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ScienceNews

MAGAZINE OF THE SOCIETY FOR SCIENCE & THE PUBLIC ■ AUGUST 2, 2008

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Found! The Last Morgan Silver Dollars

Amazing Discovery Hidden in Midwest Farm Cellar

Indiana. A farmer in America's heartland recently cashed in his long-forgotten savings, hidden away for decades in a dusty crate in his cellar—a hoard of the last Morgan Silver dollars minted by the U.S. Treasury before they ceased production for good, in 1921.

Originally purchased from a local bank for face value, the farmer had tucked them away for his retirement. Now these glittering chunks of nearly uncirculated silver history, are being released to the public by GovMint.com. While they last, you can acquire these brilliant, lustrous silver coins for as low as $29.50 apiece. Twenty-coin Bankers rolls and 10-coin Half Rolls are available.

Originally U.S. Silver Dollars were minted and stored in 1,000-coin canvas bags by the Mint.

Survival Against All Odds

By all rights these silver dollars should have been destroyed decades ago. Government silver melt-downs, including the 1918 Pittman Act, which alone destroyed 270 *million* Morgans, have decimated supplies. Millions more were called in by the government and melted for their silver content between 1921 and 1965. Today private hoards account for virtually all the surviving coins. And of those, only a fraction survive in the Virtually Uncirculated condition so coveted by collectors.

Prized Last Year Coins

These last year 90% pure silver beauties still dazzle with their Mint luster and heft. Weighing in at 26.73 grams and a diameter of 38.1 mm, they are the largest American silver coins ever to circulate. Struck from silver mined from the western Mother Lode, they are the legendary coins that built the West. Master engraver George T. Morgan fashioned a radiant profile of Lady Liberty and a majestic eagle as symbols of our nation's strength and prosperity. Today, the long-gone Morgan silver dollars are among the most sought-after coins in America.

Hot Silver Market, Hot Silver Value

Silver prices have jumped over 140% in the last two years fueling the frenzy among avid collectors, investors, and the 130 million new collectors created by the U.S. Mint's highly successful state quarters program.

Today, the market is hot for Silver coins in any condition. This same 1921 Morgan Silver Dollar currently sells elsewhere in the same grade condition for $55 apiece. But while supplies last you can get this original Virtually Uncirculated 1921 Silver Morgan for as little as $29.50 each, in quantity!

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Silver Trend Chart: Prices based on monthly averages. ©AMS, 2008.

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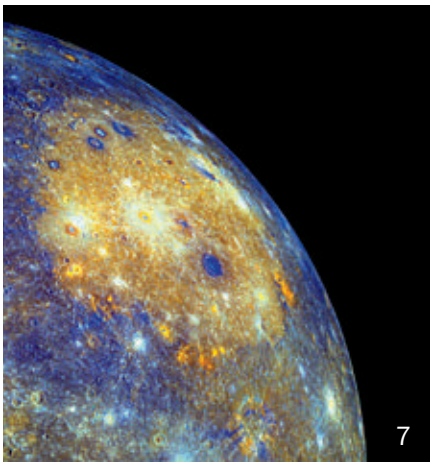
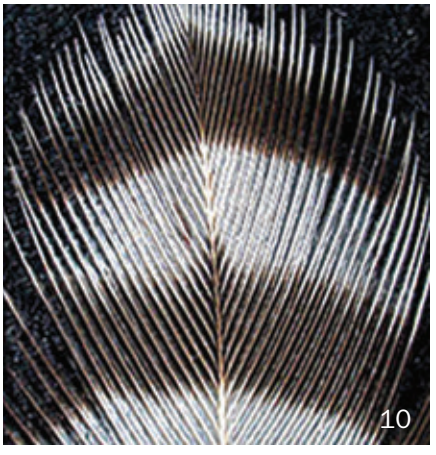
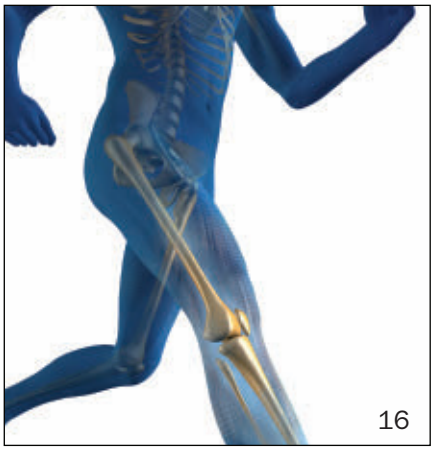
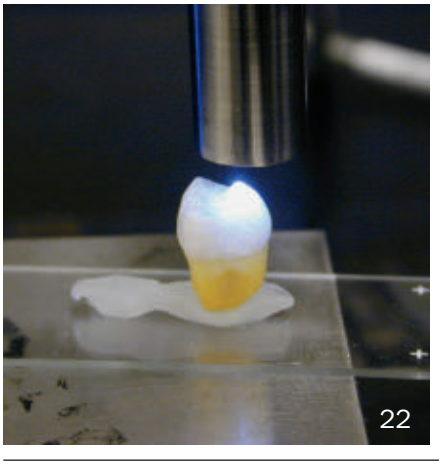








CHOO-SMITH; ISTOCKPHOTO/MPABILD; VINTHER *ET AL.*; AAAS/*SCIENCE*

AUGUST 2, 2008 • VOL. 174 • NO. 3

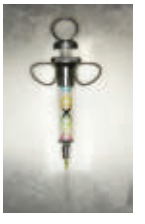
ScienceNews

In the News

Features

Essay

Departments



On the cover:
Inserting foreign genes that boost strength and endurance into DNA may appeal to athletes.
Photos: Getty/Siri Stafford; iStockphoto/luismmolina

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All the science news fit to print, doesn't

If *Science News* observed the journalistic philosophy of *The New York Times*, the magazine would be fatter than the New York City phone book. All the science news that's fit to print would never fit in anything the post office would want to deliver.

So, as it has been for nearly nine decades, *Science News* must be selective. Each issue can deliver only a small sample from the universe of scientific discovery. But at least this sample is not random. Every day our reporters and editors assess the flow of new results from journals, conferences and other sources to identify those that rank highest on the subjective scales of novelty, interest and importance.

All the stories that make the grade, given the limits of writer-power and other resources, appear online at the *Science News* website, www.sciencenews.org. Further selection narrows those down to the stories most worthy of consuming ink and paper.

Even with all that selectivity, you'll still find in *Science News* reports that you aren't likely to come across elsewhere. Few other media outlets, for example, told of the intriguing prospect for determining color patterns on the feathers of long-extinct creatures (Page 10). Some reported on a paper in *Science* about how brain cells called astrocytes pump blood to support mental activity, but few also described similar work reported in *Neuron*, as Tina Hesman Saey does in this issue (Page 5). And you might find a report on feminization of toads by agriculture elsewhere, but Janet Raloff's report (Page 9) appeared first on the *Science News* website, even before the University of Florida issued a press release about it.

As for features, Ashley Yeager's article on Raman spectroscopy (Page 22) exemplifies the kind of reporting from the cutting-edge of scientifically sophisticated research that is hard to find elsewhere.

All this is to say that our goal at *Science News* is keeping people informed about what's going on in science, without the constraints placed on, say, newspaper reporters, who may get to write only those stories that some narrow-minded editor finds interesting. And to offer stories that don't appear elsewhere because they're tough to do, requiring uncommon expertise and reportorial diligence not often available at general media outlets.

Consequently, many important stories from molecular biology, neuroscience, mathematics and physics just don't get reported at most other media outlets. You will find such stories in *Science News*, though. That's our job.

—Tom Siegfried, Editor in Chief

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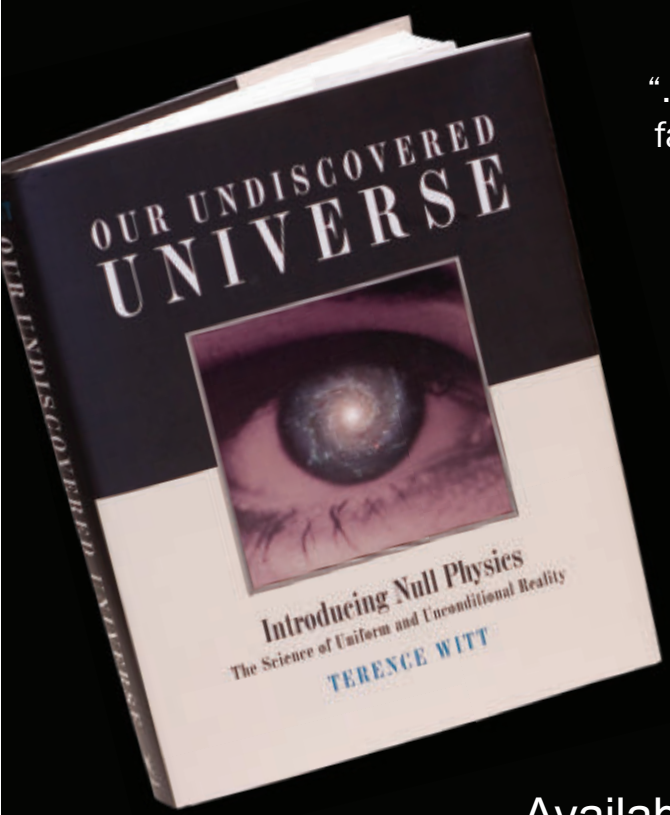

"...a significant contribution to a topic that is still far from settled."

-The Journal of the Royal Astronomical Society of Canada

"*Our Undiscovered Universe* is the mental portrait of a free thinker who is not conformed to the world of traditional physicists, and it has rarely been surpassed in the world of popular science literature."

-Dr. Hamid Rassoul, Associate Dean: College of Sciences; Founding Director of GPL; Professor: PSS, Physics and Space Science, Florida Institute of Technology

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Scientific Observations

"[Dr.] Frankenstein is so incredibly courageous and ambitious as to want to find the secret of life. He works very hard and with great imagination, and he tragically fails.... Sherlock Holmes is the opposite of romantic, and he never fails. He shows the dash of autism that may be as vital for the genius detective as for the genius scientist.... The deeply romantic and the obsessively pedantic are both part of my image of a scientific hero." — **DEVELOPMENTAL PSYCHOLOGIST UTA FRITH OF UNIVERSITY COLLEGE LONDON, IN A Q&A IN THE JUNE 3 *CURRENT BIOLOGY*.**

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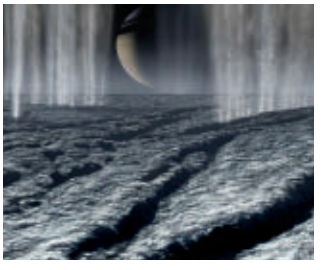
SN TODAY

Read current science news stories, updated daily. Access stories not seen elsewhere, such as Ron Cowen's coverage of evidence that one of Saturn's moons (pictured below) may host an underground ocean. Visit the Atom & Cosmos topic section on the website.



FEATURES

Watch science in action. The illustration on Page 19 of this issue has an online version, and it's animated. Watch how an injected virus can carry new genes into muscle cells and spur the body to make extra blood cells, discussed in the feature on the possibility of gene doping in this year's Olympics.

Science Past: 50 Years Ago

From *Science News Letter*, August 2, 1958

PORCUPINES GNAWED ON STONE AGE MAN'S TOOLS — Razor sharp edges on some of the bone chisels of Middle Stone Age man in Africa were found to have been put there by the needle-sharp front teeth of porcupines, Dr. Raymond A. Dart of the University of the Witwatersrand, Johannesburg, South Africa, reports. But the fact that a magnifying glass showed up the telltale marks of rodent teeth on the Stone Age tools does not mean that ancient man himself did not do the original work in splitting and shaping the animal bones. At the Kalkbank Stone Age campsite ... 3,619 bone fragments were collected. Of these, 903 had been gnawed by porcupines. "The first fact that emerges from the Kalkbank deposit," Dr. Dart stresses, "is that porcupine gnawing, even when it affects 24.95% of the bones in a deposit, does not prove that porcupines collected or split the bones they gnawed."

Science Future

August 16–24

Australia celebrates National Science Week. Visit www.scienceweek.info.au

September 18 and 19

University of Wisconsin–Madison's Holtz Center presents "Climate Change is Global." Visit sts.wisc.edu

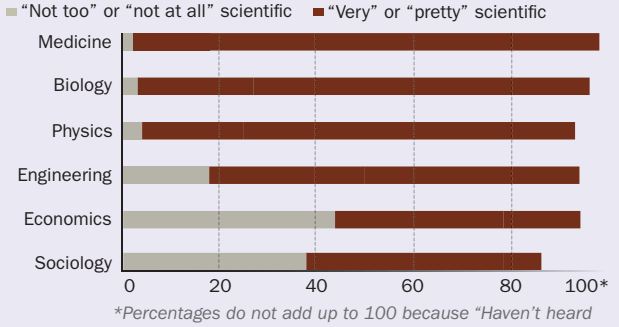
October 8

Space Shuttle Atlantis is scheduled to launch as part of the final mission to the Hubble Space Telescope. Visit www.nasa.gov/missions

Science Stats

SIZING UP SCIENCE

U.S. perceptions of the scientific nature of various fields in 2006

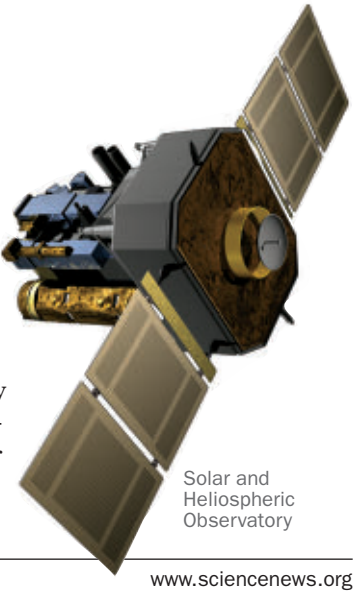


**Percentages do not add up to 100 because "Haven't heard of field" and "Don't know" responses are not shown.*

SOURCE: UNIV. OF CHICAGO, NATIONAL OPINION RESEARCH CENTER

The (-est)

The Solar and Heliospheric Observatory discovered its 1,500th comet in late June, making it the best comet catcher — more successful than all others combined. Because SOHO sits between the Earth and the sun, it sees an area of space usually obscured by daytime sky. SOHO-1500, like roughly 85 percent of SOHO's discoveries, is a fragment of a larger comet that split and plunged into the sun centuries ago.



Solar and Heliospheric Observatory

SOHO (ESA & NASA); KARL KOFOED; UK RESOURCE CENTRE FOR WOMEN IN SCIENCE, ENGINEERING AND TECHNOLOGY

“I’m used to frog embryos being able to do more than most people expect.” —KAREN WARKENTIN, PAGE 10

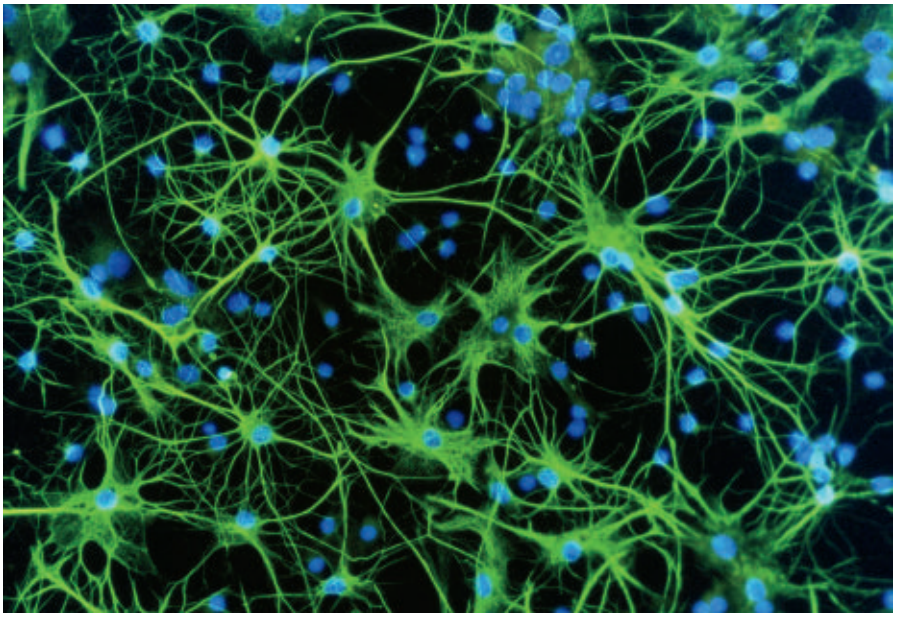
In the News

STORY ONE

Astrocytes are rising stars of the brain

Cells regulate blood flow and make fMRI possible

By Tina Hesman Saey



Astrocytes (cell body in green and nuclei in blue) were previously thought to be only support cells for neurons. New studies show astrocytes regulate blood flow in the brain, make fMRI possible and may aid neuron signaling. (Nuclei of other types of brain cells are also in blue.)

N. KEDERSHA/PHOTO RESEARCHERS, INC

Star-shaped brain cells called astrocytes are finally getting their chance to shine.

Two groups of researchers—one at MIT, the other at Harvard—have shown that astrocytes get the blood pumping to parts of the brain that are thinking hard. These cells may use blood flow and other tricks to rev up communication between neurons or slow it down, and may even play a role in storing information. The findings indicate that astrocytes are not just supporting actors for neurons; they deserve recognition as true costars.

“Astrocytes are typically forgotten,” says Venkatesh Murthy, leader of the Harvard group, but they “are right in the thick of things.”

Neurons have typically gotten the most attention from researchers because they are the brain cells that do all the thinking. But neurons cohabit the brain with a class of cells called glia, which means “glue” in Greek. Glia outnumber neurons in the human brain by a factor of 10 to one, and astrocytes are the most abundant type of glial cell.

The view of astrocytes has changed slowly over the past decade. Astrocytes were once thought to do little more than hold the brain together, and they were largely ignored. In recent years, though, scientists have learned that the star-shaped cells have a hand in guiding connections between neurons and controlling levels of chemical messengers in the brain. But those activities were viewed mainly as supporting roles. Now their central function in controlling blood flow indicates that astrocytes deserve higher billing. Without astrocytes, in fact, one of the most powerful tools of neuroscience—functional MRI—would not be possible.

Functional MRIs rely on the premise that blood flow is coordinated with neuron activity, but the mechanism that links blood flow to activity has been a mystery.

Some scientists suspected that astrocytes may play a role in blood flow because the cells have “end feet” that nestle up against synapses—the places where neurons connect—and other end feet that wrap around capillaries. But no one had proved that astrocytes could actually influence blood flow in animals.

Working with ferrets, Mriganka Sur and colleagues at MIT used an advanced microscopy technique to measure the response of astrocytes to visual stimuli. The group reported its findings June 20 in *Science*. Neurons in the visual cortex of ferrets, cats, monkeys, humans and other higher mammals are arranged in columns of cells that respond when an animal sees objects oriented in the same direction. For instance, one column would respond to the vertical edges of a building, while another close-by column would be stimulated by horizontal lines. Columns tuned to every possible orientation of a line are »

For today's top science news, visit SN Today at **www.sciencenews.org**

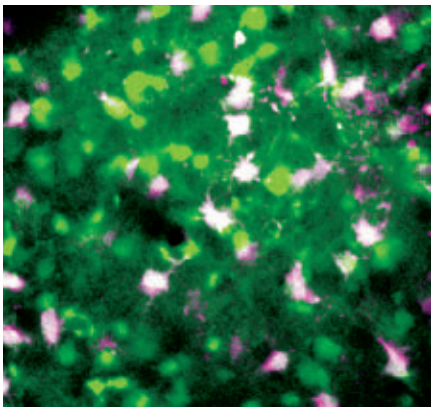
» situated close to each other in what neuroscientists call pinwheel centers.

Sur's postdoctoral researchers James Schummers and Hongbo Yu used fluorescent dyes to show when neurons and astrocytes become active. Neurons respond in split seconds to visual cues flashed into the eyes of anesthetized animals. About three to four seconds after neurons begin firing, calcium levels in the astrocytes begin to rise, a cue that the cell is active and sending signals. Blood flow through capillaries increases following the rise in calcium.

Murthy and his colleagues got similar results with neurons and astrocytes in the odor-sensing centers in the olfactory bulbs of mice. That study appeared June 26 in *Neuron*.

An astrocyte listens to the chemical conversation between neurons, soaking up neurotransmitters such as glutamate, the researchers showed. Astrocytes actually use two pathways to respond to glutamate: The cells have receptors for glutamate on the end that nestles next to the synapse, and the cells can also take up the neurotransmitter through amino acid transporters, the researchers found.

The glia are not just passively eavesdropping. They also regulate levels of neurotransmitters in the synapse, send signals to capillaries to increase blood flow to oxygen-hungry neurons and participate in gathering information, says Frank Kirchhoff, a neuroscientist at the Max Planck Institute of Experimental Medicine in Göttingen, Germany. The two new studies demonstrate that astrocytes are involved in signaling in the brain, he says.



When neurons (green) are active in the visual cortex of a ferret, astrocytes (purple) respond with increased calcium, which leads capillaries to increase blood flow.

Astrocytes don't merely pass along information from neurons to blood vessels, they also talk back to the neurons, the research demonstrates. Blocking the ability of the astrocytes to respond to glutamate caused neurons to get even more excited.

"That is direct evidence that an astrocyte is not just a pretty face sitting around soaking up [neurotransmitters], but that it also plays a role in computation," Sur says.

Each astrocyte seems to be intimately associated with a single neuron or a small number of neurons, Sur says. That was a surprise because previous research on slices of brain suggested that astrocytes work together in vast networks. Sur doesn't rule out the possibility that astrocytes coordinate with each other, but he speculates that they usually act locally — chatting with nearby neuron partners and blood cells within a 10- to 20-micrometer area. Performing similar experiments in awake animals might help answer the question, Kirchhoff suggests, because anesthetics may dampen the glial cells' responses.

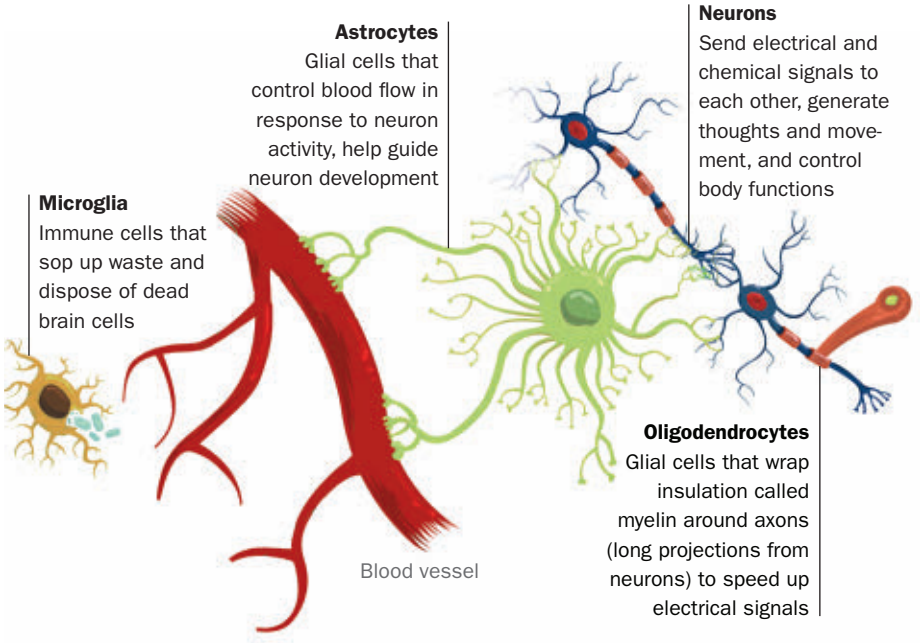
Astrocytes are pickier about responding to visual signals than neurons are, the MIT group found. The cells seem to have higher standards than neurons for the amount of stimulus they consider exciting. The researchers don't yet know whether astrocytes slow blood flow to calm over-excited neurons, or if increasing the blood supply allows neurons to work harder. And the code of calcium signaling within the astrocytes also needs to be worked out, Kirchhoff says.

Some diseases may be caused or complicated by defects in astrocyte function, Murthy says. His team is exploring whether the astrocytes' ability to control blood flow breaks down with age. The new discoveries will probably force researchers to rethink brain networks to include astrocytes, Sur adds.

"It's not often that a whole new function for a class of cells is revealed," Sur says. "It's like when we first began to understand synaptic transmission 50 years ago. The whole field is open." ■

NINDS/NATIONAL INSTITUTES OF HEALTH; JAMES SCHUMMERS AND HONGBO YU/MRIGANKA SUR LABORATORY/MIT

Back Story Brain cell roll call: three types of glial cells and a neuron



Atom & Cosmos

For longer versions of these and other Atom & Cosmos stories, visit **www.sciencenews.org**

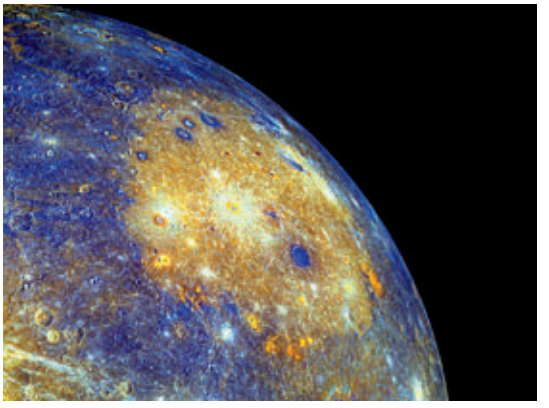
Messages from Mercury

Flyby reveals clues to volcanism, magnetism

By Ron Cowen

Mercury, the solar system's forgotten planet, is finally getting its place in the sun.

Data from the January flyby of the spacecraft MESSENGER — which will begin a year-long orbit of Mercury in 2011 — has revealed the origin of the planet's magnetic field, discovered evidence of early volcanic activity and provided a first look at the planet's surface composition, researchers report in the July 4 *Science*.



Mercury's Caloris Basin, shown in an image from the MESSENGER craft's flyby, reveals signs of volcanism.

Volcanism appears to be widespread, says Mark Robinson of Arizona State University in Tempe. For instance, the ancient Caloris Basin is filled with smooth plains that appear to have been created by the belching of vast amounts of lava. Jim Head of Brown University and collaborators found evidence of volcanic vents along the edges of Caloris. The data "open up a whole new realm" about how volcanic activity may have shaped the planet, Head says.

The only previous mission to examine Mercury close-up — Mariner 10 in the mid-1970s — found no evidence of volcanism. MESSENGER, which came within 200 kilometers of the planet, can see much finer detail.

MESSENGER data also suggest that Mercury's magnetic field is produced internally and is not a vestige of a past field.

MESSENGER — for Mercury Surface, Space Environment, Geochemistry and Ranging — will fly past Mercury again this October and in September 2009.

Voyager 2 reports from the edge

Bubble surrounding solar system seems to be lopsided

By Ron Cowen

There are no signs to announce the edge of the solar system, but when the venerable Voyager 2 spacecraft approached this final frontier last August 31, it was in for quite a shock. So were the scientists who analyzed the data radioed back to Earth.

The signals reveal that at a distance of 83.7 astronomical units (1 AU is the average Earth-sun separation), Voyager 2 had at least five encounters with a turbulent region known as the termination shock, the researchers report in the July 3 *Nature*. That's the place where the solar wind — the sun's hot supersonic wind of protons and other charged particles, which carves a bubble in space extending well beyond Pluto — slams into cold interstellar space and abruptly slows.

Analyzing the encounter is critical for understanding how the bubble interacts with surrounding space, and how the bubbles carved by other stars affect their surroundings, notes Voyager lead investigator Ed Stone of Caltech.

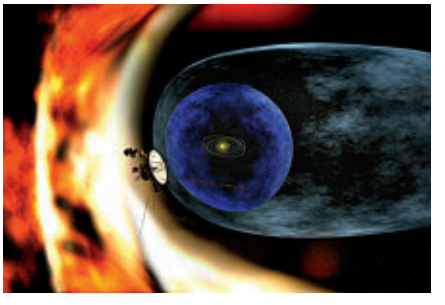
Researchers had expected that Voyager 2 would have only one encounter with the shock. The multiple crossings indicate that "the shock is not the steady structure that is predicted by the simplest theory," says Len Burlaga of NASA's Goddard Space Flight Center in Greenbelt, Md. "It is like a wave approaching a beach, that grows, breaks, dissipates and then re-forms closer to shore."

Gusts in the solar wind may cause the shock to "come and go, re-forming itself and decaying," Stone suggests.

Launched in 1977, Voyager 2 follows in the footsteps of Voyager 1, its sister craft, which headed toward the fringes of the solar system in the opposite direction, the northern celestial hemisphere, and passed through a single termination shock in 2004. The location of the shock detected by Voyager 2 — some 1.6 billion kilometers closer to the sun than the Voyager 1 shock — suggests that the solar system is lopsided. The bubble carved by the solar wind is pushed in on the southern side.

The dent may be due to extra pressure exerted by the Milky Way galaxy's magnetic field. The field is generally uniform but could have become "tilted in such a way that it's pushing more on the south than the north," Stone says.

A series of supernova explosions in the solar neighborhood about 10 million to 20 million years ago could have tilted the field, he notes.



An illustration shows Voyager 2 just inside the edge of the bubble that separates the solar system from interstellar space.

JPL/NASA; AAAS/*SCIENCE*

Body & Brain

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Dopamine's role linked to location

Desire and dread separated by mere millimeters

By Amy Maxmen

Dopamine conducts a frenzied song of craving at one end of a tiny brain region and a panic-stricken hymn at the other. Depending on where along the length of the region the neurotransmitter is triggered, it mediates emotions ranging from desire to disgust, a new study shows.

"The roles [of dopamine] may be partitioned, and perhaps defined, by anatomy," comments Emily Hueske, a neuroscientist at MIT.

The study brings researchers one step closer to explaining how dopamine performs a spectrum of functions. Dopamine interacts with spatially coded signals so that its output varies depending on where it's acting, the team reports in the July 9 *Journal of Neuroscience*.

In the long term, the finding suggests how drugs might be developed to treat dopamine-mediated disorders such as drug addiction, obesity and anxiety.

Kent Berridge, a neuroscientist at the University of Michigan in Ann Arbor, and his colleagues set out to understand how dopamine could lead to desire for a reward, and then turn around and cause fear, pain and stress.

Berridge's team focused on the nucleus accumbens, a small brain structure known as the pleasure center in mammals. The researchers tampered with dopamine and the brain chemical glutamate, known to interact with dopamine, along the length of the nucleus accumbens of rats. Allowing dopamine to act normally, the researchers injected a glutamate blocker into the front end of the brain area, turning normal rats into binge-eaters. But when the team disrupted glutamate at the back end, the rats stopped eating and became fearful — kicking up sand at the bottom of their cages, as wild rodents are wont to do when a snake or a scorpion is in their midst, Berridge says.

When researchers blocked both dopamine and glutamate, however, the rats showed neither desire nor dread, revealing that both neurotransmitters are essential in mediating the behaviors. In nature, the interaction between the two may guide a rat's responses to environmental signals. Glutamate may bring in information from the outside world, and dopamine may act on that information, Berridge suggests.

> **"Dopamine is basically saying: 'Hey, pay attention to your environment.' "**
> RICHARD PALMITER

Because the injections were so localized within the nucleus accumbens, the researchers were able to map out a millimeter-by-millimeter gradient of reactions. "The brain cares where you are exactly," Berridge says.

Behavioral neuroscientist Richard Palmiter of the University of Washington in Seattle was not shocked by the finding, because desire and dread aren't completely unrelated. Regardless of how the rat responds to a stimulus, "dopamine is basically saying: 'Hey, pay attention to your environment,' " he says.

Still, Berridge says, the work shows how motivation for a reward can turn to fear within a single structure. Describing the desire-to-fear gradient as a keyboard, he says the minute keyboard found in the rats may translate into a slightly larger, centimeter-by-centimeter keyboard in humans. Berridge speculates that the edges of "keys" are skewed in certain people, such that a sensation produces more pleasure than it should in addicts or too much fear in schizophrenia patients.

Once scientists know what underlies the front-to-back gradient, drugs could be refined to better treat separate disorders, says Charlotte Boettiger of the University of North Carolina at Chapel Hill. ■

Stem cells aid weak muscles

Transplants in mice help ameliorate genetic defect

By Tia Ghose

Skeletal muscle stem cell transplants can rebuild brawn in mice with faulty muscle-making genes, a new study finds.

The finding, reported in the July 11 *Cell*, offers hope that one day skeletal muscle stem cells from healthy people could be grafted into those with muscle disorders such as Duchenne muscular dystrophy, says study coauthor Amy Wagers of Harvard University. People with other muscle damage could also benefit, she says.

Unlike ordinary cells, skeletal muscle stem cells are able to transform into any of the types of cells that make muscles.

Because of a genetic defect, people with Duchenne don't make the protein dystrophin, which is essential for maintaining the structural integrity of muscle. Without it, muscle becomes damaged and wastes away. Wheelchair-bound by their early teens, Duchenne patients typically die soon after, when their heart and diaphragm muscles start to fail, says bioengineer Irina Conboy of the University of California, Berkeley.

Wagers and colleagues extracted stem cells from a pool of cells known to play a role in muscle growth and repair. Next, the group implanted these muscle stem cells from normal mice into mice lacking the gene to make dystrophin. Within a couple of weeks of the transplant, mice with the stem cell transplant had markedly improved muscle fibers.

"They show 94 percent recovery, which is great," Conboy says. "The first step is to restore muscle in an animal model, and that was done successfully."

Environment

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Feminization blamed on farming

Agricultural chemicals suspected in cane toad troubles

By Janet Raloff

Among toads living in farm country, gents tend to resemble the gals — both inside and out. This doesn't bode well for the hoppers impressing local ladies, much less fathering their tadpoles.

Toads and other amphibians throughout the world are under siege. Disease plagues many populations; others suffer high rates of deformities or immune suppression. In some regions, species have simply vanished without a trace.

To investigate whether these problems stem from general stress due to land development, rather than poisoning by chemicals, University of Florida biologists analyzed dozens of local adult cane toads (*Bufo marinus*). At least 20 were collected during summer nights at each of five sites in Florida. Some toads had been living in suburbs, others near anything from a little farming to heavy agriculture. As hectares of farming in the toads' vicinities increased, so did the proportion of males exhibiting a serious feminization, Krista McCoy and colleagues report in an upcoming *Environmental Health Perspectives*.

If just land disturbance — to build roads, homes, shopping malls and the like — was a sufficient stressor, the effects on toads living near suburbs should be no different than for toads living near farms. That there was a difference suggests that something about farming is to blame, such as the chemicals used on farms — many of which in isolation can cause feminization of amphibians and other animals.

At sites where half to 97 percent of nearby land was farmed, about 40 percent of the 67 non-females had typical he-toad gonads and coloring. An equal number were intersex animals, with testes and ovaries. About 20 percent of the non-females near the highest farming activity appeared outwardly male. But these superficially normal males sported a maturing Bidder's organ, as did the intersex animals.

Like the human appendix, the Bidder's organ normally has no function. But if males lose testicular function, it may mature into an ovary, says wildlife endocrinologist Louis Guillette Jr., a coauthor on the study. His team found that Bidder's organs in some of the males from the farming regions were full of eggs (although the viability of the eggs was not checked).

Feminized male toads had a female coloration, shorter forearms than normal males and fewer nuptial pads (temporary features that develop on the fingers of males who are readying to mate). Levels of testosterone, the primary macho sex hormone, were especially low in male toads from sites near substantial farming.

"I've worked with this species," says David Crews of the University of Texas at Austin, and "these are about the toughest amphibians in the world." So he was impressed by the new data, which suggest that something about nearby farming — probably runoff of pesticides or other chemicals — is "essentially remaking the individual," inappropriately "resculpting" a male tadpole's urogenital tract.

Lab studies by Tyrone Hayes of the University of California, Berkeley show that the types of gross demasculinizing changes reported in the new study would make animals sterile. Hayes has investigated gonadal changes in frogs exposed to agricultural chemicals, such as atrazine — a weed killer used by farmers raising sugarcane, a primary crop in the Florida settings where toads were sampled.

But malformed organs or a feminine appearance aren't the only mating obstacles, Hayes notes. Chemical exposures also affect behavior. "Out of every trial we've done," he says, "only two atrazine-treated males were ever able to even copulate."

Although the Florida team does not speculate on what in the tadpoles' water feminized them, Hayes says that a primary suspect has to be "atrazine, obviously." Any reproductive remodeling of the male toads' bodies probably also traces back to additional chemicals, he says.

The study area included suburban, somewhat agricultural and very agricultural land, allowing the scientists to identify "dose-dependent" effects of farming on internal organs, hormones and even outward appearance, observes Pamela Martin of Environment Canada in Burlington, Ontario. These changes "corroborated each other very well," she adds, "making for a very convincing story."

A paper by Martin's team in the July 30 *Aquatic Toxicology* makes a similar link between agricultural intensity and the feminization of male amphibians — in this case northern leopard frogs. ■

K. MCCOY ET AL./ENVIRONMENTAL HEALTH PERSPECTIVES

Mottled skin denotes a female cane toad (left), while drabber skin typifies a male (right). An intersex individual (center) has female coloration, male nuptial pads (dark color on inner fingers) and inappropriate or malformed reproductive organs. The toads were collected in Florida.

Life

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Now available in color: fossils

Pigment may have been preserved in feathers

By Davide Castelvecchi

Researchers have found what may be remnants of pigment in fossilized feathers, opening the possibility of reconstructing the colors of many long-extinct animals.

Dark stripes in a 100-million-year-old fossilized feather contain particles that closely resemble, in size and arrangement, black melanin particles in modern bird feathers, researchers will report in October in *Biology Letters*. Paleobiologist Jakob Vinther of Yale University and his collaborators used an electron microscope to examine the fossil feather — which could be from an early bird or dinosaur — as well as a 55-million-year-old bird fossil.

Researchers noticed the dark, carbon-rich microscopic granules in the 1980s but assumed them to be remnants of bacteria that had decomposed the feather.

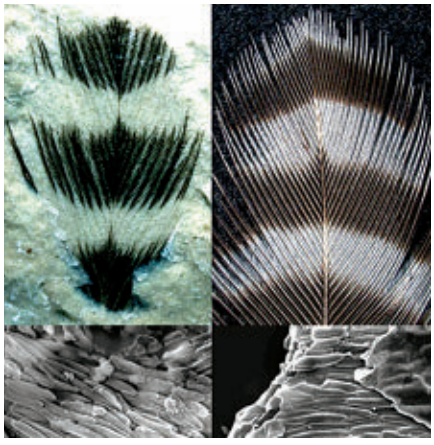
But a comparison with modern feathers shows otherwise. "You wouldn't expect bacteria to be aligned according to the orientation of the feathers," Vinther says.

The fossils may not contain any actual melanin since most organic matter breaks down before fossilizing. But, Vinther says, "melanin is very resistant to degradation," and his team is now attempting a chemical analysis of the material to see if some has survived intact.

Researchers could now look for melanin, ubiquitous in the animal kingdom, in a wide range of fossils, including ichthyosaurs, dinosaurs, insects, mollusk shells and mammals.

And while the shape of the granules is evidence of black pigment, yellow and red melanins also exist — such as in the freckles of fair-skinned humans. Cells accumulate different types of melanin in sacs of different shapes, so paleontologists may be able to find evidence for actual colors, rather than only black or shades of gray. And some animals create iridescent patterns using nanoscale structures of melanin, which might also be preserved.

"Preservation of a range of color signatures appears more than possible," says Phil Manning of the University of Manchester in England. "Once more in paleontology the preservational paradigm has been gently shifted in a positive direction."



Black stripes on a fossilized Cretaceous feather (left) resemble marks on a modern woodpecker feather (right). Scanning electron microscope images are shown at bottom.

Viewing fossils' color could reveal how animals dressed up for courtship, while finding camouflage patterns could cast new light on the environments the animals roamed, Vinther says.

Cuttlefish embryos look and learn

Before hatching, young acquire interest in crab dinners

By Susan Milius

Cuttlefish could be the first animals shown to learn visually before birth or hatching, researchers say.

Cuttlefish embryos develop in eggs that stretch and become translucent. Embryos with crabs nearby hatch into youngsters with a distinct preference for eating crabs, says Ludovic Dickel of the University of Caen in France. Without that pre-hatch view of crabs, the little cuttlefish prefer to attack shrimp, he and his colleagues report in the July *Animal Behaviour*.

Ready to learn, a cuttlefish embryo peers from its egg.

The preference develops from sight alone, Dickel says. The researchers kept the crabs in containers that prevented crab scents from getting into the water with the eggs.

Earlier work by the team showed that within a few hours of hatching, the babies need only one good look at crabs to develop a preference for them. Later on, the babies no longer learn so well. Now the window of extra-sharp learning seems to be open even before hatching, Dickel says.

Past research has shown that other species, such as ants and gulls, start learning scents and sounds as embryos, Dickel says. Cuttlefish offered a chance to test for visual learning because as the ink-stained eggs approach hatching, they swell to the point where the embryos can see through the translucent egg covering.

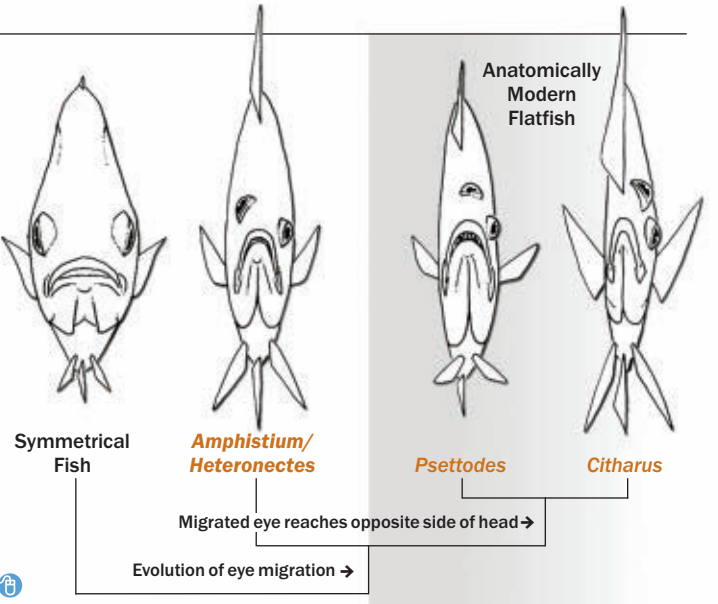
This test provides the first demonstration in any animal that embryos can learn from the sights around them, Dickel says.

"In the world in general, I think visual learning in embryos is surprising and cool," comments Karen Warkentin of Boston University. She studies defense reactions of frog embryos. "To me," she adds, "I don't think it is so surprising — in that I'm used to frog embryos being able to do more than most people expect." ■

DICKEL; VINTHER *ET AL.*

The wandering fish eye

A new look at the fossils of primitive flatfish reveals that these fish—well-known for having both eyes on one side of their heads—started out symmetrical and gradually evolved their off-kilter trait. Scientists knew that the fish's earliest ancestors had an eye on each side of the head, but evolutionary biologists had struggled to explain how the modern one-sided eye position evolved. Previous studies suggested an abrupt change. But when Matt Friedman of the University of Chicago reexamined 45-million-year-old fossils of primitive flatfish, genera *Amphistium* and *Heteronectes*, he found a transition species: One eye had moved, but it had not crossed the midline of the fish's body, as seen in today's flatfish, Friedman reports in the July 10 *Nature*. The finding supports the idea that the skeletal structure of flatfish underwent small, incremental changes over thousands to millions of years, says Alex Schreiber of St. Lawrence University in Canton, N.Y. —*Ashley Yeager*



Frogbuilding… first the toes, then the legs

Development appears out of order in coquí frog

By Rachel Ehrenberg

A small frog appears to jump-start its skeletal development, turning on genes for building feet and toes before bothering to build its legs.

While researchers are still trying to figure out how a clump of cells becomes a wing, flipper or arm, the order of developmental events has been established: The upper arm bone forms first, then the forearm, then the wrist bones and finally fingers or toes. But the new work, reported in the July/August *Evolution & Development*, hints that the gene activity that leads to limb formation may not be so clear-cut.

Francesca Mariani, a University of Southern California developmental geneticist not involved in the study, calls the idea interesting. "Maybe limb development has different ways of occurring."

The evolutionary path from ancient fish fins to the modern structures used for flying, burrowing, running and jumping has long intrigued scientists, who seek to elucidate the massive coordination of genes, cells and proteins that it takes to build an adult animal from its embryonic beginnings. Insights from the frog's fancy footwork could lead to a greater understanding of the cellular blueprint for all creatures, which one day could lead to therapies for repairing injured tissues.

Scientists say toe-building genes in embryonic frogs are turned on before the leg is fully developed (top). Older methods that stain cartilage miss the oddly timed gene activity (bottom).

Coquí frogs, *Eleutherodactylus coqui*, are already known for bypassing normal amphibian growth stages. The coquí is what scientists call a direct developer—it skips the tadpole phase, emerging from the egg as a tiny, fully formed froglet.

"These guys have managed to delete some aspects of the larval stage," says embryologist Ryan Kerney of Dalhousie University in Halifax, Canada, who conducted the research with Harvard colleague James Hanken.

The new study follows the activity of three genes known to be involved in skeletal formation in the developing embryo. In the coquí frogs, two genes were active in the budding cells that become toes before they were active in the budding cells that become a leg—evidence that the frogs rev their feet genes first.

The new work fits with a model proposed by Mariani in the May 15 *Nature*. Instead of a single management center that directs limb development from shoulder to fingertip, there might be a control center for areas close to the torso and a separate control center for the more distant structures, like wrist bones and fingers, she suggests. While Mariani isn't fully convinced the reported gene activity means the frog's budding cells are gearing up for making toes, she says "this kind of work is important. It tells you when and where the template becomes established."

R. KERNEY AND J. HANKEN/*EVOLUTION & DEVELOPMENT*; FRIEDMAN/UNIV. OF CHICAGO

Earth

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It all began with a single crack

Crumbling, not just incline, spurs a slab avalanche

By Ashley Yeager

Forecasting a snow avalanche takes more than measuring the angle of a mountain slope, researchers report in the July 11 *Science*. Whether an avalanche happens might also depend on how the snow cracks and collapses, the study suggests.

"The new theory could be a breakthrough in understanding what is going on at the very moment when an avalanche begins," says University of Edinburgh physicist Joachim Heierli, lead author of the study.

By modeling slab avalanches — the most dangerous because a snow slab breaks loose and cascades to the slope's bottom — the team found that snow fractures more easily than previously thought. Also, gravity's pull along the slope is less important than compression of the snow.

In a snow pile, a brittle, collapsible layer sits between a solid, dense snow slab on top and a rigid snow base below. The way the middle layer fractures when it's disturbed controls whether a snow pile will shear off, leading to a violent slab avalanche, or will collapse under its own weight.

Scientists had previously thought that the gravity tugging on the slope drives the avalanche and that the critical crack size to start an avalanche should increase as the slope angle decreases. But field experiments suggest this is not the case. Heierli's team addressed the discrepancy by modeling gravity's tug on the snow along the slope and the downward pull of gravity perpendicular to the slope, finding the perpendicular pull was more important.

"Some layers inside the snow are a very frail network of ice grains with lots of space in between," Heierli says. "Some arrangements may crumble like a house of cards." Fractures from crumbling can spread over large areas, even creating an avalanche on horizontal layers.

A slab avalanche begins.

"This research is really an entirely new paradigm for how the fractures that result in snow avalanches work," says Karl Birkeland of Montana State University in Bozeman.

Apollo rocks show traces of water

Study may shed light on moon formation and evolution

By Ron Cowen

A new analysis of moon rocks has revealed that the moon isn't as bone dry as researchers had thought, whetting the appetite of scientists who seek a deeper understanding of how Earth's natural satellite arose and evolved.

Because the moon is believed to have coalesced from the debris created when a Mars-sized body struck Earth some 4.5 billion years ago, the finding also suggests that Earth acquired a substantial supply of water earlier in its history than some scientists had suspected.

When the moon rocks were brought back to Earth by the Apollo astronauts, the tiny, volcanically formed glass beads inside showed no signs of water. But Alberto Saal of Brown University in Providence, R.I., and colleagues have reexamined the rocks with a more sensitive instrument, using a narrow beam of cesium ions.

The new measurements reveal that the concentration of water in the rocks is less than 50 parts per million, says coinvestigator Erik Hauri of the Carnegie Institution for Science in Washington, D.C. A critical finding, he notes, is that the concentration of water decreases dramatically from the center to the rim of the beads, suggesting that 95 percent of the water once held by the moon was lost when volcanic eruptions belched water vapor and other volatile gases. The lunar interior may originally have had an abundance of water approaching 750 ppm — similar to the amount present in Earth's upper mantle, the team reports in the July 10 *Nature*.

"This work challenges the long-standing assumption that the moon lacks indigenous water, and this result alone makes it very important to understanding the origin and early history of the moon," comments theorist Robin Canup of the Southwest Research Institute in Boulder, Colo.

Saal says it's unclear if all parts of the moon had similar concentrations of water, or if the beads only indicate the amount of water in a small section.

Answering that puzzle "will be key to unraveling what this result implies," Canup says.

If the abundances reflect an average composition, then the total mass of water originally contained by the moon would be larger than could have been delivered by meteoroids that pelted the lunar surface some 3.8 billion years ago. But if the average amount of lunar water is much lower, the finding may cast a new light on the standard model of moon formation, says Saal. That model suggests that the heat generated by the collision that created the moon would have vaporized any water.

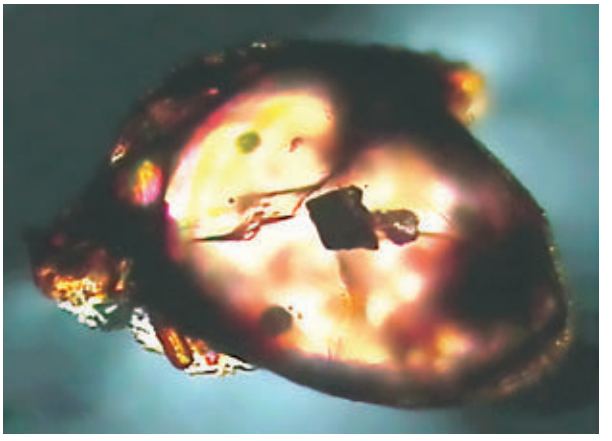
A. DUCLOS, WWW.DATA-AVALANCHE.ORG

> "If the light carbon signature is from life, then this is very big indeed." —CRAIG O'NEILL

Tiny diamonds may set earlier date for first life

Carbon isotope ratios suggest biological activity

By Sid Perkins



Analysis of microdiamonds (dark spot) in zircons suggests life could have existed 400 million years earlier than once thought.

Microdiamonds embedded in ancient zircons found in Western Australia suggest that life may have existed on Earth as early as 4.25 billion years ago.

Chemical analyses indicate that the mini-gems contain higher-than-average concentrations of the carbon-12 isotope, researchers report in the July 3 *Nature*.

Experts strongly debate whether that anomaly is evidence that life existed on Earth so soon after the planet formed, 4.6 billion years ago. If true, however, the findings would put life's earliest appearance at least 400 million years earlier than previously thought.

"If the light carbon signature is from life, then this is very big indeed," says Craig O'Neill, a geoscientist at Macquarie University in Sydney. "The trouble is, there are quite a few other mechanisms that can form light carbon signatures."

Zircons, tiny crystals of zirconium silicate, are hard, durable and chemically inert. The rocks that contain these crystals eventually erode, but often the crystals are incorporated into younger rocks, says Martin Whitehouse, an isotope geochemist at the Swedish Museum of Natural History in Stockholm. Small bits trapped when zircons cool, also known as inclusions, stay protected as the host rocks degrade over time. The zircons become tiny time capsules, holding clues about the environment.

Trace elements in zircons enable scientists to determine their age. Whitehouse and his colleagues recently measured the ratios of carbon isotopes that make up micrometer-sized diamonds embedded within some of the oldest zircons on Earth. These zircons are found in the Jack Hills of Western Australia, the remnants of rocks that originally solidified about 4.4 billion years ago.

The researchers analyzed 22 microdiamond inclusions and found that the tiny gems formed and were then incorporated into the zircons. The concentration of the heavier isotope, carbon-13, in some of the microdiamonds was about the same as that typically found deep in Earth's mantle, where natural diamonds form. However, concentrations in others were as low as 58 parts per thousand below normal.

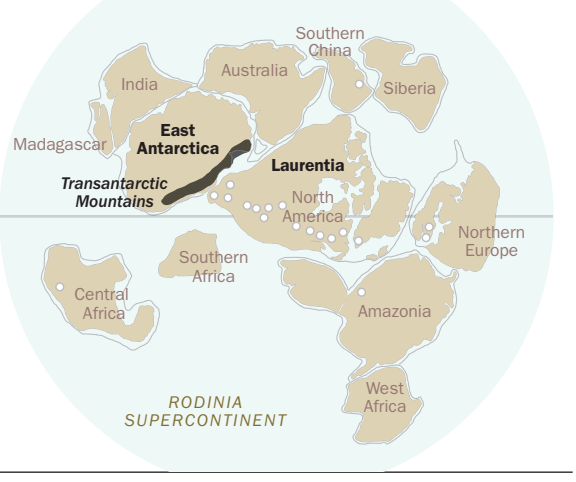
"That's a very unusual carbon signature," Whitehouse says.

Since metabolic processes that take place in cells produce isotopically light carbon, a high concentration of carbon-12 is often a sign that the carbon was generated by biologic activity, Whitehouse adds. But he agrees that other mechanisms, such as inorganic chemical reactions — including those between carbon oxides, methane, hydrogen and water, which were all constituents in Earth's early atmosphere — can yield isotopically light carbon.

The carbon-isotope ratios found in the zircons "are among the lightest ever measured," says Steven Shirey of the Carnegie Institution for Science in Washington, D.C. Although the isotopically light carbon isn't a sure sign that life existed on Earth 4.25 billion years ago, it's impossible to discount the notion, he adds.

Rock finds suggest unlikely neighbors

About 800 million years ago, East Antarctica, one of the coldest regions on Earth today, abutted what is now Death Valley, Calif. Both locales were then part of a supercontinent called Rodinia, says John Goodge of the University of Minnesota Duluth. The finding adds to an ongoing debate about how today's landmasses were arranged between 750 million and 800 million years ago. Ratios of hafnium isotopes in 1.44-billion-year-old zircons in rocks from the Transantarctic Mountains match those in zircons in the granites now found primarily in North America, which includes the landmass that was called Laurentia. Goodge and colleagues also report in the July 11 *Science* that the ratios of different elements in a basketball-sized chunk of granite recently found in East Antarctica match those found only in what is today the American Southwest. —*Sid Perkins*



ADAPTED FROM J. MEERT/UNIV. OF FLORIDA; P. RENNE, P. AHLBERG

Genes & Cells

122 years Record for longest documented and undisputed lifespan, held by the late Jeanne Calment

Strategies for fighting aging can be complex

Resveratrol, low-cal diets don't work the same way

By Tina Hesman Saey

A substance found in red wine and touted as the chemical equivalent of the fountain of youth probably acts more like a wellspring of health — with warning signs.

Resveratrol, as the chemical is known, does a pretty good job mimicking some age-defying effects found in studies of animals on calorie-restricted diets. But the substance doesn't make animals live longer, a new study shows.

At the same time, boosting levels of an enzyme believed responsible for resveratrol action and for life-extending benefits of calorie restriction does protect mice fed high-fat diets from heart problems.

But a third report links activity of the enzyme, Sirt1, and vulnerability of brain cells to damage.

The research indicates that resveratrol and low-calorie diets don't necessarily confer their benefits the same way.

"You have to carefully study the reality, and the reality is, it's complicated," says Valter Longo, a molecular geneticist at the University of Southern California.

For instance, two new studies show that each organ in the body may react differently to calorie restriction, to resveratrol or to different actions of proteins called sirtuins shown to regulate aging in yeast, roundworms and fruit flies.

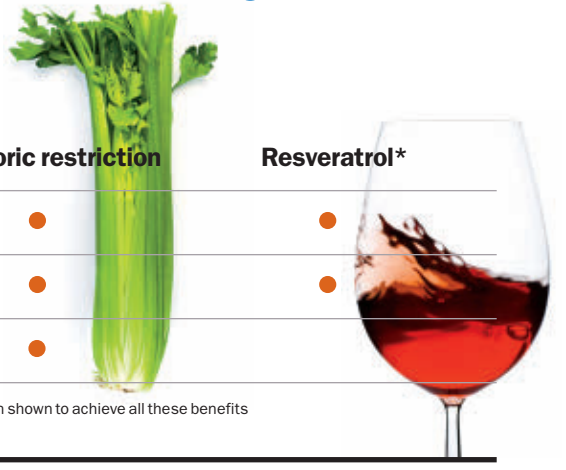
Increasing levels of the mouse sirtuin Sirt1 prevents mice from developing heart problems and fatty livers even when they are fed high-fat diets, researchers at the University of Cincinnati College of Medicine and the Spanish National Cancer Research Center in Madrid reported online June 30 in the *Proceedings of the National Academy of Sciences*. These mice with higher levels of Sirt1 eat more but also burn more calories than do mice with normal levels of the enzyme.

But Longo's group reported in the July *Cell Metabolism* that Sirt1 may affect the brain differently. Neurons grown in the laboratory were sensitive to oxidative damage when they made normal amounts of Sirt1, but reducing levels of the enzyme helped the brain cells resist stress.

An international team of researchers led by Rafael de Cabo at the U.S. National Institute on Aging reported in the August 6 *Cell Metabolism* that mice fed resveratrol had similar patterns of gene activity as mice fed only every other day. The resveratrol-treated mice had better bone health, less cataract formation and improved coordination compared with other mice their age.

Resveratrol also lowered the mice's cholesterol and made their hearts function better compared with aged mice fed a standard diet.

Ripe Old Age
Two different ways to age gracefully



* The small quantities of resveratrol in wine have not been shown to achieve all these benefits

Two paths to longer life overlap

Study identifies proteins that may play key roles in longevity

By Patrick Barry

Eating a calorie-restricted diet and being female are the best bets for living longer, at least for animals. Now scientists have discovered possible links between the two.

To find out whether these two scenarios share molecular mechanisms, Adamo Valle of the University of the Balearic Islands in Spain and colleagues compared male and female rats, some fed a normal diet and others a calorie-restricted diet.

Valle's team then compared activity levels of hundreds of proteins in the animals' livers, which help to regulate energy metabolism.

Among these proteins, 11 had different activity levels in both cases — comparing females with males and comparing normal with calorie-restricted diets, the team reports in the July *Journal of Proteome Research.*

It's the first time that scientists have found similarities between the longevity effects of gender and calorie restriction, but some scientists say that common ground is understandable.

"It doesn't surprise me at all," comments Peter DiStefano of Elixir Pharmaceuticals in Cambridge, Mass.

Valle and colleagues say the 11 proteins might affect longevity since they play roles in energy metabolism, antioxidant mechanisms, stress response and cardiovascular protection.

ISTOCKPHOTO/KATIV; ISTOCKPHOTO/MJP

Molecules

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DNA, Jim, but not as we know it

Unnatural genetic letters build stronger double helix

By Patrick Barry

If aliens have DNA, it might look something like this.

Chemists have synthesized a DNA-like molecule using unnatural versions of the A, T, C and G "letters" that make up the genetic code. The resulting molecule has greater structural stability than natural DNA and would resist breakdown by DNA-degrading enzymes in cells, the team reports in the July 9 *Journal of the American Chemical Society*.

"The artificial DNA may be a superior building scaffold for constructing medical and nanotechnological structures," says lead scientist Masahiko Inouye of the University of Toyama in Japan. "Our research opens the door to ... creating DNA-like molecules similar to natural DNA in terms of their ability for potential information storage."

While other variants of DNA have been made before, the new molecule is the first to have unnatural versions of the compounds that constitute all four letters of the genetic code. The variant is also the first to replace the bond holding each letter to the helix-shaped backbone with a more rigid triple bond. This new bond is what gives the unnatural DNA its greater stability and resistance to enzymes.

Like natural DNA, the new molecule can form a triple helix as well as a double helix.

"The DNA structure is a whole lot more pliable than we originally thought, and that's fascinating," comments Floyd Romesberg, a molecular biologist at the Scripps Research Institute in La Jolla, Calif. "This is coming along with a [chemical] structure that's been preserved for millennia and saying, 'Well, I'm bored. I want to try a different architecture.'"

Strings of DNA bind to each other in predictable ways, which makes DNA attractive as a material for engineering at the nanoscale. The ability to customize DNA's structural traits will give nanotechnologists even more control, Romesberg says.

Scientists are also developing novel drugs that use snippets of DNA or RNA to treat diseases. Enzymes in the body rapidly degrade regular RNA, comments Martin Egli, a structural biologist at Vanderbilt University in Nashville, Tenn. Egli says the chemical modifications should be easy to apply to RNA as well.

Finding the golde

PAUL J. SUTTON

Advances in gene therapy could tempt some athletes to enhance their genetic makeup, leading some researchers to work on detection methods just in case

By Patrick Barry

In early August — 8/8/08, to be precise — the curtain will rise on what many experts believe could prove to be the first genetically modified Olympics.

For the unscrupulous or overdriven Olympic athlete, the banned practice of "doping" by taking hormones or other drugs to enhance athletic prowess may seem so last century. The next thing in doping is more profound *and* more dangerous. It's called gene doping: permanently inserting strength- or endurance-boosting genes into DNA.

"Once you put that gene in, it's there for the rest of that person's life," says Larry Bowers, a clinical chemist at the U.S. Anti-Doping Agency in Colorado Springs, Colo. "You can't go back and fish it out."

Scientists developed the technology behind gene doping as a promising way to treat genetic diseases such as sickle-cell anemia and the "bubble boy" immune deficiency syndrome. This experimental medical technology — called gene therapy — has begun to emerge from the pall of early failures and fatalities in clinical

n genes

Ready, set, go. Athletes are primed for the Beijing Olympics. The desire to run faster and farther could inspire some athletes to prime their bodies down to the genes.

trials. As gene therapy begins to enjoy some preliminary successes, scientists at the World Anti-Doping Agency, which oversees drug testing for the Olympics, have started to worry that dopers might now see abuse of gene therapy in sport as a viable option, though the practice was banned by WADA in 2003.

"Gene therapy has now broken out from what seemed to be too little progress and has now shown real therapies for a couple diseases, and more coming," says Theodore Friedmann, a gene therapy expert at the University of California, San Diego and chairman of WADA's panel on gene doping.

While gene therapy research has begun making great strides, the science of detecting illicit use of gene therapy in sport is only now finding its legs. To confront the perceived inevitability of gene doping, Friedmann and other scientists have started in recent years to explore the problem of detecting whether an athlete has inserted a foreign gene — an extra copy that may be indistinguishable from the natural genes — into his or her DNA.

It's proving to be a formidable challenge. Genetic makeup varies from person to person, and world-class athletes are bound to have some natural genetic endowments that other people lack. Somehow, gene-doping tests must distinguish between natural genetic variation among individuals and genes inserted artificially — and the distinction must stand up in court.

Scientists are fighting genetics with genetics, so to speak, enlisting the latest technologies for gene sequencing or for profiling the activity of proteins to find the telltale signs of gene doping. Some techniques attempt the daunting search for the foreign gene itself, like looking for a strand of hay in an enormous haystack.

But new research could also lead to an easier and more foolproof approach: detecting the characteristic ways that an inserted gene affects an athlete's body as a whole.

Resurgence of gene therapy

In 1999, 18-year-old Jesse Gelsinger died during a gene therapy trial for a rare liver disease. Investigators later attributed his death to a violent immune reaction to the delivery virus rather than to the therapeutic gene. His death was a major setback for the field. It also may have scared away early would-be gene dopers.

> "I've had athletes come to my lectures and go to the microphone and say, 'If I took this drug, would it work with EPO and growth hormone?' I mean, they would ask this publicly."
>
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> **SALK INSTITUTE**
> **FOR BIOLOGICAL STUDIES,**
> **LA JOLLA, CALIF.**

In recent years, safety and efficacy of gene therapy have shown signs of progress in numerous clinical trials for conditions ranging from early-onset vision loss to erectile dysfunction. As scientists develop ways to use safer, weaker viruses for delivery, and as gene therapies wind their way through clinical trials, athletes and coaches might start to see gene doping as even more viable than they already do.

In the courtroom during the 2006 trial of Thomas Springstein, a German track coach accused of giving performance-enhancing drugs to high-school–age female runners, prosecutors read aloud an e-mail Springstein had written that would shock the sports world.

"The new Repoxygen is hard to get," the e-mail read, according to press reports. "Please give me new instructions soon so that I can order the product before Christmas."

Repoxygen isn't merely another doping drug such as a hormone or the latest designer steroid — it's an experimental virus designed to deliver a therapeutic gene and insert it into a person's DNA.

British pharmaceutical company Oxford BioMedica developed Repoxygen in 2002 as a treatment for severe anemia. The therapy "infects" patients with a harmless virus carrying a modified gene that encodes erythropoietin, a protein that boosts red blood cell production. This protein, often called EPO, is itself a favorite among dopers seeking to increase their oxygen capacity, and hence their endurance.

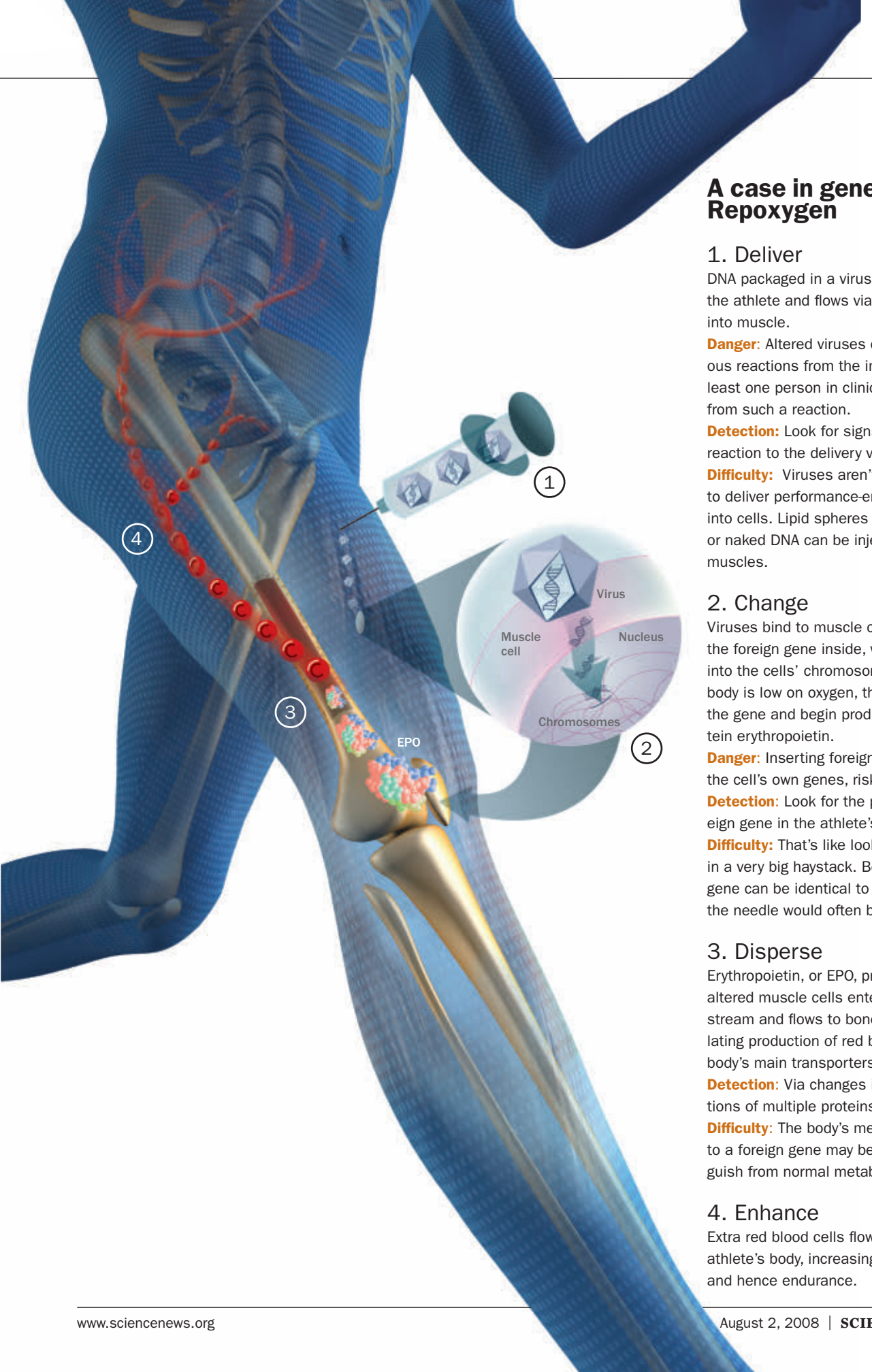
Viruses have the natural ability to inject genetic material into their host's DNA. The host's cells can translate that gene into active proteins as if the foreign gene were the cells' own. So by delivering the gene for EPO within a virus, Repoxygen could potentially increase the amounts of EPO protein — and the change would be permanent.

Athletes might also be tempted by perhaps the most tantalizing gene therapy experiment of all: the "mighty mouse." In 1998, H. Lee Sweeney and his colleagues at the University of Pennsylvania School of Medicine injected mice with a virus carrying a gene that boosted production of insulin-like growth factor 1, or IGF-1, a protein that regulates muscle growth. As a result, the mice had 15 percent more muscle mass and were 14 percent stronger than untreated mice — without ever having exercised. The treatment also prevented the decline of muscle mass as the mice grew older.

Other genetic paths to increase muscle strength and volume could include the gene for human growth hormone or segments of DNA that block a protein called myostatin, which normally limits muscle growth.

Endurance might also be boosted by the gene encoding a protein called peroxisome proliferator-activated receptor delta, or PPAR-delta. Mice engineered to have extra copies of this gene hopped onto a treadmill and, without ever having trained, ran about twice as far as unaltered mice. The extra PPAR-delta improved the ability of the mice's muscles to use fat molecules for energy, and it shifted the animals' ratio of muscle fiber types from fast-twitch toward slow-twitch fibers — a change that would improve muscle endurance in people as well. Ronald Evans and his colleagues at the Salk Institute for Biological Studies in La Jolla, Calif., published the research in 2004.

Since then, Evans says, he has been routinely approached by curious coaches



A case in gene doping: Repoxygen

1. Deliver

DNA packaged in a virus is injected into the athlete and flows via the bloodstream into muscle.

Danger: Altered viruses can elicit dangerous reactions from the immune system. At least one person in clinical trials has died from such a reaction.

Detection: Look for signs of the body's reaction to the delivery virus.

Difficulty: Viruses aren't the only way to deliver performance-enhancing genes into cells. Lipid spheres can carry DNA, or naked DNA can be injected directly into muscles.

2. Change

Viruses bind to muscle cells and deposit the foreign gene inside, where it integrates into the cells' chromosomes. When the body is low on oxygen, the cells translate the gene and begin production of the protein erythropoietin.

Danger: Inserting foreign DNA can damage the cell's own genes, risking cancer.

Detection: Look for the presence of a foreign gene in the athlete's DNA.

Difficulty: That's like looking for a needle in a very big haystack. Because the foreign gene can be identical to the natural gene, the needle would often be a strand of hay.

3. Disperse

Erythropoietin, or EPO, produced by the altered muscle cells enters the bloodstream and flows to bone marrow, stimulating production of red blood cells, the body's main transporters of oxygen.

Detection: Via changes in the concentrations of multiple proteins in blood or urine.

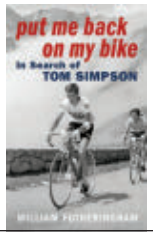
Difficulty: The body's metabolic responses to a foreign gene may be hard to distinguish from normal metabolic variations.

4. Enhance

Extra red blood cells flow throughout the athlete's body, increasing oxygen capacity and hence endurance.

J. KORENBLAT, ISTOCKPHOTO/MPABILD

Gene therapy, athletes and doping



1928
IAAF, the International Association of Athletics Federations, becomes the first international sport federation to ban doping, the use of performance-enhancing substances.

1968
The International Olympic Committee approves a ban on doping, a year after British cyclist Tom Simpson collapsed and died during the Tour de France. His autopsy revealed high levels of methamphetamine.

1998
Mighty mouse: Injecting mice with a virus carrying the gene for IGF-1 makes the animals 14 percent stronger, even without the benefit of exercise. This mouse is shown climbing a ladder while carrying weights.

1999
18-year-old Jesse Gelsinger becomes the first person to die during a gene therapy clinical trial, apparently because of a massive immune response to the virus used to deliver the genes.

2003
Gene doping is added to the World Anti-Doping Agency list of banned doping practices.

and athletes. "I've had athletes come to my lectures and go to the microphone and say, 'If I took this drug, would it work with EPO and growth hormone?' I mean, they would ask this publicly," Evans says.

"Based on athletes I've talked with, I'd say that it's a reasonable possibility that gene doping will be used in this Olympics, and I think there's a very high probability that it will be used in the next Olympics," he says.

Elusive signs

Around the time that Evans was announcing his "marathon mouse" results, WADA kicked off a funding program to focus scientific research on strategies for detecting gene doping.

"A key part of our project is to try to define what we call signatures of doping," says Olivier Rabin, a biomedical engineer and director of science for WADA. "We are looking at the impact of those kinds of genetic manipulations at different levels."

The first and most obvious approach is simply to look for the inserted gene among the roughly 6 billion "letters" of genetic code in both sets of a person's chromosomes.

For clinical gene therapy trials, finding the inserted gene is fairly easy. Scientists know the exact sequence of the gene they inserted, and often they know where on the person's chromosomes the gene should have ended up. Standard DNA sequencing techniques can reveal the genetic code for that region on the chromosomes, and the unique sequence of the inserted gene will be in plain view. With gene doping, the situation is much trickier.

"In sport, you don't know where that gene will be put, what virus was used or even what particular variety of gene was used," Friedmann says. "You don't have the advantage of knowing where to look and for what, so the argument is to look everywhere."

Another difficulty is that copies of the foreign gene wouldn't be in all of a person's cells. The gene-carrying viruses selectively target certain tissues such as muscle or liver (the liver helps to regulate muscle metabolism). Some blood cells might also take in the viruses' genetic payloads, but it's questionable whether a standard blood sample from an athlete would contain the gene. Instead, anti-doping officials would have to sample muscle tissue directly using punch biopsies, a procedure that is mildly painful.

"No one's expecting that an athlete will agree to a muscle biopsy," Friedmann says. "That's a nonstarter."

Still, direct detection of inserted genes could work in some cases. Evans points out that an artificially inserted gene for PPAR-delta would be much smaller than the natural gene. That's because the natural gene is far too big to hitch a ride on the carrier virus. Fitting the gene onto a virus means only a trimmed down version of the gene can be used. This distinctive genetic pattern would only exist in a person who had undergone gene doping.

In other cases, genes would end up in tissues where they're not normally active, making detection more straightforward. For example, the liver and kidneys normally produce the protein EPO, which makes red blood cells, but gene doping could deliver the EPO-coding gene directly to muscle tissues. The trick, then, is to find a noninvasive way to detect where EPO production is occurring inside the body.

One solution is to use medical imaging techniques such as PET scans. In research funded by WADA, Jordi Segura and his colleagues at the Municipal Institute for Medical Research in Barcelona, Spain, attached slightly radioactive "flags" to molecules made during EPO production. A standard PET scan can spot this radioactivity, revealing where EPO was being made in the bodies of mice injected with gene-doping viruses, the team reported in the October 2007 *Therapeutic Drug*

1998: LEE SWEENEY/UNIV. OF PENNSYLVANIA

2004
The World Anti-Doping Agency begins a program to fund scientific research on ways to detect gene doping.

2006
The first public evidence of a coach seeking gene doping substances for his athletes emerges in court during the trial of German coach Thomas Springstein.

June 10–11, 2008
The World Anti-Doping Agency holds the third Gene Doping Symposium, in Saint Petersburg, Russia.

Gene therapy could help an athlete change production of …	And the result could be …
Erythropoietin	Enhanced red blood cell production, thus greater oxygen delivery for endurance
Human growth factor	Increased muscle size, power and recovery from fatigue
Insulin-like growth factor	Increased number of muscle regulator cells, thus size, power and recovery from fatigue
PPAR-delta	More fat metabolism and increased muscle endurance
Myostatin	Greater muscle growth due to the inhibition of myostatin production

Monitoring. The researchers showed that production of EPO in muscle tissue was a telltale sign of gene doping.

With radioactivity that is relatively mild, the labels are routinely used in medical imaging to diagnose diseases and don't pose a significant hazard. But Friedmann notes that asking athletes to undergo such a procedure could be controversial.

Detection by proxy

Another approach is to look for signs of the viral "infection," rather than for the gene itself. Even a weakened virus could trigger a mild, and specific, immune reaction that might show up in a blood test.

Perhaps the greatest challenge facing this method is that viruses aren't the only way to deliver a gene into a doper's body. "The reality is that you can just inject naked DNA directly into tissues" with a syringe, Evans says. "Direct injection could be more local and harder to detect."

This relatively crude way to insert a gene won't spread the gene as widely through a person's body as viruses injected into the bloodstream would. But many cells near the site of injection could take in the gene, perhaps enough to improve athletic performance.

Microscopic, synthetic spheres of fat molecules called liposomes can also shuttle doping genes into the body.

To prevent dopers from evading detection by simply changing delivery vehicles, scientists are also exploring a third approach to developing tests: proteomics, the detailed study of all the proteins in the human body.

Regardless of the vehicle used, adding a new gene to the body's tightly woven web of interacting genes and proteins will cause ripples of change to spread throughout that web. "There will be a body-wide response no matter what gene you use or where in the body you put it," Friedmann says, "and those changes can be used as a signature of doping."

Painful biopsies wouldn't be required. Because the cascade of changes in protein activity would be widespread, anti-doping officials could test using blood, urine, hair or even sweat. Tools developed for the burgeoning fields of genomics and proteomics allow scientists to see the activity levels of thousands of genes or proteins simultaneously.

In preliminary unpublished experiments, Friedmann and his colleagues injected a type of muscle cell with the gene for IGF-1. Activity of hundreds of genes changed as a result, including a boost in the activity of genes that control production of cholesterol, steroids and fatty acids. All of these changes might be detectable with simple blood tests.

WADA is funding half a dozen or so ongoing studies on this proteome-based detection strategy, but research in this area is still at an early stage. "There's good reason to think that's likely to work, and a number of labs are having some nice results," Friedmann says.

As for whether any tests for gene doping will be ready in time for the Beijing Olympics, anti-doping authorities aren't giving away many hints that might help dopers evade detection. "We never say when our tests are going to be in place," WADA's Rabin says.

Even if detection methods do lag behind the games, dopers may want to think twice before assuming they're in the clear, Friedmann notes. "With stored [blood and urine] samples, one always has the option of going back some months or years later and checking again with the newest tests."

Just in case the dangers of tampering with a person's genetic makeup weren't enough of a disincentive. ■

Explore more

■ National Institutes of Health Handbook on Gene Therapy: ghr.nlm.nih.gov/handbook/therapy/genetherapy

2006: REUTERS/ARND WIEGMANN

Raman spectroscopy may offer doctors, dentists and forensic scientists a better tool for molecular detection

By Ashley Yeager

Insightful Light

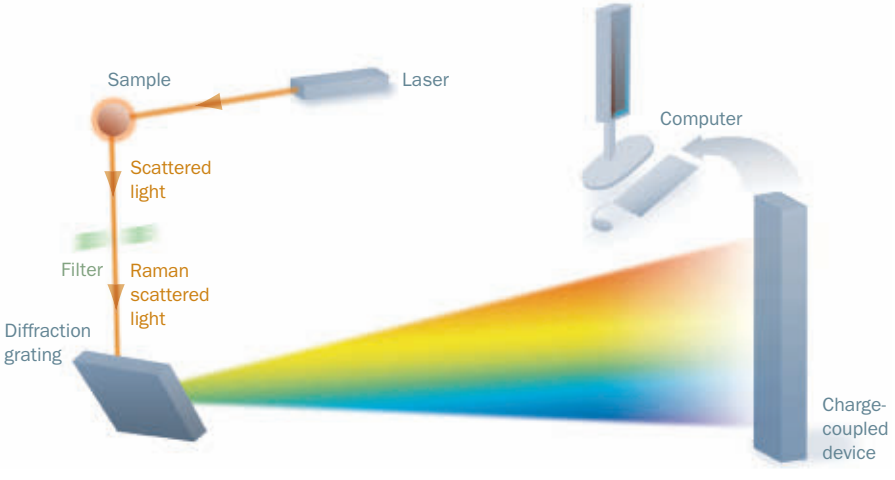
From CT, PET and MRI to the original X, a vast alphabetical arsenal of tools tells doctors what is going on inside the body. But despite their successes, these tools often fail to detect the subtle changes that signal the imminent onset of illness. Mischief at the molecular level often evades doctors' current imaging and detection abilities. So for sensing such changes, biomedical scientists are taking a tip from chemists. Using a method known as Raman spectroscopy, medical detectives are moving ever closer to exploiting the power of light to improve disease detection.

Long used in labs, spectroscopy employs light and other types of electromagnetic radiation to analyze matter. The various spectroscopic techniques reveal a molecule's unique chemical fingerprint by measuring the wavelengths of light that the molecule absorbs or emits, or by tracking how radiation scatters after interacting with a molecule. For 30 years, scientists have been eager to harness the power of Raman spectroscopy, a type of scattering spectroscopy, to image the body at the level of individual molecules. The method holds promise for pinpointing the beginnings of dental cavities and tumors. And it could even help forensic investigators nab killers sooner by lifting latent fingerprints from corpses.

A variety of researchers, from dentists and doctors to chemists, now report some of the first successes using Raman spectroscopy to probe chemicals and minerals within and on living — and dead — bodies. "Raman spectroscopy is a very powerful tool," says Cristina Zavaleta, a molecular imaging radiologist at Stanford University. But, she adds, the technique still needs some time to develop.

In recent years, scientists have rapidly overcome many of the hitches holding up the widespread use of Raman-based instruments. That progress leads many to speculate that within a few years doctors and dentists could be wheeling new, Raman-based tools into the examining room, or detectives could even be driving them to the scene of a murder.

At its simplest, a Raman spectroscope shoots a single-wavelength laser at a sample. The sample's molecules absorb, emit or scatter incoming photons. A filter captures scattered photons with the same wavelength as the laser, allowing the photons with different wavelengths to pass through. These collide with a grating that, like a prism, separates them by wavelength. The resulting pattern, or spectral fingerprint, is passed to a computer where the sample's chemical makeup is determined.



Imaging humans' insides

In Raman spectroscopy, scientists shoot a laser light at a target molecule and measure how the wavelengths of

J. KORENBLAT (SOURCE: MATERIALS SCIENCE AND METALLURGY DEPT., UNIV. OF CAMBRIDGE); ISTOCK/HOMEBREDCORGI

scattered light, in the form of photons, coming off the target compare with the laser's original wavelength. Only one in 10 million of the photons hitting the target shows an increase or decrease in wavelength. Detecting these rare photons is the challenge — and ultimately the payoff — for scientists seeking to harness the Raman effect for clinical applications.

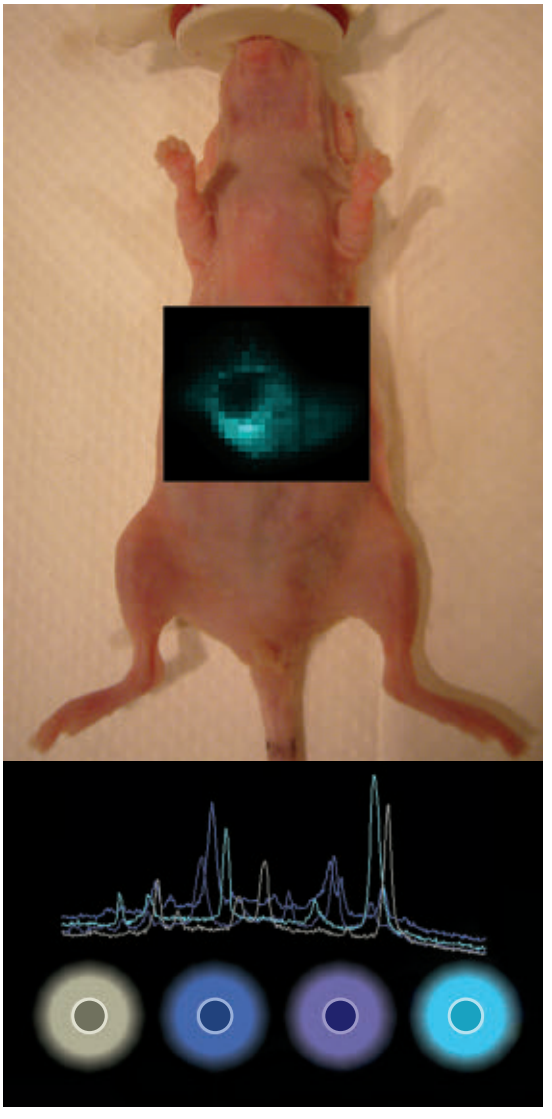
The wavelength change is called the Raman effect in honor of Indian physicist Chandrasekhara Venkata Raman, who first showed in the 1920s that measuring the changes in wavelengths of scattered photons can help scientists identify a compound's molecular makeup. He won the Nobel Prize in physics in 1930 for his work. Currently, geologists, chemists and archaeologists use the technique to study minerals in the soil, identify new materials and determine the pigments in ancient paintings, manuscripts and other artifacts.

"At this point, Raman spectroscopy is good for surface scans," says David Batchelder, a Raman researcher from the University of Leeds in England. Unlike X-rays and CT scans, existing Raman tools have yet to let doctors look inside the body. "To penetrate deep into tissues," Batchelder says, "the equipment has to be very good."

But Stanford University researchers, including Zavaleta, are on track to engineer inward-probing Raman tools. The key, the scientists discovered, is in using nanoparticles. By wrapping cancer antibodies around gold nanoparticles, the team used Raman spectroscopy to detect tumors in a living mouse.

Zavaleta and colleagues injected the nanoparticles into the mouse. Each specific antibody attached to a specific type of tumor cell. When the researchers shone laser light across the animal's body, the cells with attached antibody-coated nanoparticles showed a change in wavelength compared with the laser.

Signals coming from the antibodies are very weak, Zavaleta says. But the gold in the nanoparticles boosts the signal because the laser excites the gold cores and the metal actually shows an intensity increase in its surrounding electric fields. The Stanford team scanned the mouse's body for the excited electric fields and pinpointed the locations of the nanoparticles using a Raman microscope.



Stanford University researchers injected nanoparticles with enhanced Raman scattering activity into an anesthetized mouse. The researchers then used Raman spectroscopy and microscopy to image the mouse's liver (inset), where the particles migrated. Each nanoparticle, shown in different colors in an artist's rendering, has its own spectral fingerprint. In other experiments, the team detected key changes associated with cancer by tagging each nanoparticle with antibodies that target and bind to unique tumor markers.

JIM STROMMER, C. ZAVALETA, SANJIV GAMBHIR/STANFORD UNIV.

The microscope looks like a standard optical microscope. But researchers added the laser and a sensitive detector to the instrument to read the spectral fingerprints of the nanoparticles and then compute where in the body there were excited electric fields and changes in photons' wavelengths. Ultimately, the team's device formed an image of the mouse's internal tumors.

And, because the injected nanoparticles attached to different tumor types, the scientists were able, in one scan, to identify where different cancer cells were in the mouse's body. That single scan for many types of cancer is the novel aspect of this research, Zavaleta says. She and her colleagues reported their progress in the April 15 *Proceedings of the National Academy of Sciences*.

Aside from CT scans and X-rays, doctors are using fluorescence imaging with quantum dots to take a peek at the finer details of the human body. But the Raman technique, Zavaleta says, could exceed the capabilities of quantum dots. Doctors would need to inject only one one-thousandth the number of nanoparticles required for imaging using quantum dots. Showing that scientists can image living subjects with fewer nanoparticles has never been done successfully before, the Stanford radiologist says.

Oncologists could eventually use Raman spectroscopy during surgery to scan diseased tissue. Injecting the new nanoparticles or a variation of them into the body during an operation would show surgeons where the tiniest abnormal cells are just beginning to form. The surgeon could remove these developing cancer cells and perhaps prevent future growth and spread of the tumor, Zavaleta says.

Raman spectroscopy could also replace visual checks for tumors and diseases like cervical cancer. "In Pap smears doctors just look for cancer cells," says Batchelder, "but certain types of tumors are hard to identify. Raman technology could pick out the particular molecular processes related with this type or a par-

ticular type of tumor, making it easier to catch."

The developing technique, though, will never completely replace PET scans, MRI, ultrasound and other imaging methods, Zavaleta says. Each technique brings its own advantages to figuring out what's going on inside the body. Yet some doctors are trying to rid their offices of X-ray machines, at least the doctors that poke at people's teeth.

No drilling for the dentist

In addition to ridding the body of cancer cells, Raman spectroscopy may rid dentists of their drills.

No one likes having cavities filled. So, to avoid putting patients "under the drill," Lin-P'ing Choo-Smith and her colleagues at the National Research Council Canada's Institute for Biodiagnostics in Winnipeg are studying how to use Raman spectroscopy to spot cavities much sooner than currently possible.

Working with extracted teeth, the Canadian dental researchers have detected tiny cavities by using Raman spectroscopy to search for slight decreases in calcium hydroxyapatite, the dominant mineral component of teeth. The team presented its latest work at a meeting in June sponsored by the European Organisation for Caries Research and then discussed it again in July at a conference of the International Association for Dental Research.

Cavities, which often result from dental caries, are spots on the tooth where minerals have leached out. Bacteria in plaque play a key role in cavity formation by producing acids that leach the minerals. With less minerals in the tooth structure, the tooth begins to dissolve and can rot.

Dentists usually use X-rays and dental probes — the metal picks that can scratch at the teeth — to detect cavities. But with these tools, dentists can detect only major damage to the tooth and cavities as big as a millimeter in size. And by this stage, Choo-Smith says, the tooth can be in pretty bad shape.

"Using Raman, however, would let dentists detect small changes in mineral levels of the tooth long before a cavity actually became a cavity," Batchelder says. Dentists could detect precursors to cavities and weak spots with lesions only 100–250 micrometers deep, about the size of an individual grain of sand. The Raman tool might also detect troublesome spots between teeth.

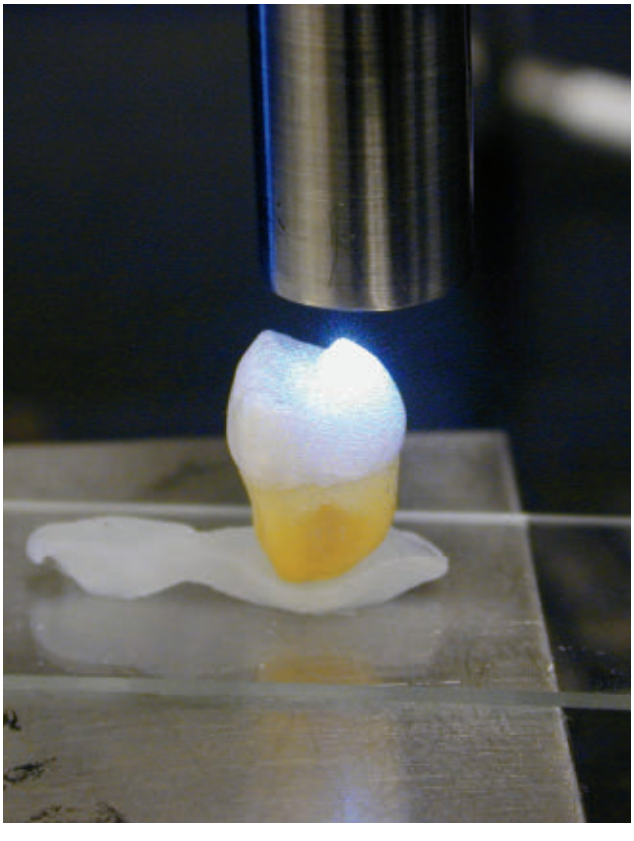
Catching the problem areas at an early stage could eliminate the dentist's need to drill, Choo-Smith says. Instead patients could self-treat the tiny, trouble areas with fluoride or antimicrobials.

Using spectroscopy coupled with an imaging technique called optical coherence tomography to detect a speck of a cavity might seem like overkill to some patients, says Cecilia Dong, a dentist at the University of Manitoba in Canada and one of Choo-Smith's collaborators. But the more information dentists have, the more accurate their diagnoses will be. That could mean less pain for patients, she adds.

What's more, Raman spectroscopy does not use ionizing radiation like X-rays do, so pregnant women and small children could be safely scanned, Dong notes. With no radiation exposure to worry about, dentists could use Raman testing every time a patient comes into the office. Frequent scanning, she says, will truly show dentists and hygienists who is doing their daily brushing and flossing.

But adapting Raman spectroscopy for the dentist's office, Choo-Smith explains, would require that dentists have a portable Raman-based unit and a miniature wand or probe to use in the mouth. Engineering and manufacturing probes for reading scattering spectroscopy emissions, specifically ones small enough to scan a tooth, is one of the greatest challenges for current Raman spectroscopy researchers.

And, while ever-smaller fiber optic cables and, in medicine, nanoparticles may help scientists add Raman spectroscopy to their disease-detecting arsenal, the development work is far from over. Still, each round of probe design and research yields clearer results. Within the next year and a half, Choo-Smith expects to take prototype probes into dentists' clinics for testing. "I think it will still be another three to five years before they will have a product to wheel into their examining rooms," she says.



Dental researchers shine laser light on an extracted tooth. A Raman spectrometer (not shown) will measure scattered photons bouncing off the tooth and read the spectral fingerprint of the tooth's minerals to detect signs of damage.

CHOO-SMITH

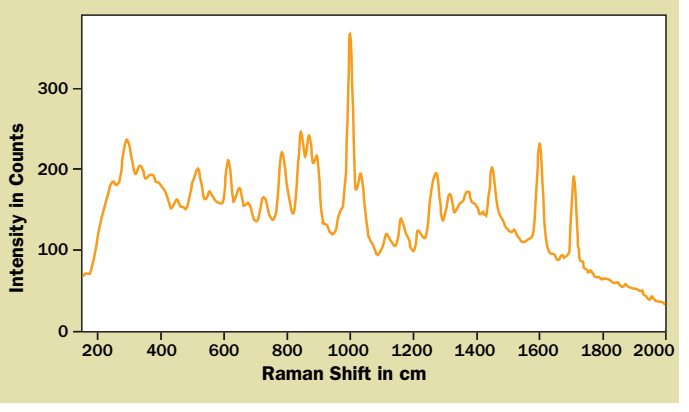
Lifting latent prints

From inside the body to inside the mouth, Raman spectroscopy shows promise for detecting the molecular fingerprints of disease. But it also could prove useful for identifying real fingerprints — such as the prints a killer leaves on a victim's body.

"Prints are really hard to lift from

corpses," says Linda Lewis, a chemist at the Oak Ridge National Laboratory in Tennessee. "Our goal, though, is to detect fingerprints on surfaces where they are not traditionally detected."

Lewis is developing a device based on Raman spectroscopy that would enable detectives to trace the chemical signatures of certain residues left by human hands — on corpses or even hard-to-analyze evidence. Working with researchers at ChemImage in Pittsburgh, Pa., and the U.S. Naval Research Laboratory in Washington, D.C., Lewis is using silver-coated nanowires, similar to Zavaleta's gold nanoparticles, to mark a killer's prints, or at least, right now, human prints left on dead animal skin.



Some companies already manufacture portable Raman spectroscopy tools for nonclinical uses. Austin, Texas–based Raman Systems Inc. sells the RSL*plus* handheld spectrometer system (top) for analyzing substances ranging from drugs like cocaine (spectrum shown) to silicon for semiconductors.

The nanowires target specific fingerprint components — such as eccrine, a watery substance that comes out of the pads of human fingers and is not well detected using current forensic methods — that give off Raman scattering emissions. "The most active signal we get right now is actually from urea," she says.

In theory, Lewis says, detectives would spray the silver-coated nanowires onto a corpse in the field and then use a Raman microscope-laser device to scan the body. The nanowires would detect particular molecules in urea, eccrine and possibly other substances. Passing the laser over the body would trigger the silver coating on the nanowires to amplify the signals emanating from the laser's scattered photons by changing the electric field. Using the microscope, which would register the chemical spectrum and locate the signals, the investigators could isolate a killer's fingerprint.

Lewis says analyzing the Raman spectroscopy scans is similar to looking at the individual pixels from a picture. Not every pixel has high peaks of light on it. Similarly, not everything gives off a Raman scattering signal. When the pixels are put together, though, the image appears in a matrix of light and dark spots. On the skin, the scattering signals from the 1-by-1-inch laser-light blocks can come together to show a fingerprint, like the pixels show the image, she says. And, once the Raman tool reveals the location of the left-behind molecules, detectives could collect the print for further analysis, just as they do now from hard surfaces.

Lewis and her colleagues are currently writing up their early results on the spectroscopy device for submission to the *Journal of Forensic Sciences*. Her team next needs to look for prints on actual decaying bodies instead of preserved pig and human skin, she says. Scanning for prints will help her team design a Raman spectroscopy device that could detect killer's prints left on bodies found 24 to 48 hours after death.

"We need to see if the prints decompose as the body does or if heat or other factors affect the signals we can get from the prints," she says.

And, although the Raman spectroscopy print identification tool is still in its testing phase, Lewis says the team wants to have something ready to go in about two years.

But corpses are not the only crime scene evidence detectives could scan for the signatures of fingerprints. Investigators could also do Raman-based analyses on explosive residues from terrorist attacks or even on heavily contaminated drug evidence. "Prints are hard to lift from these places too, and we want the device to work on all tough surfaces," Lewis says. "My far out vision, probably in 10 years, though, is to scan live skin. That would identify abuse criminals."

But creating a forensics Raman tool for widespread use means engineering nanowires more efficiently and at a lower cost. Researchers at the Naval Research Laboratory can make small quantities of nanowires, with a lot of effort, Lewis says. "The challenge is making large batches of the silver nanowires" more quickly, she says.

Medical applications for Raman spectroscopy, Batchelder notes, face similar delays. Don't expect to see Raman tools in a dentist's or doctor's office tomorrow, he says, adding that while he has seen technology improve immensely in the past 10 years, each biomedical application for Raman-based tools has had its holdups.

For medical researchers, probe design is a struggle. No commercial companies are currently invested in developing the probes, even though there is a major market for them, dental researcher Choo-Smith says. Researchers are basically going it alone, trying to build something that will bring the sensitivity of Raman spectroscopy to the examining and operating rooms. Still, scientists and doctors are optimistic, and while they recognize the obstacles, most are confident that soon they will be able to add an "R" for Raman spectroscopy to the alphabetical arsenal they use to explore the human body and catch criminals. ■

Editor's note: David Batchelder, formerly of the University of Leeds, died on June 6.

Explore more

■ University of Cambridge's tutorial on Raman spectroscopy: www.doitpoms.ac.uk/tlplib/raman/index.php

RAMAN SYSTEMS; RENISHAW INC.

DECODING THE QUANTUM MYSTERY

Signals from space to Earth could establish the reality of Einstein's worst fear

By Tom Siegfried

Every true fan of science fiction (and science too, for that matter) should be familiar with *Forbidden Planet*, the film famous for introducing the world to Robby the Robot.

The story takes place in the 23rd century on Altair-4, where the crew of the cruiser C-57D attempts to devise a contraption to communicate with Earth. "I'll bet any quantum mechanic in the service would give the rest of his life for a chance to fool around with this gadget," Chief Engineer Quinn (Richard Anderson) tells Commander Adams (Leslie Nielsen).

When the film was new, in 1956, scientists would have chortled. "Quantum mechanics" weren't repairmen for message-sending machines. It was the math for describing subatomic physics.

But it turns out that *Forbidden Planet* was prescient about more than just talking robots. No doubt the C-57D crew was trying to send a coded message back to Earth, made safe from eavesdropping by the use of quantum cryptography.

Born theoretically just a quarter century ago, quantum cryptography forms the foundation of a burgeoning research enterprise known as quantum information theory, which involves not just quantum communication but also the ambitious goal of quantum computation. The whole idea relies on the weirdness of quantum physics to enable messaging and computing schemes unattainable by ordinary means. Quantum communication promises to turn into technology the esoteric math with bizarre implications that Einstein famously refused to accept.

Even today, many knowledgeable physicists have a hard time coping with the rules of reality that quantum physics imposes. Most famous of those rules is Heisenberg's uncertainty principle, which asserts the impossibility of measuring an entity's position and velocity at the same time. (It's an odd name, though, as nothing in nature is more certain than Heisenberg's principle.) Flowing from that principle are other rules that read like riddles: Nature's basic building blocks can be particles or waves, depending on how they are observed. A particle can be in two places at once, a cat can be simultaneously alive and dead, a particle can hop from one side of a wall to another without passing through it. Quantum weirdness encompasses a diverse repertoire of confusing curiosities.

Of greatest concern to Einstein, and to many yet today, is the quantum insistence that the future is not precisely determined by the past, as it allegedly was in the clockwork universe quantified by Newton. In a quantum universe, multiple outcomes are allowed, with precisely determined odds, like a cosmic horse race in which Big Brown usually wins, but not always. A radioactive atom will probably decay within a given time, but not for sure. Einstein's desire for a deity without dice is defied repeatedly by quantum phenomena. Yet every test of the quantum rules confirms this weirdness; in any experimental challenge, quantum theory is more reliably victorious even than Tiger Woods on good knees.

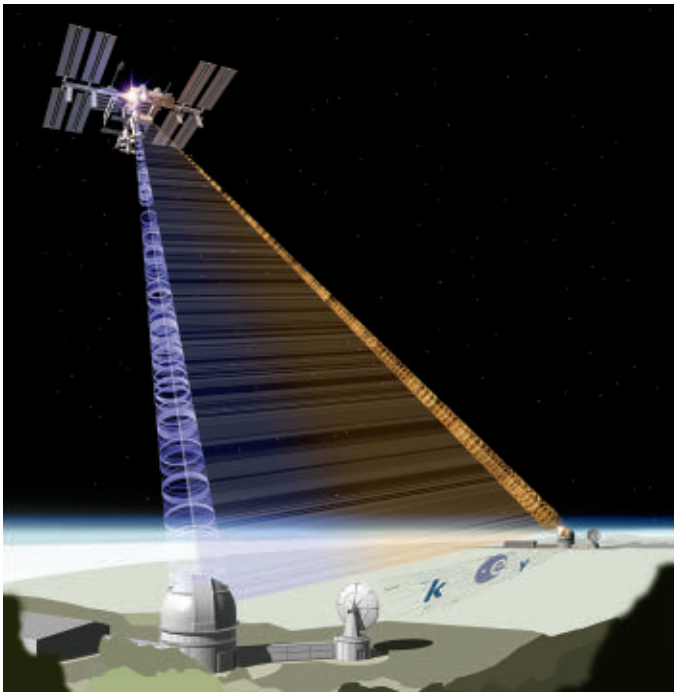
Quantum physics therefore claims cosmic authority. Einstein's theory of general relativity, for instance, is supposed to govern the cosmos on large scales, but it is widely believed to be ultimately deficient because it cannot be made compatible with quantum requirements. On the other hand, quantum physics has mostly been tested on a small scale. Quantum message sending on Earth, via light pulses transmitted through optical fibers, demonstrates that the weirdness is preserved over distances of kilometers. But that's not necessarily enough to allay all suspicion that someday quantum physics will fail.

From space, though, quantum signals could be sent simultaneously to stations much farther than current technology allows on land. So a group of physicists has devised a plan to test the universality of quantum weirdness by following the lead of *Forbidden Planet* and sending quantum messages from space to Earth.

Altair-4 is too far away, of course, but the International Space Station is conveniently nearby, and the physicists are far along in plans to use it to test quantum physics. An experimental proposal called Space-QUEST, led by physicists from the University of Vienna, calls for space-to-ground signaling using the latest in quantum communication technology.

"The use of satellites allows for demonstrations of quantum communication on a global scale, a task impossible on ground with current optical fiber and photon-detector technology," the Vienna team and their collaborators write in a new paper (online at arxiv.org/abs/0806.0945).

Some scientists wonder whether quantum weirdness will still survive at such distances. "It is an open issue whether quantum laws, originally established to describe nature at the microscopic level of atoms, are also valid in the macroscopic domain," the physicists write.



Researchers propose sending entangled photons from space to two separate labs on Earth to test quantum mechanics at large scales.

In their proposed experiment, the weirdness in question is a particular quantum property called entanglement. It's a consequence of quantum physics that was first fully noticed in the 1930s by Erwin Schrödinger and also by Einstein, neither of whom liked it very much. Entanglement is a sort of quasiphysical tie that binds, a link between two quantum particles that time and space cannot sever. It means that when particles of light — photons — interact and then go their separate ways, their ways are not really separate. The quantum math describing them retains an overlap, so that the fate of one depends, in a certain sense, on the fate of the other.

Without getting into the technicalities of polarization angles, you can think of entangled photons as something like pairs of spinning coins. If one turns up heads, the other will show tails, no matter how far the first is from the second, the quantum rules say. And it doesn't matter which coin is viewed first. There's no way to get a message from one to the other, no possible physical influence that can be transmitted to enforce this heads-tails mismatch — it just happens, instantly, as soon as one or the other photon is recorded.

It's well within the realm of current technology to produce entangled photons, and to send them off toward separate receivers. You could (as the Vienna physicists have proposed to the European Space Agency) outfit the Space Station with a device that spits out entangled photons to stations on the ground — let's say Fermilab outside Chicago and Caltech in Pasadena. When Fermilab physicists measure their photons, they can mark down a 1 for heads and a 0 for tails (that is, the corresponding polarization orientations) to generate a list of numbers known only to Fermilab and the senders on the Space Station. Caltech's scientists can compile a list of numbers the same way. Each lab can then use its list of numbers as a coding key for encrypting messages with absolute security. (Any eavesdropping on the photons would have destroyed the entanglement, alerting the physicists not to use that code.)

With Caltech and Fermilab each in possession of a set of code numbers, the Space Station could send another series of numbers (even over an open channel) to both Caltech and Fermilab, and the physicists at both locations could combine those numbers with their code keys to compute another key for secure communication between those two labs.

"Using such a scheme would allow for the first demonstration of global quantum key distribution," the physicists note in their proposal.

Global communication of quantum keys would no doubt have substantial practical applications — for secret signaling between command centers and military satellites, for instance, or for various commercial communications. The Vienna team and colleagues point out other possible uses, in synchronizing distant clocks and for research in the developing field of quantum astronomy. And space-based quantum communication would be critical to building a future quantum Internet, allowing secure communications (and perhaps computations) on a global scale.

But by far the most compelling outcome of long-distance quantum communicating would be the lesson it teaches about quantum theory's validity. The whole scheme works only if the entanglement predicted by quantum mechanics remains valid over large scales, beyond the confines of Earth-based labs.

If so, it's possible to imagine future space-based experiments using two stations orbiting at very different relative velocities, so that observers at each station would believe that their measurement of an entangled photon had occurred first. That would rule out any mystery signal telling the second photon whether the first was a 1 or 0. It would confirm what horrified Einstein — the reality of "spooky action at a distance." Scarier even than Monsters from the Id. ■

Explore more

■ Rupert Ursin *et al*. "Space-QUEST: Experiments with quantum entanglement in space." Online at arxiv.org/abs/0806.0945.

EUROPEAN SPACE AGENCY

Feedback

Iridescent shortcut

I was disappointed with your diagram of a Morpho wing in the June 7 issue ("How they shine," *SN: 6/7/08, p. 26)*. Rather than properly show different wavelengths of light interfering differently, you instead chose to cheat by keeping the wavelength the same in the two pictures and reversing the phase of the reflection from "Surface 2." By doing this, you failed to illustrate the physics and lost an opportunity to elucidate it to the reader, who may instead come away with confusion or even an incorrect understanding of the phenomenon.

MIKE SPECINER, ACTON, MASS.

Mature, or just dead

The article "Forest invades tundra" (*SN: 7/5/08, p. 26)* was very interesting, informative and disturbing. But just one note on the photo caption on Page 26. The tree indicated as "mature" may more accurately be described as dead. It appears that two inches of bark and sapwood have been burned off, leaving a well-charred inner section. If the back side of the tree does not miraculously have a nice strip of living bark attached, then that "mature tree" is surely dead. Thanks for a great science magazine.

TOM PRUNIER, ARLINGTON, VA.

Voice from the past

Now that I've seen the first four of the new *Science News* biweekly issues, I am way overdue in offering my congratulations. The new layout and design is crisp, professional and attractive; the content is as good as ever; and the whole product is more appealing. I also like the addition of your editor's column, something I think adds both a personal and professional touch and brings readers into your plans and ideas, as well as several other new, succinct features ("Science Stats" and "Scientific Observations"). *Science News* issues have long been all over our house, despite my best efforts to file them all chronologically. My family has grown up with it. My wife repeatedly exclaims about how dramatic and appealing the new format is. My grandsons, one a budding scientist/engineer, who had a gift subscription from me to the old format, like the new one even better. Any misgivings I may have had a year ago upon hearing of the possibility of reducing the frequency to once every two weeks have been decidedly put to rest. The trade-off to larger, less frequent issues is a winner, in my view.

KENDRICK FRAZIER, ALBUQUERQUE, N.M.

Editor's Note: Kendrick Frazier served as editor of Science News *from 1971 to 1977. He is now editor of* Skeptical Inquirer: The Magazine for Science and Reason.

Simpleminded voters

In modeling there are several phases. Once the model is constructed, it is validated, which means its predictions are compared to real-world data. If there are discrepancies, they are investigated and the model is revised to make the predictions close enough to actual data.

The validation steps can be very important since they basically point out the parts of the model that were not thought of. The modeling described in "Simpleminded voters" *(SN: 7/5/08, p. 22)* appears to have skipped the validation steps. It reports discrepancies between predicted results and actual results with no explanation of the discrepancies or attempt to revise the model.

It could be, for example, that voters think that behavior with reporters is an important predictor of ability to negotiate with world leaders. Voters may consider that an important factor in picking a candidate, not an excuse to avoid looking at other data. There are several other factors that could come into play, and investigating the discrepancies might tell more about the voting process.

IVAN MANN, HOOVER, ALA.

Certainly the argument that voters are more likely to vote properly when they ignore the overload of information and simply follow the party or organizational line when they cast their ballots has flaws. This is one case where statistics lie, with educated voters expressing their opinion in the voting booths based not only on information but also on logic.

Average voters have certain issues that are of top priority but may be in opposition to their political party or organization. Certainly in such a case, they should vote with their consciences and not follow the dictates of a political party. Incidentally, that is what makes each election a horse race.

NELSON MARANS, SILVER SPRING, MD.

Kudos for epigenetics article

I would like to congratulate Tina Hesman Saey on her feature article about epigenetics ("Epic genetics," *SN: 5/24/08, p. 14)*. She has conveyed, most lucidly, the fundamentals of a complex concept. As a science writer she has admirably inserted herself as a translator for those of us outside that particular area of biology. Many thanks and keep up the good work.

JIM DUNN, WARMINSTER, PA.

Science and government

Although I am in complete agreement with Steven Hyman in his June 7 column ("U.S. science policy needs to heed global realities," *SN: 6/7/08, p. 32*), he barely scratches the surface with his observations on stem cell research.

The depth of the problem caused by the impact of Bush administration ideology on the scientific community reaches earth science (global warming), human biology ("life begins at conception"), health ("abstinence only" demands, etc.), ecology (mercury, arsenic, carbon dioxide, etc.) and the variety of disciplines involved with primary research into alternative power sources. And even this is a small sample of the ongoing antiscience offensive to which we've all been subjected.

> “Governments are not very effective allocators of resources, including precious intellectual talent.”

This is not just about advancing pet projects at the expense of others, it's about sacrificing the future of our nation, and the world, at the altar of ignorance and narrow-minded, money-power ideology. After eight long, dreadful years of voodoo science and the rejection of the best the world's scientific minds have to offer, is it any wonder the leading edge the United States once had has been dulled? Is it any wonder today's new college students are avoiding the scientific endeavor?

REV. BUD ADAMS, CENTRAL SQUARE, N.Y.

Steven Hyman needs to heed global history. Wealthy countries became wealthy before their governments spent much on research. Conversely, let us recall that the resources lavished on science by the Soviet government proved of little benefit to its citizens.

Governments are not very effective allocators of resources, including precious intellectual talent. Firms and philanthropists operating in a free market are more likely to sponsor research of timely value, less likely to squander massive resources on premature exploration of scientific exotica.

The U.S. government does not spend too little on research. It spends far too much.

ALLAN WALSTAD, JOHNSTOWN, PA.

Vapor breath

Our breath is more than 99 percent water? (“Every breath you make tells of all your aches,” *SN: 7/5/08, p. 5.*) No wonder I'm so thirsty! But I'm curious — how do our bodies use all that nitrogen we breathe in but apparently not out?

BILL OSSMANN, ACTON, MASS.

To address your question, I contacted John Hunt, a respiratory medicine specialist at the University of Virginia Children's Hospital in Charlottesville, and this is his response: “Water vapor makes up more than 99 percent of the volume of the liquid exhaled breath condensate collected using current techniques — which do not condense nitrogen out of gas phase. Nitrogen gas concentrations are similar in inhaled and exhaled breath, and there is no net consumption of nitrogen by the body. Water loss in exhaled breath, although less than urinary water loss, is indeed a major reason why people get thirsty.”

— RACHEL EHRENBERG

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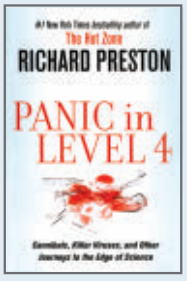
All letters subject to editing.

Panic in Level 4: Cannibals, Killer Viruses, and Other Journeys to the Edge of Science

Richard Preston

Preston's style of journalism, he says, is the equivalent of climbing into a boiling pot to better understand soup.

In this collection, Preston describes some of his close encounters with the subjects he has written about, telling, for example, how he donned a "spacesuit" to visit a high-security U.S. Army lab where researchers study Ebola virus (the subject of Preston's celebrated thriller *The Hot Zone: A Terrifying True Story*).



He goes on to describe how he climbed the tallest tree east of the Mississippi River, right after it had been killed by an invasive species—a tiny bug from Japan.

And, in another chapter, he recalls the time he spent with sufferers of a rare genetic disorder who hurt and bit themselves.

Preston, in his introduction to the book, provides some insights into his reportorial technique, including how he sometimes stops taking notes (instead relying on his memory) to put his sources at ease during especially sensitive parts of his interviews.

As for his writing style, Preston does not waste words. In terse, short sentences, he reconstructs situations, events and states of mind with a novelist's touch. But, as the author points out, the reality he describes is often more incredible than fiction.

This book gathers and slightly expands upon six long pieces Preston wrote for *The New Yorker* over several years, and includes articles on genome sequencing pioneer Craig Venter, two mathematicians obsessed with the number pi and a set of unique tapestries from the Renaissance. Reading the articles will be worthwhile, even for people who read them back then.

—**Davide Castelvecchi**

Random House, 2008, 240 p., $26.

The Drunkard's Walk: How Randomness Rules Our Lives

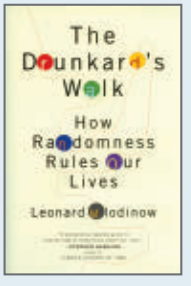
Leonard Mlodinow

People like to think they understand their world. They seek explanations for things that go well and excuses for failures. "To swim against the current of human intuition is a difficult task," Mlodinow notes.

In this guide to randomness, he explores how people misunderstand the power of praise and punishment, hot and cold career streaks, and the luck in the lottery, all because of a misunderstanding of the influence of chance.

But not to worry. Mlodinow provides lessons on what he calls "a field of subtlety," from the basic laws of probability, to regression toward the mean and availability bias. The lessons are thought-provoking because Mlodinow embeds them in a history of seemingly correct but surprisingly incorrect thinking. He pulls in examples from gambling and sports, and even explains how Apple had to make its iTunes shuffle function less random so it seemed more random to listeners.

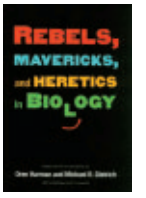
In the end, the drunkard's walk—that unpredictable stumbling—becomes a metaphor for movement through life. Success does not reflect ability and ability does not guarantee success, Mlodinow writes. But he does leave readers with a small comfort. If a baseball player takes enough swings, eventually the player will hit a home run. So, he writes, success is more about the number of times a person goes to bat.



—**Elizabeth Quill**

Pantheon Books, 2008, 272 p., $24.95.

Rebels, Mavericks, and Heretics in Biology



Oren Harman and Michael R. Dietrich (eds.)

Stories about the iconoclasts who changed their fields by challenging assumptions.

Yale Univ. Press, 2008, 416 p., $40.

Starved for Science: How Biotechnology is Being Kept Out of Africa

Robert Paarlberg

An argument that opposition to farm science hurts the poor.

Harvard Univ. Press, 2008, 235 p., $24.95.

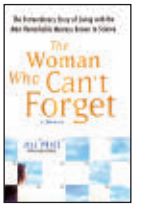
The Rhino with Glue-On Shoes: And Other Surprising True Stories of Zoo Vets and Their Patients

Lucy H. Spelman and Ted Y. Mashima (eds.)

Personal essays from more than two dozen dedicated veterinarians who care for exotic animals in U.S. zoos.

Delacorte Press, 2008, 312 p., $22.

The Woman Who Can't Forget

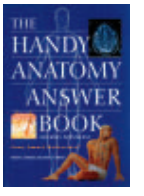


Jill Price

The memoir from an ordinary woman with an extraordinary memory.

Simon & Schuster, 2008, 263 p., $26.

The Handy Anatomy Answer Book



Naomi E. Balaban and James E. Bobick

The reference book for all the major body systems, organized through a series of questions and answers.

Visible Ink Press, 2008, 376 p., $21.95.

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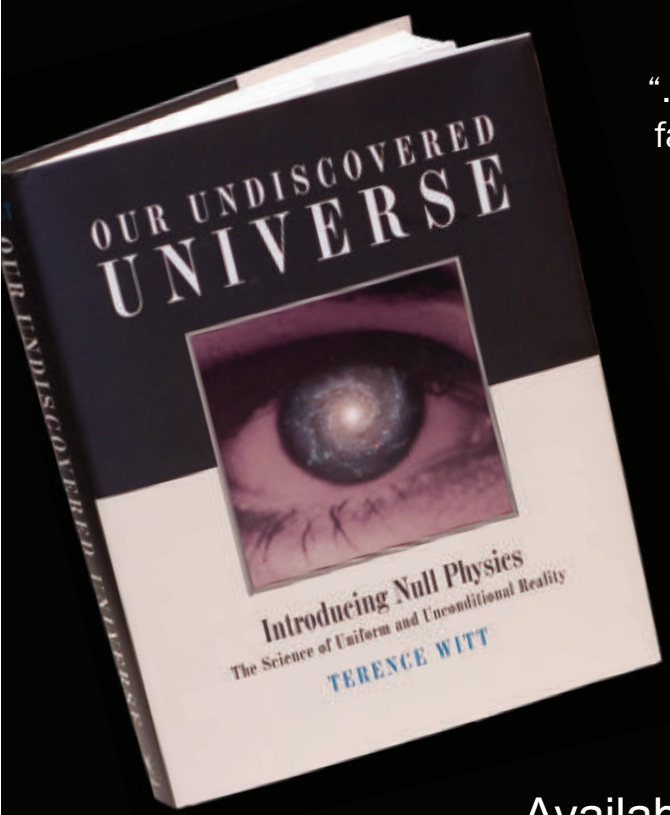

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Science should be prominent in U.S. foreign policy

On May 28, the World Science Summit held in New York City convened an assembly of prominent scientists to discuss some of the critical issues at the interface between science and society. One of the panel discussions at the summit addressed the topic of the role of science in foreign affairs. Among the participants were Harold Varmus, former director of the National Institutes of Health and now president of Memorial Sloan-Kettering Cancer Center in New York; David Baltimore, former president of Caltech and Rockefeller University in New York; and Nina Fedoroff, a plant geneticist who is the science adviser to Secretary of State Condoleezza Rice. Excerpts from their comments follow below.

Varmus: A component of my life is devoted to trying to make science a more global activity to address many of the unsolved problems that we've been hearing about.... Energy or food or water or health, every domain of activity, regionally or globally, can be influenced by science, and it's become the conviction of many of us that paying attention to science is an element of foreign policy. It is a commandment that ought to be listened to by every administration....

Science is an attractive way to try to reach out to other countries, even countries with different ideologies, because science practices common methods. Most scientists speak the same languages; science addresses issues that tend to be regional if not global; ... science profits from and often depends upon collaborations carried out in an international way; ... and science creates global public goods, information that everyone can use for the betterment of the world....

There are a lot of opportunities for any administration, especially a new one, to foster science abroad and to enhance the status of the U.S. as a partner in doing good in the world.

Baltimore: Science and technology are not limited to a space surrounded by particular political borders. Provision of clean energy in the world is perhaps the most pressing problem we have in the long run. Issues of health are international ones, especially in this era of jet-age travel. Poverty is a problem that countries have individually, but its effects spread throughout the world. Clean water affects rural and urban areas alike, and recently the provision of just basic food rations to the world's population has become a growing concern.

So we're living with a constant crisis of having spawned a population of 6.7 billion people on the Earth today and an ever increasing number as time passes. It's an enormous problem, and increasing the affluence of these individuals is something that each country is working on, and that is producing strains and challenges to stretch the resourcefulness of people throughout the world....

Science and technology are not limited to a space surrounded by particular political borders.
DAVID BALTIMORE

The AIDS epidemic ... by itself strains the resources of the world. Today we're trying to provide 33 million people with drugs to prevent the progression of AIDS; we're trying to avoid the deaths of the most productive people in society; we're trying to avoid the increase in orphaned children.

At the same time, we can't forget ... tuberculosis, malaria, other infectious diseases. We still need to be alert to new emerging infectious diseases. Actually the world has literally millions of diseases, most of which we don't know much about, in animal reservoirs, any one of which, as SARS showed us, can come out and start taking a toll in human beings....

All of this requires the marshaling of the resources of the developed world because the research that has to be carried out must be carried out in very sophisticated venues.

Fedoroff: The population has more than doubled since the middle of the 20th century, and the population experts are expecting another roughly 3 billion people to be added to the planet's population by midcentury. But here's a sobering factoid: The amount of arable land has not changed appreciably over the past half century. And it isn't likely to increase much in the future because we're losing it to urbanization, salinization and desertification as fast as we're adding it.... And now that we've decided that our crops must feed not just humans and animals but our cars as well, it's perhaps not surprising that food prices have suddenly spiked....

It's my view that our research universities and institutes as well as those of other developed nations have a unique opportunity to contribute to building the needed capacity of everything ranging from plant and agricultural sciences to small, medium and large enterprises that add value and diversify livelihoods based on science and technology. This is not just about food prices but about truly flattening the world.... It's about creating a future in which the citizens of all countries have not just the food security but the educational and economic opportunities that are today restricted largely to the developed world.

Scientists and engineers have a crucial role to play, by creating what you might call a science diplomatic core.... The notion of becoming a science diplomat, taking time out from a busy and competitive career to teach and develop research collaborations in the least advanced countries most in need of our help, is not yet on the academic radar screen. ■

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The Buddha

About Your Professor

Dr. Malcolm David Eckel is Associate Professor of Religion at Boston University. He earned his Masters in Theology at Oxford and Ph.D. in the study of comparative religion at Harvard. In 1998, Professor Eckel received the Metcalf Award for Teaching Excellence, his university's highest award for teaching.

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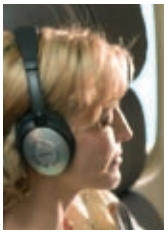
Offer Good Through: October 1, 2008

The Bose® QuietComfort® 2 Acoustic Noise Cancelling® Headphones.

Think of them as a peaceful getaway from the world around you. Whether it's the engine roar inside an airplane cabin, the bustle of the city or the distractions in the office, Bose QuietComfort 2 headphones help them fade softly into the background with the flick of a switch. You can savor delicate musical nuances without disturbing others. And when you're not listening to music, you can slip into a tranquil haven – where you can relax and enjoy peace and solitude. Clearly, these are no ordinary headphones. It's no exaggeration to say they're one of those things you have to experience to believe.



Use them as a concert hall – or a sanctuary.

"It's as if someone behind your back reached out, found the volume control for the world, and turned it way, way, down," reports *TechnologyReview.com*. Bose QC®2 headphones incorporate patented technology that electronically identifies and dramatically reduces noise, while faithfully preserving the music, movie dialogue or tranquility you desire. We designed these headphones primarily for airplane travelers. But owners soon started telling us how much they enjoy using them in other places to reduce distractions around them. They're excellent for listening to music whether you're on the go, at home or in the office.

"Forget 'concertlike' comparisons; you'll think you're onstage with the band." That's what *Travel + Leisure Golf* said when these headphones were first introduced. You'll relish the sound of a bass guitar. Or a flute. Or the delicate inflections of a singing voice. The audio is so clear you may find yourself discovering new subtleties in even your favorite music.

"The QuietComfort 2 lives up to its name, enveloping you in blissful sound in the utmost comfort. It's easy to forget they are on your head." That's what respected columnist Rich Warren reports. To enjoy peace and tranquility, simply turn them on. To add Bose quality sound, attach the included audio cord and connect them to a laptop computer, portable CD/DVD/MP3 player, in-flight audio system or home stereo. They also offer a fold-flat design for easy storage in the slim carrying case.

Try the QC2 headphones for yourself, risk free. You really must experience them to believe it. Call toll free to try these headphones for 30 days. Use them on your next trip, in your home or at the office – satisfaction guaranteed. If you aren't delighted, simply return them for a full refund.

Call 1-800-901-0256, ext. Q6560 today. The QC2 headphones are available directly from Bose – the most respected name in sound. When you call, ask about making **12 easy payments,** with no interest charges from Bose.* And discover a very different kind of headphone – QuietComfort 2 Acoustic Noise Cancelling headphones.

FREE shipping with your order.

To order or learn more:

1-800-901-0256, ext. Q6560

www.Bose.com/sciencenews

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Better sound through research®

*Bose payment plan available on orders of $299-$1500 paid by major credit card. Separate financing options may be available for select products. See website for details. Down payment is 1/12 the product price plus applicable tax and shipping charges, charged when your order is shipped. Then, your credit card will be billed for 11 equal monthly installments beginning approximately one month from the date your order is shipped, with 0% APR and no interest charges from Bose. Credit card rules and interest may apply. U.S. residents only. Limit one active financing program per customer. The distinctive design of the headphone oval ring is a trademark of Bose Corporation. Financing and free shipping offer not to be combined with other offers or applied to previous purchases, and subject to change without notice. Risk free refers to 30-day trial only and does not include return shipping. Delivery is subject to product availability. Quotes reprinted with permission: Simson Garfinkel, *TechnologyReview.com,* 7/9/03; *Travel + Leisure Golf,* 7/03; Rich Warren, *News-Gazette,* 5/19/03.