SN
SCIENCE NEWS MAGAZINE
SOCIETY FOR SCIENCE & THE PUBLIC
SEPTEMBER 3, 2016

Higgs in Sharper Focus

China's Founding Flood

Neuroscience Meets Donkey Kong

Fentanyl Fatalities

CRISPR Retooled

Tweaks to cutting-edge gene editor enhance its powers

VOL. CLVII....No. 30,000

The Stauer Times

"It's About Time"

News Flash....

Government Gets Something Right

Super Light Titanium Timepiece Loses Only One Second Every 20 Million Years.

BOULDER, Colorado The U.S. government has engineered the most ingenious, most accurate clock in the world: the F-1 U.S. Atomic Clock in Boulder, Colorado. Our extraordinary new Stauer Titanium Atomic Watch utilizes the transmissions directly from that remarkable cesium fission atomic clock to report the most precise time. This scientifically advanced timepiece will gain or lose only one second over a 20 million-year period. It is that accurate! This perfectly tuned technological invention with the super light strength of titanium is now available for UNDER $130.

Super Light Titanium has two big advantages over steel. One is corrosion resistance and the other is that titanium has the highest strength-to-weight ratio of any metal, which means that titanium is approximately 45% lighter than steel. But every other titanium watch that we can find is priced at over $400, and none of those are nearly as accurate as our atomic movement. Stauer has decided to bring these resources together in a timepiece that has the most accurate movement available today. You'll never have to set this watch. Just push one of the buttons and you are synchronized with the atomic clock in Colorado, and the hands of the watch move to the exact time position. The sleek black textured dial has luminous hands and markers plus the timepiece is water resistant to 3 ATM.

A Titanium-clad offer. This Titanium Atomic Watch exceeds the accuracy of any Swiss luxury automatic so you can be more punctual and keep most of your money in your wallet, not on your wrist. Look at your watch and we guarantee that the time is incorrect, unless you are wearing the advanced atomic technology.

The Stauer Titanium Atomic Watch is not available in stores and it comes with our 30 day money-back guarantee. If you're not completely satisfied with the accuracy, simply return the watch for the full purchase price. Includes a 2-year warranty on the movement.

Not Available in Stores

Stauer Titanium Atomic Watch ~~$195~~ *now* $129 +S&P

or **2 credit card payments of $64.50** +S&H

Call Toll-Free now to take advantage of this limited offer.

1-800-333-2045

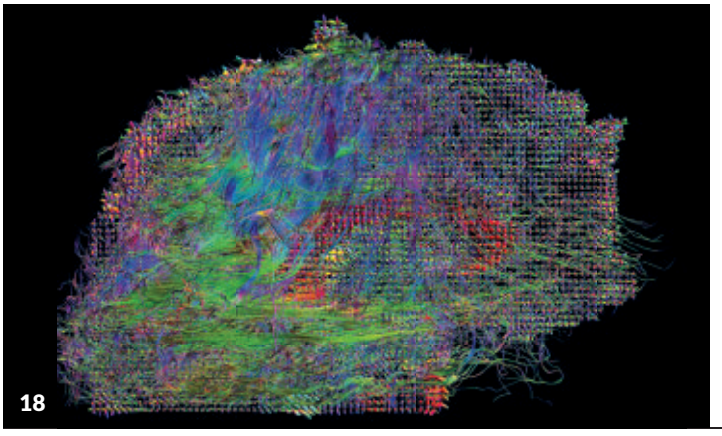
Promotional Code TTA475-10
Please mention this code when you call.

To order by mail, please call for details.

Stauer®
14101 Southcross Drive W.,
Dept. TTA475-10
Burnsville, Minnesota 55337
www.stauer.com

VOL. 190 | NO. 5

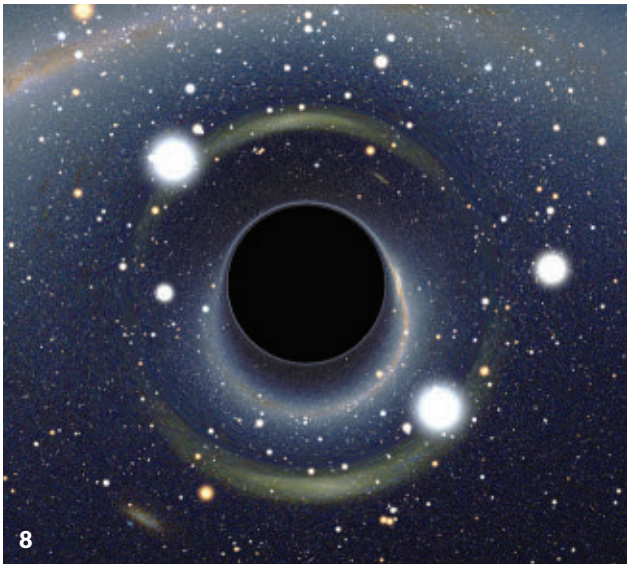
ScienceNews



18

Features

News



8

26

Departments

SOCIETY UPDATE
Explore the redesigned *Science News for Students*

COVER The gene-editing tool known as CRISPR has lots of tricks up its sleeve. *Michael Morgenstern*

CLOCKWISE FROM TOP: COURTESY OF LAB. OF NEURO IMAGING AND MARTINOS CTR. FOR BIOMEDICAL IMAGING, CONSORTIUM OF THE HUMAN CONNECTOME PROJECT (WWW.HUMANCONNECTOMEPROJECT.ORG); CYNOCLUB/ISTOCKPHOTO; ALAIN R/WIKIMEDIA COMMONS (CC BY-SA 2.5)

Bacteria display qualities that a mother would love

When my friend Steve Finkel and I get together, the talk is almost always about bacteria. He and I are both huge fans, from different angles. I'm a spectator. He studies them (*E. coli*) in his lab at the University of Southern California. I used to work down the hall from him, so I'm sure that some of my enthusiasm for the tiny creatures can be blamed on him, along with USC's out-of-control microbe-lover Ken Nealson (*Shewanella oneidensis* is his bug, among others).

Single-celled though they may be, bacteria and other microbes are far from simple. They can thrive in hostile spots — from the acidic, low-oxygen environment of the stomach to boiling hot springs or frozen tundra. Some even breathe rock (see Nealson's bug). They can adapt rapidly in rough times, switching their metabolic scheme or just going dormant. Bacteria have many admirable qualities that many of us would want for our children: grit, perseverance, flexibility and seemingly limitless creativity (albeit mostly biochemical).

Their flexibility and creativity were on full display at a recent meeting (see Page 11), a few blocks away from the *Science News* offices (and the occasion for Finkel's visit to Washington, D.C.). Reports from the meeting all involve science that takes advantage of the latest techniques for probing the bacterial experience — be that finding out how bacteria can survive without "essential" enzymes and how offensive attacks can actually give rise to bacterial cooperation. Now that bacterial genome sequencing is cheap, Finkel and fellow scientists can watch microbes evolve in the lab, in real time. Taking genetic snapshots along the way, scientists are building up a detailed picture of the genetic shifts that allow a new strain to become dominant in a given experiment. It is watching evolution in action, Finkel says, quite literally.

But microbes are organisms, much more than little sacks of evolving biochemistry. They have immune systems, of a sort. It was through studies of one bacterium's antiviral defense that scientists first discovered what's become the most versatile and headline-grabbing gene editor of all time: CRISPR/Cas9. These ingenious molecular scissors work within microbes to target viral DNA that has invaded bacteria and literally cut it to shreds. Harnessed and aimed at the DNA of other organisms, CRISPR/Cas9 has proved much easier to work with, cheaper and more precise than existing editing tools. It's been wildly successful at precisely deleting genes, helping to reveal gene functions that have long remained hidden, as Tina Hesman Saey reports on Page 22.

But even this wonder tool has its limits. So, as a legal battle over who owns the patent to the technique rages on, scientists (including the current patent holder) are already tweaking it, adjusting it, engineering it and searching for CRISPR-like alternatives, an effort Saey describes in her cover story. Some scientists are going back to the source (bacterial immune systems) to find new enzymes that might help build a library of precision gene-editing tools — one for each job.

That brings me back to why I love microbes — resilient, creative survivors that they are. Like the best humans, they are always coming up with new solutions.
— Eva Emerson, Editor in Chief

SANDY SCHAFFER

THE GREAT COURSES®

70% off

OFFER EXPIRES 09/18/16

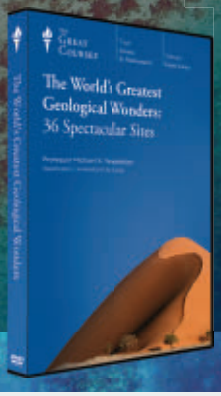
Discover Earth's Most Spectacular Locations

The World's Greatest Geological Wonders: 36 Spectacular Sites

Taught by Professor Michael E. Wysession
WASHINGTON UNIVERSITY IN ST. LOUIS

Yellowstone, the Grand Canyon, Mount Fuji. These natural wonders make many people's short lists of geologically fascinating, must-see attractions. But what about Ha Long Bay, the Columbia Glacier, or Erta Ale lava lake? They also belong on the list, as do scores of other sites featuring breathtaking vistas that showcase the grandeur of geological forces in action.

Whether you're planning your next vacation or exploring the world from home, **The World's Greatest Geological Wonders** is your gateway to an unrivaled adventure. In these 36 lavishly illustrated lectures, award-winning Professor Michael E. Wysession of Washington University in St. Louis introduces you to more than 200 of the world's most outstanding geological destinations located in nearly 120 countries—and even some geological wonders found on other planets.



LECTURE TITLES

1. Santorini—Impact of Volcanic Eruptions
2. Mount Fuji—Sleeping Power
3. Galapagos Rift—Wonders of Mid-Ocean Ridges
4. African Rift Valley—Cracks into the Earth
5. Erta Ale—Compact Fury of Lava Lakes
6. Burgess Shale—Rocks and the Keys to Life
7. The Grand Canyon—Earth's Layers
8. The Himalayas—Mountains at Earth's Roof
9. The Ganges Delta—Earth's Fertile Lands
10. The Amazon Basin—Lungs of the Planet
11. Iguazu Falls—Thundering Waterfalls
12. Mammoth Cave—Worlds Underground
13. Cave of Crystals—Exquisite Caves
14. Great Blue Hole—Coastal Symmetry in Sinkholes
15. Ha Long Bay—Dramatic Karst Landscapes
16. Bryce Canyon—Creative Carvings of Erosion
17. Uluru/Ayers Rock—Sacred Nature of Rocks
18. Devils Tower—Igneous Enigmas
19. Antarctica—A World of Ice
20. Columbia Glacier—Unusual Glacier Cycles
21. Fiordland National Park—Majestic Fjords
22. Rock of Gibraltar—Catastrophic Floods
23. Bay of Fundy—Inexorable Cycle of Tides
24. Hawaii—Volcanic Island Beauty
25. Yellowstone—Geysers and Hot Springs
26. Kawah Ijen—World's Most Acid Lake
27. Iceland—Where Fire Meets Ice
28. The Maldives—Geologic Paradox
29. The Dead Sea—Sinking and Salinity
30. Salar de Uyuni—Flattest Place on Earth
31. Namib/Kalahari Deserts—Sand Mountains
32. Siwa Oasis—Paradise amidst Desolation
33. Auroras—Light Shows on the Edge of Space
34. Arizona Meteor Crater—Visitors from Outer Space
35. A Montage of Geologic Mini-Wonders
36. Planetary Wonders—Out of This World

The World's Greatest Geological Wonders: 36 Spectacular Sites
Course no. 1712 | 36 lectures (30 minutes/lecture)

SAVE $275

DVD ~~$374.95~~ NOW $99.95
+$15 Shipping, Processing, and Lifetime Satisfaction Guarantee
Priority Code: 131447

THEGREATCOURSES.COM/2SN **1-800-832-2412**

Excerpt from the September 3, 1966 issue of *Science News*

50 YEARS AGO

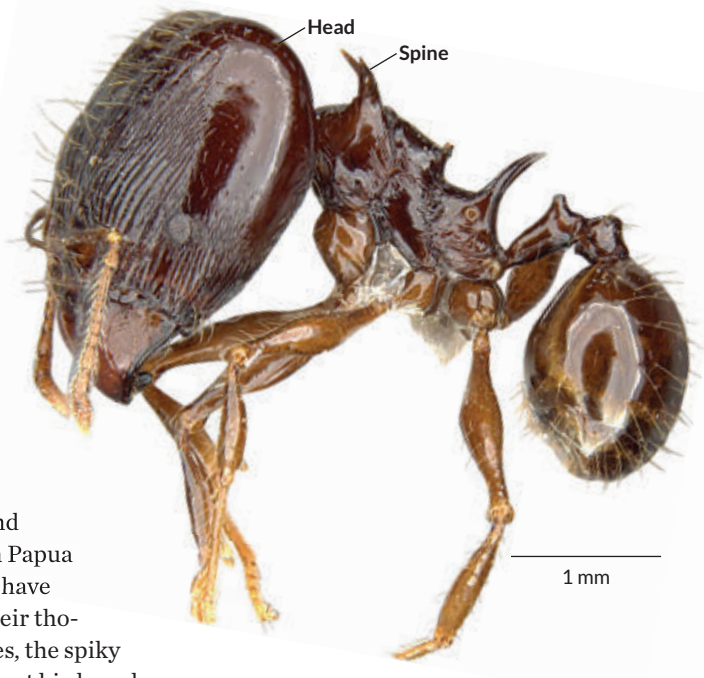
Site of seizures may be spotted with computer

Severe epilepsy that does not respond well to drugs may be attacked by computers in combination with surgery.... The computers would register information coming from electrodes implanted in the patient's brain. By reading the computer, the surgeon might then be able to spot the site of "electrical storms" which cause epileptic seizures.

UPDATE: Computers are now a central part of surgery for epilepsy. Surgeons typically measure the electrical activity of the brain, then couple those recordings with data from MRI and CT scans. Positron emission tomography and single-photon emission CT scans may further delineate the trouble spot. These techniques require computers to record and reconstruct images. Researchers are developing virtual brains, combining many technologies to map out connections and electrical function in an individual's brain. Doctors may one day use the computerized brains to guide treatment of epileptic patients, researchers report July 28 in *NeuroImage*.

INTRODUCING

Spikes may support heavy ant heads



The newly identified ant species *Pheidole drogon*, named after a dragon in *Game of Thrones*, sports spines that resemble a dragon wing and claw. The ants can't breathe fire, but the spines of some workers are filled with muscles, which may lend support to their giant heads.

The newest thorny members of a diverse genus of ants may have extra help holding their heads high.

Worker ants of the species *Pheidole drogon* and *Pheidole viserion,* found in Papua New Guinea's rainforests, have spines protruding from their thoraxes. For many ant species, the spiky growths are a defense against birds and other predators. But Eli Sarnat and colleagues suggest that these spines might also be muscular support for some *Pheidole* with oversized heads, which are probably used to crush seeds. The heads "are so big that it looks like it would be difficult to walk," says Sarnat, an entomologist at the Okinawa Institute of Science & Technology Graduate University in Japan.

Micro-CT scans of worker ants with large heads revealed bundles of thoracic muscle fibers within spines just behind their heads. Fellow worker ants with smaller heads did not have muscles in their spines, the researchers report July 27 in *PLOS ONE*. More research is needed to establish the spines' functions and understand why they evolved, Sarnat says. While buff spines may support big heads, both types probably keep predators at bay, the researchers suspect.

Researchers named the ants after two fearsome dragons, Drogon and Viserion, in the popular book and TV series *Game of Thrones*. — *Cassie Martin*

FOR DAILY USE

A view to better cornea transplants

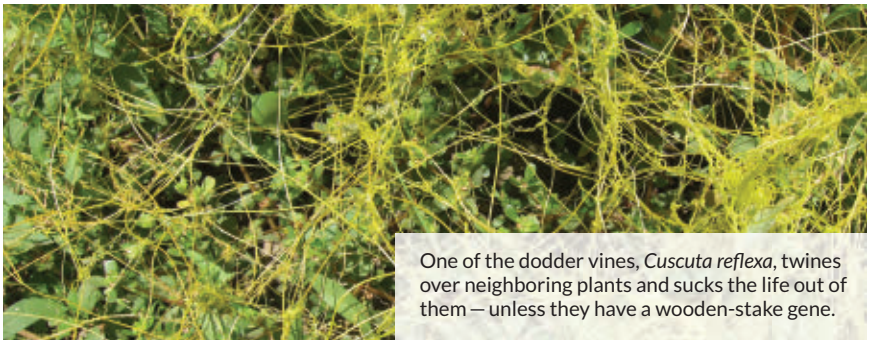
Sex matters when it comes to cornea transplants — at least for women.

Corneas are low on the list of organs that cause rejection, but it happens more often when women receive corneas from men, researchers report online July 22 in the *American Journal of Transplantation*. In data from nearly 17,000 transplants, 220 of every 1,000 male-to-female transplants failed versus 180 of every 1,000 sex-matched donations. For men, the donor's sex didn't matter.

The researchers suspect the problem is the H-Y antigen, found on the surface of most cells in a man's body. The gene that encodes H-Y is on the Y chromosome, so women don't have it. If their immune systems haven't encountered the H-Y antigen before, women's bodies may take it as a sign of a foreign invader and attack the transplant, says study coauthor Stephen Kaye, an ophthalmologist at the Royal Liverpool University Hospital in England. H-Y appears to be more of an issue in the cornea than in other organs.

If donated tissue is in short supply, however, women should take what's available, Kaye says. It's more important to get the cornea than to select who it came from. — *Amber Dance*

MASAKO OGASAWARA/OIST



One of the dodder vines, *Cuscuta reflexa*, twines over neighboring plants and sucks the life out of them — unless they have a wooden-stake gene.

IT'S ALIVE

How a tomato defeats a scary vampire plant

Forget garlic. In real life, a tomato can defeat a vampire. And researchers have now figured out the first step to vegetable triumph.

The vampires are slim, tangling vines that look like splats of orange or yellow-green spaghetti after a toddler's dinnertime tantrum. Botanically, the 200 or so *Cuscuta* species are morning glories gone bad. In the same family as the heavenly blue garden trumpets, the dodders, as they're sometimes called, lose their roots about a week after sprouting and never grow real leaves. Why bother when you can drain food and water from the neighbors?

A dodder seedling, basically a bare stem, finds that first neighbor by writhing and groping (in slow plant time) toward attractive plant odors. "The *Cuscuta* can smell its victims," says Markus Albert of the University of Tübingen in Germany.

Depending on the dodder species, victims include asparagus, melons, sugar beets, petunias, garlic, chrysanthemums and oak trees. Even worse for civilization as we know it, some *Cuscuta* species vampirize coffee plants and grapevines.

The dodder plant attaches to a wild tomato's stem and inserts teethlike haustoria to suck out nutrients (left). With the *CuRe1* gene, the plant can fight off the dodder by forming a scab so the haustoria can't penetrate (right).

Certain dodders do kill tomato plants. But not the *C. reflexa* from Asia that Albert studies; instead, it gets its skinny little haustoria whipped. Haustoria are the organs that make plant parasitism possible. When a dodder seedling brushes against tasty prey, a haustorium disk forms and pushes out from the dodder stem with a fast-growing point. "It really looks like a vampire tooth," Albert says.

If the prey is, say, a soybean plant, it's doomed. The growing dodder haustorium not only exerts force but also releases enzymes that weaken the bean's tissue. Haustorium tip cells send out projections that grasp the bean's inner ducts for water and nutrients, diverting so much that the bean starves.

A tomato plant poked by a haustorium, however, panics. A patch of cells on the stem elongate and burst, forming a scab that stops the intruder. The haustorium stalls and eventually dies.

A gene called *CuRe1* lets the tomato recognize the dodder as a threat, Albert and colleagues report in the July 29 *Science*. They transferred the gene to a normally susceptible relative and — Ha! Bite that, vampire! Albert predicts additional biochemistry could be needed to dodder-proof other crops. But for starters, researchers now know the first step in protection: A tomato's rare power to survive a scary vampire is the ability to get really scared itself. — *Susan Milius*

FROM TOP: SHIJAN KAAKKARA/WIKIMEDIA COMMONS; V. HEGENAUER *ET AL*/*SCIENCE* 2016

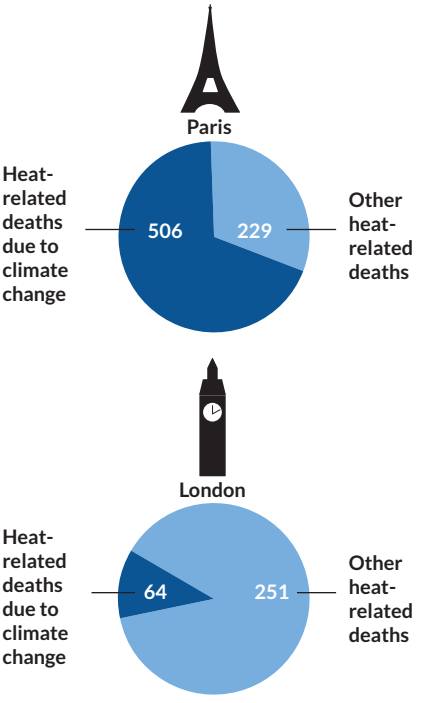
SCIENCE STATS

Global warming amplified death toll in 2003 heat wave

Climate change flaunted its deadly side during the 2003 European heat wave, which killed over 70,000 people across the continent. In London and Paris alone, global warming led to 570 more heat-related deaths than would be expected without human-caused warming, researchers estimate in the July *Environmental Research Letters*.

Daniel Mitchell of the University of Oxford and colleagues ran thousands of climate simulations with and without the influence of greenhouse gases emitted by humans. The simulations showed that 70 percent of heat-related deaths in central Paris during the heat wave and 20 percent in Greater London could be attributed to climate change. The study is the first to quantify climate change's role in the event and will inform policy makers on the risks climate change poses, the researchers say. — *Thomas Sumner*

Estimated deaths attributed to climate change in 2003 European heat wave



SOURCE: D. MITCHELL *ET AL*/*ENVIRON. RES. LETT.* 2016

HUMANS & SOCIETY

Flood tale rooted in real disaster

Deluge might have given China's first dynasty wet start

The Yellow River cuts through a gorge not far from where researchers say a landslide-created dam burst about the same time as the rise of Chinese civilization. The flood may have inspired folktales.

BY BRUCE BOWER

Ancient Chinese tales and writings about a massive flood of the Yellow River that led to civilization's rise in East Asia appear to hold water, researchers say.

A section of the Yellow River dammed by an earthquake-caused landslide broke open about 3,936 years ago, says a team led by geologist Qinglong Wu of China's Nanjing Normal University. A wall of water about a third as high as the Empire State Building charged down the Yellow River valley, possibly changing the river's course and leading to years of flooding in lowland areas inhabited by farmers, the scientists report in the Aug. 5 *Science*.

"This was one of the largest known floods on Earth over the past 10,000 years," geologist and coauthor Darryl Granger of Purdue University in West Lafayette, Ind., said August 3 at a news conference.

Remains of victims killed by an earthquake at China's Lajia site helped scientists date a flood that ravaged the Yellow River valley nearly 4,000 years ago.

That natural disaster came to be known as the Great Flood, first in folktales and later in written histories from around 3,000 years ago, the researchers propose. These accounts tell of a hero named Yu who spent decades leading efforts to dredge rivers and drain floodwaters, as well as personally fighting off supernatural beasts, following catastrophic flooding of the Yellow River. Legend has it that Yu's success enabled him to launch Chinese civilization by founding the Xia dynasty.

Some scholars regard this tale as a myth or as propaganda devised to justify centralized, imperial rule.

Historical records of the Xia dynasty are scanty, archaeologist and coauthor David Cohen of National Taiwan University in Taipei said at the news conference. New evidence of an ancient Yellow River flood "provides a tantalizing hint that the Xia dynasty actually existed," Cohen said.

Wu's team studied remains of a landslide dam along the Yellow River in north central China. The dam's remnants, found on the left and right riverbanks, included masses of soil and shattered rock typical of landslides. A scar in the earth above the right bank must have been created by the landslide, the researchers say. The dam backed up a lake that was about 200 meters deep, they estimate.

Downstream, the team found sediment and boulders carried by floodwaters. Flood sediment covered the remains of a previously excavated settlement called Lajia, located 25 kilometers downstream of the ancient dam. Cracks in the ground and flattened structures suggest an earthquake destroyed Lajia and killed its residents before the flood. That earthquake probably triggered the landslide upstream that blocked the Yellow River for about six to nine months before the natural dam burst, Wu's team says.

Radiocarbon dating of human bones and burned bits of wood from Lajia yielded an approximate age for the flood.

Great floods and other natural disasters have long played central roles in folktales and oral histories around the world. Scientists disagree about whether geological evidence of past deluges give any credence to flood stories told over hundreds of generations.

But the evidence uncovered by Wu's team shows that Emperor Yu's flood is "potentially rooted in geological events," geologist David Montgomery of the University of Washington in Seattle writes in the same issue of *Science*. "A telling aspect of the story — that it took Yu and his followers decades to control the floodwaters — makes sense in light of the geological evidence."

Despite the findings, nothing is certain about how the ancient Chinese state formed, says David Keightley of the University of California, Berkeley, who studies the origins of Chinese civilization.

If the newly documented flood did become known as the Great Flood, the Xia dynasty must have started about 3,900 years ago, Wu's group speculates. That's about 170 to 300 years later than investigators had previously estimated.

The flood's timing roughly matches up with the first appearance of China's Bronze Age urban societies, including the Erlitou culture of the Yellow River valley. Previously excavated Erlitou artifacts are remnants of the Xia dynasty, the researchers suspect. ■

FROM TOP: Q. WU; CAI LINHAI

Distinctions blur between wolf species

Mating of coyotes, grays leads to muddled canine identities

BY LAUREL HAMERS

Wolves are having something of an identity crisis. Gray wolves and coyotes might be the only pure wild canine species in North America, a new genetic analysis suggests. Other wolves — red wolves and eastern wolves — appear to be blends of gray wolf and coyote ancestry instead of their own distinct lineages.

Red wolves contain about 75 percent coyote genes and 25 percent gray wolf genes, an international team of scientists reports July 27 in *Science Advances*. Eastern wolves have about 25 to 50 percent coyote ancestry — the rest comes from gray wolves.

That finding adds another twist to the ongoing battle over wolf protection and regulation in the United States: how to protect a population that's not its own species but carries valuable genetic information.

Gray wolves used to roam much of North America, until they were hunted to near-extinction. Protection under the Endangered Species Act has helped them to rebound, but their current range is still far smaller than it used to be. Red wolves, found in the southeastern United States, and eastern wolves, found in the Great Lakes region, look similar to gray wolves but are often treated as distinct species. The two groups occupy territory where gray wolves are now scarcer (in the Great Lakes area) or completely gone (in the southeast).

The new study examined the entire genetic makeup, or genome, of 28 canids from around the world. The researchers compared the genomes of North American wolves with those of pure coyotes and Eurasian wolves to figure out what percent of each wolf's genetic material came from the gray wolf and what part came from the coyote.

Red and eastern wolves have historically mated with coyotes, the team found. Each group has a distinct ratio of gray wolf to coyote ancestry. But gray wolves have recent coyote ancestry too. That suggests that these different groups of wolves are more evolutionarily intertwined than previously believed, says Robert Wayne, a biologist at UCLA who coauthored the study

Red wolves and eastern wolves probably arose when gray wolf populations in the eastern United States were hunted by early settlers, says Doug Smith, a biologist who leads Yellowstone National Park's wolf restoration program. The declining wolf population created room for coyotes to move east, where the struggling wolves bred with them. Mixing genes with coyotes probably helped wolf populations survive in lean times.

While their coyote genes make red wolves and eastern wolves look slightly different from gray wolves, "we don't find anything incredibly unique in the red wolf that you can't find in other canines," says Bridgett vonHoldt, a biologist at Princeton University who worked with Wayne and collaborators. But red wolves are still important to protect, because "the wolf part of their genome might actually represent the last of the southeastern gray wolf." It's a similar story for the eastern wolf.

Blended species like these are hard to label, Smith says, because traditional species definitions assume clear boundaries that prevent gene sharing.

"Nothing isolates a wolf," Smith says. "They're just so capable of moving around."

Right now, wolves in the United States are managed through a patchwork of federal and state regulations. Red wolves are federally listed as endangered while gray wolves are listed as endangered in most parts of the country, including much of the Upper Midwest. Genetic mixing makes designing appropriate regulations even more challenging.

"These animals don't walk around with little name tags on them in the field," vonHoldt says. "So hybrids or admixed animals don't always look very different from a pure coyote or pure wolf."

The only way to ensure that wolf genes stick around in certain areas would be to prohibit killing of both wolves and coyotes, vonHoldt says. But such a restriction would be nearly impossible to implement.

This study is an important step, but its conclusions aren't definitive, says Paul Wilson, a biologist at Trent University in Peterborough, Canada. His own genetic research still supports the idea that the eastern wolf is its own species. Comparison with DNA from ancient North American canids — from before wolves and coyotes interbred at all — could help further clarify the debate, he says. ■

FROM LEFT: DENNIS MATHESON/FLICKR (CC BY-SA 2.0); STEFFEN239/FLICKR (CC BY-SA 2.0); CHRISTINE MAJUL/FLICKR (CC BY 2.0); MAV/WIKIMEDIA COMMONS

Eastern wolves (second from left) and red wolves (third from left) might be better described as mixtures between gray wolves (far left) and coyotes (far right) rather than as distinct species, a new genetic analysis suggests.

GENES & CELLS

Rats offer DNA clues to alcoholism

Hundreds of genes involved in drinking, new study finds

BY TINA HESMAN SAEY

Alcoholism may stem from genes being turned on and off incorrectly, a study of hard-drinking rats suggests.

Rats bred either to drink heavily or to shun alcohol have revealed 930 genes linked to a preference for alcohol, scientists report August 4 in *PLOS Genetics*.

Human genetic studies have revealed only a few of the many genetic variants thought to put people at risk for alcoholism, says Michael Miles, a neurogenomicist at Virginia Commonwealth University in Richmond. The new study takes a "significant and somewhat novel approach" to find genetic differences that may separate those who will become addicted to alcohol from those who won't.

It took decades to craft the experiment, says William Muir, a population geneticist at Purdue University in West Lafayette, Ind. Starting in the 1980s, rats bred at Indiana University School of Medicine in Indianapolis were given a choice to drink pure water or water mixed with 10 percent ethanol, about the same amount of alcohol as in weak wine. For more than 40 generations, researchers selected rats from each generation that voluntarily drank the most alcohol and bred them to create a line of rats that consume the rat equivalent of 25 cans of beer a day. Simultaneously, the researchers also selected rats that drank the least alcohol and bred them to make a line of low-drinking rats. A concurrent breeding program produced another two lines of high-drinking and of teetotaling rats.

Muir and colleagues compared complete sets of genetic instructions from 10 rats from each of the lines and identified 930 genes that differ between the high- and low-drinking lines.

Human studies known as genome-wide association studies, or GWAS, often can't determine which of many genes in a region of DNA is involved in a disease or addiction. But the rat data allowed the researchers to pinpoint the exact genetic tweaks implicated in the rats' drinking. "With GWAS, they're just trying to get down to the gene — we've got it down to the parts of the genes," Muir says.

That precision "is clearly an advance," says John Crabbe, a neuroscientist at the VA Portland Health Care System in Oregon. "No one has gone into this much detail before in any alcohol-related trait."

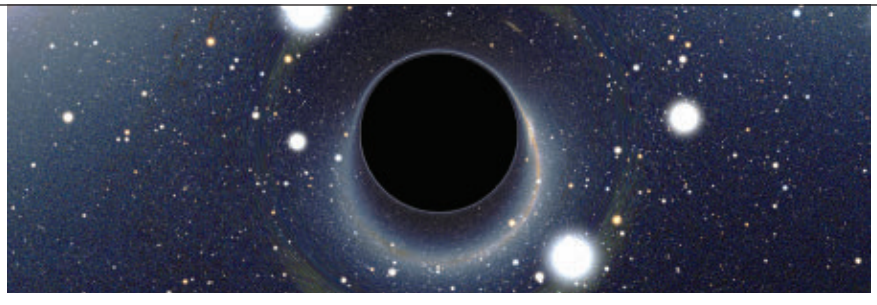
Most genetic variants associated with

ATOM & COSMOS

LIGO find offers dark matter hint

Massive black holes detected last year could be primordial

BY EMILY CONOVER



Two black holes that LIGO has detected could be dark matter, in the form of primordial black holes that formed in the infant universe. A simulated black hole is shown here.

ALAIN R/WIKIMEDIA COMMONS (CC BY-SA 2.5)

The black holes that produced the first detected gravitational waves may have exotic origins in the early universe.

When the Advanced Laser Interferometer Gravitational-Wave Observatory, LIGO, glimpsed gravitational waves from two merging black holes, scientists were surprised at how large the black holes were — about 30 times the mass of the sun (*SN: 3/5/16, p. 6*). Inspired by this finding, two papers published in *Physical Review Letters* propose that the hefty black holes were born in the universe's infancy.

Unlike run-of-the-mill black holes that form from collapsing stars, primordial black holes could have formed when dense regions of the early universe collapsed under their own gravity, some theories suggest. If they exist, primordial black holes could solve a puzzle: the identity of dark matter, the unknown source of mass in the universe that holds galaxies and galaxy clusters together. Primordial black holes could make up the universe's missing mass, an idea that counters the more popular theory that dark matter is made up of undetected particles.

A Japanese team of astrophysicists reported August 2 that LIGO's black holes may be primordial. Johns Hopkins University scientists reported May 19 that LIGO's estimated rate of black hole mergers matches that expected if dark matter consists of primordial black holes.

LIGO's massive black holes had Simeon Bird and his Johns Hopkins colleagues wondering, "Gosh — it's unexpected — what else could it be?" Bird says. Previous research had ruled out primordial black hole dark matter for all but a narrow range of masses. But that allowed range happens to overlap with the masses of the LIGO black holes.

Drawing on dark matter's known properties, Bird and colleagues estimated how often LIGO would expect to see merging primordial black holes, assuming they were the source of dark matter. This rate matched LIGO's estimated detection rate, made by assuming the one unexpectedly massive black hole merger LIGO has seen so far wasn't a fluke. Both estimates have large errors, but their agreement suggests that dark matter may be composed of primordial black holes.

Misao Sasaki of Kyoto University in

high levels of drinking weren't located within the part of a gene containing blueprints for a protein. Only four genes contained variants in their protein-producing parts. The majority of the differences were in surrounding DNA that regulates gene activity. Those changes could alter how much protein is produced, says study coauthor Feng Zhou, a neurobiologist at Indiana University School of Medicine. Altering amounts of proteins could shift biochemical reactions important for behavior.

Until recently, scientists thought alcoholism and other problems stemmed from inheriting altered forms of genes that would produce faulty proteins. "Well, that game's over," Crabbe says. Regulating gene activity is often just as important as changing the genes themselves.

The researchers don't yet know whether the genes identified in the rats lead to alcohol abuse in people. ■

Japan and colleagues also reported that LIGO could have detected primordial black holes. But the researchers found that such primordial black holes could explain only a small fraction of dark matter. This disparity boils down to differing assumptions about how primordial black holes group into pairs before merging.

"The important thing is that this can be tested," Sasaki says. More LIGO data or further studies of the cosmic microwave background — remnant light from the Big Bang's aftermath — could exclude primordial black holes as a possibility.

To better understand LIGO's black holes, "we're going to need to make more detections," says LIGO scientist Chad Hanna of Penn State. LIGO has detected a second black hole merger (*SN: 7/9/16, p. 8*), but those black holes were smaller, indicating that they formed from stars.

Eventually, subtle signs of primordial black holes may appear in gravitational wave data, says Bernard Carr of Queen Mary University of London. The eccentricity of the black holes' orbits around one another — how elliptical their paths are — could indicate whether the black holes are primordial, he says. ■

HUMANS & SOCIETY

Cancer afflicted ancient hominids

Nearly 2-million-year-old bone had possibly malignant tumor

P. RANDOLPH-QUINNEY/UCLAN

A 1.6-million- to 1.8-million-year-old toe bone sports a large growth that represents the earliest known case of a potentially fatal cancer in the human evolutionary family, researchers say.

BY BRUCE BOWER

Cancer goes way, way back. A deadly form of this disease and a noncancerous but still serious tumor afflicted members of the human evolutionary family nearly 2 million years ago, two new investigations of fossils suggest.

If those conclusions hold up, cancers are not just products of modern societies, as some researchers have proposed. "Our studies show that cancers and tumors occurred in our ancient relatives millions of years before modern industrial societies existed," says medical anthropologist Edward Odes of the University of the Witwatersrand in Johannesburg, a coauthor of both new studies. Today, however, pesticides, longer life spans and other features of the industrialized world may increase rates of cancers and tumors.

A 1.6-million- to 1.8-million-year-old hominid, either from the *Homo* genus or a dead-end line called *Paranthropus*, suffered from a potentially fatal bone cancer, Odes and colleagues say in one of two papers published in the July/August *South African Journal of Science*. X-ray techniques enabled identification of a fast-growing bone cancer on a hominid toe fossil previously unearthed at South Africa's Swartkrans Cave, the researchers report. This malignant cancer consisted of a mass of bone growth on both the toe's surface and inside the bone.

Until now, the oldest proposed cancer in hominids was an unusual growth on an African *Homo erectus* jaw fragment dating to roughly 1.5 million years ago. Critics, though, regard that growth as the result of a fractured jaw, not cancer.

A second new study, led by Patrick Randolph-Quinney, a biological anthropologist now at the University of Central Lancashire in England, identifies the oldest known benign tumor in a hominid in a bone from an *Australopithecus sediba* child. This tumor penetrated deep into a spinal bone, close to an opening for the spinal cord. Nearly 2-million-year-old partial skeletons of the child and an adult of the same species were found in an underground cave at South Africa's Malapa site (*SN: 8/10/13, p. 26*).

Although not life-threatening, the tumor would have interfered with walking and climbing, the researchers say. People today, especially children, rarely develop such tumors in spinal bones.

"This is the first evidence of such a disease in a young individual in the fossil record," Randolph-Quinney says.

X-ray technology allowed the scientists to create and analyze 3-D copies of the inside and outside of both fossils.

But studies of fossil bones alone, even with sophisticated imaging technology, provide "a very small window" for detecting cancers and tumors, cautions paleoanthropologist Janet Monge of the University of Pennsylvania Museum of Archaeology and Anthropology in Philadelphia. Microscopic analysis of soft-tissue cells, which are typically absent on fossils, confirms cancer diagnoses in people today, she says.

Without additional evidence of bone changes in and around the proposed cancer and tumor, Monge wouldn't draw any conclusions about what caused those growths.

Monge led a team that found a tumor on a 120,000- to 130,000-year-old Neandertal rib bone from Eastern Europe. Whether the tumor was cancerous or caused serious health problems can't be determined, the scientists concluded in 2013 in *PLOS ONE*. ■

BODY & BRAIN

‘Neural dust’ listens to muscles, nerves

Tiny ultrasonic implant can detect electrical activity in rats

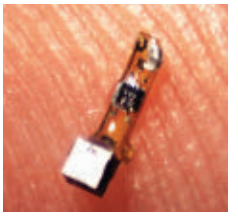
BY LAURA SANDERS

A small device with a heart of crystal can eavesdrop on muscles and nerves, scientists report in the Aug. 3 *Neuron*. Called neural dust, the device is wireless and needs no batteries, appealing attributes for scientists seeking better ways to monitor and influence the body and brain.

“It’s certainly promising,” says electrical engineer Khalil Najafi of the University of Michigan in Ann Arbor. “They have a system that operates, and operates well.”

Michel Maharbiz of the University of California, Berkeley and colleagues presented their neural dust idea in 2013. The paper in *Neuron* represents the first time the system has been used in animals. Neural dust detected activity when the researchers artificially stimulated rats’ sciatic nerves and muscles.

Unlike devices that rely on electromagnetic waves, neural dust is powered by ultrasound. When hit with ultrasound generated by a source outside the body, a specialized crystal vibrates. This mechanical motion powers the system, allowing electrodes to pick up electrical activity. This activity can then change ultrasound signals that travel back to the source, offering a readout in a way that’s similar to a sonar measurement.



This tiny sensor that responds to ultrasound (shown on a fingertip) picked up signals from rat nerves and muscles.

Neural dust may help scientists avoid some problems with current implants, such as a limited life span. For instance, implantable devices can falter in the brain’s hostile environment. “It’s like throwing a piece of electronics in the ocean and wanting it to run for 20 years,” Maharbiz says. “Eventually things start to degrade.” But having a simple device may increase the life span of such implants — though Maharbiz and colleagues don’t yet know how long the system could last.

What’s more, the brain can mount a defense against the foreign object, which can result in thick tissue surrounding the implant. Smaller systems damage the brain less. At over 2 millimeters long and just under 1 millimeter wide, a particle of the neural dust is larger than most actual specks of dust. But the system is still shrinking. “There’s a lot of room here to just really push it,” says Maharbiz. “You can keep getting smaller and smaller and smaller.”

Neural dust could be used to detect more than just electrical activity, he says. The device could be tweaked to sense temperature, pressure, oxygen or pH.

Najafi cautions that it’s unclear whether the system will prove useful for listening to nerve cell behavior inside the brain. Such an approach would need to include many different pieces of neural dust, and it’s not clear how effective that would be. ■

BODY & BRAIN

Running doesn’t make rats forget

In new study, memory loss not linked to brain cell birth

BY MEGHAN ROSEN

Exercise may not erase old memories, as some studies in animals have suggested.

Running on an exercise wheel doesn’t make rats forget previous trips through an underwater maze, Ashok Shetty and colleagues report in the Aug. 3 *Journal of Neuroscience*. Exercise or not, four weeks after learning how to find a hidden platform, rats seem to remember the location just fine, the team found.

The results conflict with two earlier papers that reported that running triggers memory loss in some rodents by boosting the birth of new brain cells. Making new brain cells rejiggers memory circuits, and that can make it hard for animals to remember what they’ve learned, says Paul Frankland, a neuroscientist at the Hospital for Sick Children in Toronto. Maybe rats are the exception, he says, “but I’m not convinced.”

In 2014, Frankland and colleagues reported that brain cell genesis clears out fearful memories in mice, guinea pigs and degus (*SN: 6/14/14, p. 7*). The team later found similar results with spatial memories. After exercising, mice had trouble remembering the location of a hidden platform in a water maze, the team reported in February in *Nature Communications*.

Shetty, a neuroscientist at Texas A&M Health Science Center in Temple, wondered if the results held true in rats. “Rats are quite different from mice,” he says. “Their biology is similar to humans.”

Using a setup similar to Frankland’s, Shetty’s team taught two groups of rats how to find a hidden platform in a water maze in eight training sessions over eight days. Then rats in one of the groups exercised on a running wheel. Four weeks later, rats in both groups performed the same in the maze test. Compared with rats that didn’t exercise, running rats had 1.5 to two times as many newborn brain cells in the hippocampus, a brain structure thought to help form new memories.

These results and other memory tests “clearly showed that exercise did not interfere with memory recall,” Shetty says. And it’s likely that exercise doesn’t harm human memories either, he says.

Frankland says maybe the rats learned the water maze too well. Shetty and colleagues trained their rodents for longer than Frankland’s team did, perhaps etching memories more deeply in the brain.

And he points out that erasing memories isn’t necessarily a bad thing. Without some sort of clearance process, “your memory is going to be full of junk.” ■

RYAN NEELY/UC BERKELEY

GENES & CELLS

‘Promiscuous’ enzymes switch jobs

Bacteria devise work-around if important genes are disabled

BY LAUREL HAMERS

When bacteria lose genes needed to make enzymes for important chemical reactions, defeat isn’t inevitable. Sometimes other enzymes will take on new roles to patch together a work-around chain of reactions that does the job, biologist Shelley Copley reported August 4.

Bacteria that can adapt in this way are more likely to survive when living conditions change, passing along these new tricks to their descendants. So studying these biochemical gymnastics is helping scientists to understand how evolution works on a molecular level.

Using different strains of *Escherichia coli* bacteria, Copley and colleagues deleted genes responsible for making crucial enzymes. The team then watched the microbes replicate for many generations to see how they worked around those limitations.

Most enzymes are highly specialized proteins: They work well to speed up only one type of reaction, the way a key fits only one lock. But some enzymes are more like master keys — they can boost multiple reactions, though they tend to specialize in one. These “promiscuous” enzymes can switch away from their specialty if conditions change.

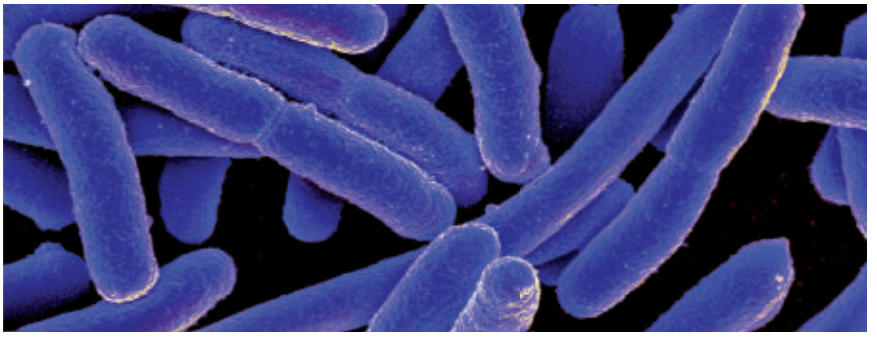
Copley’s team found that new enzymes could sub in to replace the missing ones. For instance, *E. coli* missing an enzyme needed to make vitamin B6 synthesized the vitamin using different enzymes. Surprisingly, the promiscuous enzymes didn’t directly trigger the same reaction as the enzymes they replaced. Instead, the replacement enzymes cobbled together a different (often longer) work-around series of reactions that ultimately achieved the same function.

“We were rerouting metabolism,” said Copley, of the University of Colorado Boulder.

By modifying the bacteria’s genes and forcing the microbes to survive with a more limited chemical toolkit, Copley’s work gives a more detailed look at the biochemistry underlying evolution, says biologist Gavin Sherlock of Stanford University, who was not involved in the research.

Betul Kacar, a synthetic biologist at Harvard University, says promiscuity could also be a window into the past, giving hints about enzymes’ previous roles earlier in evolutionary history. The role that an enzyme plays in a pinch could have once been its main job. “Trying to understand how novel pathways arise, what kind of mechanistic underlying forces shape those trajectories, is quite essential,” Kacar says.

Bacteria can piece together all sorts of alternative routes in response to missing enzymes, depending on environmental conditions, Copley said. The ones that are most successful are more efficient — they have fewer steps, or they yield more of the desired reaction product. ■



NIAID/FLICKR (CC BY 2.0)

When *E. coli* bacteria (shown here in false color) lose genes that make important enzymes, other enzymes find a new way to do the same job.

MEETING NOTES

Killing helps bacteria cooperate

Bacteria assassinating each other in crowds can favor the evolution of cooperation. When a *Vibrio cholerae* bacterium jostles neighbors in a crowd on crab shells, it fires a toxin injection that can kill different strains of *V. cholerae*. But siblings with the same immunity genes don’t die.

In both laboratory battles and computer simulations, neighbor-to-neighbor harpoonings over time can separate a random mix of strains into patches of same-strain clumps. The change resembles a process that separates phases of metals (the Model A order-disorder transition); it has not been reported before in living things, William Ratcliff of Georgia Tech in Atlanta said August 5. The injection and the resulting clumpy distribution favored the rise of cooperation, such as secreting substances useful to a whole community, said Georgia Tech’s Brian Hammer. — *Susan Milius*

Mixing spurs bacterial motion

Strand a fish on a tree stump, and neither swims away. But mixing two kinds of soil bacteria that are stationary on a dry surface allows the combo to expand quickly, oozing as a colony across a firm laboratory agar surface.

Over generations, the pair gets faster, Lucy McCully of the University of Massachusetts Dartmouth said August 6. In lab tests, neither *Pseudomonas fluorescens* Pf0-1 nor *Pedobacter* sp. V48 can move much without water. Yet when combined on a lab dish, a sector of some colonies bulges out unusually fast. *Pedobacter* develops the speed boost first and then something in *Pseudomonas* changes, enhancing speed even more. Over generations of commingling, evolution in one partner matters to the other: Combining one of the new speedy forms with the ancestral version of its partner lowers the speed. — *Susan Milius*

ATOM & COSMOS

Ceres is more than just a rock

Pliable layer of crust envelops dwarf planet's solid core

BY CHRISTOPHER CROCKETT

Like an interplanetary parfait, the dwarf planet Ceres appears to have layers.

A pliable outer shell of minerals, ices and salts encapsulates a core of solid rock, a new study suggests. This first peek inside Ceres — courtesy of NASA's Dawn spacecraft — can provide insight into the many ways planets and asteroids might be assembled. Ryan Park, a planetary scientist at the Jet Propulsion Laboratory in Pasadena, Calif., and colleagues report the findings online August 3 in *Nature*.

"Before we got to Ceres, we didn't know what the interior looked like," Park says. "Its evolution is more complex than what we envisioned."

Ceres is the largest body in the asteroid belt, the field of rocks between the orbits of Mars and Jupiter. The Dawn spacecraft has been orbiting Ceres since March 6, 2015. As Dawn loops around Ceres, slight changes in the spacecraft's speed — deviations of less than 0.1 millimeters per second — reveal the dwarf planet's gravity field. By combining these measurements with images that show Ceres' overall shape, the researchers deduced how mass is spread out inside. The core has a density similar to some meteorites; the shell (roughly 70 to 190 kilometers thick) is about two-thirds as dense.

Dwarf planet Ceres (seen in this image from the Dawn spacecraft) may have layers that could point to how and where it formed.

Mountains on Ceres appear to float on a deformable layer of minerals and volatile elements that easily evaporate. If Ceres were completely solid, then gravity over a mountain would be stronger than the surrounding terrain because of the increased mass. But gravity on Ceres doesn't vary with topography, the researchers find. This suggests that mountains displace mass beneath the surface, "like how a boat floats on water," Park says. To keep the underlying layer slightly flexible, Ceres' interior must be warm relative to the surface. The heat could come from radioactive decay or be left over from when Ceres formed.

This segregation of material can help researchers learn about the environment in which Ceres formed, says planetary scientist Simone Marchi of the Southwest Research Institute in Boulder, Colo. Densities within these layers allow for estimates of how much ice and radioactive material are buried beneath the surface, he says — abundances that depend on how far from the sun Ceres was born. ■

EARTH & ENVIRONMENT

India's monsoon had abrupt beginning

Origin of seasonal winds traced to nearly 13 million years ago

BY THOMAS SUMNER

The mighty monsoon winds that periodically bring rains that drench India first billowed around 12.9 million years ago.

By examining sediments piled up around islands, researchers uncovered a geologic history of the South Asian monsoon stretching back millions of years. The monsoon winds began abruptly, researchers report July 20 in *Scientific Reports*. That speedy start-up suggests that factors such as global cooling were at play in addition to the rise of the Himalayas, which scientists typically blame for the monsoon's inception.

Summer monsoon rains account for over 70 percent of India's annual precipitation. The temperature difference between the continent and the Indian Ocean drives the winds. During winter, warm air over the ocean rises and draws in cool air from the land to the north. In summer, the land becomes warmer and the winds flip direction.

The Himalayas' snow and elevation drive the temperature difference. The mountains grew over tens of millions of years, so it's difficult to determine when conditions favorable to the monsoon began. Previous estimates range from 28.7 million to 7 million years ago.

Geoscientist Gregor Eberli of the University of Miami in Florida and colleagues traveled to a place where the monsoon leaves its mark: the bottom of the Indian Ocean. Monsoon winds drive ocean currents, which carry sediments. Sediments accumulate in mounds similar to snowdrifts when currents are strong. The strong currents also pull nutrients from the seafloor toward the surface, boosting biological activity that draws oxygen from the water. That lower oxygen supply leaves a chemical trace in the sediments.

At a depth of about 500 meters below the sea surface, the researchers drilled a kilometer into the seafloor and extracted sediments dating back roughly 25 million years. A weaker precursor to the modern monsoon existed 25 million years ago, the sediment data suggest. About 12.9 million years ago, however, the winds revved up to their modern strength over the course of about 300,000 years.

The strengthening monsoon winds line up with a period of global cooling, which may have boosted the temperature difference between land and sea.

Just because the winds were blowing doesn't mean India was getting soaked, though, says Peter Clift, a geologist at Louisiana State University in Baton Rouge. The winds and rains are associated now, he says, but "that might not have always been the case." ■

JPL-CALTECH/NASA, UCLA, MPS, DLR, IDA

ATOM & COSMOS

New data give clearer picture of Higgs

LHC results allow physicists to scrutinize boson's properties

BY EMILY CONOVER

It's a Higgs boson bonanza for particle physicists, who are capitalizing on the newest data from the Large Hadron Collider to delve more deeply into the particle's properties. Scientists are keeping a keen eye out for any deviations from the standard model of particle physics, the overarching theory that describes elementary particles and their interactions.

The Higgs boson helps to explain how elementary particles obtain their mass. Its discovery in 2012 filled in the last remaining piece of the standard model (*SN: 7/28/12, p. 5*). With the newest data from the LHC, near Geneva, scientists have nailed down the Higgs' properties at the LHC's newly boosted energy. The results "strengthen the identity card of the Higgs," said Tiziano Camporesi, spokesperson for CMS, one of the LHC experiments. Camporesi discussed the new results on August 8.

The collider is now smashing protons together with 13 trillion electron volts of energy — 60 percent higher than before. The LHC has spit out more Higgs bosons at these higher energies than it did during the time it ran at its lower energy. With the new data, scientists have confirmed properties of the Higgs that were previously measured at lower energies, such as its mass (about 125 billion electron volts) and its spin (0) — a quantum version of angular momentum.

But physicists are digging even deeper, in hopes of uncovering anomalies that might lead to explanations for phenomena the standard model can't account for — such as the unidentified dark matter pervading the cosmos or the cosmic preponderance of matter over antimatter.

Sorting out the processes that generate a Higgs is first on the agenda. At higher energies, certain rare processes become more prominent. In particular, scientists are searching for a Higgs boson produced alongside two top quarks. Top quarks are the heaviest variety of the six quarks, which form larger particles like the proton and neutron. Scientists have seen hints of the production of a Higgs plus two top quarks, though not enough to meet the stringent requirements for a definitive detection. Researchers working on ATLAS, another of the LHC experiments, calculate a chance of only 3 in 1,000 to observe such hints by chance if the process does not occur.

Another way to probe the Higgs is by detecting new ways it can decay. Scientists have seen the Higgs decay into two photons — or particles of light — for example. But according to theory, Higgs bosons should decay over half of the time into bottom quarks, the second-heaviest type of quark. Bottom quarks are produced in plentiful numbers by other processes at the LHC, so sifting out evidence of Higgs bosons from the bottom-quark debris they produce is difficult. Definitive confirmation of the decay remains elusive.

By comparing the results from the new, higher-energy data with earlier LHC results, physicists can study how these processes change with energy and whether they agree with theory. In the new dataset, everything seems in order.

Many theories aiming to patch the holes in the standard model predict additional Higgs bosons, and scientists are now searching for those heavier Higgs cousins. "Who's to say there's only one? There might be more," says ATLAS researcher Carl Gwilliam of the University of Liverpool in England.

So far, the Higgs has passed all of scientists' tests, staying steadfastly consistent with theoretical predictions. "Can it really be this simple?" Nigel Lockyer, director of the Fermilab physics laboratory in Batavia, Ill., asked in a media briefing. "When we sit around and drink coffee at night, that's the kind of thing that we talk about." Higgs research, he said, is far from complete. ■

MEETING NOTES

Cooling stars hint at existence of dark matter particles

Cooling stars could shine some light on the nature of dark matter.

Certain types of stars are cooling faster than expected. That may signal the presence of hypothetical particles called axions. Such particles have been proposed to be dark matter, the unknown substance that makes up most of the universe's mass.

Researchers analyzed previous measurements of five white dwarf variable stars, which periodically grow dimmer and brighter at a rate that indicates how fast the star is cooling. The cooling was larger than predicted. Red giant stars have also shown excess cooling.

The consistent pattern could indicate something funny is going on, said Maurizio Giannotti of Barry University in Miami Shores, Fla., who presented the result August 4.

Although the cooling could be a measurement error, the researchers conclude that axions produced within the star stream outward, carrying energy away as they go and cooling the star. — *Emily Conover*

With more data, suspected new particle vanishes

Physicists' hopes have been dashed. A possible new particle hasn't been sighted in the latest data from the Large Hadron Collider near Geneva, scientists reported August 5.

Physicists from LHC experiments CMS and ATLAS unveiled hints of the particle in December (*SN: 1/9/16, p. 7*). Evidence of the particle — a bump on a plot, an excess of events at a particular energy — popped up after the LHC began smashing protons at a boosted energy.

LHC physicists had warned that the bump could be due to random fluctuations. Now, neither LHC experiment shows any sign of a wayward bump. — *Emily Conover*

HUMANS & SOCIETY

Fentanyl's fatal toll is rising

Deaths linked to opioid's rapid effects on chest muscles

BY LAURA SANDERS

For some people, fentanyl can be a lifesaver, easing profound pain. But outside of a doctor's office, the powerful opioid drug is also a covert killer.

In the last several years, clandestine drugmakers have begun experimenting with this ingredient, baking it into drugs sold on the streets, most notably heroin. Fentanyl and closely related compounds have "literally invaded the entire heroin supply," says medical toxicologist Lewis Nelson of New York University Langone Medical Center.

Fentanyl is showing up in other drugs, too. In San Francisco's Bay Area in March, high doses of fentanyl were laced into counterfeit versions of the pain pill Norco. In January, fentanyl was found in illegal pills sold as oxycodone in New Jersey. And in late 2015, fentanyl turned up in fake Xanax pills in California.

This ubiquitous recipe-tinkering makes it impossible for users to know whether they're about to take drugs mixed with fentanyl. And that uncertainty has proved deadly. Fentanyl-related deaths are rising sharply in multiple areas. National numbers are hard to come by, but in many regions around the United States, fentanyl-related fatalities have soared in recent years.

Maryland is one of the hardest-hit states. From 2007 to 2012, the number of fentanyl-related deaths hovered around 30 per year. By 2015, that number had grown to 340. A similar rise is obvious in Connecticut, where in 2012, there were 14 fentanyl-related deaths. In 2015, that number was 188.

In Massachusetts, two-thirds of people who died from opioid overdoses in the first half of 2016 showed signs of fentanyl. This wave of fentanyl-related overdoses is "horrendous," says Daniel Ciccarone of the University of California, San Francisco. What's worse, he says, "I think it's here to stay."

Fentanyl is not a new drug. Available in the 1960s, it is still used in hospitals as an anesthetic and is available by prescription to fight powerful pain. What's new, Ciccarone says, is that clandestine drug manufacturers have discovered that the euphoria-producing opioid can be made cheaply and easily — no poppy fields necessary.

Fentanyl is about 30 to 40 times stronger than heroin and up to 100 times more powerful than morphine, which means that a given effect on the body can be achieved with a much smaller amount of fentanyl. Inadvertently taking a bit of fentanyl can cause big trouble. "It's a dosing problem," Nelson says. "Because the drug is so potent, little changes in measurements can have very big implications for toxicity. That's really the problem."

That problem is made worse by the variability of illegal drugs — users often don't know what they're buying. Illegal labs aren't pumping out products with carefully calibrated doses or uniform chemical makeup. The drugs change from day to day, making it nearly impossible for a user to know what he or she is about to take, Ciccarone says.

He has seen this struggle up close. Drug users have told him that the products they buy are unpredictable. Another thing people are telling him: "That they and their friends and compatriots are dropping like flies." Tellingly, some of the most experienced drug users have recently begun doing "tester shots," small doses to get a sense of the type and dose of drug they're about to use, Ciccarone says.

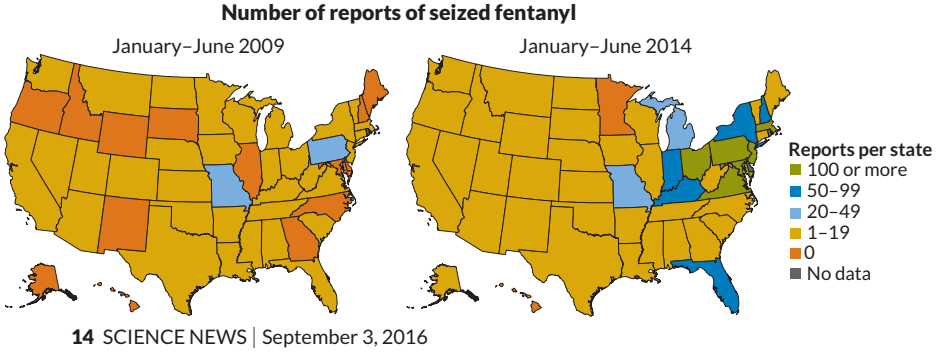
Users are right to be wary. Typically, opioids can kill by gradually depressing a person's ability to breathe. Illicit fentanyl, a recent study suggests, can kill within minutes by paralyzing muscles. Doctors have known that when injected quickly, fentanyl can paralyze chest wall muscles, prevent breathing and kill a person rapidly. That effect, called "wooden chest," might help explain the rise in fentanyl-related deaths, scientists report in the June *Clinical Toxicology*.

A quick injection of fentanyl "literally freezes the muscles and you can't move the chest," says toxicologist Henry Spiller of the Central Ohio Poison Center in Columbus. That's why doctors who dispense fentanyl in the hospital intentionally proceed very slowly and keep the opioid-counteracting drug naloxone (Narcan) on hand. "If you give it too fast, we know this occurs," Spiller says. But it wasn't known whether this same phenomenon might help explain the death rate of people using the drug illegally.

Spiller and colleagues tested postmortem concentrations of fentanyl and its breakdown product norfentanyl in 48 fentanyl-related deaths. The body usually begins breaking down fentanyl into norfentanyl within two minutes, an earlier study found. Yet in 20 of the cases, the researchers found no signs of norfentanyl, indicating death came almost immediately after first receiving fentanyl.

Naloxone can counteract the effects of opioids if someone nearby can administer the antidote. But for people whose chests quickly freeze from fentanyl, resuscitation becomes more unlikely. Fentanyl "is just a bad drug," Spiller says.

Dangerous spread In the first half of 2009, no state reported more than 49 seizures of fentanyl. In the first half of 2014, the numbers rose, with six states reporting 100 or more seizures. The maps show only the fentanyl that was analyzed by forensic labs. SOURCE: NATIONAL FORENSIC LAB. INFO. SYSTEM



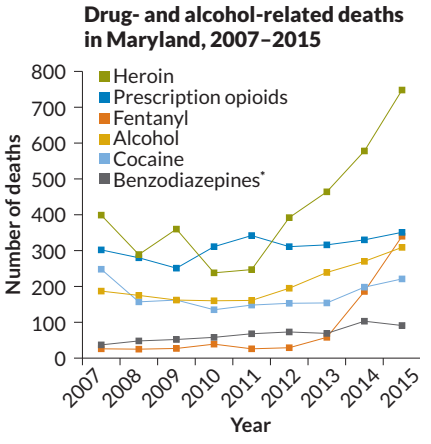
J. HIRSHFELD

Fentanyl's danger is magnified for people not accustomed to taking opioids, such as those addicted to cocaine, a situation illustrated by a recent tragedy in New Haven, Conn.

New Haven authorities noticed a string of suspicious overdoses in late June, leaving three people dead. Drug users thought they were buying cocaine, but the drugs contained fentanyl, says analytical toxicologist Kara Lynch of the University of California, San Francisco. As one of the handful of labs capable of testing blood and urine for fentanyl, hers was called on to identify the culprit. Her lab spotted fentanyl in Norco tablets back in March.

Lynch's group uses high-resolution mass spectrometry to detect many drugs' chemical signatures. But this method reveals only the drugs scientists suspect. "We can look for what we know to look for," she says. And success depends on getting the samples in the first place.

The logistical hurdles of figuring out exactly what a person took, and how much, and when, are large. Ciccarone contrasts the situation with cases of food poisoning. When people start getting sick, public health officials can figure out what lettuce people ate and test it for pathogens. The same kind of tracking system doesn't exist for drugs. His efforts to develop a system for testing illegal drugs in Baltimore broke down in part because no one had time to do the work. "The coroner is so busy right now with dead bodies," he says. "They don't have the time to test the 'lettuce.'"



Deadly surge In Maryland, deaths linked to fentanyl (orange) began a steep climb in 2013. Some of these reported deaths involved more than one substance. SOURCE: MARYLAND VITAL STATISTICS ADMINISTRATION

In the quest to curb fentanyl-related deaths, scientists and public health officials are searching for new strategies. Spiller advocates a more targeted public health message to users, one that emphasizes that fentanyl is simply a deadly drug, not just a more potent high. Ciccarone says that facilities where drug users can take illegal drugs under the care of medical personnel might reduce the number of fatalities.

For now, the scope of the problem continues to grow, Nelson says. The situation is made worse by the ingenuity of illicit drugmakers, who readily experiment with new compounds. Fentanyl itself can be tweaked to create at least 16 related forms, one of which, acetyl fentanyl, has been linked to overdose deaths. New drugs and new tweaks to old drugs rapidly evolve (*SN: 5/16/15, p. 22*), Nelson says, creating a game of whack-a-mole in which designer drugs confound public health officials and law enforcement.

"There is no single easy solution to this problem," he says. ■

LIFE & EVOLUTION

Richer homes host more kinds of bugs

Over 100 species of arthropods live inside average house

BY SUSAN MILIUS

Here's something new for real estate agents to boast about in posh neighborhoods: houses with a bigger variety of insects and spiders.

Maybe that's *not* the best selling point. But what's called a "luxury effect" appeared among more than 10,000 arthropod samples collected from the insides of 50 houses in urban and suburban Raleigh, N.C. Depending on the house, arthropods from 24 to 128 distinct scientific families showed up, says entomologist Misha Leong of the California Academy of Sciences in San Francisco. Houses in neighborhoods with higher average incomes tended toward greater diversity than houses in lower-income spots, she and colleagues report in the August *Biology Letters*. An average home had more than 100 arthropod species.

Other researchers have linked wealth with greater diversity of a neighborhood's (outdoor) birds, lizards, bats and plants. As far as Leong knows, this is the first evidence of arthropod variety as a perk of wealth.

Researchers didn't try to measure the abundance of arthropods but rather looked at the diversity. Many of the arthropod roommates found in the great indoors are so harmless that homeowners had never heard of them. Gall midge flies showed up in 100 percent of houses studied; dark-winged fungus gnats lived in 96 percent. Both were more common than Blattidae cockroaches (in 74 percent of homes).

Sheer size of bigger houses, perhaps with more room for habitat, was an important factor in the arthropod variety in wealthier neighborhoods, the researchers found. And even though the survey took place indoors, the amount of outdoor planting likewise proved important. Leong speculates that more plant variety in yards and gardens may increase arthropod diversity just by boosting the kinds of foods and habitats available.

Such results might show up in other cities if planting tastes are similar, muses Ann Kinzig of Arizona State University in Tempe, who has written about landscaping and household socioeconomic status. A luxury effect like Raleigh's might turn up in neighborhoods where rich homeowners want both a variety of different plants around a house and a consistent neighborhood look that creates big blocks of the varied greenery, she says. "But that wouldn't always have to be the preference of the rich." ■

J. HIRSHFELD

HUMANS & SOCIETY

Ape-man hoax pinned on one culprit

Probe rules out coconspirators in Piltdown Man forgery

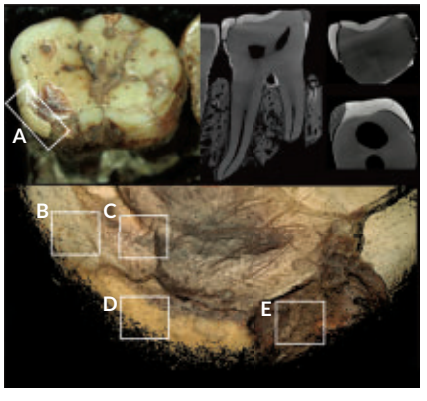
BY BRUCE BOWER

New investigations of England's infamously fraudulent Piltdown Man fossils reveal a mix of clever and clumsy methods used by one man to fool early 20th century scientists for 40 years.

Lawyer and amateur archaeologist Charles Dawson modified orangutan and human bones to resemble what scientists of the time thought a "missing link" between apes and humans might look like, say paleoanthropologist Isabelle De Groote of Liverpool John Moores University in England and colleagues. Dawson and paleontologist Arthur Smith Woodward announced the discovery of what they called *Eoanthropus dawsoni*, or Dawson's dawn man, in 1912.

Consistent forgery techniques employed on an orangutan jaw, several orangutan teeth and six braincase pieces from at least two humans point to Dawson as the lone culprit who planted faux fossils in a gravel deposit near Piltdown village, De Groote's team reports August 10 in *Royal Society Open Science*. The results are the strongest evidence to date that Dawson had no help in the hoax.

"Hopefully this is the final, or close to the final, nail in the coffin of the Piltdown story," says archaeologist Miles Russell of Bournemouth University in Poole, England.



Imaging analyses reveal new details about the Piltdown Man hoax. A photograph (upper left) and CT scan (upper right) show that the chewing surface of an orangutan tooth originally attributed to Piltdown Man was filed down. Box A at upper left denotes where chipped enamel was replaced. A closer look at the same tooth (bottom) reveals filing marks (B and C), putty (D) and a reddish brown stain (E).

As an artifact collector for a museum, with access to animal bone collections, Dawson could easily have obtained an orangutan jaw, Russell says. Russell previously argued that Dawson not only created Piltdown Man but also fabricated finds in his personal collection, including an alleged reptile/mammal hybrid fossil.

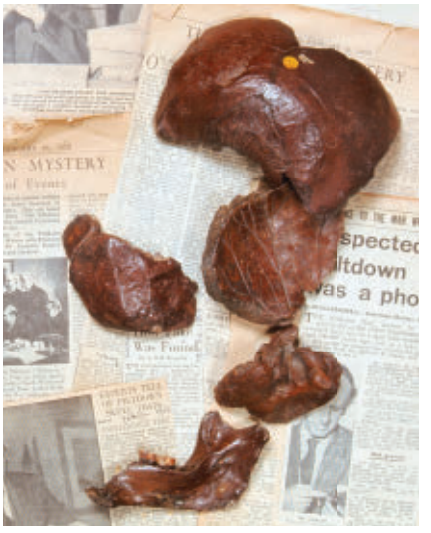
High-resolution 3-D imaging by De Groote's team shows that the orangutan jaw was cracked lengthwise, probably while being stretched by hand from its two ends. Dawson had to widen the jaw's tooth sockets to remove two molar teeth, which in great apes have telltale curved roots, the researchers say. Dawson then filed the teeth to appear more humanlike and repositioned them in their sockets. A thin layer of putty kept the teeth in place.

Since publication of a 1953 paper and a 1955 book exposing the hoax — long after Dawson's death in 1916 — a lengthy list of proposed coconspirators has accumulated. Names include Smith Woodward and French priest Teilhard de Chardin, who attended some excavations.

Dawson didn't need help, De Groote says. Imaging of the internal structure of Piltdown orangutan teeth indicates they came from the same individual. So do matching sequences of mitochondrial DNA from two teeth, one of which came from a second Piltdown site. Before he died, Dawson had informed Smith Woodward of further *Eoanthropus* finds about three kilometers from the first site.

Dawson did a better job of forging humanlike wear on a tooth from the second site. He may have learned from the comments of some early scientific critics of Piltdown Man, the researchers suspect.

Gravel was placed in cavities of two Piltdown teeth, through holes where the roots had been damaged. The cavities were plugged with pebbles held in place by the same putty used on the jaw.



Human skull fragments and orangutan teeth and a jaw from the fake fossil Piltdown Man contain clues suggesting that Charles Dawson acted alone in creating the 20th century fraud.

Dawson created his forgery from at least two human skulls, since remains from the same rear section of the braincase were planted at both Piltdown sites, De Groote's group says.

Dawson had access to medieval burials during his archaeological work. He could have selected the thickest skull fragments he could find to pass off as Piltdown Man, Russell says. Dawson knew that such bones would appear particularly apelike. Radiocarbon dating of Piltdown skull fragments is inconclusive.

To match the color of Piltdown gravel, Dawson stained his phony fossils. He did the same to nonhuman animal bones, stone tools and a carved bone that were planted as part of the sham.

Dawson's ambition to be elected a fellow of the Royal Society, an honor that he was nominated for but didn't receive, may have motivated him to fake Piltdown Man, the researchers say.

Dawson "satiated his attention-seeking by perpetrating skillful, and not so skillful, fraud," says paleoanthropologist Bernard Wood of George Washington University in Washington, D.C. Dawson's peers wanted the skull to be real as badly as Dawson wanted official recognition, so "they gave him pass after pass." ■

FROM TOP: I. DE GROOTE; I. DE GROOTE *ET AL*./*ROYAL SOCIETY OPEN SCIENCE* 2016

BODY & BRAIN

Zika vaccines work in rhesus monkeys

Three vaccines offer complete protection against Zika virus in monkeys. The results are the latest steps in the quest to create a Zika vaccine that's safe and effective for humans (*SN Online: 6/28/16*).

One vaccine, made with a purified, inactivated form of the virus — designated PIV — helped rhesus monkeys fend off infection with both a Zika strain from Brazil and one circulating in Puerto Rico, Nelson Michael and colleagues report online August 4 in *Science*. A second, DNA-based vaccine that uses snippets of Zika's genetic material to rev up the immune system was tested against a Brazilian strain. So was a third type of vaccine that relies on a virus called adenovirus to carry Zika genes into the monkeys' bodies.

The U.S. government and Inovio Pharmaceuticals have recently started human safety trials for two other DNA-based vaccine candidates. But Michael, a vaccine researcher at the Walter Reed Army Institute of Research in Silver Spring, Md., thinks the PIV vaccine may have the best shot.

"It's the one that's probably going to go the distance," he says.

DNA-based vaccines have never before been licensed for use in humans, Michael notes. The technique to make a PIV vaccine "goes back to Jonas Salk and polio," he says. Essentially, researchers grow Zika in a lab, kill it and then purify it. "It's a classic way to make a vaccine," he says. "And you know what? It works."

Human testing of the PIV vaccine will start in October. Still, Michael says evaluating many vaccine candidates is important. Any number of factors, from a bad reaction to a bankrupt manufacturer, can knock a vaccine out of the running.

"You definitely want to bet on more than one horse," he says. — *Meghan Rosen*

ATOM & COSMOS

No sign of dark matter

Before its demise, Japan's X-ray satellite Hitomi might have put to rest speculation about radiation from dark matter in a cache of galaxies. In 2014, astronomers reported that several galaxy clusters inexplicably appeared to produce X-ray photons with energies of about 3.5 kiloelectron volts. The researchers suggested that the X-rays could be from the decay of sterile neutrinos — hypothetical particles that are a candidate for the dark matter that makes up most of the universe's mass.

Before Hitomi failed on March 26, it looked at the Perseus galaxy cluster, about 232 million light-years away, but saw no sign of the previously reported X-rays, scientists report online July 25 at arXiv.org. The no-show photons make it less likely that sterile neutrinos are the dark matter particles. Hitomi spun itself to death less than six weeks after it launched, when a malfunction caused it to rotate out of control. — *Christopher Crockett*

GENES & CELLS

Scientists glimpse chemical tags

For the first time, scientists can see where molecular tags known as epigenetic marks are altered in the brain.

These chemical tags — which flag DNA or its protein associates, known as histones — don't change the genes but can change gene activity. Abnormal epigenetic marks have been associated with brain disorders such as Alzheimer's disease, schizophrenia, depression and addiction.

Researchers at Massachusetts General Hospital in Boston devised a tracer molecule that latches on to a protein that removes one type of epigenetic mark known as histone acetylation.

The scientists then used PET scans to detect where a radioactive version of the tracer appeared in the brains of eight healthy young adult men and women, the researchers report in the Aug. 10 *Science Translational Medicine*. Further studies could show that the marks change as people grow older or develop a disease. The team studied only healthy young volunteers so can't yet say whether epigenetic marking changes with age or disease. — *Tina Hesman Saey*

LIFE & EVOLUTION

Colugo gliders are primate cousins

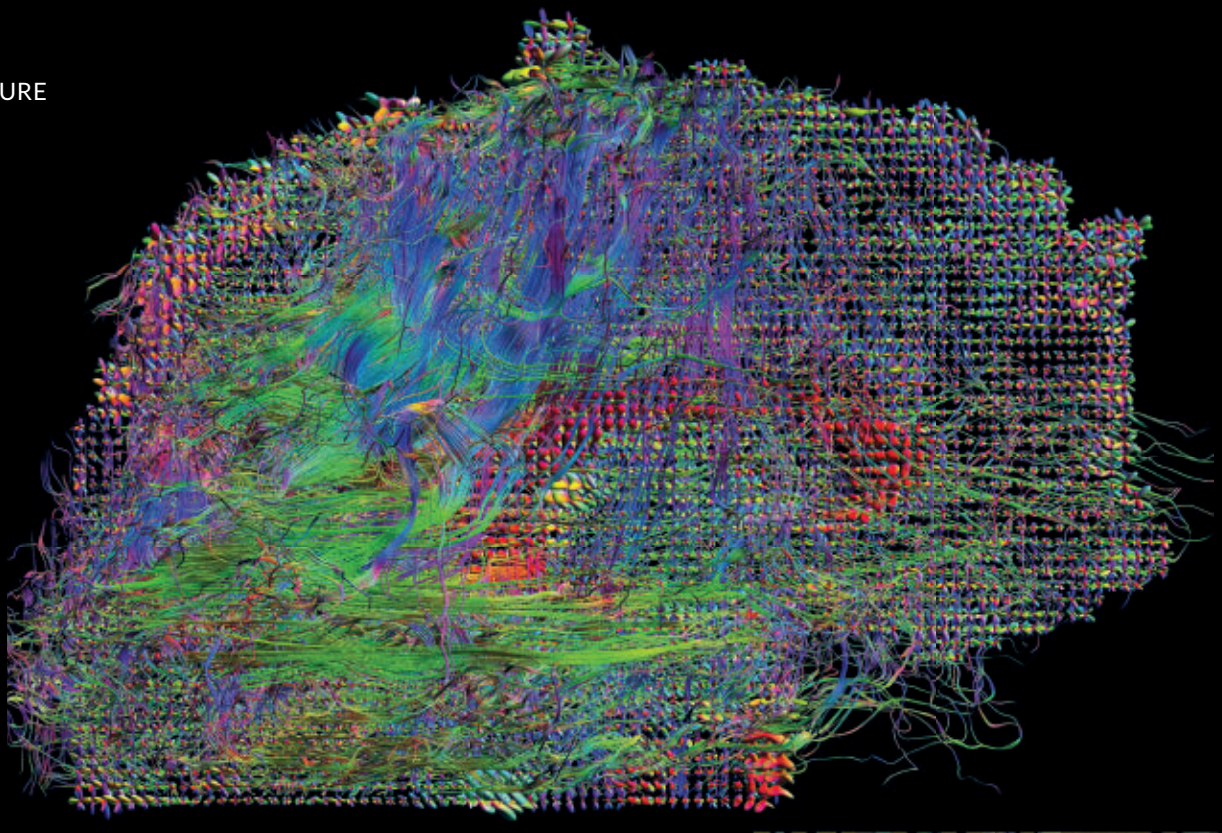
Primates may have some high-flying relatives. Colugos, small mammals that glide from treetop to treetop in forests throughout Southeast Asia, have an evolutionary history that's long been debated. Their teeth look similar to tree shrews' teeth, while other skull and genetic features resemble those of primates. (Past studies have even linked colugos to bats and other insect-eating mammals.)

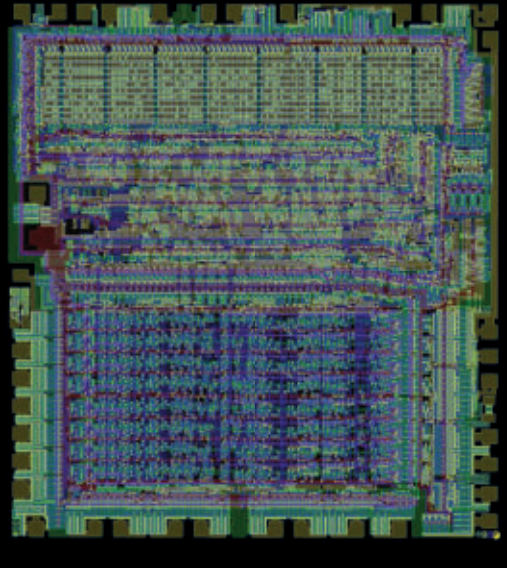
In an effort to settle the debate, William Murphy, a geneticist at Texas A&M University in College Station, and colleagues have deciphered the genome of a male Sunda colugo (*Galeopterus variegatus*) from West Java, Indonesia. Comparing colugo DNA with 21 other mammal genomes, the team found that colugos are most closely related to primates, while tree shrews took different evolutionary paths to arrive at similar traits. There are also changes in genes related to vision and gliding that are unique to colugos, the researchers report August 10 in *Science Advances*.

Key changes to certain genes may have allowed the ancient ancestors of colugos to leap and glide across the forest canopies of Southeast Asia. Mutations in some of those same genes have been linked to muscle and skeletal problems in humans.

Genetic data from colugos preserved in museums also show that the animals are more diverse than suspected. While only two species have been described in the wild, the team found at least seven separate genetic lineages, which may represent individual species. — *Helen Thompson*

V.C. MASON ET AL/SCIENCE ADVANCES 2016





GAMING THE BRAIN

Computer experiment throws shade on neuroscience methods

By Laura Sanders

Neuroscience tools didn't reveal much about the inner workings of a simple microprocessor (bottom right), so how can they grasp the much more complex brain?

Brain scientists Eric Jonas and Konrad Kording had grown skeptical. They weren't convinced that the sophisticated, big data experiments of neuroscience were actually accomplishing anything. So they devised a devilish experiment.

Instead of studying the brain of a person, or a mouse, or even a lowly worm, the two used advanced neuroscience methods to scrutinize the inner workings of another information processor — a computer chip. The unorthodox experimental subject, the MOS 6502, is the same chip that dazzled early tech junkies and kids alike in the 1980s by powering *Donkey Kong*, *Space Invaders* and *Pitfall*, as well as the Apple I and II computers.

Of course, these experiments were rigged. The scientists already knew everything about how the 6502 works.

"The beauty of the microprocessor is that unlike anything in biology, we understand it

on every level," says Jonas, of the University of California, Berkeley.

Using a simulation of MOS 6502, Jonas and Kording, of Northwestern University in Chicago, studied the behavior of electricity-moving transistors, along with aspects of the chip's connections and its output, to reveal how it handles information. Since they already knew what the outcomes should be, they were actually testing the methods.

By the end of their experiments, Jonas and Kording had discovered almost nothing.

Their results — or lack thereof — hit a nerve among neuroscientists. When Jonas presented the work last year at a Kavli Foundation workshop held at MIT, the response from the crowd was split. "A bunch of people said, 'That's awesome. I had that idea 10 years ago and never got around to doing it,'" Jonas says. "And a bunch of people were like, 'That's bullshit. You're taking the analogy way too far. You're attacking a straw man.'"

On May 26, Jonas and Kording shared their results with a wider audience by posting a manuscript on the website bioRxiv.org. Bottom line of their report: Some of the best tools used by neuroscientists turned up plenty of data but failed to reveal anything meaningful about a relatively simple machine. The implications are profound — and discouraging. Current neuroscience methods might not be up for the job when it comes to truly understanding the brain.

The paper "does a great job of articulating something that most thoughtful people believe but haven't said out loud," says neuroscientist Anthony Zador of Cold Spring Harbor Laboratory in New York. "Their point is that it's not clear that the current methods would ever allow us to understand how the brain computes in [a] fundamental way," he says. "And I don't necessarily disagree."

Differences and similarities

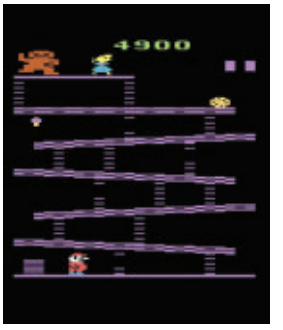
Critics, however, contend that the analogy of the brain as a computer is flawed. Terrence Sejnowski of the Salk Institute for Biological Studies in La Jolla, Calif., for instance, calls the comparison "provocative, but misleading." The brain and the microprocessor are distinct in a huge number of ways. The brain can behave differently in different situations, a variability that adds an element of randomness to its machinations; computers aim to serve up the same response to the same situation every time. And compared with a microprocessor, the brain has an incredible amount of redundancy, with multiple circuits able to step in and compensate when others malfunction.

In microprocessors, the software is distinct from the hardware — any number of programs can run on the same machine. "This is not the case in the brain, where the software is the hardware," Sejnowski says. And this hardware changes from minute to minute. Unlike the microprocessor's connections, brain circuits morph every time you learn something new. Synapses grow and connect nerve cells, storing new knowledge.

Brains and microprocessors have very different origins, Sejnowski points out. The human brain has been sculpted over millions of years of evolution to be incredibly specialized, able to spot an angry face at a glance, for instance, or remember a childhood song for years. The 6502, which debuted in 1975, was designed by a small team of humans, who engineered the chip to their exact specifications. The methods for understanding one shouldn't be expected to work for the other, Sejnowski says.

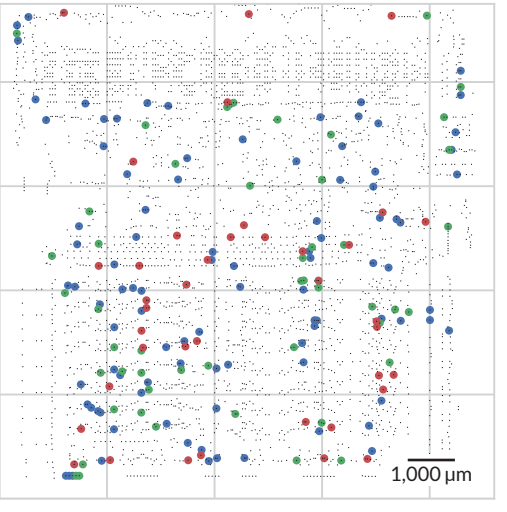
Yet there are some undeniable similarities. Brains and microprocessors are both built from many small units: 86 billion neurons and 3,510 transistors, respectively. These units can be organized into specialized modules that allow both "organs" to flexibly move information around and hold memories. Those shared traits make the 6502 a legitimate and informative model organism, Jonas and Kording argue.

In one experiment, they tested what would happen if they tried to break the 6502 bit by bit. Using a simulation to run their experiments, the researchers systematically knocked out every single transistor one at a time. They wanted to know which transistors were mission-critical to three important "behaviors": *Donkey Kong*, *Space Invaders* and *Pitfall*. The effort was akin to what neuroscientists

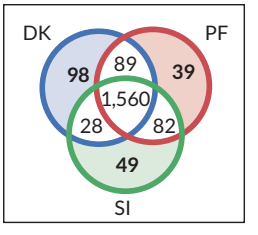


A barrel-hurling gorilla is the enemy in *Donkey Kong*, a video game powered by the MOS 6502 microprocessor. Along with *Space Invaders* and *Pitfall*, this game served as the "behavior" in a recent experiment.

Transistors that impact single games

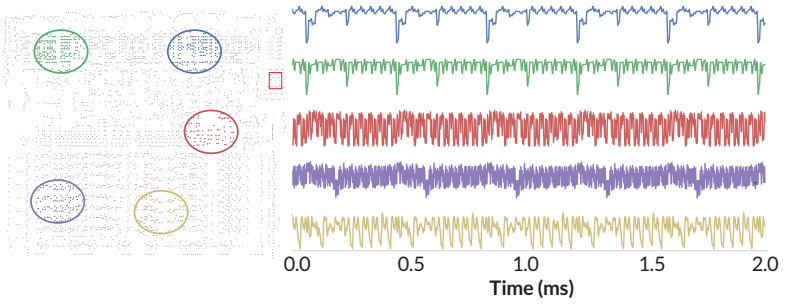


Crucial transistors



Breaking the game
With certain transistors shut down, *Donkey Kong* (blue), *Pitfall* (red) and *Space Invaders* (green) no longer worked (Venn diagram above). Some transistors (locations on microprocessor, left) damaged just one of the games.

OPPOSITE PAGE FROM TOP: COURTESY OF LAB. OF NEURO IMAGING AND MARTINOS CTR. FOR BIOMEDICAL IMAGING, CONSORTIUM OF THE HUMAN CONNECTOME PROJECT (WWW.HUMANCONNECTOMEPROJECT.ORG); GREG JAMES OF THE VISUAL 6502 PROJECT. CURRENT PAGE FROM TOP: TYLER C. HELLARD/FLICKR (CC BY-SA 2.0); E. JONAS AND K. KORDING/BIORXIV.ORG 2016



Listening in Active transistors (circles, left) produced signals (right) similar to those from nerve cells in the brain. But for the microprocessor, the signals were meaningless.

call "lesion studies," which probe how the brain behaves when a certain area is damaged.

The experiment netted 1,565 transistors that could be eliminated without any consequences to the games. But other transistors proved essential. Losing any one of 1,560 transistors made it impossible for the microprocessor to load any of the games.

Big gap

Those results are hard to parse into something meaningful. This type of experiment, just as those in human and animal brains, are informative in some ways. But they don't constitute understanding, Jonas argues. The gulf between knowing that a particular broken transistor can stymie a game and actually understanding how that transistor helps compute is "incredibly vast," he says.

The transistor "lesion" experiment "gets at the core problem that we are struggling with in neuroscience," Zador says. "Although we can attribute different brain functions to different brain areas, we don't actually understand how the brain computes."

> "Although we can attribute different brain functions to different brain areas, we don't actually understand how the brain computes."
> ANTHONY ZADOR

Other experiments reported in the study turned up red herrings — results that looked similar to potentially useful brain data, but were ultimately meaningless. Jonas and Kording looked at the average activity of groups of nearby transistors to assess patterns about how the microprocessor works. Neuroscientists do something similar when they analyze electrical patterns of groups of neurons. In this task, the microprocessor delivered some good-looking data. Oscillations of activity rippled over the microprocessor in patterns that seemed similar to those of the brain. Unfortunately, those signals are irrelevant to how the computer chip actually operates.

Data from other experiments revealed a few finds, including that the microprocessor contains a clock signal and that it switches between reading and writing memory. Yet these are not key insights into how the chip actually handles information, Jonas and Kording write in their paper.

It's not that analogous experiments on the brain are useless, Jonas says. But he hopes that these examples reveal how big of a challenge it will be to move from experimental results to a true understanding. "We really need to be honest about what we're going to pull out here."

Jonas says the results should caution against collecting big datasets in the absence of theories that can help guide experiments and that can be verified or refuted. For the microprocessor, the researchers had a lot of data, yet still couldn't separate the informative wheat from the distracting chaff. The results "suggest that we need to try and push a little bit more toward testable theories," he says.

That's not to say that big datasets are useless, he is quick to point out. Zador agrees. Some giant collections of neural information will probably turn out to be wastes of time. But "the right dataset will be useful," he says. And the right bit of data might hold the key that propels neuroscientists forward.

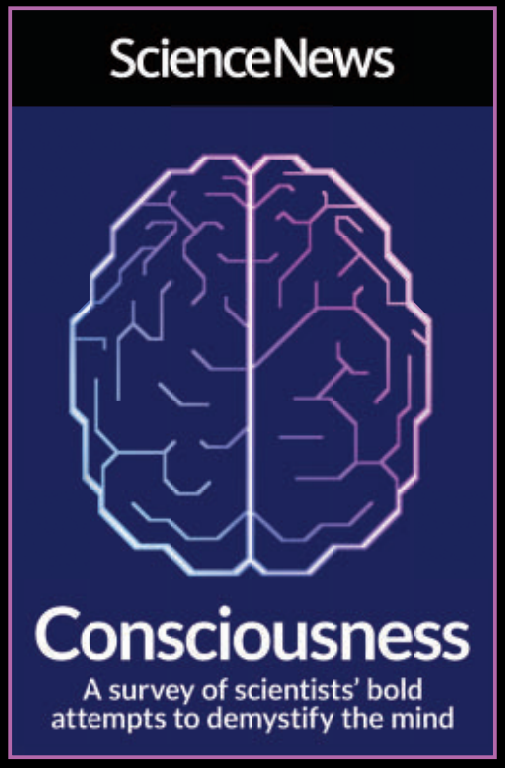
Despite the pessimistic overtones in the paper, Christof Koch of the Allen Institute for Brain Science in Seattle is a fan. "You got to love it," Koch says. At its heart, the experiment on the 6502 "sends a good message of humility," he adds. "It will take a lot of hard work by a lot of very clever people for many years to understand the brain." But he says that tenacity, especially in the face of such a formidable challenge, will eventually lead to clarity.

Zador recently opened a fortune cookie that read, "If the brain were so simple that we could understand it, we would be so simple that we couldn't." That quote, from IBM researcher Emerson Pugh, throws down the challenge, Zador says. "The alternative is that we will never understand it," he says. "I just can't believe that." ■

Explore more

■ Terrence J. Sejnowski, Patricia S. Churchland and J. Anthony Movshon. "Putting big data to good use in neuroscience." *Nature Neuroscience.* November 2014.

E. JONAS AND K. KORDING/BIORXIV.ORG 2016



Into the MIND

Scientists explore the deep questions of consciousness

Find out what they've learned at
ganxy.com/i/113816 or wherever e-books are sold.

ScienceNews

CRISPR Gets a Makeover

The gene-editing tool does one thing well, but that's just the beginning

By Tina Hesman Saey

Scientists usually shy away from using the word *miracle* — unless they're talking about the gene-editing tool called CRISPR/Cas9. "You can do anything with CRISPR," some say. Others just call it amazing.

CRISPR can quickly and efficiently manipulate virtually any gene in any plant or animal. In the four years since CRISPR has been around, researchers have used it to fix genetic diseases in animals, combat viruses, sterilize mosquitoes and prepare pig organs for human transplants. Most experts think that's just the beginning. CRISPR's powerful possibilities — even the controversial notions of creating "designer babies" and eradicating entire species — are stunning and sometimes frightening.

So far CRISPR's biggest impact has been felt in basic biology labs around the world. The inexpensive, easy-to-use gene editor has made it possible for researchers to delve into fundamental mysteries of life in ways that had been difficult or impossible. Developmental biologist Robert Reed likens CRISPR to a computer mouse. "You can just point it at a place in the genome and you can do anything you want at that spot."

Anything, that is, as long as it involves cutting DNA. CRISPR/Cas9 in its original incarnation is a homing device (the CRISPR part) that guides molecular scissors (the Cas9 enzyme) to a target section of DNA. Together, they work as a genetic-engineering cruise missile that disables or repairs a gene, or inserts something new where it cuts.

Even with all the genetic feats the CRISPR/Cas9 system can do, "there were shortcomings. There were things we wanted to do better," says MIT molecular biologist Feng Zhang, one of the first scientists to wield the molecular scissors. From his earliest report in 2013 of using CRISPR/Cas9 to cut genes in human and mouse cells, Zhang has described ways to make the system work more precisely and efficiently.

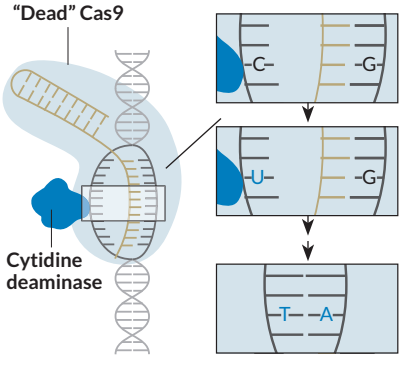
He isn't alone. A flurry of papers in the last three years have detailed improvements to the editor. Going even further, a bevy of scientists, including Zhang, have dreamed up ways to make CRISPR do a toolbox's worth of jobs.

Turning CRISPR into a multitasker often starts with dulling the cutting-edge technology's cutting edge. In many of its new adaptations, the "dead" Cas9 scissors can't snip DNA. Broken scissors may sound useless, but scientists have upcycled them into chromosome painters, typo-correctors, gene activity stimulators and inhibitors and general genome tinkerers.

Doing more Traditional CRISPR/Cas9 is one thing: a targeted scissors. A guide RNA shepherds the Cas9 enzyme to a specific stretch of DNA. Cas9 then cleaves the DNA to disable or repair a gene. Now researchers are expanding what CRISPR/Cas9 can do by converting the cutter into a platform for a host of specialized tools.

Traditional CRISPR

Changing a single base pair



A disabled or "dead" Cas9 can fix a single base typo in DNA's genetic instructions. Through a series of steps, the enzyme cytidine deaminase bolted to dead Cas9 converts a C-G DNA base pair into T-A base pair.

E. OTWELL

"The original Cas9 is like a Swiss army knife with only one application: It's a knife," says Gene Yeo, an RNA biologist at the University of California, San Diego. But Yeo and other researchers have bolted other proteins and chemicals to the dulled blades and transformed the knife into a multifunctional tool.

Zhang and colleagues are also exploring trading the Cas9 part of the system for other enzymes that might expand the types of manipulations scientists can perform on DNA and other molecules. With the expanded toolbox, researchers may have the power to pry open secrets of cancer and other diseases and answer new questions about biology.

Flexible guidance

Many enzymes can cut DNA; the first were discovered in the 1970s and helped to launch the whole field of genetic engineering. What makes CRISPR/Cas9 special is its precision. Scientists can make surgical slices in one selected spot, as opposed to the more scattershot approach of early tools. A few recent gene-editing technologies, such as zinc finger nucleases and TALENs, could also lock on to a single target. But those gene editors are hard to redirect. A scientist who wants to snip a new spot in the genome has to build a new editor. That's like having to assemble a unique guided missile for every possible target on a map. With CRISPR/Cas9, that's not necessary.

The secret to CRISPR's flexibility is its guidance system. A short piece of RNA shepherds the Cas9 cutting enzyme to its DNA target. The "guide RNA" can home in on any place a researcher selects by chemically pairing with DNA's information-containing building blocks, or bases (denoted by the letters A, T, C and G). Making a new guide RNA is easy; researchers often simply order one online by typing in the desired sequence of bases.

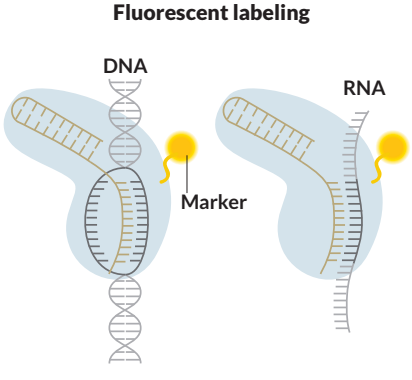
That guidance system is taking genetic engineers to places they've never been. "With CRISPR, literally overnight what had been the biggest frustration of my career turned into an undergraduate side project," says Reed, of Cornell University. "It was incredible."

Reed studies how patterns are painted on butterfly and moth wings. Color patterning is one of the fundamental questions evolutionary and developmental biologists have been trying to answer for decades. In 1994, Sean B. Carroll and colleagues discovered that a gene called *Distal-less* is turned on in butterfly wings in places where eyespots later form. The gene appeared to be needed for eyespot formation, but the evidence was only circumstantial. That's where researchers have been stuck for 20 years, Reed says. They had no way to manipulate genes in butterfly wings to get more direct proof of the role of different genes in painting wing patterns.

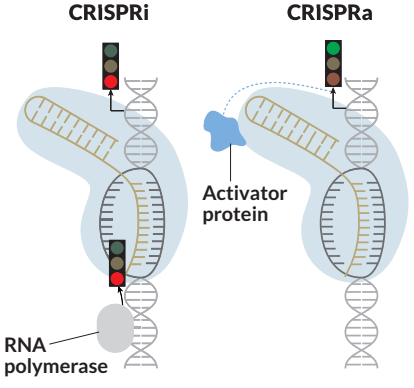
CRISPR/Cas9 can genetically manipulate butterflies; cutting a gene called *Distal-less* causes more eyespots (right) than appear on a normal wing (left).

With CRISPR/Cas9, Reed and Cornell colleague Linlin Zhang cut and disabled the *Distal-less* gene at an early stage of wing development and got an unexpected result: Rather than cause eyespots, *Distal-less* limits them. When CRISPR/Cas9 knocks out *Distal-less*, more and bigger eyespots appear, the researchers reported in June in *Nature Communications*. Reed and colleagues have snipped genes in not just one, but six different butterfly species using CRISPR, he says.

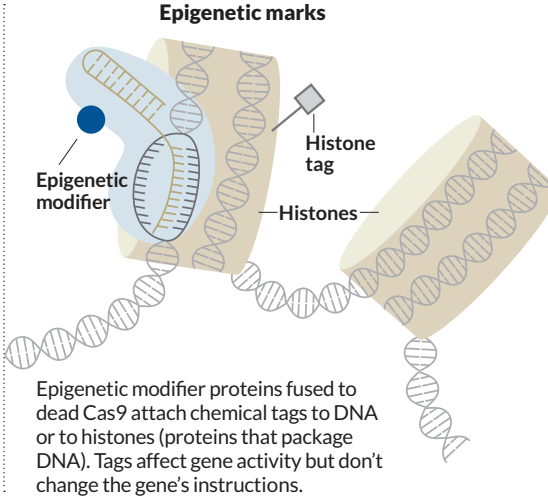
CRISPR cuts genes very well, maybe too well, says neuroscientist Marc Tessier-Lavigne of Rockefeller University in New York City. "The Cas9 enzyme is just so prolific. It cuts and recuts and recuts," he says. That constant snipping can result in unwanted mutations in genes that researchers are editing or in genes that they never intended to touch. Tessier-Lavigne and colleagues figured out how to tame the overeager enzyme and keep it from julienning the genes of human stem cells grown in lab dishes. With better control, the researchers could make one or two mutations in two genes involved



Attaching fluorescent tags to dead Cas9, researchers can locate and observe certain stretches of DNA (left) or RNA (right) in a living cell.



Dead Cas9 can block RNA polymerase from turning on a gene, a process called CRISPRi (for CRISPR interference). In CRISPRa (CRISPR activation), a protein that turns on genes is fused to dead Cas9.



Epigenetic modifier proteins fused to dead Cas9 attach chemical tags to DNA or to histones (proteins that package DNA). Tags affect gene activity but don't change the gene's instructions.

WINGS: L. ZHANG AND R.D. REED/*NATURE COMMUNICATIONS* 2016

in early-onset Alzheimer's disease, they reported in the May 5 *Nature*. Growing the mutated stem cells into brain cells showed that increasing the number of mutated copies of the genes also boosts production of the amyloid-beta peptide that forms plaques in Alzheimer's-afflicted brains. The technology could make stem cells better mimics of human diseases.

While Tessier-Lavigne and others are working to improve the CRISPR/Cas9 system, building better guide RNAs and increasing the specificity of its cuts, some researchers are turning away from snippy Cas9 altogether.

Nuanced edits

Cas9 isn't entirely to blame for the mess created when it causes a double-stranded break by slicing through both rails of the DNA ladder. "The cell's response to double-stranded breaks is the source of a lot of problems," says David Liu, a chemical biologist at Harvard University. A cell's go-to method for fixing a DNA breach is to glue the cut ends back together. But often a few bases are missing or bits get stuck where they don't belong. The result is more genome "vandalism than editing," Liu says, quoting Harvard colleague George Church.

Liu wanted a gene editor that wouldn't cause any destructive breaches: One that could A) go to a specific site in a gene and B) change a particular DNA base there, all without cutting DNA. The tool didn't exist, but in Cas9, Liu and colleagues saw the makings of one, if they could tweak it just a bit.

They started by dulling Cas9's cutting edge, effectively killing the enzyme. The "dead" Cas9 could still grip the guide RNA and ride it to its destination, but it couldn't slice through DNA's double strands. Liu and colleagues then attached a hitchhiking enzyme, whose job is to initiate a series of steps to change the DNA base C into a T, or a G to an A. The researchers had to tinker with the system in other ways to get the change to stick. Once they worked out the kinks, they could make permanent single base-pair changes in 15 to 75 percent of the DNA they targeted without introducing insertions and deletions the way traditional CRISPR editing often does. Liu and collaborators reported the accomplishment in *Nature* in May. A similar base editor, reported in *Science* in August by researchers in Japan, may be useful for editing DNA in bacteria and other organisms that can't tolerate having their DNA cut.

There are 12 possible combinations of DNA base swaps. The hitchhiking enzyme that Liu used, cytidine deaminase, can make two of the swaps. Liu and others are working to fuse enzymes to Cas9 that can do the 10 others. Other enzyme hitchhikers may make it possible to edit single DNA bases at will, Liu says. Such a base editor could be used to fix single mutations that cause genetic diseases such as cystic fibrosis or muscular dystrophy. It might even correct the mutations that lead to inherited breast cancer.

Rewriting the score

Dead Cas9 is already helping researchers tinker with DNA in ways they couldn't before. Variations on the dull blade may help scientists solve one of the great mysteries of biology: How does the same set of 20,000 genes give rise to so many different types of cells in the body?

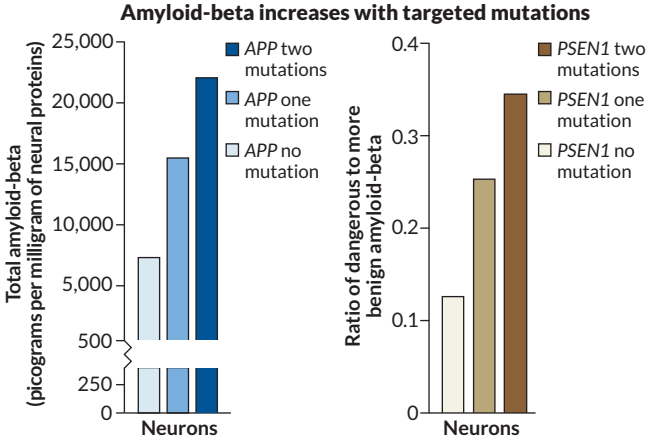
The genome is like a piano, says Jonathan Weissman, a biochemist at the University of California, San Francisco. "You can play a huge variety of different music with only 88 keys by how hard you hit the keys, what keys you mix up and the timing." By dialing down or turning up the activity of combinations of genes at precise times during development, cells are coaxed into becoming hundreds of different types of body cells.

For the last 20 years, researchers have been learning more about that process by watching when certain genes turn on and off in different cells. Gene activity is controlled by a dizzying variety of proteins known as transcription factors. When and where a transcription factor acts is at least partly determined by chemical tags on DNA and the histone proteins that package it. Those tags are known collectively as epigenetic marks. They work something like the musical score for an orchestra, telling the transcription factor "musicians" which notes to hit and how loudly or softly to play. So far, scientists have only been able to listen to the music. With dead Cas9, researchers can create molecules that will change epigenetic notes at any place in the score, Weissman says, allowing researchers to arrange their own music.

Epigenetic marks are alleged to be involved in addiction, cancer, mental illness, obesity, diabetes and heart disease. Scientists haven't been able to prove that epigenetic marks are really behind these and other ailments, because they could never go into a cell and change just one mark on one gene to see if it really produced a sour note.

One such epigenetic mark, the attachment of a chemical called an acetyl group to a particular amino acid in a histone protein, is often associated with active genes. But no one could say for sure that the mark was responsible for making those

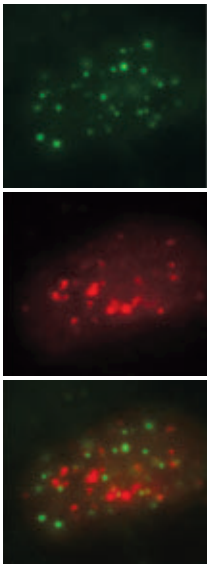
Controlling the editor Researchers tamed the Cas9 cutter so it will slice either one or both copies of a gene, then stop. Cutting the *APP* and *PSEN1* genes made mutations that mimic those in people prone to early-onset Alzheimer's disease. Neurons made more of an abnormal plaque-forming peptide with two mutations (darkest bars) than with one mutation. SOURCE: D. PAQUET *ET AL*/*NATURE* 2016



E. OTWELL

genes active. Charles Gersbach of Duke University and colleagues reported last year in *Nature Biotechnology* that they had fused dead Cas9 to an enzyme that could make that epigenetic mark. When the researchers placed the epigenetic mark on certain genes, activity of those genes shot up, evidence that the mark really does boost gene activity. With such CRISPR epigenetic editors in hand, researchers may eventually be able to correct errant marks to restore harmony and health.

Weissman's lab group was one of the first to turn dead Cas9 into a conductor of gene activity. Parking dead Cas9 on a gene is enough to nudge down the volume of some genes' activity by blocking the proteins that copy DNA into RNA, the researchers found. Fusing a protein that silences genes to dead Cas9 led to even better noise-dampening of targeted genes. The researchers reported in *Cell* in 2014 that they could reduce gene activity by 90 to 99 percent for some genes using the silencer (which Weissman and colleagues call CRISPRi, for interference). A similar tool, created by fusing proteins that turn on, or activate, genes to dead Cas9 (called CRISPRa, for activator) lets researchers crank up the volume of activity from certain genes. In a separate study, published in July in the *Proceedings of the National Academy of Sciences*, Weissman and colleagues used their activation scheme to find new genes that make cancer cells resistant to chemotherapy drugs.



CRISPR attaches fluorescent tags to chromosome endcaps, called telomeres, in a cell's nucleus (top, green) as well as to centromeres, where chromosomes are pinched together (center, red). Combining images shows where the structures are in relation to each other.

RNA revolution

New, refitted Cas9s won't just make manipulating DNA easier. They also could revolutionize RNA biology. There are already multiple molecular tools for grabbing and cutting RNA, Yeo says. So for his purposes, scissors weren't necessary or even desirable. The homing ability of CRISPR/Cas9 is what Yeo found appealing.

He started simple, by using a tweaked CRISPR/Cas9 to tag RNAs to see where they go in the cell. Luckily, in 2014, Jennifer Doudna at the University of California, Berkeley — one of the researchers who in 2012 introduced CRISPR/Cas9 — and colleagues reported that Cas9 could latch on to messenger RNA molecules, or mRNAs (copies of the protein-building instructions contained in DNA). In a study published in April in *Cell*, Doudna, Yeo and colleagues strapped fluorescent proteins to the back of a dead Cas9 and pointed it toward mRNAs from various genes.

With the glowing Cas9, the researchers tracked mRNAs produced from several different genes in living cells. (Previous methods for pinpointing RNA's location in a cell killed the cell.) In May, Zhang of MIT and colleagues described a two-color RNA-tracking system in *Scientific Reports*. Yet another group of researchers described a CRISPR rainbow for giving DNA a multicolored glow, also in living cells. That glow allowed the team to pinpoint the locations of up to six genes and see how the three-dimensional structure of chromosomes in the nucleus changes over time, the researchers reported in the May *Nature Biotechnology*. A team from UC San Francisco reported in January in *Nucleic Acids Research* that it had tracked multiple genes using combinations of two color tags.

But Yeo wants to do more than watch RNA move around. He envisions bolting a variety of different proteins to Cas9 to manipulate and study the many steps an mRNA goes through between being copied from DNA and having its instructions read to make a protein. Learning more about that multistep process and what other RNAs do in a cell could help researchers understand what goes wrong in some diseases, and maybe learn how to fix the problems.

Zhang wants to improve Cas9, but he would also like other versatile tools. He and colleagues are looking for such tools in bacteria.

CRISPR/Cas9 was first discovered in bacteria as a rudimentary immune system for fighting off viruses (*SN: 12/12/15, p. 16*). It zeroes in on and then shreds the viral DNA. Researchers most often use the Cas9 cutting enzyme from *Streptococcus pyogenes* bacteria.

But almost half of all bacteria have CRISPR immune systems, scientists now know, and many use enzymes other than Cas9. In the bacterium *Francisella novicida U112*, Zhang and colleagues found a gene-editing enzyme, Cpf1, which does things a little differently than Cas9 does. It has a different "cut here" signal that could make it more suitable than Cas9 for cutting DNA in some cases, the team reported last October in *Cell*. Cpf1 can also chop one long guide RNA into multiple guides, so researchers may be able to edit several genes at once. And Cpf1 cuts DNA so that one strand of the DNA is slightly longer than the other. That could make it easier to insert new genes into DNA.

Zhang more recently found an enzyme in the bacterium *Leptotrichia shahii* that could tinker with RNA. The RNA-cutting enzyme is called C2c2, he and colleagues reported August 5 in *Science*. Like Cas9, C2c2 uses a guide RNA to lead the way, but instead of slicing DNA, it chops RNA.

Zhang's team is exploring other CRISPR/Cas9-style enzymes that could help them "edit or modulate or interact with a genome more efficiently or more effectively," he says. "Our search is not done yet."

The explosion of new ways to use CRISPR hasn't ended. "The field is advancing so rapidly," says Zhang. "Just looking at how far we have come in the last three and a half years, I think what we'll see coming in the next few years will just be amazing." ■

Explore more

■ CRISPR/Cas9 explainer: bit.ly/CRISPR-Cas9

S. WANG ET AL/SCIENTIFIC REPORTS 2016

EXPERIENCES

Citizen science project wants your dog's DNA

Going for walks, playing fetch and now participating in genetic research are just a few things people and their dogs can do together.

Darwin's Dogs, a citizen science project headquartered at the University of Massachusetts Medical School in Worcester, is looking for good — and bad — dogs to donate DNA. The project aims to uncover genes that govern behavior, including those involved in mental illness in both people and pets.

Looking to dogs for clues about mental illness isn't as strange as it may seem. Certain breeds are plagued by some of the same diseases and mental health issues that afflict people. Researchers have learned about the genetics of narcolepsy and obsessive compulsive disorder, as well as cancer, blindness and many other ailments from studying purebred dogs. Studies of purebreds are mainly useful when the problem is caused by mutations in a single gene. But most behaviors are the product of interactions between many genes and the environment. A search for those genes can't be done with a small number of genetically similar dogs. So, Darwin's Dogs hopes to gather data on a large number of canines, including many breeds and genetically diverse mutts.

Finding behavior-related genes, such as ones that lead dogs to chew up shoes or engage in marathon fetch sessions, may give clues to genes that affect human behavior. "It seemed to me that if we could understand how [changes in DNA] make a dog so excited about chasing a ball, we could learn something about how our brains work and what goes wrong in psychiatric disease," says project leader Elinor Karlsson.

Karlsson and colleagues launched darwinsdogs.org, inviting people to answer questions about their dogs' behavior and share their pets' DNA. More than 7,000 dog owners have already signed up, and the researchers are still recruiting new volunteers.

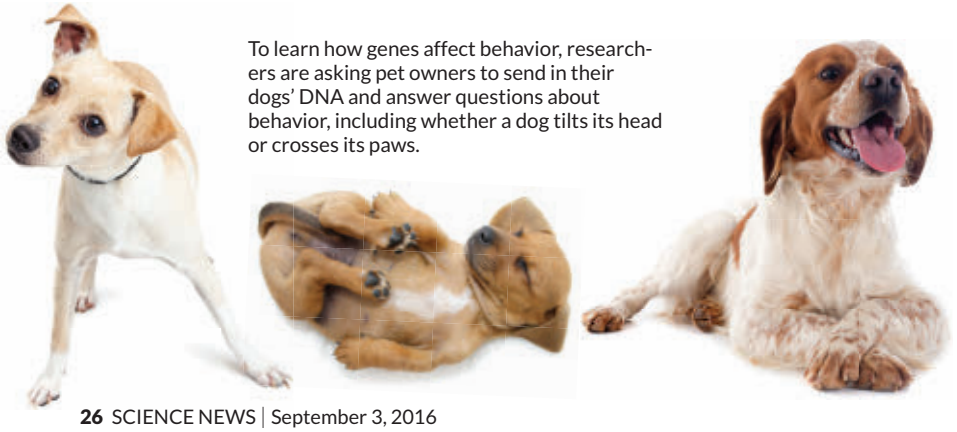
The process is simple and can be done alone with your dog, or even as a family activity. First, take an online quiz about your canine companion. The quiz is divided into multiple sections. Some sections gather basic information about your dog's appearance, exercise and eating habits; others ask about simple behaviors, such as whether your dog crosses its front paws when lying down or tilts its head. (Some questions are philosophical puzzles like whether your dog knows it is a dog.) Each question has a comment box in case you want to explain an answer. Plan to spend at least half an hour completing the questionnaire.

Once the questions are answered and the dog is registered, researchers send you a DNA sampling kit that comes with written instructions and an easy-to-follow picture guide. The kit contains a large sterile cotton swab for collecting DNA from your dog's mouth. (It's an easy procedure for the human involved, and Sally, the 14-year-old Irish setter "volunteer" *Science News* sampled, was rather stoic.) Also included is a tape measure for recording your dog's height, length, nose and collar size. When you're done, just seal the sample, measurement sheet and consent form inside the return mailer and drop it in a mailbox.

Dog owners don't need to pay a fee to participate, but they do need patience, Karlsson says. It takes time to analyze DNA, and the researchers can't say exactly how long it will be before owners (and *Science News*) learn their dogs' results. These results will include the dog's raw genetic data as well as information about the dog's possible ancestry. Knowing ancestry or particular mutations a dog carries may help veterinarians personalize a dog's care.

Dog trainers are being enlisted to give owners feedback on their dogs' personalities and to suggest activities the dogs may enjoy. Karlsson hopes to create a way for impatient owners who are willing to donate money to the project to get their reports back faster.

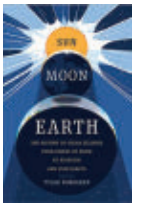
— Tina Hesman Saey



To learn how genes affect behavior, researchers are asking pet owners to send in their dogs' DNA and answer questions about behavior, including whether a dog tilts its head or crosses its paws.

FROM LEFT: ADOGSLIFEPHOTO/ISTOCKPHOTO; DOGBOXSTUDIO/SHUTTERSTOCK; CYNOCLUB/ISTOCKPHOTO

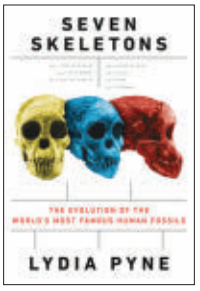
BOOKSHELF



Sun Moon Earth
Tyler Nordgren
In advance of the 2017 total solar eclipse, an astronomer traces the history of people's observations and knowledge of these rare events. *Basic Books, $26.99*

Bird Brain
Nathan Emery
With the help of stunning photos, a biologist dispels the "birdbrain" myth and explores how scientists investigate avian smarts. *Princeton Univ., $29.95*

Buy Books Reviews on the *Science News* website include Amazon.com links that generate funds for Society for Science & the Public programs.



Seven Skeletons
Lydia Pyne
VIKING, $28

BOOKSHELF

How a hominid fossil star is born

After decades of research revealing their sophisticated lives, Neandertals still can't shake their reputation as knuckle-dragging cavemen. And it's the Old Man of La Chapelle's fault.

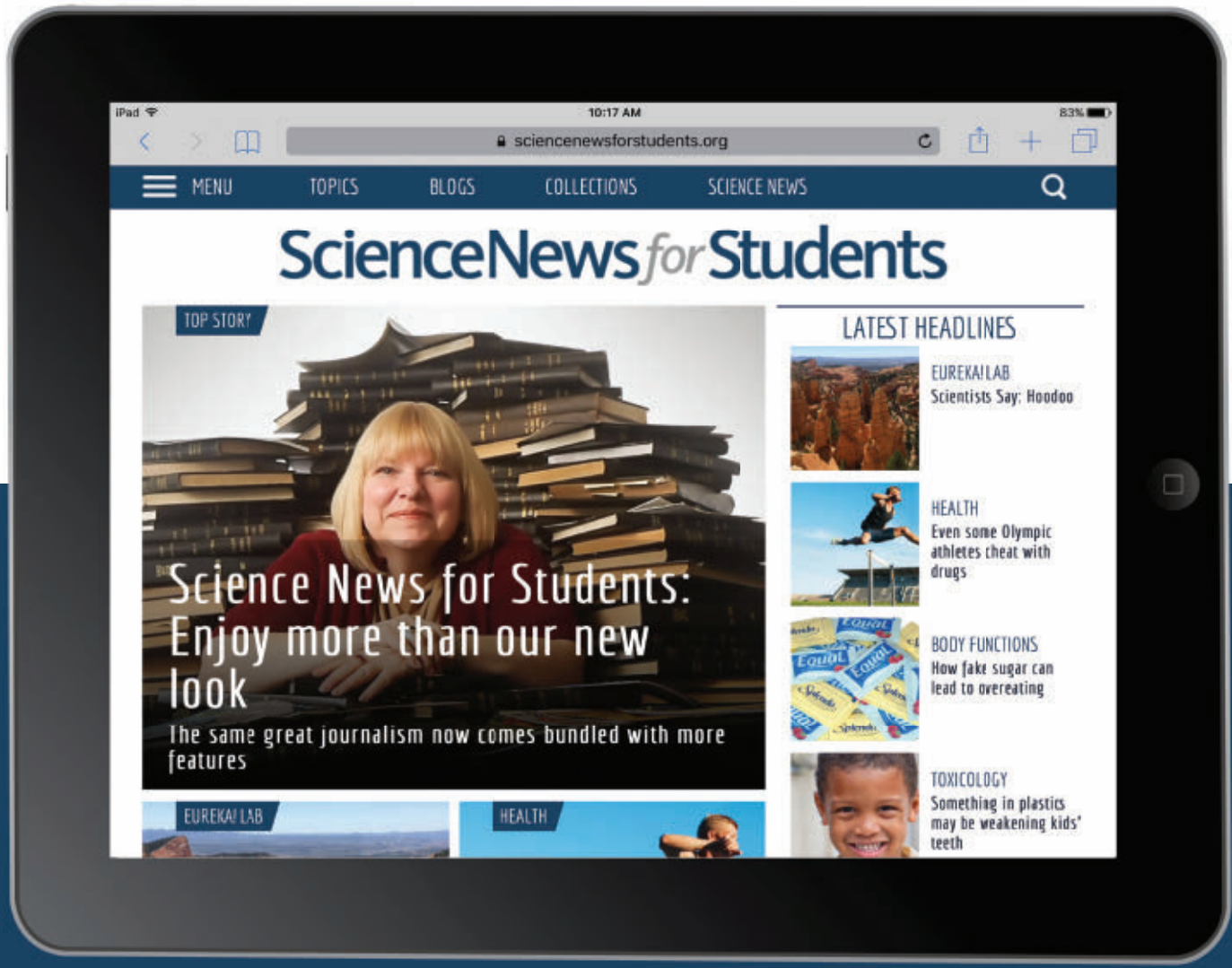
The Old Man of La Chapelle was the first relatively complete Neandertal skeleton ever found. Three French abbés discovered the bones in 1908. Soon after, geologist and paleontologist Marcellin Boule analyzed the remains. His conclusion: The ancient individual was a hunched, dim-witted savage. At the time, little was known about human evolution, and Boule's findings made headlines worldwide. The publicity helped to sear the image of the brutish Neandertal into the public's mind — so much so that even after subsequent studies determined the Old Man had arthritis and suffered from other abnormalities, it was too late to break the caveman stereotype.

The story of the Old Man and six other famous hominid fossils are the focus of Lydia Pyne's *Seven Skeletons*. Pyne, a writer and historian, considers how these fossils have shaped our views of human evolution. She also seeks to understand why some fossils end up on T-shirts and postcards, become national symbols and inspire fan fiction while others remain anonymous specimens in museum collections.

Pyne acknowledges that some experts might quibble with her list — Ardi the *Ardipithecus* (*SN: 1/16/10, p. 22*), for instance, didn't make the cut. But her selections highlight the different ways a fossil can achieve celebrity status. Catchy nicknames, media attention, unusual circumstances surrounding a discovery and even scandals can help. The diminutive hobbit, Pyne argues, benefited from being unveiled around the same time the last installment of the *Lord of the Rings* trilogy hit theaters.

Of course, scientific merit — being the first of a kind, a nearly complete skeleton or something completely unexpected — doesn't hurt either. Lucy, the first *Australopithecus afarensis* ever found, has become the yardstick by which all other hominid discoveries are now measured, Pyne explains. (One thing she underemphasizes at times, though, is the necessity of a tireless cheerleader to promote a fossil's significance.)

The book provides plenty of interesting backstory for each fossil. Readers expecting a primer on human evolution, however, will be disappointed. Pyne focuses on the cultural history of her subjects, not the actual science. But her book does provide a peek at how the field of paleoanthropology itself has evolved over the last century. — *Erin Wayman*



Explore the redesigned *Science News for Students*

Where can you find the latest news about quantum physics, cognitive science and gene editing written for tweens and teens? The newly redesigned ***Science News for Students***, of course!

Science News for Students has the same great journalism that readers have come to expect, now with even more features.

You can find videos, articles, blogs and more science-focused content on the mobile-friendly site.

Teachers can search stories by readability scores and Next Generation Science Standards.

As *Science News*' sister publication, *Science News for Students* brings readers the latest breaking scientific news — rewritten for younger audiences.

Check it out at **sciencenewsforstudents.org**

Guaranteed the most comfortable pillow you'll ever own!™

How Well Did You Sleep Last Night?

Did you toss and turn all night? Did you wake up with a sore neck, head ache, or was your arm asleep? Do you feel like you need a nap even though you slept for eight hours? Just like you, I would wake up in the morning with all of those problems and I couldn't figure out why. Like many people who have trouble getting a good night's sleep, my lack of sleep was affecting the quality of my life. I wanted to do something about my sleep problems, but nothing that I tried worked.

The Pillow Was the Problem

I bought every pillow on the market that promised to give me a better night's sleep. After trying them all, with no success, I finally decided to invent one myself. I began asking everyone I knew what qualities they'd like to see in their "perfect pillow." Their responses included: "I'd like a pillow that never goes flat", "I'd like my pillow to stay cool" and "I'd like a pillow that adjusts to me regardless of my sleep position." After hearing everyone had the same problems that I did, I spent the next two years of my life inventing MyPillow.

In the early days, Mike and his family spent countless hours hand-making each MyPillow. This hard work and dedication to "doing it right" helped MyPillow become a classic American success story.

MyPillow® to the Rescue

Flash forward eleven years and MyPillow, Mike Lindell's revolutionary pillow design, has helped 12 million people improve the quality of their sleep. MyPillow has received thousands of testimonials from customers about how MyPillow has changed their lives.

"Until I was diagnosed with various sleep issues, I had no idea why my sleep was so interrupted throughout the night. I watch Imus each morning and heard endless testimonials about MyPillow. I took his advice and ordered a MyPillow. Now I wake up rested and ready to conquer the day ahead. Thank you for helping me remember what it's like to sleep like a baby!" **- Jacqueline H.**

Lindell has been featured on numerous talk shows, including *Fox Business News* and *Imus in the Morning*. Lindell and MyPillow have also appeared in feature stories in major magazines and newspapers across the country. MyPillow has received the coveted "Q Star Award" for *Product Concept of the Year* from QVC, and has been selected as the Official Pillow of the National Sleep Foundation.

MyPillow's patented interlocking fill allows you to adjust the pillow to your individual needs regardless of sleep position.

10 YEAR WARRANTY

Unprecedented Guarantee and Warranty

I do all of my own manufacturing in my home state of Minnesota and all materials are 100% made in the U.S.A. I'm so confident MyPillow will help you, I'm offering an unprecedented 60-day money back guarantee and a 10-year warranty not to go flat! I truly believe MyPillow is the best pillow in the world and that if everyone had one, they would get better sleep and the world would be a much happier place. *God Bless.*

MADE IN THE U.S.A.

Don't wait—Order MyPillow and get sleep you've been dreaming about!

Save 50% when you use promo code "**science16**"

BUY NOW AT: mypillow.com **OR** call 800.951.3492

MyPillow®

ADVERTISEMENT

JULY 9, 2016

Rooting out terrorism

Anthropologists have moved to the front lines to determine what drives people to join terrorist organizations such as the Islamic State. New research shows that the most committed ISIS fighters revere Islamic law and identify closely with a small group of comrades, ***Bruce Bower*** *reported in "Deadly devotion"* (SN: 7/9/16, p. 18).

Some readers noted similarities between researcher **Scott Atran's** work and philosopher Eric Hoffer's 1951 book *The True Believer*. The book discusses the psychological causes of fanaticism that can be seen in political and religious movements throughout history. "It's nice to have a scientific patina applied to Hoffer's work, but his contributions to explaining the psychological bases for mass movements should always be credited," wrote **Michael Rethman**.

Atran agrees with some of Hoffer's ideas about the general conditions of fanatic devotion, including unity and self-sacrifice. But he is skeptical of other proposed conditions such as self-alienation and insecurity. "In any event, our research was driven more by trying to figure out, test and validate the cognitive and social conditions of devotion unto death regardless of personality factors," he writes. "Hoffer provides historical comparison and depth to some of these ideas. But our task is to see what can be scientifically validated as right."

Diet dilemma

Some microbes that live in the gut might cause obesity by converting fats in food into chemical signals that tell the brain to pack on the pounds, ***Tina Hesman Saey*** *reported in "Microbial signals influence obesity"* (SN: 7/9/16, p. 7).

"Then why do the olive oil fats in the Mediterranean diet not cause obesity? Why do the blubber fats in traditional Inuit diets not cause obesity? Lots more research to be done," reader **Laura Hamilton** wrote online.

Saey agrees that more research is needed, but the answer may be more complex than microbes alone. Some research, for example, is already hinting that a diet's effects may depend more on who is doing the eating than on what they are eating. Rodents on the same diet, but with different genetic makeups, may not be equally prone to gaining weight, a recent study suggests (*SN: 8/20/16, p. 13*). The same could be true for people. "So while Inuit diets may not promote obesity for them, someone else may pack on pounds after munching on blubber. Olive oil may not be healthy for everyone either," **Saey** says. "Researchers are just at the beginning of understanding how genetics, microbes and diet work together to influence health."

Dog days of yore

Dogs may have been domesticated at least twice, in Europe and Asia, during the Stone Age. Genetic analysis revealed that over time, East Asian dogs replaced dogs native to Europe, ***Tina Hesman Saey*** *reported in "DNA tells of dual origins for dogs"* (SN: 7/9/16, p. 15).

Some online readers wondered if disease played a role in shaping the ancient dog populations. "Given the ability of wolves, dogs and humans to travel long distances, it wouldn't be surprising if the Asian proto-dogs carried in fleas, internal parasites or other diseases and killed off a good portion of the European proto-dogs," **Onyxhawke** wrote. Online reader **kudjomojo** agreed, suggesting that East Asian dogs' genomes could have offered disease resistance.

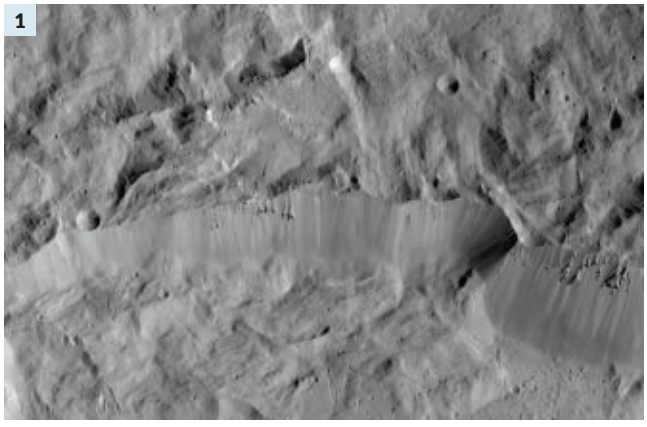
Disease spread often comes with migration to new lands. "It may also have been that the Asian dogs didn't bring the diseases but were less susceptible to diseases that may have killed European dogs," **Saey** says. Other factors could have played a part, too: Asian dogs may have had physical or behavioral traits that made them more appealing to humans and helped them become the top dogs in Europe. "It's never a gene-to-gene or genome-to-genome fight, but rather what traits the underlying genetic makeup influences that decide which dogs will have their day," she says.

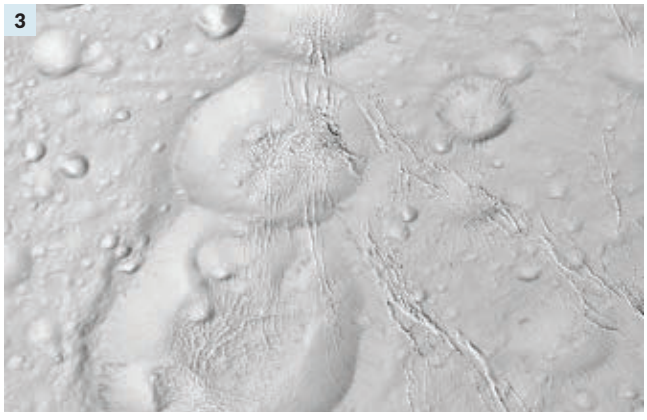
Join the conversation

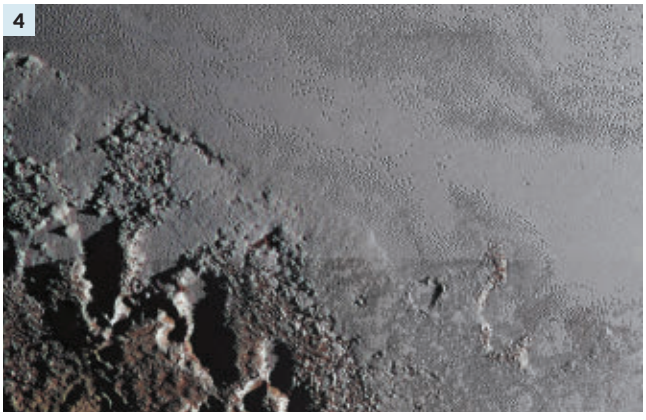
E-MAIL editors@sciencenews.org

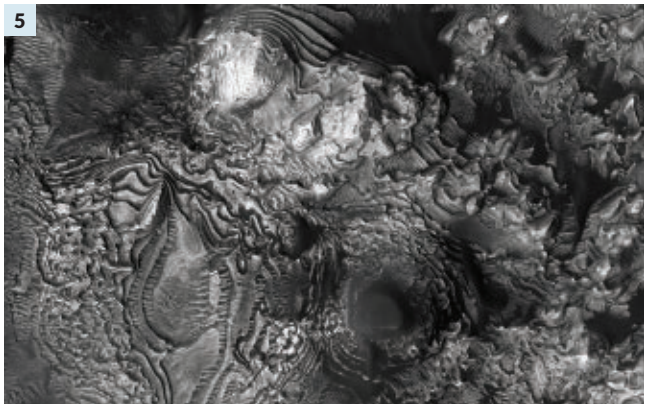
MAIL Attn: Feedback
1719 N St., NW
Washington, DC 20036

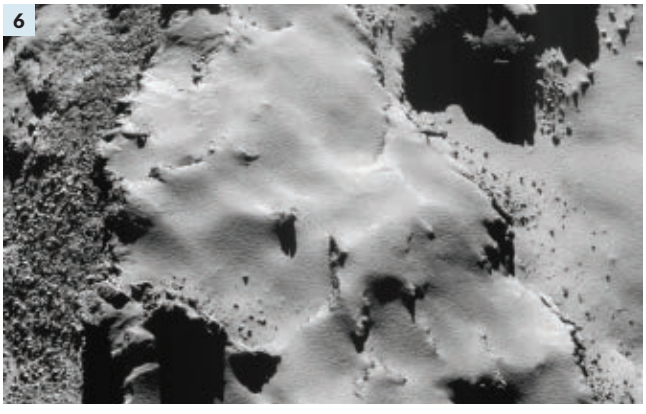
Connect with us











Out-of-this-world landscapes

Over the last several years, spacecraft have beamed back images from all across the solar system, revealing a complex tapestry of landscapes. Dust shapes the scenery on comet 67P, whereas ice rules on Pluto and the moons of Saturn. At first glance, many of these terrains seem the same — mountains, craters and canyons show up everywhere. But each world adds its own geologic signature that marks the land as utterly alien. While several of the spacecraft's missions will end in the coming year, a fleet of new explorers ensures that our interplanetary adventures are far from over. — *Christopher Crockett*

1. Cliffs rise about 4 kilometers around the crater Occator on dwarf planet Ceres. **Dawn, April 21, 2016**

2. Sunset casts long shadows east of Butes crater on Dione, a moon of Saturn. **Cassini, August 17, 2015**

3. Cracks and craters mar the icy surface of Enceladus, another Saturnian moon. **Cassini, October 14, 2015**

4. The dark highlands of Krun Macula abut the frozen pitted fields of Sputnik Planum on Pluto. **New Horizons, July 14, 2015**

5. A complex layered terrain graces Arabia Terra on Mars. **Mars Reconnaissance Orbiter, April 15, 2011**

6. Fine dust blankets a region named Ash on comet 67P/Churyumov–Gerasimenko. **Rosetta, July 18, 2016**

Amazing price breakthrough!

SAVE 90% COMPARED TO TRADITIONAL HEARING AIDS

ADVANCED HEARING AID TECHNOLOGY For Less Than $200

How can a hearing aid that costs less than $200 be every bit as good as one that sells for $2,000 or more?

The answer: Although tremendous strides have been made in Advanced Hearing Aid Technology, those cost reductions have not been passed on to you. Until now...

The **MDHearingAid PRO**® uses the same kind of Advanced Hearing Aid Technology incorporated into hearing aids that cost thousands more at a small fraction of the price.

Over 75,000 satisfied **PRO** customers agree: High quality FDA registered Hearing Aids don't have to cost a fortune.

The fact is, you don't need to spend thousands for a medical-grade hearing aid. **MDHearingAid PRO**® gives you a sophisticated high-performance hearing aid that works right out of the box with no time-consuming "adjustment" appointments.

You can contact a hearing specialist conveniently online or by phone—even after sale at no cost. No other company provides such extensive support.

Now that you know... why pay more?

TAKE ADVANTAGE OF OUR 45-DAY RISK-FREE TRIAL!

Hearing is believing and we invite you to try this nearly invisible hearing aid with no annoying whistling or background noise for yourself. If you are not completely satisfied, simply return it within that time period for a **100% refund of your purchase price.**

MDHearingAid was designed and developed by a nationally recognized ENT doctor who continues to stand behind their products.

MDHearingAid has more than 100,000 satisfied customers.

MDHearingAid offers affordable lowest-priced FDA-registered hearing aids designed and assembled in America and provides FREE after-sale expert support online or by phone.

Doctors and patients agree:

"BEST QUALITY SOUND"
"LOWEST AFFORDABLE PRICE"

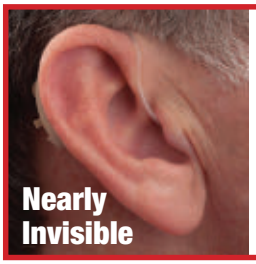
Incredible...
"I was surprised to hear sounds I had forgotten existed – the crispness of the bells we use in Church, the splash of water running, the rich overtones in music. Thank you."
– Rev. John C.

Life-Changing...
"Thank you for making an affordable hearing aid so that people like me can again be part of conversations…"
– Cathy C.

Value-Packed...
"I'm a physician and I know how much people spend on their health care. MDHearingAids are just as effective (if not more) than traditionally high-priced hearing aids."
– Dr. Chang

6 Reasons To Call Now!

1. Lowest-Priced FDA-Registered Hearing Aid In America
2. Doctor Designed, Audiologist Tested
3. World-Class Components from the U.S.A. and Europe
4. Free One-On-One After-Sale Support Online Or by Phone.
5. The Real Deal—Not an inferior Sound Amplifier
6. **Free Batteries For One Year Plus Free Shipping**



BATTERIES INCLUDED!
READY TO USE RIGHT OUT OF THE BOX!

For the Lowest Price Call Today

800-617-4879

BUY A PAIR AND SAVE $40

100% Money-Back Guarantee

Use Code **CW22** and get **FREE** Batteries for 1 Year *Plus* **FREE** Shipping

Or Visit: **TryMDHearingAid.com**

Proudly Assembled in the United States from Domestic & Imported Components

BBB A+ Rating Accredited Business

BIG SOUND. TINY PRICE.

MDHearingAid®

The incredible *Five-Star Opal Anniversary Ring* fulfills one of our long-held commitments, and celebrates yours.

1.5 total carats of genuine Ethiopian opal for under $100! PLUS, FREE matching earrings!

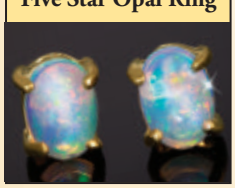
Add Some Wow to Your Vows

Put a rainbow on her finger with the opal that's taking the jewelry industry by storm.

Long ago, we made a vow: We would not produce a five-opal anniversary ring until two very specific conditions were met. First, the opals had to be of superior quality, with the joyous iridescence to delight all who saw the precious stone's colors dance in the light. Second, the price had to be right, so that we could provide the value Stauer clients expect from us. So when The New York Times style section called Ethiopian opal the "undisputed winner" of the 2014 Gem Show, we decided to pounce. The result is the astoundingly beautiful ***Five-Star Opal Anniversary Ring***.

All five of these exotic beauties possess the radiant rainbow of color we've been looking for. Arranged in a sterling silver setting finished in lustrous gold, this ring is a beautiful tribute to your lasting love.

EXCLUSIVE FREE
Five Star Opal Stud Earrings
-a $199 value-
with purchase of Five Star Opal Ring



So how about our price promise? We met that too. We want you to know there is absolutely no reason to overpay for luxury gemstones. The big name jewelers have been deceiving the public long enough, charging as much as $16,000 for an Ethiopian opal ring. We won't trump up the price to make you think it's luxurious. This ring is just as luxurious (if not more) than the big designer name rings, AND it's yours for **under $100**. I think it's safe to say we more than met our price promise. We exceeded it... by about 16,000%!

"Opal's spectacular play-of-color can display all the colors of the rainbow."
— Gemological Institute of America

"The play of color in opals is so gorgeous they sometimes don't even seem real and yet they are." — from 2015 Couture Show

Your satisfaction is 100% guaranteed. Slip this rainbow on her finger. If she's not absolutely delighted simply send it back within 60 days for a complete refund of the sale price. The stud earrings are yours to keep. See if your jewelry store can match that!

The *Five-Star Opal Ring* is one of Stauer's fastest sellers. Supplies are limited. We can't seem to keep this ring in stock. Don't miss this rare opportunity. **Plus, call today and receive the matching opal stud earrings FREE!** You'll want to catch this radiant rainbow before it's gone!

Five-Star Opal Anniversary Ring ~~$399~~*
Offer Code Price *Only* **$99** + **S&P** *Save $300!*
***Plus,* FREE opal stud earrings,** a $199 value
You must use the insider offer code to get our special sale price.

1-800-333-2045

Your Insider Offer Code: OAR182-01
Please use this code when you order to receive your discount.

Stauer®
14101 Southcross Drive W., Dept. OAR182-01,
Burnsville, Minnesota 55337 **www.stauer.com**

BBB ACCREDITED BUSINESS **Rating of A+**

CONSUMER AFFAIRS ACCREDITED

** Special price only for customers using the offer code versus the price on Stauer.com without your offer code.*

1.5 ctw Ethiopian opal • Gold-finished .925 sterling silver setting • Whole ring sizes 5–10

Smart Luxuries—Surprising Prices™