies, including the National Academy of Sciences in the U.S. "This will be an independent review," says physicist Robbert Dijkgraaf, president of the Royal Netherlands Academy of Arts and Sciences and IAC co-chair, about the evaluation requested by the U.N. and the IPCC. "We are ready to take on the important task of assuring nations around the world that they will receive sound climate advice."

The IAC hopes to have the panel's report by August. The U.N. will provide financial support for travel and meeting expenses, but the work of the review will be done for free. The panel will definitely not go through "the vast amount of data in climate science," Dijkgraaf explains. "What it will do is see what the procedures are and how they can be improved. How can we avoid, perhaps, that certain types of errors are not made?"

Dijkgraaf should know. After all, one of the IPCC errors came as a result of information provided directly by the Dutch government about the percentage of the Netherlands that lies below sea level and is therefore vulnerable to flooding from rising seas. The government corrected the percentage in a subsequent statement, from 55 to 26 percent of the country as lying below sea level.

The panel will also determine how the IPCC treats the multiplicity of opinions within various domains of climate science, such as oceanographers who disagree on the rate of sea-level rise. "We were specifically asked in our review to analyze how the IPCC deals with diverse scientific perspectives," Dijkgraaf says. "Any science goes through periodic outside review. It only strengthens the science." —*David Biello*

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such endocrine disruption has followed—some confirming that amphibians such as frogs are suffering from an atrazine onslaught, others finding no effect and others even uncovering evidence of reduced sperm count in men from agricultural regions. Atrazine and other herbicides can be found in 57 percent of U.S. streams, according to the U.S. Geological Survey.

Hayes's sex-changing experiment, however, is not without criticism. Biologist Werner Kloas of Humboldt University in Berlin charges that samples may have been contaminated by endocrine disruptors such as bisphenol A (BPA) leaching from plastic containers or being introduced during screening. He also questions the single exposure level and lack of measurement of female hormone levels in the affected frogs. For his part, Kloas in the past reviewed atrazine's effects for Syngenta and found no impact on African clawed frogs at concentrations comparable to those investigated by Hayes.

In their native habitats, African clawed frogs do not appear to be suffering from the herbicide. "Atrazine has been used widely in South Africa for the past 45 years, and our studies showed that *Xenopus* are doing equally fine in agricultural and nonagricultural areas," says zoologist Louis du Preez of North-West University in South Africa. "If atrazine had these adverse effects on *Xenopus* in the wild, surely we would have picked it up by now."

Nevertheless, the European Union has banned atrazine because of its ability to contaminate water. "I personally prefer our European habit to use the precautionary principle concerning environmental chemicals to phase out persistent compounds," Kloas says.

After declaring the chemical treatment safe in 2006, the EPA announced yet another review of the herbicide last October because of human health concerns. The chemical, after all, affects many species. "Atrazine increases aromatase and/or estrogen production in zebra fish, goldfish, caimans, alligators, turtles, quail and rats," Hayes points out. "So this is not just a frog problem."

Technology

More Food from Fungi?

Crop-enhancing microbes challenge genetic engineering

BY MICHAEL TENNESEN

To feed an exploding global population, scientists have called for a doubling of food production over the next 40 years. Genetic manipulation might seem the best way to quickly boost characteristics essential to plant growth and crop yields. New findings from different laboratories, however, suggest that fungi, bacteria and viruses could be an exciting alternative to increase agricultural productivity.

Scientists have long known that microbes can work symbiotically with plants. For instance, mycorrhizal fungi, which are associated with 90 percent of land plants, extend from roots to bring in moisture and minerals in exchange for plant carbohydrates. But microbes have recently been found among plant cells themselves and seem to confer benefits, such as more efficient photosynthesis and increased ability to fix nitrogen from the air. In fact, Mary E. Lucero, a biologist at the U.S. Department of Agriculture's Jornada Experimental Range in Las Cruces, N.M., believes that plants actively recruit these microbes rather than simply being passive hosts for them.

In the lab, Lucero has given this recruitment a hand by transferring fungi from four-wing saltbush to grama grass, which is important for grazing cattle. The fungi-infused grass grew larger and produced more seed, probably by improving nutrient uptake and water usage, she speculates. Lucero also points out that harnessing microbial help for capturing nitrogen

could reduce the need for chemical fertilizers. "It is far easier, more efficient and less expensive to inoculate a plant with a beneficial fungi than to come up with a genetically modified species," she remarks.

Rusty Rodriguez, a microbiologist with the U.S. Geological Survey's Biological Resources Division in Seattle, is trying to tackle another agricultural demon: excessive heat. In experiments to improve the ability of tomato plants to resist high temperatures, he inoculated them with fungi taken from plants near hot springs in Yellowstone National Park. The result: tomatoes that can grow at 148 degrees Fahrenheit. "That's about the internal temperature of a medium cooked prime rib," Rodriguez notes.

FUNGAL HELP: Grasses that serve as food for grazing cows have been coaxed to grow larger when injected with certain fungi.

Furthermore, by isolating a virus in the fungus, he discovered a three-way symbiosis that was required for thermal tolerance. "Without the virus the plants could handle only about 100 degrees F," Rodriguez says. The fungus and virus also conveyed heat tolerance to rice and wheat, a process that could not only boost yields but also help crops fend off the effects of climate change.

Analyzing plants from beaches, deserts and polluted areas, Rodriguez has also isolated microbes that help plants resist salt, drought and heavy metals. Curiously, the same fungi taken from plants living in unstressed areas did not confer tolerance. "It has to be the right microbe from the right habitat," Rodriguez says. Choosing microbes from heat-stressed areas could boost rice production, which drops 10 percent for every 1.8 degrees F of warming. Once acquired, however, stress-tolerant microbes can be passed in seed coatings to the plant's progeny.

Christopher L. Schardl, a plant pathologist at the University of Kentucky who studies certain species of tall fescue grass, observes that the mutualism between microbes and plants has agricultural drawbacks, too. Many microbes in plants produce biologically active alkaloids, which repel insects, birds and herbivores. In fact, in the early 1950s grazing livestock picked up a disease related to alkaloids in grass known as fescue toxicosis. It can induce tremor and stupor, as well as an aversion to further grazing. "It costs the livestock industry about $1 billion a year," says Schardl, adding that producers raising grass-fed cattle are now sowing cultivars with nontoxic fungi.

Identifying plant microbes is not easy, because microbial cells are embedded in plant tissue. Lucero uses scanning electron microscopy and new pyrosequencing techniques to identify the DNA of microbes in plant tissue.

The intensive effort, Rodriguez believes, will pay off by helping farmers meet future food demands. Modifying traits genetically is expensive, does not always work and generates a fair amount of consumer backlash. Improving crop production with the plant's own microorganisms might be more successful on a host of fronts. Says Rodriguez: "We're trying to duplicate the way it works in nature—using not genes but entire genomes from the plant's own microbial community."

Michael Tennesen is a science writer based near Los Angeles.

PET Project: Organic Catalysts Could Increase Plastics Recycling

Most discarded plastic beverage bottles can be recycled—those imprinted with a number 1 within a triangular arrow. Yet the resulting second-generation plastic is generally unusable for making new containers. Now researchers have devised a way to manufacture plastic bottles that would increase their recycling life span.

The problem with bottles made from polyethylene terephthalate (PET) thermoplastic is that the manufacturing process often needs metal oxide or metal hydroxide catalysts. These catalysts linger in the recycled material and weaken it over time, making it impractical to reuse for a third generation. Instead second-generation PET ends up in less demanding applications, such as carpets and fiberfill for coats and sleeping bags. Or it ends up as trash. In the U.S., nearly 24 billion plastic beverage containers have been incinerated, dumped in landfills or discarded as litter within the first three months of this year, according to the nonprofit Container Recycling Institute in Culver City, Calif.

A team of scientists at the IBM Almaden Research Center in San Jose, Calif., and Stanford University reports in the February 16 *Macromolecules* that it has created a family of organic catalysts that could be used to make plastics fully biodegradable and recyclable. The researchers write that organic catalysts can rival even highly active metal-based catalysts while being environmentally benign. They also believe this research might lead to a recycling process that could break polymers back down into their constituent monomers for reuse.

—Larry Greenemeier

MICHAEL BLANN *Getty Images (cow grazing)*; JOHN BLOCK *Getty Images (plastic bottles)*

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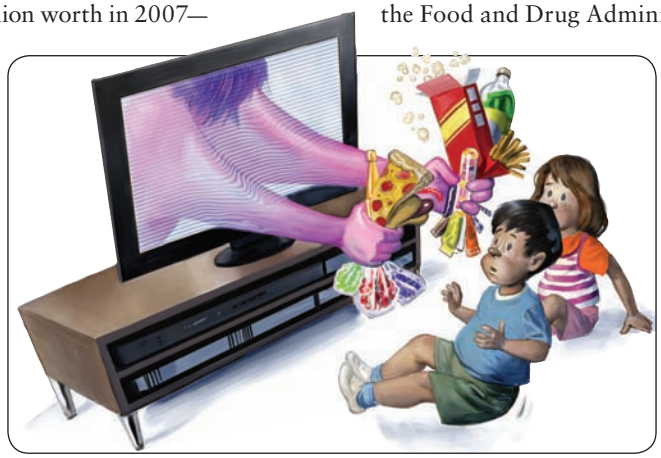
Underage, Overweight

The federal government needs to halt the marketing of unhealthy foods to kids

BY THE EDITORS

The statistic is hard to swallow: in the U.S., nearly one in three children under the age of 18 is overweight or obese, making being overweight the most common childhood medical condition. These youngsters are likely to become heavy adults, putting them at increased risk of developing cardiovascular disease, type 2 diabetes and other chronic ailments. In February, First Lady Michelle Obama announced a campaign to fight childhood obesity. Helping parents and schools to instill healthier habits in kids is an important strategy in this battle. But the government must take further steps to solve the problem.

In an ideal world, adults would teach children how to eat healthily and would lead by example. But in reality, two thirds of U.S. adults are themselves overweight or obese. Moreover, the food and beverage industry markets sugar- and fat-laden goods to kids directly—through commercials on television, product placement in movies and video games, and other media. Its considerable efforts—nearly $1.7 billion worth in 2007—have met with sickening success: a recent study conducted by researchers at the University of California, Los Angeles, found that children who see more television ads tend to become fatter. You might expect that watching TV, being a sedentary activity, is responsible for obesity, but the study found that obesity is correlated not with television per se but with advertising. The more commercial programming children watched, the fatter they got compared with those who watched a comparable amount of public television or DVDs. The majority of products marketed during children's programming are foods.



As nutritionist Marion Nestle of New York University has written, society needs to "create a food environment that makes it easier for parents and everyone else to make better food choices." Protecting children from junk-food marketing would help create conditions conducive to achieving a healthy weight.

Unfortunately, like the tobacco industry before it, the food industry cannot be trusted to self-regulate in this regard. In a study published in the March *Pediatrics,* investigators looked at the prevalence of food and beverage brands in movies released between 1996 and 2005. They noted, for instance, that although Coca-Cola and PepsiCo have pledged to not advertise during children's television programming, their products routinely appear in movies aimed at kids.

Likewise, in the March *Public Health Nutrition,* researchers reported a 78 percent increase from 2006 to 2008 in the use of cartoon characters, toys and other child-oriented cross promotions on food packaging—much of it for nutritionally bereft foods. A whopping 65 percent of these cross promotions came from food manufacturers that have opted into the Children's Food and Beverage Advertising Initiative, sponsored by the Council of Better Business Bureaus, which promises to limit advertising to kids but allows participants to decide for themselves whether to restrict in-store marketing. Such examples of ineffectual commitments on the part of the food industry abound.

In December a group of U.S. agencies—the Federal Trade Commission, the Centers for Disease Control and Prevention, the Food and Drug Administration, and the Department of Agriculture—proposed standards for foods and beverages that are marketed to children between the ages of two and 17. The agencies sensibly recommended that such foods must provide a meaningful contribution to a healthy diet by meeting specified requirements; that the amounts of saturated fat, trans fat, sugar and salt in these foods must not exceed limits set by the group; and that certain clearly healthy foods—such as those that are 100 percent fruits, vegetables or whole grains—may be marketed to kids without meeting the other two standards.

The interagency working group is due to submit a report containing its final recommendations to Congress by July 15. The standards are worthy but have one problem: as they stand, they would be voluntary. They should be mandatory, not optional, and the FDA should implement and enforce them.

The estimated cost of treating obesity-related ailments in adults was $147 billion for 2009. With the health care system already faltering, allowing companies to decide for themselves whether to peddle junk food to kids is a fox-and-henhouse policy this country simply cannot afford any longer. ■

ILLUSTRATION BY MATT COLLINS

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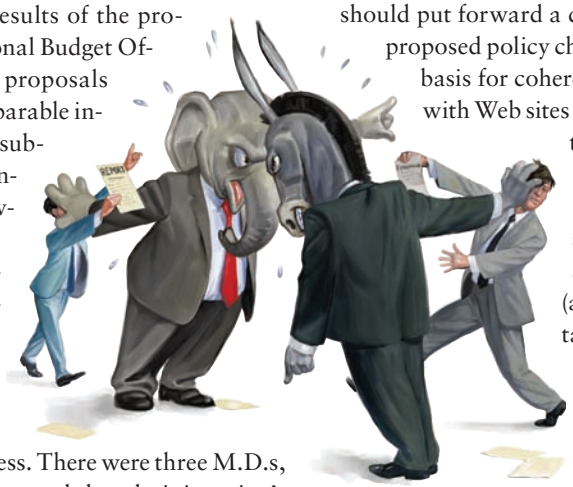
Flying Blind in Policy Reforms

Health care, climate change and other complex topics demand more expert and public debate

BY JEFFREY D. SACHS

The long and divisive fight over U.S. health care reform exposed basic weaknesses in the processes of governance. As is so often true in American politics these days, politicians and lobbyists kept complex subjects to themselves, pushing expert discussion and systematic public debate to the sidelines. Although the final legislation expands coverage, and I favor it for that reason, it falls far short of the changes we need to lower costs and improve health outcomes.

During 14 months of debate over health care, the administration did not put forward a clear, analytical policy white paper on the aims, methods and expected results of the proposed reforms. Only the Congressional Budget Office's budget scoring of legislative proposals was even partly systematic; no comparable independent analysis exists on other substantive issues. The actual health consequences of the legislation were never reviewed or debated coherently.



The one-day Health Care Summit in February epitomized the problem. The president, the vice president, the secretary of Health and Human Services and the president's health czar (a lawyer) were together with 38 members of Congress. There were three M.D.s, all Republican congressmen who opposed the administration's plans, but no public health specialists, health economists, speakers for civil society, leaders of health maintenance organizations or representatives of other health care organizations. The debate was all about who would pay for what, not about how to organize health delivery to achieve better, lower-cost outcomes.

One might think that the real action had all happened earlier, in congressional hearings, in brainstorming sessions and in the bargaining sessions with key stakeholders. Yet the earlier process was relentlessly driven by political and lobbying calculations and without the informed participation of the American people, who were left to vent at Tea Parties and on blog sites. The mammoth legislation is impenetrable, a widely noted fact. Experts were never invited systematically to comment or debate about it so as to help the public and politicians understand the issues. The lack of clear policy documents from the administration meant that the public had little basis for reaction other than gut instincts and fearful sentiments fanned by talk-show hosts.

In general, our political system regularly puts around the table people who are not the best equipped to find deep solutions to our problems. Certainly it has also done so on climate change, with the nation's expert community kept at arms length from the legislative drafting process. As with health care, the outcome has been House and Senate draft legislation that lacks public support. The same has been true on Afghanistan: the "war cabinet" has lacked real expertise on that country's culture, economy and development challenges, and the U.S. public has remained uninformed of true options.

As a start toward better policy making, the administration should put forward a detailed analysis justifying each major proposed policy change. That white paper could form the basis for coherent public debate and reflection, along with Web sites where outside experts would be invited to share opinions accessible to the public. The public, too, would be invited to blog about that position paper. A version of the draft legislation understandable to lay readers would also be posted (alongside the more technical and inevitable legalese) and opened to online commentaries by experts and the public. The administration and Congress would rely more heavily on external advisory panels to tap into the nation's wealth of expertise and to draw on the views of business, academia and other sectors of society.

In our governance systems today, the intrinsic complexity of the challenges easily outpaces the gut instincts and amateurism of the existing government machinery. I would not presume or recommend that decisions be left to the purported experts, who often represent special interests or have their own biases or narrow views. Still, a systematic vetting of policy options, with recognized experts and the public commenting and debating, will vastly improve on our current policy performance, in which we often fly blind or hand the controls over to narrow interests and viewpoints. ■

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

SCI AM An extended version of this essay is available at **www.ScientificAmerican.com/may2010**

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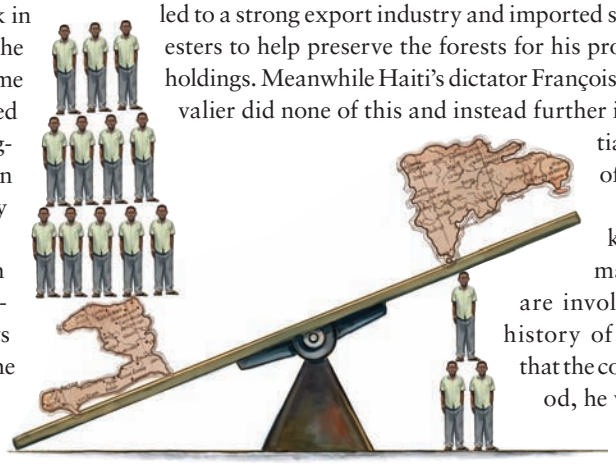
Doing Science in the Past

The comparative method of historical science helps to explain Haiti's poverty

BY MICHAEL SHERMER

History is not often thought of as a science, but it can be if it uses the "comparative method." Jared Diamond, professor of geography at the University of California, Los Angeles, and James A. Robinson, professor of government at Harvard University, employ the method effectively in the new book they have co-edited, *Natural Experiments of History* (Harvard University Press, 2010). In a timely study comparing Haiti with the Dominican Republic, for example, Diamond demonstrates that although both countries inhabit the same island, Hispaniola, because of geopolitical differences one ended up dirt poor while the other flourished.

Christopher Columbus's brother Bartolomeo colonized Hispaniola in 1496 for Spain, establishing the capital at Santo Domingo on the eastern side of the island. Two centuries later, during tensions between France and Spain, the Treaty of Ryswick in 1697 granted France dominion over the western half of the island. Because France was richer than Spain at this time and slavery was an integral part of its economy, it turned western Hispaniola into a center of slave trade with staggering differences in population: about 500,000 slaves in the western side of the island as compared with only 15,000 to 30,000 slaves in the eastern side.



That difference in population pressures, along with France's hunger to import more timber from Haiti, magnified the influence of geographic factors. Weather fronts for Hispaniola come from the east and dump rain on the Dominican side of the island, leaving the Haitian side naturally drier and with less fertile soils for agricultural productivity. Haiti's need for farmland and timber rapidly deforested the already sparse trees on its side of the island, with disastrous consequences: soil erosion, loss of timber for building and of wood for charcoal fuel, heavier sediment loads in rivers and decreased watershed protection that reduced the potential for hydroelectric power. This negative feedback cycle of environmental degradation for Haiti set it up for squalor.

When both the Haitians and Dominicans gained their independence in the 19th century, we see other comparative differences. Haitian slave revolts were violent, and Napoleon's draconian intervention for restoring order resulted in the Haitians distrusting Europeans and eschewing future trade and investments, imports and exports, immigration and emigration. Haitian slaves had also developed their own Creole language spoken by no one else in the world, which further isolated Haiti from cultural and economic exchanges. Collectively, those barriers meant that Haiti did not benefit from factors that typically build capital, wealth and affluence and that might have led to prosperity under independence. In contrast, Dominican independence was relatively nonviolent; the country shuttled back and forth for decades between independence and control by Spain, which in 1865 decided that it no longer wanted the territory. Throughout this period the Dominicans spoke Spanish, developed exports, traded with European countries, and attracted European investors, as well as a diverse émigré population of Germans, Italians, Lebanese and Austrians, who helped to build a vibrant economy.

Finally, even when both countries succumbed to the power of evil dictators in the mid-20th century, Rafael Trujillo's control of the Dominican Republic involved considerable economic growth because of his desire to enrich himself personally, but his policies led to a strong export industry and imported scientists and foresters to help preserve the forests for his profiteering timber holdings. Meanwhile Haiti's dictator François "Papa Doc" Duvalier did none of this and instead further isolated the Haitians from the rest of the world.

Diamond acknowledges that many other factors are involved in the long history of this island but that the comparative method, he writes, "consists of comparing—preferably quantitatively and aided by statistical analyses—different systems that are similar in many respects but that differ with respect to the factors whose influence one wishes to study."

At the heart of all science is the isolation of a handful of powerful factors that account for the majority of the variance in what is being measured. Employing the comparative method with such natural experiments of history is no different from what sociologists and economists do in comparing natural experiments of society today. So it is time for scientists to respect history as a science and for historians to test their historical hypotheses by the comparative method and other techniques. ■

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

PHOTOGRAPH BY BRAD SWONETZ; ILLUSTRATION BY MATT COLLINS

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Human Uniqueness and the Future

We must adjust to our unparalleled ability to shape the world's evolution

BY LAWRENCE M. KRAUSS

What is human uniqueness, and how did it contribute to what we could now call behavioral modernity? How did it develop? And what implications does it have for understanding our present and future? This past February the Origins Project that I direct at Arizona State University helped to convene an interesting meeting of paleontologists, anthropologists, primatologists, evolutionary biologists, geneticists, archaeologists and psychologists to attempt to address such questions, among others.

I began the meeting by pointing out that when some people heard about its subject, they had asked me what was so unique about humans? Surely all animals are unique in their own way, and although we have special traits, so do bees and giraffes. But as my A.S.U. colleague Kim Hill has put it, "Even before the invention of agriculture, human communities may have eventually numbered around 70 million individuals … as *Homo sapiens* spread over the planet more broadly than any other large vertebrate. No creature on earth lives in cohesive social units that rival this complexity or biomass."

And spread over the planet we have. Several months ago in this column I commented on our species's capacity to breach, and sometimes tear down, the barriers that nature imposed on our evolution. More recently, a report by Kevin N. Laland of the University of St. Andrews in Scotland and his colleagues in *Nature Reviews Genetics*, building on an earlier proposal by Robert Boyd of the University of California, Los Angeles, and Peter J. Richerson of U.C. Davis, argued that human culture, defined as any learned behavior, including technology, has been the dominant natural selection force on modern humans.

Which brings me to the present. The vigorous, vehement and vexed reactions to any piece I have written that mentions "climate change," combined with the power of greed on the one hand and the struggle for subsistence on the other, have convinced me there is no chance that governments will significantly reduce the output of industrial greenhouse gases in time to stave off considerable change to the planet's climate and to human habitats.

So it is perhaps time to think more about how we will respond to the range of possible environmental changes. Such planning should include the good, the bad and the ugly.

The good? Some regions of the planet that are not now conducive to agriculture surely one day will be. The bad? The possibilities here, it seems, vastly outweigh the good, with the worst case probably involving the displacement of several billion people from the poorest coastal regions of the world, with concomitant social, economic and political upheaval, possible starvation from regional losses in agriculture, and rises in international tensions, terrorism and political instability. The ugly will include the need, for example, to brace for the ever more jarring effects of extreme weather patterns, the extinction of a huge range of animal and plant species, and the invasion into new latitudes of predators and pests.

I don't think such effects will mean the end of humanity or even the end of civilization. I just see a changed world (although I would be very surprised if it were a better world) to which we will have to adapt. It will produce the ultimate example of gene-culture co-evolution: our technology will change the world, and it will dramatically affect natural selection, not just for a whole range of species but for humans as well. And it will reflect human uniqueness in the sense I described earlier: our evolutionary success may compete with that of microbes in our impact on the earth's environment.

Once again I am reminded of discussions during our Origins meeting in which Curtis W. Marean of A.S.U. described the evolution of hominids who lived near the southern tip of Africa for almost 100,000 years, during which dramatic sea-level rises and falls caused migrations, changes in hunting and dietary patterns, and developments of new technology. Those individuals, who may have been the ancestors of all of us, survived. I expect we will, too. What is new is that the environmental selection for hominids of the future will be induced by human culture and technology of today in ways we might have been able to alter rationally had we been rational enough. ■

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

PHOTOGRAPH BY JOHN BOSWELL; ILLUSTRATION BY MATT COLLINS

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Through Neutrino Eyes

Neutrinos are no longer just a curiosity of physics but a practical tool for astronomy

By Graciela B. Gelmini, Alexander Kusenko and Thomas J. Weiler

KEY CONCEPTS

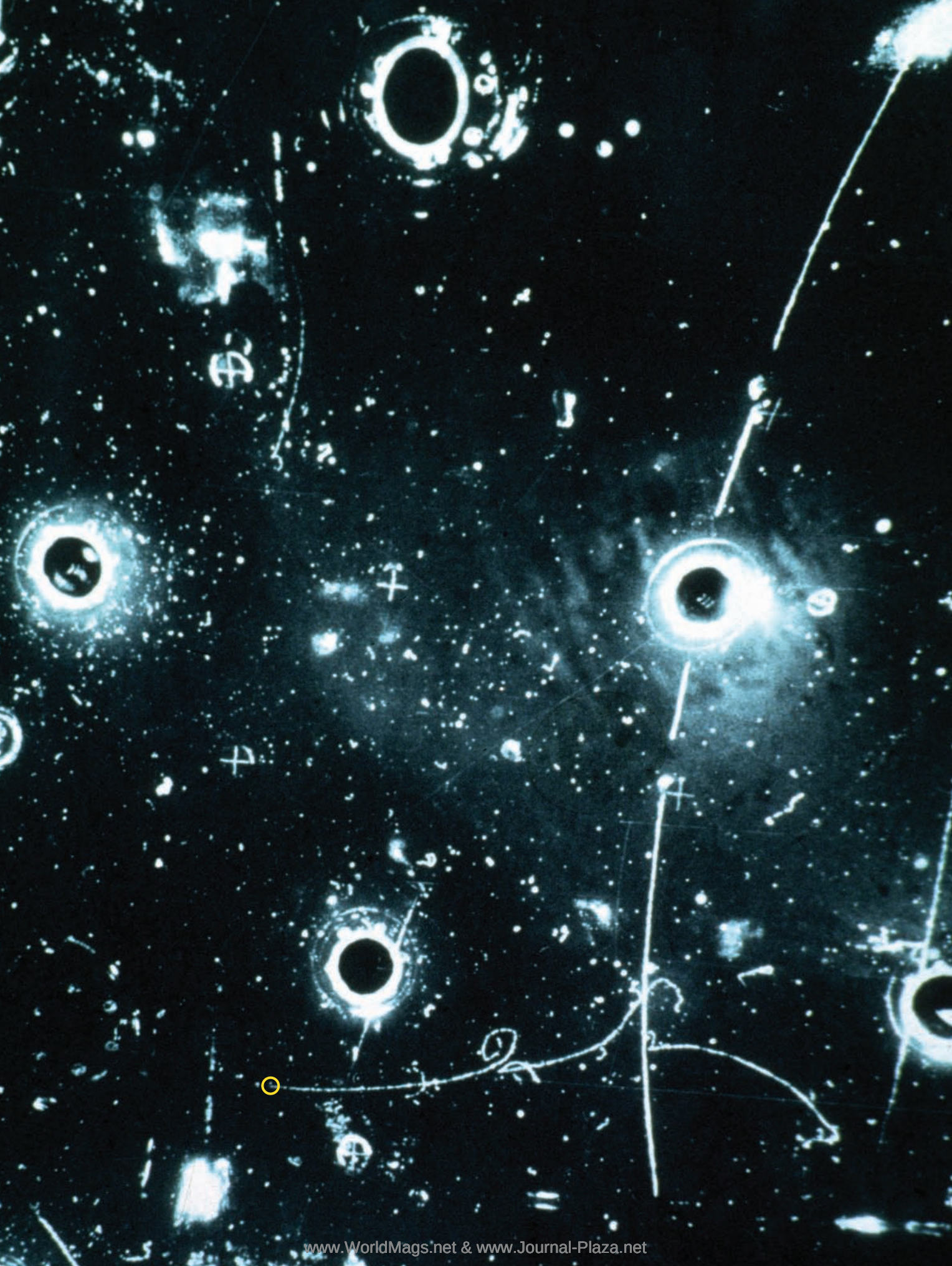
- Neutrinos will give astronomers a type of x-ray vision far better than actual x-rays. Being the most unreactive type of subatomic particle, they pass through intervening matter as though it were hardly there—revealing the cores of stars and other dramatic but otherwise hidden places in the cosmos.
- Alas, the very property that makes neutrinos so useful means they tend to fly through detectors without registering. Only this year have instruments become sensitive enough to detect cosmic sources unequivocally.
- Neutrinos come in multiple varieties and can metamorphose in midflight. This peculiar property provides additional information about their celestial origins.

—The Editors

When the Nobel Foundation awarded Ray Davis and Masatoshi Koshiba the 2002 Nobel Prize in Physics, it could have chosen to emphasize any of their many accomplishments. Davis made his name detecting neutrinos from the sun—the first of these notoriously elusive particles ever seen from beyond our planet—and Koshiba discovered them coming from the great supernova explosion of 1987. Their work was an experimental tour de force and helped to establish that neutrinos, which theorists had assumed were massless, in fact have a small mass. Yet the Nobel Foundation recognized Davis and Koshiba, above all, for establishing a new branch of science: neutrino astronomy.

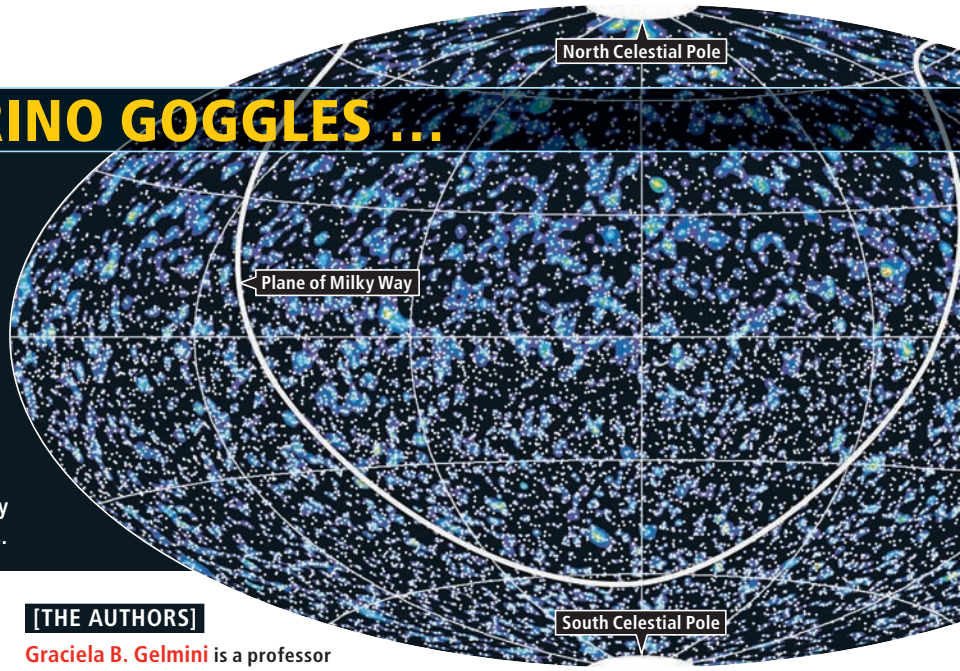
With their work, neutrinos graduated from a theoretical novelty to a practical way to probe the universe. In addition to studying neutrinos to glean the particles' properties, scientists can now use them to lift the veil on some of the hidden mysteries of the universe. In an undertaking akin to the construction of giant optical telescopes a century ago, astronomers have been designing and building vast neutrino telescopes in anticipation of seeing new wonders. These observatories have already caught tens of thousands of neutrinos and made pictures of the sun in neutrinos.

INVISIBLE NEUTRINO enters a bubble chamber from the left and kicks an electron (*circled in yellow*) onto a tortuous journey (*squiggly line*). This iconic image, made by CERN's Gargamelle bubble chamber in 1972, helped to prove the Standard Model of particle physics and set the stage for the use of neutrinos in astronomy.



[OBSERVATIONS]

IF YOU HAD NEUTRINO GOGGLES ...



THE SKY IN NEUTRINOS

Through those goggles, the sky might look something like this image, made by the half-completed IceCube observatory from April 2008 to May 2009. The nearly 20,000 neutrinos (*dots*) come from both the cosmos and from Earth's upper atmosphere; subtracting off the estimated atmospheric production leaves a possible cosmic signal (*colored*). (The signal is only "possible"; it will take the full IceCube to identify astronomical sources unambiguously.) IceCube sees both the northern and southern skies because Earth is nearly transparent to all but the highest-energy neutrinos.

COURTESY OF CERN (*preceding page*); COURTESY OF THE ICECUBE COLLABORATION (*sky in neutrinos*)

Neutrinos from other cosmic sources are hard to tell apart from those produced in Earth's upper atmosphere, but instruments should be able to do so by this time next year.

At that point, the floodgates of discovery will open, and a particle once derided as unobservable may become indispensable. Neutrinos can reveal things that light is blind to. When we study the sun with light, we are seeing only the surface—just the uppermost few hundred kilometers of gas. Although the energy powering sunlight originates in nuclear reactions at the core, sunlight itself is absorbed and reemitted trillions on trillions of times by the intervening layers of gas, and only very near the surface does it stream freely into space. In contrast, with neutrino eyes we directly see the central fusion engine—the hottest, innermost 1 percent of the sun's volume. The neutrinos created there pass through the sun's outer layers almost as if they were empty space.

Neutrinos also will allow us to peer deep into supernovae, other stellar explosions such as gamma-ray bursts, and disks swirling around supermassive black holes. The observatories now under construction should catch sight of about one supernova a year within the nearest 50 or so galaxies. They may also see some of the hundreds of gamma-ray bursts that go off every year, not to mention even more exotic celestial objects that may be going entirely unnoticed. But like every powerful tool, the neutrino takes some getting used to. It requires astronomers to approach their subject in a new way.

The Benefits of Being Antisocial

To a particle physicist, a neutrino is similar to an electron, except for its lack of electric charge, which makes it immune to the electric and magnetic forces that dominate the everyday world. When you sit on a chair, electric repulsion prevents you from falling through. When chemicals react, atoms swap or share electrons. When a material absorbs or reflects light, charged particles react to an oscillating electromagnetic field. Neutrinos, being electrically neutral, pass right through solid matter, play no role in atomic or molecular physics, and are almost completely invisible.

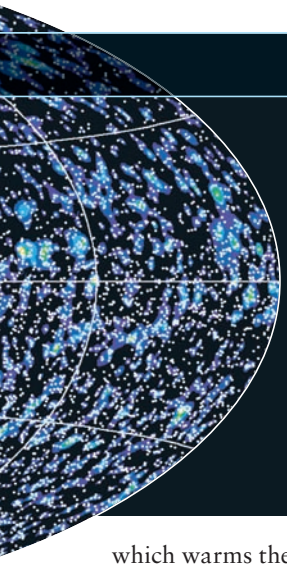
The known types of neutrinos do participate in the weak nuclear force that is responsible for radioactive beta decay and fusion of the heavier elements, but this force, as its name suggests, is feeble except over extremely short distances. Thus, neutrinos barely interact with other particles. To detect them, physicists and astronomers must monitor large volumes of matter, looking for the rare occasion when a neutrino leaves a mark. If cosmic neutrinos collectively have as much energy as cosmic rays (the protons and ions that bombard our planet), as astronomers expect, it will take a cubic kilometer of material to capture a decent sample of them. The biggest observatories are approaching this size [*see box on page 43*].

Physicists have also postulated other neutrinos, so-called sterile neutrinos, that are so standoffish they barely respond even to the weak force; the force of gravity may be their dominant connection to the rest of the universe. These neutrinos are even more challenging to detect [*see box on page 44*].

Aloof though they may be, neutrinos are active participants in the drama of the cosmos. They are a necessary by-product of beta decay,

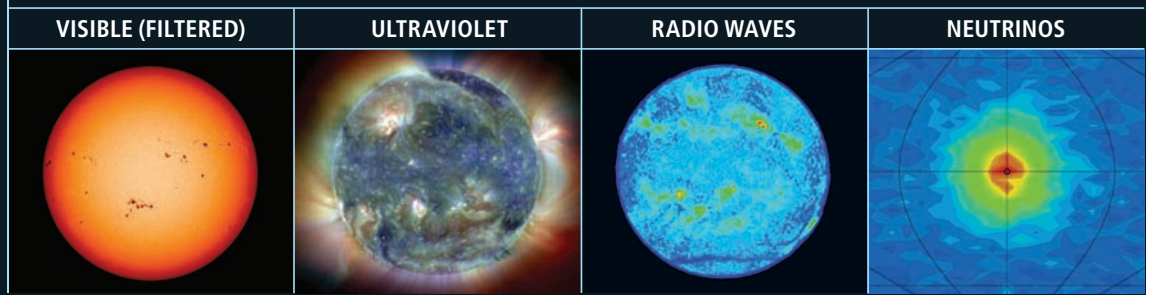
[THE AUTHORS]

Graciela B. Gelmini is a professor of physics at the University of California, Los Angeles. As a high school student in Argentina, she considered careers in art, philosophy and astronomy before settling on physics. "Physicists had better *mate*," she recalls, referring to the national drink (and to local slang for brains). Alexander Kusenko, also at U.C.L.A., finished his physics degree after being drafted by the Soviet army and then went to Stony Brook University on an exchange program that worked so well he never went back. He and Gelmini are both on the Pierre Auger Observatory team. Thomas J. Weiler thought he would grow up to be a cowboy but got distracted by quantum mechanics and relativity theory at Stanford University and the University of Wisconsin–Madison. He is now a professor of physics at Vanderbilt University and a member of the Extreme Universe Space Observatory team. "There are too many cowboys out there anyway," he says.



"SEEING" THE SUN

Astronomers have seen the sun at every wavelength of light, and now they have seen it in neutrinos. The image is blurry—the Super-Kamiokande experiment that made it has a resolution of 26 degrees, whereas the sun is 0.5 degree wide (*black circle*)—but is still a technological milestone. Whereas light shows only the surface of the sun, neutrinos expose the core.



which warms the debris of exploded stars and the interiors of planets and is a crucial intermediate step in stellar nuclear fusion. They are also decisive in one of the two major types of supernovae, those that result from the implosion of a massive star at the end of its life. The implosion compresses the core of the star to nuclear densities and releases 10^{58} neutrinos in a span of 10 to 15 seconds. In such numbers, even the most antisocial particle cannot help but become the life of the party. Neutrinos account for 99 percent of the total energy released by the cataclysm. Observing them thus lets us see the 99 percent of the picture that ordinary telescopes miss, including the decisive early stages. The detection of neutrinos from the 1987 event confirmed the basic theory of stellar collapse [see "The Great Supernova of 1987," by Stan Woosley and Tom Weaver; Scientific American, August 1989]. The detectors now available will be able to provide a real-time movie of stellar collapse, rebound and explosion.

Whatever their origins, neutrinos have no difficulty reaching Earth. Not only do they pass through gas and dust, they can cross the entire universe no matter how high their energy is. That is not true of light. The most energetic form of light, gamma rays, is attenuated by the cosmic background radiation—the haze of microwaves left over from the big bang and the accumulated starlight and radio waves of past eons. Gamma-ray photons with energies of 100 tera-electron-volts (TeV) go barely a few tens of millions of light-years. Energetic cosmic rays are blocked, too.

Neutrinos are thus one of the few ways astronomers have to study the most powerful phenomena in nature. They may be hard to catch but are worth the effort.

Flavorful Science

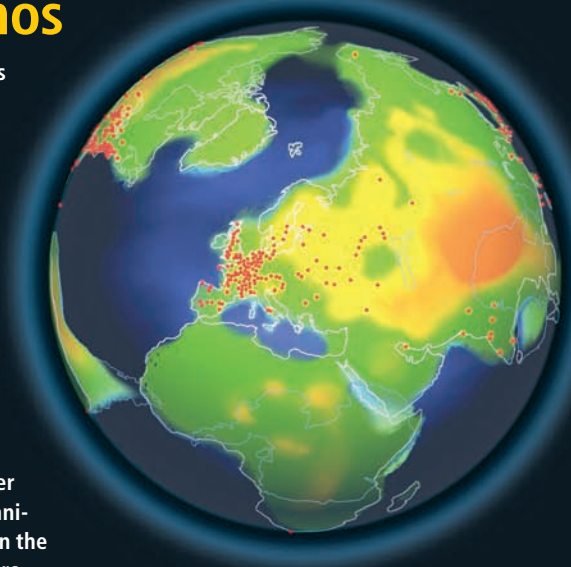
Besides being aloof, neutrinos have another distinctive feature: their strange ability to metamorphose. Like all elementary matter particles, they come in three versions, called flavors. The electron (e) has two heavier replicas, the muon (μ) and the tau (τ), and each has a neutrino partner: the electron-neutrino (ν_e), the muon-neutrino (ν_μ) and the tau-neutrino (ν_τ).

But whereas the electron, the muon and the tau have specific masses, the three neutrino flavors do not. If you measure the mass of a neutrino with a given flavor, you get one of three answers at random, with a certain probability for each. Conversely, if you measure the flavor

[TERRESTRIAL SOURCES]

Earth, by the Light of Neutrinos

Our own planet glows feebly in neutrinos, as this artist's conception shows (colors represent intensity). Natural radioactivity releases them, and geophysicists have started to use neutrino observations to determine the distribution of radioactive isotopes. Other sources include cosmic-ray collisions in the upper atmosphere, possible annihilation of dark matter in the core, and nuclear reactors.



COURTESY OF SOHO/EIT CONSORTIUM/MDI TEAM, COURTESY OF ESA/NASA/SOHO, COURTESY OF STEPHEN WHITE *University of Maryland/NRAO/AUI* AND COURTESY OF SUPER-KAMIOKANDE COLLABORATION (*suns, left to right*); GEORGE RETSECK (*Earth*)

of a neutrino with a given mass, you get one of three answers. A neutrino can have either a specific flavor or a specific mass but not both at the same time. Neutrino mass states are labeled by number, ν_1, ν_2 and ν_3, which are distinct states from ν_e, ν_μ and ν_τ.

Neutrinos thus violate a basic intuition we have about objects. A basketball weighs 22 ounces, a baseball five ounces. But if balls behaved like neutrinos, a basketball would sometimes be 22 ounces, sometimes five ounces. In this respect, neutrinos are rather like people, with our multiple group identities. For instance, scientists may have both an institutional affiliation and a political party affiliation at the same time. Surveys show that 6 percent of scientists are Republicans, but that does not mean 6 percent of scientific laboratories are associated with the Republican party. Rather, in a typical laboratory, six out of 100 randomly chosen scientists happen to be Republican. Likewise, a ν_1 neutrino interacting in a detector may manifest itself as a ν_e, ν_μ or ν_τ with a calculable probability.

Flavor determines how neutrinos partake in the weak nuclear force, and mass determines how they propagate through space. For instance, beta decay produces neutrinos of a single flavor, ν_e. As these particles fly through space, their flavor is unimportant; it is their mass state that dictates their behavior. The ν_e is a mixture of a ν_1, ν_2 and ν_3 in proportions that, for technical reasons, physicists call mixing angles. Instead of a single type of particle, physicists must now keep track of three. Eventually the neutrinos react with material in a detector, and here again it is the flavor that matters. If the relative proportions of mass states have remained unchanged, they will add up to the original flavor again (which, for beta decay, is ν_e).

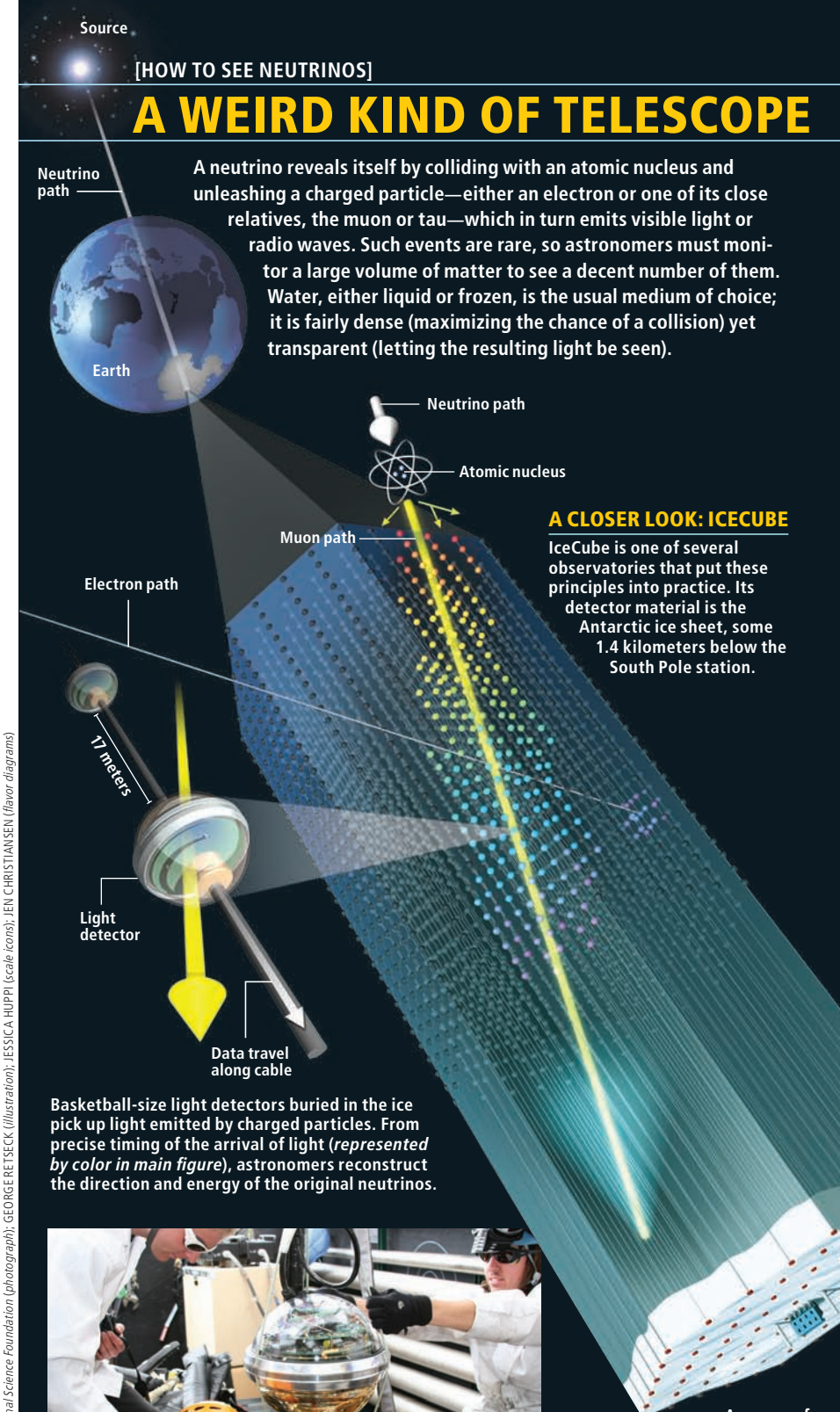
But that need not be the case. When the particles are propagating as mass states, they become vulnerable to new effects that can alter the mixture, thereby changing their flavor. This process is what causes neutrinos to metamorphose.

By the principles of quantum mechanics, each mass state corresponds to a wave with a certain wavelength. The waves overlap and interfere with one another. To use an acoustic metaphor, a neutrino is like a sound wave consisting of three pure tones. As anyone who has ever tuned a musical instrument knows, superposed sound waves having slightly different pitch (or wavelength) exhibit "beats," an oscillation of their sound intensity. In the case of neutrinos, a difference in mass acts like a differ-

[HOW TO SEE NEUTRINOS]

A WEIRD KIND OF TELESCOPE

A neutrino reveals itself by colliding with an atomic nucleus and unleashing a charged particle—either an electron or one of its close relatives, the muon or tau—which in turn emits visible light or radio waves. Such events are rare, so astronomers must monitor a large volume of matter to see a decent number of them. Water, either liquid or frozen, is the usual medium of choice; it is fairly dense (maximizing the chance of a collision) yet transparent (letting the resulting light be seen).



A CLOSER LOOK: ICECUBE

IceCube is one of several observatories that put these principles into practice. Its detector material is the Antarctic ice sheet, some 1.4 kilometers below the South Pole station.

Basketball-size light detectors buried in the ice pick up light emitted by charged particles. From precise timing of the arrival of light (*represented by color in main figure*), astronomers reconstruct the direction and energy of the original neutrinos.

Scientists started work during the 2005–2006 southern summer and hope to wrap it up in the coming summer. They drill 2.5-km holes using hot water and lower the photodetectors on a cable.

An array of detectors on the surface identifies cosmic rays that can confound neutrino detection.

COURTESY OF REINA MARUYAMA *National Science Foundation (photograph)*; GEORGE RETSECK *(illustration)*; JESSICA HUPPI *(scale icons)*; JEN CHRISTIANSEN *(flavor diagrams)*

OBSERVATORY SPECS	DESIGN
SUPER-KAMIOKANDE Location: North of Nagoya, Japan Detector volume: 50,000 cubic meters Date of operation:1996– Angular resolution: 26 degrees Energy range: 10^8–10^{12} eV	Photodetectors line a giant water tank in a zinc mine. Physicists have proposed expanding it 20-fold, creating Hyper-Kamiokande.
PIERRE AUGER OBSERVATORY Location: South of Mendoza, Argentina Detector volume: 30,000 km^3 (telescope coverage), 20,000 m^3 (ground detectors) Date of operation:2004– Angular resolution: 0.5–2 degrees Energy range: 10^{17}–10^{21} eV	Primarily a cosmic-ray detector, Auger also sees high-energy neutrinos using an array of 1,600 small water tanks. In addition,ultraviolet telescopes look for particle collisions in the atmosphere.
ANTARCTIC IMPULSE TRANSIENT ARRAY (ANITA) Location: McMurdo Station, Antarctica Detector volume: 1,000,000 km^3 Dates of flights: 2006–2007, 2008–2009 Angular resolution: 1–2 degrees Energy range: 10^{17}–10^{21} eV	A balloon flies above Antarctica for one month to scan for radio waves that can be traced to high-energy neutrinos colliding with the ice sheet.
ASTRONOMY WITH A NEUTRINO TELESCOPE AND ABYSS ENVIRONMENTAL RESEARCH (ANTARES) Location: Mediterranean Sea near Marseille, France Detector volume: 0.05 km^3 Date of operation: 2008– Angular resolution: 0.3 degree Energy range: 10^{13}–10^{16} eV	Twelve strings of photodetectors anchored to the seafloor look for collisions in the water. It is one of three pilot projects for the KM3NeT, a cubic-kilometer neutrino telescope scheduled for construction from 2011 to 2015.
ICECUBE Location: South Pole Detector volume: 1 km^3 Estimated date of completion: 2011 Angular resolution: 1–2 degrees Energy range: 10^{11}–10^{21} eV	Eighty-six strings of light-sensitive detectors (and in some cases radio antennas) are lowered into the ice through a drill hole, where they freeze into place. It is a scaled-up verison of the earlier AMANDA experiment.
EXTREME UNIVERSE SPACE OBSERVATORY (EUSO) Location: International Space Station Detector volume: 1,000,000 km^3 of air (equivalent to 1,000 km^3 of ice) Estimated date of completion: 2015 Angular resolution: 1–2 degrees Energy range: 10^{19}–10^{21} eV	An ultraviolet telescope in the Japanese Experiment Module will monitor Earth's atmosphere for tracks of charged particles.

WHICH FLAVOR OF NEUTRINO WAS IT?

Each type, or flavor, unleashes its respective particle—an electron-neutrino lets loose an electron, a muon-neutrino a muon, and tau-neutrino a tau. From their telltale light patterns, the flavor can be distinguished with a 25 percent confidence.

The electron interacts with atoms and dumps its energy, lighting up a nearly spherical volume.

The muon, being less interactive, travels a kilometer or more, creating a cone of light.

The tau rapidly decays. Its creation and demise create two spheres—a "double bang"—of light.

ence in pitch, and the beats cause an oscillation of flavor with distance [*see box on page 45*].

The sun, for example, produces electron-neutrinos. Before they reach Earth, they become a mix of all three flavors. The pioneering experiments of Davis and Koshiba were sensitive only to electron-neutrinos, so they missed the muon- and tau-neutrinos into which many of the electron-neutrinos had metamorphosed during their journey. It took a detector sensitive to all three neutrino flavors, the Sudbury Neutrino Observatory detector in Canada in 2001 and 2002, to detect a representative sample of particles [see "Solving the Solar Neutrino Problem," by Arthur B. McDonald, Joshua R. Klein and David L. Wark; Scientific American, April 2003].

Another well-established example of neutrino metamorphosis occurs when neutrinos are created in Earth's upper atmosphere. Cosmic rays collide with nuclei in the air, creating unstable particles called pions that subsequently decay into electron- and muon-neutrinos. These neutrinos then propagate through the air and solid planet as mass states. The farther they travel by the time they are detected, the more of the muon-neutrinos turn into tau-neutrinos. Consequently, neutrino observatories see half as many muon-neutrinos coming up from below (having traveled from the opposite side of the planet) as from overhead (having gone from the upper atmosphere straight to the ground).

Fun with Ratios

For astronomers, flavor is to neutrinos what polarization is to light: a property that can encode information. Just as a celestial source can emit light with a given polarization, it produces neutrinos with certain flavors, and by measuring the flavor, astronomers can figure out what processes must have operated within the source. The trick is to mentally undo the metamorphosis that the neutrinos underwent on their journey.

If we could measure precisely the energy of a neutrino and how far it traveled, we would know where in the oscillation cycle it ended up and could calculate the relative proportions of the three flavors. We lack this precision. Over large distances and long times, neutrinos oscillate so many times that we cannot keep track of the flavor mix—it looks like a blur to us. Instead we take a statistical average, described by a so-called flavor propagation matrix. From this matrix, astronomers can deduce what an observed ratio must originally have been.

For instance, it is thought that many neutrinos

[DARK MATTER?]

Fecundity of Sterile Neutrinos

Astronomers used to think that neutrinos might make up the mysterious dark matter of the universe. That idea fell into disfavor when neutrinos turned out to be too lightweight—at most a millionth of the mass of the electron. But scientists still hold open the possibility that as yet unobserved neutrinos, known as sterile neutrinos because they do not respond to the weak nuclear force, might be out there and might be heavy enough to do the trick.

Sterile neutrinos might seem utterly impossible to detect, but the same was once said of ordinary neutrinos. One thought is that they might have distinctive effects on astronomical objects. For instance, supernova explosions might emit them. Because such explosions are inherently asymmetric, more neutrinos would come off in one direction than others and the stellar remnant would recoil in the opposite direction at hundreds of kilometers per second. In fact, astronomers do observe such a recoil, and it has long been a mystery.

In addition, sterile neutrinos might be unstable and decay into x-ray photons. The Chandra X-ray Observatory discovered faint x-ray emission hinting at a sterile neutrino with a hundredth of the mass of the electron, and the Suzaku x-ray mission saw a weak signal that could have come from a sterile neutrino. Decays of sterile neutrinos might also have ionized hydrogen in the early universe or even helped to skew the universe in favor of matter over antimatter. For now, though, the evidence is too tenuous to reach any conclusions.

—G.B.G., A.K. and T.J.W.

come from extreme-energy collisions of photons with protons. This process occurs in cosmic-size particle accelerators—found at the shock fronts of supernova remnants and in the jets squirted out by black holes of all sizes—as well as in deep space where cosmic rays slam into the cosmic background radiation. The collisions produce charged pion particles, which decay to muons and muon-neutrinos. The muons in turn decay to electrons and electron-neutrinos, among other things. The resulting stream of neutrinos is one part ν_e, two parts ν_μ and no ν_τ—a flavor ratio of 1:2:0. Looking up the pertinent values in the propagation matrix, we find that this ratio evolves into 1:1:1. If an Earthly experiment sees other than 1:1:1, then the pion-decay chain cannot be the source of the neutrinos.

In some cases, the pion might lose energy by colliding with other particles or emitting radiation while traveling on a curved trajectory in a magnetic field. If so, the muon into which it decays becomes irrelevant as a high-energy neutrino source, and the initial flavor ratio is instead 0:1:0. According to the propagation matrix, the ratio at Earth will be 4:7:7 rather than 1:1:1. If an experiment finds that the flavor is 1:1:1 for lower-energy neutrinos but 4:7:7 for higher-energy ones, astronomers can infer the particle density and magnetic field strength of the source.

Neutrinos can also come from so-called beta-beam sources. In cosmic particle accelerators, high-speed atomic nuclei can exchange pions or simply fall apart, leading to a fast beam of neutrons. The neutrons undergo radioactive beta decay, emitting a pure stream of electrons and electron-neutrinos, for a flavor ratio of 1:0:0. After processing with the propagation matrix, the flavor ratio that emerges at Earth is 5:2:2.

Whatever the initial mix of flavors is, the two flavors ν_μ and ν_τ arrive at Earth in equal numbers. This equality, which reflects a deeper symmetry that physicists have yet to explain, is noteworthy because tau-neutrinos will always turn up in telescopes even though no known astrophysical source produces them.

The flavor ratio can discriminate the workings of celestial objects as no other source of information can. Together with gamma rays and cosmic rays, neutrinos will spell out the dynamical mechanism and energy budget of nature's mightiest dynamos. They can determine whether cosmic particle accelerators are purely electromagnetic (in which no neutrinos are produced) or involve heavy particles (in which neutrinos do emerge). They might even help solve a mystery that is on every astronomer's top-10 list: How are the highest-energy cosmic rays produced? Some cosmic rays are so potent that they seem to defy known physics. Neutrinos can probe the interior of whatever is spitting them out.

They can reveal other natural processes as well. The decay of dark matter particles might yield neutrinos in a ratio of 1:1:2, which evolves to roughly 7:8:8. In certain quantum theories of gravity, the very fabric of spacetime undulates on microscopic scales. Very high energy neutrinos have very short wavelengths that might be sensitive to these fluctuations. The fluctuations might act to scramble the flavor, leading to an observed ratio of 1:1:1. In the future, physicists may be able to use the measurement of a ratio other than 1:1:1 to rule out certain classes of theories and determine the energy levels at which quantum-gravitational effects come into play.

Another exotic process is the decay of a heavy neutrino into a lighter variety, which would alter the flavor ratio. From studying solar neutrinos, physicists have found that ν_1 is lighter than ν_2, but they do not know which of ν_1 and ν_3 is the lightest. If astronomers found a flavor ratio of 4:1:1, it would mean that neutrinos are indeed unstable and that ν_1 is the lightest. A ratio of 0:1:1 would favor ν_3.

Historically, astronomy began with observations of the universe in visible light and gradually expanded to infrared, microwave, radio, x-rays and gamma rays. Neutrinos continue the trend. The coming decade will be the golden age of neutrino astronomy. ■

JEN CHRISTIANSEN; GEORGE RETSECK (*source* and *Earth*)

NEUTRINO METAMORPHOSIS

Unlike other types of particles, neutrinos mutate as they travel through space. Astronomers must mentally undo this effect to reconstruct what the neutrinos used to be and what produced them.

CONFLICTED IDENTITY

A neutrino has this uncanny ability to mutate because it has dual identities. It can be one of three flavors and have one of three masses, but a given flavor does not imply a given mass, or vice versa.

FLAVOR determines how the particle interacts with matter.

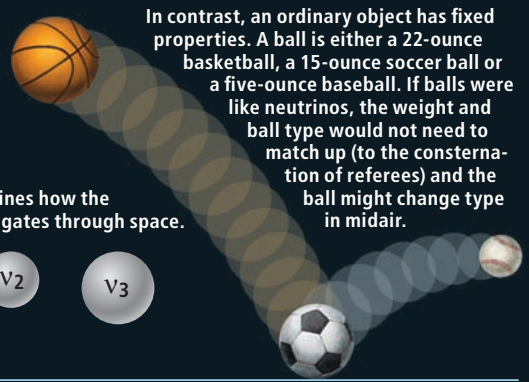
ν_e Electron-neutrino

ν_μ Muon-neutrino

ν_τ Tau-neutrino

MASS determines how the particle propagates through space.

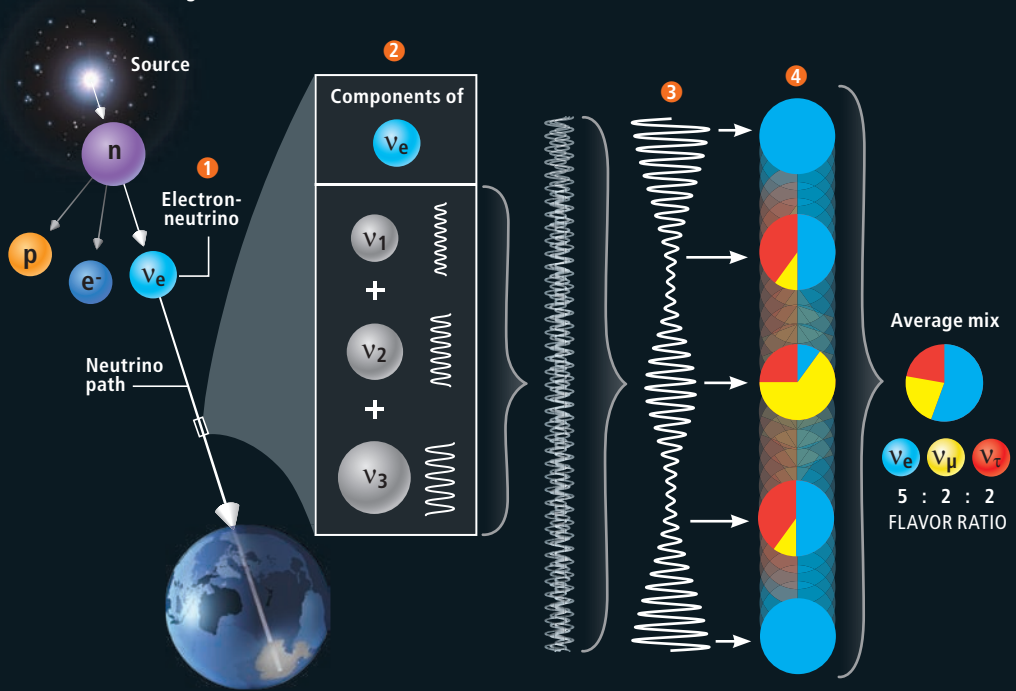
ν_1 ν_2 ν_3



In contrast, an ordinary object has fixed properties. A ball is either a 22-ounce basketball, a 15-ounce soccer ball or a five-ounce baseball. If balls were like neutrinos, the weight and ball type would not need to match up (to the consternation of referees) and the ball might change type in midair.

FLAVOR OSCILLATIONS

When created or detected, a neutrino has a specific flavor. For instance, the beta decay of a neutron creates an electron-neutrino 1. This neutrino has no specific mass but is a mix of all three possibilities—represented by a sum of three waves with different wavelengths 2. As the neutrino propagates, the waves become misaligned, so they no longer add up to the original flavor but to some mix of all three flavors 3. The mix varies as the neutrino travels 4. Here the average mix is 5:2:2—which means a detector has a five-ninths chance of seeing it as an electron-neutrino and a fourth-ninths chance as a muon- or a tau-neutrino.



FLAVOR MIXES

Astrophysical processes produce distinctive flavor mixes, which astronomers can deduce by accounting for the metamorphosis. Muon- and tau-neutrinos always arrive in equal proportions, a consequence of their intrinsic symmetry.

Source	Ratios at Source	Ratios at Earth
Neutron decay	$1\nu_e{:}0\nu_\mu{:}0\nu_\tau$	$5\nu_e{:}2\nu_\mu{:}2\nu_\tau$
Pion decay (complete)	1:2:0	1:1:1
Pion decay (incomplete)	0:1:0	4:7:7
Dark matter decay (example)	1:1:2	7:8:8
Spacetime foam	Any	1:1:1
Neutrino decay (ν_1 lightest)	Any	4:1:1
Neutrino decay (ν_3 lightest)	Any	0:1:1

Some cosmic rays are so potent they seem to defy known physics. Neutrinos can probe the interior of whatever is spitting them out.

MORE TO EXPLORE

Flavor Ratios of Astrophysical Neutrinos: Implications for Precision Measurements. Sandip Pakvasa, Werner Rodejohann and Thomas J. Weiler in *Journal of High Energy Physics*, Article No. 5; February 1, 2008. **arxiv.org/abs/0711.4517**

High Energy Cosmic Rays. Graciela B. Gelmini in *Journal of Physics: Conference Series*, Vol. 171, No. 1, Paper No. 012012; June 29, 2009. **arxiv.org/abs/0903.4716**

Sterile Neutrinos: The Dark Side of the Light Fermions. Alexander Kusenko in *Physics Reports*, Vol. 481, Nos. 1–2, pages 1–28; September 2009. **arxiv.org/abs/0906.2968**

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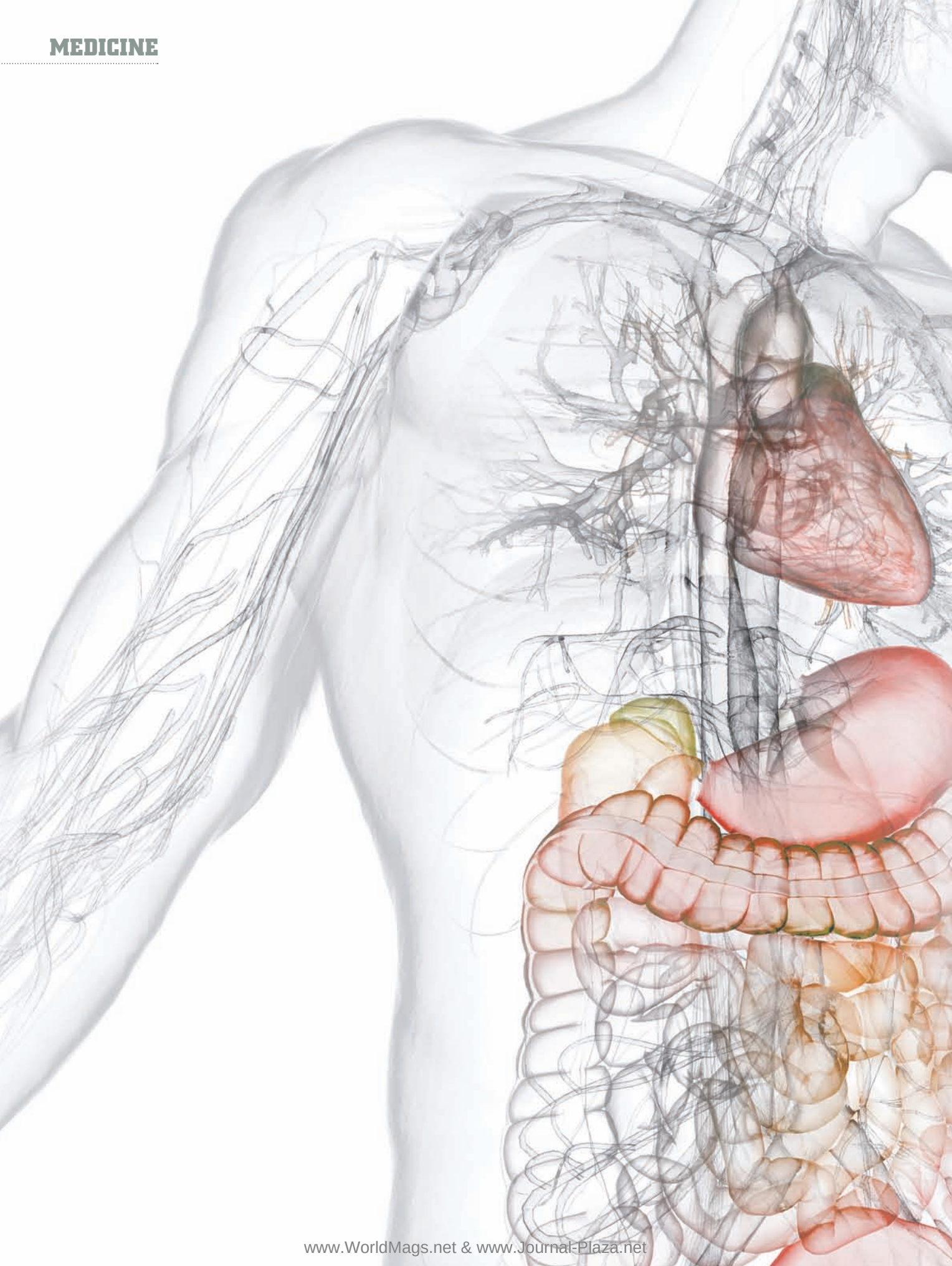
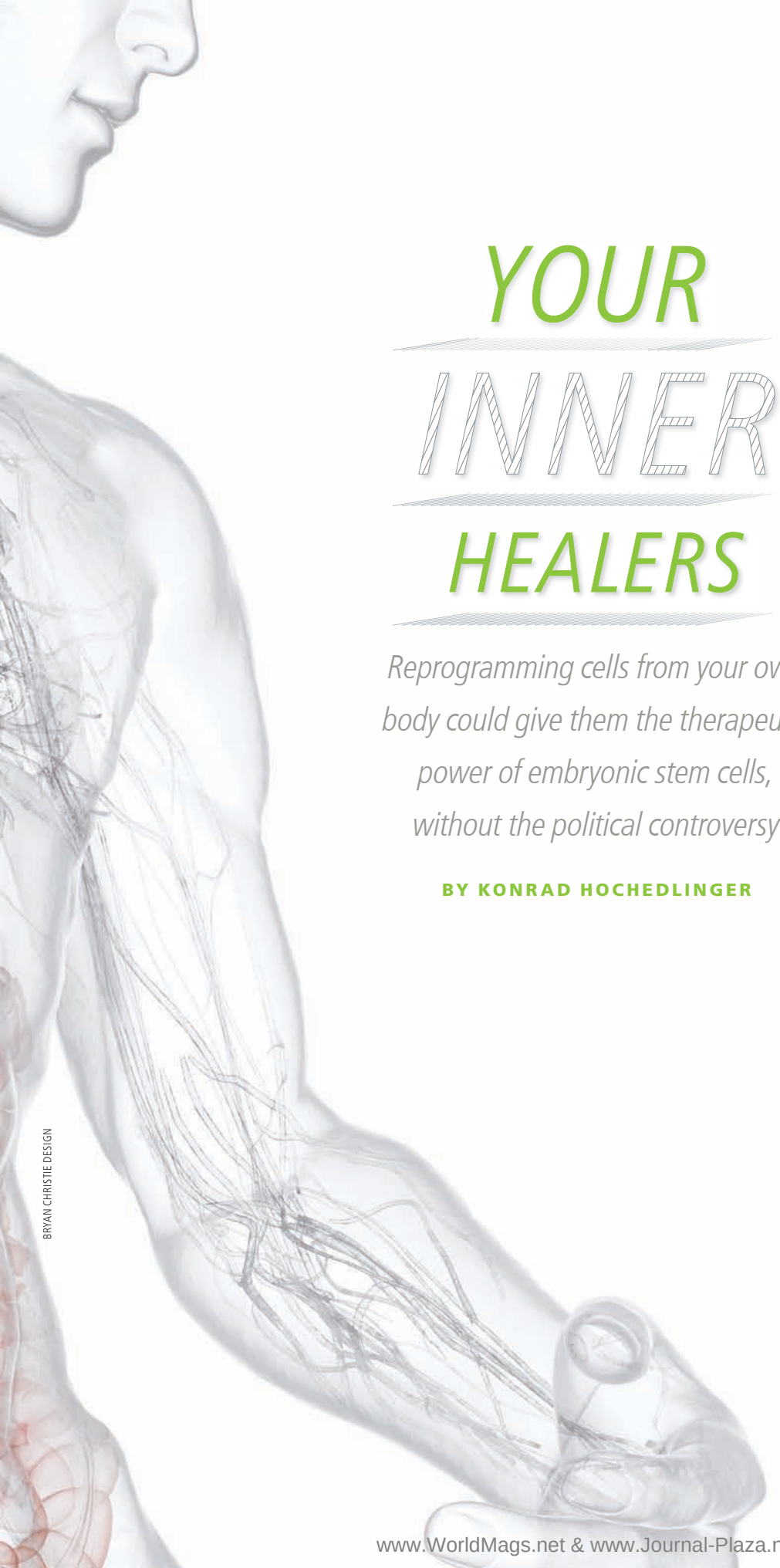




BRYAN CHRISTIE DESIGN

YOUR INNER HEALERS

Reprogramming cells from your own body could give them the therapeutic power of embryonic stem cells, without the political controversy

BY KONRAD HOCHEDLINGER

KEY CONCEPTS

- Induced pluripotent stem cells are mature body cells that have been made to change their identities and revert to an embryolike state—without the help of eggs or embryos.
- Rejuvenating the normal body cells of any individual—then converting them to any of the 220 human cell types—could yield new disease treatments and custom replacement tissues.
- Scientists are now working to understand how these cells are able to reverse their biological clocks and whether the newest kind of stem cell will prove as powerful as embryonic cells.

—The Editors

I remember my excitement one morning in the winter of 2006 when I peered through a microscope in my laboratory and saw a colony of cells that looked just like embryonic stem cells. They were clustered in a little heap, after dividing in a petri dish for almost three weeks. And they were glowing with the same colorful fluorescent markers scientists take as one sign of an embryonic cell's "pluripotency"—its ability to give rise to any type of tissue in an organism's body. But the cells I was looking at did not come from any embryo: they were regular adult mouse cells that had seemingly been rejuvenated by the addition of a simple cocktail of genes.

Could it really be so easy to roll back the internal clock of any mammalian cell and return it to an embryonic state? I was not the only one wondering at the time. Shinya Yamanaka of the University of Kyoto and his colleagues had just published a groundbreaking study in August 2006 that revealed their formula for creating what they called induced pluripotent stem cells (iPSCs) from the skin cells of mice. Researchers had been struggling for years to understand and control the enormous potential of embryonic stem cells to produce customized tissues for use in medicine and research—as well as contending with political and ethical controversies over the use of embryos, scientific setbacks and false hopes generated by previous "breakthroughs" that did not pan out. So stem cell scientists were surprised and a little bit skeptical of the Japanese group's results at first. But that morning in the lab, I could see firsthand the results of following Yamanaka's recipe.

Other scientists were also able to reproduce his achievement, and improved techniques for making and testing iPSCs have come rapidly over the past few years. Today thousands of scientists worldwide are working to develop the potential of iPSCs to help in understanding and treating human diseases that have so far defied cures, such as type 1 diabetes, Alzheimer's disease and Parkinson's disease. The possibility of changing a cell's identity just by delivering a few select genes has transformed the way scientists think about human development as well.

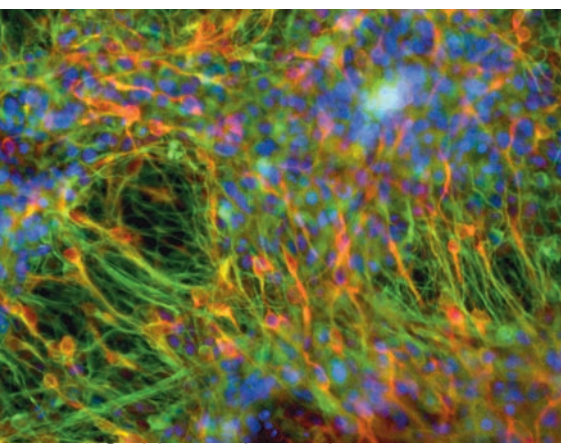
Throughout human history people have dreamed of finding a Fountain of Youth to escape the consequences of aging and disease.

Throughout history people have dreamed of finding a Fountain of Youth to escape the consequences of aging and disease, and the ability to return an adult body cell to an embryonic state would certainly appear to be as close as humanity has come to that fantasy so far. Of course, the technology is still in its infancy. Many important questions must be answered before anyone can say whether iPSCs will change the practice of medicine or even whether they will actually prove equivalent to the more controversial embryonic stem cells.

Primordial Power

To understand the hopes inspired by the discovery of iPSCs, one must return to what makes embryos so special. Current iPSC studies rely heavily on techniques and concepts developed in work with embryonic cells over the past 30 years, particularly the phenomenon of pluripotency. Mammalian development is normally a one way-street, where cells become progressively more specialized and less versatile with time, a process called differentiation. Only during a brief window very early in development do all the cells within an embryo possess the ability to become any of the 220 cell types in the human body. Extracting those cells and growing them in culture gives rise to embryonic stem cells. The ability of true embryonic stem cells to indefinitely maintain their capacity to generate any tissue type defines the term "pluripotent."

Even in a late-stage embryo, stem cells have specialized to the extent that they can give rise only to specific families of cell types, such as those in muscle and bone. These cells are considered "multipotent," but they are no longer pluripotent. In an adult, all that remains of those precursors are so-called adult stem cells that replenish mature cells within a tissue. Blood stem cells continuously regenerate the 12 different blood and immune cell types, for exam-



THERAPEUTIC PROMISE

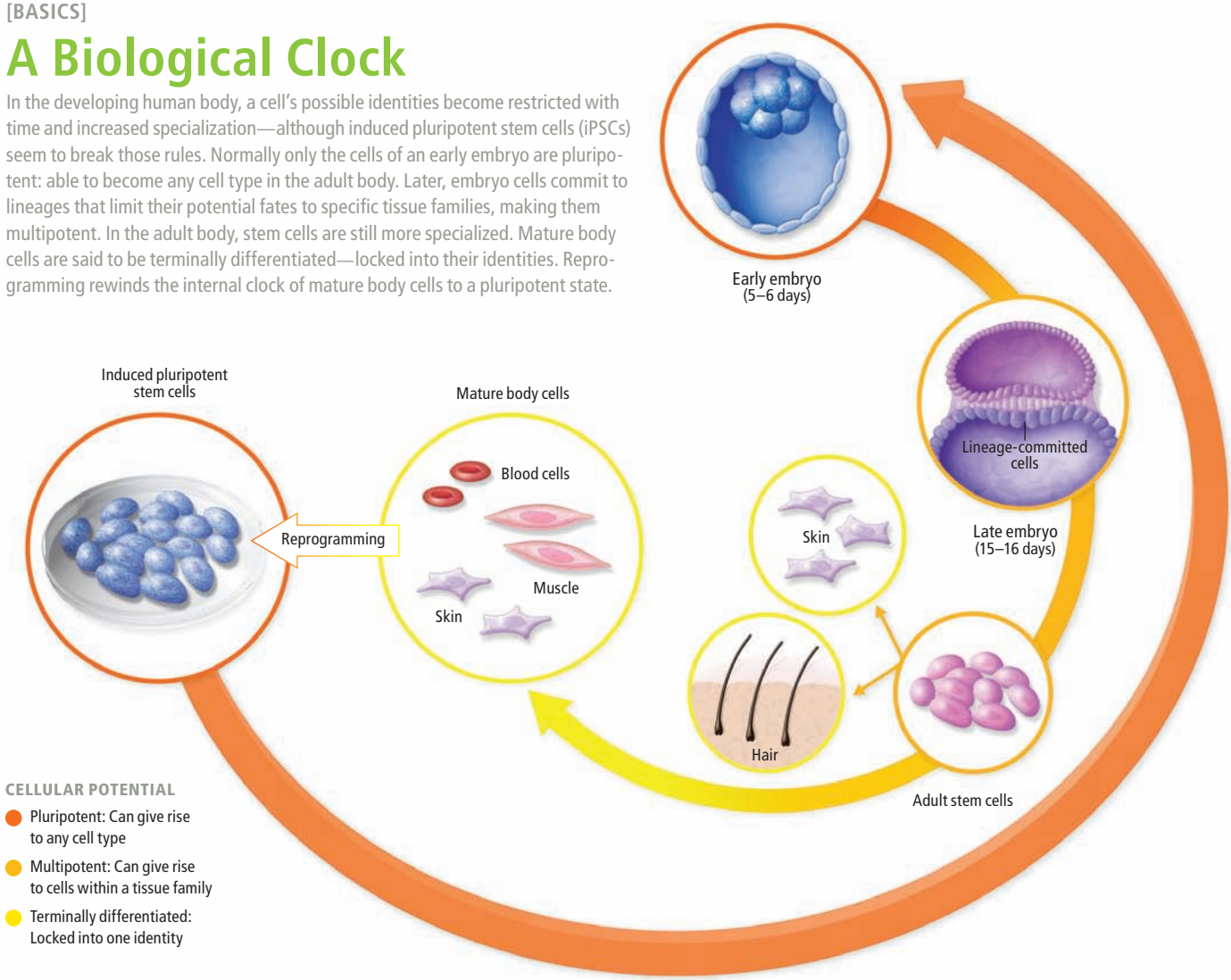
Neurons (*left*) were generated from induced pluripotent cells that were made from the skin cells of patients with Parkinson's disease. With the ability to take a mature body cell and convert it to an embryonic state, then into any desired tissue type, scientists will be able to study how a variety of diseases arise, develop and test drugs that hinder the disease process and, eventually, produce healthy replacement tissues for use in treating illnesses.

COURTESY OF HYESOO KIM AND LORENZ STUDER *Sloan-Kettering Institute*

[BASICS]

A Biological Clock

In the developing human body, a cell's possible identities become restricted with time and increased specialization—although induced pluripotent stem cells (iPSCs) seem to break those rules. Normally only the cells of an early embryo are pluripotent: able to become any cell type in the adult body. Later, embryo cells commit to lineages that limit their potential fates to specific tissue families, making them multipotent. In the adult body, stem cells are still more specialized. Mature body cells are said to be terminally differentiated—locked into their identities. Reprogramming rewinds the internal clock of mature body cells to a pluripotent state.



ple, and skin stem cells are responsible for regrowing our skin and hair every few weeks.

In mammals the one thing that never happens under normal circumstances is for a cell to dedifferentiate, that is, revert back to a more primitive type. Indeed, the only exception to this rule is cancer cells, which can become less differentiated than the tissue in which they first arise. Unfortunately, some cancer cells can also continue to divide endlessly, displaying an immortality similar to that of pluripotent cells.

Until recently, the only way to turn back the developmental clock of a normal adult cell was through elaborate manipulations to trick it into behaving like an embryonic cell, a process termed cellular reprogramming. The oldest approach to achieving reprogramming is somatic cell nuclear transfer, or "cloning," which involves injecting the genetic material from an adult cell into an egg cell whose own DNA has been removed. This DNA-egg hybrid then develops into an early-stage embryo from which pluripotent stem cells can be extracted.

CLONING

Transferring the nucleus of a mature cell into an egg is another method of reprogramming a person's adult DNA to an embryonic state. Attempts to derive embryonic stem cells from human-clone embryos have so far failed for unknown reasons.

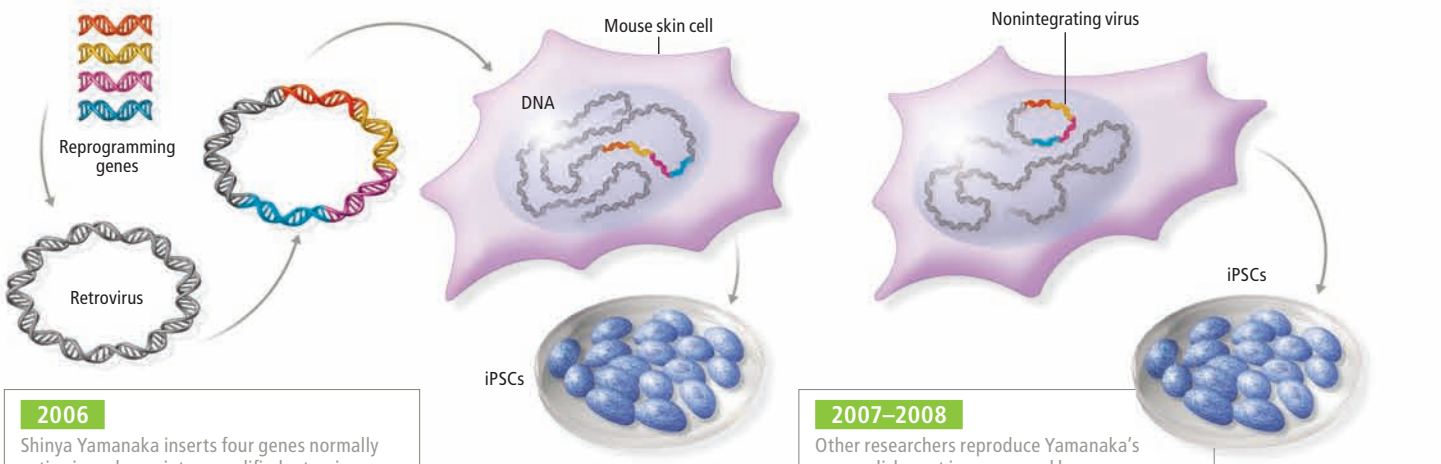
Since the cloning of Dolly the sheep was revealed in 1997 and the first isolation of human embryonic stem cells in 1998, nuclear transfer has received considerable attention as a possible means of producing custom-tailored pluripotent stem cells to replace any tissue damaged through injury or disease. Poorly understood factors within the egg do seem to genuinely rejuvenate the genetic material of the adult donor cell—even telomeres, the caps protecting the ends of chromosomes that wear away with age, are restored to a youthful state. Yet despite progress with animals, attempts to produce human embryonic stem cells through cloning have remained unsuccessful.

Yamanaka and his group went around this impasse by taking a novel approach to turning

TAMI TOLPA (*illustration*); PHILIPPE PSAILA *Photo Researchers, Inc.* (*stem cell nuclear transfer*)

Rapid Progress toward Safe Cell Rejuvenation

Just four years ago scientists in Japan first showed that a set of genes ferried by a retrovirus could transform the skin cells of adult mice into pluripotent stem cells. Many researchers have since been working to achieve the same end in simpler, safer and more efficient ways—key steps to making therapy a reality.



2006

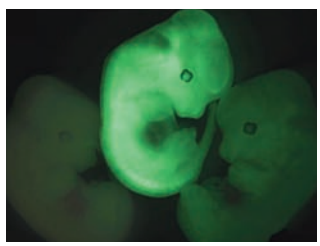
Shinya Yamanaka inserts four genes normally active in embryos into a modified retrovirus, which he then injects into mouse skin cells. The virus inserts the genes into the mouse DNA, and the genes then begin reprogramming the skin cells into induced pluripotent stem cells (iPSCs).

2007–2008

Other researchers reproduce Yamanaka's accomplishment in mouse and human cells. Experiments also show that delivery of the four reprogramming genes by viruses that do not permanently integrate into cellular DNA still succeeds in producing iPSCs.

adult cells directly into pluripotent cells without the use of eggs or embryos. Instead of introducing adult genetic material into an egg, they reasoned that introducing the genes normally active only in embryos into an adult cell might be sufficient to reprogram that cell into an embryolike state. Their first feat was to identify a cocktail of two dozen different genes that are turned on in pluripotent cells but silent in adult cells. When introduced into skin cells using retroviruses as delivery vehicles, these genes then almost magically reprogrammed the identity of the skin cells into that of pluripotent cells. With further experiments, Yamanaka then found that only four genes—*Oct4*, *Sox2*, *Klf4* and *c-Myc*—were actually necessary to produce iPSCs.

As soon as several independent laboratories, including mine, successfully reproduced the results, this magic trick became a biological fact. By now about a dozen different adult cell types from a total of four different species (mouse, human, rat and monkey) have been reprogrammed into iPSCs, and certainly more will follow. The discovery of iPSCs is so thrilling to stem cell researchers because they can circumvent the technical complexities of cloning and avoid most of the ethical and legal constraints associated with human embryo research. This new pluripotent cell type is not without its own problems, however. Quality control and safety are the main focus of iPSC research right now, as scientists work to establish what these cells really are and what they are capable of doing.



TESTING CELLS' TRUE POTENTIAL

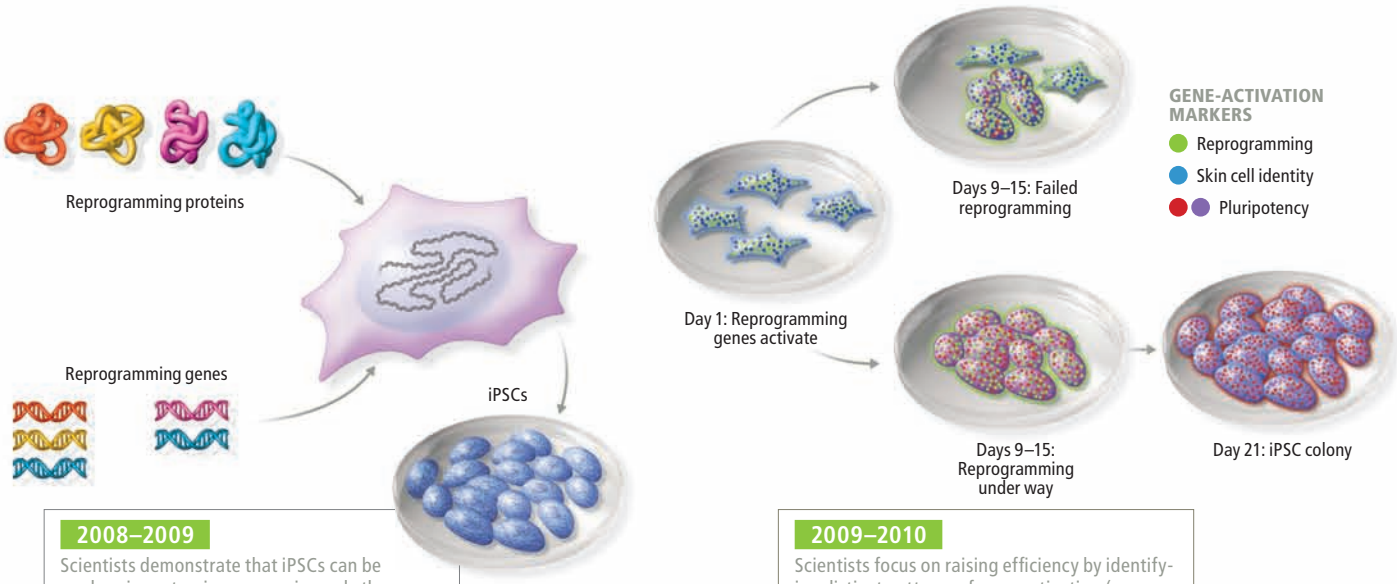
Gold-standard laboratory tests to determine whether stem cells are truly pluripotent aim to demonstrate that the cells can give rise to any tissue type in the body. When injected into an early mouse embryo, for example, fluorescently marked pluripotent cells should integrate throughout the body of the developing mouse (*bright green, above*). Finding alternative methods of verifying the pluripotency of human iPSCs is an important goal.

Identity Crisis

Although iPSC colonies may look like embryonic stem cells under a microscope and may display the molecular markers associated with pluripotent cells, the unequivocal proof of their pluripotency comes from functional testing—can the cells do all the things a pluripotent cell, by definition, can do? Even embryo cell colonies can contain some dud cells that do not display the pluripotency of a true embryonic stem cell, and scientists have developed a few routine tests to gauge a cell's pluripotency. With increasing stringency, they are: the ability of stem cells to produce a wide variety of body cell types in a petri dish when exposed to the appropriate developmental cues; the ability of stem cells to produce a teratoma (a type of tumor containing cells from all embryonic tissue lineages) when injected under the skin of a mouse; and the capacity, when injected into an early-stage mouse embryo, to contribute to the development of all tissue lineages, including germ cells, in the resulting newborn mouse.

Whereas embryonic stem cells generally pass all these tests, many iPSCs do not. Closer examination of the cells that fail has revealed that the viruses used to deliver the four key repro-

TAMI TOLPA (*illustration*); COURTESY OF ALEXANDER MEISSNER *Harvard University* AND MARIUS WERNIG *Stanford University* (*mouse embryos*)



2008–2009

Scientists demonstrate that iPSCs can be made using retroviruses carrying only three of the original Yamanaka reprogramming genes, then only two, or just by introducing the proteins encoded by the four reprogramming genes directly into cells.

2009–2010

Scientists focus on raising efficiency by identifying distinct patterns of gene activation (revealed by fluorescent markers) characterizing cells that will successfully convert to iPSCs. Skin cell identity and reprogramming-gene markers give way to pluripotency markers.

gramming genes into skin cells are often not properly shut off, and important genes in the cells' original DNA are not properly turned on, resulting in cells that have lost their skin cell identity without gaining a pluripotent identity. These partially reprogrammed cells therefore do not qualify as authentic pluripotent cells.

Ongoing studies of iPSCs that do pass all the pluripotency tests are aimed at pinpointing the differences that distinguish a "good" from a "bad" iPSC. Thorsten Schlaeger, George Daley and their colleagues at Harvard University, for example, recently identified a pattern of gene activity in skin cells undergoing the lengthy (about three weeks) process of changing their identity to that of pluripotent cells. The fluorescent markers displayed by these cells during the transition distinguished them from cells in the same colony that would not ultimately become iPSCs, and so this marker pattern could be used as an early indicator of successful conversion.

Because scientists cannot ethically perform the most stringent pluripotency test by injecting human iPSCs into human embryos, it is absolutely critical to ensure that human iPSCs fulfill all other criteria of pluripotency. These include the complete silencing of the potentially harmful viruses employed to deliver the reprogramming genes. Yamanaka's team members discovered, for example, that one third of the mice that they had generated by injecting iPSCs into developing mouse embryos later formed cancers as a consequence of residual retrovirus activity.

One of the main problems with using retroviruses as gene-delivery vehicles is that these kinds of viruses (HIV is one example) integrate themselves directly into the host cell's DNA strand, becoming a part of its genome. This ability allows the added genes to reside permanently and remain active in the host cell, but depending on where the virus inserts itself, it can cause DNA damage that sparks cancerous changes in the cell. In efforts to produce safer iPSCs, therefore, many labs have developed methods that avoid permanent genetic manipulation of cells.

My research group has used a modified type of adenovirus, which normally causes the common cold in humans, to deliver the four reprogramming genes into mouse cells without integrating into the cellular genome. Adenoviruses persist inside the cells for only a short period—just long enough to convert them into iPSCs. When we injected the resulting pluripotent cells into mouse embryos, they readily became incorporated into the developing animals, which were all tumor-free as adults. This discovery, along with several alternative approaches to producing virus-free iPSCs, should eliminate a major roadblock to one day applying iPSCs directly in human therapies.

[THE AUTHOR]

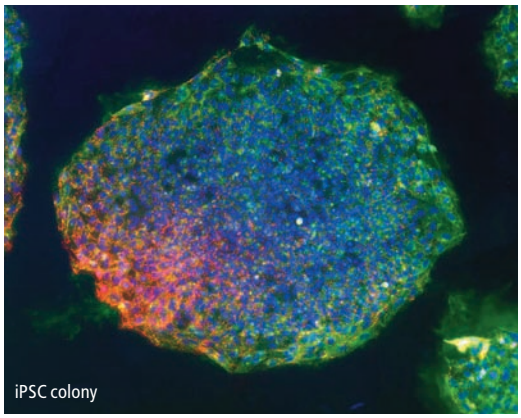
Konrad Hochedlinger is associate professor of stem cell and regenerative biology at Harvard University and a faculty member of the Harvard Stem Cell Institute and the Howard Hughes Medical Institute. In his laboratory at Massachusetts General Hospital, he works toward understanding the biology of stem cells and cellular reprogramming and their potential use in the treatment of disease. He is also a scientific adviser to iPierian, a biopharmaceutical company developing products based on stem cells.

COURTESY OF SAM RILEY *Massachusetts General Hospital*

[THERAPY POSSIBILITIES]

Custom-Tailored Cells to Cure Disease

An ability to transform a patient's skin or blood cells into iPSCs and then into any other type of cell could cure diseases in two ways: in the very near future, by allowing scientists to "model" illnesses and test drugs in a petri dish and, perhaps in another decade, by repairing or replacing diseased tissues.



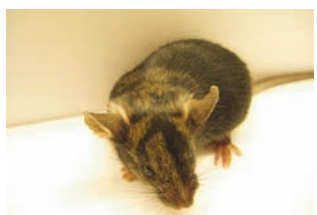
iPSC colony

APPLICATION	STATUS
DISEASE MODELING Convert iPSCs derived from patients into the affected tissue type, then study disease progression and drug responses in those cells	■ Human iPSCs have already been used to generate 12 tissue types, including cells representing diverse disorders such as Parkinson's disease and diabetes ■ Symptoms of smooth muscular atrophy and familial dysautonomia have been "treated" in cultured cells
CELL THERAPY Convert iPSCs derived from a sick patient into healthy cells for transplantation into that individual	■ 10 years or more in the future ■ iPSC-derived neurons have been transplanted into rats to treat a version of Parkinson's ■ iPSC-derived blood progenitor cells with corrected sickle cell anemia genes cured the disease in mice

Ultimately, researchers hope to produce iPSCs without using any type of virus, but instead by simply exposing adult cells to a combination of drugs that mimic the effect of the reprogramming genes. Sheng Ding of the Scripps Research Institute, Douglas A. Melton of Harvard and others have already identified chemicals that can substitute for each of the four reprogramming genes in that each chemical activates a pathway of molecular interactions inside a cell that would be activated by the gene. When the four drugs have been tried together, however, they proved insufficient to make pluripotent cells. It may only be a matter of time, though, until researchers find the right cocktail and concentration of drugs to reprogram body cells into iPSCs without ever using viruses.

Healing Cells?

Because pluripotent cells are capable of generating any type of tissue in the body, the application that most captures the public imagination is the possibility of using iPSCs to produce replacement parts for cells and organs damaged by disease: neurons lost to Parkinson's or a spinal cord injury, for instance, or cardiac tissue destroyed by a heart attack. The ability to convert adult cells from the intended recipient of such a transplant into pluripotent cells and then coax those cells into the desired tissue would mean the replacement part is perfectly matched, genetically and immunologically, with the recipient's body. Moreover, easily accessible skin cells could be used to produce any kind of needed cell, including those in hard-to-reach organs and tissues, such as the brain or pancreas.



ETHICS UNCLEAR

Injecting iPSCs into a developing mouse embryo yields a chimeric animal (*above*) that displays the presence of foreign cells in its mixed coat colors. The same technique could, in theory, create a chimeric human embryo; iPSCs could also theoretically generate sperm and eggs to produce a human embryo through traditional in vitro fertilization. The pluripotency of iPSCs thus could raise some of the same ethical issues as human embryo research.

This technique also offers the possibility of repairing disease-causing genetic mutations before reintroducing the new cells, an approach that has been used with the adult stem cells that naturally regenerate some tissues. Success has been limited, though, because those precursor cells are notoriously difficult to grow and manipulate outside the body.

Recent experiments in mice suggest that treating genetic disorders in this manner with iPSCs is indeed feasible. Specifically, Rudolf Jaenisch of the Massachusetts Institute of Technology showed in 2007 that iPSCs could cure sickle cell anemia in an animal. The disease results from a single genetic mutation that causes red blood cells to adopt a deformed crescentlike shape. In this proof-of-concept study, investigators first reprogrammed skin cells from the mice into iPSCs. They then replaced the disease-causing gene in the iPSCs with a healthy version and coaxed the "repaired" iPSCs into becoming blood-forming stem cells. After transplantation back into the anemic mice, the healthy precursors produced normal red blood cells. In principle, this method could be applied to any other disease in humans for which the underlying gene mutation is known.

The multimillion-dollar question is how long it might take before iPSCs can be used to treat people. For the reasons already outlined, safety and control are absolutely essential before any iPSC-derived cells could be tested in humans. Current strategies to push embryonic stem cells or iPSCs into fully differentiated mature cell types cannot yet efficiently eliminate the occasional immature stem cells that might

COURTESY OF WILLIAM COLLINS *Deepak Srivastava Lab, Gladstone Institute of Cardiovascular Disease (iPSC)*; COURTESY OF KONRAD HOCHEDLINGER AND MATTHIAS STADTFELD *Massachusetts General Hospital (mouse)*

seed a tumor. An example underscoring why this is such a problem comes from a recent experiment in transplanting iPSC-derived dopamine-making neurons, which are the cells lost in Parkinson's patients, into rats suffering a version of the human disease. Although the rats clearly benefited from the engrafted cells, some of the animals also eventually developed teratomas in their brain.

In light of the fast pace of discoveries so far, however, it is optimistic but not unreasonable to estimate that such obstacles could be overcome in as little as 10 years, and transplantation of iPSC-derived cells might then be ready for human testing to begin. But iPSCs could well demonstrate their therapeutic value much sooner. The study and treatment of many tissue-destroying diseases, such as type 1 diabetes, Alzheimer's and Parkinson's, are limited by scientists' ability to obtain the affected tissues for study or to grow them in cultures for extended periods, and iPSCs could therefore be of enormous service in so-called disease modeling.

The idea is to derive iPSCs from affected patients' skin or blood cells and then convert them into the cell types involved in the patients' diseases. Both Clive N. Svendsen of the University of Wisconsin–Madison and Lorenz Studer of the Sloan-Kettering Institute recently derived iPSCs from the cells of patients with the devastating disorders smooth muscular atrophy and familial dysautonomia, respectively. When the iPSCs were transformed into the cell types affected in each of those diseases, the cultured cells recapitulated the abnormalities just as they are seen in patients.

This process could allow researchers to study the development of a disease in a petri dish, with the advantage of having a potentially endless supply of new cells, because the original iPSCs can be maintained indefinitely. Ultimately, the goal of academic scientists as well as pharmaceutical companies is to use these petri dish models to better understand the disease process and identify novel drugs to treat the illness.

This extremely promising use of iPSCs is not far off at all. Indeed, when Svendsen and Studer exposed their cell cultures to experimental drugs in each study, the disease "symptoms" were partially alleviated in the cells. This principle can now be applied to many other disorders for which treatments do not yet exist, and unlike transplanting cells into individuals, the result may be the development of drugs from which millions could benefit.

CELLS FOR SALE

The first commercially marketed product made from human iPSCs, a heart cell line called iCell Cardiomyocytes, is intended for use by pharmaceutical companies to test the effects of potential heart drugs.

MORE TO EXPLORE

Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors. Kazutoshi Takahasi and Shinya Yamanaka in *Cell,* Vol. 126, No. 4, pages 663–676. Published online August 10, 2006.

Epigenetic Reprogramming and Induced Pluripotency. Konrad Hochedlinger and Kathrin Plath in *Development,* Vol. 136, No. 4, pages 509–523; February 15, 2009.

Induced Pluripotent Stem Cells and Reprogramming: Seeing the Science through the Hype. Juan Carlos Izpisúa Belmonte, James Ellis, Konrad Hochedlinger and Shinya Yamanaka in *Nature Reviews Genetics*, Vol. 10, No. 12, pages 878–883. Published online October 27, 2009.

Find an enriched multimedia version of this article at **www.ScientificAmerican.com/interactive**

Challenges and Hope

Although iPSCs clearly circumvent some of the ethical and legal controversies surrounding embryonic cells, their pluripotency has yet to be completely understood or controlled, and embryonic stem cells therefore remain the gold standard for any pluripotent cell type.

Important unanswered questions include the practical issue of whether the conversion of body cells into iPSCs and the conversion of iPSCs into therapeutically relevant cell types can ever be made efficient enough for widespread use. Also unresolved is whether iPSCs retain any memory of the body cell type from which they are derived, a factor that could limit their ability to be converted into any other type of cell. We have gained some insight into the mechanisms by which a mature cell transforms into a pluripotent cell, but the process of reprogramming—how only a few genes manage to rewire the entire program of a mature cell into that of an embryonic cell—is still largely a black box.

Tackling such questions will require the continued use of embryonic cells as a reference point and will determine whether embryonic stem cells may be more effective for certain types of applications and iPSCs for others. Moreover, as truly pluripotent cells, iPSCs may raise ethical issues similar to concerns over embryonic cells because, in theory at least, iPSCs could be used to generate human embryos [*see box on opposite page*].

Nevertheless, from a scientific standpoint progress in the field of cellular reprogramming in recent years is truly astounding. Advances in cloning and, more recently, the discovery of iPSCs have refuted the old dogma that the identity of cells is irreversibly locked once they have differentiated. Both techniques have raised the possibility, at least, of reprogramming the identity of a body cell from one type of tissue into that of any other tissue type just by manipulating a few genetic switches. Understanding how this rewiring works at a mechanistic level will keep researchers energized and busy for years to come.

Only time can reveal whether iPSCs or related technologies will indeed become the modern Fountain of Youth. I personally think there is a good chance they will. Certainly iPSCs will continue to influence approaches to the study and treatment of many devastating diseases and have the potential to revolutionize medicine in the 21st century as profoundly as vaccines and antibiotics did in the 20th century. ■

Revolutionary RAIL

High-speed trains are coming to the U.S.

BY STUART F. BROWN

FAST LANE: CALIFORNIA'S planned high-speed line, shown here in an artist's impression, will likely be the first true high-speed rail line to be built in the U.S. With more than $11 billion in financing secured, construction could begin as early as next year.

America is an absurdly backward country when it comes to passenger trains. As anyone who has visited Europe, Japan or Shanghai knows, trains that travel at nearly 200 miles per hour have become integral to the economies of many countries. With its celebrated Tokaido Shinkansen bullet trains, Central Japan Railway has for the past five decades carried billions of passengers between Tokyo and Osaka in half the time it would take to fly [*see box on next page*]. A new Madrid-to-Barcelona express train runs at an average speed of 150 miles per

KEY CONCEPTS

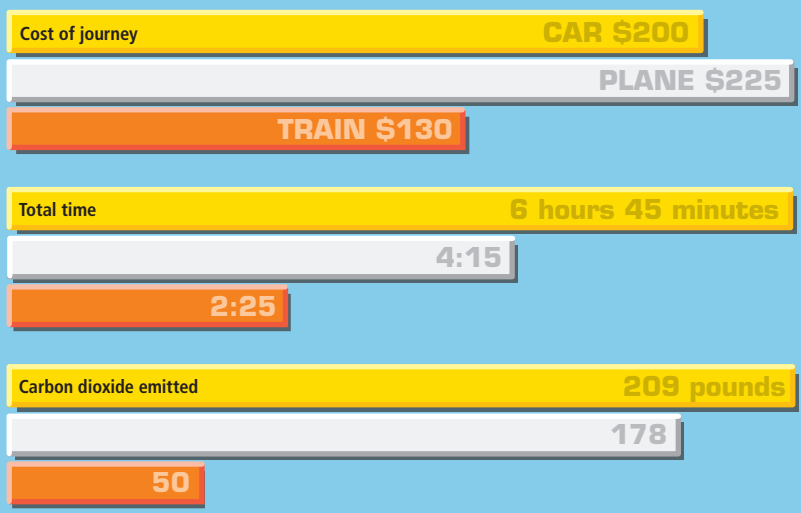
- Unlike Japan, France and other countries, the U.S. has no true high-speed train lines.
- A recent influx of federal money is spurring hope that long-planned projects could finally be built.
- Such projects include both steel-wheels-on-rails and magnetic levitation technology.

—The Editors

[HEAD-TO-HEAD]

The Benefits of Rail

The rail line that stretches the 320 miles between Tokyo and Osaka in Japan demonstrates a few of the benefits of high-speed trains. The figures below all refer to a one-way trip between the central business districts of each city.



SOURCES: U.S. Government Accountability Office, Reuters, Bureau of Transportation Statistics, Japan Central Railway.

▲ ALTERNATE ROUTE: Japan's Tokaido Shinkansen bullet trains carry 150 million passengers every year.

hour; since its inception two years ago, airline traffic between the two cities has dropped by 40 percent. In contrast, Amtrak's showcase Acela train connecting Boston to Washington, D.C., averages just 70 mph. That figure is so low because many sections of the Acela's tracks cannot safely support high speeds, even though the train itself is capable of sprints above 150 mph. Think of it as a Ferrari sputtering down a rutted country lane.

There has been a recent push to change all this. Earlier this year the Department of Transportation announced the recipients of $8 billion in stimulus funding designed to spread high-speed rail across the U.S. The 2010 federal budget requests an additional $1 billion in rail construction funds in each of the next five years. And in 2008 California voters approved a $9-billion bond measure to initiate an ambitious high-speed rail network that would connect Los Angeles to San Francisco and, eventually, Sacramento and San Diego.

Questions remain, however, about exactly what kind of passenger system will be built. In the decades since the federal government last pursued rail as a viable way to transport passengers—not just freight—train technology has advanced significantly, with advanced high-speed lines spreading through Europe and, more recently, across mainland China.

And what exactly qualifies as "high speed" by the guidelines of the stimulus funding is open to interpretation. Federal authorities, eager to spread the wealth to as many congressional districts as possible, are financing a bevy of incremental improvements to existing lines. In many cases, these projects will only marginally increase passenger rail speeds.

On the other end of the technological spectrum, some efforts aim to bypass wheels-on-rail systems by using magnetic levitation, or maglev technology, in which passenger cars float above a concrete guideway. Momentum for the technology comes in a number of forms. Although maglev trains have been in development for decades, the first (and, thus far, only) commercial system entered service in 2004. For mountainous regions of the U.S., the technology represents the only viable solution to the problem of steep gradients that would otherwise cripple standard rail lines. And perhaps most important, the technology has received a stunning vote of confidence from the world's foremost experts in building and operating commercial high-speed passenger rail lines.

The Maglev Option

The Central Japan Railway (CJR) has by far the world's largest body of experience in operating high-speed trains, having run the sleek wheels-on-rail Shinkansen bullet trains connecting the population centers of Tokyo, Nagoya and Osaka since 1964. Yet the realities of running the bullet system are now spurring CJR's interest in maglev. Every night a marching army of 3,000 railway workers descends on a 12-mile section

COURTESY OF CALIFORNIA HIGH-SPEED RAIL AUTHORITY (*preceding pages*); LUCY READING-IKKANDA (*bar chart*); TOSHIYUKI AIZAWA Getty Images (*trains*)

of Shinkansen track, scrutinizing the rights-of-way, replacing worn components and assuring precision alignment of the rails. The following night they labor on the next 12-mile section of track. The work never ends.

The company must invest all this costly effort because even small imperfections in the tracks can trigger serious vibrations in the speeding trains. These vibrations, in turn, increase wear and tear on the infrastructure. The deterioration of rails, train wheels and the overhead catenary wires supplying electricity to locomotives increases exponentially with the train's running speed. Truly high-speed rail turns out to be murder on the hardware. If the nighttime maintenance work on the Shinkansen line takes longer than expected, its 309-train daily schedule is thrown into chaos.

Hoping to avoid such difficulties, the company plans to construct a high-speed maglev line called the Tokaido Shinkansen Bypass, which it aims to complete by 2025. Although this would not be the world's first commercial maglev line—a 19-mile shot connecting Shanghai's airport with its financial center opened in 2004—at 180 miles, it will be by far the most ambitious. Yoshiyuki Kasai, CJR's chair, told a gathering of transportation officials in Washington, D.C., last June that maglev would be less expensive than traditional high-speed rail in the long run because of less costly upkeep demands over the life cycle of the system. CJR also says maglev promises to reduce trip times because the trains accelerate and slow down much more rapidly than wheel-on-rail trains can.

More significant for the prospects of maglev technology in the U.S., maglev propulsion allows trains to climb much steeper gradients than standard high-speed rail lines can. It is the only way fast trains could pass through much of the western U.S.'s jagged terrain.

The problem for classic technology is traction. Locomotives' steel wheels can maintain only so much adhesion to steel rails before they start to slip, and the train stalls. Common and unpredictable conditions such as rain, snow, ice and even wet leaves place a limit on the steepness of the grade a train can climb or safely de-

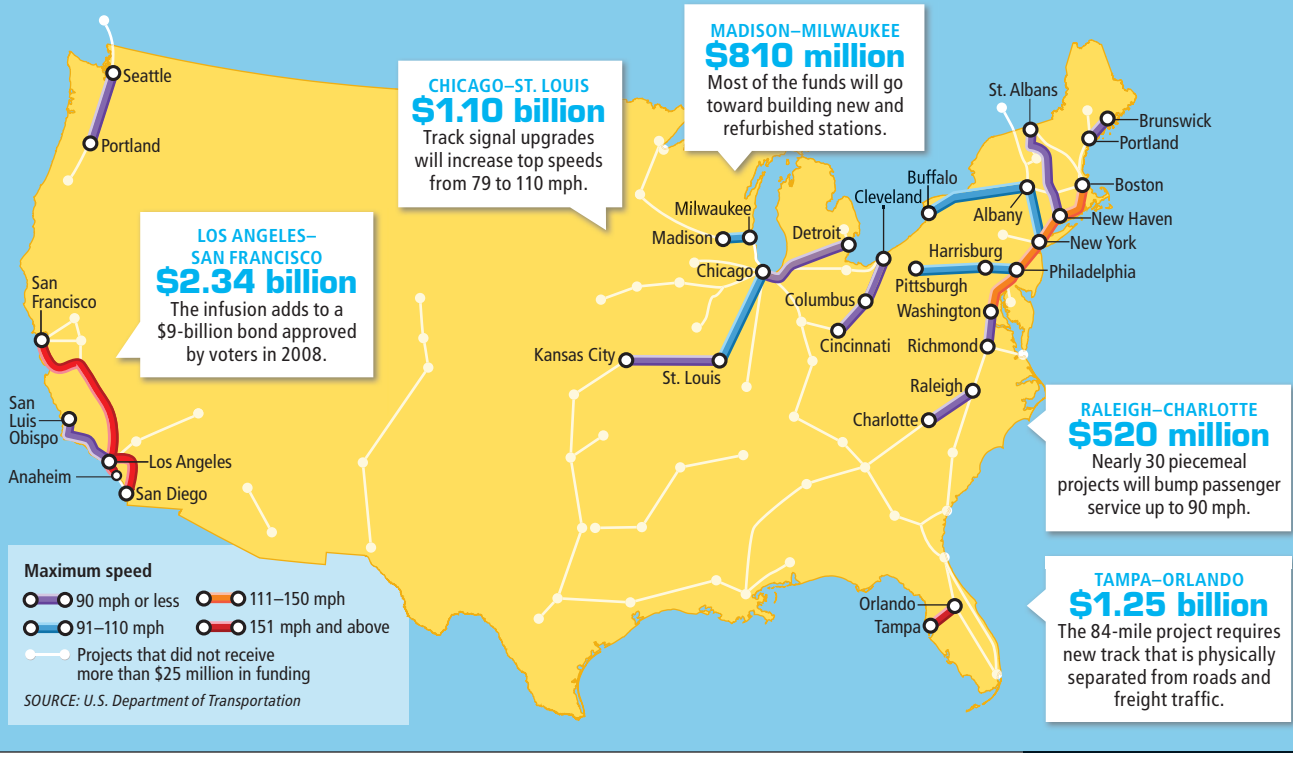
[THE AUTHOR]

Contributing editor Stuart F. Brown has been covering transportation topics such as rail, automobiles, trucks, boats, aircraft and spacecraft since 1984. His work been recognized by the American Association of Engineering Societies, the American Chemical Society and the Institute of Electrical and Electronics Engineers.

[FUNDING]

THE FEDERAL EXPRESS

In January the government announced the recipients of $8 billion in stimulus funds for high-speed rail. The biggest individual slices went to true high-speed projects in California and Florida; the rest of the money will be used to incrementally improve passenger service on lines shared with freight trains. The colored lines below mark all projects awarded more than $25 million; the boxes highlight the five biggest winners.



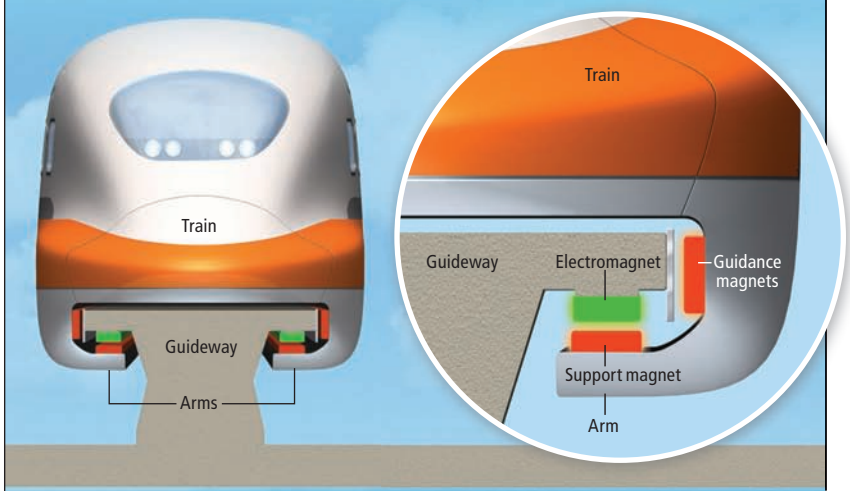
NILES A. JAEGER (*Brown*); JESSICA HUPPI (*map*)

[HOW IT WORKS]

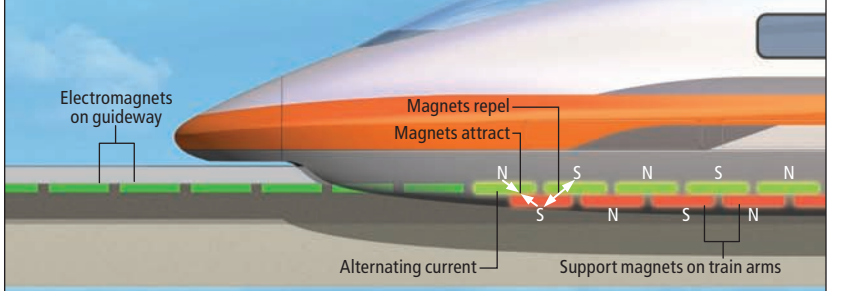
THE PULL OF MAGLEV

The Central Japan Railway has announced that it will build a 200-mile-long line that will use magnetic levitation—or maglev—technology. Maglev systems employ magnetic fields to lift and propel trains above concrete guideways. Because it eliminates the friction between steel wheels and rails, the approach not only raises speeds, it significantly reduces wear on the system, leading to lower maintenance costs. Planners in Colorado, Nevada and California hope to bring similar systems to the U.S.

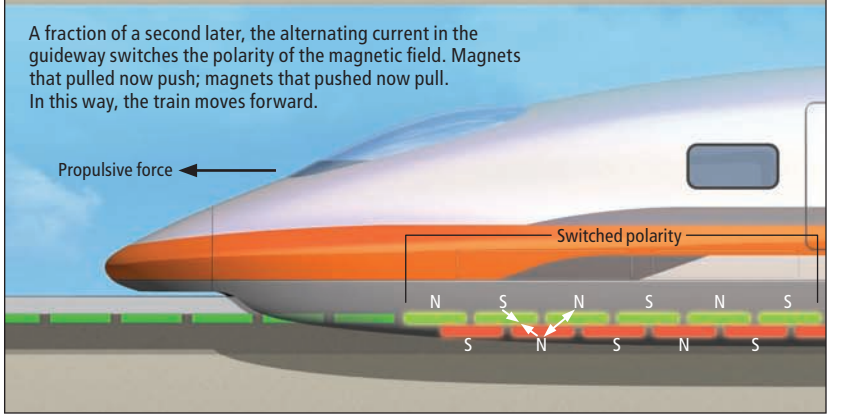
▼ **LEVITATION:** In a maglev system, arms on each side of the train reach around and below an elevated concrete guideway. Electromagnets on the underside of the guideway attract support magnets installed in the train's arms. Sophisticated control systems balance the weight of the train against the magnets' pull, keeping the train a constant distance from the track. In addition, guidance magnets on each side ensure that the train stays centered.



▼ **PROPULSION:** Old-fashioned trains have locomotives. In a maglev, the guideway does most of the work. Inside the guideway an alternating current creates a moving magnetic field that pulls the support magnets on the train's arms. By varying the frequency of the alternating current, the train can accelerate or decelerate as needed. The current goes through only the section of guideway that has the train directly above it.



A fraction of a second later, the alternating current in the guideway switches the polarity of the magnetic field. Magnets that pulled now push; magnets that pushed now pull. In this way, the train moves forward.



scend. Because of this limitation, grades on railways in the U.S. are generally kept below 3 percent, and grade maximums of 2 percent or less are most common.

Maglev lines, in contrast, have no steel-on-steel contact, so traction does not pose the challenge it does on a wheels-on-rails line. Maglev lines can climb a 10 percent grade, which permits planners to select more expeditious routes when laying out new rights-of-way through hilly terrain.

The technology also allows for high-speed transport in areas that would otherwise remain impassable. The Rocky Mountain Rail Authority recently completed an 18-month study of building two intersecting high-speed train lines running along about 400 miles of Colorado's north-south and east-west interstate highways. It concluded that the trains need to be maglev, because some of the grades along the highways reach 7 percent. "You're going through the Rocky Mountains," says Harry Dale, the rail authority's chair. He also notes that because magnetic forces, not physical adhesion, propel and slow the train, Colorado's "snow and ice problem goes away."

Dale believes that the maglev trains built by Transrapid International, a joint venture of the German firms Siemens and ThyssenKrupp, could do the job. Transrapid is the manufacturer of the Shanghai airport system, which has whisked more than 17 million passengers from Shanghai to its airport at peak speeds of 267 mph. Transrapid's maglev trains use conventional electromagnets; the Japanese, on the other hand, have been researching technology that employs superconducting electromagnets not unlike those found inside the Large Hadron Collider. While the superconducting approach provides greater clearance between train and guideway as a precaution against earthquakes, the magnets must be cooled with liquid helium, an expensive and unwieldy proposition.

The Fast Route

Competing proposals for a passenger train line connecting Las Vegas to southern California further demonstrate just how important maglev technology can be. Urban planners have dreamed of linking Las Vegas to Los Angeles with fast trains for decades. "This is an ideal corridor for high-speed trains because you are connecting one of the biggest entertainment districts in America with southern California, one of the largest population centers," says engineer Thom-

GEORGE RETSECK

as Bordeaux, senior transportation manager at Parsons Transportation, an engineering firm in Las Vegas. The cities are 270 miles apart—right in the sweet spot between 100 and 500 miles where train travel is more convenient than either driving or flying. And the land between those two cities is little more than sand and scrub, a blank canvas on which to paint the tracks.

Unfortunately, the Los Angeles basin is flanked to the east by the San Bernardino and San Jacinto mountain ranges. Any high-speed line penetrating these natural obstacles would have to scale grades of up to 7 percent, which is only feasible using maglev technology. The California-Nevada Super Speed Train project aims to do just that, connecting Las Vegas with Anaheim, a large city just south of Los Angeles.

The alternative to maglev technology is to avoid the L.A. basin area altogether. The DesertXpress, as the project is called, would build a traditional high-speed rail line that links Las Vegas to Victorville, a high desert outpost more than an hour and a half from downtown Los Angeles (this assumes no traffic, which is an anomaly in L.A.). While it would not require advanced technology, it also would not take passengers anywhere they would want to go.

The DesertXpress will also fail to connect to the planned California high-speed rail system that will link Los Angeles to San Francisco. The California project was one of the two big winners in this year's stimulus fund giveaway, along with an 84-mile route connecting Tampa and Orlando in Florida. When the stimulus money is combined with the $9 billion secured in the 2008 voter referendum, the California project will have in hand more than a quarter of its $40-billion projected total cost. Construction is likely to begin as early as 2011.

Exclusive Access

Regardless of whether maglev or conventional rail-on-wheels technology is used, an inviolable requirement for safe fast-train operation is having special tracks dedicated to the high-speed trains, no exceptions permitted. That is where Amtrak's pokey Acela line, which shares its route with freight and slower passenger trains, was born to fail.

Another necessity is laying out the track so that there are no grade-level crossings, which is where most crashes happen involving trains and road-going vehicles. Time and time again, people try to drive around a closed crossing gate to beat the train, or pedestrians who are unaware that oncoming locomotives project very little sound in front of them notice a train when it is too late to escape. Depending on a route's terrain, lots of overpasses, underpasses and tunnels may be needed to keep the rest of the world out of the exclusive path of the fast trains.

Why has it taken so long for the U.S. to get onboard with technologies that are already ripe? The short answer: passenger trains have not been a federal priority for quite some time. The nation spent decades building interstate highways and airports; investment in tracks suitable for fast trains dwindled to almost nothing. American railroads became almost exclusively low-speed haulers of heavy freight.

But the recent push for green transportation, along with the realization that the nation's highways and airports are already operating past capacity, could bring fast trains into vogue—at least in a few key regions of the country. ■

[COST COMPARISON]

Maglev vs. Traditional High-Speed Rail

The existing and planned high-speed train projects listed below demonstrate that the cost of a project depends greatly on individual circumstances. The most important factors include the terrain the line must pass through (mountainous areas are more costly), how densely populated the area is, the cost of labor, and the technology being used.

Line	Estimated construction cost per mile (millions)	Status	Technology	Length (miles)
Yatsushiro to Kagoshima	$82	Completed 2004	Wheels on rail	79
Barcelona to Madrid (*pictured above*)	$39	Completed 2008	Wheels on rail	468
Los Angeles to San Francisco	$63	Proposed	Wheels on rail	520
Las Vegas to Victorville	$22	Proposed	Wheels on rail	183
Las Vegas to Anaheim	$48	Proposed	Maglev	269
Baltimore to Washington, D.C.	$132	Proposed	Maglev	40

MORE TO EXPLORE

High Speed Passenger Rail. Report of the U.S. Government Accountability Office, GAO-09-317, March 19, 2009. **www.gao.gov/products/GAO-09-317**

The Third Way: Will a Boom in Government Investment Bring True High-Speed Rail to the U.S.? Michael Moyer in *Scientific American*, Vol. 301, No. 2, pages 15–16; August 2009.

California High-Speed Rail Authority Web site: **www.cahighspeedrail.ca.gov**

Transrapid maglev technology demonstration: **http://bit.ly/transrapid**

GEORGE RETSECK

Uncanny SIGHT in the BLIND

Some people who are blind because of brain damage have "blindsight": an extraordinary ability to react to emotions on faces and even navigate around obstacles without knowing they can see anything

BY BEATRICE DE GELDER

The video my colleagues and I shot is amazing. A blind man is making his way down a long corridor strewn with boxes, chairs and other office paraphernalia. The man, known to the medical world as TN, has no idea the obstacles are there. And yet he avoids them all, here sidling carefully between a wastepaper basket and the wall, there going around a camera tripod, all without knowing he has made any special maneuvers. TN may be blind, but he has "blindsight"—the remarkable ability to respond to what his eyes can detect without knowing he can see anything at all. [To see the film of the experiment, go to www.ScientificAmerican.com/may2010/blindsight.]

TN's blindness is of an extremely rare type, caused by two strokes he suffered in 2003. The strokes injured an area at the back of his brain called the primary visual cortex, first on his left hemisphere and five weeks later on the right. His eyes remained perfectly healthy, but with his visual cortex no longer receiving the incoming signals he became completely blind.

This study of TN navigating along the hallway is probably the most dramatic demonstration of blindsight ever reported. Other patients who have lost vision because of damage to the primary visual cortex have exhibited less spectacular but equally mysterious cases of the phenomenon—responding to things they cannot consciously see, ranging from simple geometric shapes to the complex image of a person's face expressing an emotion. Scientists have also induced a similar effect in healthy people, by temporarily "switching off" their visual cortex or by outfoxing it in other ways.

Today research into blindsight seeks to understand the range of perceptual abilities that may be retained by the cortically blind and to determine which brain regions and neuronal pathways are responsible. The knowledge being gained says something about us all, because even if we never suffer a catastrophic injury resembling TN's, the same unconscious brain

KEY CONCEPTS

- Some people who are blind because of brain damage exhibit "blindsight"—responses to objects and images they cannot consciously see.
- Blindsight can detect many visual features, including colors, motion, simple shapes, and the emotion expressed by a person's face or posture.
- Researchers are mapping the ancient brain areas responsible for blindsight and exploring the limits of this remarkable ability.

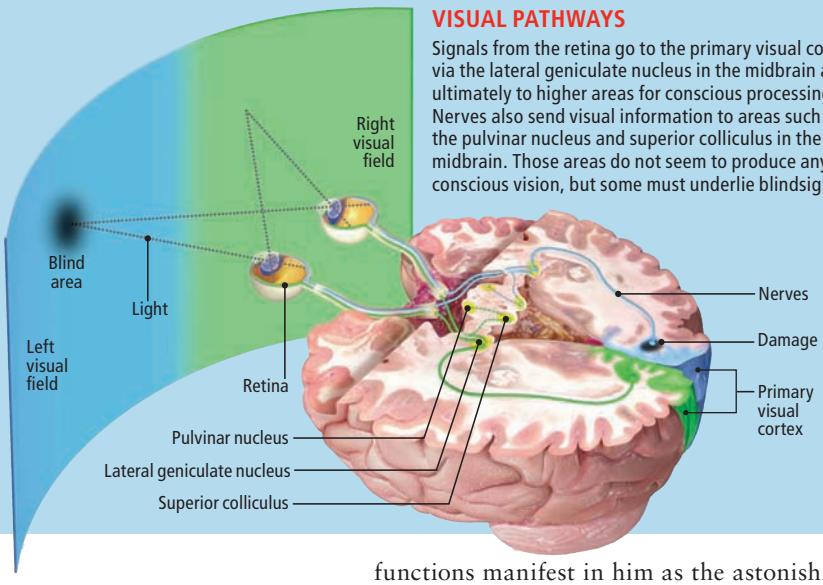
—The Editors

DARREN BRAUN

[BASICS]

What Is Blindsight?

Conscious vision in humans depends on a region of the brain called the primary visual cortex (*below*). Damage there causes blindness in corresponding areas of the visual field. "Blindsight" occurs when patients respond in some way to an item displayed in their blind area, where they cannot consciously see it. In a dramatic demonstration of the phenomenon, a patient called "TN" navigated an obstacle course despite his total blindness (*right*).



VISUAL PATHWAYS

Signals from the retina go to the primary visual cortex via the lateral geniculate nucleus in the midbrain and ultimately to higher areas for conscious processing. Nerves also send visual information to areas such as the pulvinar nucleus and superior colliculus in the midbrain. Those areas do not seem to produce any conscious vision, but some must underlie blindsight.

NAVIGATING BLIND

Suspecting patient TN might exhibit blindsight, researchers, including Lawrence Weiskrantz (*shown with TN above*), asked him to walk down a cluttered hallway, telling him it was empty. TN avoided all the obstacles, even though he remained unaware of them and of his meandering path. Video of the experiment is online at www.ScientificAmerican.com/may2010/blindsight.

functions manifest in him as the astonishing ability to see without knowing are surely a constant, invisible part of our own daily existence.

A Controversial History

As long ago as 1917, doctors reported cases like blindsight—then called residual vision—in soldiers injured in World War I. Half a century would pass, however, before more organized and objective research into the capacity began. First, Lawrence Weiskrantz and his student Nicholas K. Humphrey, both then at the University of Cambridge, studied surgically altered monkeys in 1967. Then, in 1973, Ernst Pöppel, Richard Held and Douglas Frost of the Massachusetts Institute of Technology measured the eye movements of a patient and found he had a slight tendency to look toward stimuli that he could not see consciously.

These discoveries spurred further systematic investigations of animals lacking the primary visual cortex (also called V1), most of them conducted by Weiskrantz and his collaborators. A number of studies established that animals retain significant visual abilities after removal of their visual cortex (for example, detecting movement and discriminating shapes).

Weiskrantz and his co-workers also began studies in 1973 with a person known as DB who had recently lost part of his visual cortex in surgery to remove a tumor. The wider research community, however, initially greeted reports of human blindsight with great skepticism.

Disbelief about blindsight is not surprising, because the phenomenon seems counterintuitive, if not outright contradictory. After all, how could people see without knowing that they see? Just as it does not make sense to say that I do not know if I am in pain, it also does not make sense, on the face of it, to suggest that somebody can see something when he insists he is blind.

Yet we do not always know that we can see. Nor do we always know that we cannot. The relation between seeing and knowing is more complicated than we commonly assume. For instance, people with normal sight have a blind spot, although we are not usually aware of this hole in our sight or handicapped by it.

Another reason for disbelief was the paucity of human evidence: subjects with cortical blindness who can be studied are rare. The primary visual cortex is only a few centimeters across in adults, and brain damage is seldom restricted to just that area, knocking out the patient's vision yet leaving other faculties intact enough for meaningful research on what the brain continues to perceive. Even so, it is now clear that many more patients with damage to the visual cortex have blindsight than scientists realized in the past, and skepticism has abated.

It is now clear that many more patients with damage to the visual cortex have blindsight than scientists realized in the past.

KEITH KASNOT (*illustration*); BEATRICE DE GELDER (*photograph*)

Most of these patients still have some functioning in the primary visual cortex. Many have damage to only a small part of V1, leading to a small island of blindness in their visual field; others lose the entire left or right half of V1, leaving them blind across the corresponding (opposite) half of their visual field. Blindsight in these cases involves detecting objects or images presented in the blind area, where the patient cannot see them consciously.

Traditional methods for studying vision in humans have relied on the viewers' verbal reports of what they perceive. Tested in that way, subjects will report not seeing anything in the blind part of their visual field. More indirect methods, however, can reveal that these unseen visual stimuli actually do influence how a patient responds.

In some experiments, patients show clear physiological changes, such as constriction of the pupil, as signs of unconscious seeing. And subjects can react differently to items shown in the intact visual field depending on what is presented at the same time in the blind field. When asked to guess which of several alternative items are displayed in the blind field, a patient may answer correctly almost every time.

Another important experimental tool is neuroimaging, which can provide direct evidence about the brain regions involved in blindsight and the pathways that the visual information travels. Brain imaging has been instrumental in dispelling lingering suspicions that some spared pieces of cortex might explain residual vision.

Collectively, these various kinds of experiments have revealed that people can unconsciously detect a wide range of visual attributes, including color, simple shapes such as X and O, simple motion, and the orientation of lines or gratings. Large shapes, as well as very fine detail, seem hard to detect. For instance, patients detect features of a grating most effectively if its lines are comparable to venetian blinds viewed from about 1.5 to 4.5 meters (five to 15 feet).

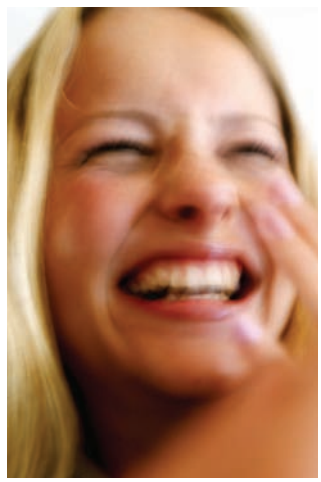
We were inspired to try the navigation experiment with TN by research Weiskrantz and Humphrey did in the 1970s: a monkey with no primary visual cortex freely moved around a room cluttered with objects without bumping into any of them. Nevertheless, we were amazed when TN made his way along the hallway with no collisions at all. Personalized psychophysical tests to assess his conscious vision had not found any visual functioning, including detection of big targets.

TN's ability to move down the corridor was reminiscent of sleepwalking, another phenomenon in which people exhibit a capacity to perform in some way without having any awareness of their actions. Indeed, when we questioned him afterward, he insisted he had simply walked along the hallway: he was not only unaware of seeing anything but also oblivious to how he had maneuvered around the unseen objects. He was at a loss to explain or even to describe his actions.

WHAT CAN BE DETECTED?

Blindsight is strongest when visual details are about the size of a quarter viewed from five to 15 feet away. It can detect an assortment of basic visual properties, including:

- Simple shapes
- Arrays of lines
- Objects appearing or disappearing
- Movement
- Color
- Orientation of lines



▲ **BLINDSIGHT can also recognize emotions being expressed by a person, but not who the person is or what the person's gender is.**

Blindsight for Emotions

Moving around is one of the most fundamental tasks an animal faces, so perhaps it should not be surprising that the brain has ways to support navigation even when the primary visual cortex and conscious vision are hobbled. As a social species, humans also depend for their survival on successful communication with others. They must recognize other people, along with their gestures and signs of what they are thinking. With such thoughts in mind, my collaborators and I began to wonder in the late 1990s if people with cortical damage could detect visual displays such as the emotion on a face or the meaning of a body posture in the usually inaccessible parts of their visual field.

In 1999 we started conducting tests using movies of faces. Vision researchers generally consider faces to be visually complex—far more difficult to process than gratings and other elementary shapes—but a face is a very natural form for the human brain to handle. Our patient, GY, had lost all of his primary visual cortex on the left side in childhood, rendering him blind on the right side of his visual field. We found he could reliably guess the expression appearing on faces he did not consciously perceive, but he seemed truly blind to a variety of nonemotional facial attributes such as personal identity and gender.

To study blindsight of emotions further, in 2009 we exploited a phenomenon called emotional contagion, a tendency to match one's own facial expressions to those of others that we see. Researchers measure emotional contagion with a procedure called facial electromyography, by which electrodes on a subject's face record nerve signals going to muscles involved in smiling or frowning. We used this technique on GY and DB while showing them still images of faces and whole bodies expressing happiness or fear.

All the stimuli triggered emotional reactions as measured by electromyography, irrespective of whether the image was on the patient's sighted side or his blind side. In fact, surprisingly, the

ANTHONY MARSLAND *Getty Images (happy)*; GETTY IMAGES (*sad*)

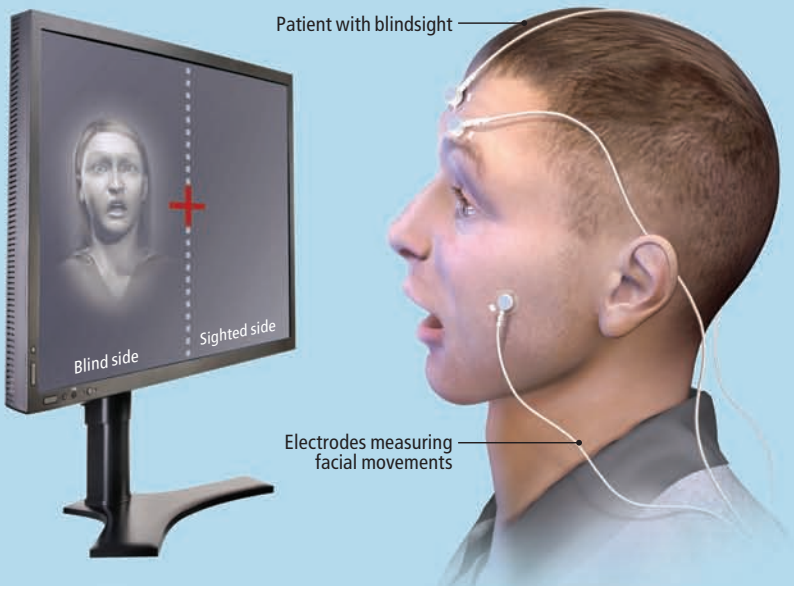
[EXPERIMENTS]

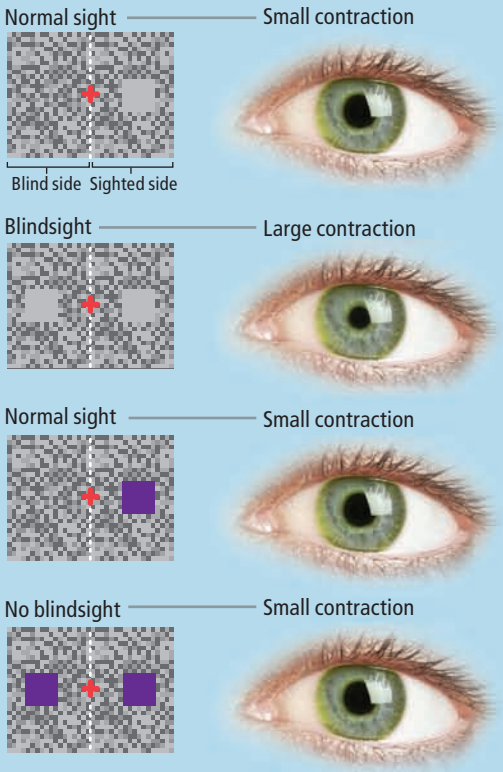
Investigating Blindsight

Because total cortical blindness like patient TN's is rare, studies of blindsight often use patients blind on one side of their visual field. The patient stares at a fixed point while images are presented on each side. The subject may be asked to "guess" what is on the blind side or to press a button on seeing items on the sighted side. Equipment may monitor brain activity and measure involuntary responses such as tiny facial movements and pupil dilation.

▼ DOES BLINDSIGHT SEE EMOTIONS?

Patients shown images on their blind side of people expressing emotions correctly guessed the emotion most of the time. Facial muscles used in smiling and frowning reacted in ways that matched the kind of emotion in the unseen image (*below, exaggerated*). Thus, the emotions were recognized without involving conscious sight. The effect worked with images of faceless bodies as well as faces, implying that patients were recognizing an emotion and not merely mimicking a facial expression unconsciously.





▲ WHAT BRAIN AREAS DOES BLINDSIGHT USE?

Researchers showed patients gray and purple squares, knowing the superior colliculus region in the midbrain receives no signals from the retina about purple objects. Gray squares but not purple ones triggered signs of blindsight such as greater pupil contractions. These results, along with neuroimaging of the patients in action, imply that the superior colliculus plays a critical role in blindsight.

MAPPING NEURAL PATHWAYS

Researchers are using advanced imaging techniques to attempt to trace the neural pathways that visual information travels in the brain to produce blindsight.

One such method is a kind of magnetic resonance imaging called diffusion tensor imaging, which relies on water diffusing more rapidly along neurons than across them.

Diffusion tensor imaging has mapped bundles of neurons that may be responsible for blindsight of emotions. The pathway connects the pulvinar nucleus and superior colliculus to the amygdala, which plays a key role in processing emotions.

unseen images produced a faster response than those seen consciously. We also monitored pupil dilations, a measure of physiological arousal. The unseen fearful images produced the strongest effect—seemingly the more we are consciously aware of an emotional signal, the slower and weaker is our reaction.

One school of thought holds that emotional contagion arises because people unconsciously mimic the expressions they see, without necessarily recognizing the emotion itself. But because our patients reacted not only to faces but also to bodies (which had blurred faces), we concluded that they were perceiving and responding to the emotion.

Blindsight for All

Because the number of suitable patients for blindsight studies is extremely small, inducing the phenomenon temporarily in people with completely healthy brains is a valuable tool for conducting controlled experiments. One technique uses visual "masking," more popularly known as the use of subliminal images: a visual stimulus flashes before the experimental subject very briefly, followed immediately by a pattern in the same location. The pattern interferes with conscious processing of the fleeting subliminal image, leaving the subject with no conscious awareness of seeing it, but experiments can tease out objective evidence that it was seen. Other experiments temporarily disable the visual cortex by applying magnetic fields to the back of the head, a technique called transcranial magnetic stimulation.

Numerous studies have shown that healthy subjects can reliably "guess" the nature of a stimulus even when it is presented too briefly for them to perceive it consciously or when transcranial magnetic stimulation is disabling their visual cortex. Much research has also investigated how normally sighted observers react to emotional stimuli they cannot see consciously. Even before such blindsight experiments got under way, studies in animals and humans suggested that structures in the subcortex (areas of the

KEITH KASNOT (*experiment and eyes*); LUCY READING-IKKANDA (*squares*)

brain that are deeper and more evolutionarily ancient than the cortex) can initiate appropriate responses before areas such as the visual cortex have analyzed the stimulus in detail. This nonconscious system seems to operate in parallel with the normal, predominantly cortical, processing routes. These subcortical areas that are activated by subliminal emotional stimuli are the leading suspects in processing emotions detected by blindsight in permanently blind patients.

Yet scientists continue to debate whether these temporary forms of blindness induced in normally sighted people are the true functional equivalent of blindsight in patients with permanent cortical damage. In particular, visual-masking techniques, such as the use of subliminal images, permit the visual cortex to process information as usual but interfere with further conscious processing. Consequently, "blindsight" of subliminal images could be a quite distinct phenomenon from blindsight in patients, involving its own characteristic assortment of brain regions. Transcranial magnetic stimulation presumably mimics cortical damage closely, but to know whether the resulting blindsight actually involves the same neuronal pathways requires experiments that combine the technique with neuroimaging.

Conversely, after an injury, a patient's brain (even an adult's) may start rewiring itself to compensate for the loss. Such neural plasticity could well create pathways for blindsight that are not present in the normally sighted people who are studied using transcranial magnetic stimulation and visual masking. Until these issues are better understood, studies of patients with injuries will remain crucial for fathoming how noncortical regions produce residual vision.

Neural Pathways

Research has not yet fully determined the neural structures responsible for blindsight in the cortically blind, but the most likely candidate to play a central role is a brain region called the superior colliculus (SC), which sits in a part of the subcortex called the midbrain. In nonmammals such as birds and fish, the SC is the main structure receiving input from the eyes. In mammals it is overshadowed by the visual cortex but remains involved in controlling eye movements, among other visual functions. Blindsight would exploit information that travels from the retina to the SC without first going through the primary visual cortex.

Last year my colleagues and I showed that this midbrain area is essential for translating a visual signal that cannot be consciously perceived into an action. Specifically, we had a patient press a button whenever we showed him a square on his sighted side. Sometimes we simultaneously presented a square on his blind side. Sometimes we used gray squares and sometimes purple ones. We chose a purple hue that only one type of light-detecting cone cell in the retina detects, knowing that the SC receives no inputs from that type; it is blind to this purple.

A gray square on our patient's blind side accelerated his response and made his pupils constrict more—a sign of processing the stimulus—whereas a purple square had neither effect. In other words, he exhibited blindsight of gray stimuli but not purple ones. Brain scans showed that his SC was most strongly activated only by the gray stimulus on his blind side. Some other areas in the midbrain have been suspected of being involved in blindsight instead of the SC, but in our experiment their activity seemed unrelated to the occurrence of blindsight.

These findings show that the SC acts in the human brain as an interface between sensory processing (sight) and motor processing (leading to the patient's action), thereby contributing to visually guided behavior in a way that is apparently separate from the pathways involving the cortex and entirely outside conscious visual experience. Blindsight of emotions displayed by people also involves the SC as well as other areas in the midbrain, such as the amygdala.

Blindsight has captured a lot of attention from philosophers, who are intrigued by the paradoxical idea of seeing without knowing that one sees. The idea, of course, is only a paradox if "seeing" is always taken to mean "consciously seeing." That mind-set was a stumbling block to acceptance of blindsight by scientists, delaying progress in understanding the role of unconscious seeing in human cognition.

It can also be a stumbling block for patients suffering from cortex-based loss of vision, preventing them from unlocking the potential of their residual visual skills in their everyday lives. For example, TN views himself as a blind person, and he will remain totally dependent on his white cane until he is convinced he can see without knowing it. Training may also help. After three months of daily stimulation, cortically blind patients were better at detecting targets in their blind field. Whether training in realistic conditions could lead to improved navigation skills is, like so many other features of blindsight, a question for future research. ■

[THE AUTHOR]

Beatrice de Gelder is professor of cognitive neuroscience and director of the Cognitive and Affective Neuroscience Laboratory at Tilburg University in the Netherlands. She is also on the faculty of the Athinoula A. Martinos Center for Biomedical Imaging in Charlestown, Mass. De Gelder investigates the neuroscience behind processing of faces and emotions and the ways cognition and emotion interact in both healthy and damaged brains.

MORE TO EXPLORE

Unseen Facial and Bodily Expressions Trigger Fast Emotional Reactions. Marco Tamietto et al. in *Proceedings of the National Academy of Sciences USA,* Vol. 106, No. 42, pages 17661–17666; October 20, 2009.

Collicular Vision Guides Nonconscious Behavior. Marco Tamietto et al. in *Journal of Cognitive Neuroscience,* Vol. 22, No. 5, pages 888–902; May 2010.

Affective Blindsight. Beatrice de Gelder and Marco Tamietto in *Scholarpedia,* Vol. 2, No. 10, page 3555; 2007. Available at **www.scholarpedia.org/article/Affective_blindsight**

Helen, a Blind Monkey Who Sees Everything. Video from 1971. Available at **bit.ly/blindsightmonkey**

COURTESY OF M. KRET

Arctic Plants

Global warming is dramatically revamping not only the ice greening some parts and browning others. The alterations

KEY CONCEPTS

- A detailed set of aerial photos taken in the 1940s for oil exploration in northern Alaska has provided the most graphic evidence that the Arctic tundra is turning shrubbier and is "greening."
- Satellite remote sensing indicates that, in sharp contrast, the boreal forests south of the tundra are "browning"—the result of dry conditions, more intense fires, and insect infestations.
- Both the greening and the browning can be attributed to global climate change. These ecosystem transitions are likely to profoundly affect the wildlife and human inhabitants of the region and may even intensify global warming.

—The Editors

The year was 1944. World War II was showing signs of winding down, but predictions that the Japanese would fight to the bitter end had the Allies gravely concerned that they would run out of gasoline for the war effort. The 23-million-acre Naval Petroleum Reserve in northern Alaska was a prime location for finding new sources of oil, and the U.S. Navy decided to explore. But the navy had a problem: no maps. So it decided to take an exceptionally detailed set of aerial photographs.

Basing out of Ladd Field, near Fairbanks, surveyors mounted a massive K-18 camera in the open door of a twin-engine Beechcraft. Over several years, flying low and slow, they took thousands of photographs of Alaska's North Slope, extending from the Arctic Ocean south to the Brooks Range, and of the forested valleys on the south side of the range—itself a part of the boreal forest of evergreens and deciduous trees that stretches across a large swath of the Arctic [*see map on page 68*].

Feel the Heat

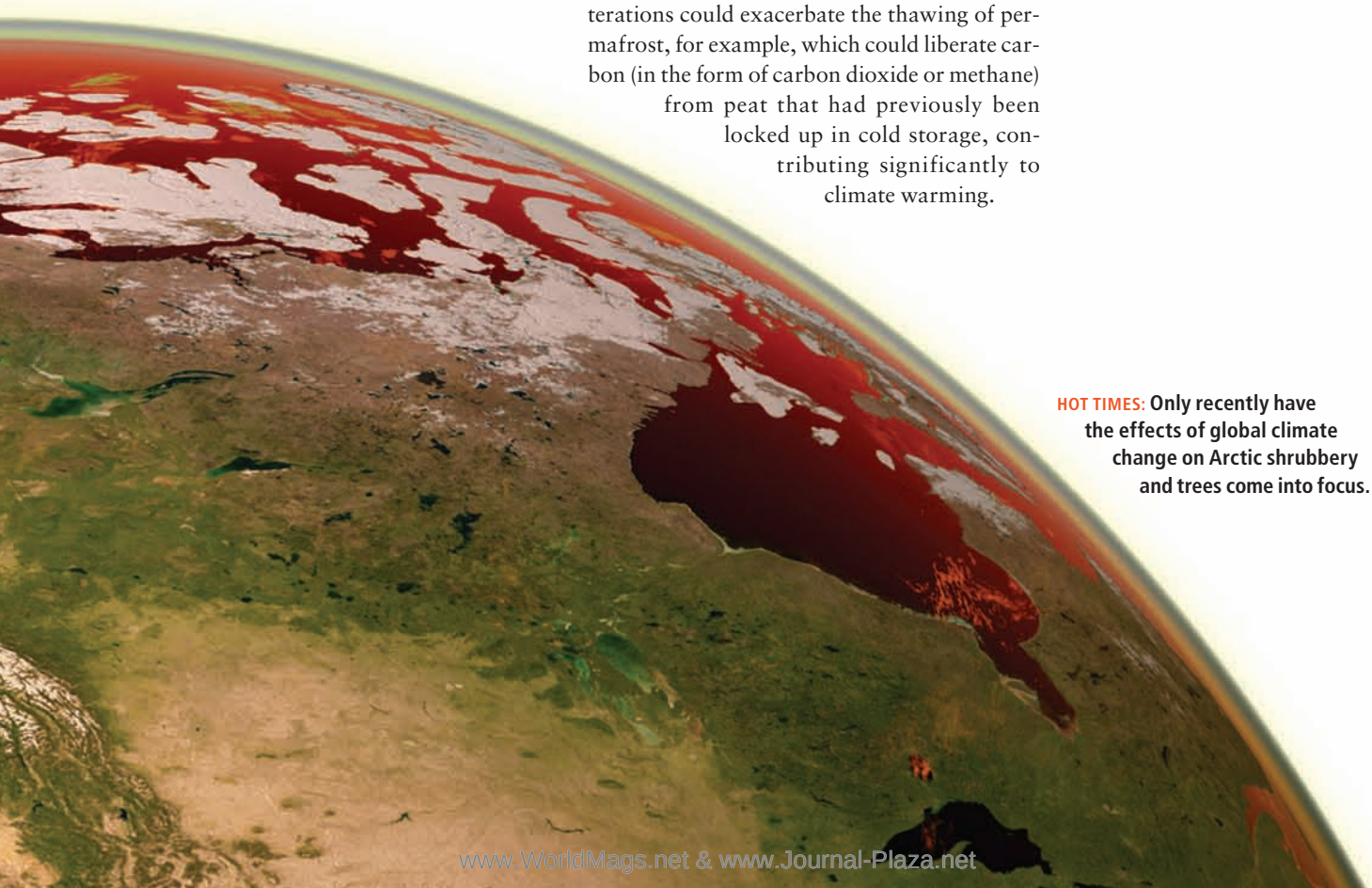
but also tundra and forests at the top of the world, could exacerbate climate change

By Matthew Sturm

The nine-by-18-inch negatives produced pictures so sharp that hoofprints of moose were visible. Some images were worthy of Ansel Adams, but more important, the full set has proved to be a crucial part of the evidence revealing how Arctic and sub-Arctic lands have been responding to climate change.

That question is pressing because the answers will help local inhabitants figure out what steps they need to take to cope with the changes. Approximately four million people live in the Arctic, and the climate shifts are affecting subsistence hunting, commercial logging, transportation and infrastructure.

Moreover, unexpectedly fast changes in land cover could have global ramifications. These alterations could exacerbate the thawing of permafrost, for example, which could liberate carbon (in the form of carbon dioxide or methane) from peat that had previously been locked up in cold storage, contributing significantly to climate warming.

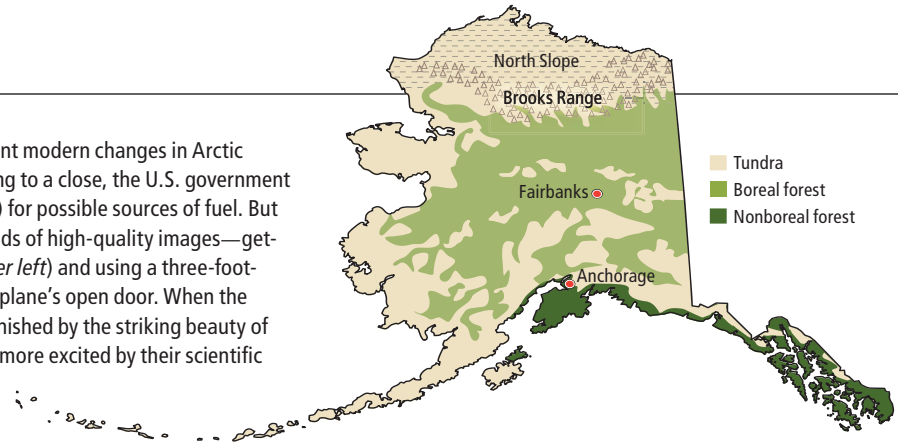


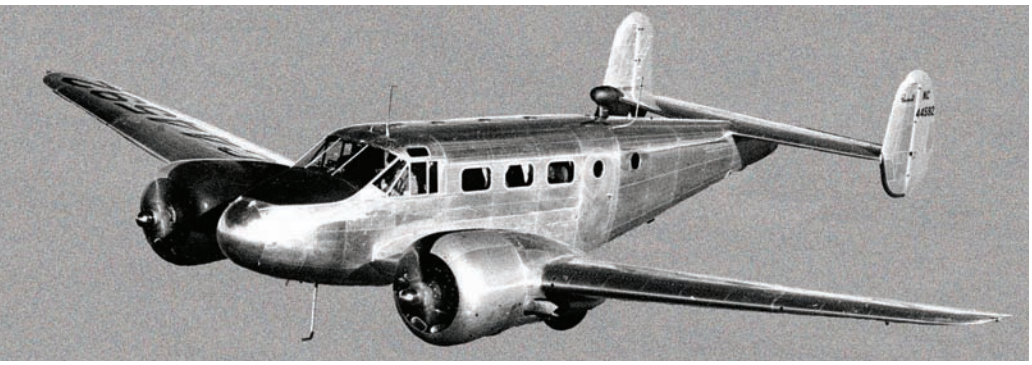
HOT TIMES: Only recently have the effects of global climate change on Arctic shrubbery and trees come into focus.

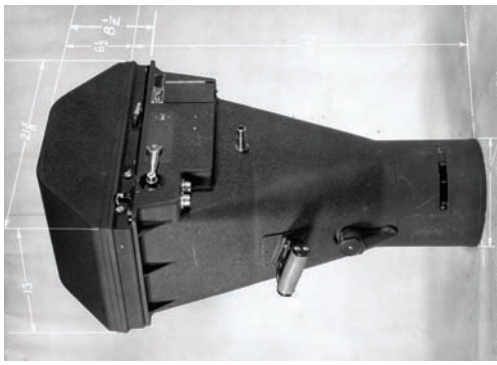
[HELP FROM HISTORY]

Sixty Years Ago

A World War II–era project has inadvertently helped document modern changes in Arctic vegetation. Worried about oil supplies as the war was drawing to a close, the U.S. government decided to survey Alaska's North Slope (*dashed area on map*) for possible sources of fuel. But no useful maps existed. So U.S. Navy surveyors took thousands of high-quality images—getting the shots by flying low in a twin-engine Beechcraft (*lower left*) and using a three-foot-long, large-format K-18 camera (*lower right*) mounted in the plane's open door. When the author obtained the photographs decades later, he was astonished by the striking beauty of many of them (*example at bottom of page*). But he was even more excited by their scientific import: he and his co-workers went on to reshoot the same locations and compare the images, thereby documenting profound changes in the vegetation.







JEAN-FRANCOIS PODEVIN AND NASA (*preceding pages*); JESSICA HUPP (*map*); AP PHOTO (*airplane*); COURTESY OF NATIONAL MUSEUM OF THE U.S. AIR FORCE (*camera*)

How to Measure Greening

Even before a polar bear on a tiny ice floe made the cover of *Time* magazine in 2006 , it was clear that the Arctic sea ice was melting rapidly [see "Meltdown in the North," by Matthew Sturm et al.; Scientific American, October 2003]. By the 1990s those of us who study climate change in the Arctic had good reason to think that Arctic vegetation was also changing, but our tools for tracking terrestrial alterations were not as effective as those for sea ice. White sea ice contrasts starkly with dark ocean water, which makes the ice and water amenable to monitoring from satellites and airplanes. In contrast, climate-driven variations in tundra—treeless regions where the subsoil is permanently frozen—and forest can be subtle, sometimes just a slow alteration in the mix of plant species rather than a sharp shift from one type of ecosystem to another. Vegetation changes can take years, even decades, before they become detectable.

We did have strong hints about what type of changes to look for, however. Greenhouse experiments on the tundra had shown that fertilization and artificial warming of the soil could produce dramatic growth of shrubs at the expense of nonwoody tundra plants such as sedges and mosses. Dwarf birch plants, for example, that had previously been knee high grew to head height in a matter of years. Based on this evidence, our best guess was that tundra warming would trigger an increase in biomass, possibly an explosive one—mainly in the form of more and bigger shrubs. Farther south, in the boreal forests, the tree line had been advancing both northward and upslope to higher altitudes for centuries. The expectation was that warming would accelerate this march.

But nothing was certain. At the time, various research groups were trying to detect shifts in vegetation using remote sensing or intensive studies of small plots on the ground, so my colleagues Chuck Racine and Ken Tape and I reasoned we could best contribute new informa-

tion by looking for change using old photographs—if we could find such documents. During our search, an archivist mentioned that he had some navy air photos from the 1940s in his warehouse. Were we interested? He was planning to throw them away soon because of limited storage space. I held my breath until a sample arrived. As the photos slid out of the envelope onto my desk, I was stunned. They were perfect for our work, and they were beautiful. Eventually we had about 6,000 on our shelves.

In the summer of 2000 we began our study, concentrating on the tundra. The definition of tundra, with its low-growing vegetation and permanently frozen subsoil, does little to convey the great beauty and complexity of this ecosystem. Covering about 5 percent of the earth's land surface, most tundra is a thick carpet of mosses, lichens and sedges (which look like grasses), with a smattering of other vascular plants and dwarf shrubs. From the air this collection of plants appears to be a low green carpet, plush and smooth. On the ground, it is a mosaic of many plants, all spongy and tiring to walk on, although when dry, delightful to lounge on. And it is anything but flat. The sedges and other plants grow into bumps called tussocks, or hummocks, that are the bane of anyone who has tried to walk far over the tundra. Rising up to half a meter high, these bumps are often unstable at the top, flopping over when weighted and sending hikers tumbling to the ground or twisting their ankles. Typically the dwarf shrubs hide in the creases between tussocks, although dense patches of head-high shrubs often cluster near water.

The higher the latitude, the more barren the tundra becomes, until the shrub component vanishes. Finally, even the mosses and lichens give way to vast areas of bare soil, known as polar desert. To the south, the tundra transitions first into a smattering of spruce trees, then into a patchwork of tundra and forest, and finally into the boreal forest, also called taiga. The transition from tundra to taiga can be abrupt, or it can spread over tens of kilometers. In Alaska the boundary is largely coincident with the southern edge of the Brooks Range.

To take the repeat photos we needed, we flew in a helicopter with the doors off, armed with copies of the old photos. Circling until we could match the earlier view as closely as possible, we often found ourselves barely 15 meters off the deck, a revelation that gave us added respect for our World War II predecessors in their fixed-wing plane. With care, we could achieve a fairly close match. Over four summers we rephotographed more than 200 locations. In the evenings we would compare the new photos with the old for an informal assessment. In image after image, individual shrubs were bigger than they had been 50 years earlier (yes, individual shrubs were still alive and identifiable!). Patches of shrubs had filled in, and the patches had expanded into tundra where shrubs had previously been smaller than our detection limit of about 50 centimeters high. Willow, birch and alder, the big three of Arctic shrubs, were all expanding in range and getting larger. We were particularly impressed by one pattern of shrub advance we nicknamed "shock troops," where shrubs had colonized old river terraces and tundra flats, taking over hectares of previously shrub-free territory in a few short decades.

The reality of the transformation was driven home when we field-checked the photos. Shrubs that appeared in our new photos as small dark circles proved to be as tall as a person. These were often ringed by halos of smaller shrubs, which the larger bush appears to protect from harsh winds and blowing snow. In some places, the shrubs were so thick they formed impene-

ARCTIC LINGO

Albedo: The extent to which an object or surface reflects light from the sun. Snow and ice are superior reflectors. They return to space up to 85 percent of sunlight, thus limiting warming of the land.

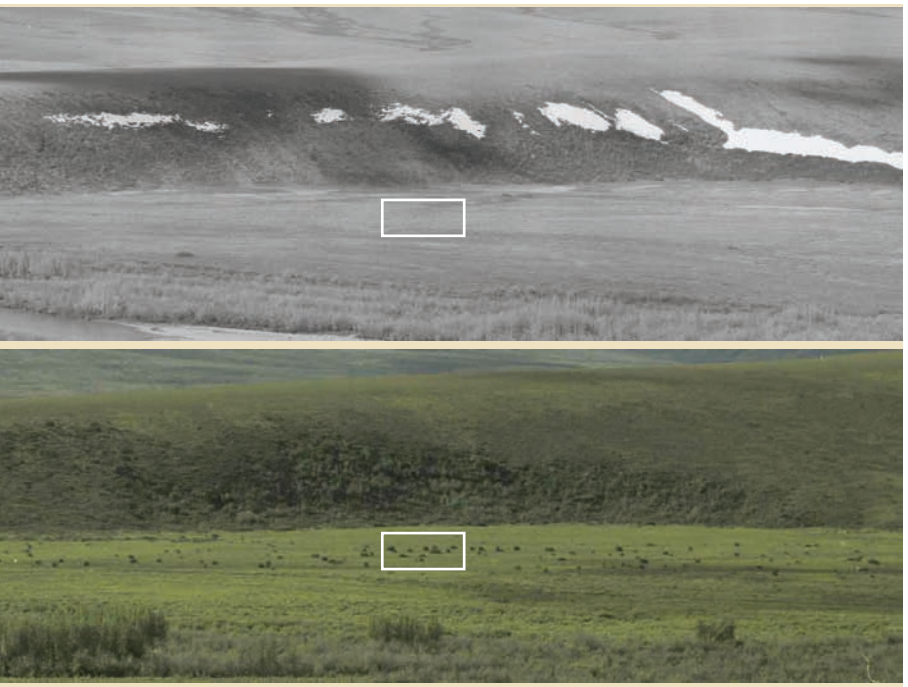
Taiga, or boreal forest: The forests in and just south of the Arctic Circle; they consist mainly of conifers and constitute the world's largest ecosystem.

Tundra: Treeless region in the Arctic where the subsoil is permanently frozen, and the ground is covered by dense, low vegetation.

To see other striking images from the U.S. Navy survey, visit **www.ScientificAmerican.com/arctic-plants**

COURTESY OF U.S. NAVY

PHOTO FROM 1940S, taken by U.S. Navy surveyors, shows gullies along the Colville River filled with drifted snow from the winter.



COMPARISON of photographs taken of Alaska's North Slope in the 1940s and at the same time of year early in the 21st century presents graphic evidence of an increase in plant growth. The color image, from 2002, highlights human-height "shock troop" shrubs marching across a tundra terrace where they were originally absent.

Climate shifts in the Arctic are affecting hunting, logging, transportation and infrastructure locally and exacerbating warming worldwide.

trable thickets. By the end of the second summer, after we had thrashed our way through dozens of shrub jungles, we coined the phrase "shrubby Arctic" to capture what was happening to the landscape. In all, the photos documented that shrubs had been expanding in an area of northern Alaska measuring more than 200,000 square kilometers.

But what was happening to the tundra outside of Alaska and in the taiga forests to the south? To answer this question, my colleagues Scott Goetz, Doug Stow, Skip Walker, Gensuo Jia and Dave Verbyla were using the radiometers on NOAA weather satellites to measure changes in those sites as well as in Alaska. Computing an index called NDVI (normalized difference vegetation index) based on reflectance in the red and near-infrared bands, they were finding that the greenness of the tundra was increasing. Greenness correlates with biomass and new growth, and the researchers interpreted their findings to mean that the shrub component of the tundra was expanding. The increase in NDVI was most pronounced in Arctic Alaska, western Canada and Siberia but could be detected in Scandinavia and other parts of the Arctic as well. Other colleagues—Bruce Forbes in Russia, Greg Henry in the Canadian High Arctic and Paul Grogan in central Arctic Canada—were finding similar results from their on-the-ground studies, while the recollections of Arctic residents in Alaska, Canada and Russia added support to the idea that a pan-Arctic increase in shrubs was under way.

A close comparison of the most recent satellite record of tundra greening with our photo-based map of shrub change provides one additional detail: the NDVI is increasing not only in the tundra areas where the photos show more large shrubs but also where only dwarf shrubs (below the photo detection limit) can currently be found. These small shrubs between tussocks are ubiquitous, and they are plastic: they can alter their growth form when growing conditions improve, attaining substantial size. With mini shrubs already in place over a vast area, the tundra regions are preconditioned for rapid growth.

Such a phenomenon would not be unprecedented. The paleo-record—pollen found in sediment cores—shows an abrupt increase in shrub pollen about 8,000 years ago. Known informally as the "birch explosion," it seems to mark a time when shrubs swept across the tundra landscape.

A Surprise in the Forest

The satellite records revealed an even more startling result in the vast boreal forests south of and ringing the tundra. Although studies confirmed that the tree line was continuing to move northward and to higher elevations, in many places the satellites indicated that behind this advancing front the forests were losing biomass and becoming less productive. The forests were browning—drying and dying—while the tundra was greening, a fact that seems to contradict the conventional wisdom concerning the forest response to climate warming.

About 10 years ago Glenn Juday and Martin Wilmking, then at the University of Alaska Fairbanks, started collecting a set of tree ring samples from near Fairbanks and south of the Brooks Range that have helped unravel the apparent contradiction. Instead of the customary positive correlation—higher temperatures in summer produce better growth and wider rings—they began to find stands in which higher temperatures had produced smaller rings and more slowly growing trees. In western Alaska, where it was wetter, they found the trees grew more vigorously as it warmed, but as they moved east into drier country, they discovered smaller rings, distressed trees and struggling, even dying, tree

COURTESY OF U.S. NAVY (*top landscape comparison*); COURTESY OF KEN TAPE (*bottom landscape comparison and scrub halo*); COURTESY OF GASIUS R. SHAVER *Marine Biological Laboratory (greenhouse structure)*

stands. The warmer summers were just too dry.

Two other dendrochronologists, Andi Lloyd of Middlebury College and Andy Bunn of Western Washington University, using every boreal tree ring record they could uncover, confirmed that the browning of the boreal forests was a pan-Arctic phenomenon and that although it predominated in spruce trees, it occurred in all boreal tree species. The exact causes of the declining tree growth are still being worked out, but drought and heat stress are two primary suspects, because browning has been observed more commonly in dry continental sites and in the southern part of each species' range.

The trees have been getting hammered in two other ways as well, both thought to be linked to the warming climate—increased insect outbreaks and a rise in the frequency and size of forest fires. In Alaska, big forest-fire seasons seem to be coming about every five years rather than every 10, and infestations of insects such as the spruce bark beetle, which have ravaged more than 500,000 hectares of prime forest in Alaska so far, appear to be intensifying.

Predicting the Future Is Hard to Do

The changes taking place on the tundra and in the boreal forests present an ironical symmetry. The boreal forests have encroached on an estimated 11,600 square kilometers of the southern edge of the Alaskan tundra in 50 years, yet over the same period they have been drying out, burning up and suffering insect damage behind their advancing front. Juday and others suggest that the outcome is going to be a conversion from forest to grassland. At the same time, the tundra is becoming increasingly shrubby and junglelike. Does the future have in store a switch, where the forest will begin to look a lot like tundra, while the tundra looks more and more like forest?

The problem with answering this question is our limited ability to understand the linked processes that are driving the vegetation changes, let alone predict their future course. Even though the Arctic sea ice is a simple system of just water and ice that responds in principle to physical rules that can be coded into models, the ice has been declining at a rate that is twice as fast as that predicted by 13 of the scientific community's best large-scale models. Current predictions are for an ice-free Arctic Ocean in 40 years, but these predictions are more extrapolations of observed changes than model results. For the tundra and boreal forests, with their great biological complexity and competing feedback mechanisms—some that dampen growth and some that accelerate it—the existing models are still too simplistic to produce accurate predictions.

In a recent paper, my group tried to address the prediction question for tundra shrubs using a simple model of shrub population growth and the contrasting photos. To our surprise, the model indicated that the shrub expansion started about 150 years ago, near the end of the Lit-

My gut feeling is that the tundra landscape is likely to change faster than predicted by our crude model.

EXPERIMENTS and observations support the photographic evidence that the tundra is becoming shrubbier. In greenhouse studies that artificially warmed the soil (*below;* greenhouse covering has been removed), shrubs grew to head height, while those in normal soil stayed about knee high. And observations in nature (*right*) indicate that bigger shrubs, in a so-called halo effect, protect smaller ones from the elements and thus encourage growth in concentric rings (*marked by lines*) around a big one—resulting in a much greener tundra.

[THE AUTHOR]

Soon after completing a doctorate at the University of Alaska Fairbanks in 1987, Matthew Sturm went to work for the U.S. Army Corps of Engineers, where he is a research scientist. Recently he led a 4,000-kilometer snowmobile traverse across Alaska and Arctic Canada. Sturm's interest in shrubs and trees developed during an earlier trip, when he got stuck in deep snow in a willow patch. After several hours of tugging on snowmobiles and packing down snow, he realized that maybe the shrubs had an impact on snow cover—which ultimately led to the studies reported in this article.

tle Ice Age. We had expected the expansion to correspond with the rapid Arctic warming that has taken place since the 1970s. On the other hand, the timing coincided nicely with the first appearance of moose, those long-legged shrub browsers, on Alaska's North Slope. It also coincided with the onset of tree line expansion.

The model results imply that, in part, the shrubs have been slowly expanding in response to a natural warming cycle that began well before the industrial revolution. Other lines of evidence, however, suggest that although this expansion probably started because of natural warming, it is continuing, and apparently accelerating, because of human-aided warming. In the region where shrubs are expanding, the past four decades have also seen a marked increase in the retreat of glaciers, an increase in the rate of permafrost warming and an advance in the onset of spring (as revealed by freeze-up and break-up dates for rivers and lakes)—all of which have been tied to climate change accelerated by human activities. Sadly, we are unlikely to find a set of photos from the 1900s, which is what we would need to establish that the rate of shrub expansion was slower between 1900 and 1950 than between 1950 and the present.

BIG FOREST-FIRE SEASONS in Alaska now seem to come much more frequently, and the fires are more intense. Fires and insect damage together are browning the once green boreal forest. Shrubs thrive in these burned areas and, with their greater biomass and branching, increase the possibility of still more fires in the future.

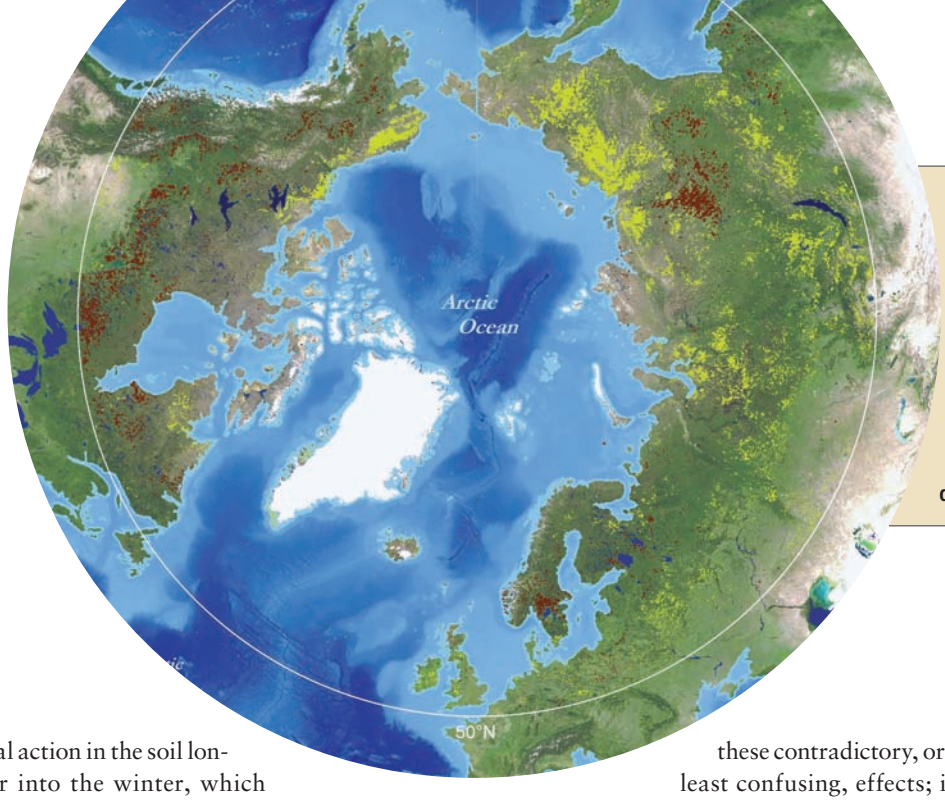
The same simple model predicted that it will take at least 150 years before shrub-rich areas are completely covered with shrubs; where there are no shrubs now, it will take even longer. The danger with trusting this prediction, though, is that the model does not allow for catastrophic effects such as fire that might abruptly alter the vegetation (shrubs tend to thrive in disturbed areas), nor does it include feedback effects that might speed up the change. My gut feeling is that our prediction is too conservative and that the tundra landscape is likely to change faster than predicted by our crude model.

One source of this suspicion is the aftermath of actual fires. From July to September 2007 during exceptionally dry weather, for example, the largest lightning-caused tundra fire on record burned on the North Slope, scorching more than 100,000 hectares. My colleague Chuck Racine visited the area in July 2009. In many places, shrubs had already resprouted. In similar, older tundra burn areas in western Alaska, shrub cover expanded by as much as a factor of eight in 30 years. Increasing lightning strikes and drying conditions could lead to more fires. Moreover, the shrubs, with their greater biomass and branching, increase the likelihood of fire in the future, creating a positive feedback effect.

Of the other potential feedback effects that operate on the tundra, we know of at least two positive ones related to the winter snow cover. It may seem strange to think of winter having any impact on the growth of shrubs, because they do their growing in the summer, but winter processes determine soil and water conditions for the following growing season. The importance of winter to Arctic plants lies in its long duration. The tundra is covered by snow nine months of the year and the taiga seven months, making the predominant color of these regions white, not green.

One of the feedback processes works like this: where shrubs manage to overtop the nearby tussocks, they trap snow in the winter, producing drifts that deepen the snow cover around them. Snow is an excellent insulator, nearly as good as a down quilt (this is because the snowpack may be as much as 75 percent air). Where the deeper snow insulates the ground better, soil temperatures are higher than they would otherwise be. In some shrub zones we have found temperatures at the base of the snow to be 10 degrees Celsius greater than in adjacent tussock areas. The warmer conditions promote micro-

COURTESY OF MATTHEW STURM (*Sturm*); ALASKA STOCK (*fire*)



MAP OF THE ARCTIC, based on satellite data collected and analyzed by Scott Goetz and his colleagues at the Woods Hole Research Center, reflects changes in the state of the tundra and boreal forest between 1982 and 2005. Consistent with other work, the analyses show that shrub growth increased (*light green areas*) and that the forest underwent drying and tree losses (*brown areas*).

bial action in the soil longer into the winter, which stockpiles more nutrients so that come summer, the shrubs get a boost. Fertilized shrubs grow vigorously, so they become taller, thereby trapping more snow in the ensuing winters, reinforcing the cycle.

The other snow-related feedback effect derives from the albedo (reflectivity) of the snow. The dark branches of tall shrubs protrude above the snow during winter and particularly in spring. These branches absorb solar energy many times better than the white snow, enough to cause local warming and accelerated melting in the spring, producing an earlier start to the growing season and stimulating the shrubs to grow larger still.

Individually, the winter feedback effects are easy to understand, but because they are not independent of one another or of summer processes (some of which are well understood, others not), the net effect is uncertain. For example, the deeper drifts produced by shrubs should in principle take longer to melt in spring than the surrounding undrifted snow. Can the albedo effect overcome the enhanced depth effect, or does the drifting trump the accelerated melting? In summer, shading and leaf litter are two potential feedback processes not fully understood. Shading by an enhanced shrub canopy is known to produce lower summer soil temperatures, potentially working against the winter snowdrift enhancement of microbial action. Leaf litter from the shrubs alters the nutrient loading around the shrubs, potentially spurring growth.

Many investigators are busy trying to model these contradictory, or at least confusing, effects; indeed, several groups are developing predictive models of tundra and boreal forest change. But one of the biggest wild cards in their deck is whether the future climate will bring more snow or less. If this terrestrial science follows the example of efforts to understand the vanishing sea ice, it will be our ability to physically track the ongoing changes and project those into the future, rather than computer models alone, that will answer the big questions. Not surprisingly, photograph pairs from Alaska are being used as test data in model development.

We were certainly lucky that the navy took exceptional photos on Alaska's North Slope—and that we managed to get our hands on them. Serendipity is as important in science as in other aspects of life. Had we not found the photos, we might not have realized as soon as we did that a transformation in landscape potentially as profound as the loss of sea ice was taking place in front of our eyes. The photos are the most graphic and easily comprehended evidence, although without satellites and the careful work of dendrochronologists, we would not know other parts of the story.

The challenge now is to work out a method to predict what will unfold on Arctic lands and how fast. The complexity of biological systems makes the task difficult. Nevertheless, if we do not do it quickly, the changes are likely to overtake us, forcing us to react rather than anticipate. I am fairly certain now, however, that this story is being played out in three colors: green, brown and white. ■

MORE TO EXPLORE

Recent Climate Warming Forces Contrasting Growth Responses of White Spruce at Treeline in Alaska through Temperature Thresholds. M. Wilmking et al. in *Global Change Biology,* Vol. 10, No. 10, pages 1724–1736; October 2004.

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COURTESY OF SCOTT GOETZ *Woods Hole Research Center*

A Better Lens on DISEASE

Computerized pathology slides may help doctors make faster and more accurate diagnoses

BY MIKE MAY

KEY CONCEPTS

- A remake of pathology, a profession that has processed samples the same way for more than 100 years, is long overdue.
- Emerging techniques allow computerized images of biopsies to be manipulated in novel ways.
- Ultimately, digital pathology will allow for more precise diagnoses of tissue samples, whether from an oncologist's office or a crime scene.

—The Editors

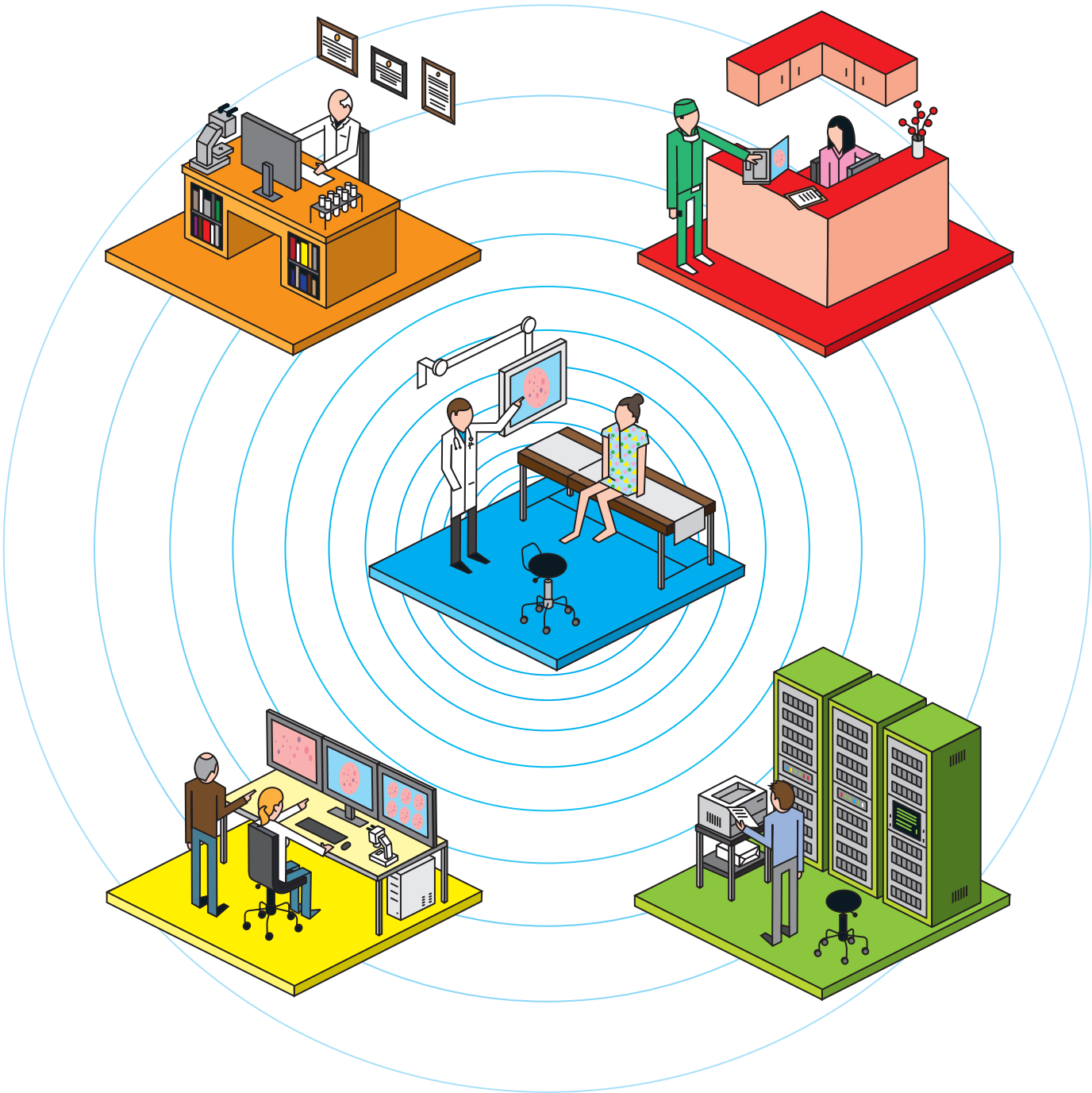
In the late 1990s Dirk G. Soenksen imagined a new future for pathology. At the time, pathologists often sat on telephone books to get a good view through their microscopes, yet Soenksen's children viewed high-resolution monitors when merely playing Nintendo. "Why can't microscopists look at computer monitors, too?" he wondered.

That question sent Soenksen on an extended journey, beginning in his garage. After 18 months of intense laboring, he emerged as the head of a newly created digital-pathology company called Aperio, which he now runs in Vista, Calif. Beyond merely moving images of diseased tissues from microscopes to computers, his technology—as well as that of other start-ups and even established health care companies—promises to make anatomical pathology, which involves the interpretation of biopsies, far more quantitative. This advance should, in turn, enhance the accuracy of diagnosing diseases and help physicians track the effectiveness of a treatment so that any needed changes can be made promptly.

Most pathologists already use computers in some way, if only to make notes in patient files. Beyond a computer monitor, assorted notepads and piles of papers usually cover a pathologist's desk. Only a research pathologist, however, is likely to be able to inspect a sample as a digital file. In general, today's pathologists lack the ability to make or obtain digitized slides, and review of such slides is approved by the U.S. Food and Drug Administration for only a few medical applications, all related to breast cancer.

For now, the hundreds of millions of pathology slides prepared annually get handled as they have for more than 100 years. A tissue sample gets cut into paper-thin, or thinner, sections, and a stain brings out specific features. Then, a pathologist puts the glass slide under a microscope. In a breast cancer biopsy, for example, a pathologist looks for a range of features in the tissue, including the number of abnormal cells in the section and the tumor grade, the latter depending on features such as cell structure. "Now this is done by eyes over the microscope, looking at every little point," says George K. Michalopoulos, chair of the department of pathology at the University of Pittsburgh.

In fact, pathologists do not look at every spot on every slide, but digitized versions could be inspected more thoroughly. A computer could analyze each pixel on every digital slide. And it could find and measure attributes indicative of health and disease—such as internal structure, color, texture and intensity of every pixel in ev-



ery cell. A pathologist hunched over a microscope would assess those same attributes in only a small number of the cells.

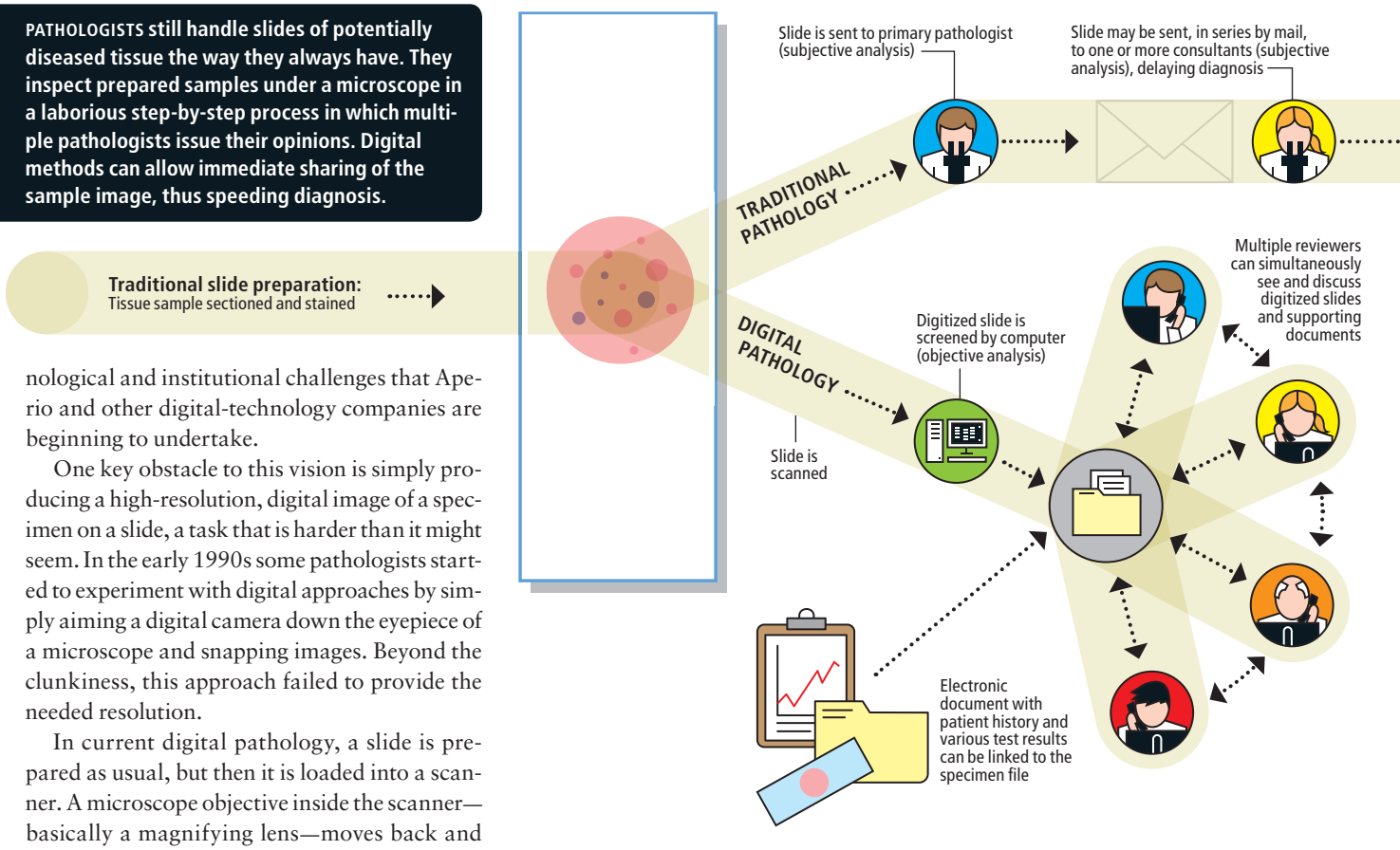
Turning to computers, though, will not take pathologists out of the picture. Instead digitizing slides can actually bring more pathologists into the process of making a diagnosis and thereby avoid medical error. Michalopoulos says that consulting with others on a diagnosis is "part of daily living in pathology." But today, he says, "you put a glass slide in the mail, and it takes two or three days—even with the fastest methods—to get there." With digital pathology, a tissue image could be sent electronically to others or, more likely, posted on a secure Web site and made available for a consultation with a pathologist on the other side of the world in just seconds. If consulting on a slide was that much easier, that much faster, pathologists might confer even more than they do already. As Michalopoulos says, "A consultation is the only way to resolve disputes, and experts often disagree. So you need to send slides to outside experts."

In combination, these two broad advances—more quantitative analysis and faster image sharing for consultation—serve as the main rationale for digitizing pathology samples. Getting there, though, will depend on solving a series of tech-

DIAGNOSIS MADE EASIER by the use of digitized slides of tissue samples will transform pathology, one of the few analytical professions to lag in adopting full-scale computerization.

QUICKHONEY

PATHOLOGISTS still handle slides of potentially diseased tissue the way they always have. They inspect prepared samples under a microscope in a laborious step-by-step process in which multiple pathologists issue their opinions. Digital methods can allow immediate sharing of the sample image, thus speeding diagnosis.



nological and institutional challenges that Aperio and other digital-technology companies are beginning to undertake.

One key obstacle to this vision is simply producing a high-resolution, digital image of a specimen on a slide, a task that is harder than it might seem. In the early 1990s some pathologists started to experiment with digital approaches by simply aiming a digital camera down the eyepiece of a microscope and snapping images. Beyond the clunkiness, this approach failed to provide the needed resolution.

In current digital pathology, a slide is prepared as usual, but then it is loaded into a scanner. A microscope objective inside the scanner—basically a magnifying lens—moves back and forth over the slide, and imaging technology, such as a CCD (charge-coupled device) camera, captures the image. Speed is of the essence in digital pathology. The scanner from Aperio, for example, can digitize a typical sample—about 15 millimeters on a side, or roughly the dimensions of a stamp—at a resolution of 0.5 micron per pixel, in about two minutes.

Those numbers reveal a fundamental challenge. Digitizing just one such slide to the resolution needed for detailed viewing requires 900 million pixels. By comparison, a photograph that is 4 × 5 inches and scanned at 300 dots per inch—a standard resolution for printing in a magazine—is composed of only 1.8 million pixels. So the digitized pathology slide requires 500 times more pixels. Digitizing the images faster requires faster electronics both to collect and to process the data. Some scanners acquire an image on a glass slide in square pieces, called tiles, and then software stitches them into a complete digital slide. Other devices, such as Aperio's, scan a slide in stripes, like a fax machine, and build the image on the fly.

No matter how fast a scanner operates, the speed is never enough. "We probably [prepare] 1.5 million glass slides a year, not counting specialty stains and so on," says Jonhan Ho, a skin pathologist at the University of Pittsburgh Medical Center. With a single scanner running at two minutes per slide, scanning slides for that one medical center for a year would take three million minutes—more than five years of scanning 24 hours a day, seven days a week.

Is Digital Good Enough?

The other looming question is whether pathologists looking at slides from Aperio and other companies on a computer screen can identify tissue abnormalities as well as they can when examining standard slides under a microscope. Drazen M. Jukic and some of his colleagues at the Pittsburgh medical center compared traditional pathology and digital techniques in an article in *Human Pathology* in 2006. For the most part, these pathologists found the digital files to be about as good as microscope slides in terms of enabling them to diagnose diseases by reviewing the images.

If digital pathology is only just as good as age-old methods, what could make it better? An ability to share slides easily is one answer. The Net Image Server, together with the OlyVIA viewer software from Olympus, for example,

MORE TO EXPLORE

Digital Pathology Image Analysis: Opportunities and Challenges. Anant Madabhushi in *Imaging in Medicine,* Vol. 1, No. 1, pages 7–10; October 2009. Available at **www.futuremedicine.com/doi/abs/10.2217/iim.09.9**

Digitizing Pathology. Jeffrey M. Perkel in *Bioscience Technology,* Vol. 34, No. 2, pages 8–12; February 23, 2010. Available at **www.biosciencetechnology.com/Articles/2010/02/Imaging-Digitizing-Pathology**

QUICK HONEY (*icons*); JEN CHRISTIANSEN (*infographic*)

works much like an ordinary Web page. Instead of sending digitized slides—which can be gigabytes and bigger in size (as much information as three compact discs could contain)—this software creates a repository of slides on a Web site or on a server.

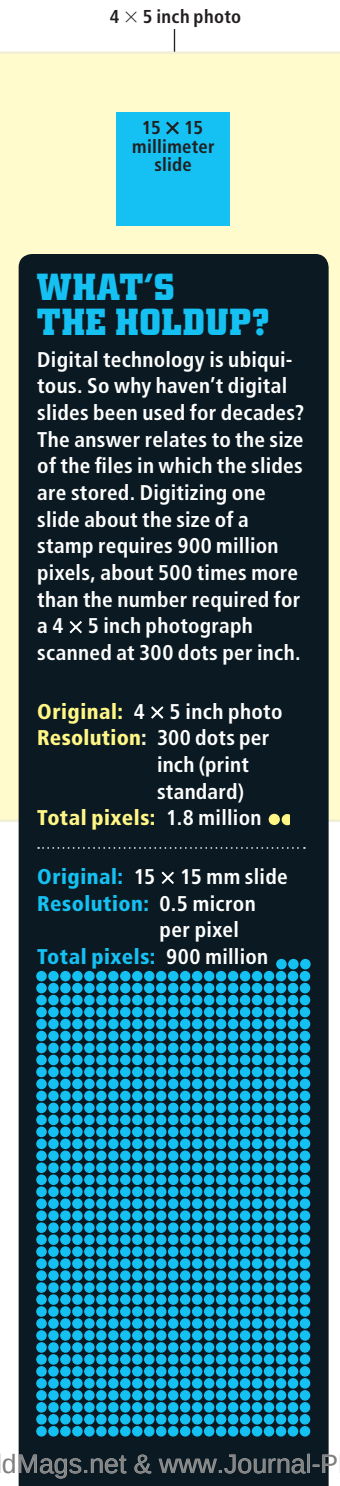
When a pathologist clicks on a thumbnail, the Olympus software downloads enough of the image to fill a viewing box on the screen. It is a lot like looking up an address on Google Earth, where a user gets a viewing box's worth of a satellite image. The viewer can see more of the satellite image by simply clicking and dragging with a mouse. The same can be done with OlyVIA. If a pathologist sends only pieces of a big file, others can view the digitized tissue images over a digital subscriber line (DSL) or cable connection to the Internet.

Although electronic sharing will make it easier and faster for pathologists to consult with one another, that feature alone does not bring completely new capabilities to medicine. But computerized image analysis may bring about a more fundamental transformation. Aperio and others have developed analytical software and are working on making advanced versions.

In certain cases, such as inspecting breast cancer images, pathologists can already move into the digital era. For instance, roughly one quarter of breast cancers create abnormally high levels of a protein called human epidermal growth factor receptor 2, or HER2 for short. This protein can be revealed in samples of breast tissue by staining the protein so that it can be seen in a tissue slide.

Traditionally pathologists look at these slides for the intensity of staining and the number of cells that are colored. Visual estimates of the extent of staining (the intensity measurement) can be quite variable between pathologists. Digitization, combined with software that measures intensity in every pixel, quantifies intensity measurements, allowing analyses to become more uniform and dependable.

So far only technologies from Aperio and BioImagene in Sunnyvale, Calif., are cleared by the FDA for interpreting digital slides for HER2 levels on a computer monitor. Leaders of digital-pathology companies, though, hope that more endorsements are on the way and that the technology will continue to advance. "In the future, not even very far away," says Gene Cartwright, head of Omnyx, a Pittsburgh digital-pathology company, "the computer might show you things that your eye might not see." As an example, he imagines pathologists wanting to quantify many stains used on the same slide. "If there were five stains and you want to judge their intensity by eye, forget it," he explains. "You can't do it, but it's pretty easy for a computer to analyze the intensity of different colors."



Future Fixes

Although several companies offer software for the clinical environment, pathologists themselves must be enticed into using these systems. To help that along, developers are focusing on creating a "cockpit" for pathologists. A monitor could display the digital slides of a gross specimen removed during surgery, as well as a patient history and reports summarizing various other test results.

"That will take a number of years," Soenksen says. "You need to integrate the digital-slide information with a hospital's laboratory information system, with the radiology system, and other systems. You will need all of those interfaces to enable sharing." He adds, "Those interfaces are being established one at a time, and every interface is a custom development."

Despite the challenges, digital pathology is already coming to the clinic. But it is starting in niches, like the inspection of breast cancer markers. "A hospital might start by using digital pathology for 20 percent of its samples and then expanding that over several years," Cartwright says. "No one will go cold turkey in replacing conventional scopes."

And the issue of resisting change will always linger. "A pathologist feels at home with a microscope," Ho declares. "It's a tool, like a scalpel or stethoscope. It's an extension of our fingertips, and there's resistance to taking away the microscope."

Bit by bit, digital pathology will continue to work its way into clinical pathology—and expand, along the way, into forensics. Pathologists will interact more, quantify more, and develop increasingly objective ways to diagnose diseases and judge how well a treatment is working. ■

Mike May is a freelance science and technology writer who lives near Houston.

Breeding Cassava

KEY CONCEPTS

- Cassava roots are the main source of calories for millions of people living in the tropics, but they are poor in protein, vitamins and other nutrients.
- Scientist have created cassava varieties with improved nutritional value, higher yields, and resistance to pests and disease.
- A combination of traditional breeding, genomics and molecular biology techniques could lead to further breakthroughs.

—The Editors

The world's third-largest source of calories has the potential to become a more productive and more nutritious crop, alleviating malnutrition in much of the developing world

By Nagib Nassar and Rodomiro Ortiz

The diet of more than 800 million people revolves around neither wheat, nor corn, nor rice. Instead in many countries the main staple consists of the starchy roots of a plant variously called cassava, tapioca, manioc or yuca (not to be confused with the succulent plant yucca). Indeed, cassava contributes more to the world's calorie budget than any other food except rice and wheat, which makes it a virtually irreplaceable resource against hunger. Throughout the tropics, families typically cultivate it for their own consumption on small parcels of land, although in Asia and in parts of Latin America the plant is also grown commercially for use in animal feed and starch-based products. The root's nutritional value, however, is poor: it contains little protein, vitamins or other nutrients such as iron. Better varieties of cassava could thus effectively alleviate malnutrition in much of the developing world.

Because of that promise, the two of us and our colleagues at the University of Brasilia and others are devoted to creating hardier, more productive and more nutritious varieties and

ANDY CRAWFORD *Getty Images*

to Feed the Poor

making them widely available to farmers in developing countries. Our team focuses largely on applying traditional breeding techniques to form hybrids between cassava and its wild relatives, taking advantage of traits that have evolved in the wild plants over millions of years. This approach is less costly than genetic engineering and does not raise the safety concerns that make some people wary of genetically modified crops. Meanwhile researchers and nonprofit organizations in the developed world have begun to take an interest and have produced genetically modified cassava varieties for the same purposes. The recent completion of a draft genome sequencing of cassava may open the way to further improvements.

Tropical Favorite

The shrubby plant *Manihot esculenta*—the scientific name for cassava—and its wild relatives of the genus *Manihot* originate in Brazil. Indigenous peoples first domesticated the plant, and Portuguese sailors took it to Africa in the 16th century; from there its use spread to tropical Asia, reaching as far as Indonesia. Africa now produces more than half (51 percent) of the world's annual output of more than 200 million metric tons; Asia and Latin America harvest 34 and 15 percent, respectively.

The roots, resembling elongated sweet potatoes, can be eaten directly, either raw or boiled, or can be processed into granules, pastes or flours. In Africa and some parts of Asia, people also consume the leaves as a green vegetable, which provides protein—a dry cassava leaf is up to 32 percent protein—and vitamins A and B.

Cassava requires low investment in capital and labor. It tolerates drought and acidic or infertile soils fairly well; quickly recovers from damage caused by pests and diseases; and is efficient at converting the sun's energy into carbohydrates. In fact, whereas the edible part of grain

[WORLDWIDE PRODUCTION]

Who Grows Cassava?

Cassava is a favorite of subsistence farmers throughout the tropics and especially in Africa, where more than half of production is concentrated. The plant grows easily from small cuttings and tolerates drought and infertile soils. Its roots can be pulled out at any time of the year for a quick calorie fix. Like noodles, bread or rice, it accompanies dishes that are as varied as the local cuisines. In some countries it is also grown commercially.

crops is at best only 35 percent of the plant's total dry weight, in cassava it is about 80 percent. Moreover, cassava can be planted at any time of the year, and harvesting can be delayed by months or even by a year. Thus, farmers often keep some plants in the field as a kind of insurance against unforeseen food shortages. It is no wonder that the crop has become a favorite of subsistence farmers in nearly every region where it can grow and that it has become an integral part of local traditions and cuisines.

The crop, however, has disadvantages as well. It has a short shelf life, and if unprocessed, it usually goes bad within a day. Moreover, cassava plants within a given region tend to be genetically uniform, which makes crops vulnerable: a disease or pest that damages one plant will likely sicken them all. But most of all, the lack of nutrients other than carbohydrates makes cassava a risky food to rely on excessively.

Hybrid Technology

One of us (Nassar) first became interested in improving cassava as a young agronomist in his native Egypt. In the early 1970s—a time of widespread famines in sub-Saharan Africa—he visited Brazil to study the plant in its original environment. He then decided to relocate, eventually becoming a naturalized Brazilian. In 1975 at the University of Brasilia, with a small grant from Canada's International Development Research Center, he began to assemble a living collection of wild *Manihot* species, which could serve as a library of useful traits that could be added to cassava. Traveling the country, often on foot or by bicycle, he collected specimens and took them back to Brasilia, where he and his collaborators would eventually grow 35 different species.

This biodiversity resource would prove crucial in the development of new varieties, both at the university and elsewhere. One of the first results achieved by the team was the creation in 1982 of a hybrid breed with higher protein content. Cassava roots are typically just 1.5 percent protein, compared with wheat's 7 percent protein or more. In particular, the roots are deficient in sulfur-containing essential amino acids such as methionine, lysine and cysteine. The new hybrid variety had up to 5 percent protein content. The Brazilian government is now seeking ways to reduce the country's dependence on foreign wheat by adding cassava flour to wheat; using higher-protein cassava would help preserve the daily

ROOM FOR IMPROVEMENT

Although cassava is a readily available source of calories for many of the world's poor, excessive reliance on it can lead to malnutrition. In particular, it is a poor source of protein, vitamins A and E, iron and zinc. The plant has other shortcomings:

- It is highly perishable if not processed.
- It is usually planted from cuttings, leading to genetic uniformity and to vulnerability to pests and diseases.
- Certain varieties, if not cooked properly, can cause cyanide poisoning, leading to paralysis and death.

MAPPING SPECIALISTS; SOURCE: FOOD AND AGRICULTURE ORGANIZATION (*map*); GETTY IMAGES (*tapioca starch*); COURTESY OF NEIL PALMER *CIAT* (*bowl of cassava starch*); ANDRE BARANOWSKI *Getty Images* (*boiled yuca*)

intake of protein for millions of Brazilians.

Hybridization between cassava and wild relatives, as well as selective breeding between different strains of cassava, may also help create varieties containing other important nutrients. The Brasilia team has shown that certain wild *Manihot* species are rich in essential amino acids, iron, zinc, and carotenoids such as lutein, beta-carotene and lycopene. Beta-carotene in particular is an important source of vitamin A, a lack of which results in progressive eye damage—a serious and widespread problem in the tropics of Africa, Asia and Latin America. Given cassava's status as a staple in the tropics, high-carotenoid varieties could contribute significantly to solving vitamin A deficiencies in the developing world. In the past three years the team has bred highly productive cassava varieties containing up to 50 times as much beta-carotene as regular cassava, and it is now in the process of testing these varieties with local farmers.

Another major project has focused on changing the plant's reproductive cycle. Cassava's ordinary mode of reproduction, by pollination, produces seedlings of types not identical to the mother plant and frequently lower in yield. Farmers thus commonly plant cuttings from existing plants rather than sowing seed. Cutting, however, enables viruses and bacteria to contaminate a plant. Generation after generation, the microorganisms accumulate, which eventually can impair a plant's yield. Like many other flowering plants, certain wild *Manihot* species, including the treelike relative of cassava *M. glaziovii,* procreate both sexually and asexually, and the asexually produced seeds sprout into plants that are basically clones of the mother plant. Through more than a decade of efforts focused on interspecies breeding, the Brasilia researchers recently obtained a cassava variety that can reproduce both sexually and asexually, by making two types of seeds, just like its wild relative. Once further work is completed, this variety will be ready to be distributed to farmers.

M. glaziovii possesses other useful genes that may help feed millions of people living on arid land. A hybrid of *M. glaziovii* and cassava typically displays two types of roots. Some, like those in cassava, swell up with starch and are edible. The second type of root reaches farther underground, where it can tap into deeper water sources. These traits make the hybrids among the best cassava varieties for use in semiarid regions, such as northeastern Brazil or certain of the savanna regions of sub-Saharan Africa. Some have shown tolerance to drought when tested by farmers in Petrolina, one of the driest regions of Brazil. The team is now improving these hybrids to combine high yield and tolerance to drought by backcrossing them with a productive variety of cassava and then selecting high-yield offspring that can be distributed more widely.

A different kind of manipulation—the time-honored technique of grafting—offers another way to increase yields of cassava's tuberous roots, as Indonesian farmers first discovered in the 1950s. Grafting stalks of species such as *M. glaziovii* or *M. pseudoglaziovii* (or hybrids of the two) onto cassava stocks has increased root production in test plots as much as sevenfold. Unfortunately, in many countries the practice of grafting is hampered by the lack of availability of these hybrids.

Pest Insurance

Beyond enhancing nutrition and production, selective breeding and crossbreeding with wild species have been crucial in counteracting the

[THE AUTHORS]

Nagib Nassar, a native of Cairo, has a Ph.D. in genetics from the University of Alexandria in Egypt. He has researched cassava at the University of Brasilia since 1975, creating varieties that have been adopted by farmers in Brazil and exported to cassava breeders in Africa. Rodomiro Ortiz was born in Lima, Peru. He received a Ph.D. in plant breeding and genetics from the University of Wisconsin–Madison and is a former director of resource mobilization at the International Maize and Wheat Improvement Center in Texcoco, Mexico.

CASSAVA FARMER checks his crop in Huila in the Colombian Andes.

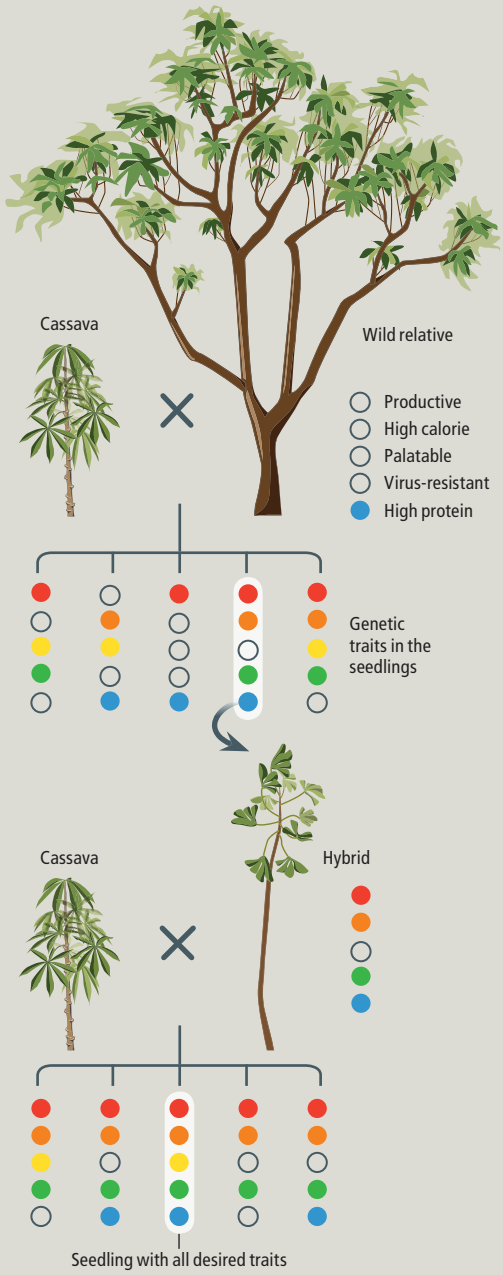
COURTESY OF NEIL PALMER *CIAT* (*cassava farmer*); COURTESY OF ANGELA GORGEN (*Nassar*); COURTESY OF CIMMYT CORPORATE COMMUNICATIONS (*Ortiz*)

[CONVENTIONAL BREEDING]

Ancient Meets Modern

Wild relatives of cassava, including the treelike *Manihot glaziovii* (*left*), often have traits that would benefit the crop but lack many of the desirable traits of the domesticated species. In the time-honored technique of backcrossing, breeders obtain the right combination of all traits by producing many generations of hybrids, often aided by modern tools such as genetic markers, which reveal the presence of a trait in a seedling without the need to grow it into a plant.

HOW MARKER-ASSISTED BREEDING WORKS



spread of pests and diseases. Improving resistance to the cassava mosaic virus ranks among the most important achievements in cassava science. In the 1920s the spread of the mosaic virus in the East Africa territory of Tanganyika (now Tanzania) triggered a famine. Two English scientists working in Tanzania hybridized cassava with *M. glaziovii*, saving the crop after about seven years of efforts. In the 1970s mosaic came back and threatened areas in Nigeria and Zaire (now Democratic Republic of the Congo). Researchers at the International Institute of Tropical Agriculture (IITA) in Nigeria used *M. glaziovii* and its hybrids originating from the University of Brasilia's collection and again produced mosaic-resistant cassava. That newly bred variety gave rise to a family of mosaic-virus-resistant varieties now cultivated on more than four million hectares in sub-Saharan Africa; in the intervening decades, Nigeria has become the world's top cassava producer. Still, viruses undergo frequent genetic mutations, and someday new mosaic strains will likely break the resistance bred into the cassava varieties. Hence, preemptive breeding will always be necessary to stay ahead of the disease.

The cassava mealybug (*Phenacoccus manihoti*) is one of the most virulent pests besetting this crop in sub-Saharan Africa. This insect, which kills plants by sucking out their lymph, was especially devastating in the 1970s and early 1980s; it destroyed plantations and nurseries to such an extent that production virtually came to a halt. Toward the end of the 1970s the IITA and research partners elsewhere in Africa and in South America introduced a predator wasp from South America that lays eggs in mealybugs, so that the wasp larvae eventually devour the mealybugs from the inside. As a result of this effort, the cassava mealybug was held in check across most of Africa's cassava-producing areas in much of the 1980s and through the 1990s. In a few small areas of Zaire this system did not work well because of a rise in the parasite wasp's own predators. In the middle of the past decade the Brasilia team searched wild *Manihot* species for a reliable solution to this problem and found mealybug-resistance traits—once again in *M. glaziovii*. Mealybug-resistant varieties are now grown by small farmers in the region surrounding Brasilia and can be exported to other countries should the mealybug plague come back.

Looking ahead, we anticipate that new, valuable traits could come from breeding chimeras. A chimera is an organism having two or more

JESSICA HUPPI (*illustrations*); COURTESY OF FOREST AND KIM STARR (*photograph*)

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[GENETICALLY MODIFIED CASSAVA]

The Biotech Way

Genetic engineering, now widely adopted in U.S. agriculture, is beginning to show results in cassava as well. But genetically modified versions are unlikely to become widely available soon, and some worry that research funding is giving short shrift to cheaper, more traditional methods of developing new varieties.

Major advances have come from an international collaboration called BioCassava Plus. The group has created varieties of cassava rich in zinc, iron, protein, beta-carotene (a source of vitamin A) and vitamin E by using genes from other organisms—including algae, bacteria and other plants.

"We hit our target," says BioCassava Plus lead researcher Richard Sayre of the Donald Danforth Plant Science Center in St. Louis. All the new transgenic varieties are now in field trials on test plots in Puerto Rico, and the program has received the green light to start field trials in Nigeria. Traditional breeding can get beta-carotene into cassava, he says, but for iron and zinc only genetic engineering has shown results so far. Meanwhile Sayre's team is working on combining all the new traits into a single variety.

The project is funded by the Bill & Melinda Gates Foundation and by Monsanto. (Monsanto's support came with strings attached: the corporation reserves the right to charge for the use of the varieties if a farmer's gross income exceeds $10,000 a year.)

GENETICALLY MODIFIED cassava seedlings

Peter Beyer of the University of Freiburg in Germany calls the BioCassava Plus achievements a breakthrough. "The step from here to the product, however, is still a big one," he adds. Beyer should know: the beta-carotene-rich "golden rice" that he and his collaborators first announced in 2000, making the cover of *Time,* is only now nearing approval in several countries. Engineering new organisms may be fast, he notes, but demonstrating that they are safe for the environment and for consumption and breeding them into varieties that are palatable to local tastes is not: 10 to 12 years is the norm. "Regulators simply do not allow you to proceed as quickly as with a variety that has been bred traditionally," Beyer says.

Beyond not necessarily being faster than conventional breeding, genetic engineering is also much more expensive, and sometimes genes that work well in one organism do not work quite as well in a completely different one. "A lot of people have kind of drunk the Kool-Aid" about genetic engineering's promise, says Doug Gurian-Sherman of the Union of Concerned Scientists. Consequently, it tends to get a disproportionate amount of research funding. "I think to put all your eggs in one basket is a huge mistake," he remarks, adding that public funding agencies should help restore a balance. *—Davide Castelvecchi, staff editor*

genetically distinct tissues growing within it. There are two principal types of chimera. In sectorial chimeras, two different longitudinal sectors of tissue are visible in a plant organ, but their growth is not stable, because one of the tissues grows faster than the other and may soon occupy the entire shoot. In the second type of chimera, called periclinal, the external part of the shoot surrounds the internal one and may be more stable than a sectorial chimera. Trials are under way at Brasilia to develop a method of grafting that will produce stable periclinal chimeras using tissue from *M. glaziovii*. Such an approach may lead to continuous root enlargement every time a chimera stalk is planted. Chimeras have so far shown promising productivity and seem to adapt especially well to semiarid areas.

Cassava should be a high priority of agricultural science, but traditionally it has not been. Only a handful of research laboratories have studied this plant, perhaps because it is cultivated in the tropics, far from where most scientists of the developed world work. This dearth of research investment has meant that average yearly yields in South and Central America and in Africa are no more than 14 tons per hectare, even though field research shows that, with some improvements, cassava could grow four times as plentifully and feed many more people—both in areas where it is already grown and elsewhere.

Some interest is beginning to emerge in the developed world, however. Researchers at the Donald Danforth Plant Science Center in St. Louis are leading a project to insert genes—coming from other plant species or from bacteria—into cassava to increase its nutritional value and extend its shelf life [*see box above*].

The sequencing of the cassava genome, which is now in its first published draft, will likely boost the development of transgenic cassava. It will also aid conventional breeding programs through the technique of marker-assisted breeding, which relies on information gleaned from genetic analysis to guide the breeding of desired traits. Establishing a global network to coordinate efforts of all institutions that conduct research on cassava would ensure that the potential of this crop does not go to waste. ■

MORE TO EXPLORE

Back to the Future of Cereals. Stephen A. Goff and John M. Salmeron in *Scientific American,* Vol. 291, No. 2, pages 42–49; August 2004.

Future Farming: A Return to Roots? Jerry D. Glover, Cindy M. Cox and John P. Reganold in *Scientific American,* Vol. 297, No. 2, pages 82–89; August 2007.

Failure to Yield: Evaluating the Performance of Genetically Engineered Crops. Doug Gurian-Sherman. Union of Concerned Scientists, 2009. Available at **www.ucsusa.org/food_and_agriculture**

COURTESY OF SHANTHA J. R. PIERIS

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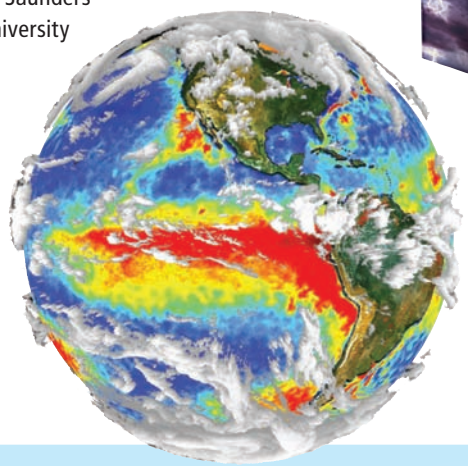
Decoding Weather ▪ Inelegant Universe ▪ History of the Pill

BY KATE WONG

THE ENCYCLOPEDIA OF WEATHER AND CLIMATE CHANGE: A COMPLETE VISUAL GUIDE
by Juliane L. Frye, Hans-F. Graf, Richard Grotjahn, Marilyn N. Raphael, Clive Saunders and Richard Whitaker. University of California Press, 2010 ($39.95)



The science of weather—from cloud formation (*right*) to approaches to slowing and reversing climate change—is clearly and succinctly explained in this wide-ranging, well-illustrated volume.

EXCERPT

A TEAR AT THE EDGE OF CREATION: A RADICAL NEW VISION FOR LIFE IN AN IMPERFECT UNIVERSE
by Marcelo Gleiser. Free Press, 2010 ($25)

For centuries scientists have been searching for a single theory of the universe that reveals an elegantly simple order behind the apparent complexity of the natural world. That quest continues today with the hunt for a "grand unified theory" that joins Einstein's theory of relativity with the laws governing quantum mechanics. This is a misguided mission, argues physicist and former "Unifier" Marcelo Gleiser of Dartmouth College. It is the messiness of the universe—not the beautiful symmetries—that holds the key to its origins. Here he describes grappling with 16th-century German astronomer Johannes Kepler's unified model of the cosmos, which proposed that the arrangement of the six planets then known could be understood as a tidy series of nested spheres and polyhedra.

"How could someone so wrong be so utterly convinced of being right? We have much to learn from Kepler's mistake. In hindsight, it's easy for us to ridicule his creation. After all, there aren't six planets, but eight. If he could have seen them with the naked eye, he would never have proposed his model, and his career would have taken a different turn. Kepler's blindness was his blessing. He constructed a model of the world with the data he had available. At any given time, including ours, this is the best that anyone can do. What we can measure will always limit our view of reality. Kepler's mistake was to give his vision of reality a finality it didn't deserve. Glimpsing at the hidden code of Nature proved so cathartic that he was bewitched and took his belief for the truth. Kepler's mistake was to forget that a final theory is impossible because we will never know all of reality. Then and now, any science that is tainted with blind belief will lead us astray. I looked again at Kepler's creation: a nested finite cosmos, a geometric dream, ordered and precise. At that moment, I knew that my days as a Unifier were over."

ALSO NOTABLE

BOOKS

- **Anatomy of an Epidemic: Magic Bullets, Psychiatric Drugs and the Astonishing Rise of Mental Illness in America**
  by Robert Whitaker. Crown, 2010 ($26)
- **Mystery Cults of the Ancient World**
  by Hugh Bowden. Princeton University Press, 2010 ($39.95)
- **Bursts: The Hidden Pattern behind Everything We Do**
  by Albert-Laszlo Barabasi. Dutton Adult, 2010 ($26.95)
- **A Vast Machine: Computer Models, Climate Data, and the Politics of Global Warming**
  by Paul N. Edwards. MIT Press, 2010 ($32.95)

- **America and the Pill: A History of Promise, Peril, and Liberation**
  by Elaine Tyler May. Basic Books, 2010 ($25.95)
- **In the Empire of Ice: Encounters in a Changing Landscape**
  by Gretel Ehrlich. National Geographic, 2010 ($28)
- **Duel at Dawn: Heroes, Martyrs, and the Rise of Modern Mathematics**
  by Amir Alexander. Harvard University Press, 2010 ($28.95)
- **Second Nature: The Inner Lives of Animals**
  by Jonathan Balcombe. Palgrave Macmillan, 2010 ($27)
- **Stepping-Stones: A Journey through the Ice Age Caves of the Dordogne**
  by Christine Desdemaines-Hugon. Yale University Press, 2010 ($30)
- **The Little Book of String Theory**
  by Steven Scott Gubser. Princeton University Press, 2010 ($19.95)
- **Superbug: The Fatal Menace of MRSA**
  by Maryn McKenna. Free Press, 2010 ($26)

FOLKS WE FOLLOW ON TWITTER

- **Bug Girl, entomologist (@bug_girl)**
- **Chris Rowan, geologist at the University of Edinburgh (@Allochthonous)**
- **Eric R. Weinstein, economist and mathematician (@EricRWeinstein)**
- **A. Garrett Lisi, physicist and surfer (@garrettlisi)**
- **Deborah Blum, science writer and professor at the University of Wisconsin–Madison (@deborahblum)**

NASA

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140-Character Study

What if everyone had always been on Twitter at the same time?

BY STEVE MIRSKY

Have you joined the Twitterverse? All over the world millions of people are posting their 140-or-fewer-character tweets online via Twitter. As a confirmed Twitterer, I wondered what it might have been like if Twitter, and all its users, had been around for, oh, the past few thousand years.

PythyinGreece Had amazing insight into right triangles. Add squares of sides = square of hypo. Could be useful.

Euclidmenot Working on something (book series called Elements) to drive 10th graders nuts 4 thousands of years. Conic section alone will make them cry.

Aristophanesridiculous @Euclidmenot Conic section? I thought you said COMIC section. HaHA, I still got it! Hey, frogs are funny, yes?

Arkymeets Note to self: take more baths. Do some of my best thinking in the tub.

Galiheyo You know what moves when they show you the torture instruments? Your colon. I'm gonna be ixnay on the eetstway for an ilewhay.

Libnits Made way to figure out area under a curve by dividing into smaller and smaller sections until width of each disappears, call it calculus.

AppleNewt @Libnits You made that up? You couldn't make up a bedtime story for a 2-yr-old. Making a kid, BTW, sounds disgusting.

Libnits @AppleNewt Keep sitting under trees, maybe something big will fall on you next time.

AppleNewt @Libnits Apple falls near you, best idea you have is "Ooh, let's make applesauce."

HairyAlbert @AppleNewt Pick on somebody your own size. Btw, your gravity's wrong. Just a teeny bit most of the time, but hey. @Euclidmenot You too.

Euclidmenot @HairyAlbert Prove it.

OzAScarecrow @PythyinGreece The sum of the square roots of any two sides of an isosceles triangle is = to the square root of the remaining side!

Mendelayoff @Euclidmenot Calling my thing Periodic Table of the Elements. Different elements from yours. OK?

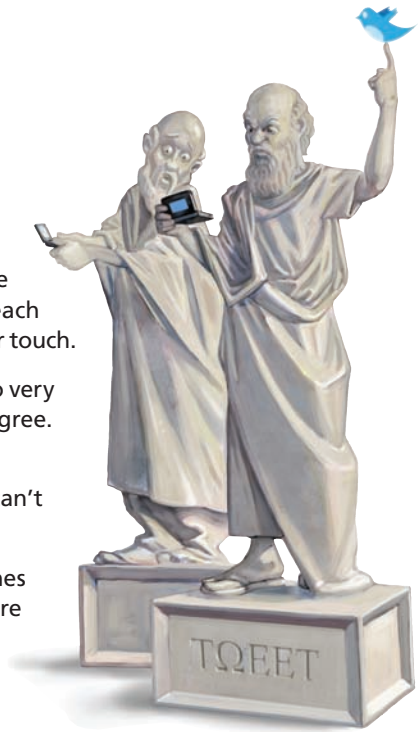
Euclidmenot @Mendelayoff We're like two lines that go next to each other for infinity but don't ever touch.

PythyinGreece @OzAScarecrow So very wrong, but congrats on the degree. At least you're failing upward.

AppleNewt @PythyinGreece You can't fall upward.

HairyAlbert @Euclidmenot Two lines that never touch? Those lines are gonna touch, trust me.

ChuckinDown Worms and barnacles again today. I don't feel so good.



PythyinGreece @AppleNewt I said he was FAILing upward, not falling upward. You're doing too much alchemy, get fresh air.

HairyAlbert @Mendelayoff I'll take number 99 on your table.

AlfieWallace @ChuckinDown Are you eating the worms and barnacles? Hey, did you get the package I sent?

ChuckinDown @AlfieWallace Yes, got package. Adding to my tummy troubles. We need to talk.

Curieous Went through thousands of pounds of pitchblende to get a speck of radium. I hate pitchblende.

InAHuff It snowed in DC, which proves beyond a shadow of a doubt that there is no global warming. I rest my case.

Beefranklin @InAHuff I risked my life in electrical storms for guys like you?

Bigstick99 @HairyAlbert Hey, I'm also number 99. There's a lot of interesting physics in ice hockey.

InAHuff @Bigstick99 But the hockey stick is broken!

Beefranklin @InAHuff Seriously, you're embarrassing us.

HairyAlbert @Bigstick99 I prefer elevator races.

SJGould I'm supposed to say something in 140 characters? That's ludicrous. It's absurd. It's beyond ridiculous. In fact, it's impossible. What idio

RogerToryPete Tweet! ■

PHOTOGRAPH BY FLYNN LARSEN; ILLUSTRATION BY MATT COLLINS