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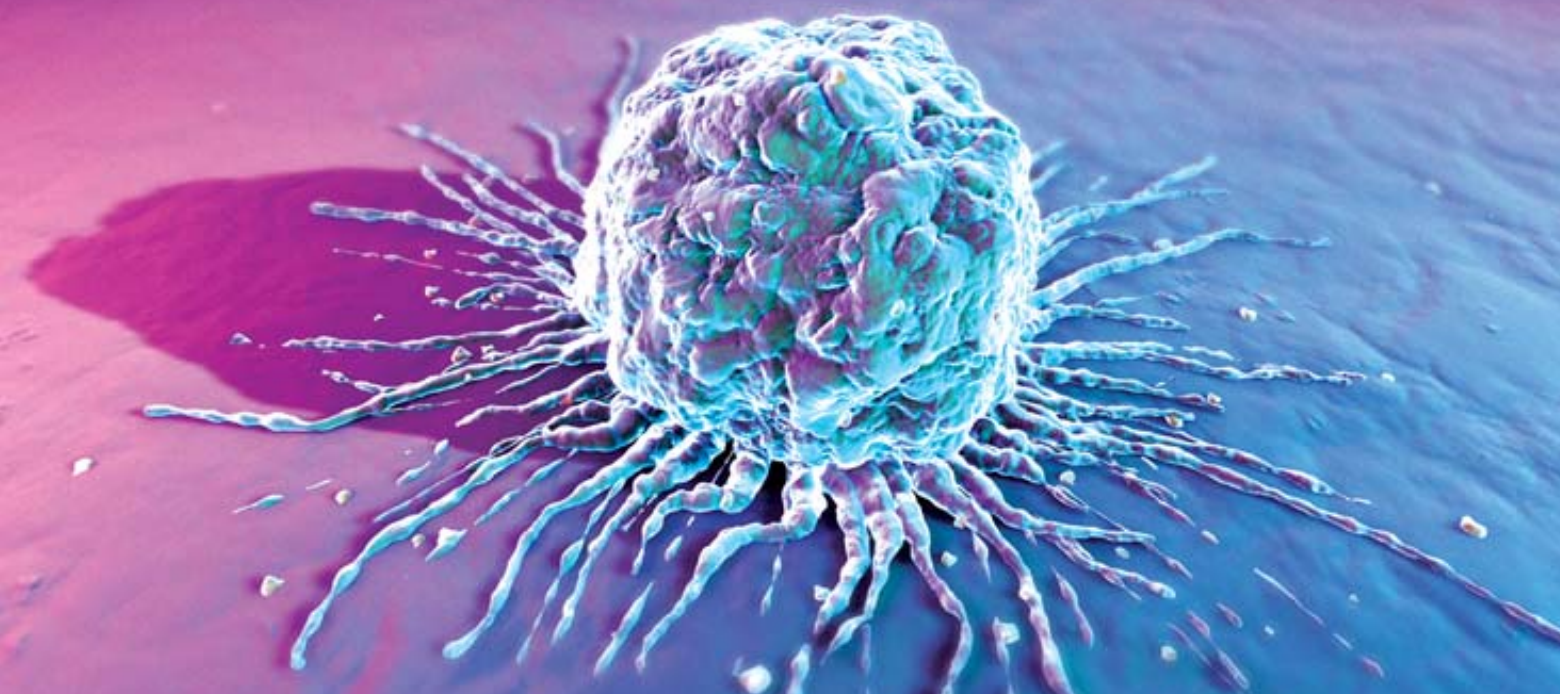


Superlenses and Metamaterials

Bird's-Eye View of Color

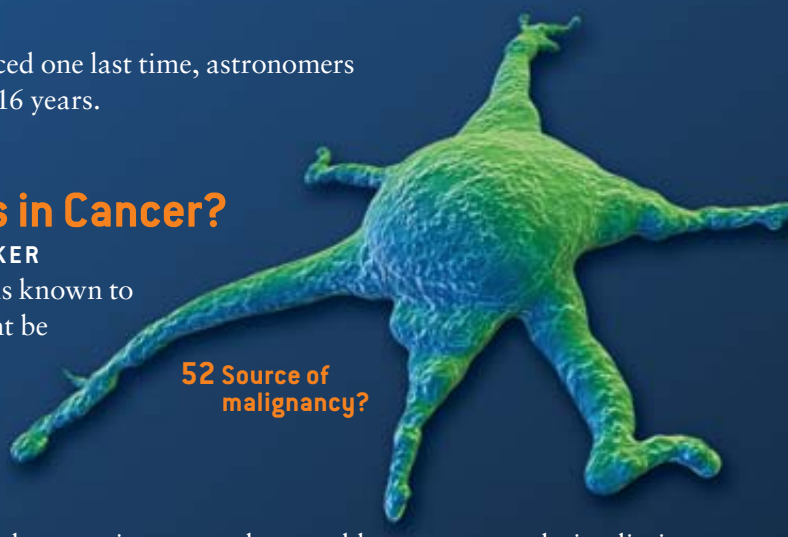
The Real CSI: Forensic Science

july 2006

contents

features

SCIENTIFIC AMERICAN Volume 295 Number 1



52 Source of malignancy?

departments

100

32

Michael Kremer, Harvard University 39

columns

Cover image by Jeff Johnson, Hybrid Medical Animation; photograph at left by Kathleen Dooher.

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Cell Phones on a Plane

… so I said that there was, like, NO WAY I'd go out with him unless … WAIT A SEC! … It looks like we're finally over the Rockies, so I should be there in TWO HOURS! … Really? Excellent! … So, anyhow, I told him that he'd better …

For many of us, the prospect of spending time trapped in an airline cabin listening to a passenger chatter into a cell phone may evoke thoughts of a 1950s horror-movie-like title: "Cell Phone Hell at 33,000 Feet!" Despite the current ban on cellular telephony, that possibility came a bit closer to reality in late 2004, when the U.S. Federal Communications Commission began reviewing a proposed regulation that would permit the use of cell phones in flight. Although no decision date has been set, telecommunications companies and some airlines are champing at the bit to provide these wireless services.

CAN YOU hear me now?

DONNA MCWILLIAM *AP Photo*

But beyond the anticipation of dollar signs and aural torture to come, recent research indicates that there may be sound safety reasons to continue the existing FCC and Federal Aviation Administration prohibitions on cell phone use in the air.

Experts have debated for years whether it is safe to use cell phones and personal electronic devices (PEDs) such as laptop computers and gaming devices on airplanes. Although crews have submitted numerous reports of errors in avionics (electronic navigation, communications and flight management) systems that ceased after all PEDs were shut down, many specialists consider this evidence to be anecdotal. Further, skeptics doubt that any interference from these devices would lead to mishaps, particularly if they were deactivated during takeoffs and landings. After all, no air accident or near miss has been definitively attributed to radio emissions from PEDs. When confronted with such data in the past, the airline industry has simply responded by installing better shielding around avionics systems and adopting other mitigation strategies.

Recently, however, researchers at Carnegie Mellon University concluded that cell phones and other PEDs could endanger the normal operation of critical navigation systems on aircraft. After monitoring radio emissions from portable electronics during airline flights (with an antenna and spectrum analyzer that fit into a carry-on bag), they estimate that an average of one to four cellular calls are made from the cabin during each trip—despite the ban. The researchers also determined that some of the emissions from mobile phones occurred in frequencies employed by Global Positioning System (GPS) receivers, which are increasingly vital for safe landings. In addition, the study warned that avionics that operate at non–cell phone frequencies could encounter interference when nearby wireless signals interact and generate spurious spikes in other frequency ranges.

Given the new research, we recommend that further study be performed before lifting the in-flight prohibition of cell phones. First, the aviation agencies should collect more complete data on aerial wireless-interference incidents. Next, the government should enlist a competent technical organization to characterize the onboard radio-frequency environment more accurately. The aviation industry, the FCC and the FAA should also better coordinate their risk analyses of mobile phone use. Finally, the FAA and the airlines should attempt to convince the flying public that restrictions on the operation of electronic devices are enforced to reduce real safety risks, not to gain some commercial advantage such as protecting existing Airfone-type in-flight phone services.

Being trapped on a plane with cell phone junkies is one thing, but the possibility that their calls could cause a crash is an issue no one should take lightly.

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New Monkey Genus Is First in 83 Years

In 1923 explorers in what is now known as the Democratic Republic of Congo brought out a specimen of a monkey with grayish green fur, a red face and webbed digits. Dubbed Allen's swamp monkey, or *Allenopithecus nigroviridis*, the primate was the most recent new genus of primate discovered—until now. Scientists have determined that a monkey previously known only from photographs belongs to a new genus.

BLOG: I.D. Rigs Its Own Trial

Still smarting from the shellacking handed them in the *Kitzmiller v. Dover* decision, the neocreationists appear to be manufacturing their own feel-good opportunities now.

PODCAST: Interview with Frank Wilczek

The Nobel Prize–winning physicist talks about his new book, *Fantastic Realities*, as well as his research and the current and future state of physics. His wife, Betsy Devine, recounts taking the phone call from Stockholm informing Wilczek that he had been awarded the 2004 Nobel Prize in Physics.

Ask the Experts

Could certain frequencies of electromagnetic waves or radiation interfere with brain function?

Amir Raz, assistant professor of clinical neuroscience at Columbia University, explains.

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Letters

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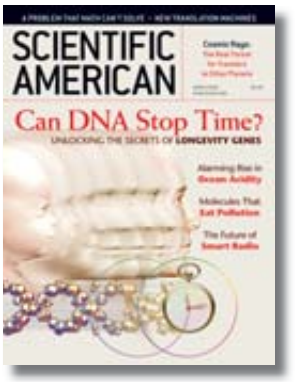
IT COULD BE SAID that March's issue was "problematic": at first glance, the title of "The Limits of Reason," by Gregory Chaitin, might have proved somewhat deflating. Chaitin's logical exploration of the insolvability of the number "omega" implicitly threw down the gauntlet at the human impulse to tackle every problem with the assumption that it has a solution, even if not immediately ascertainable. And, true to form, readers responded with a broadside of questions, challenges—and solutions.



Of more pragmatic concern was Scott C. Doney's "The Dangers of Ocean Acidification," which examined a not unsolvable (we hope) environmental problem caused by increased seawater absorption of fossil-fuel carbon. Finally, in "Unlocking the Secrets of Longevity Genes," David A. Sinclair and Lenny Guarente pinpointed a handful of genes that may be key to solving an age-old problem: ending diseases of the elderly and extending the human life span. Just think of how many more issues of your favorite science mag you could read.

SEA CHANGE

In "The Dangers of Ocean Acidification," Scott C. Doney did not mention other acid-base chemistry systems in the ocean that might buffer or control pH in the long term. Silicate acid-base chemical equilibriums—mainly solid-phase alumino-silicate (clay)-aqueous solution reactions—have been suggested as possible systems controlling long-term ocean pH, at least in the deep sea.

Björn Warnqvist
Täby, Sweden

DONEY REPLIES: In the 1960s some scientists hypothesized that equilibrium reactions between seawater and silicate minerals controlled the composition of inorganic salts in seawater. This was dubbed "reverse weathering," because it required the chemical transformation and uptake of some elements onto highly weathered clays in marine sediments. This hypothesis has mostly fallen out of favor as a dominant factor in ocean chemistry because of both the discovery of deep-sea hydrothermal vents (which act as both chemical sources and sinks) and only limited findings of reverse weathering reactions.

Silicate rocks, however, do play an important role in the carbon cycle, because high atmospheric carbon dioxide (CO_2) concentrations accelerate the weathering of rocks on land; on timescales of hundreds of thousands to millions of years, atmospheric and oceanic CO_2 concentrations reflect in part a balance between volcanic CO_2 emissions and terrestrial silicate weathering.

LOST IN TRANSLATION

It is interesting to note that in "The Elusive Goal of Machine Translation," by Gary Stix, the translation of the expression "blowing snow" is given as "*pouderie*." Both the editors and the author had only one word of French to translate in this article, and they blew it! The word is *poudrerie*. This certainly illustrates the difficulty, complexity and pitfalls associated with translation.

As a physicist, I welcome the advent of any progress in automatic translation, as it will allow one to access scientific work written in all languages. For many scientists, the language of nature is more interesting to translate than human dialects are, and this work is better left to machines. So if you want me to translate some article into French, it better be one with meaningful and interesting scientific content. The other choice is to outsource it to India or China!

J.H.P. Claude Bouchard
Munster Hamlet, Ontario

EXTENDING THE SENIOR MOMENT

Regarding your cover story, "Unlocking the Secrets of Longevity Genes," by David A. Sinclair and Lenny Guarente,

if the *SIR* class of genes has so many benefits and so few (if any) side effects, why aren't they "on" all the time? To put it a different way, what is the evolutionary advantage to having them "off"?

Matt Prager
New York City

SINCLAIR AND GUARENTE REPLY: *This is a very good question, with two possible answers: First, the force of natural selection declines rapidly once we replace ourselves with children, so there is no reason for it to preserve a trait that fosters very long lived people or animals. Second, the* SIR *genes are activated to help the body get through a crisis, which includes temporarily reducing fertility and the ability to store energy as fat. When food is abundant, however, a species would gain a stronger survival advantage by reproducing and storing fat for leaner times. That is why we want to turn the genes on with drugs only at an appropriate stage of life.*

IRREDUCIBLY INCOMPRESSIBLE

Maybe I am missing something obvious, but in "The Limits of Reason," Gregory Chaitin's assertion of the incompressibility of omega is flawed. Doesn't the fact that the author can accurately describe in the space of a single article the properties and qualities of the number omega without actually enumerating it in its entirety implicitly prove that omega is indeed compressible?

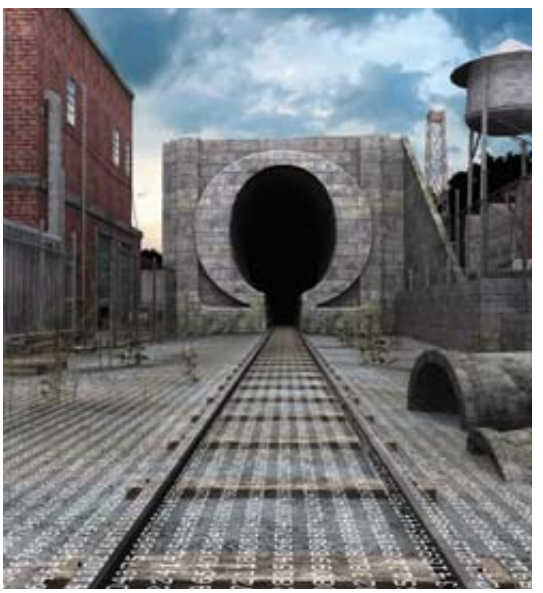
Matthew Tatuś
Little Rock, Ark.

The central point of Chaitin's fascinating discussion—that there is an infinite number of unprovable but true mathematical assertions (in the sense of the thing to be proved being much longer than the proof)—raises two interesting questions. First, can anything be said about the number of *provable* statements? Could it be shown, for example, that there is a countable infinity of such propositions? Second, is there any record or source for archiving those statements that are unprovable but are believed to be true? We can find proved theorems in books and papers; can we find "unprovable truths" somewhere?

R. Stephen Berry
Department of Chemistry
University of Chicago

CHAITIN REPLIES: *To address Tatuś, my article defines omega but indirectly, in a way that doesn't enable one to determine its value. Furthermore, there is no way to do that. That is why omega is interesting.*

Yes, as Berry suggests, the number of provable statements is also a countable infinity. But there is no central repository for unprovable statements.



Ω PROBLEM: **A finite computer program can reveal only a finite number of omega's digits; the rest remain shrouded in obscurity.**

COLOR COMMENTARY

In "What You See Is What You Say" [News Scan], Charles Q. Choi stated that most of the world's languages use a single word for "blue" and "green." I found this fact intriguing, but on checking, I discovered that English, French, Spanish, Portuguese, German, Dutch, Japanese, Korean, Latin, Chinese, Russian, Italian and Swahili all have different words for the two colors. In fact, so far I have not found a language that does not distinguish between them.

Is Choi wrong, or is there a vast family of blue-green color-blind languages that I have not yet located?

James Walpole
Lincolnshire, U.K.

CHOI REPLIES: *In 1999 anthropologist Brent Berlin and linguist Paul Kay of the University of California, Berkeley, reported finding that most unwritten languages of nonindustrial societies do not have separate color terms for green and blue but rather use a single term to cover these regions of color space—for instance, Tarahumara, an indigenous language of Mexico.*

This is not true, however, of oral languages only. The Japanese word aoi *and the Vietnamese word* xanh *refer to what English speakers would call blue or green. (Japanese also has* midori, *which refers exclusively to what English speakers would call green.) Irish uses the word* glas *to cover the green-gray range and* uaine *for bright green, whereas Welsh uses* glas *for green, gray and blue and has other words for green and gray. In contrast, the English word "blue" refers to much of what Russian would refer to as either* goluboy *or* siny.

ERRATA In "Unlocking the Secrets of Longevity Genes," by David A. Sinclair and Lenny Guarente, the name of Sinclair's company was given as Sirtis. The correct name is Sirtris.

In answer to the question "How do electric eels generate a voltage, and why don't they get shocked?" [Ask the Experts], it was stated that each electrogenic eel cell carries a charge of a little less than 100 microvolts. It should be millivolts.

In "What You See Is What You Say," by Charles Q. Choi [News Scan], the statement "The view from the right eye is processed in the brain's left hemisphere," should read "The views from both eyes' right visual fields are processed in the left hemisphere."

KENN BROWN; CONCEPT BY DUSAN PETRICIC

50, 100 & 150 Years Ago

FROM *SCIENTIFIC AMERICAN*

Looking into Atoms ▪ Solid Earth, Molten Lava ▪ Dangerous Travel

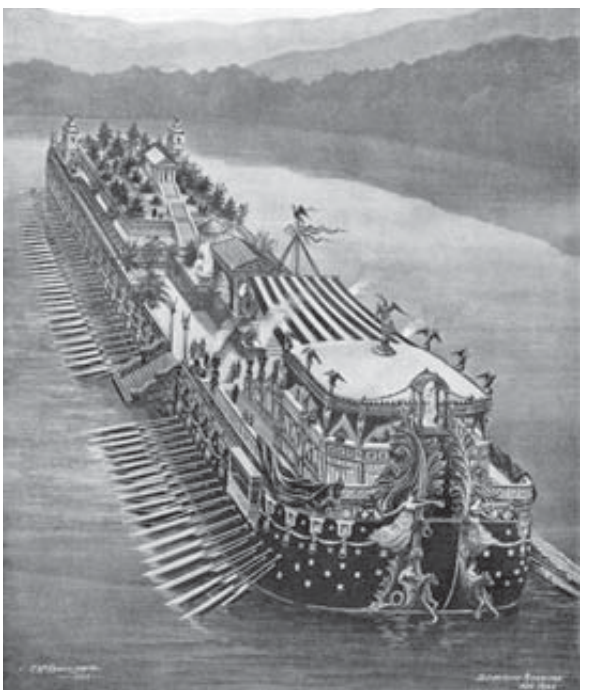
JULY 1956

PEEKING INTO ATOMS—"Today the most backward schoolboy knows that atoms are real. He even knows what they look like. The picture of a little round nucleus surrounded by a cloud of electrons is practically the trademark of our time. In 1951 the author began to think about a new way of examining nuclei. The idea was to shoot very high-speed electrons at them and see how the electrons were deflected, or, as the physicist says, scattered. At Stanford University in 1951 a great linear accelerator was being built that would produce an intense beam of electrons at energies approaching a billion electron volts. The corresponding wavelength would be measured in a few fermis. This is short enough to reveal nuclear structure in considerable detail.—Robert Hofstadter." [*Editors' note: Hofstadter was awarded a Nobel Prize in Physics in 1961 for this work.*]

COMMUNIST CHEER—"The 14 U.S. and seven British physicists who attended last month's high-energy physics conference in Moscow were impressed by the congeniality of their hosts and the absence of secrecy. The relaxed atmosphere seemed at least partly due to political changes within the Soviet Union. Victor F. Weisskopf of the Massachusetts Institute of Technology reported that Soviet research was already benefiting from the return to universities and institutes of many scientists who had been held in labor camps. The release of prisoners, he said, has gone far to eliminate the atmosphere of fear in the Soviet Union."

JULY 1906

IMPERIAL ROMAN GALLEY—"Buried under the waters of Lake Nemi lie two pleasure galleys, which belonged to the Emperors Tiberius and Caligula, and which contain art treasures that have been coveted for five hundred years. It is because of their unusual size (war galleys were much smaller) that the vessels, it is inferred, must have been used as pleasure barges. From the investigations of the divers we may glean much of the construction of the vessels, even though we may not be able to present an absolutely accurate restoration [*see illustration*]."



ANCIENT BARGE from Lake Nemi, Italy—a reconstruction, 1906

RADIOACTIVE BURNERS—"The earth is no longer regarded as an immense sphere of liquid or semi-liquid material surrounded by a solid crust of indeterminate thickness, but as a fairly solid globe. If we dismiss the idea that lava reservoirs are but the projections of a central molten mass (because such projections would have solidified millions of years ago), the next step is to ascertain what may be the cause of the lava's internal heat. Major Clarence E. Dutton holds that the heat must be generated in or surrounding the molten lava. It is admitted that the earth contains either radium or radio-active minerals. Calculations have been made, rough, to be sure, but still sufficiently accurate, which tend to prove that the heat developed by subterranean radium is far greater than can be radiated into space."

JULY 1856

PERILOUS RAILROADS—"Neither in safety nor comfort can our railroads or those of England compare with those of Prussia. During the past year not a single life has been lost in Prussia by any neglect on the part of their management, and only two lives were lost altogether. After all, there are some things in despotic countries worthy of imitation, and this is assuredly the case in railroad management. Our railroads are more safe than they were a few years ago; there is room for improvement. As yet, the life of a republican citizen is apparently esteemed of but little value by our public carriers."

NEBUCHADNEZZAR, NOT—"The London *Atlas* says that Colonel Rawlinson has lately found a mummy which is believed to be that of Nebuchadnezzar. The face, which is eminently handsome, is covered with a golden mask. Some *wooly horse* speculation, no doubt. Where's Barnum?"

POLICY

A Regulation on Regulations

AN OBSCURE LAW IS EVOLVING INTO A BLUDGEON AGAINST GOVERNMENT REGULATION **BY PAUL RAEBURN**

In January 2001 the *New England Journal of Medicine* published a study showing that reducing salt in the diet could lower blood pressure, even in people without hypertension. The National Heart, Lung and Blood Institute, which funded the study, quickly posted a press release on its Web site announcing the findings.

The Salt Institute, an industry group, was stung by the study's results. Unable to challenge the data on scientific grounds, the institute found another way to attack them. It filed a petition under the Data Quality Act—a law ironically intended to ensure that regulations are based on solid science—arguing that the findings did not meet the act's standards and that the heart institute had therefore broken the law by posting them.

The dispute eventually moved to the courts, where a district judge dismissed the industry's challenge. The institute appealed, and in March a federal appeals court again dismissed the petition. The Salt Institute, which was joined in the suit by the U.S. Chamber of Commerce, has yet to decide whether to take the case to the Supreme Court.

It was the first time the right to petition in court under the Data Quality Act was challenged, but it will most likely not be the last. Nobody keeps an exact tally, but something like 100 Data Quality Act petitions have been filed with dozens of different government agencies. Most have been initiated by industry groups, disputing scientific reports that could lead to tougher regulations. If subsequent petitions are accepted by the courts, the litigation could tie up government reports indefinitely, long before their data could lead to any government action.

The law, also known as the Information Quality Act, was enacted in 2000 without public debate. "It was passed in the middle of the night as an appropriations rider," says Rena Steinzor, a University of Maryland law professor. The act consists of a mere

A HIGHER CAUSE: Lobbyist James J. Tozzi (*left*) is fighting for medical marijuana as part of a complex strategy to add judicial teeth to a law that allows for challenges to government scientific reports that are often the basis for new regulations.

COURTESY OF CRE (*left*); JUSTIN SULLIVAN *Getty Images* (*right*)

two paragraphs in a longer appropriations bill. It says that the White House Office of Management and Budget (OMB) should ensure "the quality, objectivity, utility, and integrity of information … disseminated by Federal agencies." That seems reasonable, Steinzor admits: "Who can argue with the idea that data should be correct?"

In practice, however, the act could turn into an "über-statute that can challenge all rule making" by the federal government, she says. "Somebody could challenge the rule making and lose, lose, lose—and then file an appeal under the Data Quality Act."

The federal government's regulatory actions are already subject to opposition in court. What the Data Quality Act does is attempt to extend those challenges to reports that are strictly informational, such as the heart institute's press release. In the absence of the Data Quality Act, its research could not be taken to court.

The Data Quality Act was written not by a member of Congress but rather by James J. Tozzi, a lobbyist and the founder of the Center for Regulatory Effectiveness. Tozzi acknowledges that although the act could shut down government regulations, its effect would mainly be on inefficient regulations. The reason, he says, is that filing a Data Quality Act petition is difficult, and it can be turned down by the agency it is aimed at, the OMB or ultimately by the courts.

Thomas O. McGarity, a professor at the University of Texas School of Law and president of the Center for Progressive Reform, disagrees. "It costs nothing to file a Data Quality Act request, and if you get judicial review, you can shut down the government."

Given the Salt Institute's setback, its case is dead unless one of two things happens: it appeals to the Supreme Court, hoping for a decision saying that courts can accept Data Quality Act petitions. Or the act's defenders go to Congress to ask it to amend the law to allow judicial review. In the meantime, petitioners can continue to take their cases to court in other appellate jurisdictions.

Tozzi, a one-time New Orleans jazz musician, has a more improvisational approach to going back to court. Because courts may not be sympathetic to industry, he is using the act to argue that the government has ignored data showing marijuana is helpful to cancer patients and others. "The FDA issued a statement saying that medical marijuana has no medical uses," Tozzi says. That is at variance with a National Academy of Sciences report that found it did have benefits. He reasons that the courts might take a more sympathetic view of suffering cancer patients than they did of the Salt Institute. "It's a case where you have industry trying to establish a precedent for itself by hiding behind sick people," says Sean Moulton of OMB Watch, a Washington, D.C., nonprofit.

Industry's success with the Data Quality Act is now being imitated by a few public-interest groups, including some confronting the Fish and Wildlife Service's failure to list species as endangered when the data argue otherwise. But most are waiting to see whether Congress amends the act. "If they do," McGarity says, "they're going to wish they hadn't."

Paul Raeburn writes about science, policy and the environment from New York City.

INFORMATION WARFARE

The Data Quality Act, enacted by Congress without public input, has spawned perhaps 100 petitions challenging government regulations. They include:

- **A petition challenging the Environmental Protection Agency's listing of certain chemicals as "likely carcinogens." The Washington Legal Foundation and the American Council on Science and Health questioned the agency's use of animal studies to predict human cancer risk.**
- **The Partnership for the West's filing that challenges the Fish and Wildlife Service's proposed listing of the greater sage grouse as threatened or endangered. The group says that the FWS overstates the risk to the grouse and that listing it would paradoxically increase risks to the grouse's survival.**
- **A whistle-blower, Andrew Eller, at the FWS argued that the service was manipulating data to allow the approval of inappropriate land development in the habitat of the Florida panther.**

BIOLOGY

An Immune Portal

PROTEIN MAY BE A KEY TO AUTOIMMUNE DISORDERS **BY JENEEN INTERLANDI**

As a medical student in Germany, Stefan Feske studied two Turkish brothers born with severe combined immunodeficiency syndrome, or SCIDS, a rare, life-threatening genetic disease characterized by a seriously debilitated immune system. Because the boys' T cells could not take up calcium, their immune systems would not work. These siblings provided Feske and his collaborators with a unique opportunity to track down a key protein involved in this process by studying human cells in

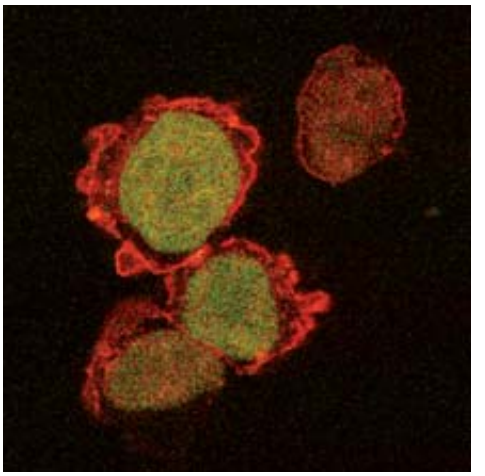
BUILDING ON PAST SUCCESSES

The targeting of ion-channel proteins by pharmaceutical companies has yielded several blockbuster drugs, virtually all of which are directed at the cardiovascular and central nervous systems. Proteins similar to Orai 1, which may be part of the calcium-ion immune channel, have been the target of powerful drugs such as Norvasc, which treats high blood pressure, and Xanax, an antianxiety medication. In 2002 alone, this class of drugs generated more than $12 billion in revenues, according to a study by Synta Pharmaceuticals in Lexington, Mass.

which it was already dysfunctional. "You cannot do this for every gene hunt," says Feske, now an assistant professor of pediatrics at Harvard Medical School.

That search ended recently with the discovery by Feske and his Harvard collaborators, Anjana Rao and Yousang Gwack, of Orai 1, a protein that may be part of the ion channel that admits calcium into T cells, a step required to set the body's immune response in motion. The group's endeavors, reported in the May 11 issue of *Nature*, represent several years of investigations that were part of a larger 20-year effort to track down this critical cog in immune functioning.

Because the pathway that this channel participates in has been conserved throughout evolution, fruit flies and humans still make and use many of the proteins involved in much the same way. Recognizing this similarity, Gwack, now a research associate in pathology at Harvard, developed a genetic screen in fruit flies that complemented Feske's patient studies. By expressing a key human protein in fruit fly cells, Gwack was able to search for the elusive calcium channel in the fly's smaller genome. His data, combined with a genetic analysis of the siblings' extended family, led the team to a single gene that was mutated in both patients. Gwack named the new protein encoded by



LONG-SOUGHT PROTEIN called Orai 1 (*red-stained area*) may be a critical subunit of the immune system's calcium channel.

STEFAN FESKE *CBR Institute*

the gene Orai 1, after the keeper of heaven's gate in Greek mythology.

Ion channels facilitate the movement of specific molecules, such as calcium or potassium, into and out of cells. Because these proteins span the cell membrane, they make a particularly appealing target for finding new drugs. "The problem for most drugs is that they have to get into the cell," Feske says. Getting into a cell means getting past its membrane, something ion channels were made to accomplish.

Drug companies around the world have been searching for ion channels specific to the immune system, especially a particular calcium channel, whose genetic identity has evaded researchers for two decades. The discovery of Orai 1, which may be a subunit of the immune system's calcium channel, represents a major breakthrough in that initiative. "The impact is going to be huge," says Michael Xie, director of ion-channel research at Synta Pharmaceuticals in Lexington, Mass., which is developing drugs that interact with this calcium channel. "Inhibition of this immune channel could provide one of the most direct means of manipulating the immune response."

Because drugs that block this passageway would stifle the body's immune response, they could be useful in treating a variety of autoimmune disorders, such as allergies and rheumatoid arthritis, which occur when the body's immune system turns against itself. Scientists also hope further research on Orai 1 will lead to better drugs for preventing transplant rejection, which occurs when the immune system attacks a donor organ. Drugs that home in on this apparently immune-specific calcium channel could avoid side effects, such as kidney impairment and neurotoxicity, caused by other transplant drugs, which interact with molecules found in several types of cells.

Still, more work remains before scientists can be certain of the role that Orai 1 plays. It is possible, for example, that the newly discovered protein is not a component of the channel itself but rather a modulator, or key, that opens and closes the channel like a doorway. And even if Orai 1 turns out to be a channel protein, it may be only one of the components that makes up the channel. "It's not the end of the story," Gwack says. "But the whole field is getting very, very hot now."

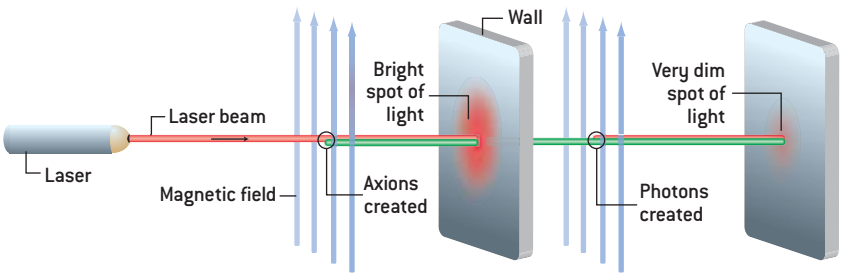
Jeneen Interlandi is a science writer based in New York City.

PHYSICS

A Hint of Axions

AN EXPERIMENT MAY HAVE SEEN AN ELUSIVE NEW PARTICLE **BY GRAHAM P. COLLINS**

Named after a laundry detergent and originally proposed to clean up a problem with particle physics, axions are curious critters. Axions produced during the big bang could be lurking all around us, contributing to the dark matter that constitutes 22 percent of the universe. Other axions, freshly formed inside the sun, could be streaming through us. And according to a paper published in March, laboratory-made axions might have been detected for the first time by an experiment in Italy known as PVLAS (*p*olarization of the *v*acuum with a *las*er).



LIGHT BEAM experiment that would confirm the existence of axions passes a laser beam through a strong magnetic field, converting some photons to axions (*green beam*). The axions penetrate a wall before passing through another magnetic field that converts some of the particles back to photons, which form an extremely faint spot on the far wall.

SAVING A SYMMETRY

Physicists originally proposed the axion as part of a scheme to explain why the strong nuclear force preserves so-called CP symmetry, which relates the properties of particles and antiparticles. Calculations using the Standard Model of particle physics showed that the strong force could preserve CP only if a certain parameter in the theory was zero, and yet quantum effects tend to make the parameter nonzero. In 1977 Helen R. Quinn and Roberto D. Peccei, then at Stanford University, showed that by changing the parameter into a quantum field, its value would be driven to zero by a natural process. A side effect of the new field would be the existence of a new particle—the axion.

Axions are posited to have exceedingly low mass—less than a millionth that of an electron—and are electrically neutral. They interact only very weakly with other particles, making detection difficult. But physicists predict that a tiny fraction of any photons passing through a magnetic field will change into axions. (That is how the sun is predicted to produce them.) Indeed, the Italian experiment, based at the National Laboratories of Legnaro and led by Emilio Zavattini and Giovanni Cantatore of the INFN Trieste, saw evidence for axions in the behavior of a laser beam. The beam's polarization was rotated by 10 millionths of a degree after transiting 44,000 times back and forth through an extremely strong magnetic field. Such rotation is just the fingerprint expected if some photons converted to invisible axions, or more precisely, what physicists call axion-like particles.

From its data, the PVLAS group infers the mass of the putative axions and how strongly they interact. Puzzlingly, however, the results contradict other observations and do not fit with constraints deduced from astrophysics. In particular, the CERN Axion Solar Telescope (CAST) ran for six months in 2003 and failed to detect any axions arriving from the sun. That result would seem to rule out a large swath of possible masses and interaction strengths, including the values seen by PVLAS. Furthermore, if axions interact as strongly as PVLAS indicates, they should be produced in large quantities in stars, causing stars to grow old much faster than they are known to.

Such considerations "put the bar pretty high before one can accept the PVLAS results," says axion expert Pierre Sikivie of the University of Florida and CERN. On the other hand, he adds, "these people are very competent, and they have worked on it a long time." By all accounts, the PVLAS researchers have been careful to exclude effects that could be confounding the data; moreover, in work that is not yet published, the group has also obtained consistent results with a different laser. Some theorists have already proposed ways to reconcile the PVLAS results with those of CAST and other astrophysical limits.

Only further experiments will determine the truth. If the PVLAS results are correct, then axions should appear in an experiment known as "shining a light through a wall." The idea is this: A laser beam is sent through a strong magnetic field at an opaque wall. Some of the photons in the beam are converted to axions, which pass through the wall. On the other side, another magnetic field induces a small fraction of the axions to convert back to photons, which can be detected. Such an experiment, using a large, strong magnet and sensitive photon detectors, would convincingly confirm (or refute) the PVLAS results in a matter of minutes. Research groups, including the PVLAS team, are gearing up to perform that experiment. By the end of the year the axion could be a firm addition to the particle menagerie—or back on physicists' most-wanted list.

LUCY READING-IKKANDA

Not So Super

WILL ANTIBODY THERAPIES RECEIVE ADDED SCRUTINY? BY CHARLES Q. CHOI

The drug's inventors called their creation a "superantibody." They hoped that it would be capable of activating immune cells other antibody drugs could not on their own. The moniker for the compound, targeted at autoimmune disease or leukemia, was TGN1412, made by TeGenero, based in Würzburg, Germany. On March 13 six previously healthy volunteers given the antibody in a routine test of its safety were sent to intensive care.

Although all the men are out of critical condition, one patient who went into a three-week coma after taking the drug may lose bits of his fingers and toes. Several medical experts assert that these results, which came after experiments with TGN1412 on rabbits and monkeys at up to 500 times the human dose, highlight the need for caution in designing trials of biotechnology drugs that work through novel mechanisms.

Animal trials hinted that the drug activates mostly regulatory T cells. Unlike other T cells, which kill infected cells or secrete inflammatory molecules known as cytokines, regulatory T cells dampen immune responses. The hope was that the antibody could help suppress autoimmune disorders such as rheumatoid arthritis and might prompt T cells to attack leukemia.

To activate T cells, one receptor responds to a specific foreign invader, or antigen, and another, CD28, signals a green light for an immune response. TGN1412, however, can trigger T cells without the aid of an antigen by simply latching onto a region on CD28 near the cell membrane that other molecules do not target.

Preliminary investigations from the U.K. Medicines and Healthcare Products Regulatory Agency (MHRA) concluded that the root of the problem lay not in contamination or incorrect dosages but with TGN1412 itself. Although the scientists interviewed cautioned that they had not examined the as yet unreleased clinical data, they conjectured that instead of activating mostly regulatory T cells, TGN1412 activated all T cells. That occurence could have led to a massive release of immune molecules, a cytokine storm, that can produce shock and multiorgan failure.

Different results in humans and monkeys pointed to the stem of the Y-shaped antibody, known as the Fc region, as a suspect. In monkeys, the stem might not have bound to cells or might have latched on in a manner that did not trigger a response. In humans, however, it could have yielded unpredictable results after it bound either to non–T cells it was not supposed to or to other immune cells not expressing CD28, contends immunologist Carl June of the University of Pennsylvania. A recent finding suggests that humans may not have certain brakes on their immune systems that nonhuman primates do.

BAD REACTION: The boyfriend of Myfanwy Marshall became seriously ill after receiving an experimental drug at a London hospital.

EDMOND TERAKOPIAN *PA/AP Photo*

TGN1412 could slow the pace of development of the roughly 1,000 clinical grade antibodies in the pipeline, June says. He noted that gene therapy clinical trials led inadvertently to an unexpected death, effectively shutting down research for a number of years. The field's comeback arrived only with a huge increase in regulatory burdens that made it virtually impossible for smaller companies to participate. Still, June predicts that "17 or so antibodies have been approved so far. Their worth has been proven. Big pharma is into antibodies, so it won't die on the vine."

Charles Q. Choi is a frequent contributor.

HYPERREACTIVE HUMANITY

Ajit Varki of the University of California, San Diego, and his colleagues discovered that 20 times more T cells from chimpanzees and other great apes expressed immune-dampening proteins known as Siglecs than human ones did and at 10 to 100 times higher levels per cell, which could explain human T cell hyperreactivity. Varki has asked drugmaker TeGenero for a TGN1412 sample to test his theory, but the company has refused. The scientists reported their findings online May 8 via the *Proceedings of the National Academy of Sciences USA*.

As scientists go forward, better understanding of how TGN1412 works could lead to therapies that take advantage of its immune-triggering activity, perhaps to boost the effectiveness of vaccines. "Maybe something can be salvaged out of the situation," says Carl June of the University of Pennsylvania.

Who Pays?

FUROR ERUPTS OVER TOLL COLLECTING ON THE INTERNET

BY WENDY M. GROSSMAN

What we think of as the Internet—e-mail, the Web, instant messaging—is in reality a set of applications that run over the network the way a word processor runs on a computer. The bits those applications transfer are carried by the physical infrastructure provided by telephone companies such as Verizon and AT&T, cable outfits such as Comcast, and even electric utility firms. Now those same Internet access providers want to charge the largest content providers for premium access—in essence, an extra fee for the use of a digital "fast lane" to reach customers.

EQUAL ACCESS by Internet content providers is at issue in the debate over network neutrality.

Google, Microsoft and consumer groups, among others, are protesting, noting that open access to the telecommunications network spawned the innovations of the past 20 years. They argue that new network services and consumer access to vital information could be stifled by added fees. The tempest has resulted in several bills being introduced in the U.S. Congress to preserve "network neutrality": the principle that all traffic over the Internet is treated the same, even that of the company providing the bandwidth. No bits get priority, unless a higher class of service is offered to all at no extra charge. No traffic, moreover, can be blocked by the network operator.

The present panic began in November 2005, when AT&T CEO Edward E. Whitacre, Jr., told *Business Week* that services such as Google, Yahoo! and Vonage ought to be paying AT&T to deliver customers to them. Otherwise, he said, AT&T would have no incentive to invest in upgrading its network. Since then, executives from BellSouth, Qwest and Verizon have stated publicly that they want to be able to favor traffic from content providers that have paid for better service or to slow down traffic for IP telephony or streaming video that poses a direct threat to their revenue. Network neutrality again raises the perennial issue of how pricing for communications bandwidth can create impediments to new Web-based applications and services. Vinton Cerf, coauthor of the TCP/IP protocols by which the Internet operates and now a vice president at Google, has called the proposals from phone and cable companies an effort to create a "toll road" in the middle of the Internet. The Internet's old guard has never trusted the telecommunications industry and points to recent behavior as a reason for opposing multitiered pricing.

Verizon recently settled a class-action suit over its spam filters' blocking of many legitimate e-mail domains. It has also fought to stop municipalities such as Philadelphia from setting up their own wireless networks, and Comcast has been known to prohibit virtual private network connections that give employees secure access to company networks from home. Despite telephone and cable company claims that competition is working well, the U.S.'s thousands of dial-up Internet service providers have given way in most areas to only one or two choices of broadband providers, whether phone (AT&T, Verizon, BellSouth) or cable (Comcast).

A technical argument against these new pricing proposals relates to how they might complicate exchange of information on the Internet by blocking, say, video or music files needed for building a blog or Web site. "When you look at network neutrality, you ought to look at its effect on services and Internet applications such as blogs," says Daniel Weitzner of the World Wide Web consortium. "What makes blogs interesting is the concatenation of information from lots of points around the Web."

Telecommunications executives have compared tiered pricing to a retailer offering customers faster delivery for free if they purchase a certain amount of goods. But as they say on the Net, TANSTAAFL ("there ain't no such thing as a free lunch"). Ultimately, someone must pay—and there is a good chance that it will be consumers who end up with the bill.

Wendy M. Grossman writes about information technology from London.

NEUTRALITY PARTISANS

In early May, Representative Edward Markey of Massachusetts introduced the Network Neutrality Act of 2006, which would prohibit network operators from giving priority to certain data over their networks.

Markey's bill is one of six attempts that have been put forward this year to legislate the principles of network neutrality.

PHOTODISC RED/GETTY IMAGES

A New Take on Hybrids

FORMER SKEPTICS DEVELOP AN ALTERNATIVE HYBRID SYSTEM **BY STEVEN ASHLEY**

Toyota's flagship gas-electric hybrid sedan Prius represents the epitome of the emerging "green car" category in the mind of the buying public. Although hybrids are still only a blip on the automobile sales charts, the market-leading model has been the most effective tool in the car industry's effort to wrap itself in an eco-friendly cloak. But even with the success of this niche market, General Motors, DaimlerChrysler and BMW have mostly remained on the sidelines, unconvinced of the hybrid's practicality and marketability. (They shied away from having to swallow the added cost of the hybrid's extra electric motors, batteries and so forth—the "hybrid premium" that has thus far failed to fully appear in sticker prices.)

But that view seems to have changed. A consortium of the three firms is working on an alternative technology called a two-mode hybrid to challenge Toyota's supremacy.

As in most hybrids, the two-mode system marries a gasoline engine with electric motors. And it recaptures braking energy as battery power, shuts down the engine at stops and can operate at slow vehicle speeds on electricity alone. Unlike Toyota's single-mode Hybrid Synergy Drive, however, the two-mode offers enhanced fuel efficiency not only in stop-and-go traffic but also on the highway, producing a 25 percent improvement in combined mileage over standard models. In addition, the new design can accommodate vehicles large and small as well as rear-, front- or all-wheel-drive models.

In a typical single-mode hybrid, engine power drives a planetary gear set (which multiplies the torque from the power source) that splits the power between the drive axle and an electric motor. The system's first electric motor operates as a generator, converting that mechanical rotation into electric current, which can then either recharge the battery or power a second electric motor that produces drive-axle torque, depending on the driving conditions.

In contrast, the two-mode system contains two electric motors sandwiching two planetary gear sets, which are separated by two electronic clutches that together form a pair of electric continuously variable transmissions. The system can thus deliver a continuous spectrum of gear ratios that overlays four fixed gears sized to provide operating "sweet spots" at which the engine can achieve enhanced fuel economy or traction power for rapid acceleration, hill climbing or trailer pulling. "It switches between modes seamlessly, without the driver realizing it," explains GM's Larry Nitz.

Single-mode systems are efficient at low speeds mainly because they can propel the car without the engine. At higher velocities, when engine power is required, however, running the electric motors yields less benefit because transmitting power through the motors and a variable transmission is nearly 25 percent less efficient than sending it through a mechanical path that uses gears, Nitz says. At high speeds, the two-mode system improves fuel mileage by relying on electric-motor assist and cylinder deactivation—shutting down part of the engine when extra power is not required. Real-time computer controls match the most favorable operating configuration to each driving situation to optimize power and torque as needed.

The two-mode's mechanical components are cheap and reliable, whereas the single-mode's electric motors and power electronics tend to be more costly and tricky to run, says Andreas Truckenbrodt of DaimlerChrysler. The new system also avoids the big, heavy electric motors that a single-mode vehicle needs to accelerate to top speed and to compensate for its lack of gearing.

GM's Chevrolet Tahoe and DaimlerChrysler's Dodge Durango SUVs will receive the two-mode in late 2007 and early 2008, respectively. Although BMW has not yet revealed its plans, the German car maker's Wolfgang Epple confirms that each company will adapt the system to its own engines and brand—for instance, a two-mode in a BMW X5 sport wagon would perform differently from one in a Tahoe or a Durango.

GENERAL MOTORS CORPORATION

BIG, HIGH-POWERED VEHICLES, such as this GMC Graphyte concept SUV, will be targeted for the two-mode hybrid system, because boosting mileage ratings will save more fuel than using the same technology in smaller cars and trucks.

GREEN OR GREENWASHING?

- **Honda was the first to introduce a fuel-sipping, lower-emission hybrid into the American market (the two-door Insight).**
- **Toyota currently sells more hybrid vehicles than its competitors combined. It even licenses hybrid patents to Ford and supplies components to Nissan.**
- **Hybrids have enabled car makers to project the image of being green, even while purveying fleets of gas-guzzling but high-profit pickup trucks and sport utility vehicles—a public relations strategy critics call "greenwashing." They also help the companies meet federal Corporate Average Fuel Economy (CAFE) standards.**

BY THE NUMBERS

Virtual Skulduggery

INTERNET CRIME MAY BE A BRAKE ON PRODUCTIVITY **BY RODGER DOYLE**

The Internet, which seemed like science fiction a generation ago, has become a supernational reality, with more than a billion people worldwide now having access. But with growth, there has come crime, and indeed the Internet is now where pedophiles prowl and identities are stolen.

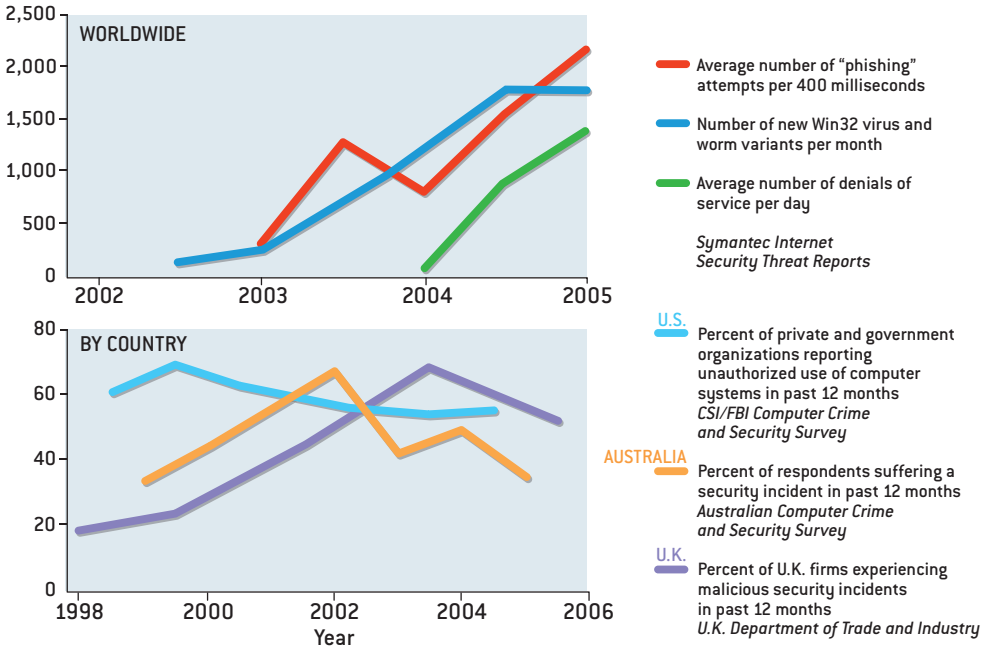
Part of the blame must go to law enforcement agencies, which have been slow to adjust to the radically different conditions of the virtual world. Police accustomed to relying on physical evidence, eyewitnesses and confessions, were suddenly confronted with evidence in digital form; in place of an eyewitness was a log file, a transcript of a server's activity. Most disconcerting, the crime scene was no longer in the neighborhood but in a computer half a world away. In addition, cyber crime seemed to mutate into new enigmatic forms, forcing bewildered police to learn new tricks. From the early days, when hackers sent out viruses for the sheer joy of creating consternation, to the present, when sophisticated cyber criminals threaten to close down a Web site—"denial of service" in the jargon of the Internet—the authorities have had difficulty keeping up.

The general feeling is that crime on the Net is growing. Indicators produced by Symantec Corporation, which measures illegal activity worldwide via more than 40,000 sensors placed in home and corporate computers, show that illegal Internet activity has increased recently (*top graph*). On the other hand, nationwide surveys of organizations suggest a decreasing or stabilizing trend of attacks, perhaps reflecting improved protection measures (*bottom graph*).

The apparent surge in Internet crime in the new millennium as suggested by the top graph has degraded the usefulness of the Net as a marketplace for goods. Consumer surveys show that in January and February of this year only 55 percent of Americans believed that Internet financial transactions were "safe and secure," a decline from the high of 70 percent recorded in 2003. To the extent that the Internet is the prime tool for enhancing services such as retailing and banking, productivity growth in the huge services sector is retarded by virtual crime.

Rodger Doyle can be reached at rodgerpdoyle@verizon.net

SELECTED INDICATORS OF ILLEGAL INTERNET ACTIVITY



RODGER DOYLE

MALEFACTORS WITHOUT BORDERS

International efforts, such as those of the Council of Europe, which is engaged in a worldwide program to standardize national laws and practices relating to cyber crime, have been progressing slowly. Recently, the efforts of law enforcement agencies have been complicated by the apparent large-scale movement of organized crime onto the Internet, which happened because of growing opportunities for illicit profit. Add to this the lax enforcement in developing countries, such as Nigeria, home of the advance-fee scam, and the Internet is ripe for exploitation by individual malefactors and organized crime.

FURTHER READING

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E-Crime: A Rapid Evidence Assessment. Matthew Williams, 2006. www.cybercrimeresearch.com/publications.htm

DATA POINTS: SAVE THE INSECTS

Dell Computer had $56 billion in sales during its last fiscal year. That amount, however, is less—by a billion—than the estimate of the value that bees, dung beetles and other insects bring every year to the U.S. economy. Cornell University entomologist Jon E. Losey and Mace Vaughan of the Xerces Society for Invertebrate Conservation in Portland, Ore., made the first ever estimate of "services" provided by wild insects in a study that appeared in the April issue of the journal *Bioscience*—one that the authors acknowledge is "very conservative"—only a small fraction of the actual benefits furnished by creatures considered by many to be mere pests. Without insects, the authors note, human life on earth would eventually be extinguished.

Value of crop production from pollination by native insects: $3 billion

Crop losses averted by beneficial insects from predation or parasitism of agricultural pests: $4.5 billion

Percent of native pests controlled by other insects: 65

Economic losses averted every year by burial of livestock waste by dung beetles: $380 million

Amount spent for hunting, fishing and observing wildlife that relies on insects as a food resource: $50 billion

Number of North American bird species that are primarily insectivores: 395

SOURCE: BioScience, *April 2006*

MEDICINE

From Brain to Heart

Roughly 5 percent of patients laid low by strokes experience heart attacks soon afterward, sometimes without any prior known history of cardiac disease. Now researchers have found a region of the brain that, when damaged by a stroke, appears to cause a 15 times greater risk for ensuing heart muscle injury. Workers at Massachusetts General Hospital analyzed 50 patients with stroke caused by arterial blockage who also had elevated levels of enzymes released by damaged cardiac muscle. Magnetic resonance imaging scans pinpointed the right insular area as the culprit, a region deep inside the brain linked with the part of the nervous system that sets off stress-related responses. The findings could help prioritize stroke patients at risk of heart attacks for protective therapy. Future studies may also reveal which stroke patients are more likely to develop pneumonia or disruptions in heart rhythm. The research appears in the May 9 *Neurology*. —*Charles Q. Choi*

ASTROPHYSICS

New Way to Create Elements

For decades, scientists have known that supernovae, the explosive deaths of giant stars, trigger reactions to forge most of the heavy elements in the universe. Textbook reactions cannot explain the emergence of unusual isotopes of metals such as molybdenum and ruthenium seen in the sun and meteorites. Now researchers report that antineutrinos, ghostly particles with tiny masses, might generate these rare ingredients. In the first seconds after a supernova, a region rich in protons emerges around the dead star's core, which has most likely collapsed into a neutron star. In the April 14 *Physical Review Letters*, investigators at the University of Basel in Switzerland and their colleagues suggest antineutrinos streaming in huge numbers from the neutron star could irradiate the protons and turn some into neutrons, which build stable, heavy isotopes. This process could assist in explaining the surprisingly large number of certain heavy elements, such as strontium, seen in otherwise metal-poor stars. —*Charles Q. Choi*

SUPERNOVAE may generate unusual metal isotopes.

NEUROSCIENCE

What Role for New Neurons?

Adult rodents form more new neurons than usual when placed in spacious habitats with toys and running wheels, so researchers had supposed that neuron formation, called neurogenesis, also causes the decreased anxiety as well as the enhanced learning and memory brought on by richer environments. Looking to test the connection further, Columbia University researchers precisely irradiated and disabled the hippocampal region where mice form new neurons. Surprisingly, when placed in enriched surroundings, the irradiated mice performed just as well as intact rodents in spatial learning tests and were equally less anxious. The result suggests neurogenesis is not responsible for the effects of enrichment, at least in mice, the investigators note in the April 30 online *Nature Neuroscience*. The study also raises tantalizing questions about the role of neurogenesis in humans, as some research has suggested that the process is important in the treatment of depression. —*JR Minkel*

ENRICHED environments may decrease anxiety—without neurogenesis.

MARK GARLICK *Photo Researchers, Inc. (top)*; CORBIS *(bottom)*; ILLUSTRATION BY MATT COLLINS

PARTICLE PHYSICS

Mass Change

Constants of nature are expected to remain, well, constant, but physicists now find that the masses of protons or electrons might have varied over time. Researchers at the Free University of Amsterdam and their colleagues investigated the wavelengths absorbed by hydrogen gas irradiated with extreme ultraviolet laser beams in their laboratory. They compared it with readings taken at the European Southern Observatory in Chile from the glow of hydrogen clouds that had absorbed radiation from distant quasars, light that originated 12 billion years ago. The positions of certain wavelengths in both cases depend on the proton-to-electron mass ratio. Currently protons are roughly 1,836 times the mass of electrons. In the April 21 *Physical Review Letters*, the scientists reported that the proton-to-electron mass ratio has apparently decreased by one fifty-thousandth in the interval since the universe's youth.

These findings complement recent contentious observations that the fine-structure constant, which describes the overall strength of the electromagnetic force, has increased slightly. —*Charles Q. Choi*

ASTRONOMY

Traces of Gravity

Astronomers seem to invoke collisions, however improbable, when they cannot explain odd features of the solar system. Triton circles Neptune in reverse of its sister moons, for example, and the prior best guess was that Triton flew in from afar and knocked another moon out, like a well-struck cue ball. But if a pair of objects orbiting each other waltzed past Neptune, the one moving slower relative to the planet could have been snared by its gravity and begun orbiting the planet, and the other would have continued on its way, argue researchers in the May 11 *Nature*. Many such binary pairs have been spotted on the solar system's periphery over the past few years. Similarly, gravity, rather than a glancing blow from a protoplanet, might also account for Uranus and its moons' 98-degree axial tilt relative to the planet's orbital plane. Based on accepted trajectories for the young gas giants, a simulation reported in the April 27 issue of *Nature* indicates that the wobbling spin of Saturn could have nudged Uranus on its side during close encounters between the pair. —*JR Minkel*

AXIAL TILT of Uranus (*below*), as seen from the vicinity of one of its moons.

PARASITOLOGY

Island of Resistance

In the quest to squelch malaria, biotechnologists have sketched plans to introduce a gene into mosquitoes that would confer resistance to the malaria parasite, *Plasmodium falciparum*, which the insects transmit between people. Now it seems that nature may have beat researchers to the punch. A group collected thousands of *Anopheles gambiae* mosquitoes from huts in Mali and let some of their offspring feed on blood from an infected villager. Of 101 different pedigrees, a surprising 22 showed no trace of *Plasmodium* on dissection, reports the group in the April 28 *Science*. The resistance appears to stem from a gene or genes on a small patch of chromosome the researchers have dubbed the *Plasmodium* resistance island. Lead author Kenneth Vernick of the University of Minnesota speculates that another strategy to combat malaria might be to selectively target bugs carrying the susceptibility gene variant, perhaps with a recently discovered lethal fungus that appears to prefer *Plasmodium*-ridden mosquitoes. —*JR Minkel*

MALARIA protozoa (*upper right*), near blood cells.

RON MILLER (*top*); EYE OF SCIENCE/PHOTO RESEARCHERS, INC. (*bottom*)

BRIEF POINTS

- **Paleontologists discovered in western Patagonia what may be one of the largest carnivorous dinosaurs ever. The new species, *Mapusaurus roseae*, is bigger than *Tyrannosaurus rex*, slightly more immense than its cousin, *Gigantosaurus*, and appears to have hunted in packs.**

  Announcement by Museo Carmen Funes, Plaza Huincul, Argentina, and University of Alberta, April 17

- **Pass the hummus: Americans who consumed a Mediterranean diet—meals with vegetables, fruits, legumes, some fish and alcohol, along with low amounts of dairy and meat products—experienced a lower risk of Alzheimer's disease as they grew older. The study was the first that examined the relation between Alzheimer's and general dietary patterns.**

  Annals of Neurology, published online April 18

- **Deforming the crystal structure of silicon, the workhorse of electronics, changes its properties so that the material becomes capable of carrying a light-based signal. The invention raises the possibility of replacing electronic components with much faster optical ones.**

  Nature, May 11

- **Jellyfish produce some of the fastest movements in the animal kingdom. A camera that captures 1.4 million frames per second determined that jellyfish stinging cells discharged in 700 nanoseconds and struck with the force of some bullets.**

  Current Biology, May 9

The human understanding when it has once adopted an opinion ... draws all things else to support and agree with it. And though there be a greater number and weight of instances to be found on the other side, yet these it either neglects and despises ... in order that by this great and pernicious predetermination the authority of its former conclusions may remain inviolate.
—*Francis Bacon,* Novum Organum, *1620*

The Political Brain

A recent brain-imaging study shows that our political predilections are a product of unconscious confirmation bias By MICHAEL SHERMER

Pace Will Rogers, I am not a member of any organized political party. I am a libertarian. As a fiscal conservative and social liberal, I have found at least something to like about each Republican or Democrat I have met. I have close friends in both camps, in which I have observed the following: no matter the issue under discussion, both sides are equally convinced that the evidence overwhelmingly supports their position.

This surety is called the confirmation bias, whereby we seek and find confirmatory evidence in support of already existing beliefs and ignore or reinterpret disconfirmatory evidence. Now a functional magnetic resonance imaging (fMRI) study shows where in the brain the confirmation bias arises and how it is unconscious and driven by emotions. Psychologist Drew Westen led the study, conducted at Emory University, and the team presented the results at the 2006 annual conference of the Society for Personality and Social Psychology.

Politicians need a peer-review system.

During the run-up to the 2004 presidential election, while undergoing an fMRI bran scan, 30 men—half self-described as "strong" Republicans and half as "strong" Democrats—were tasked with assessing statements by both George W. Bush and John Kerry in which the candidates clearly contradicted themselves. Not surprisingly, in their assessments Republican subjects were as critical of Kerry as Democratic subjects were of Bush, yet both let their own candidate off the hook.

The neuroimaging results, however, revealed that the part of the brain most associated with reasoning—the dorsolateral prefrontal cortex—was quiescent. Most active were the orbital frontal cortex, which is involved in the processing of emotions; the anterior cingulate, which is associated with conflict resolution; the posterior cingulate, which is concerned with making judgments about moral accountability; and—once subjects had arrived at a conclusion that made them emotionally comfortable—the ventral striatum, which is related to reward and pleasure.

"We did not see any increased activation of the parts of the brain normally engaged during reasoning," Westen is quoted as saying in an Emory University press release. "What we saw instead was a network of emotion circuits lighting up, including circuits hypothesized to be involved in regulating emotion, and circuits known to be involved in resolving conflicts." Interestingly, neural circuits engaged in rewarding selective behaviors were activated. "Essentially, it appears as if partisans twirl the cognitive kaleidoscope until they get the conclusions they want, and then they get massively reinforced for it, with the elimination of negative emotional states and activation of positive ones," Westen said.

The implications of the findings reach far beyond politics. A jury assessing evidence against a defendant, a CEO evaluating information about a company or a scientist weighing data in favor of a theory will undergo the same cognitive process. What can we do about it?

In science we have built-in self-correcting machinery. Strict double-blind controls are required in experiments, in which neither the subjects nor the experimenters know the experimental conditions during the data-collection phase. Results are vetted at professional conferences and in peer-reviewed journals. Research must be replicated in other laboratories unaffiliated with the original researcher. Disconfirmatory evidence, as well as contradictory interpretations of the data, must be included in the paper. Colleagues are rewarded for being skeptical. Extraordinary claims require extraordinary evidence.

We need similar controls for the confirmation bias in the arenas of law, business and politics. Judges and lawyers should call one another on the practice of mining data selectively to bolster an argument and warn juries about the confirmation bias. CEOs should assess critically the enthusiastic recommendations of their VPs and demand to see contradictory evidence and alternative evaluations of the same plan. Politicians need a stronger peer-review system that goes beyond the churlish opprobrium of the campaign trail, and I would love to see a political debate in which the candidates were required to make the opposite case.

Skepticism is the antidote for the confirmation bias. SA

Michael Shermer is publisher of Skeptic *(www.skeptic.com) and author of* Science Friction.

BRAD HINES

Ecology and Political Upheaval

Small changes in climate can cause wars, topple governments and crush economies already strained by poverty, corruption and ethnic conflict By JEFFREY D. SACHS

Careful study of the long-term climate record has shown that even a minor shock to the system can cause an enormous change in outcome, a nonlinear response that has come to be called "abrupt climate change." Less well recognized is that our social and economic systems are also highly sensitive to climate perturbations. Seemingly modest fluctuations in rainfall, temperature and other meteorological factors can create havoc in vulnerable societies.

Recent years have shown that shifts in rainfall can bring down governments and even set off wars. The African Sahel, just south of the Sahara, provides a dramatic and poignant demonstration. The deadly carnage in Darfur, Sudan, for example, which is almost always discussed in political and military terms, has roots in an ecological crisis directly arising from climate shocks. Darfur is an arid zone with overlapping, growing populations of impoverished pastoralists (tending goats, cattle and camels) and sedentary farmers. Both groups depend on rainfall for their livelihoods and lives. The average rainfall has probably declined in the past few decades but is in any case highly variable, leaving Darfur prone to drought. When the rains faltered in the 1980s, violence ensued. Communities fought to survive by raiding others and attempting to seize or protect scarce water and food supplies.

Public debates tend to neglect powerful ecological effects because we focus on politics.

A drought-induced famine is much more likely to trigger conflict in a place that is already impoverished and bereft of any cushion of physical or financial resources. Darfur was also pushed over the edge by ethnic and political conflict, with ambitious, violent and unscrupulous leaders preying on the ethnic divisions. These vulnerabilities, of course, have not been unique to Darfur. Several studies have shown that a temporary decline in rainfall has generally been associated throughout sub-Saharan Africa with a marked rise in the likelihood of violent conflict in the following months.

Africa is certainly not alone in experiencing the linkages of climate shocks and extreme social instability. Rainfall shifts associated with El Niño cycles have had similarly catastrophic consequences. The massive 1998 El Niño produced huge floods off the coast of Ecuador, which destroyed a considerable amount of export crops and aquaculture. That led to a failure of loans to Ecuador's already weak banking system, which in turn helped to provoke a bank run, an unprecedented economic collapse and eventually the ouster of the government. Halfway around the world the same El Niño caused an extreme drought in Indonesia, coinciding with Asia's massive financial crisis. Indonesia's drought and resulting food shortage contributed to financial and political destabilization and to the end of President Suharto's 31-year rule. As in Ecuador, the short-term economic collapse was by far the largest in Indonesia's modern history.

Climate skeptics who ask impatiently why we should care about "a degree or two" increase in the global mean temperature understand neither the climate nor the social and economic systems in which we live. Both climate and society are subject to great instability, nonlinear responses and high unpredictability. Climate changes may influence storms, droughts, floods, crop yields, disease vectors and much more, well beyond what the current "average" forecasts suggest. And the resulting ecological effects, especially on societies already facing hunger or financial and political fragility, can be enormous and dire. Our public debates tend to neglect these powerful effects because we focus on politics and only rarely on the underlying environmental pressures.

Once we recognize the ecological risks to our economic well-being and even to our national security, we will begin to look much harder for practical approaches to mitigating the pressures that our global society is now placing on the earth's ecosystems. We will then need to increase our preparations for the intensified shocks that are surely on their way. The intertwined strategies of mitigation and adaptation will be the topics of future columns. SA

Jeffrey D. Sachs is director of the Earth Institute at Columbia University and of the U.N. Millennium Project.

ARNOLD ADLER

Reprogramming Biology

Tinkering with our genetic programs will extend longevity By RAY KURZWEIL

Biology is now in the early stages of a historic transition to an information science, while also gaining the tools to reprogram the ancient information systems of life. Our electronic devices typically update their software every few months, yet the 23,000 software programs called genes inside our cells have not changed appreciably in thousands of years. As we begin to understand biology in terms of its information processes, however, we are developing realistic models and simulations of how disease and aging progress and ways to reprogram them.

RNA interference (RNAi), which science learned about only in the past several years, can turn specific genes off. Because many types of illness depend on gene expression at some point, RNAi heralds a breakthrough technology. One example of a gene that we would like to turn off is an insulin receptor gene that tells fat cells to hold on to every calorie. When that gene was blocked in the fat cells of mice during a study at the Joslin Diabetes Center, those mice ate a lot but remained thin and healthy. They lived almost 20 percent longer.

Versions of our cells will be made "younger" by correcting DNA errors.

Innovative means of adding beneficial genes to patients' bodies are starting to overcome the hurdles for gene therapy. United Therapeutics, a company I advise, has licensed and adapted a technique that modifies cells in vitro, verifies that the new genetic information has been properly inserted, replicates the modified cell millions of times and then injects those cells back into the bloodstream, where they embed themselves into the right tissues. This method has cured fatal pulmonary hypertension in animals and is entering human trials.

Another important line of attack is to regrow our own cells, tissues and even whole organs. A major benefit of this "therapeutic cloning" technique will be the ability to create tissues from versions of our cells that have been made "younger" by correcting DNA errors and senescence-related changes. For example, we will be able to create heart cells from your skin-derived stem cells and introduce them into your system through the bloodstream. Over time, the new cells will replace your old ones, resulting in a rejuvenated heart.

Nanotechnology can go beyond the limitations of biology. Harvard University and Massachusetts Institute of Technology researchers have designed nanoparticles that latch onto cancer cells, burrow inside and release toxins to destroy them. Another scientist cured type 1 diabetes in rats with a nanoengineered device that uses seven-nanometer pores to controllably release insulin while blocking antibodies.

Our ability to understand and even reprogram the brain is also accelerating. The latest in vivo scanners can image individual interneuronal connections firing in real time. IBM has begun an ambitious effort to simulate a substantial portion of the cerebral cortex at a detailed level. Rising numbers of artificial neural implants can replace diseased tissue, such as an FDA-approved one for Parkinson's patients that allows software updates to be downloaded from outside the body.

As an information technology, biology is subject to what I call the "law of accelerating returns." Such technologies double their price performance and capacity in less than a year. Sequencing DNA has come down in price by half annually, from $10 per base pair in 1990 to under a penny today. The amount of genetic data we have sequenced has more than doubled every year. At this rate, we will increase the capability of these technologies by a factor of 1,000 in less than a decade and by a billion in 25 years.

Human life expectancy was only 37 years in 1800. Our ability to reprogram biology will dramatically increase it again, but this progression will be much faster. I expect that within 15 years, we will be adding more than a year annually to remaining life expectancy. So my advice is: take care of yourself the old-fashioned way for a while longer, and you may get to experience the remarkable century ahead in full. SA

An expanded version of this essay is available online at www.sciam.com/ontheweb

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Ray Kurzweil is a pioneering inventor, recipient of the National Medal of Technology and author. His most recent book is The Singularity Is Near: When Humans Transcend Biology.

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Dangling a Carrot for Vaccines

Drug companies do not see much of a market in treating diseases of developing nations. Michael Kremer hopes to change that—with a plan that taps the profit motive By JR MINKEL

It's a gray, drizzly March day at Harvard University. Economist Michael Kremer is recalling his postcollegiate year, 1985, spent teaching high school in Kenya, contracting malaria, recovering and watching sick Kenyans fare worse than he. Melancholy enters his voice. "The burden of disease is just very clear," he nearly sighs. "This is a terrible crisis. It seems vital to put the same sorts of entrepreneurial spirit and effort, and creativity, unleashed by the market sector"—he laughs dryly, as if in disbelief—"to work on these diseases as is being done for the diseases in rich countries."

KATHLEEN DOOHER

MICHAEL KREMER: DRUGS TO THE POOR

- **Advocates the use of advanced market commitments (AMCs), in which donors agree to pay high prices for vaccines on condition that they later be sold cheaply to poor nations.**
- **On whether companies can be coaxed into making vaccines for neglected diseases: "If you make it attractive enough, they will."**

Poor nations labor under the weight of malaria, AIDS, tuberculosis and a score of diseases lesser known in rich countries, but they cannot afford to pay the prices companies want for drugs. Whereas some might denounce the pharmaceutical industry's profit seeking, Kremer wants to harness it. He has championed the idea that governments and other donors should try to make a malaria or tuberculosis vaccine as attractive to industry as the average drug market is. "I want them to do the same thing for malaria they would do for breast cancer," he says.

Right now research and development for neglected vaccines occurs primarily through public-private partnerships, which have invigorated the field in the past half a decade. Nonprofit groups such as the International AIDS Vaccine Initiative channel money from donors into deals with biotech and pharma companies. Industry involvement is growing, says Michel Zaffran, deputy executive secretary of the Global Alliance for Vaccines and Immunization, "but it's still not at the level one would like to see." Aid groups negotiate with drugmakers to procure vaccines for poor nations, but industry remains wary it will be haggled down to an unwelcome price.

Kremer advocates constructing a kind of artificial market for a vaccine. A donor would commit to paying a certain sum, a few hundred million dollars up to perhaps $5 billion, on delivery of a viable vaccine. Once a vaccine is manufactured, the donor would purchase it at a high price per dose until the sum is exhausted; thereafter, the company would be obligated to supply the vaccine to poor countries at a low price. "The idea is quite simple, and it really gets at the heart of the problem—that there are insufficient markets in the developing world to attract industry," remarks Wendy Taylor, founder of BIO Ventures for Global Health.

The recipient of a MacArthur fellowship in 1997,

the 41-year-old Kremer is adept at sketching out institutional fixes for problems in developing countries. To ease these nations' debt, he has argued that the international community should regard loans to odious regimes as loans to the ruling despots themselves, perhaps dissuading banks and other private lenders. To break up black markets surrounding the antiquities of poor countries, he proposes leasing the artifacts to museums.

His first foray into financial incentives for disease treatment was in 1998, when he studied the idea that the public sector could buy out the patents of working vaccines. A year later Kremer had an inspirational conversation with Jeffrey D. Sachs, a development economist at Columbia University. The concept evolved into a vaccine purchase fund, in which a donor would commit to buying doses of an already manufactured vaccine—something the World Bank had also recommended. "We were both quite enthusiastic about the idea of buying out the product," Kremer says. At a colloquium, Sachs and Kremer outlined the idea in front of attendees from international aid groups and industry, who were not immediately persuaded.

Malaria or tuberculosis vaccines should be as attractive to industry as the average drug market is.

Undaunted, Kremer published a pair of subsequent papers laying out the rationale, design challenges and trade-offs. He envisioned the purchase commitment as a long-term contract specifying clinical criteria, setting up an independent adjudicating committee and requiring poor countries that wanted the vaccine to make a small co-payment.

"The details of how this is done will make a big difference," Kremer acknowledges. One trade-off hinges on the commitment's payment structure, which could range from a competition that awards a sum to the first company that develops a vaccine to a more marketlike approach, in which any product meeting the clinical requirements is eligible for purchase. By judiciously selecting the price and quantity of doses that they commit to, donors can choose to reward the fast development of an initial vaccine or the introduction of subsequent, possibly superior products, Kremer says.

One criticism leveled at advanced market commitments (AMCs), as the purchase commitments are now called, is that they would encourage industry to dust off abandoned, mediocre vaccine candidates. To Kremer, that is the whole point: "If they have something they think has a 10 percent chance, I want them to take that off the shelf."

To succeed, the commitment has to minimize industry's risk of supplying vaccines to a single buyer, the donor, who might decide to pay the lowest price possible once a vaccine was developed. The U.S. government's Project BioShield illustrates the danger. Enacted in 2004, it allocated $5.6 billion over 10 years to stimulate development of vaccines and drugs for potential terrorist threats. The government has purchased drugs from a few biotech firms. But BioShield's original rules, now modified, gave administrators discretion in whether, how much and at what price to buy, and some companies that sunk millions into drug development were left without a customer.

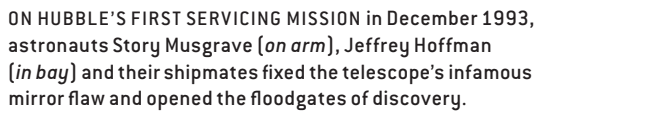
The Center for Global Development, where Kremer is a nonresident fellow, convened a working group in 2003 to study the feasibility of purchase commitments. Made up of economists, lawyers, public health experts and representatives from industry, the group published its recommendations last year, including sample contracts. It advocated allowing multiple companies to share in an AMC, in part to attract more industry participation, and letting poor countries refuse a vaccine, in case circumstances changed. These efforts caught the attention of the Group of Seven nations. In its December meeting last year, the G7 called for a pilot proposal from the World Bank for one of six diseases: malaria, HIV, tuberculosis, rotavirus, pneumococcus or human papillomavirus.

The concern persists that AMCs might compete with public-private partnerships. A commitment would have to be designed to tie up funds only on completion of a vaccine, Kremer emphasizes. "There was a tendency earlier on to present this as an alternative to up-front funding," he admits. "We're not trying to take the public sector out of this."

Indeed, getting industry, donors and the public sector working together seems key to making an AMC work. Industry still faces uncertainty about how much vaccine poor countries would want to buy and how to set a long-term price in advance. The G7 has asked the World Bank and the Global Alliance for Vaccines and Immunizations to help improve demand forecasting and other implementation issues. Robert Hecht of the International AIDS Vaccine Initiative notes that the international vaccine procurement system and laws governing liability and intellectual property also need further development. "There are many people who doubt it will actually work, and there are many who hope it will," Zaffran says.

If Kremer errs on the side of overexuberance, it stems partly from his desire to help those sharing the lot of the Kenyans he knew and partly from his belief as an economist in the power of institutions to shape incentives. "There's a tendency for this whole debate over pricing of drugs in the developing world to be framed in terms of access versus incentives," he says—poverty versus profit. "Both sides in that debate are taking the existing institutions as given. I'm trying to think about ways to make the market work to the advantage of people." SA

JR Minkel is a frequent contributor.



ON HUBBLE'S FIRST SERVICING MISSION in December 1993, astronauts Story Musgrave (*on arm*), Jeffrey Hoffman (*in bay*) and their shipmates fixed the telescope's infamous mirror flaw and opened the floodgates of discovery.

Hubble's Top 10

By Mario Livio

As they wait for the space telescope to be serviced one last time, astronomers reflect on its discoveries over the past 16 years

Few telescopes in history have had such a profound effect on astronomical research as the Hubble Space Telescope. Yet its influence is not what most people think. By and large, it has not made singular discoveries—achievements that are its and its alone. Instead Hubble has taken what were hints and suspicions from ground-based observations and turned them into near certainties. It has worked in concert with other observatories to provide a multihued view of the cosmos. It has forced theorists to rethink broad-brush theories and to construct new ones that explain astronomical phenomena in much finer detail. In short, Hubble has been extremely influential not by standing apart from other instruments and techniques but mainly by becoming deeply integrated with them.

In April the telescope passed its 16th anniversary in space. Its achievements, both in providing astronomers with unprecedented detail and in bringing a glimpse of the wonders of the universe to homes worldwide, have been somewhat overshadowed of late by the debate over its future. As NASA struggles to resume space shuttle flights, Hubble continues to deteriorate; unless astronauts can reach and refurbish it, the telescope could reach the end of its useful life as early as mid-2008. Arrival at this crossroads has spurred me to take stock of Hubble's—and astronomy's—past decade and a half, which many researchers consider a golden age of their field.

I present below my (admittedly biased) choices of Hubble's 10 most riveting contributions, from its revelations about smallish objects such as planets, progressing to galaxies and the universe as a whole. It is extremely difficult to do justice in one article to all that Hubble has contributed. At the time of writing, its archive contained more than 27 terabytes of data and was growing by 390 gigabytes a month. The data have been the basis for 6,300 scientific papers. Moreover, the telescope continues to produce astonishing science. Working with other observatories in the past year, Hubble has discovered two additional satellites of Pluto; an unexpectedly (and paradoxically) massive galaxy in the very early universe; and a planetary-mass companion to a brown dwarf, itself not much heavier than a planet. We should consider ourselves lucky to live in an era in which we have seen for the first time features of the universe that humans were once able to probe only with their imaginations.

NASA

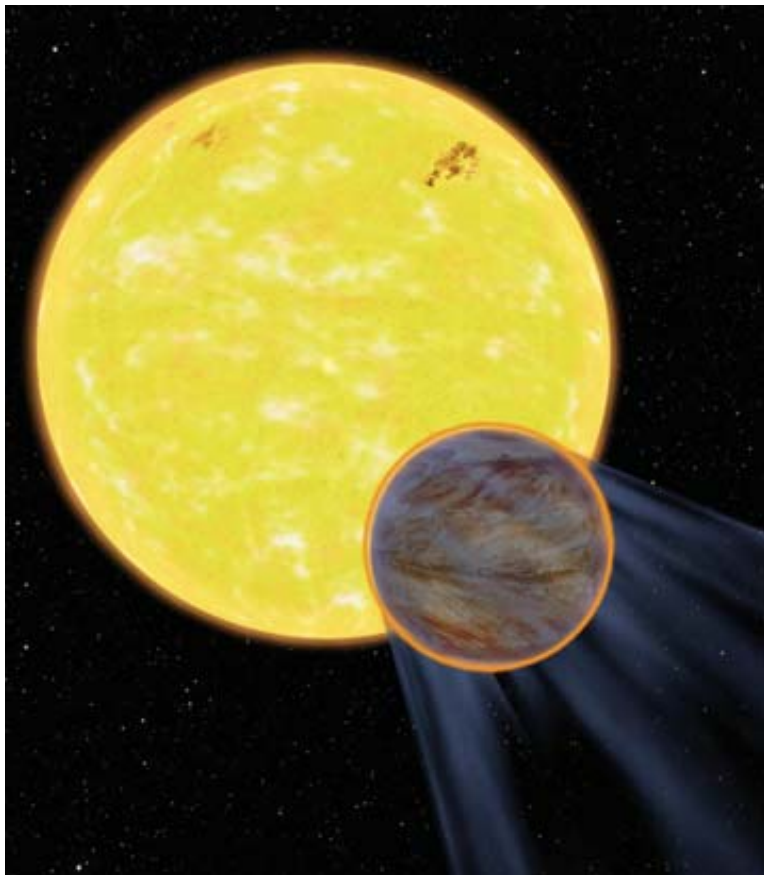
1 The Great Comet Crash

From a cosmic perspective, the impact of Comet Shoemaker-Levy 9 into Jupiter was unremarkable: the cratered surfaces of rocky planetary bodies and satellites already bear testimony that the solar system is a shooting gallery. From a human perspective, however, the collision was a once-in-a-lifetime event: it is thought that on average a comet plows into a planet only once every 1,000 years.

A year before Shoemaker-Levy 9's demise, Hubble images revealed that it had split into about two dozen fragments, a "string of pearls." The first fragment smashed into Jupiter's atmosphere on July 16, 1994, followed by the rest over the following week. Images showed plumes resembling nuclear mushroom clouds rising above Jupiter's horizon, falling and spreading within 10 minutes of impact. The resulting scars lasted for months.

The rarity of the images alone makes them valuable, but the shots also raised an intriguing question about the gas giant's composition. At one site, waves rippled outward at 450 meters per second. The leading explanation is that they are gravity waves, in which the restoring force is buoyancy, as when you try to force a piece of wood into water and it bobs up and down. If so, then the properties of the waves suggest that the ratio of oxygen to hydrogen in the water cloud where the waves propagated is 10 times as high as in the sun. Yet if Jupiter formed from the gravitational breakup of a primordial disk of dust and gas, as some theories posit, its composition should be the same as that of the disk—and therefore similar to that of the sun. The discrepancy remains unresolved.

EIGHT IMPACT SITES (some overlapping or barely visible) mar Jupiter's southern hemisphere in this image, taken July 22, 1994. Below, a plume rises like a mushroom cloud above the rim of the planet six minutes after an impact on July 16.



SILHOUETTE OF A PLANET, shown in this artist's conception, is inferred from Hubble measurements of the brightness of the host star.

2 Extrasolar Planets

In 2001 the American Astronomical Society asked planetary scientists to vote on what they thought had been the biggest discovery of the previous decade. They chose the detection of planets outside our solar system. Today researchers know of about 180 such bodies. Most have been found by ground-based telescopes observing the small wobble that the gravitational tug of a planet introduces in the motion of its host star. Yet these observations provide the barest amount of information: just the size and ellipticity of the planet's orbit and a lower limit on its mass.

Hubble has followed up by focusing on those planets whose orbital planes are aligned with our line of sight, so that they cross periodically in front of their stars and block some of their light—an event known as a transit. Hubble observations of the first discovered transiting planet, the companion to the star HD 209458, have given the most detailed information about any planet outside our solar system. It is 30 percent lighter than Jupiter yet 30 percent larger in diameter, probably because the blast of radiation from its parent star has caused it to bloat. The Hubble data are so precise that they would reveal broad rings and massive satellites around the planet if they existed; they do not. Most impressive is that Hubble has made the first measurements of the composition of a world around another star. The atmosphere contains sodium, carbon and oxygen, and its hydrogen is evaporating into space to create a cometlike tail. These observations are a precursor to searches for the chemical signs of life elsewhere in the galaxy.

DON DIXON (*illustration*); NASA AND HUBBLE SPACE TELESCOPE COMET TEAM (*top*); NASA AND STScI (*bottom*)

3 Death Throes

Theory predicts that a star with a mass between eight and 25 times that of our sun ends its life in a supernova explosion. When the star exhausts its usable fuel, it abruptly loses the constant struggle to hold up its own weight. Its core collapses to form a neutron star—an inert, hyperdense remnant—and the outer gas layers are ejected at 5 percent of the speed of light.

Testing this theory has been difficult, however, because no supernova has gone off in our galaxy since 1680. On February 23, 1987, astronomers got the next best thing: a supernova in one of the Milky Way's satellite galaxies, the Large Magellanic Cloud. Hubble had not yet been launched, but three years later it began to track the progress of the event. It soon uncovered a three-ring system around the exploded star. The central ring appears to represent the narrow waist of an hourglass-shaped puff of gas, and the larger rings are the edges of two teardrop-shaped lobes, evidently created by the star a few tens of thousands of years before it exploded. In 1994 Hubble began seeing spots brighten in sequence along the central ring: the supernova ejecta smacking into the ring. Observations of the ring continue to illuminate the endgame of the star.

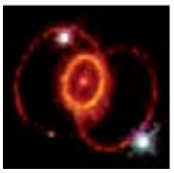
Unlike their more massive counterparts, sunlike stars are thought to die gracefully by ejecting their outer gaseous layers in a nonexplosive process that takes about 10,000 years. As the hot central core of the star is exposed, its radiation ionizes the ejected gas, causing it to glow in vibrant green (emitted by ionized oxygen) and red (ionized hydrogen). The result is called, somewhat misleadingly, a planetary nebula. Some 2,000 are known today. Hubble has revealed extraordinarily complex shapes in unprecedented detail.

Some of the nebulae exhibit a set of concentric rings like bull's-eyes, possibly indicating that the ejection process was episodic rather than continuous. Oddly, the inferred elapsed time between ejection episodes, about 500 years, is too long to be explained by dynamic pulsations (in which the star contracts and expands, in a gentle tussle between gravity and gas pressure) and too short to represent thermal pulsations (in which the star is driven out of equilibrium). The precise nature of the observed rings is therefore unclear.

NASA, ESA, STScI AND CHRISTOPHER BURROWS (*inset*); DON DIXON (*left*); NASA, ESA, HEIC AND HUBBLE HERITAGE TEAM STScI/AURA (*right*)

WHEN A SHOCK WAVE from Supernova 1987A crashed into a preexisting ring of gas, hot spots began lighting up.

Artist's reconstruction



Hubble image

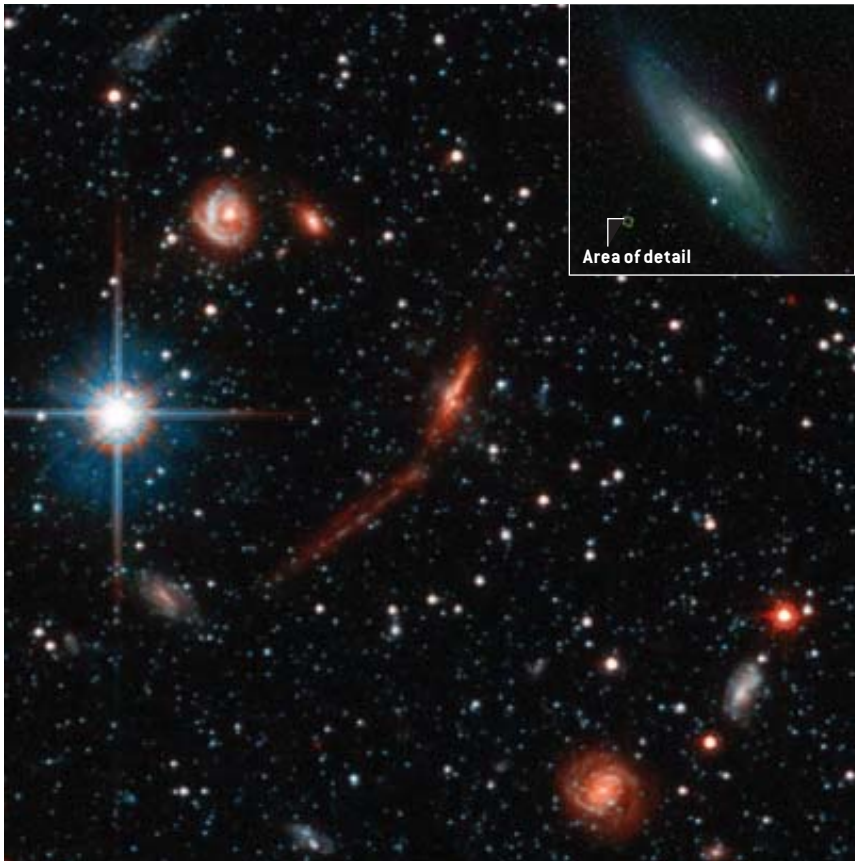
CAT'S-EYE NEBULA is one of the most complex known planetary nebulae, which are thought to be created by dying sunlike stars.

4 Cosmic Birthing

For a long time, astronomers have known that narrow, spouting streams of gas are the signposts of stellar birth. A nascent star can send out a pair of collimated jets several light-years in length. How it does so is not fully understood. The most promising hypothesis involves a large-scale magnetic field threading the dusty, gaseous disk surrounding the young object. Ionized matter, forced to flow along the magnetic field lines, gets flung out like beads on rotating wires. Hubble has supported this theoretical picture by providing the first direct evidence that these jets indeed originate at the center of the disk.

Another expectation, which Hubble overturned, was that the circumstellar disks would be deeply embedded within their parent clouds and would therefore be impossible to see. In fact, Hubble revealed dozens of protoplanetary disks, or "proplyds," often silhouetted against nebulae. At least half the young stars surveyed possess such disks, demonstrating that the raw materials for planet formation are ubiquitous in the galaxy.

LOOKING LIKE MALFORMED AMOEBAS, dust disks surround embryonic stars in the Orion Nebula. Each image is 2,040 astronomical units square.



ODDLY YOUNG STARS on the outskirts of the Andromeda galaxy (*inset*) could be shards from a galaxy collision. (Several background galaxies also appear in this image.)

5 Galactic Archaeology

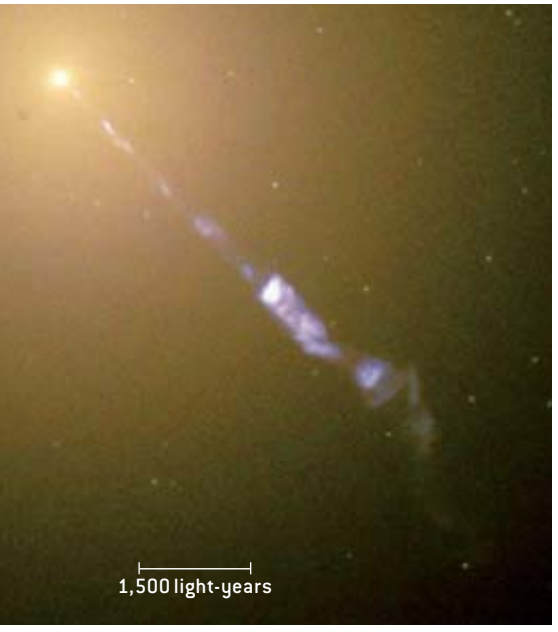
Astronomers think that large galaxies such as the Milky Way and neighboring Andromeda grew by assimilating smaller ones. The record of this tangled past should be written into the arrangement, ages, compositions and velocities of their stars. Hubble has been instrumental in deciphering this history. An example was its observations of Andromeda's stellar "halo," the tenuous spherical cloud of stars and star clusters that surrounds the main galactic disk. Astronomers found that halo stars come in a wide range of ages: the oldest are 11 billion to 13.5 billion years old; the youngest are six billion to eight billion years old. The latter are like children in a nursing home. They must have wandered in from some younger galaxy (such as a satellite galaxy that was assimilated) or from some younger region within Andromeda itself (namely, the disk, if it became disrupted by a passing or colliding galaxy). The Milky Way's halo does not contain significant numbers of comparatively young stars. So even though Andromeda and the Milky Way have similar shapes, Hubble data suggest that the two galaxies have had very different histories.

THE AUTHOR

MARIO LIVIO is one of the most wide-ranging researchers in astronomy today, studying dark energy, supernova explosions, extrasolar planets and accretion onto compact objects. He is currently at the Space Telescope Science Institute in Baltimore. His recent popular book, *The Equation That Couldn't Be Solved,* discusses symmetry and its role in things ranging from the selection of mates to the laws of physics. In what remains of his time after research and writing, he is an amateur art historian with an extensive library of museum catalogues.

NASA, ESA AND T. M. BROWN *STScI (top)*; BILL SCHOENING, VANESSA HARVEY/REU PROGRAM/NOAO/AURA/NSF *(inset)*; NASA, J. BALLY *University of Colorado*, H. THROOP *Southwest Research Institute* AND C. R. O'DELL *Vanderbilt University (bottom)*

PLASMA JET, thought to be generated by an accreting black hole of three billion solar masses, squirts out of galaxy M87.



6 Supermassive Black Holes Galore

Since the 1960s astronomers have reasoned that quasars and other active galactic nuclei—bright, violent cores of galaxies—are powered by giant black holes feasting on matter. Hubble observations have firmed up this general scenario. Almost every galaxy it has observed carefully has turned out to have a black hole lurking at its hub. Two findings have been particularly significant. First, high-resolution images of quasars reveal that they reside in bright elliptical galaxies or in interacting galaxies, suggesting that it takes a certain sequence of events to feed the central black hole. Second, the mass of the giant black hole is tightly correlated with the mass of the spherical bulge of stars surrounding the galactic center. The correlation suggests that the formation and evolution of a galaxy and its black hole are intimately connected.

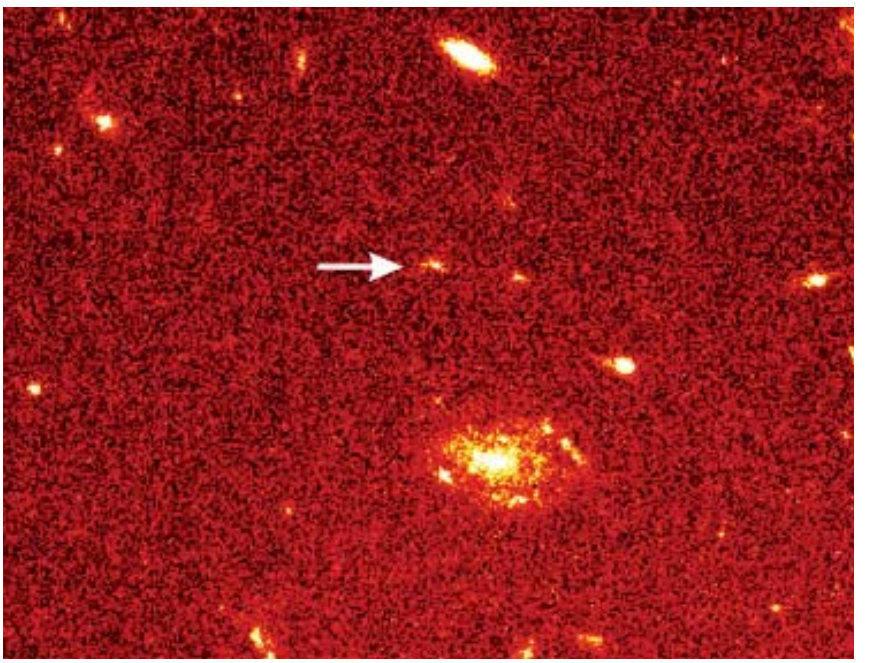
7 The Largest Explosions

Gamma-ray bursts (GRBs) are short flashes of gamma rays lasting between a few milliseconds and tens of minutes. They come in two distinct classes depending on whether they last longer or shorter than about two seconds; the longer ones produce lower-energy photons than the shorter ones do. Observations by the Compton Gamma Ray Observatory, the x-ray satellite BeppoSAX and ground-based observatories have attributed the long-duration bursts to the core collapses of massive, short-lived stars—in other words, to a type of supernova. The question is why only a small fraction of supernovae produce GRBs.

Hubble has found that whereas supernovae occur throughout the regions of star formation in galaxies, long-duration GRBs are concentrated in the very brightest regions, where the most massive stars reside. Furthermore, compared with supernova host galaxies, the hosts of long GRBs are significantly fainter, more irregular and less endowed with heavy elements. This is important because massive stars deficient in heavy elements generate stellar winds that are weaker than those blown out by their enriched counterparts. Over the course of their lives, they retain more of their mass; when they expire, they are heavier. The collapse of their cores tends to produce not a neutron star but a black hole. In fact, astronomers attribute long GRBs to collimated jets generated by rapidly spinning black holes. The deciding factors for whether a core collapse produces a GRB appear to be the mass and rotation rate of the progenitor star at the time of its death.

Identifying short-duration bursts has proved to be more difficult. Only last year were a few finally pinpointed by the HETE 2 and Swift satellites. Hubble and the orbiting Chandra X-ray Observatory revealed that these bursts give off less energy overall than long-duration ones and occur in a wider variety of galaxy types, including elliptical galaxies where stars are no longer forming. Apparently the short bursts are associated not with massive, short-lived stars but rather with the corpses of those stars. The most plausible hypothesis is that the short-duration bursts arise from a merger of two neutron stars.

HOST GALAXY of gamma-ray burst 971214 shows up as a modest smudge (*next to arrow*).



NASA AND HUBBLE HERITAGE TEAM *STScI/AURA* (*top*); NASA, S. R. KULKARNI AND S. G. DJORGOVSKI *California Institute of Technology* AND CALTECH GRB TEAM (*bottom*)

BILLIONS OF TIMES FAINTER than anything the naked eye can see, distant galaxies are strewn across the Hubble Ultra Deep Field.

8 The Edge of Space

One of the overarching goals of astronomy is to trace the development of galaxies and their precursors as close as possible to the big bang. To get an idea of what the Milky Way once looked like, astronomers have sought to take pictures of galaxies of various ages, from infancy to maturity. To this end, Hubble, coordinating with other observatories, has taken long exposures of small patches of sky—the Hubble Deep Fields, the Hubble Ultra Deep Field and the Great Observatories Origins Deep Survey—to bring out the most distant (hence most ancient) galaxies.

These supersensitive images have uncovered galaxies that existed when the universe was only a few hundred million years old, about 5 percent of its present age. These galaxies were smaller in size and more irregular in shape than modern ones, as one would expect if today's galaxies formed from the agglomeration of smaller ones (as opposed to the breakup of larger ones). Going even further back in time is the main aim of Hubble's successor, the James Webb Space Telescope, currently under construction.

The deep observations have also traced the waxing and waning of star formation in the universe at large over cosmic time. The rate seems to have reached its peak around seven billion years ago and has fallen 10-fold since then. When the universe was relatively young—one billion years old—the star formation rate was already high, about a third of its peak value.

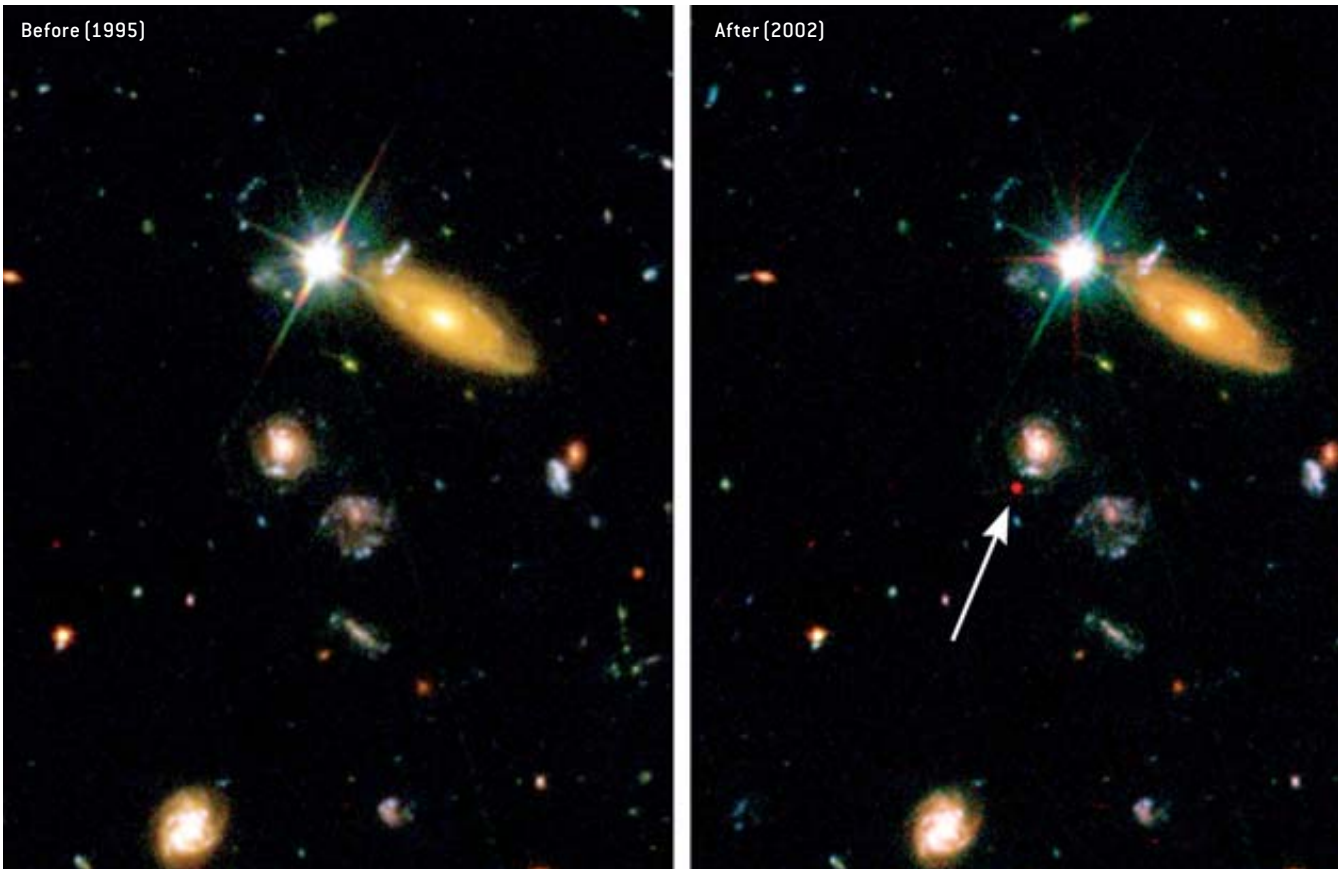
9 The Age of the Universe

Observations by Edwin Hubble and others in the 1920s showed that we live in an expanding universe. Galaxies are flying apart from one another in a systematic pattern, implying that the fabric of space itself is stretching. The Hubble constant (H_0) is a measure of the current rate of expansion, which is the key parameter in determining the age of the universe. The reasoning is simple: H_0 is the rate at which galaxies are moving apart from one another; thus, neglecting any acceleration or deceleration, the inverse of H_0 sets the time when they must have all been lumped together. The value of H_0 also plays a role in the growth of galaxies, the production of light elements and the timing of the phases of cosmic evolution. It should therefore come as no surprise that accurately measuring the Hubble constant was a major goal for the eponymous space telescope from the outset.

In practice, finding the value meant ascertaining the distance to nearby galaxies, a notoriously difficult task that produced more than its share of controversy in the 20th century. The telescope did the definitive study of Cepheid variables—stars whose distinctive pulsations reveal their intrinsic brightness and hence their distance—in 31 galaxies. The resulting value of H_0 has a precision of about 10 percent. Together with measurements of the cosmic microwave background, the value of the Hubble constant indicates an age of 13.7 billion years for the universe.

PULSATING CEPHEID STARS, like the one shown in this artist's conception, are the gold standard for estimating intergalactic distances.

NASA, ESA, S. BECKWITH *STScI* AND HUBBLE ULTRA DEEP FIELD TEAM (*top*); DON DIXON (*bottom*)



DISTANT SUPERNOVA, discovered by comparing images from different times, helped to reveal a momentous transition from cosmic deceleration to acceleration.

10 The Accelerating Universe

In 1998 two independent teams of astronomers dropped a bombshell: the expansion of the universe is accelerating. Astronomers had generally assumed it must be decelerating, because galaxies attract one another gravitationally and should retard their mutual separation. What propels the acceleration is widely considered to be the biggest mystery in physics today. The working hypothesis is that the universe contains some hitherto unseen constituent known as dark energy. A combination of Hubble, ground-based and microwave-background observations suggests that this dark energy makes up about three quarters of the total energy density of the universe.

The acceleration began about five billion years ago, before which time the expansion had been decelerating. In 2004 Hubble discovered 16 distant supernovae that span this crucial transition. These observations placed more meaningful constraints on theories for what the dark energy could be. The simplest (though, in some ways, most mysterious) possibility is that it is a form of energy embodied in space itself, even when otherwise empty. For the time being, no other instrument is as vital to the hunt for distant supernovae to pin down dark energy. Hubble's role in the study of dark energy is perhaps the single biggest reason that astronomers have been so keen for NASA to keep the telescope going. SA

NASA AND J. BLAKESLEE *Johns Hopkins University*

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2 **Searching for Shadows of Other Earths.** Laurance R. Doyle, Hans-Jörg Deeg and Timothy M. Brown. Vol. 283, No. 3, pages 58–65; September 2000.

3 **The Extraordinary Deaths of Ordinary Stars.** Bruce Balick and Adam Frank. Vol. 291, No. 1, pages 50–59; July 2004.

4 **Fountains of Youth: Early Days in the Life of a Star.** Thomas P. Ray. Vol. 283, No. 2, pages 42–47; August 2000.

6 **The Galactic Odd Couple.** Kimberly Weaver. Vol. 289, No. 1, pages 34–41; July 2003.

7 **The Brightest Explosions in the Universe.** Neil Gehrels, Luigi Piro and Peter J. T. Leonard. Vol. 287, No. 6, pages 84–91; December 2002.

8 **Galaxies in the Young Universe.** F. Duccio Macchetto and Mark Dickinson. Vol. 276, No. 5, pages 92–99; May 1997.

9 **The Expansion Rate and Size of the Universe.** Wendy L. Freedman; Vol. 267, No. 5, pages 54–60; November 1992.

10 **From Slowdown to Speedup.** Adam G. Riess and Michael S. Turner. Vol. 290, No. 2, pages 62–67; February 2004.

Stem Cells: The Real Culprits in Cancer?

By Michael F. Clarke and Michael W. Becker

A dark side of stem cells—their potential to turn malignant—is at the root of a handful of cancers and may be the cause of many more. Eliminating the disease could depend on tracking down and destroying these elusive killer cells

After more than 30 years of declared war on cancer, a few important victories can be claimed, such as 85 percent survival rates for some childhood cancers whose diagnoses once represented a death sentence. In other malignancies, new drugs are able to at least hold the disease at bay, making it a condition with which a patient can live. In 2001, for example, Gleevec was approved for the treatment of chronic myelogenous leukemia (CML). The drug has been a huge clinical success, and many patients are now in remission following treatment with Gleevec. But evidence strongly suggests that these patients are not truly cured, because a reservoir of malignant cells responsible for maintaining the disease has not been eradicated.

Conventional wisdom has long held that any tumor cell remaining in the body could potentially reignite the disease. Current treatments therefore focus on killing the greatest number of cancer cells. Successes with this approach are still very much hit-or-miss, however, and for patients with advanced cases of the most common solid tumor malignancies, the prognosis remains poor.

Moreover, in CML and a few other cancers it is now clear that only a tiny percentage of tumor cells have the power to produce new cancerous tissue and that targeting these specific cells for destruction may be a far more effective way to eliminate the disease. Because they are the engines driving the growth of new cancer cells and are very probably the origin of the malignancy itself, these cells

KENN BROWN

ONE AMONG THOUSANDS of tumor cells may be a cancer stem cell responsible for driving the disease.

are called cancer stem cells. But they are also quite literally believed to have once been normal stem cells or their immature offspring that have undergone a malignant transformation.

This idea—that a small population of malignant stem cells can cause cancer—is far from new. Stem cell research is considered to have begun in earnest with studies during the 1950s and 1960s of solid tumors and blood malignancies. Many basic principles of healthy tissue genesis and development were revealed by these observations of what happens when the normal processes derail.

Today the study of stem cells is shedding light on cancer research. Scientists have filled in considerable detail over the past 50 years about mechanisms regulating the behavior of normal stem cells and the cellular progeny to which they give rise. These fresh insights, in turn, have led to the discovery of similar hierarchies among cancer cells within a tumor, providing strong support for the theory that rogue stemlike cells are at the root of many cancers. Successfully targeting these cancer stem cells for eradication therefore requires a better understanding of how a good stem cell could go bad in the first place.

Stem cells' power to self-renew already exempts them from the rules.

Orderly Conduct

THE HUMAN BODY is a highly compartmentalized system made up of discrete organs and tissues, each performing a function essential to maintaining life. Individual cells that make up these tissues are often short-lived, however. The skin covering your body today is not really the same skin that you had a month ago, because its surface cells have all since sloughed off and been replaced. The lining of the gut turns over every couple of weeks, and the life span of the platelets that help to clot blood is about 10 days.

The mechanism that maintains a constant population of working cells in such tissues is consistent throughout the body and, indeed, is highly conserved among all complex species. It centers on small pools of long-lived stem cells that serve as factories for replenishing supplies of functional cells. This manufacturing process follows tightly regulated and organized steps wherein each generation of a stem cell's offspring becomes increasingly specialized.

This system is perhaps best exemplified by the hematopoietic family of blood and immune cells. All the functional cells found in the blood and lymph arise from a single common parent known as the hematopoietic stem cell (HSC), which resides in bone marrow. The HSC pool represents less than 0.01 percent of bone marrow cells in adults, yet each of these rare cells gives rise to a larger, intermediately differentiated population of progenitor cells. Those in turn divide and differentiate further through several stages into mature cells responsible for specific tasks, ranging from defending against infection to carrying oxygen to tissues [*see box on opposite page*]. By the time a cell reaches that final functional stage, it has lost all ability to proliferate or to alter its destiny and is said to be terminally differentiated.

The stem cells themselves meanwhile remain undifferentiated, a state they maintain through their unique capacity for self-renewal: to begin producing new tissues, a stem cell divides in two, but only one of the resulting daughter cells might proceed down a path toward increasing specificity. The other daughter may instead retain the stem cell identity. Numbers in the overall stem cell pool can thus remain constant, whereas the proliferation of intermediate progenitors allows populations of specific hematopoietic cell types to expand rapidly in response to changing needs.

The capacity of stem cells to re-create themselves through self-renewal is their most important defining property. It gives them alone the potential for unlimited life span and future proliferation. In contrast, progenitors have some ability to renew themselves during proliferation, but they are restricted by an internal counting mechanism to a finite number of cell divisions. With increasing differentiation, the ability of the progenitors' offspring to multiply declines steadily.

The practical significance of these distinctions can be observed when hematopoietic stem cells or their descendants are transplanted. After the bone marrow of a mouse is irradiated to destroy the native hematopoietic system, progenitor cells delivered into the marrow environment can proliferate and restore hematopoiesis temporarily, but after four to eight weeks those cells will die out. A single transplanted hematopoietic stem cell, on the other hand, can restore the entire blood system for the lifetime of the animal.

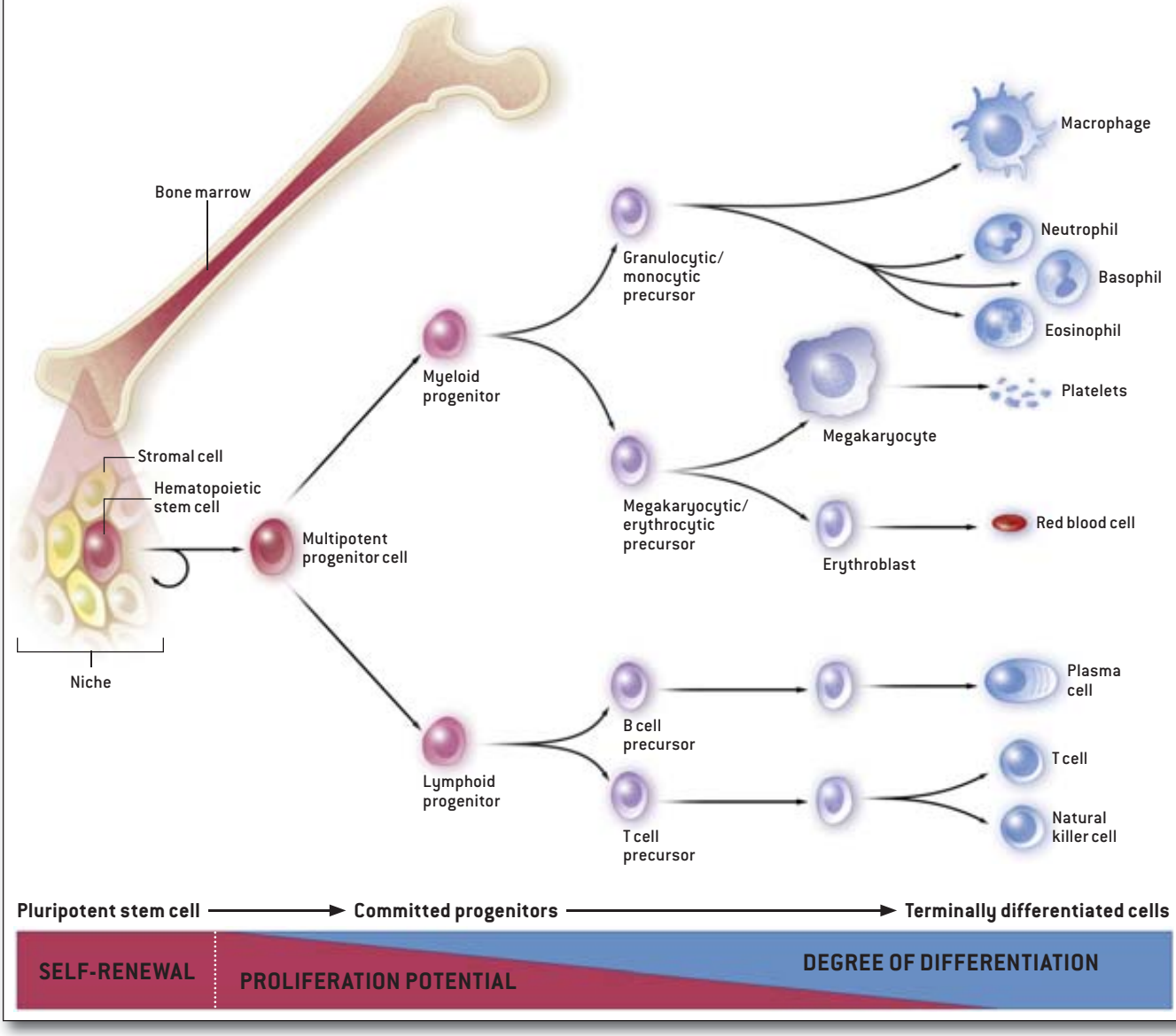
The hematopoietic system's organization has been well understood for more than 30 years, but similar cellular hierarchies have recently been identified in other human tissues, including brain, breast, prostate, large and small intestines,

Overview/*Cancer Stem Cells*

- Cancer cells are often perceived as all having the same potential to proliferate and expand the disease, but in many types of cancer only a small subset of tumor cells has that power.
- The tumor-generating cells share key traits with stem cells, including an unlimited life span and the ability to generate a diverse range of other cell types, and are therefore considered cancer stem cells.
- These malignant progenitors are believed to spring from regulatory failures in damaged stem cells or their immediate offspring.
- Cancer treatments must target cancer stem cells to eradicate the disease.

HIERARCHY IN BLOOD-FORMING CELLS

Stem cells in the blood-forming, or hematopoietic, system illustrate principles governing the activity of stem cells in other tissues as well. A small population of hematopoietic stem cells (HSC) in the bone marrow is the source of most of the different blood and immune cell types that circulate in the human body. HSCs reside in an environmental niche, surrounded by stromal cells that provide important regulatory signals to the stem cell. When new blood or immune cells are needed, an HSC divides to produce one daughter cell that remains in the niche and retains the long-term HSC identity and another short-lived daughter termed a multipotent progenitor cell (MPP). The MPP, in turn, divides to produce progenitors committed to generating cells in the myeloid (blood) or lymphoid (immune) lineages. As the descendants of progenitors become increasingly specialized they experience a programmed decline in their ability to proliferate until they stop dividing and are said to be terminally differentiated. Only the stem cell retains unlimited proliferative potential through its ability to renew itself indefinitely by dividing without differentiating.



and skin. Principles of regulated stem cell behavior are also shared across these tissues, including specific mechanisms for controlling stem cell numbers and for directing decisions about the fates of individual cells. Several genes and the cascades of events triggered by their activity—known as genetic pathways—play key roles in dictating stem cells' fate and function, for example. Among these are signaling pathways headed by the *Bmi-1*, *Notch*, *Sonic hedgehog* and *Wnt* genes. Yet most of these genes were first identified not by scientists studying stem cells but by cancer researchers, because their pathways are also involved in the development of malignancies.

Many such similarities between stem cells and cancer cells

TAMI TOLPA

have been noted. The classical definition of malignancy itself includes cancer cells' apparent capacity to survive and multiply indefinitely, their ability to invade neighboring tissues and to migrate (metastasize) to distant sites in the body. In effect, the usual constraints that tightly control cellular proliferation and identity seem to have been lifted from cancer cells.

Normal stem cells' power to self-renew already exempts them from the rules limiting life span and proliferation for most cells. Stem cells' ability to differentiate into a broad range of cell types allows them to form all the different elements of an organ or tissue system. A hallmark of tumors, too, is the heterogeneity of cell types they contain, as though the tumor were a very disorderly version of a whole organ. Hematopoietic stem cells have been shown to migrate to distant parts of the body in response to injury signals, as have cancer cells.

In healthy stem cells, strict genetic regulation keeps their potential for unlimited growth and diversification in check. Remove those control mechanisms, and the result would be something that sounds very much like malignancy. These commonalities, along with growing experimental evidence, suggest that failures in stem cell regulation are how many cancers get started, how they perpetuate themselves, and possibly how malignancies can spread.

Several possible paths to malignancy become apparent.

Achilles' Heel

THE PRESENCE OF STEM CELLS in certain tissues, especially those with high cell turnover such as the gut and the skin, seems to be an overly complicated and inefficient system for replacing damaged or old cells. Would it not appear to make more sense for an organism if every cell could simply proliferate as needed to supply replacements for its injured neighbors? On the surface, perhaps—but that would make every cell in the body a potential cancer cell.

Malignancies are believed to arise when an accumulation of "oncogenic" changes to key genes within a cell leads to the abnormal growth and transformation of that cell. Gene mutations typically happen through a direct insult, such as the cell being exposed to radiation or chemicals, or simply through random error when the gene is improperly copied before cell division. Because the rare stem cells are the only long-lived cells in the organs where most cancers develop, they represent a much smaller potential reservoir for cumulative genetic damage that could eventually lead to cancer. Unfortunately, because stem cells are so long-lived, they also become the most likely repository for such damage.

Indeed, stem cells' longevity would explain why many cancers develop decades after tissues are subjected to radiation—the initial injury may be only the first in a series of mutations required to transform a healthy cell into a malignant one. In addition to accumulating and preserving these oncogenic scars, a stem cell's enormous proliferative capacity makes it an ideal target for malignancy. Because nature so strictly regulates self-renewal, a cell population already possessing that ability would need fewer additional mutations for malignant transformation than would cells lacking that capacity.

With these considerations in mind, several possible paths to malignancy become apparent. In one model, mutations occur in the stem cells themselves, and their resulting loss of control over self-renewal decisions produces a pool of stem cells predisposed to malignancy. Subsequent additional oncogenic events that trigger proliferation of the malignant cells into a tumor might happen in the stem cells or in their descendants, the committed progenitor cell population. A second model holds that oncogenic mutations initially occur in stem cells but that the final steps in transformation to cancer happen only in the committed progenitors. This scenario would require the progenitors' lost self-renewal capacity to be somehow reactivated.

Current evidence supports both models in different cancers. And at least one example exists of both processes playing a role in different stages of the same disease. Chronic myelogenous leukemia is a cancer of the white blood cells caused by the inappropriate fusion of two genes. Insertion of the resulting fused gene will transform a normal hematopoietic stem cell into a leukemia stem cell. Untreated, CML invariably progresses to an acute form known as CML blast crisis. Catriona Jamieson and Irving Weissman, both then at the Stanford University School of Medicine, demonstrated that in patients who progressed to CML blast crisis, the specific additional genetic events responsible for this more virulent version of the disease had conferred the ability to self-renew on certain progenitor cells.

Steady Pursuit

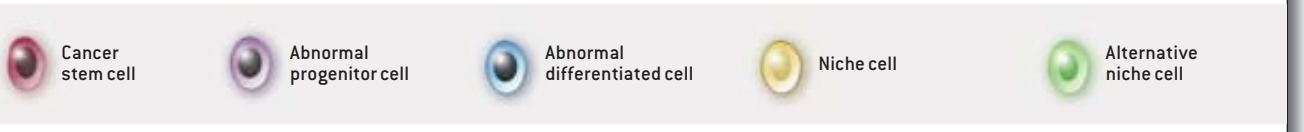
OVER THE PAST DECADE, evidence that stem cells could become malignant and that only certain cancer cells shared a variety of traits with stem cells strengthened the idea that the driving force underlying tumor growth might be a subpopula-

THE AUTHORS

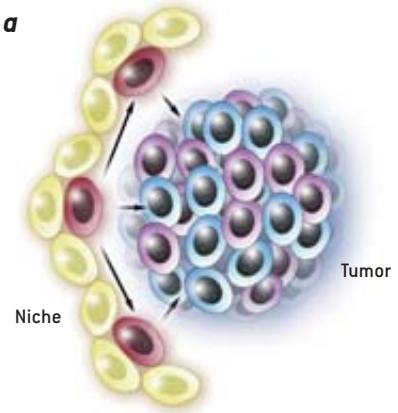
MICHAEL F. CLARKE and *MICHAEL W. BECKER* worked together in Clarke's laboratory at the University of Michigan at Ann Arbor, where breast tumor stem cells were first isolated in 2003. Clarke is now associate director, as well as professor of cancer biology and of medicine, at the Stanford Institute for Stem Cell Biology and Regenerative Medicine. He continues to work on identifying cancer stem cells and the mechanisms by which they, as well as normal stem cells, regenerate. Becker is assistant professor of medicine in the hematology and oncology division of the University of Rochester Medical Center. Becker's research focus is characterizing leukemic stem cells, and his clinical work centers on peripheral blood and bone marrow transplantation.

POSSIBLE PATHS TO CANCER

The existence of cancer stem cells that drive tumor growth has been established in several blood cancers and a handful of solid tumor types, but how these malignant stem cells arise is still uncertain. Like a normal stem cell, a cancer stem cell has the ability to self-renew by dividing without differentiating and can therefore potentially give rise to an unlimited number of the abnormal differentiated cells that make up the bulk of a tumor. Those progeny have a finite life span and are not themselves tumorigenic—that is, they cannot generate new cancer cells. The behavior of normal stem cells is tightly controlled by their own genetic programming in concert with signals they receive from their environmental niche. Changes in the way cancer stem cells carrying oncogenic gene mutations respond to niche signaling may therefore play an important role in the cells' final transition to malignancy (*a, b* and *c*). Alternatively, mutations in the stem cell might be preserved in its immature descendants, the progenitor cells, which subsequently undergo further mutations that reactivate the self-renewal capacity normally possessed only by stem cells (*d*). Evidence of all these possibilities has been observed in different cancers.

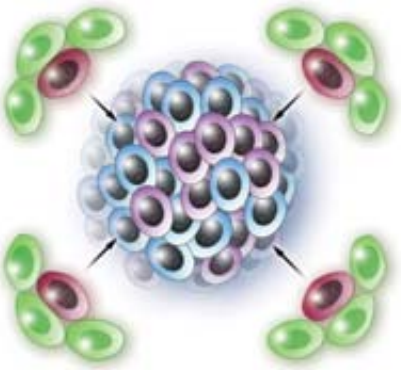


a



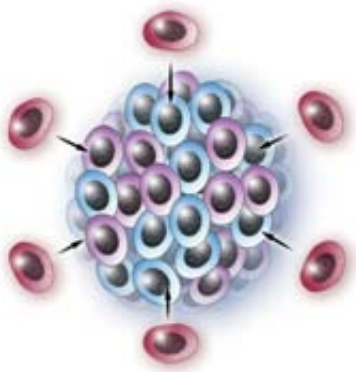
EXPANDED NICHE. Cancer stem cells with oncogenic mutations are held in check by healthy niche signals until a further alteration in the cancer stem cells or in the niche causes the niche to expand. The larger niche allows the malignant stem cells to increase their own population and consequently the number of abnormal cells they generate.

b



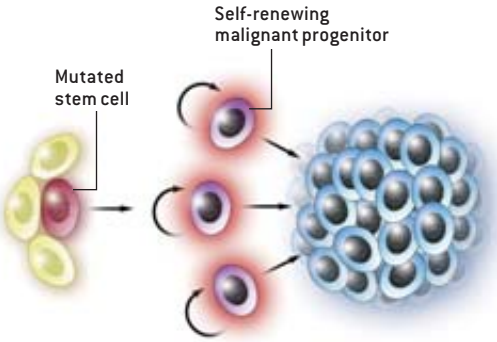
ALTERNATIVE NICHE. Oncogenic mutations in cancer stem cells include changes that enable the cells to adapt to a new niche. The cancer stem cells can expand their own numbers and proliferation and possibly invade neighboring tissues or metastasize to distant locations in the body.

c



NICHE INDEPENDENCE. Mutation renders stem cells that are already predisposed to malignancy independent of niche signaling, lifting all normal environmental controls on the cancer stem cells' self-renewal and proliferation.

d



SELF-RENEWAL MUTATION. Progenitor cells predisposed to malignancy by oncogenic mutations inherited from their parent stem cell undergo further mutation that restores the ability to self-renew. These progenitors thereby gain unlimited life span and tumorigenic capacity and become cancer stem cells.

TAMI TOLPA

Cornering Cancer Stem Cells

Techniques for sorting live cancer cells and for determining whether they possess the ability to self-renew have led to the positive identification of cancer stem cells within larger cancer cell populations. In the cancers listed below, the malignant stem cells have been demonstrated capable of self-renewal and able to regenerate the entire mixture of cell types found in the original tumor. Those properties mean that a small number of cancer stem cells could have given rise to the whole tumor, could continually replenish its much larger cell population—the majority of which is nontumorigenic—and could reconstitute the original cancer even if most or all of the tumor were destroyed. Eradicating the disease would therefore require treatments to target the cancer stem cells successfully.

CANCER TYPE (year cancer stem cells identified)
Acute myeloid leukemia (1994)
Acute lymphoblastic leukemia (1997)
Chronic myelogenous leukemia (1999)
Breast (2003)
Multiple myeloma (2003)
Brain (2004)
Prostate (2005)

tion of stemlike cancer cells. The theory has a longer history, but in the past the technology to prove it was lacking.

By the 1960s a few scientists were already beginning to note that groups of cells within the same tumor differed in their ability to produce new tumor tissue. In 1971 C. H. Park and his colleagues at the University of Toronto showed that within a culture of cells taken from an original, or "primary," myeloma (a cancer affecting plasma cells in bone marrow), the cells displayed significant differences in their ability to proliferate. At the time, Park's group could not interpret this phenomenon decisively, because at least two explanations were possible: all the cells might have had the ability to multiply in culture but by chance only some of them did, or else a hierarchy of cells was present in the tumor and cancer stem cells were giving rise to cells that were nontumorigenic, or incapable of proliferation.

Philip J. Fialkow of the University of Washington had already demonstrated in 1967 that the stem cell model was probably the correct one for leukemia. Using a cell-surface protein marker called G-6-PD, which can identify a cell's lineage, Fialkow showed that in some women with leukemia, both the tumorigenic cells as well as their more differentiated nontumorigenic progeny had all arisen from the same parent cell.

These early studies were critical in the development of the stem cell model for cancer, but they were still limited by researchers' inability to isolate and examine different cell populations within a tumor. A key event in stem cell biology, therefore, was the commercial availability, beginning in the 1970s, of an instrument called a flow cytometer, which can automatically sort different living cell populations based on the unique surface markers they bear.

A second crucial event in the evolution of cancer stem cell studies was the advent during the 1990s of conclusive tests for self-renewal. Assays to establish self-renewal in human cells did not exist until Weissman of Stanford and John E. Dick of the University of Toronto developed methods that allowed normal human stem cells to grow in mice. Using flow cytometry and this new mouse model, Dick began in 1994 to publish a series of seminal reports identifying cancer stem cells in leukemia. In 2003 Richard Jones of Johns Hopkins University identified a cancer stem cell population in multiple myeloma.

Earlier the same year our own laboratory group at the University of Michigan at Ann Arbor had published the first evidence of cancer stem cells in solid tumors. By transplanting sorted populations of cells from human breast tumors into mice, we were able to confirm that not all human breast cancer cells have the same capacity to generate new tumor tissue. Only one subpopulation of the cells was able to re-create the original tumor in the new environment. We then compared the phenotype, or physical traits, of those new tumors with that of the patient samples and found that the profile of the new tumors recapitulated the original. This finding indicated that the transplanted tumorigenic cells could both self-renew and give rise to all the different cell populations present in the original tumor, including the nontumorigenic cells.

Our study attested to the presence of a hierarchy of cells within a breast cancer similar to those identified in blood malignancies. Since then, the investigation of cancer stem cell biology has exploded, as labs across the world continue to find similar subpopulations of tumorigenic cells in other forms of cancer. In 2004, for example, the laboratory of Peter Dirks of the University of Toronto identified cells from primary human central nervous system tumors with the capacity to regenerate the entire tumor in mice. In addition, he found a high number of the purported cancer stem cells present in one of the fastest-growing forms of human brain cancer, medulloblastoma, compared with far fewer tumorigenic cells found in less aggressive brain tumor types.

A related area of recent intensive investigation is also providing support for the cancer stem cell model. The signaling environment, or niche, in which tumors reside appears to strongly influence the initiation and maintenance of malignancy. Studies of normal body cells as well as of stem cells have already established the essential role of signals emanating from surrounding tissue and the supportive extracellular matrix in sustaining a given cell's identity and in directing its behavior. Normal cells removed from their usual context in the body and placed in a dish have a tendency to lose some of their differentiated functional characteristics, for example. Stem cells, in contrast, must be cultured on a medium that provides signals telling them to remain undifferentiated, or they will quickly begin proliferating and differentiating—seemingly as though that is their default programmed behavior, and only the niche signals hold it in check.

In the body, stem cell niches are literal enclaves surrounded by specific cell types, such as stromal cells that form connective tissue in the bone marrow. With a few exceptions, stem cells always remain in their niche and are sometimes physically attached to it by adhesion molecules. Progenitor cells, on the other hand, move away from the niche, often under escort by guardian cells, as they become increasingly differentiated.

The importance of niche signaling in maintaining stem cells' undifferentiated state and in keeping them quiescent until they are called on to produce new cells suggests that these local environmental signals could exert similar regulatory control over cancer stem cells. Intriguing experiments have shown, for example, that when transplanted into a new niche, stem cells predisposed to malignancy because of oncogenic mutations will nonetheless fail to produce a tumor. Conversely, normal stem cells transplanted into a tissue environment that has been previously damaged by radiation do give rise to tumors.

Many of the same genetic pathways identified with signaling between stem cells and their niche have been associated with cancer, which also suggests a role for the niche in the final transition to malignancy. For example, if malignant stem cells were being held in check by the niche but the niche was somehow altered and expanded, the malignant stem cell pool would have room to grow as well. Another possibility is that certain oncogenic mutations within cancer stem cells could permit them to adapt to a different niche, again letting them increase their numbers and expand their territory. Still a third alternative is that mutations might allow the cancer stem cells to become independent of niche signals altogether, lifting environmental controls on both self-renewal and proliferation.

Closing In

THE IMPLICATIONS of a stem cell model of cancer for the way we understand as well as treat malignancies are clear and dramatic. Current therapies take aim against all tumor cells, but our studies and others have shown that only a minor fraction of cancer cells have the ability to reconstitute and perpetuate the malignancy. If traditional therapies shrink a tumor but miss these cells, the cancer is likely to return. Treatments that specifically target the cancer stem cells could destroy the engine driving the disease, leaving any remaining nontumorigenic cells to eventually die off on their own.

Circumstantial evidence supporting this approach already exists in medical practice. Following chemotherapy for testicular cancer, for example, a patient's tumor is examined to assess the effects of treatment. If the tumor contains only mature cells, the cancer usually does not recur and no further treatment is necessary. But if a large number of immature-looking—that is, not fully differentiated—cells are present in the tumor sample, the cancer is likely to return, and standard protocol calls for further chemotherapy. Whether those immature cells are recent offspring that indicate the presence of cancer stem cells remains to be proved, but their association with the disease prognosis is compelling.

Stem cells cannot be identified based solely on their appearance, however, so developing a better understanding of the unique properties of cancer stem cells will first require improved techniques for isolating and studying these rare cells. Once we learn their distinguishing characteristics, we can use that information to target cancer stem cells with tailored treatments. If scientists were to discover the mutation or environmental cue responsible for conferring the ability to self-renew on a particular type of cancer stem cell, for instance, that would be an obvious target for disabling those tumorigenic cells.

Destroy the engine driving the disease, leaving nontumorigenic cells to die off.

Encouraging examples of this strategy's promise have been demonstrated by Craig T. Jordan and Monica L. Guzman of the University of Rochester. In 2002 they identified unique molecular features of malignant stem cells believed to cause acute myeloid leukemia (AML) and showed that the cancer stem cells could be preferentially targeted by specific drugs. Last year they reported their discovery that a compound derived from the feverfew plant induces AML stem cells to commit suicide while leaving normal stem cells unaffected.

Some research groups are hoping to train immune cells to recognize and go after cancer stem cells. Still others are exploring the use of existing drugs to alter niche signaling in the hope of depriving cancer stem cells of the environmental cues that help them thrive. Yet another idea under investigation is that drugs could be developed to force cancer stem cells to differentiate, which should take away their ability to self-renew.

Most important is that cancer investigators are now on the suspects' trail. With a combination of approaches, aimed at both targeting genetic pathways unique to the maintenance of cancer stem cells and disrupting the cross talk between tumor cells and their environment, we hope to be able soon to find and arrest the real culprits in cancer. SA

MORE TO EXPLORE

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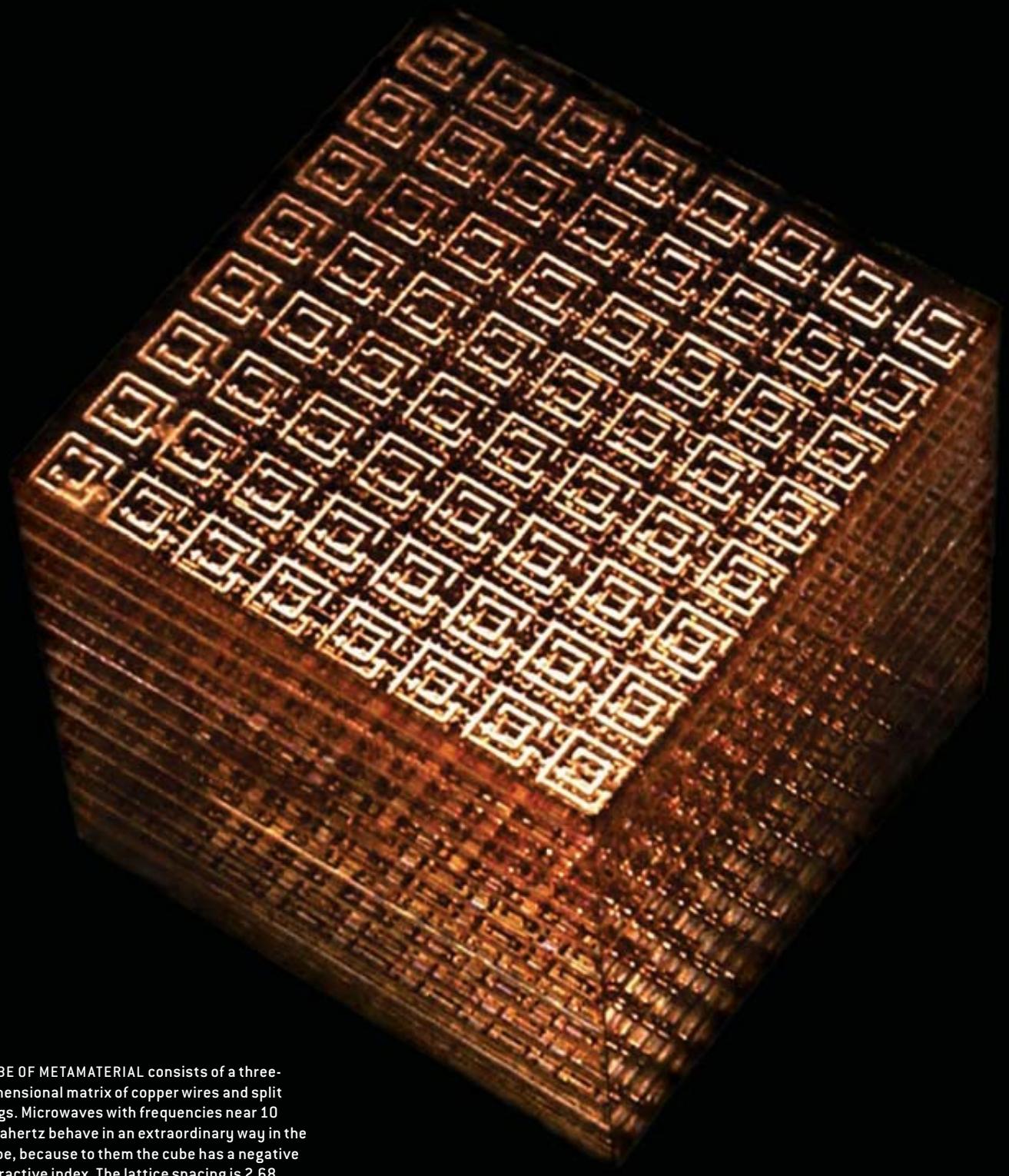
THE QUEST FOR THE



CUBE OF METAMATERIAL consists of a three-dimensional matrix of copper wires and split rings. Microwaves with frequencies near 10 gigahertz behave in an extraordinary way in the cube, because to them the cube has a negative refractive index. The lattice spacing is 2.68 millimeters, or about one tenth of an inch.

Superlens

Built from "metamaterials" with bizarre, controversial optical properties, a superlens could produce images that include details finer than the wavelength of light that is used

By John B. Pendry and David R. Smith

Almost 40 years ago Russian scientist Victor Veselago had an idea for a material that could turn the world of optics on its head. It could make light waves appear to flow *backward* and behave in many other counterintuitive ways. A totally new kind of lens made of the material would have almost magical attributes that would let it outperform any previously known. The catch: the material had to have a negative index of refraction ("refraction" describes how much a wave will change direction as it enters or leaves the material). All known materials had a positive value. After years of searching, Veselago failed to find anything having the electromagnetic properties he sought, and his conjecture faded into obscurity.

A startling advance recently resurrected Veselago's notion. In most materials, the electromagnetic properties arise directly from the characteristics of constituent atoms and molecules. Because these constituents have a limited range of characteristics, the millions of materials that we know of display only a limited palette of electromagnetic properties. But in the mid-1990s one of us (Pendry), in collaboration with scientists at Marconi Materials

Technology in England, realized that a "material" does not have to be a slab of one substance. Rather it could gain its electromagnetic properties from tiny structures, which collectively create effects that are otherwise impossible.

The Marconi team began making these so-called metamaterials and demonstrated several that scattered electromagnetic waves unlike any known materials. In 2000 one of us (Smith), along with colleagues at the University of California, San Diego, found a combination of metamaterials that provided the elusive property of negative refraction.

Light in negative-index materials behaves in such strange ways that theorists have essentially rewritten the book on electromagnetics—a process that has included some heated debate questioning the very existence of such materials. Experimenters, meanwhile, are working on developing technologies that use the weird properties of metamaterials: a superlens, for example, that allows imaging of details finer than the wavelength of light used, which might enable optical lithography of microcircuitry well into the nanoscale and the storage of vastly more data on optical disks. Much remains to be done to turn such visions into reality, but now that Veselago's dream has been conclusively realized, progress is rapid.

Negative Refraction

TO UNDERSTAND HOW negative refraction can arise, one must know how materials affect electromagnetic waves. When an electromagnetic wave (such as a ray of light) travels through a material, the electrons within the material's atoms or molecules feel a force and move in response. This motion uses up some of the wave's energy, affecting the properties of the wave and how it travels. By adjusting the chemical composition of a material, scientists can fine-tune its wave-propagation characteristics for a specific application.

But as metamaterials show, chemistry is not the only path to developing materials with an interesting electromagnetic response. We can also engineer electromagnetic response by creating tiny but macroscopic structures. This possibility arises because the wavelength of a typical electromagnetic wave—the characteristic distance over which it varies—is orders of magnitude larger than the atoms or molecules that make up a material. The wave does not "see" an individual molecule but rather the collective response of millions of molecules. In a metamaterial, the patterned elements are considerably smaller than the wavelength and are thus not seen individually by the electromagnetic wave.

As their name suggests, electromagnetic waves contain both an electric field and a magnetic field. Each component induces a characteristic motion of the electrons in a material—back and forth in response to the electric field and around in circles in response to the magnetic field. Two parameters quantify the extent of these responses in a material: electrical permittivity, ε, or how much its electrons respond to an electric field, and magnetic permeability, μ, the electrons' degree of response to a magnetic field. Most materials have positive ε and μ.

Another important indicator of the optical response of a material is its refractive index, n. The refractive index is simply related to ε and μ: $n = \pm\sqrt{\varepsilon\mu}$. In every known material, the positive value must be chosen for the square root; hence, the refractive index is positive. In 1968 Veselago showed, however, that if ε and μ are both negative, then n must also take the negative sign. Thus, a material with both ε and μ negative is a negative-index material.

A negative ε or μ implies that the electrons within the material move in the opposite direction to the force applied by the electric and magnetic fields. Although this behavior might seem paradoxical, it is actually quite a simple matter to make electrons oppose the "push" of the applied electric and magnetic fields.

Think of a swing: apply a slow, steady push, and the swing obediently moves in the direction of the push—although it does not swing very high. Once set in motion, the swing tends to oscillate back and forth at a particular rate, known technically as its resonant frequency. Push the swing periodically, in time with this swinging, and it starts arcing higher. Now try to push at a faster rate, and the push goes out of phase with respect to the motion of the swing—at some point, your arms might be outstretched with the swing rushing back. If you have been pushing for a while, the swing might have enough momentum to knock you over—it is then pushing back on you. In the same way, electrons in a material with a negative index of refraction go out of phase and resist the "push" of the electromagnetic field.

Metamaterials

RESONANCE, the tendency to oscillate at a particular frequency, is the key to achieving this kind of negative response and is introduced artificially in a metamaterial by building small circuits designed to mimic the magnetic or electrical response of a material. In a split-ring resonator (SRR), for example, a magnetic flux penetrating the metal rings induces rotating currents in the rings, analogous to magnetism in materials

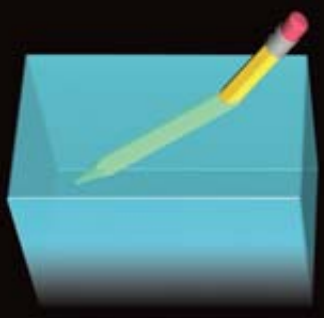
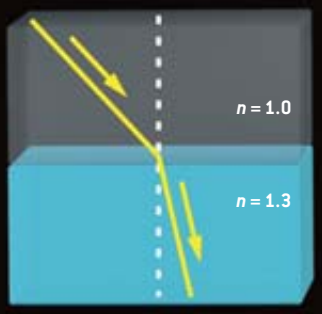
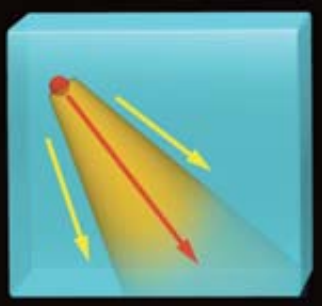
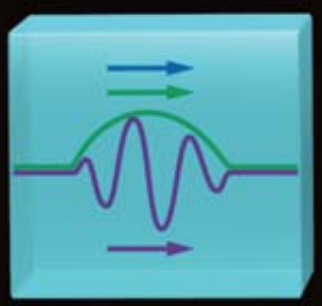
Overview/*Metamaterials*

- Materials made out of carefully fashioned microscopic structures can have electromagnetic properties unlike any naturally occurring substance. In particular, these metamaterials can have a negative index of refraction, which means they refract light in a totally new way.
- A slab of negative-index material could act as a superlens, able to outperform today's lenses, which have a positive index. Such a superlens could create images that include detail finer than that allowed by the diffraction limit, which constrains the performance of all positive-index optical elements.
- Although most experiments with metamaterials are performed with microwaves, they might use shorter infrared and optical wavelengths in the future.

MINAS H. TANIELIAN *Boeing Phantom Works* (*page 60*)

NEGATIVE-INDEX WEIRDNESS

In a medium with a negative index of refraction, light (and all other electromagnetic radiation) behaves differently than in conventional positive-index materials in a number of counterintuitive ways.

POSITIVE-INDEX MEDIUM		NEGATIVE-INDEX MEDIUM
A pencil in water appears bent because of the water's higher refractive index.		A pencil embedded in a negative-index medium would appear to bend all the way out of the medium.
When light travels from a medium with low refractive index (*n*) to one with higher refractive index, it bends toward the normal (*dashed line at right angles to surface*).		When light travels from a positive-index medium to one with a negative index, it bends all the way back to the same side of the normal.
A receding object appears redder because of the Doppler effect.		A receding object appears bluer.
A charged object (*red*) traveling faster than the speed of light generates a cone of Cherenkov radiation (*yellow*) in the forward direction.		The cone points backward.
In a positive-index medium, the individual ripples of an electromagnetic pulse (*purple*) travel in the same direction as the overall pulse shape (*green*) and the energy (*blue*).		The individual ripples travel in the opposite direction to the pulse shape and the energy.

MELISSA THOMAS

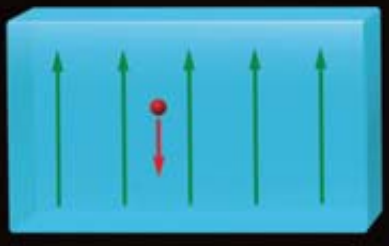
[*see box below*]. In a lattice of straight metal wires, in contrast, an electric field induces back-and-forth currents.

Left to themselves, the electrons in these circuits naturally swing to and fro at the resonant frequency determined by the circuits' structure and dimensions. Apply a field below this frequency, and a normal positive response results. Just above the resonant frequency, however, the response is negative—just as the swing pushed back when pushed faster than its frequency. Wires can thus provide an electric response with negative ε over some range of frequencies, whereas split rings can provide a magnetic response with negative μ over the same frequency band. These wires and split rings are just the building blocks needed to make a wide assortment of interesting metamaterials, including Veselago's long-sought material.

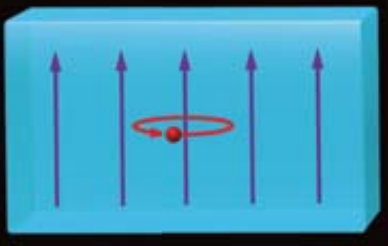
ENGINEERING A RESPONSE

The key to producing a metamaterial is to create an artificial response to electric and magnetic fields.

IN AN ORDINARY MATERIAL



An electric field (*green*) induces linear motion of electrons (*red*).



A magnetic field (*purple*) induces circular motion of electrons.

IN A METAMATERIAL

Linear currents (*red arrows*) flow in arrays of wires.

Circular currents flow in split-ring resonators (SRRs).

METAMATERIAL STRUCTURE

A metamaterial is made by creating an array of wires and SRRs that are smaller than the wavelength of the electromagnetic waves to be used with the material.

The first experimental evidence that a negative-index material could be achieved came from the experiments by the U.C.S.D. group in 2000. Because the most stringent requirement for a metamaterial is that the elements be significantly smaller than the wavelength, the group used microwaves. Microwaves have wavelengths of several centimeters, so that the metamaterial elements could be several millimeters in size—a convenient scale.

The team designed a metamaterial that had wires and SRRs interlaced together and assembled it into a prism shape. The wires provided negative ε, and SRRs provided negative μ: the two together should, they reasoned, yield a negative refractive index. For comparison, they also fashioned an identically shaped prism out of Teflon, a substance having a positive index with a value of $n = 1.4$. The researchers directed a beam of microwaves onto the face of the prism and detected the amount of microwaves emerging at various angles. As expected, the microwave beam underwent positive refraction from the Teflon prism but was negatively refracted by the metamaterial prism. Veselago's speculation was now reality; a negative-index material had finally been achieved.

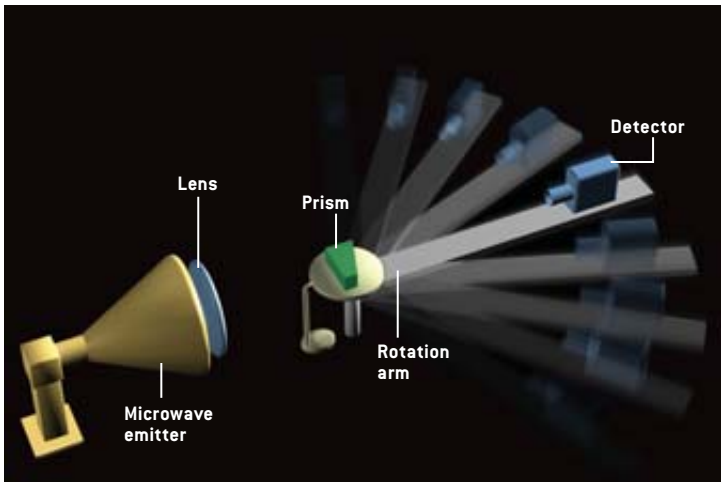
Or had it?

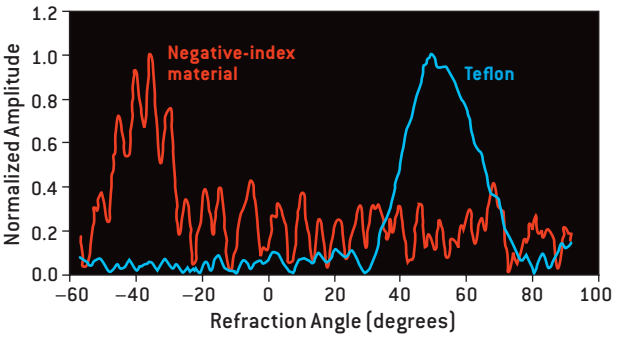
Does It Really Work?

THE U.C.S.D. EXPERIMENTS, along with remarkable new predictions that physicists were making about negative-index materials, created a surge of interest from other researchers. In the absence of metamaterials at the time of Veselago's hypothesis, the scientific community had not closely scrutinized the concept of negative refraction. Now with the potential of metamaterials to realize the madcap ideas implied by this theory, people paid more attention. Skeptics began asking whether negative-index materials violated the fundamental laws of physics. If so, the entire program of research could be invalidated.

One of the fiercest discussions centered on our understanding of a wave's velocity in a complicated material. Light travels in a vacuum at its maximum

MELISSA THOMAS





EXPERIMENT CARRIED OUT at Boeing Phantom Works in Seattle using first a metamaterial prism and then a Teflon (positive-index) prism confirmed the phenomenon of negative refraction. The Teflon refracted microwaves by a positive angle (*blue line*); the metamaterial by a negative angle (*red line*).

speed of 300,000 kilometers per second. This speed is given the symbol c. The speed of light in a material, however, is reduced by a factor of the refractive index—that is, the velocity $v = c/n$. But what if n is negative? The simple interpretation of the formula for the speed of light suggests that the light propagates backward.

A more complete answer takes cognizance that a wave has two velocities, known as the phase velocity and the group velocity. To understand these two velocities, imagine a pulse of light traveling through a medium. The pulse will look something like the one shown in the last illustration in the box on page 63: the ripples of the wave increase to a maximum at the center of the pulse and then die out again. The phase velocity is the speed of the individual ripples. The group velocity is the speed at which the pulse shape travels along. These velocities need not be the same.

In a negative-index material, as Veselago had discovered, the group and phase velocities are in opposite directions. Surprisingly, the individual ripples of the pulse travel backward even as the entire pulse shape travels forward. This fact also has amazing consequences for a continuous beam of light, such as one coming from a flashlight wholly immersed in a negative-index material. If you could watch the individual ripples of the light wave, you would see them emerge from the target of the beam, travel backward along the beam and ultimately disappear into the flashlight, as if you were watching a movie running in reverse. Yet the energy of the light beam travels forward, away from the flashlight, just as one expects. That is the direction the beam is actually traveling, the amazing backward motion of the ripples notwithstanding.

In practice, it is not easy to study the individual ripples of a light wave, and the details of a pulse can be quite complicated, so physicists often use a nice trick to illustrate the difference between the phase and group velocities. If we add together two waves of different wavelengths traveling in the same direction, the waves interfere to produce a beat pattern. The beats move at the group velocity.

In applying this concept to the U.C.S.D. refraction experiment in 2002, Prashant M. Valanju and his colleagues at the University of Texas at Austin observed something curious. When two waves of different wavelengths refract at the interface between a negative- and a positive-index material, they refract at slightly different angles. The resulting beat pattern, instead of following the negatively refracting beams, actually appears to exhibit positive refraction. Equating this beat pattern with the group velocity, the Texas researchers concluded that any physically realizable wave would undergo positive refraction. Although a negative-index material could exist, negative refraction was impossible.

Assuming that the Texas physicists' findings were true, how could one explain the results of the U.C.S.D. experiments? Valanju and many other researchers attributed the apparent negative refraction to a variety of other phenomena. Perhaps the sample actually absorbed so much energy that waves could leak out only from the narrow side of the prism, masquerading as negatively refracted waves? After all, the U.C.S.D. sample involved significant absorption, and the measurement had not been taken very far away from the face of the prism, making this absorption theory a possibility.

The conclusions caused great concern, as they might invalidate not only the U.C.S.D. experiments but all the

THE AUTHORS

JOHN B. PENDRY and *DAVID R. SMITH* were members of a team of researchers who shared the 2005 Descartes Research Prize for their contributions to metamaterials. They have collaborated on the development of such materials since 2000, Pendry focusing on the theory and Smith on experimentation. Pendry is professor of physics at Imperial College London, and recently his main interest has been electromagnetic phenomena, along with quantum friction, heat transport between nanostructures, and quantization of thermal conductivity. Smith is professor of electrical and computer engineering at Duke University. He studies electromagnetic-wave propagation in unusual materials and is currently collaborating with several companies to define and develop novel applications for metamaterials and negative-index materials.

MELISSA THOMAS (*left*); MELISSA THOMAS; SOURCE: MINAS H. TANIELIAN *Boeing Phantom Works* (*right*)

phenomena predicted by Veselago as well. After some thought, however, we realized it was wrong to rely on the beat pattern as an indicator of group velocity. We concluded that for two waves traveling in different directions, the resulting interference pattern loses its connection with the group velocity.

As the arguments of the critics began to crumble, further experimental confirmation of negative refraction came. Minas Tanielian's group at Boeing Phantom Works in Seattle repeated the U.C.S.D. experiment with a very low absorption metamaterial prism. The Boeing team also placed the detector much farther from the prism, so that absorption in the metamaterial could be ruled out as the cause of the negatively refracted beam. The exemplary quality of the data from Boeing and other groups finally put an end to any remaining doubts about the existence of negative refraction. We were now free to move forward and exploit the concept, albeit chastened by the subtlety of the new materials.

Beyond Veselago

AFTER THE SMOKE of battle cleared, we began to realize that the remarkable story that Veselago had told was not the final word on how light behaves in negative-index materials. One of his key tools was ray tracing—the process of drawing lines that trace out the path that a ray of light should follow, allowing for reflection and refraction at the interface of different materials.

Ray tracing is a powerful technique and helps us understand, for example, why objects in a swimming pool appear closer to the surface than they actually are and why a half-submerged pencil appears bent. It arises because the refractive index of water (n equals about 1.3) is larger than that of air, and rays of light are bent at the interface between the air and the water. The refractive index is approximately equal to the ratio of the real depth over the apparent depth.

Ray tracing also implies that children swimming in a negative-index pool would appear to float above the surface. (A valuable safety feature!) The entire contents of the pool—and its container—would also appear above the surface.

Veselago used ray tracing to predict that a slab of negatively refracting material, with index $n = -1$, should act as a lens with unprecedented properties. Most of us are familiar with positive-index lenses—in cameras, magnifying glasses, microscopes and telescopes. They have a focal length, and where an image is formed depends on a combination of the focal length and the distance between the object and the lens. Images are typically a different size than the object, and the lenses work best for objects along an axis running through the lens. Veselago's lens works in quite a different fashion from those [*see box below*]: it is much simpler, acting only on objects adjacent to it, and it transfers the entire optical field from one side of the lens to the other.

So unusual is the Veselago lens that Pendry was compelled to ask just how perfectly it could be made to perform. Specifically, what would be the ultimate resolution of the Veselago lens? Positive-index optical elements are constrained by the diffraction limit to resolve details that are about the same size or larger than the wavelength of light reflected from an object. Diffraction places the ultimate limit on all imaging systems, such as the smallest object that might be viewed in a microscope or the closest distance that two stars might be resolved by a telescope. Diffraction also determines the smallest feature that can be created by optical lithography processes in the microchip industry. In a similar manner, diffraction limits the amount of information that can be optically stored on or retrieved from a digital video disk (DVD). A way around the diffraction limit could revolutionize optical technologies, allowing optical lithography well into the nanoscale and perhaps permitting hundreds of times more data to be stored on optical disks.

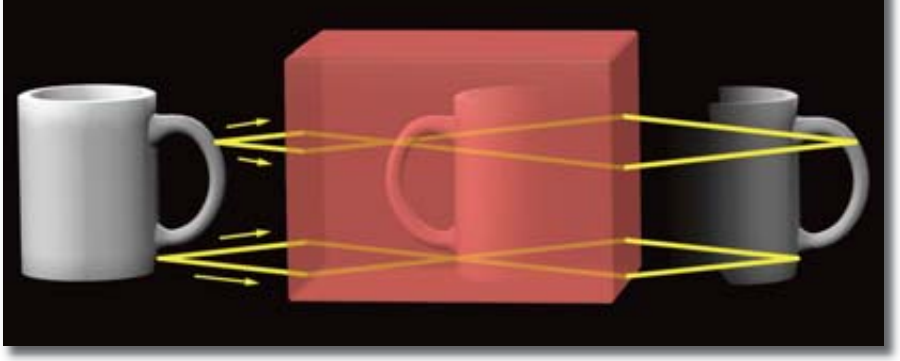
To determine whether or not negative-index optics could surpass the positive version, we needed to move beyond ray tracing. That approach neglects diffraction and thus could not be used to predict the resolution of negative-index lenses. To include diffraction, we had to use a more accurate description of the electromagnetic field.

The Superlens

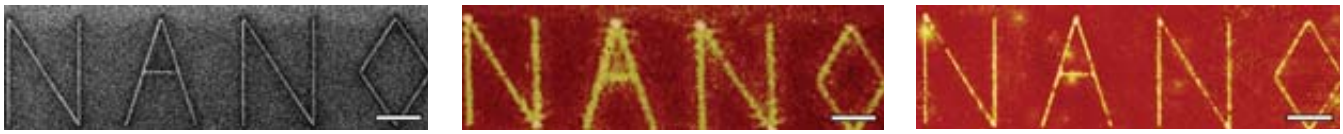
DESCRIBED MORE accurately, all sources of electromagnetic waves—whether radiating atoms, a radio antenna or a beam of light emerging after passing through a small aperture—produce two distinct types of fields: the far field and the near field. As its name implies, the far field is the part that is radiated far from an object and can be captured by a lens to form an image. Unfor-

THE SUPERLENS

A rectangular slab of negative-index material forms a superlens. Light (*yellow lines*) from an object (*at left*) is refracted at the surface of the lens and comes together again to form a reversed image inside the slab. The light is refracted again on leaving the slab, producing a second image (*at right*). For some metamaterials, the image even includes details finer than the wavelength of light used, which is impossible with positive-index lenses.



MELISSA THOMAS



THIN LAYER OF SILVER acts like a superlens over very short distances. Here the word "NANO" is imaged with a focused ion beam (*left*), optically without a superlens (*middle*) and optically with a 35-nanometer layer of silver in place (*right*). Scale bar is 2,000 nanometers long. With the superlens, the resolution is finer than the 365-nanometer wavelength of the light used.

tunately, it contains only a broad-brush picture of the object, with diffraction limiting the resolution to the size of the wavelength. The near field, on the other hand, contains all the finest details of an object, but its intensity drops off rapidly with distance. Positive-index lenses stand no chance of capturing the extremely weak near field and conveying it to the image. The same is not true of negative-index lenses.

By closely examining the manner in which the near and far fields of a source interacted with the Veselago lens, Pendry concluded in 2000—much to everyone's surprise—that the lens could, in principle, refocus both the near and far fields. If this stunning prediction were true, it would mean that the Veselago lens was not subject to the diffraction limit of all other known optics. The planar negative-index slab has consequently been called a superlens.

In subsequent analysis, we and other researchers found that the resolution of the superlens is limited by the quality of its negative-index material. The best performance requires not just that the refractive index $n = -1$, but that both $\varepsilon = -1$ and $\mu = -1$. A lens that falls short of this ideal suffers from drastically degraded resolution. Meeting these conditions simultaneously is a severe requirement. But in 2004 Anthony Grbic and George V. Eleftheriades of the University of Toronto showed experimentally that a metamaterial designed to have $\varepsilon = -1$ and $\mu = -1$ at radio frequencies could indeed resolve objects at a scale smaller than the diffraction limit. Their result proved that a superlens could be built—but could one be built at the still smaller optical wavelengths?

The challenge for scaling metamaterials to optical wavelengths is twofold. First, the metallic conducting elements that form the metamaterial microcircuits, such as wires and SRRs, must be reduced to the nanometer scale so that they are smaller than the wavelength of visible light (400 to 700 nanometers). Second, the short wavelengths correspond to higher frequencies, and metals behave less like conductors at these frequencies, thus damping out the resonances on which metamaterials rely. In 2005 Costas Soukoulis of Iowa State University and Martin Wegener of the University of Karlsruhe in Germany demonstrated experimentally that SRRs can be made that work at wavelengths as small as 1.5 microns. Although the magnetic resonance becomes quite weak at these short wavelengths, interesting metamaterials can still be formed.

But we cannot yet fabricate a material that yields $\mu = -1$ at visible wavelengths. Fortunately, a compromise is possible. When the distance between the object and the image is much smaller than the wavelength, we need only fulfill the condition $\varepsilon = -1$, and then we can disregard μ. Just last year Richard Blaikie's group at the University of Canterbury in New Zealand and Xiang Zhang's group at the University of California, Berkeley, independently followed this prescription and demonstrated superresolution in an optical system. At optical wavelengths, the inherent resonances of a metal can lead to negative permittivity (ε). Thus, a very thin layer of metal can act as a superlens at a wavelength where $\varepsilon = -1$. Both Blaikie and Zhang used a layer of silver about 40 nanometers thick to image 365-nanometer-wavelength light emanating from shaped apertures smaller than the light's wavelength. Although a silver slab is far from the ideal lens, the silver superlens substantially improved the image resolution, proving the underlying principle of superlensing.

Toward the Future

THE DEMONSTRATION of superlensing is just the latest of the many predictions for negative-index materials to be realized—an indication of the rapid progress that has occurred in this emerging field. The prospect of negative refraction has caused physicists to reexamine virtually all of electromagnetics. Once thought to be completely understood, basic optical phenomena—such as refraction and the diffraction limit—now have new twists in the context of negative-index materials.

The hurdle of translating the wizardry of metamaterials and negative-index materials into usable technology remains. That step will involve perfecting the design of metamaterials and manufacturing them to a price. The numerous groups now working in this field are vigorously tackling these challenges. SA

XIANG ZHANG University of California, Berkeley

MORE TO EXPLORE

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What Birds

Evolution has endowed birds with a system of color vision that surpasses that of all mammals, including humans

See

By Timothy H. Goldsmith

MARTIN HARVEY *Peter Arnold, Inc.*

We humans customarily

assume that our visual system sits atop a pinnacle of evolutionary success. It enables us to appreciate space in three dimensions, to detect objects from a distance and to move about safely. We are exquisitely able to recognize other individuals and to read their emotions from mere glimpses of their faces. In fact, we are such visual animals that we have difficulty imagining the sensory worlds of creatures whose capacities extend to other realms—a night-hunting bat, for example, that finds small insects by listening to the echoes of its own high-pitched call.

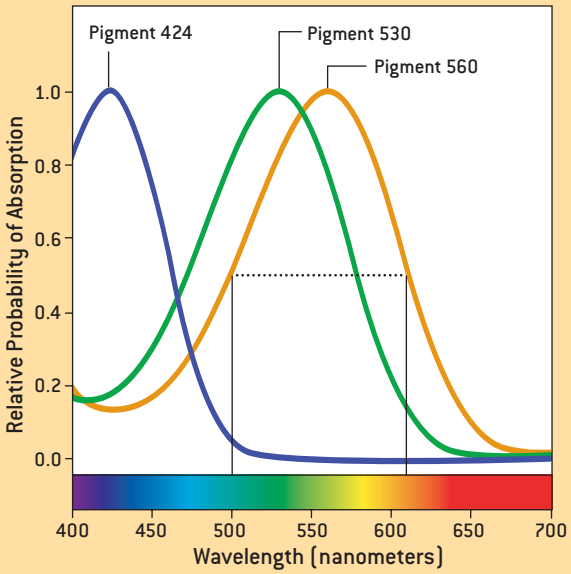
Our knowledge of color vision is, quite naturally, based primarily on what

AFRICAN GROUND HORNBILL (*Bucorvus leadbeateri*), like all birds, sees the world in a rich tapestry of color that we can scarcely imagine. Birds have this capacity because they have retained color-processing cone cells in the eye that mammals lost millions of years ago.

Human Color Vision

Humans and some other primates see the colors that they do as a result of interactions among three types of cone cells in the retina of the eye. Each cone type contains a different pigment that is sensitive to a given range of wavelengths of light. The three types of cones are maximally sensitive at about 560, 530 and 424 nanometers.

The two thin vertical lines in the graph rise from wavelengths that are absorbed equally by pigment 560. Even though photons from rays with a wavelength of 500 nanometers (*in the blue-green*) have more energy than photons from rays having a wavelength of 610 nanometers (*in the orange*), both cause the same response of the pigment and thus cause the same excitation of the cone cell. A single cone cell therefore cannot reveal to the brain the wavelength of the absorbed light. To distinguish one wavelength from another, the brain must compare signals from cones with different visual pigments.



humans see: researchers can easily perform experiments on cooperative human subjects to discover, say, what mixtures of colors look the same or different. Although scientists have obtained supporting information from a variety of other species by recording the firing of neurons, we remained unaware until the early 1970s that many vertebrates, mostly animals other than mammals, see colors in a part of the spectrum that is invisible to humans: the near ultraviolet.

The discovery of ultraviolet vision began with studies of insects—and with the curiosity of a remarkable Englishman, Sir John Lubbock, Lord Avebury. Friend and neighbor of Charles Darwin, member of Parliament, banker, archaeologist and naturalist, Lubbock discovered sometime before 1882 that in the presence of UV light, ants would pick up their pupae and carry them to dark areas or to areas illuminated by longer wavelengths of light. Then, starting in the mid-1900s, Austrian naturalist Karl von Frisch and his students (and their students) showed that bees and ants not only see UV light as a distinct color but use ultraviolet in skylight as part of a celestial compass.

The finding that a great many insects perceive UV light led briefly to the idea that this spectral region provides a private sensory channel that avian predators cannot see. Nothing, however, could have been further from the truth. Work of the past 35 years has shown that birds, lizards, turtles and many fish have UV receptors in their retinas. Why, then, are mammals so different? What caused them to have impoverished color vision? The search for answers has turned up a fascinating evolutionary story and led to fresh insights into the extraordinarily rich visual world of birds.

Overview/*An Evolutionary Tale*

- Color vision of vertebrates depends on cone cells in the retina. It turns out that birds, as well as lizards, turtles and many fish, have four types of cone cells, whereas most mammals have only two types.
- The progenitors of mammals had the full complement of cones, but during a period in their evolution when they were mainly nocturnal—and thus color vision was not crucial to their survival—early mammals lost two types of cone cells.
- The ancestors of a group of Old World primates, which includes humans, "reclaimed" a third cone by means of mutation of one of the existing cones.
- Most mammals, however, still have only two cones, making mammalian color vision—even that of humans and their kin—distinctly limited when compared with the visual world of birds.

How Color Vision Evolved

THE DISCOVERIES are best understood if one first knows some basic details of how any organism perceives color. First, a common misconception must be put to rest. It is true, as many youngsters learn in school, that objects absorb some wavelengths of light and reflect the rest and that the colors we perceive "in" objects relate to the wavelengths of the reflected light. But color is not actually a property of light or of objects that reflect light. It is a sensation that arises within the brain.

Color vision in vertebrates begins with the cone cells in the retina, the layer of nerve cells that transmits visual signals to the brain. Each cone contains a pigment that consists of some variant of the protein opsin, linked to a small molecule called retinal, closely related to vitamin A. When the pigment absorbs light (or, more precisely, absorbs discrete packets of energy called photons), the added energy causes the retinal to

JEN CHRISTIANSEN; SOURCE: TIMOTHY H. GOLDSMITH

change shape, triggering a cascade of molecular events leading to excitation of the cone cell. This excitation in turn leads to activation of retinal neurons, one set of which fires impulses in the optic nerve, conveying information to the brain about the light received.

The more intense a light, the more photons are absorbed by the visual pigments, the greater the excitation of each cone, and the brighter the light appears. But the information conveyed by a single cone is limited: by itself, the cell cannot tell the brain which wavelength of light caused its excitation. Some wavelengths are absorbed better than others, and each visual pigment is characterized by a spectrum that describes how absorption varies with wavelength. A visual pigment may absorb two wavelengths equally, but even though their photons contain different energies, the cone cannot tell them apart, because they both cause the retinal to change shape and thus trigger the same molecular cascade leading to excitation. All a cone can do is count the photons it absorbs; it cannot distinguish one wavelength from another. Hence, a cone can be equally excited by an intense light at a relatively poorly absorbed wavelength and by a dim light at a readily absorbed wavelength.

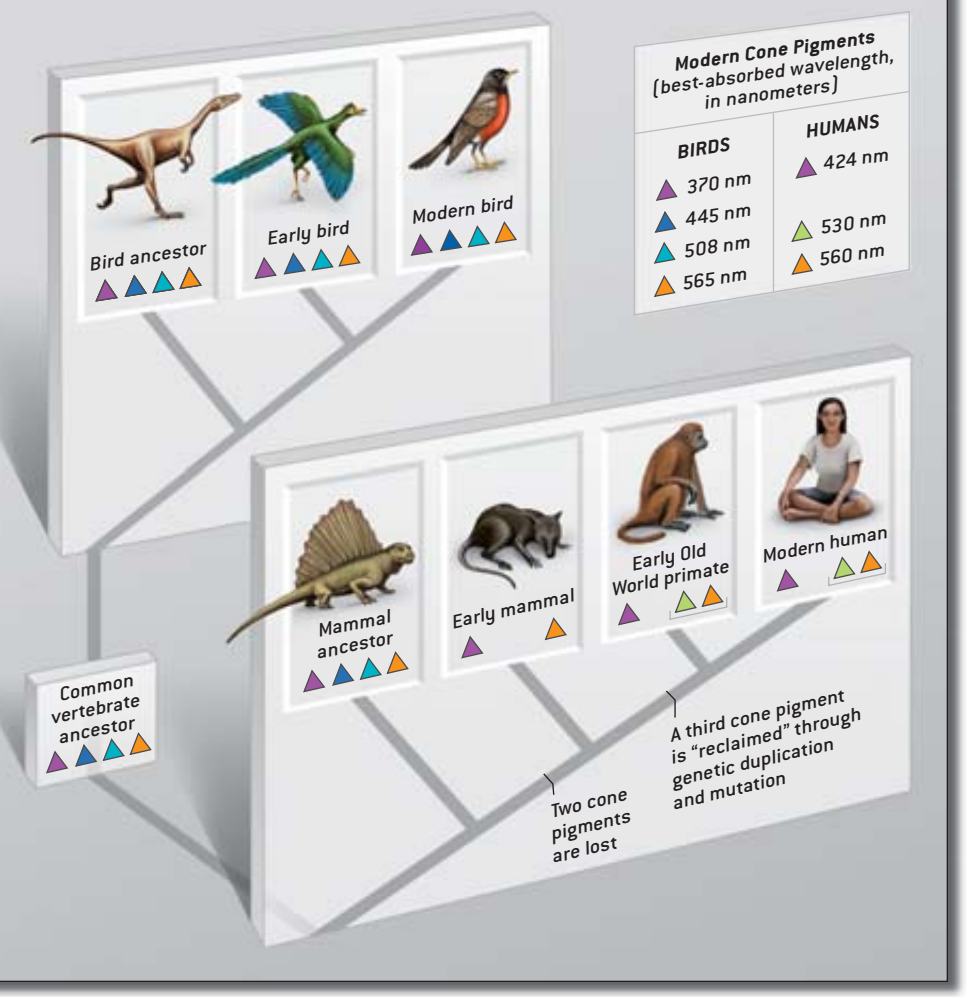
The important conclusion to draw here is that for the brain to see color, it must compare the responses of two or more classes of cones containing different visual pigments. The presence of more than two types of cones in the retina allows an even greater capacity to see different colors.

The opsins that distinguish one cone from another have provided a way to study the evolution of color vision. Researchers can figure out the evolutionary relations of opsins in the various classes of cones and from different species by examining the sequences of nucleotide bases (or DNA "letters") in the genes that code for these proteins. The resulting evolutionary trees reveal that opsins are ancient proteins that existed before the emergence of the predominant groups of animals that populate the earth today. We can trace four lineages of vertebrate cone pigments, named descriptively after the spectral region in which they are most sensitive: long-wavelength, mid-wavelength, short-wavelength and ultraviolet. All major groups of vertebrates have rods in the retina as well as cones. The rods, which contain the visual pigment rhodopsin, provide vision in very dim light. Rhodopsin is similar in both structure and absorption characteristics to the cone pigments most sensitive to

THE AVIAN ADVANTAGE

By analyzing the DNA of contemporary species, scientists have been able to look back in time and determine how cone pigments have changed as vertebrates have evolved. The work indicates that very early vertebrates had four cone types (*colored triangles*), each containing a different pigment. Mammals lost two of these cones during their early evolution, very likely because these animals were nocturnal and cones are not needed for vision in dim light. Birds and most reptiles, in contrast, retained four spectrally different cone pigments.

After the dinosaurs died out, mammals began to diversify, and the lineage that gave rise to the Old World primates of today—African monkeys, apes and humans—"reclaimed" a third cone through duplication and subsequent mutation of the gene for one of the remaining pigments. Because humans evolved from this primate lineage, we are unlike most of our fellow mammals in having three cones (instead of two) and trichromatic color vision—an improvement, but nothing to challenge the more nuanced visual world of birds.



JEN CHRISTIANSEN; SOURCE: TIMOTHY H. GOLDSMITH

wavelengths in the middle of the visual spectrum, and it evolved from those pigments hundreds of millions of years ago.

Birds have four spectrally distinct cone pigments, one drawn from each of the four evolutionary lineages. Mammals, however, typically have only two cone pigments, one maximally sensitive in the violet and the other sensitive at long wavelengths. The likely explanation for this paucity is that during their early evolution in the Mesozoic (245 million to 65 million years ago), mammals were small, secretive and nocturnal. As their eyes evolved to take advantage of the night, they became increasingly dependent on the high sensitivity of rods and less dependent on color vision. Consequently, they lost two of the four cone pigments that their ancestors once possessed—pigments that persist in most reptiles and birds.

Flamingo

COLOR is not actually a property of light or of objects that reflect light. It is a sensation that ARISES WITHIN THE BRAIN.

The demise of the dinosaurs 65 million years ago presented mammals with new opportunities for specialization, and they began to diversify. One group—among which were the progenitors of humans and the other Old World primates living today—took up a diurnal life, spread out into the trees, and made fruit an important part of their diet. The colors of flowers and fruits frequently contrast with the surrounding foliage, but mammals, with only one long-wavelength-sensitive cone pigment, would have been unable to see contrasting colors in the green, yellow and red regions of the spectrum. A solution for these primates, though, was present in the evolutionary toolbox.

Occasionally in the cell divisions that occur during the formation of eggs and sperm, an unequal exchange of parts of chromosomes leads to production of a gamete that possesses a chromosome containing extra copies of one or more genes. If subsequent generations maintain these extra genes, natural selection may preserve useful mutations that arise in them. As Jeremy Nathans and David Hogness, working at Stanford University, have shown, something of this kind occurred during the past 40 million years in the visual system of our ancestral Old World primates. The unequal exchange of DNA in a reproductive cell and subsequent mutation of an extra copy of a gene for a pigment sensitive to long wavelengths resulted in the creation of a second long-wavelength-sensitive pigment, which had a shift in its wavelength of maximum sensitivity. This primate lineage thus differs from that of other mammals in having three cone pigments instead of two and trichromatic color vision.

Though a significant improvement, this system does not equip us with the quintessence of color vision. Ours is still the result of an evolutionary reclamation job and remains one pigment short of the tetrachromatic visual system found in birds and in many reptiles and fish. Our genetic heritage also handicaps some of us in another way. Both our genes for long-wavelength-sensitive pigments lie on the X chromosome. Because males possess only one X chromosome, mutations in either of the pigment genes can leave the affected male with a diminished capacity to distinguish between reds and greens. Females suffer from this kind of color blindness less often, because if a pigment gene is damaged on one copy of the X chromosome they can still make the pigment under the guidance of the healthy gene on their other copy of X.

Cone pigments are not the only elements that were lost from the retina during the early evolution of mammals. Each cone of a bird or reptile contains a colored oil droplet; these droplets no longer exist in mammalian cones. The droplets, which contain high concentrations of molecules called carotenoids, are placed so that light passes through them just before reaching the stack of membranes in the outer segment of the cone where the visual pigment is located. The oil droplets function as filters, removing short wavelengths and narrowing the absorption spectra of the visual pigments. This reduces the spectral overlap between pigments and increases the number of colors that, in principle, a bird can discern.

Testing Color Vision in Birds

THE PRESENCE of four types of cones containing different visual pigments certainly implies that birds have color vision. Yet a direct demonstration of the ability to see colors requires behavioral experiments in which birds show that they can discriminate colored objects. These experiments must also eliminate other cues, such as brightness, that the birds might be using. Although researchers have performed experiments of this type on birds, they began examining the role of UV cones only in the past couple of decades. My former student Byron K. Butler and I decided to use the technique of color

THE AUTHOR

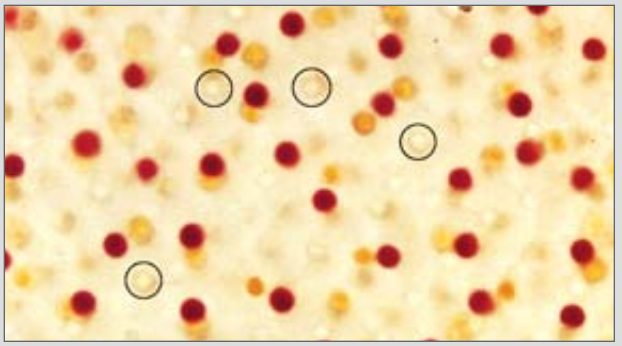
TIMOTHY H. GOLDSMITH is professor emeritus of molecular, cellular and developmental biology at Yale University and a fellow of the American Academy of Arts and Sciences. He has studied vision of crustaceans, insects and birds during a span of five decades. He also nurtures an interest in the evolution of human cognition and behavior and has enjoyed thinking and writing with legal scholars in association with the Gruter Institute for Law and Behavioral Research. For a dozen years before retiring, Goldsmith taught a science course for students in the humanities and social sciences and, with William Zimmerman, wrote the text *Biology, Evolution, and Human Nature*.

BORIS ROESSLER *DPA/Corbis*

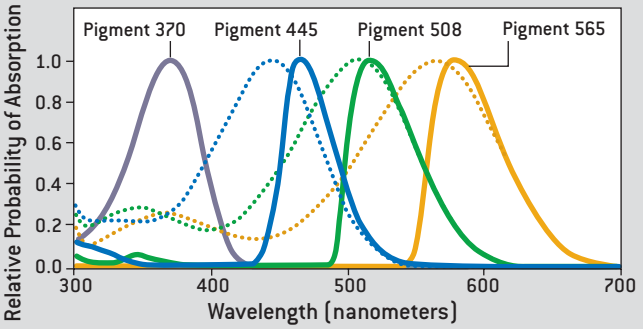
THE IMPORTANCE OF CONE OIL DROPLETS

Cones of birds and many other vertebrates have preserved several features lost from the cones of mammals. The most important of these for color vision is oil droplets. The cones of birds contain red, yellow, nearly colorless and transparent droplets. A micrograph of a chickadee retina (*left*) clearly reveals the yellow and red droplets; black rings mark several colorless droplets. All but the truly transparent droplets act as filters that remove light having short wavelengths.

The filtering effect narrows the spectral sensitivity of three of the four cones of birds and shifts it to longer wavelengths (*graph*). By restricting the wavelengths to which the cones respond, the droplets enable the birds to distinguish more colors than they would see distinctively without the droplets. Ozone in the upper atmosphere absorbs wavelengths shorter than 300 nanometers; therefore, ultraviolet vision for birds involves only the near ultraviolet: the wavelength band from 300 to 400 nanometers.



FILTERING EFFECT OF DROPLETS



matching to explore how the four cones participate in vision.

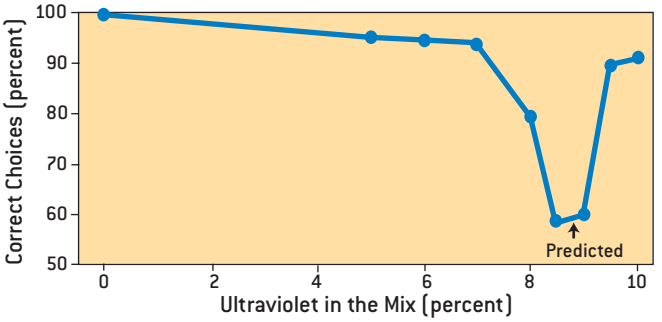
To grasp how color matching works, first consider our own color vision. A yellow light excites both types of long-wavelength cones in humans. Furthermore, it is possible to find a mixture of red and green lights that excites the same two cones to exactly the same extent, and this mixture will be perceived by a viewer as the same yellow seen when the pure yellow light is presented. In other words, two physically different lights may match in color—a reminder that the perception of color is produced in the brain. Our brains discriminate colors in this region of the spectrum by comparing the outputs of the two long-wavelength cones.

Armed with knowledge of the physical properties of the four cones and the oil droplets, Butler and I were able to calculate what mixture of red and green wavelengths birds should see as having the same hue as a particular yellow wavelength. Because human and avian visual pigments are not identical, this mixture was different from what we would predict for humans asked to make the same color match. If the birds responded to the lights as we predicted, that result would confirm our measurements of visual pigments and oil droplets and would allow us to go on to explore whether and how the ultraviolet-sensitive cones are involved in color vision.

We used as subjects small Australian parakeets called budgerigars (*Melopsittacus undulatus*). We trained the birds to associate a food reward with a yellow light. A budgerigar sat on a perch from which it viewed a pair of lights about three feet away. One was the yellow training light, the other a variable mixture of red and green. During testing, a bird flew to the light where it anticipated food. If it went to the yellow, a small seed hopper opened briefly, and the bird got a quick snack. If it went to the wrong light, it got no reward. We changed the mixture of red and green in an irregular sequence, as well as varying the positions of the two lights so the birds were unable to associate food with either the right or left side. We also changed the intensity of the training light so the birds would be unable to use brightness as a cue.

At most mixtures of red and green, the birds were readily able to select the yellow training light and get their reward of seed. But when the mixture contained about 90 percent red and 10 percent green—a proportion we calculated would match the yellow hue of the training light—the birds became confused, and their choices became erratic.

EVIDENCE FOR UV VISION IN BIRDS



DO BIRDS REALLY SEE UV WAVELENGTHS as distinct colors? In an experiment, the author and his colleagues showed that they do. The researchers trained parakeets to distinguish a violet training light from light made up of mixtures of blue and UV. When the mixture had only about 8 percent UV, it matched the hue of the training light and the birds made many errors. Their choices fell to chance at the point (*arrow*) where the author had calculated—on the basis of measurements of the visual pigments and oil droplets in bird cones—that the colors would match.

TIMOTHY H. GOLDSMITH (*micrograph*); JEN CHRISTIANSEN; SOURCE: TIMOTHY H. GOLDSMITH (*illustrations*)

Reassured that we could predict when birds would see color matches, we sought similar evidence to show that UV cones are contributing to tetrachromatic color vision. In this experiment we trained the birds to receive food at a violet light and explored their ability to distinguish this wavelength from mixtures of blue and a broad band of wavelengths in the near UV. We found that the birds could clearly distinguish the violet light from most mixtures. Their choices fell to chance, however, at 92 percent blue and 8 percent UV, the proportions we calculated would make the hue of the mixture indistinguishable from the violet training light. This result means that UV wavelengths are seen as distinct colors by birds and that UV cones participate in a tetrachromatic visual system.


Macaw

Scientists were unaware until the 1970s that many animals see colors in THE NEAR ULTRAVIOLET.

Beyond Human Perception

OUR EXPERIMENTS provided evidence that birds use all four cones in their color vision. But it is difficult—impossible, in fact—for humans to know what their perception of colors is actually like. They not only see in the near ultraviolet, but they also can see colors that we cannot even envision. As an analogy, we might say that our trichromatic color vision can be represented in a triangle, whereas their tetrachromatic color vision requires an additional dimension, giving a tetrahedron or triangular pyramid. The space above the floor of the tetrahedron encompasses a variety of colors that lie beyond direct human experience.

How might birds make use of this wealth of color information? In many species of birds, males are much more brightly colored than females, and following the discovery of UV sensitivity, researchers sought evidence that UV colors not visible to humans might influence mate choice.

In one line of research, Muir Eaton, then at the University of Minnesota, studied 139 species of birds in which the sexes look the same to a human observer. Based on measurements of wavelengths of light reflected from the plumage, he deduced that in more than 90 percent of these species, the eye of a bird sees differences between males and females that ornithologists had not previously recognized.

In a study of males from 108 species of Australian birds, Franziska Hausmann and an international group of col-

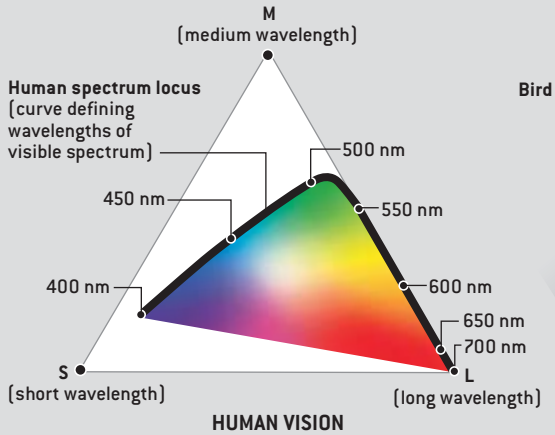
MARTIN HARVEY *Corbis (top photograph)*; ARTHUR MORRIS *Corbis (bottom photograph)*; JEN CHRISTIANSEN; SOURCE: TIMOTHY H. GOLDSMITH *(illustrations)*

A VIRTUAL PEEK INTO THE VISUAL WORLD OF BIRDS

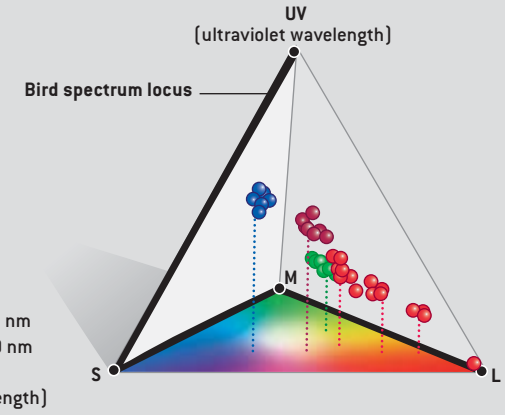
The color vision of humans can be mapped as a triangle. All the colors of the spectrum that we humans can see plot along the heavy black curve lying inside the triangle, and all the many other colors that are made by mixtures of lights lie below the curve.

To map the color vision of a bird, we need to add another dimension, and the result is a solid, a tetrahedron. All the colors that do not activate the UV receptor lie in the floor of the tetrahedron; however, because the cone oil droplets increase the number of colors a bird can see [*as explained in top box on preceding page*], the spectrum locus follows the edges of the triangular floor rather than the shark fin shape of the human color triangle. The colors that involve the UV receptor fall in the space above the floor. For example, the red, green and blue plumage of the painted bunting (*photograph*) reflects varying amounts of UV light in addition to the colors that we humans see (*graph*).

To indicate graphically the colors that the female bunting sees when she looks at her mate, we have to move from the plane of the triangle to the three-dimensional volume of the tetrahedron.



HUMAN VISION



BIRD VISION


MALE PAINTED BUNTING

Imagining a UV World

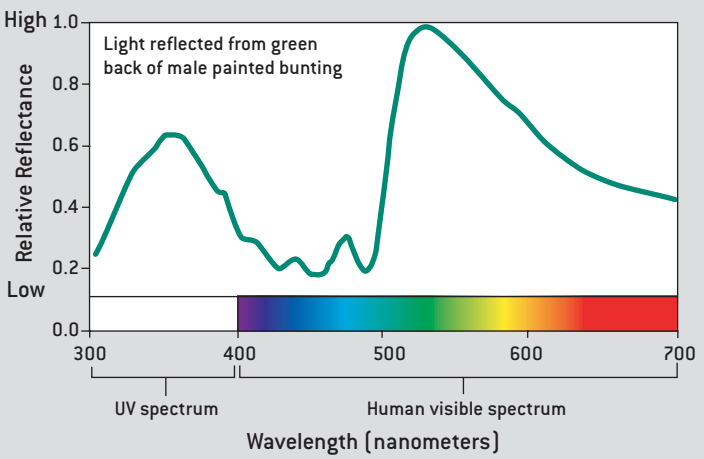
Although no one knows what the world looks like to birds, these images of black-eyed Susans offer a glimpse of how an ability to see ultraviolet light might change the way the world looks. To us, the center of the flower is a small dark disk (*left*). But a camera equipped to detect only ultraviolet light "sees" patterns invisible to us, including a much larger dark ring (*right*). These photographs were made by Andrew Davidhazy, a professor of imaging and photographic technology at the Rochester Institute of Technology. —*The Editors*

leagues found colors with a UV component significantly more often in plumage that is involved in courtship displays than in feathers from elsewhere on the birds. Furthermore, groups in England, Sweden and France have studied the blue tit (*Parus caeruleus*), a Eurasian near relative of chickadees of North America, and starlings (*Sturnus vulgaris*), with results indicating that females are in fact attracted to those males that show the brightest UV reflectance. Why should this matter? UV reflectance from the plumage of birds depends on the submicroscopic structure of feathers, so it can serve as a useful indicator of the health of male birds. Amber Keyser and Geoffrey Hill of the University of Georgia and Auburn University have shown that male blue grosbeaks (*Guiraca caerulea*) with the most, brightest and most-UV-shifted blue in their plumage are larger, hold the most extensive territories with abundant prey, and feed their offspring more frequently than other males do.

More generally, having a UV receptor may give an animal an advantage in foraging for food. Dietrich Burkhardt of the University of Regensburg in Germany has shown that the waxy surfaces of many fruits and berries reflect UV light that might advertise their presence. Jussi Viitala of the University of Jyväskylä in Finland and colleagues have found that small falcons called kestrels are able to locate the trails of voles visually. These small rodents lay scent trails of urine and feces that are reported to reflect UV light, making them visible to the UV receptors of kestrels, particularly in the spring before the scent marks are covered by vegetation.

People unaware of these intriguing findings often ask me, "What does ultraviolet vision *do* for birds?" The question seems to imply that sensitivity to UV must be a peculiarity or even a feature that self-respecting birds should be able to live happily without. We are so locked into the world of our own senses that, although we readily understand and fear a loss of vision, we cannot conjure a picture of a visual world beyond our own. It is humbling to realize that evolutionary perfection is a will-o'-the-wisp and that the world is not quite what we imagine it to be when we measure it through a lens of human self-importance. SA

The colors reflected from small regions of feathers are represented by clusters of points: bright red for the breast and throat, darker red for the rump, green for the back, and blue for the head. (We cannot, of course, show the colors the bird sees, because no human can perceive those colors.) The more ultraviolet in the color, the higher the points are above the floor. There is a distribution of points within each of the clusters because the wavelengths of reflected light vary within the regions, such as what we humans see as the red areas of the breast and throat.



MORE TO EXPLORE

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A POWER GRID FOR THE HYDROGEN ECONOMY

Cryogenic, superconducting conduits could be connected into a "SuperGrid" that would simultaneously deliver electrical power and hydrogen fuel

By Paul M. Grant, Chauncey Starr and Thomas J. Overbye

On the afternoon of August 14, 2003, electricity failed to arrive in New York City, plunging the eight million inhabitants of the Big Apple—along with 40 million other people throughout the northeastern U.S. and Ontario—into a tense night of darkness. After one power plant in Ohio had shut down, elevated power loads overheated high-voltage lines, which sagged into trees and short-circuited. Like toppling dominoes, the failures cascaded through the electrical grid, knocking 265 power plants offline and darkening 24,000 square kilometers.

That incident—and an even more extensive blackout that affected 56 million people in Italy and Switzerland a month later—called attention to pervasive problems with modern civilization's vital equivalent of a biological circulatory system, its interconnected electrical networks. In North America the electrical grid has evolved in piecemeal fashion over the past 100 years. Today the more than $1-trillion infrastructure spans the continent with millions of kilometers of wire operating at up to 765,000 volts. Despite its importance, no single organization has control over the operation, maintenance or protection of the grid; the same is true in Europe. Dozens of utilities must cooperate even as they compete to generate and deliver, every second, exactly as much power as customers demand—and no more. The 2003 blackouts raised calls for greater government oversight and spurred the industry to move more quickly, through its IntelliGrid Consortium and the GridWise program of the U.S. Department of Energy, to create self-healing systems for the grid that may prevent some kinds of outages from cascading. But reliability is not the only challenge—and arguably not even the most important challenge—that the grid faces in the decades ahead.

A more fundamental limitation of the 20th-century grid is that it is poorly suited to handle two 21st-century trends: the relentless growth in demand for electrical energy and the coming transition from fossil-fueled power stations and vehicles to cleaner sources of electricity and transportation fuels. Utilities cannot simply pump more power through existing high-voltage lines by ramping up the voltages and currents. At about one million volts, the electric fields tear insulation off the wires, causing arcs and short circuits. And higher currents will heat the lines, which could then sag dangerously close to trees and structures.

It is not at all clear, moreover, how well today's infrastructure could support the rapid adoption of hybrid vehicles that draw on electricity or hydrogen for part of their power. And because the power system must continuously match electricity consumption with generation, it cannot easily accept a large increase in the unpredictable and intermittent power produced from renewable wind, ocean and solar resources.

We are part of a growing group of engineers and physicists who have begun developing designs for a new energy delivery system we call the Continental SuperGrid. We envision the SuperGrid evolving gradually alongside the current grid, strengthening its capacity and reliability. Over the course of decades, the SuperGrid would put in place the means to generate and deliver not only plentiful, reliable, inexpensive and "clean" electricity but also hydrogen for energy storage and personal transportation.

Engineering studies of the design have concluded that no further fundamental scientific discoveries are needed to realize this vision. Existing nuclear, hydrogen and superconducting technologies, supplemented by selected renewable energy, provide all the technical ingredients required to create a SuperGrid. Mustering the social and national resolve to create it may be a challenge, as will be some of the engineering. But the benefits would be considerable, too.

Superconducting lines, which transmit electricity with almost perfect efficiency, would allow distant generators to compensate for local outages. They would allow power plants in different climate regions to bolster those struggling to meet peak demand. And they would allow utilities to construct new generating stations on less controversial sites far from population centers.

SuperGrid connections to these new power plants would provide both a source of hydrogen and a way to distribute it widely, through pipes that surround and cool the superconducting wires. A hydrogen-filled SuperGrid would serve not only as a conduit but also as a vast repository of energy, establishing the buffer needed to enable much more extensive use of wind, solar and other renewable power sources.

A hydrogen-filled SuperGrid would serve not only as a conduit but also as a vast repository of energy.

Overview/*A Continental SuperGrid*

- As the 2003 blackouts in North America and Europe vividly testify, the current power grid is struggling to meet growing demand for electricity and the coming shift from fossil-fueled power and cars to cleaner sources of energy.
- For several years, engineers have been designing a new infrastructure that would enable cities to tap power efficiently from large nuclear and renewable energy plants in distant and remote locations.
- SuperCables would transmit extraordinarily high electrical current nearly resistance-free through superconducting wires. The conduits would also carry ultracold hydrogen as a liquid or high-pressure gas to factories, vehicle fueling stations, and perhaps one day even to home furnaces and boilers.

PRECEDING PAGES: SLIM FILMS; CORBIS (*background satellite image*); BOB SACHA *Corbis* (*wind power*); ALAN SCHEIN PHOTOGRAPHY *Corbis* (*office buildings*); PREMIUM STOCK/CORBIS (*power plant*); GEORGE STEINMETZ *Corbis* (*aerial view of houses*); CORBIS (*solar arrays and substation*); BMWAG, MÜNCHEN (*hydro car*); ZUMA PRESS (*clean vehicles*); AMERICAN SUPERCONDUCTOR, INC. (*superconducting cable*); ROBERT HARDING *World Imagery/Corbis* (*houses*)

And it would build the core infrastructure that is a prerequisite if rich economies are to move away from greenhouse-gas-emitting power plants and vehicles.

A New Grid for a New Era

A CONTINENTAL SUPERGRID may sound like a futuristic idea, but the concept has a long history. In 1967 IBM physicists Richard L. Garwin and Juri Matisoo published a design for a 1,000-kilometer transmission cable made of niobium tin, which superconducts at high currents. Extraordinary amounts of direct current (DC) can pass resistance-free through such a superconductor when the metal is chilled by liquid helium to a few degrees above absolute zero. The scientists proposed a DC cable with two conductors (made of superconducting wire or tape) that together would carry 100 gigawatts—roughly the output of 50 nuclear power plants.

Garwin and Matisoo were exploring what might be possible, not what would be practical. It would not make sense to inject that much power into one point of the grid, and liquid helium is a cumbersome coolant. But their ideas inspired others. In the following decades, short superconducting cables were built and tested to carry alternating current (AC) in Brookhaven, N.Y., and near Graz, Austria, with the latter operating connected to the local grid for several years.

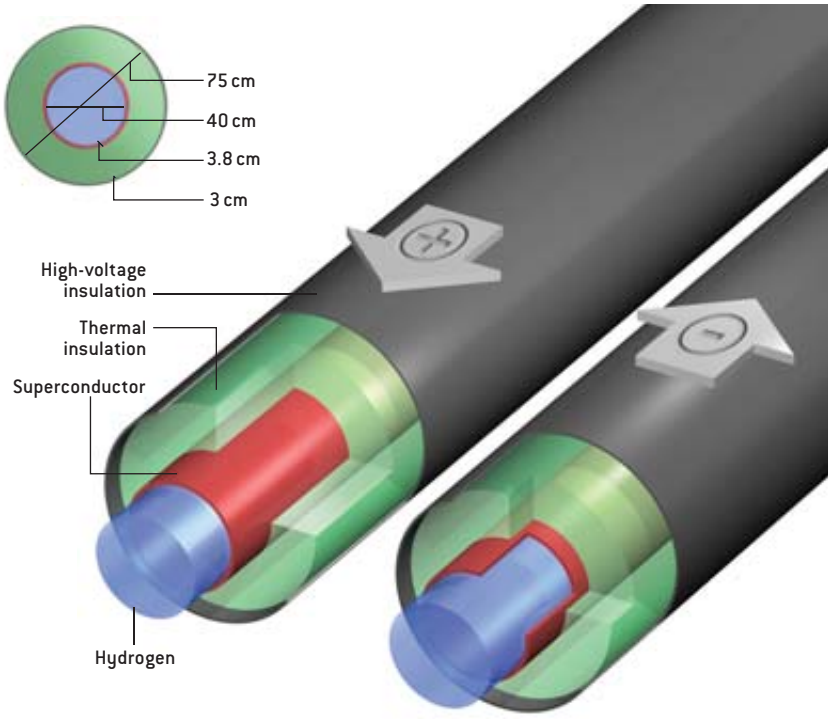
Ten years after the discovery of high-temperature superconductivity, a technical study by the Electric Power Research Institute (EPRI) concluded that with liquid nitrogen as a coolant, a five-gigawatt DC "electricity pipe" could compete economically with a gas pipeline or conventional overhead lines for transmission distances of 800 kilometers or more. Two of us (Grant and Starr) developed the idea further in papers that explored how ultracold hydrogen—either liquid or supercritical gas—might both chill the superconducting wires and deliver energy in chemical form within a continental-scale system. In 2002 and 2004 the third author (Overbye) organized workshops at which dozens of experts detailed a plan for a 100-meter pilot segment, precursor to a 50-kilometer intertie between existing regional grids.

It is important to develop prototypes soon, because existing electrical grids are increasingly reaching the point of maximum loading—and, as the blackouts indicate, occasionally exceeding it. As total generating capacity in the U.S. has risen by almost a quarter in the past five years, the high-voltage transmission grid has grown in size by just 3.3 percent. Yet society's appetite for energy continues to grow rapidly: the U.S. Energy Information Administration forecasts that by 2025 annual energy use in the U.S. will hit 134 trillion megajoules (127 quadrillion BTUs), over a quarter greater than it was in 2005.

The rising demand poses two problems: where to get this new energy and how to distribute it. Fossil fuels will probably still supply a large fraction of our energy 20 years from now. But global competition for limited petroleum and natural gas resources is intense, and even mild production shortages can send prices skyrocketing, as we have seen in the past few months. Concern

SUPERCABLES

SuperCables could transport energy in both electrical and chemical form. Electricity would travel nearly resistance-free through pipes (*red*) made of a superconducting material. Chilled hydrogen flowing as a liquid (*blue*) inside the conductors would keep their temperature near absolute zero. A SuperCable with two conduits, each about a meter in diameter, could simultaneously transmit five gigawatts of electricity and 10 gigawatts of thermal power (*table*).



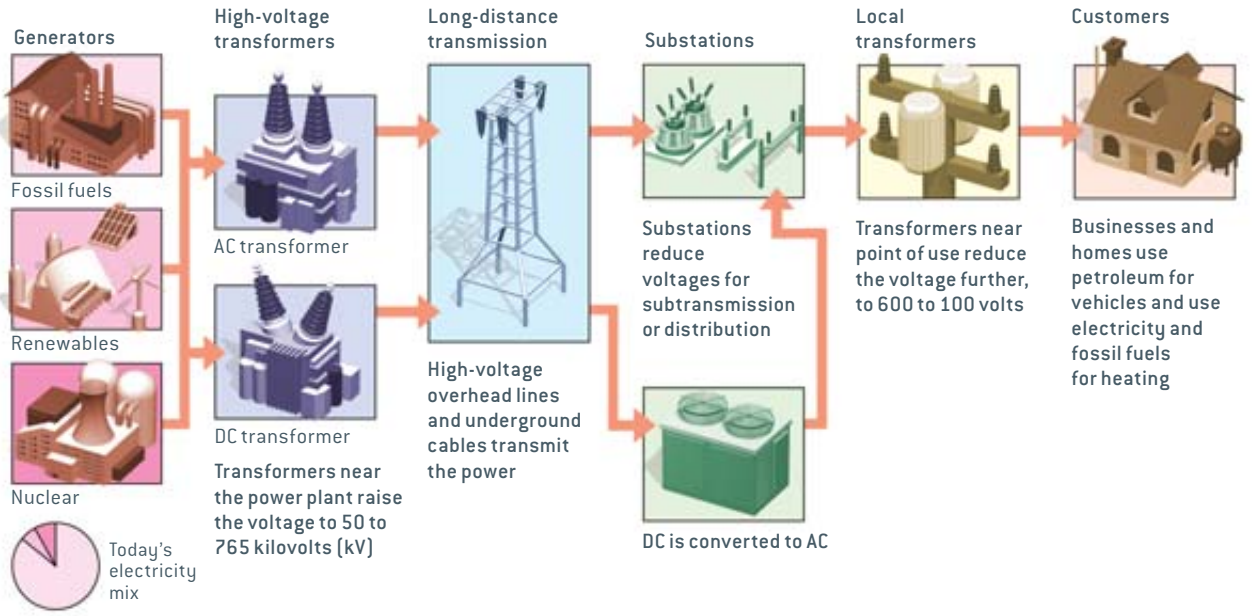
	Voltage/Temperature	Flow rate	Power delivered
DC circuit	+50,000 volts and −50,000 volts	50,000 amperes	5,000 megawatts electric
Liquid hydrogen	20 kelvins	0.6 cubic meter/second in each pipe	10,000 megawatts thermal

SLIM FILMS

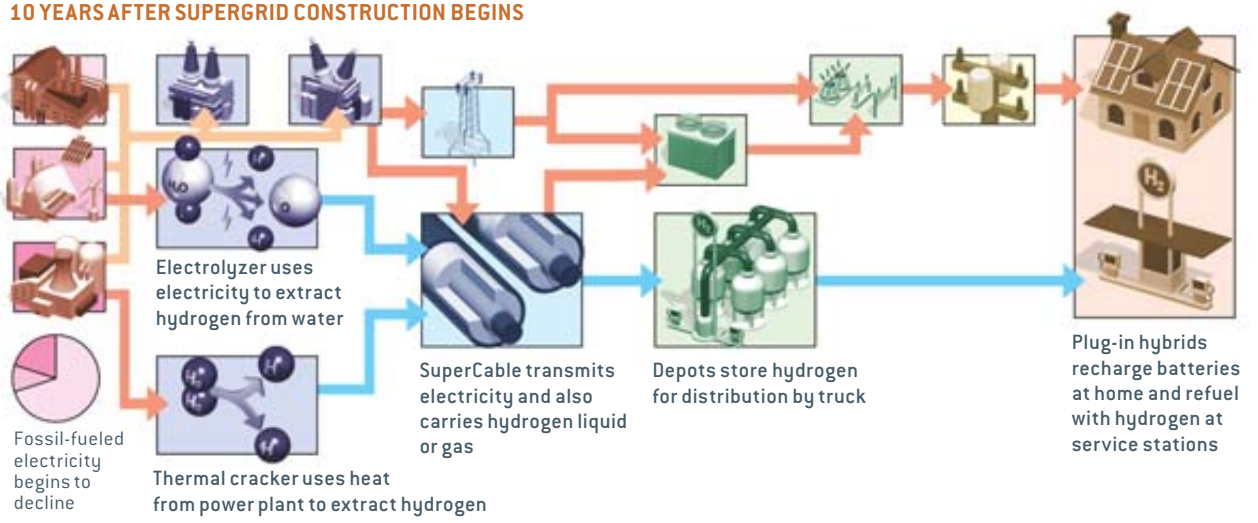
THE EVOLUTION OF A SUPERGRID

Transition to a SuperGrid would take at least a generation to complete. The evolution would inject new technologies into every level of the infrastructure: generators, transformers, power transmission and consumption.

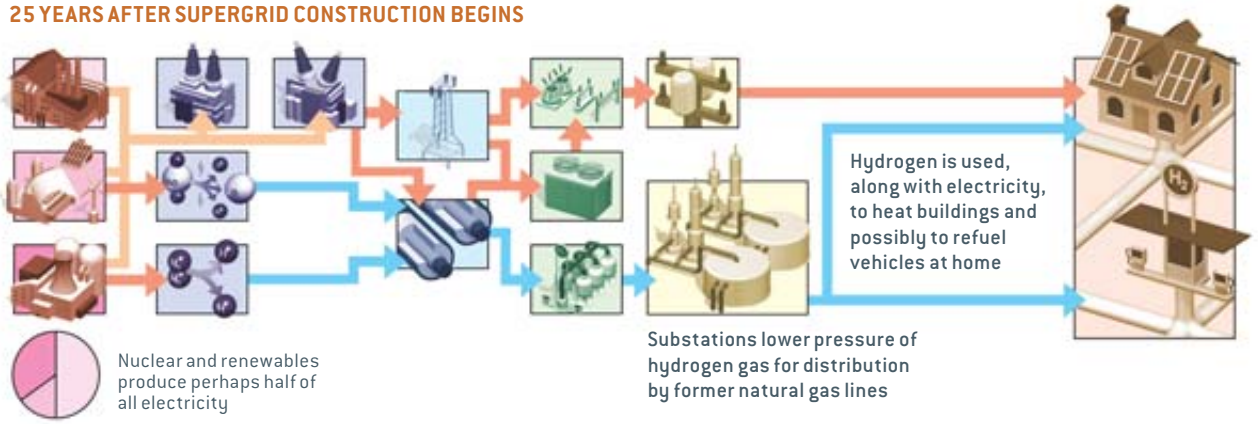
TODAY



10 YEARS AFTER SUPERGRID CONSTRUCTION BEGINS



25 YEARS AFTER SUPERGRID CONSTRUCTION BEGINS



SLIM FILMS

over greenhouse warming is leading to other constraints.

If we have an opportunity to move away from our dependence on fossil fuels, clearly we should take it. But fully exploiting nonfossil energy sources, including wind, solar, agricultural biomass and in particular advanced nuclear power, will require a new grid for this new era. To distribute trillions of kilowatt-hours of extra electricity every year, the U.S. grid will have to handle roughly 400 gigawatts more power than it does today.

The current infrastructure can be enhanced only so far. New carbon-core aluminum wires can be stretched more tautly than conventional copper wires and so can carry perhaps three times as much current before sagging below safe heights. And U.S. utilities will take advantage of provisions in the 2005 Energy Act that make it easier to open new transmission corridors.

But high-voltage lines are already approaching the million-volt limit on insulators and the operating limits of semiconductor devices that control DC lines. AC lines become inefficient at distances around 1,200 kilometers, because they begin to radiate the 60-hertz power they carry like a giant antenna. Engineers will thus need to augment the transmission system with new technologies to transport hundreds more gigawatts from remote generators to major cities.

Next-Generation Nuclear

ONE OF OUR GOALS in designing the SuperGrid has been to ensure that it can accept inputs from a wide variety of generators, from the smallest rooftop solar panel and farmyard wind turbine to the largest assemblage of nuclear reactors. The largest facilities constrain many basic design decisions, however. And the renewables still face tremendous challenges in offering the enormous additional capacity required for the next 20 years. So we built our concept on a foundation of fourth-generation nuclear power.

The 2005 Energy Act directed $60 million toward development of "generation IV" high-temperature, gas-cooled reactors. Unlike most current nuclear plants, which are water-cooled and so usually built near large bodies of water—typically near population centers—the next-generation reactors expel their excess heat directly into the air or earth.

In newer designs, the nuclear reactions slow down as the temperature rises above a normal operating range. They are thus inherently resistant to the coolant loss and overheating that occurred at Chernobyl in Ukraine and Three Mile Island in Pennsylvania [see "Next-Generation Nuclear Power," by James A. Lake, Ralph G. Bennett and John F. Kotek; SCIENTIFIC AMERICAN, January 2002].

Like all fission generators, however, generation IV units will produce some radioactive waste. So it will be least expensive and easiest politically to build them in "nuclear clusters," far from urban areas. Each cluster could produce on the order of 10 gigawatts.

Remote siting will make it easier to secure the reactors as well as to build them. But we will need a new transmission technology—a SuperCable—that can drastically reduce the cost of moving energy over long distances.

SuperCables

FOR THE ELECTRICITY PART of the SuperGrid, where we need to move tens of gigawatts over hundreds of kilometers, perfect conductors are a perfect fit. Although superconducting materials were discovered in 1911 and were fashioned into experimental devices decades ago, it is only quite recently that the refrigeration needed to keep them ultracold has become simple enough for industrial use. Superconductors are now moving beyond magnetic resonance imaging scanners and particle accelerators and into commercial power systems.

For example, the DOE has joined with power equipment manufacturers and utilities to produce prototypes of superconducting transformers, motors, generators, fault-current limiters and transmission cables. Other governments—notably Japan, the European Union, China and South Korea—have similar development programs. Three pilot projects now under way in the U.S. are demonstrating superconducting cables in New York State on Long Island and in Albany and in Columbus, Ohio.

These cables use copper oxide–based superconducting tape cooled by liquid nitrogen at 77 kelvins (–196 degrees Celsius). Using liquid hydrogen for coolant would drop the temperature to 20 kelvins, into the superconducting range of new compounds such as magnesium diboride [see "Low-Temperature Superconductivity Is Warming Up," by Paul

For moving tens of gigawatts over hundreds of kilometers, perfect conductors are a perfect fit.

THE AUTHORS

PAUL M. GRANT worked for IBM for 40 years, starting in 1953 at age 17 as a pinsetter at the company bowling alley. After earning a Ph.D. in physics at Harvard University, he joined the San Jose Research Laboratory, where he participated in the discovery of high-temperature superconductivity. From 1993 to 2004, Grant was a science fellow at the Electric Power Research Institute (EPRI), which was founded by *CHAUNCEY STARR* in 1973. Starr, a 1990 recipient of the U.S. National Medal of Technology, did early research on cryogenics, managed the atomic energy division of Rockwell International, co-founded the American Nuclear Society, and was president of EPRI for more than a decade. *THOMAS J. OVERBYE,* who holds the Fox Family Professorship in Electrical and Computer Engineering at the University of Illinois at Urbana-Champaign, contributed to the official investigation of the 2003 North American blackout.

C. Canfield and Sergey L. Bud'ko; SCIENTIFIC AMERICAN, April 2005].

All demonstrations of superconducting cables so far have used AC power, even though only DC electricity can travel without resistance. Even so, at the frequencies used on the current grid, superconductors offer about one two-hundredth the electrical resistance of copper at the same temperature.

The SuperCable we have designed includes a pair of DC superconducting wires, one at plus 50,000 volts, the other at minus 50,000 volts, and both carrying 50,000 amps—a current far higher than any conventional wire could sustain. Such a cable could transmit about five gigawatts for several hundred kilometers at nearly zero resistance and line loss. (Today about a tenth of all electrical energy produced by power plants is lost during transmission.)

A five-gigawatt SuperCable is certainly technically feasible. Its scale would rival the 3.1-gigawatt Pacific Intertie, an existing 500-kilovolt DC overhead line that moves power between northern Oregon and southern California. Just four SuperCables would provide sufficient capacity to transmit all the power generated by the giant Three Gorges Dam hydroelectric facility in China.

Because a SuperCable would use hydrogen as its cryogenic coolant, it would transport energy in chemical as well as electrical form. Next-generation nuclear plants can produce either electricity or hydrogen with almost equal thermal efficiency. So the operators of nuclear clusters could continually adjust the proportions of electricity and "hydricity" that they pump into the SuperGrid to keep up with the electricity demand while maintaining a flow of hydrogen sufficient to keep the wires superconducting.

Electricity and Hydricity

THE ABILITY TO CHOOSE among alternative forms of power and to store electricity in chemical form opens up a world of possibilities. The SuperGrid could dramatically reduce fuel costs for electric- and hydrogen-powered hybrid vehicles, for example.

Existing hybrids run on gasoline or diesel but use batteries to recover energy that otherwise would go to waste. "Plug-in" hybrids that debuted last year use electricity as well as gas [see "Hybrid Vehicles," by Joseph J. Romm and Andrew A. Frank; SCIENTIFIC AMERICAN, April]. BMW, Mazda and others have demonstrated hydrogen hybrids that have two fuel tanks and engines that burn hydrogen when it is available and gasoline when it is not. Many automakers are also developing vehicles that use onboard fuel cells to turn hydrogen back into electricity by combining it with oxygen.

Even the most efficient automobiles today convert only 30 to 35 percent of their fuel energy into motion. Hydrogen fuel-cell hybrids could do significantly better, reaching 50 percent efficiencies with relative ease and eventually achieving 60 to 65 percent fuel efficiencies.

Replacing even a modest percentage of petroleum-based transportation fuels would require enormous amounts of both hydrogen and electricity, as well as a pervasive and efficient delivery infrastructure. The SuperGrid offers one way to realize this vision. Within each nuclear cluster, some reactors could produce electricity while others made hydrogen—without emitting any greenhouse gases.

By transporting the two together, the grid would serve both as a pipeline and as an energy store. For example, every 70-kilometer section of SuperCable containing 40-centimeter-diameter pipes filled with liquid hydrogen would store 32 gigawatt-hours of energy. That is equivalent to the capacity of the Raccoon Mountain reservoir, the largest pumped hydroelectric facility in the U.S.

By transforming electricity into a less ephemeral commodity similar to oil or natural gas, the new grid could allow electricity markets to tolerate rapid swings in demand more reliably than they do today. SuperGrid links crossing several time zones and weather boundaries would allow power plants to tap excess nighttime capacity to meet the peak electricity needs of distant cities [*see illustration on opposite page*]. By smoothing out fluctuations in demand, the low-loss grid could help reduce the need for new generation construction.

The SuperGrid could go a long way, too, toward removing one of the fundamental limitations to the large-scale use of inconstant energy from wind, tides, waves and sunlight. Renewable power plants could pump hydrogen onto the grid, rather than selling electricity. Alternatively, baseline generators could monitor the rise and fall in electrical

PUMP-FILLED LAKE atop Raccoon Mountain in Tennessee stores enough potential energy to create 32 gigawatt-hours of electricity when drained through its hydroelectric dam. Every 70 kilometers of SuperCable would store an equivalent amount of energy in the form of hydrogen.

TENNESSEE VALLEY AUTHORITY

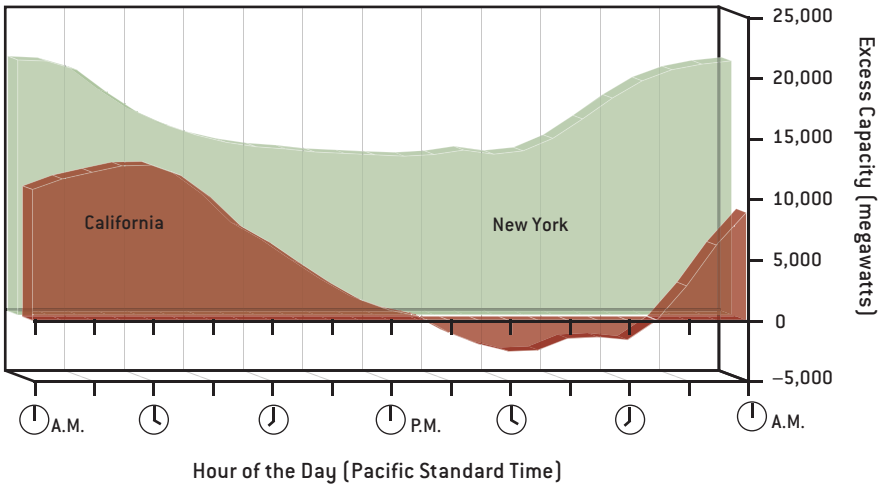
output from these plants and might be able to use electrolysis to shift their electricity/hydricity blend to compensate.

Charging Ahead

NO MAJOR SCIENTIFIC advances are needed to begin building the SuperGrid, and the electric utility industry has already shown its interest in the concept by funding a SuperGrid project at EPRI which will explore the numerous engineering challenges that integrating SuperCables into the existing power grid will pose. The largest of these is what to do if a SuperCable fails.

The grid today remains secure even when a single device, such as a high-voltage transmission line, fails. When a line sags into a tree, for example, circuit breakers open to isolate the line from the grid, and the power that was flowing on the wire almost instantaneously shifts to other lines. But we do not yet have a circuit-breaker design that can cut off the extraordinary current that would flow over a SuperCable. That technology will have to evolve. Grid managers may need to develop novel techniques for dealing with the substantial disturbance that loss of such a huge amount of power would cause on the conventional grid. A break in a SuperCable would collapse the surrounding magnetic field, creating a brief but intense voltage spike at the cut point. The cables will need insulation strong enough to contain this spike.

Safely transporting large amounts of hydrogen within the SuperCable poses another challenge. The petrochemical industry and space programs have extensive experience pumping hydrogen, both gaseous and liquid, over kilometer-scale pipelines. The increasing use of liquefied natural gas will reinforce that technology base further. The explosive potential (energy content per unit mass) of hydrogen is about twice that of the methane in natural gas. But hydrogen leaks more easily and can ignite at lower oxygen concentrations, so the hydrogen distribution and storage infrastructure will need to be airtight. Work on hydrogen tanks for vehicles has already produced coatings that can withstand pressures up to 700 kilograms per square centimeter.



CONTINENT-WIDE SUPERGRID could help avoid brownouts and overloads by allowing operators to shift huge amounts of power over long distances. On a hot summer day, for example, demand for electricity in California (*red*) can exceed the state's active generating capacity for several hours. But generators in New York State have surplus capacity (*green*), so they can make up the deficit.

Probably the best way to secure SuperCables is to run them through tunnels deep underground. Burial could significantly reduce public and political opposition to the construction of new lines.

The costs of tunneling are high, but they have been falling as underground construction and microtunneling have made great strides, as demonstrated by New York City's Water Tunnel Number 3 and the giant storm sewers in Chicago. Automated boring machines are now digging a 10.4-kilometer-long, 14.4-meter-diameter hydroelectric tunnel beside the Niagara River, at a cost of $600 million. Recent studies at Fermilab estimated the price of an 800-kilometer-long, three-meter-wide, 150-meter-deep tunnel at less than $1,000 a meter.

SuperCables would carry many times the power of existing transmission lines, which helps the economic case for burial. But the potential for further technology innovation and the limits imposed by the economics of underground construction need more exploration.

To jump-start the SuperGrid, and to clarify the costs, participants in the 2004 SuperGrid workshop proposed constructing a one-kilometer-long SuperCable to carry several hundred megawatts. This first segment would simply test the superconducting components, using liquid nitrogen to cool them. The project could be sponsored by the DOE, built at a suitable national laboratory site, and overseen by a consortium of electric utilities and regional transmission operators. Success on that prototype should lead to a 30- to 80-kilometer demonstration project that relieves real bottlenecks on today's grid by supplementing chronically congested interties between adjacent regional grids.

Beyond that, price may largely determine whether any country will muster the political and social will to construct a SuperGrid. The investment will undoubtedly be enormous: perhaps $1 trillion in today's dollars and in any case beyond the timescale attractive to private investment. It is difficult to estimate the cost of a multidecade, multigenerational SuperGrid effort. But one can judge the ultimate benefits: a carbonless, ecologically gentle domestic energy infrastructure yielding economic and physical security. SA

MORE TO EXPLORE

National Energy Planning for the Century. Chauncey Starr in *Nuclear News,* Vol. 45, No. 31, pages 31–35; February 2002. Available at **www.w2agz.com/SG%20-Bibliography.htm**

The SuperCable: Dual Delivery of Chemical and Electric Power. Paul M. Grant in *IEEE Transactions on Applied Superconductivity,* Vol. 15, No. 2, pages 1810–1813; June 2005.

Proceedings of the 2002 and 2004 SuperGrid conferences are available at **supergrid.uiuc.edu**

W. WAYT GIBBS

Attorneys, investigators and educators have felt the impact of television's popular forensics programs

CSI: REALITY

By Max M. Houck

Forensic science has been the backbone of mystery stories from Edgar Allan Poe's Dupin adventures to Sir Arthur Conan Doyle's Sherlock Holmes tales to Jack Klugman's *Quincy* television series to today's wildly successful forensics shows. Holmes's methods presaged many actual techniques for linking physical evidence to the perpetrator of a crime, such as blood testing. Forensic science was codified as a profession in the early 1900s and exploded into the public consciousness in the 1990s with the advent of DNA analysis.

Forensics has never been more popular or popularized: eight crime dramas, including *CSI: Crime Scene Investigation* and its sibling programs, made it into the top 20 shows last October. On one Thursday that month, 27 percent of all American televisions that were turned on were tuned to *CSI*. On cable, CourtTV's *Forensic Files,* a documentary-style series featuring real crimes and real scientists, airs four days a week. Such programs give the impression that forensic laboratories are fully staffed with highly trained personnel, stocked with a full complement of state-of-the-art instrumentation and rolling in the resources to close every case in a timely fashion.

The gap between public perception and reality, however, is vast. And the popularity of these shows has led to complaints of a "CSI effect": at least some lawyers and judges have the impression that jurors schooled on *CSI,* which has been on the air since 2000, now demand unreasonable levels of physical evidence in trials. Whether the CSI effect truly exists as a quantifiable influence on courtroom behavior is still a subject of debate. Of no debate, though, is the effect that the CSI programs have had on the activities of police, who now collect more pieces of physical evidence than ever before; in academia, where some forensics programs are growing exponentially; and in overburdened working laboratories, which are a far cry from the glitzy, blue-lit analysis palaces of TV.

The Effect in the Courtroom

IN ONE OF THIS SEASON'S episodes of *CSI,* the plot included a television crew recording the activities of the fictional crime scene investigators. Lead researcher Gil Grissom rebuffs the TV crew's attempts, saying, "There's too many forensics shows on TV." Numerous attorneys and judges who believe that jurors are afflicted with the CSI effect would agree. But to what extent do *CSI* and its relatives influence the expectations that jurors bring to trials?

The press started to pay attention to the issue in 2003, collecting anecdotes from attorneys and judges about what appeared to be a change in the behavior of jurors. In 2005 Oregon district attorney Josh Marquis, vice president of the National District Attorneys Association, told *CBS News,* "Jurors now expect us to have a DNA test for just about every case. They expect us to have the most advanced technology possible, and they expect it to look like it does on television." Indeed, jurors in a Los Angeles murder case complained that a bloody coat had not been tested for DNA, even though such tests were unnecessary: the defendant had already admitted to having been at the crime scene. The judge noted that TV had taught jurors about DNA tests but not about when they should be used. In a study in Delaware of how juries deal with evidence, one juror tangling with a complex DNA case complained that these kinds of problems did not happen "on *CSI*."

Attorneys blamed the CSI effect when a Baltimore jury acquitted a man of murder—testimony from two eyewitnesses was trumped by a lack of physical evidence. "I've seen a big change in jurors and what they expect over the last five years," defense at-

BRAD SWONETZ

PAUCITY OF PHYSICAL EVIDENCE led to acquittal of actor Robert Blake (*shown kissing his attorney after the verdict*) in the murder of his wife, Bonny Lee Bakley, in 2001, despite Blake's having motive and opportunity. His attorney holds Blake's ankle monitor aloft. In a subsequent civil case, Blake was found liable for the wrongful death.

NICK UT *AP Photo*

CSI effect: not guilty by reason of TV?

torney Joseph Levin of Atlantic City, N.J., told a local newspaper. "Jurors can ask questions of the judge while in deliberations, and they're asking about what they see as missing evidence. They want to know where the fingerprints are or the DNA. If it's not there, they want to know why." In the California murder trial of actor Robert Blake, prosecutors tried to persuade the jury by establishing Blake's motive and opportunity, and they presented witnesses who testified that Blake asked them to kill his wife. But no gunshot residue or blood spatter evidence was presented, and Blake was acquitted. A juror was quoted as saying that if the prosecutor "had all that information, that would have meant [Blake] was guilty." The defeat was the prosecutor's first in 50 murder cases.

Before *CSI* became popular, attorneys mostly worried about whether a jury was going to understand the complexity of DNA evidence. Now, though, many spend time clarifying the difference between television and reality—it is common for lawyers to ask prospective jurors about their exposure to forensics-themed TV programs. And some prosecutors are attempting to preempt any potential fallout from the CSI effect. In trials in Arizona, Illinois and California, they have put so-called negative evidence witnesses on the stand to alert jurors to the fact that real-life detectives often fail to find physical evidence, such as DNA or fingerprints, at crime scenes.

Several legal experts have argued, however, that the CSI effect may be illusory. The newspaper that quoted Atlantic City lawyer Levin also noted that Superior Court Judge Albert Garofolo said, "My initial reaction might have been 'Yes, there is a CSI effect.' But I think this may be more of a suspicion than anything else. There's a feeling this could be real, but in truth I can't recall a situation where I've heard a jury say they were expecting more."

In 2005 in the *Wall Street Journal*, Simon Cole of the department of criminology, law and society at the University of California, Irvine, and his student Rachel Dioso wrote: "That television might have an effect on courtrooms is not implausible.... But to argue that 'C.S.I.' and similar shows are actually raising the number of acquittals is a staggering claim, and the remarkable thing is that, speaking forensically, there is not a shred of evidence to back it up. There is a robust field of research on jury decision-making but no study finding any C.S.I. effect. There is only anecdotal evidence."

What appears to be the first study of the CSI effect was published in February by Kimberlianne Podlas, an attorney and assistant professor of media law and ethics at the University of North Carolina at Greensboro. Podlas concluded that the chances of, and reasoning for, acquittals were the same for frequent *CSI* viewers as for prospective jurors who did not watch the show—she saw no CSI effect. Several participants, however, said that a lack of forensic testing was an issue, despite the fact that physical evidence would not have resolved the hypothetical charges. Studies of real juries have been advocated, and at least five graduate students (three in the U.S. and two in England) are preparing theses examining the effect.

Overview/*Science vs. Fiction*

- Prosecutors, judges and police officers have noted what they believe to be a so-called CSI effect whereby the popular television forensics programs have led jurors to have unreasonable expectations for the quality and quantity of physical evidence.
- Any CSI effect in courtrooms is still unproved. But the television programs have led to an increase in the collection of physical evidence, contributing to issues of storage and personnel shortages.
- The television shows have also undoubtedly led to an explosion of interest in forensics evidence on college campuses, where enrollment in forensics science studies has greatly increased since the *CSI* series went on the air.

What Is Real?

WHETHER OR NOT forensics shows are measurably influencing the demands and decisions of juries, television is un-

questionably giving the public a distorted view of how forensic science is carried out and what it can and cannot do. The actors playing forensic personnel portrayed on television, for instance, are an amalgam of police officer/detective/forensic scientist—this job description does not exist in the real world. Law enforcement, investigations and forensic science are each sufficiently complex that they demand their own education, training and methods. And specialization within forensic laboratories has been the norm since the late 1980s. Every forensic scientist needs to know the capabilities of the other subdisciplines, but no scientist is an expert in every area of crime scene investigation.

In addition, laboratories frequently do not perform all types of analyses, whether because of cost, insufficient resources or rare demand. And television shows incorrectly portray forensic scientists as having ample time for every case; several TV detectives, technicians and scientists often devote their full attention to one investigation. In reality, individual scientists will have many cases assigned to them. Most forensics labs find backlogs to be a major problem, and dealing with them often accounts for most requests for bigger budgets.

Fictional forensics programs also diverge from the real world in their portrayal of scientific techniques: University of Maryland forensic scientist Thomas Mauriello estimates that about 40 percent of the forensic science shown on *CSI* does not exist. Carol Henderson, director of the National Clearinghouse for Science, Technology and the Law at Stetson University College of Law, told a publication of that institution that jurors are "sometimes disappointed if some of the new technologies that they think exist are not used." Similarly, working investigators cannot be quite as precise as their counterparts on the screen. A TV character may analyze an unknown sample on an instrument with flashing screens and blinking lights and get the result "Maybelline lipstick, Color 42, Batch A-439." The same character may then interrogate a witness and declare, "We know the victim was with you because we identified her lipstick on your collar." In real life, answers are seldom that definite, and the forensic investigator probably would not confront a suspect directly. This mismatch between fiction and reality can have bizarre consequences: A Knoxville, Tenn., police officer reported, "I had a victim of a car robbery, and he saw a red fiber in the back of his car. He said he wanted me to run tests to find out what it was from, what retail store that object was purchased at, and what credit card was used."

Groaning under the Load

DESPITE NOT HAVING all the tools of television's CSI teams, forensic scientists do have advanced technologies that are getting more sophisticated all the time. Initial DNA-testing methods in the late 1980s required samples the size of a quarter; current methods analyze nanograms. The news routinely reports the solution of a cold case, a suspect excluded or a wrongful conviction overturned through advanced forensic technology. Databases of DNA, fingerprints and firearms ammunition have become important resources that can link offenders to multiple crimes.

Nevertheless, far from being freed to work telegenic miracles, many labs are struggling under the increasing demands they face. As police investigators gain appreciation for the advantages of science and also feel pressure to collect increasing amounts of evidence, they are submitting more material from more cases for forensic analysis. Police detectives who at one time might have gathered five pieces of evidence from a crime scene say they are collecting 50 to 400 today. In 1989 Virginia labs processed only a few dozen cases. The number of cases being submitted this year has ballooned into the thousands. Of course, not every item at a crime scene can or should be collected for testing. The remote chance of an item being significant has to be weighed against the burden of backlogged cases. But social, professional and political pressures based on unrealistic expectations engendered by television mean that if an officer brings in a bag filled with cigarette butts, fast-food wrappers and other trash, chances are good that most of the items will be scheduled for analysis.

And all that work will have to be done, in many cases, by already overloaded staffs. For example, the state of Massachusetts has 6.3 million people outside of Boston and eight DNA analysts for that region. (Boston has three analysts of its own.) New York City has eight million people and 80 DNA analysts. But Massachusetts and New York City have similar rates of violent crime (469.4 versus 483.3 per 100,000), which is the kind of crime most likely to involve DNA evidence. Massachusetts,

Who will analyze all the evidence?

COURTESY OF WASHINGTON STATE POLICE LABORATORY

STORING AND TRACKING MILLIONS of items of evidence pose significant challenges to law-enforcement agencies and forensic laboratories.

CSI MULTITASKER Catherine Willows combines roles of real-life investigators.

Fictional TV investigators

like many other states, thus appears to be woefully understaffed. Thankfully, the state has recognized this imbalance and has authorized the hiring of more forensic DNA analysts.

A consequence of the new trends, then, is exacerbation of the already disturbing backlog problem. A study recently published by the Department of Justice's Bureau of Justice Statistics found that at the end of 2002 (the latest available data), more than half a million cases were backlogged in forensic labs, despite the fact that tests were being processed at or above 90 percent of the expected completion rate. To achieve a 30-day turnaround time for the requests of that year, the study estimated a need for another 1,900 full-time employees. Another Justice Department study showed that the 50 largest forensic laboratories received more than 1.2 million requests for services in 2002: the backlog of cases for these facilities had doubled in the course of one year. And these increases have happened even though crime rates have fallen since 1994.

Another side effect of the increased gathering of physical evidence is the need to store it for various lengths of time, depending on local, state or federal laws. Challenges for storing evidence include having the computers, software and personnel to track the evidence; having the equipment to safely stow biological evidence, such as DNA; and having adequate warehouse space for physical evidence. In many jurisdictions, evidence held past a certain length of time may be destroyed or returned. Storage can be a critical issue in old or cold cases—the Innocence Project at the Benjamin N. Cardozo Law School in New York City has found that the evidence no longer exists in 75 percent of its investigations into potentially wrongful convictions.

Just keeping track of the evidence that does exist can be problematic: a 2003 study by the American Society of Crime Laboratory Directors indicated that more than a quarter of American forensic laboratories did not have the computers they needed to track evidence. Mark Dale, director of the Northeast Regional Forensic Institute at the University at Albany and former director of the New York Police Department Laboratory, estimates that more than 10,000 additional forensic scientists will be needed over the next decade to address these various issues. In addition, appropriate modernization of facilities will cost $1.3 billion, and new instruments will require an investment of greater than $285 million.

The Effect on Campus

ON THE POSITIVE SIDE, through *CSI* and its siblings, the public has developed a fascination with and respect for science as an exciting and important

THE AUTHOR

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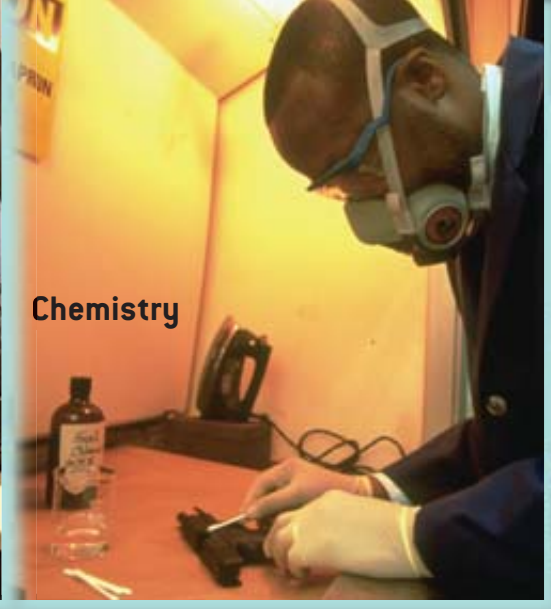


often have expertise in multiple areas of specialization.

MATT YORK *AP Photo (interrogator)*; STEVE LISS *Corbis/Sygma (chemistry)*; ANNA CLOPET *Corbis (DNA analysis)*

profession unseen since the Apollo space program. Enrollment in forensic science educational programs across the U.S. is exploding. For example, the forensic program at Honolulu's Chaminade University went from 15 students to 100 in four years. At my institution, West Virginia University, the forensic and investigative sciences program has grown from four graduates in 2000 to currently being the third largest major on campus, with more than 500 students in the program.

The growth of existing programs and the advent of new ones have been such that the National Institute of Justice, in collaboration with West Virginia University, produced a special report, *Education and Training in Forensic Science: A Guide for Forensic Science Laboratories, Educational Institutions and Students*. The report formed the basis for an accreditation commission under the American Academy of Forensic Sciences. As of this past January, 11 programs had received provisional, conditional or full accreditation.

CSI's popularity may have also affected the demographics of forensic science. In the 1990s women and minorities were underrepresented as leads in television series with a scientific theme; the current slate of CSI dramas, however, has generally improved this representation. Women are now in the majority in forensic science educational programs in the U.S. and in much of the profession. Two thirds of forensic science laboratory management personnel are currently male, a figure sure to decrease as the newer women workers advance.

The best result of public interest in forensics, though, would be increased investment in forensics research. In the past, most research was conducted in police laboratories working on specific, case-related questions. But for technologies to advance markedly, testing is needed in the controlled environment of the academic laboratory. Such labs could investigate questions that clearly require more research. For example, recent legal challenges have called into question the long-held assumption of the absolute uniqueness of fingerprints, tool marks, bite marks, bullet striations and handwriting matches.

As forensic science is increasingly relied on, it must become more reliable: a recent National Institute of Justice report to Congress stated that basic research is needed into the scientific underpinning of impression evidence, such as tire marks or footprints; standards for document authentication; and firearms and tool-mark examination. The report also recommended that the federal government sponsor research to validate forensic science disciplines, addressing basic principles, error rates and standards of procedure. Clearly, more funding for such research would be beneficial: one must wonder why the U.S. spent a mere $7 million this fiscal year for basic forensic science research through the National Institute of Justice when $123 million was spent on alternative medicine through the National Institutes of Health.

One of the most fundamental obligations of any democratic government to its citizens is to ensure public safety in a just manner. Forensic science is an integral and critical part of the criminal justice process. In the 21st century properly educated, well-equipped, fully staffed forensic science laboratories are essential to the fulfillment of that obligation. The popular interest in forensic science is at an all-time high, as are the challenges to the veracity of forensic science methods and capacities. Even if no so-called CSI effect exists in the courtroom, the real effect is the realization of the need for the advancement of forensic science laboratories and research. SA

MORE TO EXPLORE

The CSI Effect: Fake TV and Its Impact on Jurors in Criminal Cases. Karin H. Cather in *The Prosecutor,* Vol. 38, No. 2; March/April 2004.

Public Forensic Laboratory Budget Issues. Perry M. Koussiafes in *Forensic Science Communications,* Vol. 6, No. 3; July 2004. Available at **www.fbi.gov**

Trace Evidence Analysis: More Cases in Forensic Microscopy and Mute Witnesses. Max M. Houck. Elsevier/Academic Press, 2004.

Fundamentals of Forensic Science. Max M. Houck and Jay A. Siegel. Elsevier/Academic Press, 2006.

For updates on forensic science legislation, visit: **www.crimelabproject.com/**

A FAREWELL TO KEYWORDS

By Gary Stix

A picture may be worth a kilo of words, but typing into Google Image the single word "rosebud" returns about 60,000 pictures.

The power of an individual keyword is both good and bad. It can find a virtual stack of Web pages. But it is unable to differentiate between the flower in bloom and legendary film director Orson Welles's scowl. Ideally, an Internet user should be able to use the likeness of a rose to tell a search engine to find others like it.

The idea of using images to search images is not new. About a decade ago software emerged that could match one photograph to another or take a graphic representation—say, a large red dot on a green background—and track down pictures of a rose in a database [see "Finding Pictures on the Web," by Gary Stix; SCIENTIFIC AMERICAN, March 1997]. This type of search—which collectively came to be known as content-based image retrieval—has progressed only slowly beyond the graduate-project stage.

Major search engines have yet to implement this form of image retrieval to mill through their indexes of images, the largest of which contain links to billions of photographs and graphics. Still, research by both industry and academia has achieved some intriguing advances of late that sidestep the need for keywords—and address the challenge of analyzing the content of images in large databases.

Dial and Shoot

THE RECENT PROLIFERATION of Web-enabled camera phones and PDAs—and the still persistent difficulty of using thumb and forefingers on undersize keypads to input keywords—opens opportunities for those who can find a way to pull results off the Web by sending a query in the form of an image captured by a phone's camera.

The reigning obsession with search technology has elicited new ways of using images to track down information on the Web

Microsoft Research has identified a list of uses for a cell phone camera as a Web input device. A prospective buyer interested in information about a new stove could photograph the appliance in a department store and relay the image as a file to a server that can return to the user's cell phone a Web page from *Consumer Reports*. A picture of the *Mona Lisa* could yield an art history page. A shot of a nearby landmark building might produce a map showing the user's present location. "It brings the Web closer to the real world," says Larry Zitnick, a member of Microsoft Research's Redmond, Wash., laboratory. "It's kind of like having the Web look at what you're looking at." Another group at Microsoft's Asian research laboratory in Beijing works on a similar project, and eventually the two efforts could merge.

Among the challenges faced by these investigators is finding ways to create search algorithms powerful enough to comb through the image content of the entire Web. Zitnick and his colleagues have demonstrated a system that can take a "query" photograph captured from a cell phone camera and then send it to a server that matches it with already captured, or "training," images, each of which provides a link to the relevant Web site. Zitnick wants to craft a database populated with the billions of images captured by a search engine, such as MSN Search. Currently the system, which still lacks a name, can perform retrievals from among tens of thousands of images in two to four seconds, an interval that needs to be reduced to a fraction of a second.

AARON GOODMAN

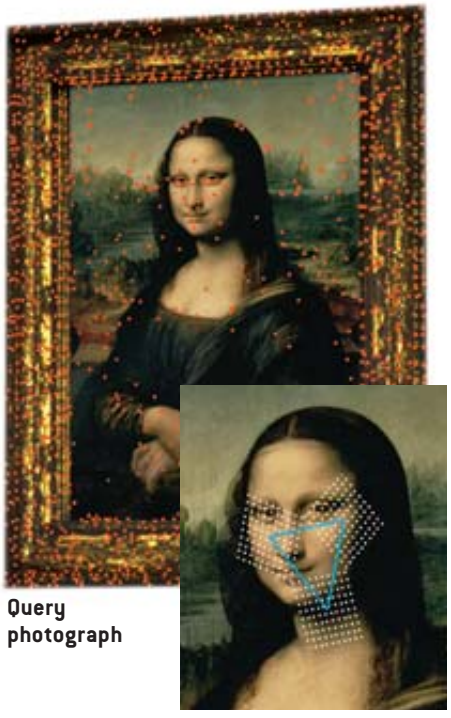
SNAPSHOTS taken by a cell phone camera may be used to search the Web.

SEARCHING THE WEB BY PHOTO AND PHONE

In a project at Microsoft Research, a photograph snapped by a cell phone camera is used to look on the Web for matching images or information related to the picture.

1 A search begins when someone snaps a picture with a cell phone camera—a shot of the *Mona Lisa,* for instance—and sends the image to an image server via the Web. The server contains training images—copies of photographs gathered from all over the Web, which have been indexed and saved for matching with query images.

2 To speed the search for a match, the image server tries to find "features," dark areas surrounded by light areas, or vice versa (*red dots*). Each feature forms the center of a square patch of pixels (often a 10-by-10 grid), and some of these features are grouped into sets of three that are a specified distance from one another (*as indicated by blue triangle at right*).



Query photograph

To prepare the system, a computer analyzes a training photograph from a Web page for distinctive features of the image that consist of dark areas surrounded by light areas, or vice versa. Some of the features are bunched into groups of three, based on a calculation of how far one is from the other. Each feature represents the center point of a 10-by-10 square patch of pixels. The grouping of three patches is called a triplet, some 5,000 of which are typically identified in a training image. The location of each triplet is stored as an entry in a huge table that is designed to minimize the amount of computation required to search any individual entry. A query image is also separated into triplets; these triplets are matched with those in the table, and then Web pages containing a matched image are sent to the user's cell phone [*see box on these two pages*]. The investigators chose triplets as the basis of comparison instead of single patches because a triplet encompasses a larger area of the overall image, a property that should reduce the risk of generating an erroneous match between a query and a training image.

As with most image-recognition applications, performance is far from perfect, with detection rates averaging about 80 percent. Detection of flat objects that have highly detailed surfaces—a description that fits many consumer products—has a better rate, however. And if performance constraints are loosened to allow for most people's expectation of a Web search—retrieval of not one but several links—the detection rate can be enhanced still further. Although an image search may return more than one Web site, its ability to match specific photographic features between the query images and the training images—a door, for instance—means that the number of images returned to the user would be fewer and better targeted than the number found in the usual text search.

To expand the range of searchable objects, Zitnick wants to improve the system's ability to find mirrorlike surfaces or things with complex three-dimensional shapes, such as plants. The system, nonetheless, will never encompass the full range of visually detectable objects. "It's going to be useful for certain things, and for others, it's going to fail miserably," he says.

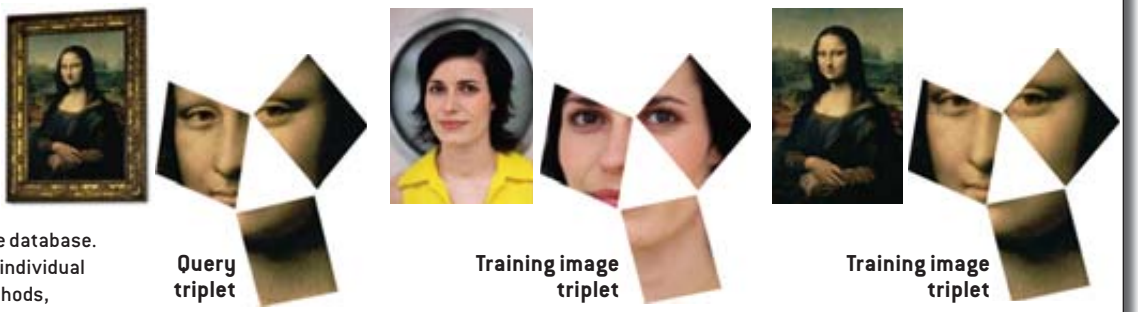
Looking for Cheesecake

THE CHALLENGE of perusing the vast expanse of the Web for images remains a preoccupation for Google as well. The search-engine powerhouse does not let on the specifics of future plans, but its researchers have started to present papers on their doings at technical conferences. Full image-to-image matching or recognizing an individual object, such as a chair, takes a backseat, in the company's view, to the more pragmatic issue of how to provide simple generalizations about the content of billions of images. Is, for instance, that pinkish color in a particular photograph that of naked flesh or a snapshot of an Art Deco structure in Miami's South Beach? From the Web's earliest days, image-searching efforts have been plagued by the risk of having unwanted pornography turn up in the results.

"We want to make sure that images are classified as containing adult content by using not only keywords and URLs but also image analysis," says Google researcher Shumeet Baluja. The Mountain View, Calif., company has developed—and actually implemented—a system that can differentiate with middling accuracy pictures that are naughty or nice, according to a paper from one conference. Eschewing shape-classification methods that can take from seconds to minutes

AARON GOODMAN (*hand holding cell phone*); LOUVRE, PARIS, FRANCE/GIRAUDON/BRIDGEMAN ART LIBRARY (*Mona Lisa painting*)

3 Group of three patches—called triplets—from the camera's query photograph is compared with triplets from training images to locate a match. An average of 5,000 triplets are collected for each query photograph and compared with all triplets from training images in the database. Comparing triplets, instead of the individual patches used by other search methods, enhances the likelihood of finding a match.



4 A mathematical algorithm ensures that all patches are depicted at the same scale and in the same orientation. When the triplet comparisons identify a match with a training image, the correspondence will be verified as correct if a set of pixels at the center points of the picture match (*green squares*).

5 Once a match is verified, a Web page on which the training image appears is sent to the user's cell phone.

M. THOMSEN *zefa/Corbis (head shot of woman)*

to process, researchers have reported that they can detect half the adult pics among a test set of 1.5 billion thumbnail images during an eight-hour interval using 2,500 computers—a rate of about 20 images a second. A Web surfer does not have to wait eight hours: with such a tool, the user who wants to screen out porn simply instructs the search engine to omit the links that have already been tagged for questionable content.

The system works by combining modules for detecting 27 features, among them skin color, connected pixels (signifying a visual continuum of color that could represent flesh, for instance), skin texture and the presence of a face. Skin comprises a lot of colors, and many everyday objects assume the colors of flesh. One component of the detector looks for an object—perhaps a building—that often has the appearance of skin but can be distinguished by specific features, such as long, straight edges. The pictures turned up and flagged by the system can be filtered out. These tagged images serve as one component of Google's "image-safe search," a user-selected option in Google Images that also analyzes URLs and other text content to make decisions on what is inappropriate.

To be useful for Web-wide image perusal, any component algorithm in a larger search module would, above all, have to be fast and efficient. Two of the Google researchers on the adult-filtering project—Baluja and Henry Rowley—have dramatically reduced the amount of information required to determine the sex or orientation of a face. The resulting acceleration in processing time is important because users look for people perhaps more than any other type of image. Google would like a better way to determine whether Britney Spears or Tony Blair is really in a picture. It has crafted a variety of image filters—one of which tries to identify a person's gender. Others examine a person's clothes or age.

The gender and facial-pose filters crafted by Baluja and Rowley are created by measuring the intensity (lightness and darkness) of pairs of pixels within a 20-by-20 patch taken from an image that includes the face of a man or a woman in one case and distinct facial poses in another. A separate algorithm first makes an educated guess as to the location of a face in an image before the pose-determination filter does its job. The filter has been trained so that it need examine only 150 pairs of pixels in a single 20-by-20 patch in the facial area before predicting with 99 percent accuracy whether a face is in one of five poses (frontal, right-half profile, and so on). Although they are suited to a variety of uses, both the gender and face-pose classifiers are being incorporated into Google's image-safe search feature.

The Google team tends to downplay technical virtuosity for its own sake. "We take a pragmatic approach to research," comments Peter Norvig, the company's engineering search quality director. "We prefer to finesse a problem if we can. We don't have to solve the object-recognition problem 100 percent." Given the density of information in any photograph, the key to success for an image-searching tool is to make each pixel count. SA

MORE TO EXPLORE

Boosting Sex Identification Performance. Shumeet Baluja and Henry Rowley. Innovative Applications of Artificial Intelligence, 2005.

Large Scale Image-Based Adult-Content Filtering. Henry A. Rowley, Yushi Jing and Shumeet Baluja. International Conference on Computer Vision Theory and Applications, 2006.

Larry Zitnick's home page: **http://research.microsoft.com/~larryz/**

VASCULAR STENTS

Expanding Use

Implantation of stents—mesh cylinders that widen clogged arteries—is growing so fast that some doctors say the procedure is overused. Yet the inserts have been evolving for 20 years, proponents note, and represent an alternative to more invasive open surgery.

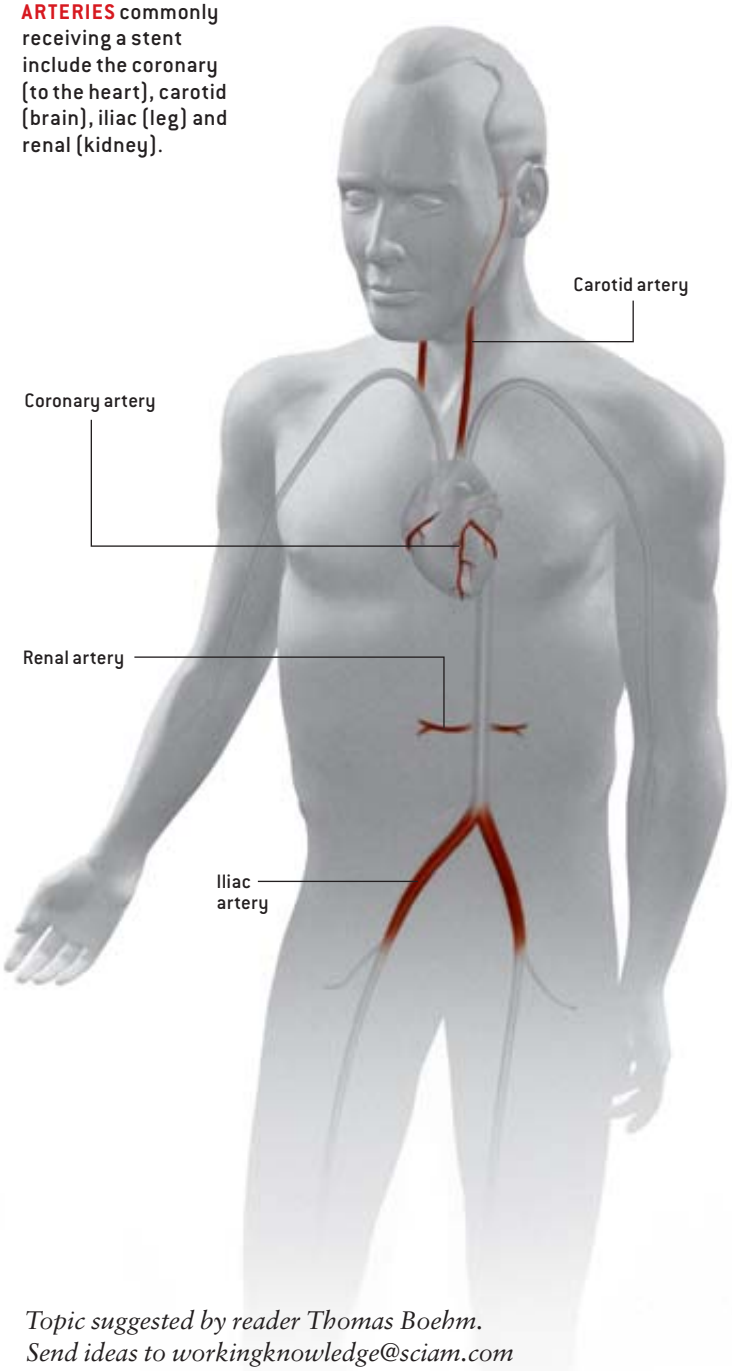
For decades, coronary patients whose arteries had been narrowed by accumulated plaque underwent open-heart surgery; a section of healthy artery or vein was sewn in as a bypass around the compromised vessel. Similar measures were taken with patients who had blocked arteries elsewhere, or the artery was cut open and the plaque scraped out. The advent of balloon angioplasty reduced the intrusiveness for certain patients; a balloon was fed along a catheter to the blockage, then expanded to crack and compress the plaque, leaving a wider conduit for blood flow. Yet arteries often renarrowed if walls recoiled or if fibrous tissue grew.

Stents are put in place with a similar balloon procedure, but they keep the artery open [*see illustrations on opposite page*]. The leading targets by far are the coronary arteries that feed blood to heart muscle, but other vessels are increasingly being serviced.

The first stents, approved in the early 1990s, were stainless steel. Later, self-expanding stents made from a "shape-memory" nickel-titanium alloy appeared. Stents coated with polymers that time-release drugs to prevent tissue ingrowth were approved in the U.S. in 2003 and broadened use. Critics say doctors underestimate surgical risks and are too quick to insert them. But Michael Jaff, medical director of the Massachusetts General Hospital Vascular Center in Boston, says "coronary stents have revolutionized patient care." Although about 30 percent of heart patients experienced renarrowing with a plain stent, the rate with medicated stents is below 10 percent. "There is solid science and massive study" proving that drug-eluting coronary stents are superior, Jaff notes. For other applications, "stents still look favorable, but there is less science to prove it."

Manufacturers are moving full speed ahead. Brian Firth, vice president for medical affairs at Cordis Corporation, says his company is developing stents for the superficial femoral artery in the thigh and the popliteal artery below the knee. "Stents are going up, and that trend is likely to continue," he states. —*Mark Fischetti*

ARTERIES commonly receiving a stent include the coronary (to the heart), carotid (brain), iliac (leg) and renal (kidney).



KEN EWARD *BioGrafx*

Topic suggested by reader Thomas Boehm. Send ideas to workingknowledge@sciam.com

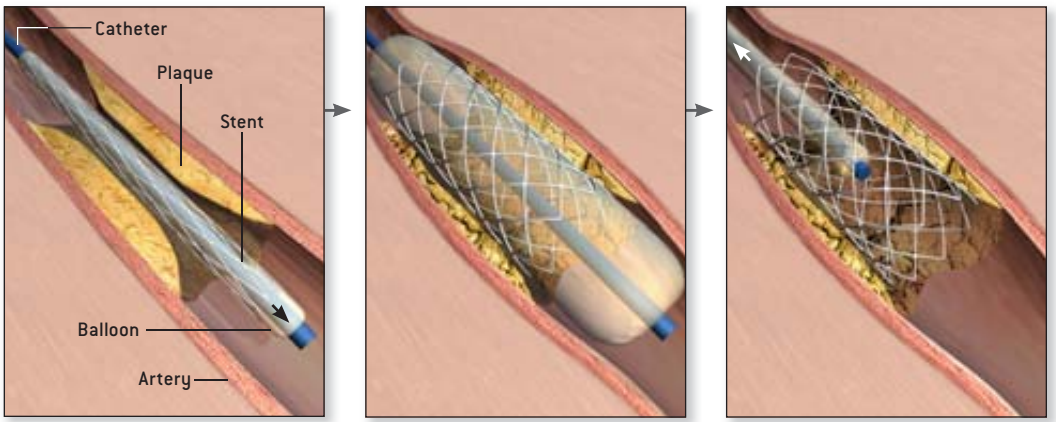
DID YOU KNOW...

- PLAQUE CATCHER: Stent procedures crack plaque, which could release bits of debris. Most organs tolerate the crumbs with little clinical effect, according to L. Nelson Hopkins, chair of the neurosurgery department at the State University of New York at Buffalo. But debris that lodges in an artery to the brain could cause a stroke. Several companies have therefore devised filters for carotid stenting that catch plaque [*see illustrations below*]. In some cases, balloons are used to shut down blood flow during the procedure, and suction catheters remove debris before normal flow is restored.

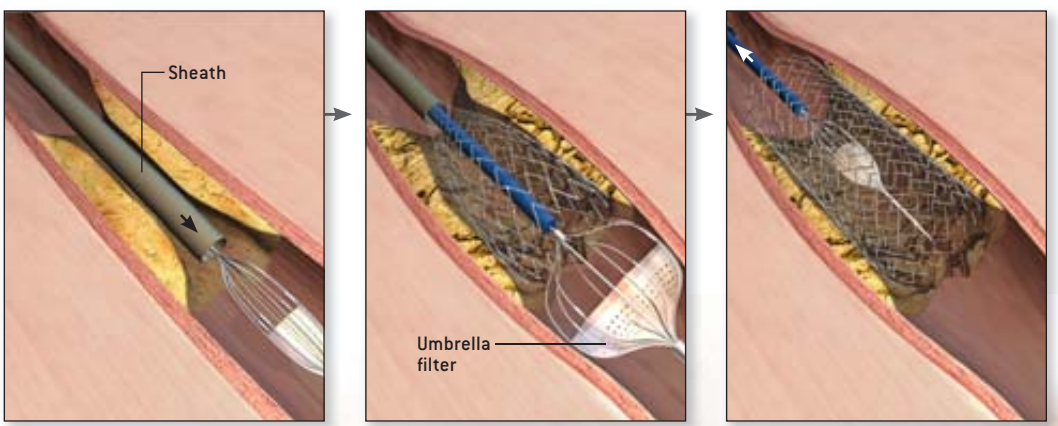
- CLOT NOT: Blood clots can form at any surgical site or around any implanted device. Stent patients are typically put on a medication that blocks platelets from coagulating, for a month to a year, and aspirin, the mainstay antiplatelet drug.

- ONE SIZE DOES NOT FIT ALL: Stents are carefully sized to a patient's target artery, determined initially with imaging and then during the procedure itself. Most coronary arteries are two to four millimeters in diameter, carotid arteries four to six millimeters. Balloon-expandable stents are preferred for coronary operations because their final width can be precisely set with the balloon. Self-expanding stents are more crush-resistant and are therefore favored for carotid applications because those arteries lie close to the skin, where a regular stent could be dangerously narrowed by external pressure.

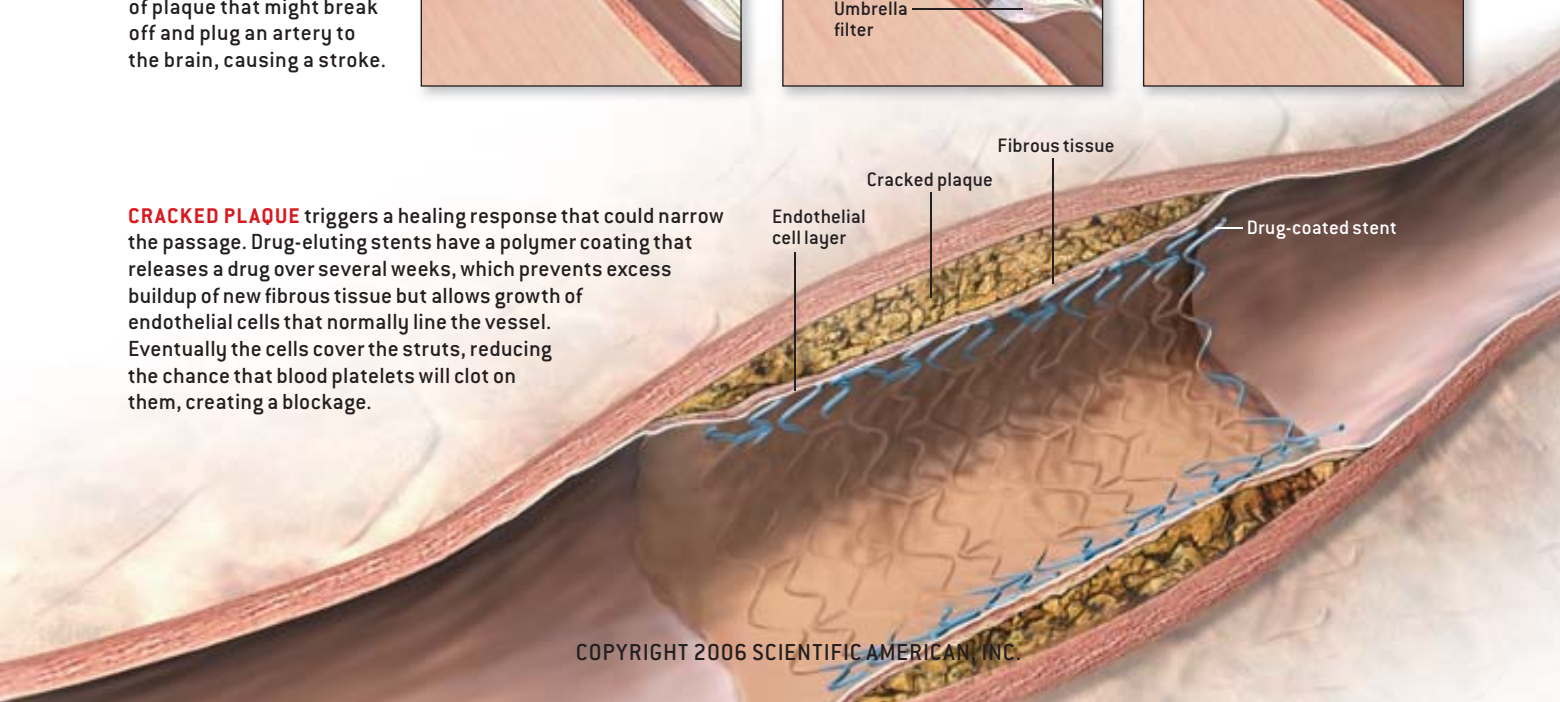
BALLOON-EXPANDABLE stents, used in most coronary arteries, are crimped onto a balloon and fed by a catheter to the site. The balloon is inflated (perhaps several times), opening the stent and cracking and compressing plaque. The balloon is then deflated and withdrawn.



SELF-EXPANDING stents are used in most carotid applications. The stent is squeezed inside a tight sheath. As the sheath is retracted, the stent expands. A balloon may be applied later to further embed the plaque and stent. An umbrella filter may be used during procedures to catch bits of plaque that might break off and plug an artery to the brain, causing a stroke.



CRACKED PLAQUE triggers a healing response that could narrow the passage. Drug-eluting stents have a polymer coating that releases a drug over several weeks, which prevents excess buildup of new fibrous tissue but allows growth of endothelial cells that normally line the vessel. Eventually the cells cover the struts, reducing the chance that blood platelets will clot on them, creating a blockage.



Standing Up to Dance and Sing

HOW WE BECAME HOMINID, THEN HUMAN **BY BLAKE EDGAR**

THE FIRST HUMAN: THE RACE TO DISCOVER OUR EARLIEST ANCESTORS
by Ann Gibbons
Doubleday, 2006 ($26)

THE SINGING NEANDERTHALS: THE ORIGINS OF MUSIC, LANGUAGE, MIND, AND BODY
by Steven Mithen
Harvard University Press, 2006 ($25.95)

In the early 1980s, when I studied anthropology, human fossils older than about four million years amounted to a few inscrutable scraps. Just as accumulating molecular evidence from humans and apes pointed to the period between four million to six million years ago as the likely time frame for when we and they last shared a common ancestor, the fossil side of the story abruptly ended. What a difference a decade makes.

With the discovery in 1992 and 1993 of 17 specimens from Ethiopia later described as the new genus and species *Ardipithecus ramidus*, an early fossil record began to emerge. New fossils, both slightly younger and much older than the 4.4-million-year-old *ramidus* remains, soon followed. And with new fossils came new names and competing claims for being the oldest demonstrable human ancestor, or hominid. Besides *Ardipithecus*, *Orrorin* (in 2000) and *Sahelanthropus* (in 2002) sought their place on the hominid roll call with the more familiar fossils of *Australopithecus* and *Homo*. As veteran *Science* magazine correspondent Ann Gibbons quips, "The human story was beginning to look as complicated as a Tolstoy novel, with new characters appearing unexpectedly as the book of life unfolded."

In *The First Human*, Gibbons provides the first popular account of these intriguing discoveries and of rivalry and collaboration among the discoverers. An engrossing, fast-paced read, her story unfolds in many remote and rugged locales, from the Middle Awash of Ethiopia to the Tugen Hills of Kenya and the Djurab Desert of Chad.

Gibbons tells of hard-driven, dedicated teams contending with extreme heat, blowing sand, illness and other hazards of fieldwork in Africa, where success demands years, or decades, of persistence. After all, hominids may not have been common creatures in their day, and only fortuitous circumstances of gentle, rapid burial in suitable sediments kept a carcass from being a carnivore's meal, allowing it perchance to fossilize.

Gibbons seems as interested—if not more so—in personalities and politics as in the identities and significance of her protagonists' fossils. She is not the first to recognize that conflict as well as camaraderie accompanies the quest for human origins, and the scientists she portrays do possess the stuff of dramatic characters. There is the meticulous, mercurial paleontologist Tim White, co-leader of an international team with an unparalleled track record of spectacular discoveries, from the oldest modern human skull to one of the oldest human ancestors. And zoologist Meave Leakey, who has stepped out from the shadow of the most famous surname in human origins research to make singular contributions of her own. And Michel Brunet, a French expert on ancient hoofed mammals, inspired by Charles Darwin and Louis Leakey to pursue hominids.

Brunet bucked the odds by not looking for fossils in the celebrated cradle of humankind, East Africa's Rift Valley. He went to Chad, which hinted at its human fossil potential as early as 1961. Another hominid would not come to light there until 1995, but Brunet's team found that australopithecine jawbone and then explored much older sites. In 2001 a Chadian student on Brunet's team unearthed the cranium nicknamed "Toumaï." Formally named *Sahelan-*

OLDEST KNOWN HUMAN ANCESTOR was found in Chad in 2001. French paleontologist Michel Brunet (*center*) examines the fossil with Chadian colleagues Ahounta Djimdoumalbaye (*right*) and Mackaye Hassane Taisso, who found the skull.

PATRICK ROBERT *Corbis*

thropus tchadensis, it is currently the oldest known hominid skull and pushes the emergence of our evolutionary line as far back as seven million years ago—as Gibbons writes, "so ancient that Brunet said that Toumaï could 'touch with its finger' the last ancestor shared by humans and chimpanzees."

Early hominids largely looked and acted like apes. With one key difference: they stood and walked upright. This change in posture and mobility had profound implications for our evolution and "may have initiated the greatest musical revolution in human history." That is the ironic conclusion of Reading University archaeologist Steven Mithen, who continues his search for the essence of human behavior in his latest book, *The Singing Neanderthals*.

Particularly within the past two million years, early humans refined the ability to walk, run and jump. With big brains and bottoms, spring-loaded legs, and sophisticated sensorimotor control, they could also dance, Mithen argues, if not sing.

With a fascinating blend of neurology, anatomy, archaeology, developmental psychology and musicology, Mithen seeks the source of our propensity for making music, a universal human feature that has been strangely neglected compared with the origin of language. Darwin, naturally, touched on the topic, positing that unable to woo with words, our ancestors "endeavored to charm each other with musical notes and rhythm."

Essential to both bipedal locomotion and music, rhythm plays a pivotal role as well in language. Music and language share other intriguing attributes. Both can move or manipulate us. Both can be spoken, written or gestured. Both possess hierarchical structure. And both seem to activate multiple regions of our brains.

Mithen takes on linguist Steven Pinker's assertion that music is just an entertaining invention, not a crucial biological adaptation like language. He carefully constructs and deliberately lays out his argument that music's evolution holds the key to language.

Yes, language ultimately supplanted music's role in emotional expression and became our means of conveying ideas and information. Music, however, still stirs our most basic emotions. Until the relatively recent advent of syntactic language in modern humans, Mithen maintains, it was music that helped hominids find a mate, soothe a child, cheer a companion or provide a group's social glue.

Like language, much of music does not fossilize. We have elegant bird-bone flutes as old as 36,000 years from sites in Germany and France—unequivocal musical instruments. Beyond that, one is hard-pressed to display tangible evidence of music's role in prehuman society. Mithen must speculate that Neandertals, for instance, strummed stalactites, drummed on mammoth skulls or otherwise made music without leaving a trace. But step inside a cave used by prehistoric people, and it is easy to appreciate its acoustic potential. By drawing data from a diverse range of disciplines, Mithen makes a persuasive case that our ancestors got rhythm and brings to prehistory a sense of sound. SA

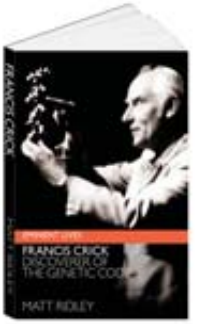
Blake Edgar is a science editor and writer. He is co-author of From Lucy to Language, *forthcoming in a revised edition from Simon & Schuster, and of* The Dawn of Human Culture *(John Wiley & Sons, 2002).*

THE EDITORS **RECOMMEND**

FRANCIS CRICK: DISCOVERER OF THE GENETIC CODE

by Matt Ridley. Atlas Books/HarperCollins, 2006 ($19.95)

"Because of the momentous nature of his discovery Francis Crick must eventually be bracketed with Galileo, Darwin, and Einstein as one of the great scientists of all times," Ridley writes in this first biography of the co-discoverer of the structure of DNA. "He trained his mind to be exquisitely good at solving nature's puzzles using logic, had the courage to take on the biggest problems, and threw himself exuberantly into the task, never letting prejudice stand in the way of reason. Throughout, he stayed true to himself: ebullient, loquacious, charming, sceptical, tenacious."

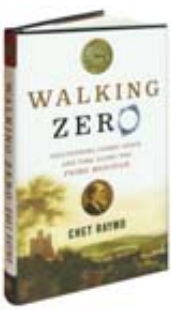


Ridley, a well-known British science writer, unfolds Crick's life from its modest beginnings on "a middle-class street in a middle-size town in the… English Midlands" through his uninspired physics career (six years designing magnetic mines for the Royal Navy) to his sudden switch into biology at the age of 31, when "with the bravado of a bankrupt gambler," he tried to decide what he would solve first, "the secret of the brain or the secret of life." In a stunning combination of visual and intellectual imagination, he and James Watson figured out the double helix of DNA, the secret of life. At age 60 he immigrated to California and focused his logic and energy on the nature of consciousness. He died in 2004, at 88, still working on this second quest.

WALKING ZERO: DISCOVERING COSMIC SPACE AND TIME ALONG THE PRIME MERIDIAN

by Chet Raymo. Walker & Company, 2006 ($22.95)

The story of the prime meridian is in itself fascinating: in 1884 an international agreement fixed a meridian of zero longitude and standard time through southeast England. But Raymo, a physicist and science writer who wrote a popular weekly column for the *Boston Globe,* goes beyond this tale. He uses an actual walk along the meridian as a "thread on which to hang" a history of astronomy, geology and paleontology. Stops at sites near the meridian include Newton's rooms at Cambridge, Darwin's house at Downe, the infamous town of Piltdown, and the place where the first dinosaur fossils were discovered. A walk with this delightful writer is the best exercise a reader could have.



For the Birds

HAWKING INTERESTING AVIANS IN THE URBAN ENVIRONMENT **BY STEVE MIRSKY**

New York City is lousy with birds, and I mean that in a good way: I once counted 20 species in an hour in my backyard in the Bronx, with rufous-sided towhees and American redstarts making cameo appearances beside the usual mourning doves and sparrows. The city is also clearly a human-dominated landscape. So the American Museum of Natural History was a good choice to host a late April conference called "Conserving Birds in Human-Dominated Landscapes." I went because in the Alfred Hitchcock movie *The Birds,* I rooted for the crows. (I also sided with the giant insects in *Starship Troopers*. Although I did back the humans in the *Matrix* movies. Well, in the first one.)

One of the speakers at the conference was Andrew Balmford of the University of Cambridge. In 2003 Balmford was named one of the "Scientific American 50," a celebration of research leaders "who have contributed to the advancement of technology in the realms of science, engineering, commerce and public policy." Balmford was recognized for his work on the economics of habitat preservation. So naturally we talked about inebriation and Pokémon.

Balmford discussed some birds' abilities to prosper among humans. The wood pigeon, for example, seems to have thrived in England by leaving its traditional woodland environment for the fields, where it has switched from a mostly fruit diet to crops (which some farmers aren't cooing about). Some wood pigeons have even taken up residence in towns and cities, where they hang out near bars—because of the great opportunities such establishments afford for the distribution of food directly onto the sidewalk. If you get my drift. (When I mentioned this pigeon propensity to a friend, he asked, "Food that was thrown out?" To which I responded, "Well, not *out*.")

As for the fictional cartoon creatures, in 2002 Balmford and his colleagues published a short report in the

journal *Science* called "Why Conservationists Should Heed Pokémon." His two sons had an interest in the local flora and fauna, whereas most of their friends were much more engaged by Pokémon characters. "And it turns out there is actually a field guide to Pokémon creatures in which you can learn all their different names and all their different attributes," Balmford says, "just like you would about birds of the eastern U.S." Balmford decided to find out which group of creatures most kids knew better: a sampling of the real animals and plants in their area or the Pokémon organisms. You know where this is going.

According to the *Science* paper, "For wildlife, mean identification success rose from 32 percent at age 4 to 53 percent at age 8 and then fell slightly; for Pokémon, it rose from 7 percent at age 4 to 78 percent by age 8, with children aged 8 and above typically identifying Pokémon 'species' substantially better than organisms such as oak trees or badgers." Says Balmford of that finding, "We obviously felt that was rather sad. Sad and rather worrying, but it also maybe can give us some food for thought about how we market natural history to kids to capture their imaginations."

Such inspiration should be possible, because birds really are incredibly charismatic. Here's one possible sample pitch for the get-kids-into-birds campaign: Now, I admit to almost complete ignorance about Pokémon characters, which I would imagine do incredible things, like shoot fire out of their blowholes or eat rocks or design a high-mileage, low-emission SUV or other magical things. But birds can do some pretty amazing things themselves. Some can outrun thoroughbred horses, others can pluck fish out of raging rivers with their feet, a few can see a rabbit a mile away. And of course, the big one—they fly! In fact, numerous residents of Metropolis, when getting their first glimpse of no less a personage than Superman, shouted, "Look, up in the sky! It's a bird!" SA

ILLUSTRATION BY MATT COLLINS; PHOTOGRAPH BY FRANK VERONSKY

Q Why is most of the ground brown?

Steven Allison, an ecology researcher at the University of California, Irvine, provides this answer:

Large amounts of carbon in inorganic forms absorb most visible wavelengths of light and give soils their characteristic dark brown shades. (When carbon inputs to the soil are low because of erosion or lack of plant growth, we see the red, yellow or gray hues of the underlying minerals.) The more interesting question then is: Why does soil have so much carbon?

Soils around the globe hold 1,500 to 2,300 petagrams—or as much as two quintillion grams—of carbon. That is two to three times the amount of carbon stored in the world's plants. A large fraction of this soil carbon is ancient—hundreds to thousands of years old. How is that possible when so many species of bacteria, fungi and other invertebrates decompose and consume soil carbon?

After plants die, decomposers assimilate some of their carbon and respire the remainder as carbon dioxide. When decomposers themselves die, their carbon also can be consumed and respired by other decomposers.

Several factors, however, may block the action of decomposers. Many of the microorganisms secrete enzymes to break organic compounds into small molecules, which they can then take up. But they cannot easily degrade all forms of soil carbon. Material from the cell walls of dead microbes reacts with other carbon compounds in the soil to form complex polymers. Many of these polymers are called humic compounds, and they build up in soil because their chemical structures can withstand enzymatic attacks. Along with similar molecules called polyphenols, humic compounds can bind to and inactivate the very enzymes that could potentially degrade them.

Other environmental factors diminish the efficiency of microbial enzymes. If soils are nitrogen-poor, microbes may not have the nutrients available to build enzymes. And because some enzymes require oxygen as a substrate, anoxic conditions (as in waterlogged bogs or peat lands) often cause soil carbon to accumulate.

Q Why do rainbows form instead of straight bands of colors? And why do they appear to touch the ground?

—A. Wolpin, Athens, Ga.

Jeff Waldstreicher, a meteorologist with NOAA's National Weather Service, explains:

Sunlight passing through raindrops creates rainbows via a process called refraction. Refraction is the bending of light as it passes from one medium to another. When sunlight hits a raindrop, it does not move as fast through the water as it does through the atmosphere, and consequently it turns a little. The light then turns again as it leaves the raindrop and returns to the air at its original speed. When light hits the rain at just the right angle, it is refracted through a raindrop and into our eyes, causing us to see a rainbow.

Because they have different wavelengths, the various colors of light refract slightly differently when they pass between mediums, which is why rainbows appear as a continuous band of colors with red on top and violet on the bottom.

A typical raindrop is spherical, and so its effect on sunlight is symmetrical about an imagined axis connecting the center of the drop and the sun. Thus, the rainbow is actually a circle centered on the point directly opposite the sun from the observer—the so-called antisolar point. We do not perceive the full circle, because the earth gets in the way. The closer the sun is to the horizon, the more of the circle we see. Right at sunset, we would observe a full semicircle of the rainbow with the top of the arch 42 degrees above the horizon. The higher the sun is in the sky, the less of the arc is visible above the horizon. SA

For a complete text of these and other answers from scientists in diverse fields, visit www.sciam.com/askexpert

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