Rosetta's Comet Rendezvous Makes Space History

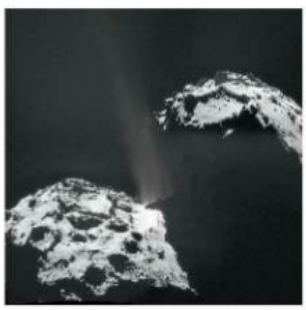
On Aug. 6, the European Space Agency's Rosetta spacecraft went where no man, or probe, had gone before: into orbit around a comet. The rendezvous marked the end of a 4 billion-mile journey and the start of a 17-month orbital mission designed to understand the changes comets undergo as they approach the sun.

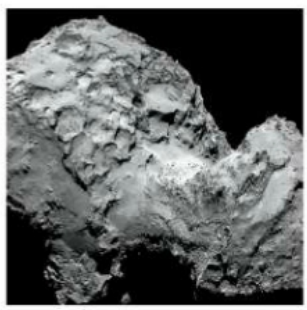
Because comets contain material from when the sun and planets formed, Rosetta can answer questions about the evolution of the solar system and the origin of water (and possibly life) on Earth.

Just weeks after arriving near Comet 67P/Churyumov-Gerasimenko, Rosetta delivered the sharpest-ever views of a nucleus — the frozen mass of rock and ice at a comet's heart. The spacecraft's camera revealed it as a double-lobed object that some mission scientists referred to as a "rubber ducky," complete with a head, neck and body. Pocked with craters and littered with boulders, the nucleus measures about 2.5 miles across at its widest.

As of press time, Rosetta is scheduled to drop a lander, named Philae, in mid-November onto a site on the comet's surface named Agilkia — another space exploration first. Together, the two spacecraft will map the comet's surface, analyze its chemical composition and study the gases and dust particles ejected as the sun's heat warms the ice in the nucleus. Philae should survive for a few months, and Rosetta will last until the end of 2015 or beyond, so the probes will be able to examine changes in 67P as it heads toward its closest approach to the sun in August. — RICHARD TALCOTT

Read the latest news on Rosetta at **DiscoverMagazine.com/Rosetta**





TOP: ESA/ROSETTA/MPS FOR OSIRIS TEAM MPS/UPD/LAM/IAA/SSO/INTA/UPM/DASP/IDA. BOTTOM: ESA/ROSETTA/MPS FOR OSIRIS TEAM MPS/UPD/LAM/IAA/SSO/INTA/UPM/DASP/IDA (3); SECOND IMAGE FROM LEFT, ESA/ROSETTA/NAVCAM/DAMIA BOUIC

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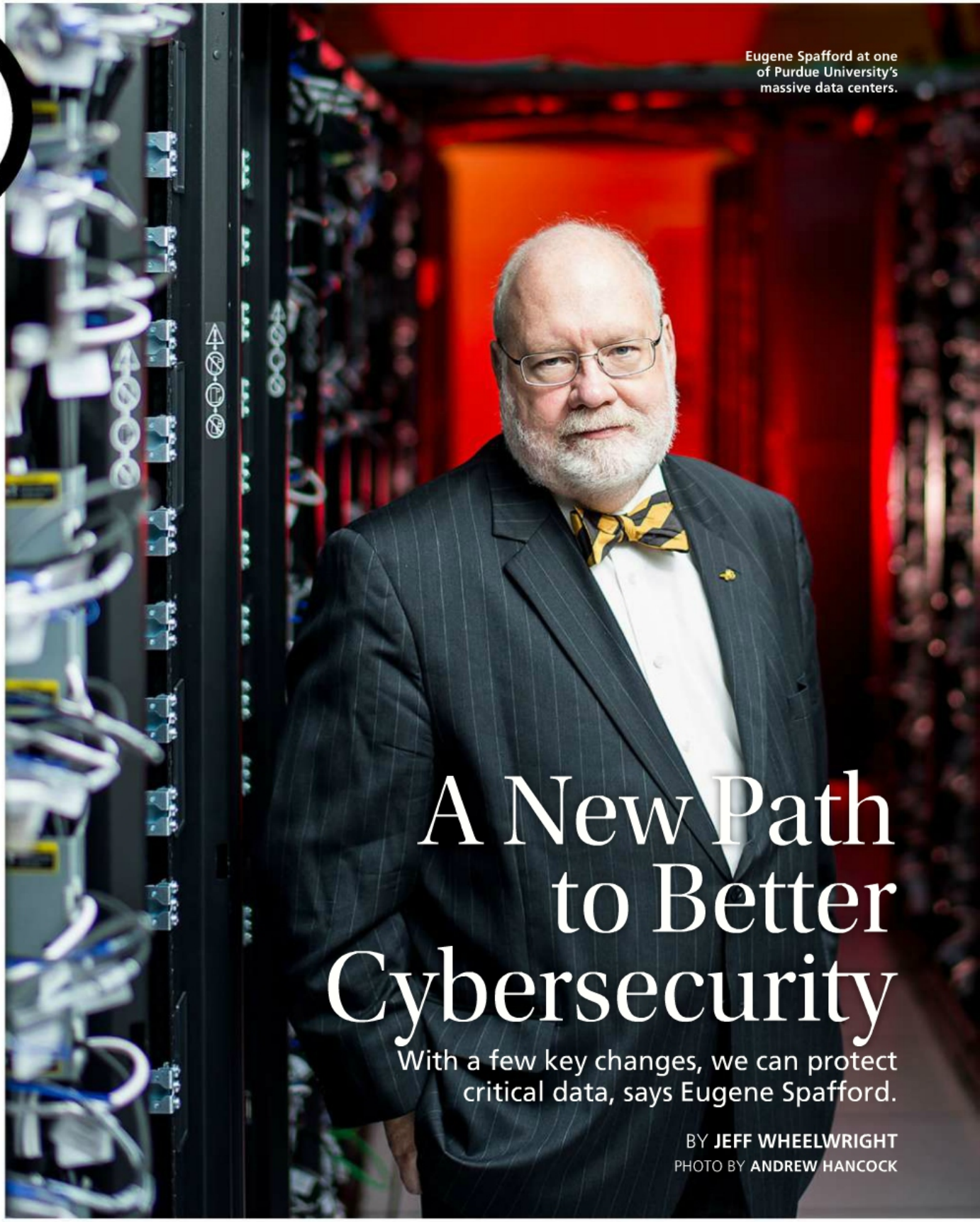


Eugene Spafford at one of Purdue University's massive data centers.

A New Path to Better Cybersecurity

With a few key changes, we can protect critical data, says Eugene Spafford.

BY **JEFF WHEELWRIGHT**
PHOTO BY **ANDREW HANCOCK**

It was a terrible year for the health of computer systems. Cyberthieves stole credit- and debit-card numbers from up to 56 million customers of the retail giant Home Depot, even more than the 40 million they stole in 2013 from Target. At JPMorgan Chase, 76 million bank accounts were compromised. The Heartbleed bug poked a big hole in widely used encryption software, and the Bash bug exposed millions of computers to malware. A Russian gang made off with more than a billion email addresses and passwords and compromised a half-million websites.

What's going on, and what can we do about it? *Discover* spoke with Eugene Spafford, a longtime computer security expert and director of Purdue University's Center for Education and Research in Information Assurance and Security (CERIAS).

As you look over the recent incidents, what do they tell you about the state of our cybersecurity?

The Home Depot and Target breaches were examples of how our commercial infrastructure is very vulnerable to those who want to exploit it. As criminals increase their sophistication, they will pick bigger and more complex targets. That targeting won't be for the intellectual challenge — it will be because bigger targets have more to offer. Theft of millions of credit card transactions provides a huge body of information to break up and resell to other criminals. Theft of medical data, design and marketing plans, and financial information is a growing business with little in the way to discourage it.

It took months before the Home Depot and Target breaches were detected. It took more time before the companies patched their software, then assured customers that the patched systems were safe. Can we really trust that such ad hoc fixes to existing programs will protect us from credit card fraud?

The software industry has built a response mechanism around the idea that flaws in products can be patched and that somehow the "patchability" is a substitute for sound design. Unfortunately, as we have seen with a great many incidents, it takes time to discover and analyze each flaw, and the patches take time to apply. The Heartbleed and Shellshock (Bash) flaws took years to discover, for instance — with the Shellshock flaw reported as being present for nearly 25 years! Then, too, some flaws may never get fixed everywhere. This combination of factors means sloppy design is ensuring that our overall infrastructure will be riddled with vulnerabilities for the foreseeable future.

What about the theft of passwords by Russian gangsters?

It's unlikely we'll be able to identify and apprehend the people who've stolen all those passwords because of the difficulty of investigating and prosecuting computer crime. But for them to get the passwords means that they somehow found weaknesses in lots of vendors that they were able to exploit. The Target breach, the collection of passwords and a number of other incidents this year all point to a significant, well-funded, technically talented criminal element that is actively attacking and exploiting systems, from home users up to major corporations.

If you were the cybersecurity czar, what steps would you recommend?

This is an area that needs more fundamental research on how to change the way we build and deploy things, not simply on how to patch what's there. An awful lot of the federal research funding is, how do we fix Windows, how do we fix Linux, how do we make a stronger PC. That's not going back and questioning fundamental assumptions.

We are currently using general-purpose, mass-market computing platforms to do things that don't really require that level of generality. It makes them vulnerable to a wider variety of attack than they would be if they were custom-built.

If we build systems that do only one or two things, they're less likely to be attacked. Your microwave oven has software inside that's used to make it run. If that's not connected anywhere and it doesn't do anything else, like calculate your taxes and store your recipe files and send email, it can't be attacked by outside mechanisms. Yes, it might be more expensive to build a new system or to remove components from an existing system. But being in business means you also have a duty to your customers and society not to endanger them unnecessarily with what your product does.

We've also got to move the job of combating malicious cyberactivity away from the military and more into law enforcement. A lot of what the federal government does is that it tries to mandate from a centralized, top-down approach. By default, most information flows to a small number of federal agencies. That's not the right approach. What we really need is a local view.

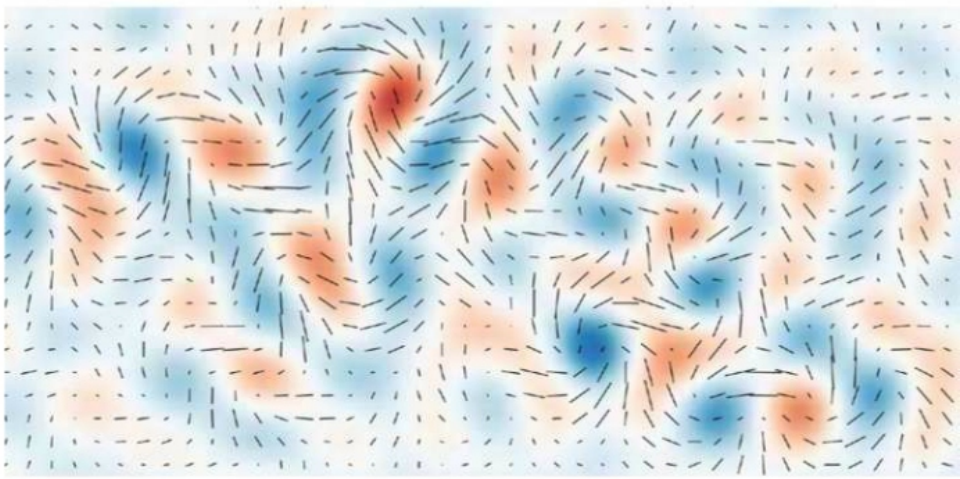
You've proposed a local extension service for small, local businesses, something akin to the agricultural extension service.

If you found an unusual proliferation of caterpillars eating everything in your garden, you wouldn't contact somebody in Washington to come look at them. You would find your local extension service, and you would take a sample in, and they would give you advice as to what it was and how to respond. I think we need to adopt that kind of model for cyber — have an extension service, at a local level, that people can go to for classes, advice as to what software to get and help to identify a problem.

5

What Made the Bang so Big?

Earlier in 2014, cosmologists thought they were finally closing in on an answer to that age-old question, "How did it all begin?" In March, Harvard astrophysicist John Kovac announced that a small telescope at the South Pole called BICEP2 (short for Background Imaging of Cosmic Extragalactic Polarization) had captured signals that apparently come from "the first trillionth of a trillionth of a trillionth of a second in the history of the universe."



This telltale swirling pattern of light may be evidence of cosmic inflation.

Independent confirmation was still needed, said Kovac, who heads the BICEP2 team, but if the result held up, it would mean scientists were on the verge of witnessing and understanding the moment of creation for our cosmos. Then data from the European Space Agency's Planck space telescope rolled in six months later, casting doubt over the earlier result. (See "Clouded by a Veil of Dust," opposite page.) The world won't know the final verdict until the BICEP2 and Planck scientists release their joint report.

The BICEP2 telescope in Antarctica looked for the cosmic pattern.

Assuming its findings are validated, BICEP2 will have amassed the strongest support yet for cosmic inflation, a theory that attempts to explain exactly what happened during the Big Bang, the universe's explosive birth event. Inflationary theory holds that our newborn universe started as a tiny fleck of matter, less than one-billionth the size of a proton, and grew exponentially fast — expanding faster than the speed of light, in fact, while doubling in size at least 100 times.

Inflation is the brainchild of MIT physicist Alan Guth, who came up with the idea in 1979. "I didn't think it would be tested in my lifetime," says Guth, because when he dreamed up the theory, no one could conceive of a practical way to verify it.

The runaway expansion lasted from about 10^{-36} of a second to 10^{-32} of a second after the Big Bang, but it would have deformed space violently enough to produce gravitational waves, just as a vibrating drumhead emits sound waves. These gravitational waves generated during inflation would be so weak by now, 13.8 billion years after the Big Bang, that they'd be undetectable. But in 1997, five physicists hit upon a possible strategy: Inflationary gravity waves could distort the light left over from the Big Bang in a discernible way.

Eons after the primordial blast, this remnant light fills all space, constituting a faint glow everywhere in the sky known as the cosmic microwave background, or CMB. The key lies in determining how that vestigial light is polarized — basically, how the light waves are oriented. Inflation-era gravity waves, which alternately stretch and compress space as they pass through, would leave a permanent mark in the cosmic radiation background, adding a twist to the CMB polarization. This distinctive, swirling pattern is called a B-mode. If astronomers could detect that, they would, in effect, see the fingerprint of inflation.

BICEP2 was specifically designed to look for this pattern. From 2010 to 2012, the telescope observed a small patch of sky visible from Antarctica. Kovac and his co-investigators — Jamie Bock of Caltech, Chao-Lin Kuo of Stanford and Clem Pryke of the University of Minnesota — then spent over a year scrutinizing the data. "We checked it 14 different ways to make sure it was consistent," Kovac says, before announcing they had identified the telltale vortex-like pattern expected from

TOP: BICEP COLLABORATION. BOTTOM: STEFFEN RICHTER, HARVARD UNIVERSITY

gravitational waves generated during inflation.

The researchers believe the signal they detected was cosmic in origin and did not come from our own galaxy, although that point has come under question. The big issue is whether the BICEP2 investigators properly accounted for the effects of dust within our own galaxy, as it could also have given rise to the swirling B-mode pattern.

While that's being straightened out, the BICEP2 team is moving ahead, poring over new data from the South Pole's Keck Array, which is part of the series of experiments co-led by Kovac and his colleagues. BICEP3, BICEP2's more sensitive successor, is set to begin a three-year observational run in early 2015. And several competing groups are going after the B-mode signal as well.

If the original claims are substantiated and the emerging picture of the universe's beginning is upheld, what would that mean? First, it would tell us that gravitational waves, predicted by Einstein's century-old theory of general relativity, really do exist. Second, it would greatly clarify our understanding of the Big Bang, telling us, as Guth puts it, "what banged and why it banged." Third, it would build an almost ironclad case for inflation.

Some uncertainty would still persist because cosmologists don't fully grasp the underlying physics behind inflation. But the story of our universe's first moments would, nevertheless, come into sharper focus than ever before — far beyond what many observers had deemed possible. — STEVE NADIS

CLOUDED BY A VEIL OF DUST

Euphoria overtook the science world on March 17, when members of the BICEP2 team announced the discovery of gravitational waves that represented the "first tremors of the Big Bang." A couple of months later, two independent analyses claimed the BICEP2 researchers had underestimated the effects of dust in our galaxy, as it could produce the pattern they had attributed to gravitational waves.

On Sept. 22, data from the Planck space telescope showed that the portion of the sky BICEP2 studied contained more galactic dust than previously assumed. The two teams have joined forces to determine whether the signal BICEP2 detected originated, at least in part, from gravitational waves, or if it's entirely explained by dust.

The results should appear in late 2014. Meanwhile, astronomers are continuing the kinds of observations undertaken by BICEP2, which are still regarded as the most promising means of witnessing the birth throes of our universe. — S.N.

COURTESY OF KINDMAN

Thousands of plants crowd a grow room owned by Kindman, a Denver cannabis dispensary. In 2014, Colorado became one of the first states to legalize the drug.

6

Marijuana Goes Legit, but the Future of Research Is Hazy

In 1969, Carl Sagan wrote anonymously that marijuana helped him reach "devastating insights." If he were writing today, he might use his real name. The stigma of dope is seemingly going up in smoke — but there are still surprisingly few studies on the drug.

In 2014, Alaska, Oregon and the District of Columbia legalized recreational marijuana, and sales began in Colorado and Washington, which adopted similar measures in 2012. Twenty-three states now allow the use of medical marijuana. In a February poll by the Pew Research Center, a majority of Americans — 54 percent — said pot should be legal. Just four years ago, 41 percent supported legalization.

But the growing acceptance of marijuana has done little to ease research restrictions. The federal government still classifies pot as a highly restricted drug, and it can take years to secure approval for studies. Even in states where researchers can legally buy top strains like Ghost Train Haze at the corner pot store for their personal use, they must use a single federally approved strain for their studies. Yet that strain is low on a chemical credited with many of the plant's touted medical benefits.

Philippe Lucas, vice president for research at Tilray, a medical marijuana producer in British Columbia, says America's loss is Canada's gain. There, a research project can use pot from a licensed producer.

So, is the ever-more-accessible drug safe to use? The few studies on marijuana yield no clear answer. Scientists have demonstrated that pot impairs driving, though other researchers say high drivers often compensate with added caution. Other studies suggest pot hammers short-term memory, and one found that frequent use can lower IQ, though it has received criticism for overstating the link. Research published in October suggests that regular pot smoking increases the risk of developing chronic bronchitis. As for marijuana's widely touted medicinal benefits, the scant research in that area suggests that chemicals in pot called cannabinoids may reduce pain and inflammation.

The FDA is considering reclassifying weed into a less restrictive category. If it does, much of the red tape would vanish, and researchers could be able to use retail strains in their studies — and not just as a Saganesque aid to creative scientific thinking. — EMMA MARRIS

7

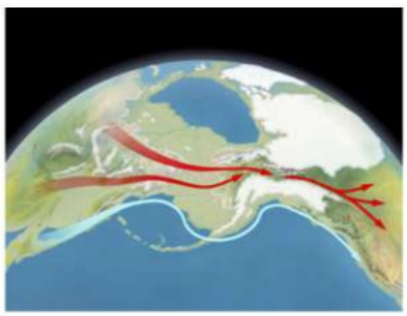
Ancient Genome Sequences Settle First Americans Debate

A toddler boy and a teenage girl have settled a contentious debate in archaeology more than 12,000 years after their deaths.

In February, researchers published the first ancient American human genome, sequencing DNA from the remains of a boy known as Anzick-1, who was buried about 12,600 years ago in what is now western Montana. The child's genes proved conclusively for the first time that Native Americans are descended from an Asian population that migrated across Beringia — a land bridge now submerged between Siberia and Alaska — at least 15,000 years ago.

"The archaeological and genetic stories are beginning to mesh," says Mike Waters, an archaeologist at Texas A&M University and a member of the Anzick-1 team. "It's been a long-held belief that the First Americans gave rise to Native Americans, but having the genetics verified that there were direct or close ties."

Particularly satisfying to Waters, the findings refute a competing theory about First Americans. Based on similarities in tool design between the American Clovis culture, to which Anzick-1 likely belonged, and that of a southwestern European Ice Age culture, some researchers had been promoting the Solutrean hypothesis: that the Americas were first settled by Europeans who crossed the Atlantic, possibly in skin kayaks.



Arrows show the flow of human migration across the Bering land bridge from Asia.

A child's remains were found at the base of this cliff in Montana, along with Clovis tools (left).

"Anzick clearly shows direct descendency — and continuity — of Native Americans all the way back to Central Asia," Waters says. "The Solutrean ship has sunk."

Anzick-1's resting place is the oldest credible burial site found in the Americas — and the only one associated with the Clovis culture, known in particular for its fluted spear points. The child's remains were found in 1968 during construction on land belonging to the Anzick family.

Recognizing the find's scientific significance but aware of Native American cultural sensitivities, the family kept the remains secure for more than 40 years. They turned down several requests to study Anzick-1's remains until they were approached by Waters and University of Copenhagen paleobiologist Eske Willerslev.

Sequencing Anzick-1's genome was no easy task, according to Willerslev. "Without a doubt, this was the most demanding genome to date that I have ever sequenced," he says. "With Anzick-1, there was a tremendously low amount of human DNA left — less than 2 percent. The rest was microbial [contamination]."

Although Willerslev is accustomed to sequencing ancient DNA samples in about a year, it took him

FROM TOP: MICHAEL WATERS; SARAH ANZICK; GARY HINCKS/SCIENCE SOURCE

In the Hoyo Negro cave, diver Susan Bird works on the skull of Naia, whose DNA is over 10,000 years old.

PAUL NICKLIN/NATIONAL GEOGRAPHIC

more than three years to sequence Anzick-1's genome because of the DNA's poor condition and his desire to deep sequence the material, repeating the process multiple times for the most accurate results.

Those results were impressive: Anzick-1's genome showed his people were directly ancestral to 80 percent of Native Americans stretching from the Pacific Northwest to southern Chile. And the boy was closely related to the other 20 percent, groups living in Arctic Canada and Greenland.

Meanwhile, in an underwater Mexican cave, the skeleton of a girl, whom researchers call Naia, was revealing secrets of her own.

According to a study published in *Science* in May, the sequencing of Naia's mitochondrial DNA — dated between 12,000 and 13,000 years old — confirmed a shared genetic lineage with modern Native Americans.

Unlike Anzick-1, Naia's remains — the most complete skeleton of an ancient American ever found — include the skull. The teenager, found in the Yucatan Peninsula's Hoyo Negro cave, had a prominent forehead, narrow face and wide-set eyes. These facial characteristics are seen on most of the other ancient American skulls known to researchers but are not associated with modern Native Americans, a disparity that had fueled alternate theories of the continent's first settlers. But Team Naia found no genetic evidence that the girl was related to any other population.

The difference between Paleoamerican and modern Native American facial features is likely a combination of additional waves of migration from Siberia, via Beringia, and genetic drift, a gradual change in appearance and other traits as populations divide, migrate and adapt, says Jim Chatters, a Seattle-area anthropologist who led the multinational study of Naia.

"Anzick and Naia say the same thing, that you have Beringians here very early," Chatters says. "They are two different pieces of a puzzle that's producing one picture."

—GEMMA TARLACH

8

The Year in Fraud

The suicide of a stem cell researcher in Japan last summer prompted a great deal of soul searching in science. Yoshiki Sasai's death came after a scandal involving two papers retracted for fraud — the most high-profile case of scientific misconduct in 2014. But it was far from the only one.

Serious questions were also raised about stem cell research by Harvard's Piero Anversa. We learned more about Cory Toth, a former diabetes researcher at the University of Calgary, whose lab fabricated data in nine published articles. And we saw the discovery of an apparent ring to generate positive assessments, aka peer reviews, of submitted manuscripts, 60 of which wound up being retracted.

It might seem, then, that 2014 was an *annus horribilis* in the world of science fraud. For many in the public, which pays for much of this research in tax dollars, news of these events may have come as a rude awakening. But at Retraction Watch, when we see and hear that kind of commentary, we feel a little like the police captain in *Casablanca* who proclaims he's "shocked, shocked!" to learn there is gambling at Rick's, only to be handed his winnings a moment later.

We started Retraction Watch in 2010, and every year since then, we've witnessed at least a few cases big enough to warrant headlines: anesthesiologist Yoshitaka Fujii, record holder for retractions at 183; Diederik Stapel, whose groundbreaking social psychology work was almost entirely fabricated; Joachim Boldt, the German critical-care specialist and previous retraction record holder. The list goes on.

So what can we learn from all these scandals? Are scholarly journals and their editors, who insist that their peer-reviewed studies are more trustworthy than everything else the public hears about science, little better than carnival barkers hawking bogus trinkets?

The short answer is no. Journals and publishers are, for the most part, doing a good job. They increasingly use software to screen manuscripts for plagiarism, and some even employ statistics experts to review papers for signs of data fabrication. In the Fujii case, for example, the British journal *Anaesthesia* had a stats guru analyze Fujii's articles. His verdict: The chances that the data were valid were infinitesimal.

It's impractical to apply this sort of extensive scrutiny to every one of the nearly 2 million manuscripts submitted each year. But conducting statistical reviews of papers that get flagged during the editorial process — or, perhaps more important, after publication — is an achievable goal, one that would make a significant contribution to the integrity of the scientific literature.

In fact, post-publication peer review is an emerging phenomenon in scholarly publishing. On sites like PubPeer, researchers critique papers, pointing out everything from errors or other problem spots to potentially manipulated images and other evidence of misconduct. One of the reasons there seems to be more fraud is simply that we're better at finding it.

Many scientists, journal editors and publishers have reacted warily to PubPeer and its ilk. Some contend that the anonymity of the post-publication reviewers breeds witch hunts and harms innocent bystanders. But the sites are doing a service by catching horses even though they have already left the barn. In addition, small but growing efforts have also begun, to test whether research holds up by repeating — in scientific parlance, replicating — experiments in cancer and psychology research.

All of these efforts underscore a critical point, one that science may need some time to embrace: The paper is not sacrosanct. It does not come into the world like a flawless, shining deity immune to criticism or critique. If more scientists come to think of a new publication as a larval stage of scientific knowledge and if fewer schools and funding agencies prize the high-profile journal article — basing tenure, grant and promotions on it — then researchers will feel less pressure to cut corners and manufacture dramatic results.

Reporting on cases in which scientists have committed fraud can be disheartening, even heartbreaking. But for every fraudster out there, we know there are dozens of scientists who are quick to correct the record when they discover problems in their work. And they rail against the reluctance of many of their peers to do the same. Sadly, many scientists are worried that acknowledging any fraud in their midst will discourage funding.

We are guided by the old chestnut: The cover-up is worse than the crime. If the growing awareness of an ongoing problem has led to more transparency, the scientific process, and the public who benefits from the knowledge it generates, will be better off. — ADAM MARCUS AND IVAN ORANSKY, CO-FOUNDERS OF RETRACTIONWATCH.COM

KATIE EDWARDS/IKON IMAGES/CORBIS

The "Spinosaurus: Lost Giant of the Cretaceous" exhibition at the National Geographic Museum in Washington, D.C.

First Dinosaur to Menace Land and Water

Uncovered in Saharan Morocco, a new specimen of the dinosaur *Spinosaurus aegyptiacus* helped researchers confirm that the 50-foot carnivore was the largest land predator ever known. And that's probably the least interesting thing about the strange animal; *Spinosaurus* is also the only aquatic dinosaur ever identified.

"*Spinosaurus* breaks the mold. It's not just another *T. rex*-like predator, only bigger," says Nizar Ibrahim, the University of Chicago paleontologist who led the dig. When it comes to its bones, "to be honest, one of the best modern analogs for it is the penguin."

Spinosaurus lived about 95 million years ago in the massive river systems of what's now northern Africa. It was a powerful swimmer, with a crocodilian snout, broad feet that may have been webbed, shortened but heavily muscled hind limbs and a propulsive tail similar to that of some fish.

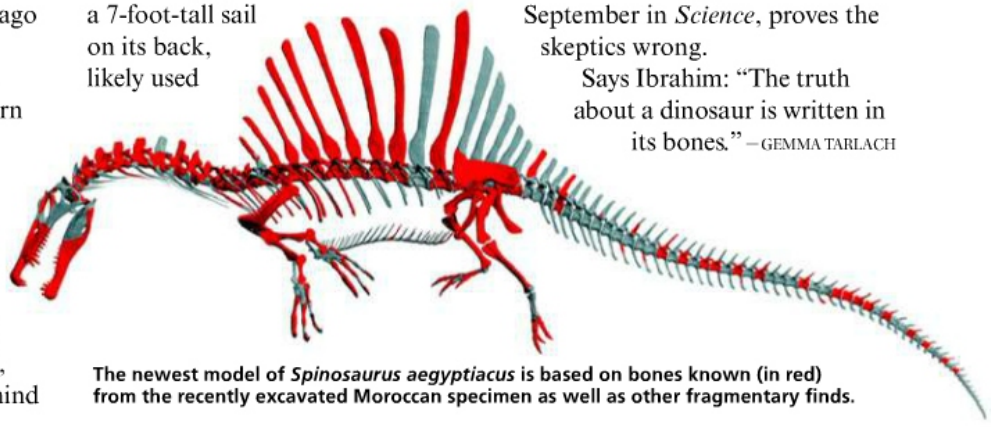
Using CT scans of the new fossil to create a digital model of the dinosaur, Ibrahim and colleagues also discovered that *Spinosaurus* is the only dinosaur that evolved to lose the central cavity in its limb bones. The adaptation, which provides buoyancy control, can be seen today in aquatic animals such as the hippo and, yes, the penguin.

The megapredator also had a 7-foot-tall sail on its back, likely used for display.

Although its anatomy suggests *Spinosaurus* spent at least some time on land, the dinosaur's front-heavy mass and shorter hind limbs meant it had an ungainly, slothlike posture.

The only other partially complete *Spinosaurus* was destroyed during World War II, making study with modern methods impossible. Some paleontologists had doubted the bizarre chimera even existed. The new finding, published in September in *Science*, proves the skeptics wrong.

Says Ibrahim: "The truth about a dinosaur is written in its bones." — GEMMA TARLACH



The newest model of *Spinosaurus aegyptiacus* is based on bones known (in red) from the recently excavated Moroccan specimen as well as other fragmentary finds.

FROM TOP: REBECCA HALE/NATIONAL GEOGRAPHIC; SKELETAL RECONSTRUCTION BY IBRAHIM, ET AL. 2014, SCIENCE/AAAS

10

Quantum Photo Finish

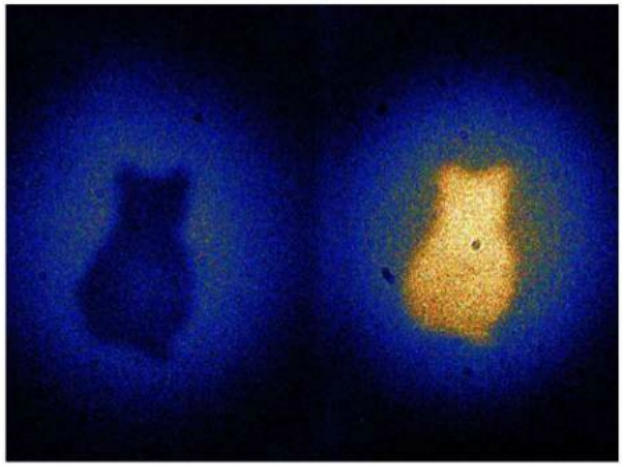
In a dark lab in Vienna, physicists did something incredible: They shined a laser through a cat-shaped hole in some cardboard, resulting in a glowing, red feline image. The twist: The light in the image didn't go through the hole in the cardboard.

The work, published in August, started with a single beam of light. To create a typical image, the entire beam would shine on the cardboard hole. Some light particles, or photons, would pass through, making up an image. The other photons would be blocked.

This time, the physicists took advantage of a weird quantum process called entanglement. Entangled photons are fundamentally linked, carrying some of the same information about each other even after they're separated. Think twins with ESP. "Spooky action at a distance," according to Albert Einstein.

After shining the light beam through a crystal to entangle the photons, the physicists split the beam in two, letting half of each entangled pair pass though the cat cutout. The other half traveled to a detector — a special camera — carrying the cat-shaped information from their twins' journeys.

"I didn't expect the images to come out so well," says physicist Gabriela Lemos, the lead author of the paper.



Images of a cat-shaped cutout created by photons that, due to quantum entanglement, didn't go through the cat cutout.

Interestingly, the twin photons weren't totally identical. The unobserved photons that went through the cat-shaped hole were too low in energy to be visible, while the detected twins were high-energy and visible. The team hopes others can use this unique property to image objects, such as delicate biological samples, that a more energetic, visible beam might otherwise destroy. — SHANNON PALUS

2014 World Debut: New Species Series

Can You See Me Now?

2014 World Debut: **New Species Series**

Amblyopsis hoosieri

Type of animal: Eyeless cavefish

Description: Completely colorless; 2 to 3 inches long; anus on underside of neck

Home: Southern Indiana

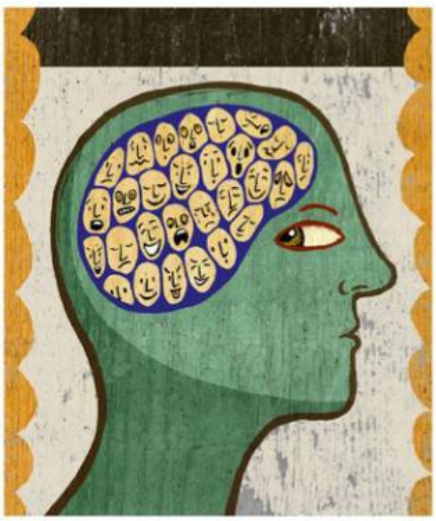
Fun fact: Unlike others of its kind, *A. hoosieri* lacks a debilitating mutation in the rhodopsin gene, which is an important gene for vision. That means it could see just fine … if it had eyes. Researchers named the fish after the Indiana Hoosiers basketball team — but not to imply the players might be visually challenged. The name honors several famous fish scientists who worked at Indiana University, as well as the species's proximity to the university. Plus, the lead author is a Hoosier fan. — BRENDA POPPY

FROM TOP: GABRIELA BARRETO LEMOS; MATTHEW NIEMILLER/ZOOKEYS

Schizophrenia Study Finds New Genetic Links

11

Schizophrenia, which affects 1 in 100 people worldwide and an estimated 2.4 million Americans, exacts tremendous social costs and great human suffering. Drugs can calm the inner voices, delusions and hallucinations, but few patients recover fully, and there is no cure. Nor are there predictive tests or internal markers for the disease — it must be diagnosed by outward signs alone. But this problem is at last yielding to progress on the genetic front.



In July, an international consortium of schizophrenia researchers, mounting what it calls the largest biological experiment in the history of psychiatry, reported 108 regions in the genome associated with schizophrenia. Two dozen of these genetic links had been recorded before, but more than 80 were new. Neuroscientists now have many more avenues for exploring the biological underpinnings of the disorder.

Originally thought to stem from bad parenting, schizophrenia tends to cluster in families, implicating DNA. The risk of the disease rises the closer one is related to a patient. Until recently, gene scans were unsuccessful in turning up links to schizophrenia.

"When we started, we got a lot of things wrong," says Patrick Sullivan, a geneticist and psychiatrist at the University of North Carolina. "We had no clear fix on the problem. What was the best study design? How many samples did we need? Also, in the '80s, genotyping [reading DNA's sequence of letters] was really expensive. Every time a new technology came along, we gave it a shot, but schizophrenia was way more complicated than we thought."

Sullivan is principal investigator for the Psychiatric Genomics Consortium, which includes "nearly everyone in the world who's working on schizophrenia," he says. The consortium's broad-scale analyses included 35 research groups that have integrated genetic samples from a total of 150,000 subjects — 37,000 of whom have schizophrenia and 113,000 healthy controls. The unprecedentedly large sample allows a glimpse of the genetic basis of the disease that smaller, earlier studies didn't have the statistical power to see. The specific method employed was a genome-wide association study, or GWAS.

Because DNA's code varies slightly from person to person, GWAS seeks to identify the places where a schizophrenic's genome differs from a healthy person or from another schizophrenic. The genotyping technology can distinguish a million possible sequences across each sample, the goal being to show the variants that are more prevalent in the patients than in healthy subjects.

The good news from the study was that many of the variants associated with the disorder made biological sense. Some, for example, pointed to genes that expressed themselves in brain cells, or that involved immune function, a previously established connection. Another important hit was at DRD2, the gene for the dopamine receptor, which is targeted by antipsychotic drugs. The bad news — which really wasn't news to the investigators — was that the variants were fairly common in the population, but their effect was weak. They weren't blockbuster genes like those for cystic fibrosis or Huntington's disease, single flaws making for straightforward predictions. The risk of schizophrenia to someone who carries one of these markers is increased by as little as one-tenth of a percent.

Thomas Insel, director of the National Institute of Mental Health, describes schizophrenia as polygenic, meaning that genes probably act in networks to produce it. "The genome works like a symphony, not like a soloist," he says. "If you line up these [variants] and determine the likely function of the genes, do they tell the same story?" The next task will be to engineer neurons in cell cultures so that they manifest one or more of the variants. "Does this alter any aspect of how neurons develop or how they fire?" Insel wants to know.

"The goal of this work is to understand the neurobiology," Sullivan stresses. "So the molecular basis is polygenic. Are we going to sit back and cry because schizophrenia didn't turn out like we hoped it would? It's complicated. That's the scientific challenge." – JEFF WHEELWRIGHT

ILLUSTRATION WORKS/CORBIS

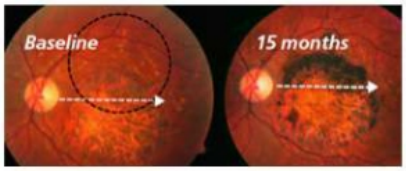
12

Stem Cells Make Insulin, Restore Retinas

Since embryonic stem cells were first cultured in the lab more than 30 years ago, researchers have talked up their therapeutic potential. Able to differentiate into dozens of tissue types, stem cells might be used to regenerate organs and treat numerous diseases.

The proof has been slow to come, however. "You've been hearing about them for decades, but where's the beef?" asks Robert Lanza, chief scientist at Advanced Cell Technology and a pioneer of regenerative medicine. The field has been dogged by political and religious opponents, who object to the destruction of human embryos during the harvest of cells.

So there was extra satisfaction in October when two scientific teams, Lanza's and a group led by Harvard University's Douglas Melton, each announced advances. The group at Harvard's Stem Cell Institute coaxed human embryonic stem cells into pancreatic cells. Transplanted into diabetic mice, the cells secreted insulin and cured the mice in 10 days. The next step — Melton says it's the last hurdle before human trials — will be to shield the foreign cells from rejection by the body's immune system.



Researchers used stem cells to create retinal pigment epithelium cells, which were transplanted into a patient's retina (left) in an area depicted by the black circle. After 15 months, the new cells had grown.

Lanza's therapeutic target has been the eye — specifically, eyes failing from macular degeneration. The study included 18 patients, half with age-related macular degeneration and half with Stargardt's macular dystrophy, the leading causes of blindness in adults and juveniles. From the embryonic stem cells, the researchers produced a type of tissue called retinal pigment epithelium (RPE). Growing RPE cells in quantity, they injected them into one eye of each patient. The subjects were followed for an average of two years.

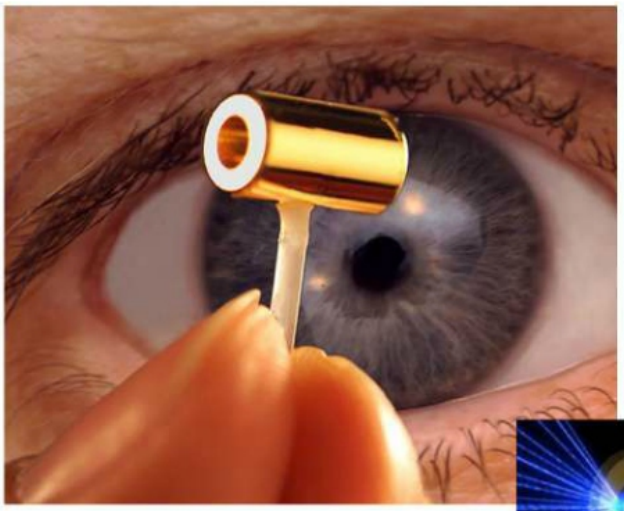
Not only were there no adverse effects from the transplanted cells — this was primarily a safety trial — but 10 patients showed marked improvements in vision, and the eyesight in another seven seems to have stabilized.

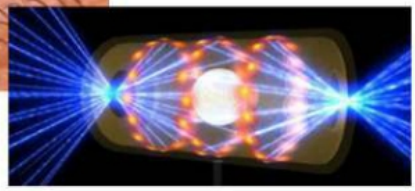
Since it's now possible to reprogram adult cells to make tissues like RPE, Lanza expects the controversy over stem cells to subside. He also plans to use embryonic cell lines "where we extract a cell and don't damage the embryo. We will be able to satisfy all but a small number of people."

— JEFF WHEELWRIGHT

13

A Promising Spark for Lab-Made Fusion





The cylinder (above) that contains the fuel capsule is just a few millimeters wide. A rendering (right) shows the laser beams entering the capsule, where they compress and heat the fuel to trigger nuclear fusion.

In a lab east of San Francisco, physicists trained 192 lasers on a plastic sphere the size of a BB. Inside were ingredients for a powerful fusion reaction similar to the kind that makes our sun hot and glowing.

When they switched the lasers on, the Lawrence Livermore National Laboratory scientists found that more energy came out of the fuel than went in. The research, reported in February, is a crucial milestone toward tapping the power of lab-made fusion.

In fusion reactions, hydrogen isotopes meld together, creating high-energy alpha particles. The key to increasing the captured energy was to keep these particles trapped inside the container, feeding energy back into the reaction.

To make fusion a viable renewable energy source, scientists still have work to do: Some of the lasers' energy was lost before even making it to the tiny bead. The energy produced needs to increase at least a hundredfold for the total energy it takes to turn on a fusion reaction to be less than the total energy gained. Still, this is a spark. — SHANNON PALUS

TOP: STEVEN SCHWARTZ AND ROBERT LANZA. BOTTOM: LAWRENCE LIVERMORE NATIONAL LABORATORY/NATIONAL IGNITION FACILITY (2)