

SCIENCE NEWS MAGAZINE

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APRIL 29, 2017

Seeking Signs of Autism

Entanglement to the Max

Why Squid Are Smart

Proton Enigmas

Exploring the diversity of venomous fish

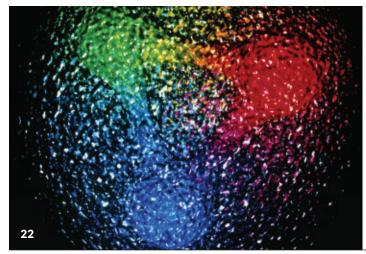
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COVER The devil firefish (*Pterois miles*) of the Indian Ocean and Red Sea has venomous spines to thwart predators. *Cigdem Sean Cooper/Shutterstock*



Scientists find amazement in what's most familiar

For her 7th birthday, my niece received a very special gift — a compound light microscope with a set of slides. As soon as we got it out of the package, she became a diligent young investigator, studying the leg of a fly, dog cardiac muscle and onion epidermal cells. But it wasn't the pre-

pared slides that captivated her most. She wanted to investigate more familiar things. We plucked hairs from our heads to see what they looked like, and collected dirt from various spots across the yard to compare and contrast. Sitting at the dining room table, she drew big circles on notebook paper and sketched her newfound views. The world she thought she knew was suddenly unexpected.

At one time or another, a similar feeling must have motivated researchers studying the proton (Page 22). Here's a basic constituent of matter that, as physics writer Emily Conover writes, makes up stars, planets and people (also, peonies, blue jeans and gelato — a few of my favorite familiar things). The proton has been observed, albeit indirectly, for about a century. Its place at the center of the atom is etched into our minds. Heck, we even control it — smashing protons together at near light-speed in giant particle colliders.

Yet for those who look a little closer, there are many surprises: Protons are made up of more fundamental particles called quarks and gluons. Some of the quarks stick around but others are more ephemeral, popping in and out of existence. Exactly how all the proton's parts add up to make the whole remains murky, as do some of the proton's key properties. Scientists don't know its precise size, nor do they understand its spin. Supposedly the particle should (rarely) decay, but no one has detected a proton's death. Microscopes aren't much help, so scientists use souped-up tools with lasers, mirrors and magnets to see in a different way, to become more intimate with the world they thought they knew.

Glass frogs may not be familiar to most of us, but biologists who spent many years' worth of rainy seasons searching for moms and egg clutches became wellacquainted with these amphibians (Page 16). Known glass frog caregivers have almost always been dads. But it now appears that by briefly pressing their bellies against the clutches, many moms have an important role, too. As one evolutionary biologist commented: "Parental care is perhaps more common and diverse in animals than we realize.... We just might have to look a bit harder for it."

And then there are the tropical fang blennies, well-known among home aquarium enthusiasts. New research (Page 28) reveals that the venom of one fang blenny species acts on opioid receptors, probably working as a sedative rather than causing pain. Close investigations with micro-CT scans, chemical analyses and experiments in mice show that these familiar fish have evolved a survival strategy surprisingly different from that of other venomous creatures.

Investigate means to study closely. But looking isn't sufficient for science. You also have to get to know something well enough to appreciate what you see. By building understanding, recognizing patterns and forming questions, scientists prepare themselves to spot the unexpected. Whether it's dirt from the front yard or much smaller constituents of matter, there's always something more to discover. — *Elizabeth Quill, Acting Editor in Chief*

PUBLISHER Maya Ajmera ACTING EDITOR IN CHIEF Elizabeth Quill

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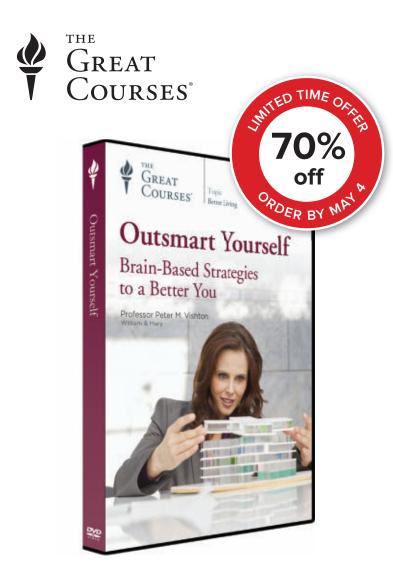


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NOTEBOOK



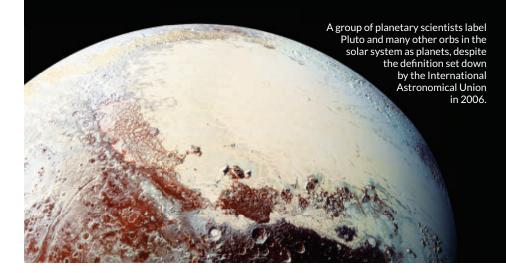
Excerpt from the April 29, 1967 issue of *Science News*

50 YEARS AGO

Drifting theories shake up geology

Continental drift, a theory often considered amusing but rarely important, seems about to become the focus of a revolution in geology. At the least, it has already split the geological community into those who find the evidence for it "formidable" and those who think it is not yet formidable enough to constitute a proof.

UPDATE: That continents shift is now widely accepted and explained by plate tectonics. Plenty of evidence supports the idea that the Earth's outer layer is divided into large slabs that gradually move over the mantle. But researchers don't agree on when the plates first began shifting. New evidence from ancient rocks found in Canada suggests the slipping and sliding didn't get going until Earth was at least a billion years old (SN: 4/15/17, p. 8). In about 250 million years from now, the continents may drift together into a supercontinent called Amasia (SN: 1/21/17, p. 18).



SOAPBOX What's a planet?

Pluto is a planet. It always has been, and it always will be, says Will Grundy of Lowell Observatory in Flagstaff, Ariz. Now he just has to convince the world. "wanderer" and included the sun, moon, Mercury, Venus, Earth, Mars, Jupiter and Saturn. Eventually the moon and sun were dropped from the list and Uranus and Neptune were added, along with Pluto, after its discovery in 1930. The idea of a planet as a roundish, rocky or gaseous body that orbits the sun stuck, until 2006.

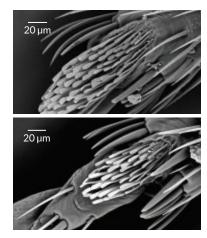
For centuries, the word "planet" meant

FOR DAILY USE

Tropical bedbugs outclimb common species

Some bedbugs are better climbers than others, and the bloodsuckers' climbing prowess has practical implications.

To detect and monitor bedbugs, people use an array of strategies, from DIY setups to dogs. Pitfall traps placed near the base of furniture are highly effective for detecting and monitoring an infestation. The traps, which rely on smooth inner walls to prevent escape, are sold around the world. But they have been tested primarily with *Cimex lectularius*, the most common bedbug species in the United States.



The leg of an adult female tropical bedbug (top) appears hairier than an adult female common bedbug's leg (bottom) under a scanning electron microscope.

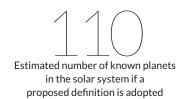
Tropical bedbugs (C. hemipterus), it turns out, can easily scale the walls of pitfall traps, Chow-Yang Lee, an entomologist at Universiti Sains Malaysia in Penang, and colleagues found in lab tests. While 24 to 76 percent of tropical bedbugs in the study escaped traps, no more than 2 percent of common bedbugs made it out of most traps. In measurements of vertical frictional force, tropical bedbugs also came out on top. Further investigation of the species' feet revealed extra hairs on the tibial pads of tropical bugs. These hairs may give legs a better grip on trap walls, the researchers propose online March 15 in the Journal of Economic Entomology. Tropical bedbugs live in some regions of Africa, Australia, Japan, China and Taiwan. They have recently been spotted in Florida. - Helen Thompson

FROM TOP: NASA, JHUAPL, SWRI; D.Y. KIM ET AL/JOURNAL OF ECONOMIC ENTOMOLOGY 2017

That's when the International Astronomical Union narrowed the definition, describing a planet as any round body that orbits the sun and has moved anything nearby out of its way, either by consuming objects or flinging them into space. Pluto failed to meet the last criterion (*SN:* 9/2/06, *p.* 149), so it was demoted to a dwarf planet.

Almost overnight, the solar system was down to eight planets. "The public took notice," Grundy says. It latched onto the IAU's definition — perhaps a bit prematurely. The definition has flaws, he and other planetary scientists argue. First, it discounts the thousands of exotic worlds that orbit other stars and also rogue ones with no star to call home (*SN*: 4/4/15, p. 22).

Second, it requires that a planet cut a clear path around the sun. But no planet does that — Earth, Mars, Jupiter and Neptune share their paths with asteroids, and objects crisscross



planets' paths all the time.

Third, objects far from the sun need to be big to cut a clear path. Even a rock the size of Earth out in the Kuiper Belt wouldn't have the heft required to gobble down or eject objects from its path.

Grundy and colleagues (all members of NASA's New Horizons mission to Pluto) laid out these arguments against the IAU definition of a planet March 21 at the Lunar and Planetary Science Conference in The Woodlands, Texas.

Grundy prefers simpler criteria: any round object in space that is smaller than a star. By that definition, Pluto is a planet. So is the asteroid belt object Ceres. So is Earth's moon. "There'd be about 110 known planets in our solar system," Grundy says. Plenty of exoplanets and rogue worlds would fit the bill as well.

The reason for the tweak is to keep the focus on the features — the physics, geology and atmosphere — of the world itself, rather than worry about what's going on around it, Grundy says.

The New Horizons mission (*SN:* 12/26/15, p. 16) has shown that Pluto is an interesting world with active geology, an intricate atmosphere and other features associated with planets in the solar system. It makes no sense to write off Pluto because it doesn't fit one criterion. The public could easily readopt the small world as a planet, Grundy says, though astronomers might be a tougher sell.

"People have been using the word correctly all along," he says, suggesting we stick with the original definition. That's his plan. -Ashley Yeager

MYSTERY SOLVED Nectar offers DIY muscle protection

Hawk moths have a sweet solution to muscle damage.

Manduca sexta moths dine solely on nectar, but the sugary liquid does more than fuel their bodies. The insects convert some of the sugars into antioxidants that protect the moths' hardworking muscles, researchers report in the Feb. 17 *Science*.

When animals expend a lot of energy, like hawk moths do as they rapidly beat their wings to hover at a flower, their bodies produce reactive molecules, which attack muscle and other cells. Humans and other animals eat foods that contain antioxidants that neutralize the harmful molecules. But the moths' singular food source — nectar — has little to no antioxidants.

So the insects make their own. They send some of the nectar sugars through an alternative metabolic pathway to make antioxidants instead of energy, says study coauthor Eran Levin, an entomologist now at Tel Aviv University. Levin and colleagues say this mechanism may have allowed nectar-loving animals to evolve into powerful, energy-intensive fliers. -*Elizabeth S. Eaton*



INTRODUCING Touchy tyrannosaur

Behind their ferocious facades, tyrannosaurs were probably touchyfeely. A new species of tyrannosaur may have had highly sensitive organs in its face able to detect touch and temperature, researchers report March 30 in *Scientific Reports*.

Daspletosaurus horneri was identified based on several skulls found in northern Montana. The 9-meter-long dino lived

about 75 million years ago. *D. horneri's* facial bones were coarse and lumpy, says study coauthor Thomas Carr, a vertebrate paleontologist at Carthage College in Kenosha, Wis. Nerve holes riddled the dino's snout and jaw bones. Crocodilians, close relatives of dinos with specialized sensory organs in their facial scales, have similar texture and wiring. The dinosaur's snout would have been as sensitive as a "giant fingertip," Carr says, good for gently picking up its young. All tyrannosaurs probably had these sensory organs, the researchers suggest.—*Elizabeth S. Eaton*

Daspletosaurus horneri (illustrated) and other tyrannosaurs may have had sensitive snouts and jaws.



Genes & Cells Cephalopod smarts tied to RNA edits

Molecular revisions have also slowed the animals' evolution

BY TINA HESMAN SAEY

Octopus, squid and cuttlefish don't always follow the rules laid out in their DNA. Straying from prescribed genetic instructions may have increased the cephalopods' thinking prowess, but if so, it came at a cost, a new study suggests.

Once genes have been copied from DNA into RNA, these cephalopods heavily edit the genes' protein-making directions, researchers report in the April 6 *Cell*. The study included a squid species, two octopus species and a cuttlefish species, all coleoids, or shell-less cephalopods. Each species contained 80,000 to 130,000 RNA sites that had been edited. This high level of editing contrasts with only 1,150 edited sites in RNA from a nautilus and 933 in a mollusk.

RNA editing changes one of the information-carrying subunits of RNA from the nucleotide adenosine to one called inosine. That substitution can change how a cell reads the genetic instructions to build proteins, exchanging one amino acid for another not specified by the DNA instructions. Generally, such tweaks to proteins have harmful effects, and evolution has gradually weeded out the changes. In the brains of humans and other mammals, less than 1 percent of RNA editable sites change protein-coding instructions.

But squid, octopus and cuttlefish edit about 11 to 13 percent of the proteinbuilding RNAs in their brains, computational biologists Noa Liscovitch-Brauer and Eli Eisenberg of Tel Aviv University

and colleagues discovered. Cephalopods edit RNA in other tissues, too, but not as much as in the brain.

Some genes have multiple editable sites. Octopus and their brethren may edit all of the sites, or edit some but not others. Adding up all the pos-

sible edited and unedited combinations could produce hundreds to thousands of different versions of a protein within a cell. "It introduces immense complexity and diversity," says Eisenberg.

All four coleoid cephalopod species share 1,146 editing sites in 443 proteins, the researchers discovered. Exactly why the species edit RNAs in the same place isn't yet clear, but such sharing is a signal that editing at those sites was important

allow cephalopods flexibility in thinking, which could contribute to complex behaviors such as unlocking cages or using tools.

RNA editing could

RNA editing probably reduced genetic diversity of cephalopods (cuttlefish shown) but may have also boosted their intelligence.

in cephalopod evolution.

Editing was especially prevalent in genes responsible for the structure and function of nerve cells in the brain, says study coauthor and neuroscientist Joshua Rosenthal of the Marine Biological Laboratory in Woods Hole, Mass. Such RNA editing could allow cephalopods flexibility in thinking, which could contribute to complex behaviors such as unlocking cages or using tools.

Nautilus species are related to octopus, squid and cuttlefish but aren't known for their smarts. Nautiluses also tend not to edit RNA. That's not proof that RNA editing contributes to cephalopod intelligence, "but it's good reason to hypothesize," Eisenberg says.

So much RNA editing has downsides, though, the researchers say, including slowed evolution. For an RNA to be edited, it must fold into complex shapes and have a stretch in which the single-stranded molecule forms a double strand. DNA mutations that would block the doublestranded structures are not welcome near RNA editable sites, the researchers found. DNA mutations provide the

> genetic diversity needed for evolution, so limiting DNA alterations in favor of RNA editing has slowed evolution in these species. About 10 to 26 percent fewer DNA mutations than expected are found in RNA edited genes in coleoid cephalopods, Eisenberg and

colleagues calculate.

RNA editing is clearly important in those species, says Jianzhi Zhang, an evolutionary geneticist at the University of Michigan in Ann Arbor. Although the findings are intriguing, he thinks the researchers have not proved a connection between complex behavior and RNA editing. "The question is, 'What is it doing?' I don't have an answer, but I think this is the most important question."

Virus may trigger celiac disease

Gluten interaction confuses immune cells, study suggests

BY ELIZABETH S. EATON

A common, usually harmless virus may trigger celiac disease. Infection with the suspected culprit, a reovirus, could cause the immune system to react to gluten as if it were a dangerous pathogen instead of a benign food protein, researchers report in the April 7 *Science*.

In mice, the reovirus T1L tricked the immune system into attacking food molecules, prompting an inflammatory response, virologist Terence Dermody of the University of Pittsburgh and colleagues found.

"Viruses have been suspected as poten-

tial triggers of autoimmune or food allergy–related diseases for decades," says Herbert Virgin, a viral immunologist at Washington University School of Medicine in St. Louis. This study provides new data on how a viral infection can affect the immune system, Virgin says.

Almost everyone gets infected with a reovirus, and almost no one gets sick, Dermody says. But if the first exposure to gluten in childhood occurs during infection, the virus may turn the immune system against the food protein.

The immune system either allows foreign substances to pass through the body peacefully, or it goes on the attack. In people with celiac disease, gluten is treated like a pathogen; the immune response damages the small intestine's lining, causing symptoms like bloody diarrhea.

Celiac disease has been associated with two genetic features. Though 30 to 40 percent of people in the United States have one or both of these features, only 1 percent have been diagnosed with the disease. This disparity suggests there is an environmental trigger.

In mice engineered to have one of those genetic features, T1L appeared to trick the immune system into seeing gluten as an enemy, Dermody and colleagues found. The key interaction occurs in the mesenteric lymph nodes, where gluten meets dendritic cells. These immune cells dictate whether the immune system ignores a substance. T1L also engages with the dendritic cells, fooling the cells to treat gluten, like the virus, as a threat.

Dermody and colleagues also found that people with celiac disease have higher levels of reovirus antibodies than people without the disease.

If T1L is a true trigger of celiac disease in humans, a vaccine could be developed for at-risk kids, Dermody says. Other viruses may also stimulate the disease.

ATOM & COSMOS

Early galaxy lived fast and died young

Discovery raises questions about how collections of stars form

BY ASHLEY YEAGER

A hefty red, dead galaxy in the early universe appears to have bulked up too fast.

The galaxy, seen as it was when the universe was only 1.65 billion years old, weighs at least three times as much as the Milky Way but has stopped making stars. Other galaxies at that time tend to be smaller and continue to churn out stars. How such a monster was made in less than a billion years, then shut down so quickly isn't clear, says Karl Glazebrook of Swinburne University of Technology in Australia. Finding the behemoth may

EONARD DOUBLET/SWINBURNE UNIV. OF TECH.



force astronomers to rethink galaxy formation to explain why some grow up fast, while others develop slowly, he and colleagues report in the April 6 *Nature*.

Astronomer Peter Behroozi of the University of California, Berkeley is not convinced that a rewrite is warranted just yet. "The galaxy is certainly not typical, but it is consistent with the broad diversity of galaxies coming out of theoretical models," he says.

Glazebrook's group used Hawaii's Keck Observatory to study the spectrum — a catalog of light by wavelength — of galaxy ZF-COSMOS-20115. The data confirm that it stopped making stars 500 million to a billion years before the epoch in which it was observed. The data also indicate the galaxy created the mass of over 1,000 suns each year. Contempora-

Galaxy ZF-COSMOS-20115 (illustrated) formed stars rapidly but then suddenly stopped, becoming red and dead by the time the universe was only 1.65 billion years old. neous galaxies typically generate a mass of less than 100 suns annually. With such rapid star formation, the galaxy probably matured in less than 100 million years.

Perhaps the galaxy got so large by colliding with another galaxy. A big merger stirs up and compresses gas to high densities, triggering intense star formation. These events often last less than 100 million years, much shorter than the billion-year timescales for a normal galaxy's star formation. In merger galaxies, gas is consumed quickly because stars form fast. If the gas runs out, star formation stops.

If massive galaxy mergers do exist, they are probably rare, says Cornell University astronomer Dominik Riechers. That's because galaxies form as matter pools together and collapses due to gravity over cosmic time. In the young universe, few regions would have had enough gravity to form massive galaxies, Riechers says.

In 2014, however, Glazebrook and colleagues reported finding a bunch of objects, including ZF-COSMOS-20115, that fit the profile of massive red, dead galaxies in the early universe. Studying the other galaxies' spectra could confirm that those candidates are inactive, too.

MATTER & ENERGY

Entangled atoms break record

Two teams of physicists push quantum effect to larger scales

BY EMILY CONOVER

In a feat of quantum one-upmanship, two teams of scientists have staked new claims of linking whopping numbers of atoms at the quantum level.

Researchers in Geneva demonstrated quantum entanglement of 16 million atoms, smashing the previous record of about 3,000 entangled atoms (*SN Online: 3/25/15*). Meanwhile, scientists from Canada and the United States used a similar technique to entangle over 200 groups of a billion atoms each. The teams reported their results online March 14 in a pair of papers posted at arXiv.org.

Through quantum entanglement, seemingly independent particles become intertwined. Entangled atoms can no longer be considered separate entities and make sense only as part of a whole — even if the atoms are far apart. The process typically operates on small scales, hooking up tiny numbers of particles, but the researchers convinced atoms to defy that tendency.

"It's a beautiful result," says atomic physicist Vladan Vuletic of MIT, who was part of the team that demonstrated the earlier, 3,000-atom entanglement. Quantum effects typically don't appear at the large scales that humans deal with every day. Instead, particles' delicate quantum properties are wiped out through interactions with the messy world. But under the right conditions, quantum effects like entanglement can persist. "What this work shows us is that there are certain types of quantum mechanical states that are actually quite robust," Vuletic says.

Both teams demonstrated entanglement using "quantum memory" devices. Consisting of a crystal interspersed with rare-earth ions – exotic elements like neodymium and thulium – the quantum memories were designed to absorb a single photon and reemit it after a short delay. The single photon is collectively absorbed by many rare-earth ions at once, entangling them. After tens of nanoseconds, the quantum memory emits an echo of the original photon: another photon continuing in the same direction as the photon that entered the crystal.

By studying the echoes, the scientists quantified how much entanglement occurred in the crystals. The more reliable the timing and direction of the echo, the more extensive the entanglement was. While the U.S.-Canadian team based its measurement on the timing of the emitted photon, the Swiss team focused on the direction of the photon.

The quantum memory devices aren't new technologies. "The experiments are not complicated," says physicist Erhan Saglamyurek of the University of Alberta in Canada, who was not involved with the research. Instead, the advance is mainly in the theoretical physics the researchers established to quantify the entanglement that was expected to arise inside such quantum memories. This development allowed the researchers to confirm that such large numbers of particles were actually entangled, Saglamyurek says.

Scientists from the two research teams declined to comment, as the papers reporting the work are still undergoing peer review.

The results don't have any obvious practical use. Instead, the work grows out of technology that is being developed for its potential applications: Quantum memories could be used in quantum communication networks to allow for storage of quantum information.

Physicists hope to push weird quantum effects to larger and larger scales. For quantum entanglement, "it would be a dream if you could make that visible to the naked eye," says Jakob Reichel, a quantum physicist at École Normale Supérieure in Paris. The latest results don't go that far. "It's not a revolution," Reichel says. But, "I think it helps us [get] a better feeling for entangled states."



Ruins of ancient palace in Mexico unearthed

Remnants of a royal palace in southern Mexico, dating to around 2,300 to 2,100 years ago, come from what must have been one of the Americas' earliest large, centralized governments, researchers say.

Excavations completed in 2014 at El Palenque uncovered a palace with separate areas where a ruler conducted affairs of state and lived with his family, say archaeologists from the American Museum of Natural History in New York City. Only a ruler of a bureaucratic state could have directed construction of this all-purpose seat of power, the investigators conclude online March 27 in Proceedings of the National Academy of Sciences.

The palace, the oldest such structure in the Valley of Oaxaca, covered as many as 2,790 square meters, about half the White House's floor area (an aerial view of an excavated section of the palace is shown). A staircase opened to an inner courtyard that probably served as a place for the ruler and his advisers to reach decisions, hold feasts and – based on human skull fragments found there – perform ritual sacrifices, the scientists suggest. – *Bruce Bower*

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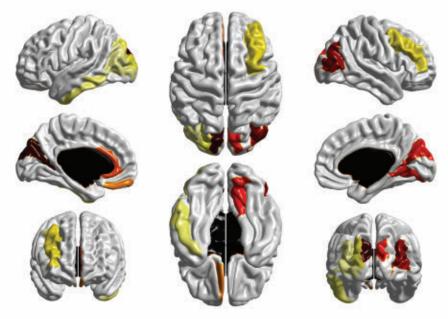
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BODY & BRAIN Scientists seek early signs of autism

Biomarkers could aid diagnosis and lead to treatment strategies

BY LAURA SANDERS

Soon after systems biologist Juergen Hahn published a paper describing a way to predict whether a child has autism from a blood sample, the notes from parents began arriving. "I have a bunch of parents writing me now who want to test their kids," says Hahn, of Rensselaer Polytechnic Institute in Troy, N.Y. "I can't do that."

That's because despite their promise, his group's results, reported March 16 in *PLOS Computational Biology*, are nowhere close to a debut in a clinical setting. The test will need to be confirmed and repeated in different children before it can be used to help diagnose autism. Still, the work of Hahn and colleagues, along with other recent studies, illustrates how the hunt for a concrete biological signature, a biomarker, of autism is gaining speed.

Currently, pediatricians, child psychologists and therapists rely on behavioral observations and questionnaires, measures with limitations. Barring genetic tests for a handful of rare mutations, there are no blood draws, brain scans or other biological tests that can reveal whether a child has — or will get — autism. Objective tests would be incredibly useful, helping provide an early diagnosis that could lead to therapy in the first year of life, when the brain is the most malleable. A reliable biomarker might also help distinguish various types of autism, divisions that could reveal who would benefit from certain therapies. And some biomarkers may reveal a deeper understanding of how the brain normally develops.

Scientists are simultaneously sanguine and realistic about the prospect of uncovering solid autism biomarkers. "We have great tools that we've never had before," says psychiatrist Joseph Piven of the University of North Carolina School of Medicine in Chapel Hill. Scientists can assess genes quickly and cheaply, gather sophisticated information about the shape and behavior of the brain, and rely on large organized research collaborations aimed at understanding autism. "That said, I've done this long enough to know that people make all kinds of claims: 'In the next five years or the next 10 years, we're going to do this," Piven says. The reality, he says, is more challenging.

Hahn agrees. "I think it will take quite

Brain features may someday help doctors diagnose autism. High-risk babies who went on to develop autism had more rapid growth in certain parts of their brains than low-risk babies who didn't develop autism. Darker colors indicate a bigger difference in growth rate; black regions weren't analyzed.

a bit longer" to find clinically useful biomarkers, he says. "It's not what parents want to hear. The thing is, this is a very difficult medical disease with many different manifestations."

Researchers have turned up differences in the brain between people with and without autism, including size and growth patterns, connections between areas and cell behavior. But the variability in autism symptoms — and causes — has prompted scientists to look beyond the brain in the search for biomarkers.

"Autism may not be purely a brain disorder," says Eric Courchesne, a neuroscientist at the University of California, San Diego. Scientists are looking for important clues to autism in gut microbes, skin cells, the immune system and factors that circulate in the blood.

That was the rationale behind Hahn and colleagues' experiment, which compared compounds in the blood of 83 children with autism with those of 76 children without the disorder. The researchers focused on a group of molecules implicated in autism. These molecules carry out an intricate series of metabolic reactions called folatedependent one-carbon metabolism and transsulfuration. Earlier work suggested that these processes are altered in people with autism.

Hahn and colleagues developed a statistical tool that examined the relationships between 24 of these molecules. Instead of looking at the concentration of each individual player, the team wondered if a more global view would help. "Could you find patterns in these that give you a much more predictive pattern than if you look at them one by one?" Hahn asks. The answer, their results showed, was yes.

The statistical tool correctly identified 97.6 percent of the children with autism and 96.1 percent of the children without. Just two of 83 children on the autism spectrum were misclassified as not having autism, and three of 76 children without autism were misclassified as having the disorder. Compared with other methods described in the scientific literature, "the numbers we got out were very, very good," Hahn says.

Those results are "quite interesting as an example of a blood test," says Dwight German, a neuroscientist at the University of Texas Southwestern Medical Center in Dallas. But as a researcher who also works on blood-based biomarkers of autism, German is familiar with a huge caveat: Blood can be fickle. Medications, age and even time of day can influence factors in the blood, he says. "There's an awful lot of testing you have to do to show that what you're measuring is related to the disorder and not what they ate for breakfast."

If these metabolic differences are present just after birth, the blood test could be an extremely early indicator of autism. But much more work is needed to validate the new approach, including tests on children younger than 3, Hahn says.

Other issues need to be resolved, too. When tested on 47 siblings of people with autism, children who presumably share genetics and environment with an affected sibling but who don't have the disorder themselves, the statistical tool's performance worsened a bit. The tool incorrectly classified four of the 47 siblings as having autism.

For tougher distinctions between high-risk kids like these, scientists have had success looking back to the brain. Recently, Piven and colleagues studied babies born to parents who already had a child with autism. These "baby

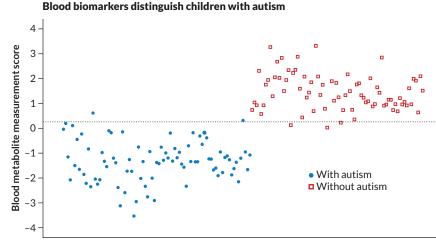
sibs" have about a one in five chance of developing autism themselves, a rate higher than that of a child without a sibling with autism. By studying this high-risk group, Piven and colleagues have found brain features that are associated with even more risk.

Researchers had sus-

pected that at some point early in life, brains grow too much in children who will go on to develop autism. Piven and colleagues scanned the brains of 106 babies with older siblings with autism at 6, 12 and 24 months of age. The researchers also included 42 low-risk infants.

At 6 and 12 months of age, the 15 babies who went on to develop autism had more growth in the outer surface of their brains, the cortex, than both the high-risk babies who didn't develop autism and the low-risk babies, the researchers reported in the Feb. 16 *Nature*. A computer program that analyzed brain growth predicted whether

Blood test After a newly devised mathematical analysis assigned a score based on the level of blood metabolites, samples from children with autism (blue) were clearly distinguishable from samples from kids without autism (red). The method, however, is not ready for use in the clinic.



these high-risk infants would go on to develop autism. On a second set of babies, the classification performed well, successfully identifying eight out of 10 babies who would go on to develop autism by 24 months of age.

Other work by Piven and colleagues has turned up other brain differences

Scientists are simultaneously sanguine and realistic about the prospect of uncovering solid autism biomarkers. in high-risk babies. Babies who will go on to develop autism have more cerebrospinal fluid on a certain part of the outer layer of their brains than those who don't develop the disorder. But the results, published online March 6 in *Biological Psychiatry*, fell short of the predictive power of the

brain overgrowth results.

Both of these brain scan studies apply only to high-risk babies. It's not known whether similar tests would work on children without siblings with autism. But it's possible that these types of detailed findings can help distinguish varieties of autism, and those are distinctions that must be made before scientists can make progress, Piven says. "We call [autism] one thing, but it's many, many different things. And until we are able to grapple with that in a more meaningful way, it's sort of an intractable problem."

Child and adolescent psychiatrist Robert Hendren of the University of California, San Francisco envisions a time when this collection of disorders collectively called autism are all cataloged in detail, thanks to biomarkers. "We'll call it autism 23 or autism 14, and we'll say, 'We know this is the process that's going on, and this is how we're going to personalize our treatments for this person.'"

On the way to that goal, a big breakthrough is unlikely, Piven says. It's not like the discovery of penicillin for bacterial infections. "You give it, and 10 days later, everything is fine. This isn't going to be like that." Even so, the breadth and enthusiasm of the field is promising, he says. "This whole idea of looking at early biomarkers is a new way of thinking, and we have enormous capabilities to make this reality."

Genetic risk of second cancer tallied

Inherited mutations up childhood survivors' odds of later tumors

BY AIMEE CUNNINGHAM

A second cancer later in life is common for childhood cancer survivors, and scientists now have a sense of the role genes play when this happens. A project that mined the genetic data of a group of survivors finds that 11.5 percent carry inherited mutations that increase the risk of a subsequent cancer.

"We've always known that among survivors, a certain population will experience adverse outcomes directly related to therapy," says epidemiologist and team member Leslie Robison of St. Jude Children's Research Hospital in Memphis, Tenn. The project sought "to find out what contribution genetics may play." The team presented the work April 3.

"The results validate the thoughts of those of us who believe there is a genetic risk that increases the risk of second malignancies" in addition to the risk related to treatment, says David Malkin, a pediatric oncologist at the University of Toronto.

Five-year survival rates for kids with cancer have reached over 80 percent. But some survivors develop a later cancer due to radiation or chemotherapy. The team examined 3,007 survivors of pediatric cancer who routinely undergo evaluation at St. Jude. About a third had leukemia as kids. By age 45, 29 percent of survivors had developed new tumors, often in the skin, breast or thyroid.

The team cataloged each survivor's DNA and looked at 156 cancer predisposition genes. Of the survivors, 11.5 percent had a problematic inherited mutation in one of these genes. Some genes convey a higher risk than others, so the team looked at a subset of 60 genes for which only one mutated copy in each cell is enough to cause disease. These 60 genes also have high penetrance — a mutated copy is highly likely to lead to a cancer. Nearly 6 percent of survivors had a problematic mutation in one of these genes.

Survivors were also divided based on whether they had radiation therapy as kids. Nearly 17 percent of survivors who hadn't received radiation had a problematic mutation in the subset of 60 genes. These survivors had an increased risk for any second cancer. Those with both a mutation in one of the 60 genes and radiation in their treatment history had a higher risk for specific kinds of second cancers: breast, thyroid or sarcomas, tumors in connective tissues.

Based on these estimates of genetic risk, the team says survivors not given radiation should undergo genetic counseling if any second cancer develops. But for survivors who had radiation, counseling would be useful only when a secondary breast, thyroid or sarcoma tumor develops in a site that received radiation therapy, says St. Jude epidemiologist and project member Carmen Wilson. Counseling can provide guidance on health practices, reproductive choices and implications for relatives who may also have the mutation, Robison says.

The data could help with future cancer prevention, Robison says. The team would like to create prediction models that consider treatment, genetics and other clinical information to place survivors into different risk groups. "It's eventually going to have clear implications for how these patients are clinically managed, and how we either prevent or ameliorate the adverse effects," he says.

Malkin notes that when an individual got treatment is another factor influencing risk for second cancers, as treatments and doses have changed over time. He also thinks the reported percentage of survivors at risk is lower than expected. "Expanding the pool of genes to look at will be very informative," he says.

MEETING NOTE

Engineered immune cells can boost cancer survival

Immune cells engineered to hunt and destroy cancer cells may help some people with acute lymphoblastic leukemia, or ALL, live much longer. Outcomes depend on disease severity before treatment, oncologist Jae Park reported April 3.

In ALL – expected to strike 5,970 people and kill 1,440 in the United States in 2017 – immune cells called B cells grow out of control in bone marrow and can spread to



other tissues. Five-year survival rates are 71 percent. But after a relapse, less than 10 percent of people survive for five years, said Park, of

Engineered CAR-T cells (one in red, attacking a leukemia cell) were effective for some people against relapses of leukemia over the long term. Memorial Sloan Kettering Cancer Center in New York City.

Park and colleagues genetically engineered T cells from 51 people whose leukemia came back or who didn't respond to chemotherapy. These "CAR-T cells" kill the rogue B cells. Of 20 people who had leukemia cells making up less than 5 percent of their bone marrow, 95 percent had a complete response to treatment. Most are still alive with no signs of leukemia; one patient has been in remission for five years.

But 31 people whose leukemia cells composed more than 5 percent of their bone marrow didn't fare as well. After good initial responses to the therapy, the cancer came back a median of 6.3 months later. Patients survived a median of 17 months, but some are still alive after three years.

Park isn't sure why CAR-T cells work better for some people than others. But, he said, the therapy "still provides better survival than traditional treatments." – *Tina Hesman Saey*

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BODY & BRAIN

Dengue may stoke Zika infections

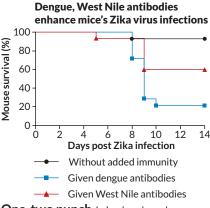
Rogue antibodies help virus enter cells, experiments find

BY AIMEE CUNNINGHAM

Being immune to a virus is a good thing, until it's not. That's the lesson from a study that sought to understand the severity of recent Zika outbreaks. Experiments suggest that prior exposure to dengue or West Nile can worsen a Zika infection.

"Antibodies you generate from the first infection ... can facilitate entry of the Zika virus into susceptible cells, exacerbating the disease outcome," says virologist Jean K. Lim. Lim, of the Icahn School of Medicine at Mount Sinai in New York City, and colleagues report the results online March 30 in *Science*.

The study is the first to demonstrate this effect in mice, as well as the first to implicate West Nile virus, notes Sharon Isern, a molecular virologist at Florida Gulf Coast University in Fort Myers.



One-two punch Lab mice given dengue or West Nile antibodies were more likely to die in the two weeks after a Zika virus infection than mice without those antibodies.

Zika is similar to other types of flaviviruses, sharing about 60 percent of its genetic information with dengue virus and West Nile virus.

Exposure to a virus spurs the body to create antibodies, which typically prevent illness from later infections with the virus. That's not the case for a phenomenon called antibody-dependent enhancement that has been described in dengue patients (*SN: 6/25/16, p. 22*). Dengue

virus has four versions; when a person with immunity to one type gets sick with another type, the illness is worse. Antibodies from the previous exposure help the subsequent dengue virus infect cells.

In one experiment with cell samples, Zika infected cells more efficiently when the virus was mixed with blood plasma from dengue- or West Nile–exposed donors than with plasma from individuals with neither illness. Zika was most aggressive in the presence of dengue.

In mice, more than 93 percent given plasma free of dengue or West Nile survived a Zika infection. But for mice given plasma with dengue antibodies, nearly 80 percent had died by the 10th day of infection. Of mice given plasma with West Nile antibodies, about 40 percent died from the Zika infection.

"This is important because in places where the Zika virus is causing outbreaks, such as South America, there are currently other circulating viruses, such as dengue, which is highly prevalent," says Lim. Zika has entered the United States, where an estimated 3 million residents harbor antibodies to West Nile.

Big quake hopscotched across faults

New Zealand temblor jumped farther than thought possible

BY THOMAS SUMNER

A seemingly impossible earthquake that rattled New Zealand last November casts doubt on how well seismologists can forecast quakes involving multiple faults.

Retracing the path of the magnitude 7.8 temblor using satellite and seismic data, researchers discovered that the quake involved at least 12 major faults and was far more widespread and powerful than predicted by seismic hazard assessments. Such assessments are crucial to designing earthquake-resistant buildings.

The quake, which hit New Zealand's South Island, released pent-up energy along more than 170 kilometers of faults, including ones thought to be too spread out for a rupture to jump between, scientists report online March 23 in *Science*. "This crazy event showed us just how little we knew," says study coauthor Ian Hamling, a geophysicist at GNS Science in Avalon, New Zealand. Many quake simulations artificially limit how far a rupture can hop. Those restrictions, Hamling says, should be toned down or removed.

Quakes that involve multiple faults have been difficult to study, says Thomas Jordan, director of the Southern California Earthquake Center in Los Angeles. His team recently relaxed restrictions on how far a rupture can jump in simulations that forecast the risk of California earthquakes. Making those predictions more accurate will require more observations of complex quakes, Jordan says.

New Zealand's shaking is caused by the ongoing collision of the Australian

and Pacific tectonic plates. When an earthquake occurs, the shaking can trigger earthquakes on nearby faults in a game of seismic hopscotch. A seismic event's overall intensity depends in part on the total length of ruptured faults.

Forecast calculations often assume that a rupture can't jump between faults if the gap is more than 4 or 5 kilometers wide. The New Zealand quake, however, crossed a roughly 15-kilometer-wide gap. That's based on a reconstruction Hamling and colleagues created using GPS data of ground movement and satellite images of how the landscape shifted. Had the rupture stopped at that gap, Hamling estimates, the quake would have released roughly a tenth the amount of energy.

The researchers aren't sure how the quake crossed the gap. The rupture may have continued deep underground before returning to the surface, they propose, or traveled along unmapped faults near the surface to bridge the gap.

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LIFE & EVOLUTION

Glass frog moms do care after all

Just a few hours of maternal attention help eggs survive

BY SUSAN MILIUS

Glass frogs often start life with some tender care from a source scientists didn't expect: frog moms.

Maternal care wouldn't be news among mammals or birds, but amphibian parenting intrigues biologists because dads are about as likely as moms to evolve as the caregiver sex. And among New World glass frogs (family Centrolenidae), what little parental care there is almost always is dad's job — or so scientists thought, says Jesse Delia of Boston University.

Months of nights searching leaves in Mexico, Panama, Colombia, Ecuador and Peru, however, have revealed a widespread world of brief, but important, female care. In examining 40 species, Delia and Laura Bravo-Valencia, now at Corantioquia, a government environmental agency in Colombia, found that often mothers lingered over newly laid eggs for up to several hours. By pressing their bellies against the brood, moms hydrated the jelly-glop of eggs and improved offspring chances of survival, Delia, Bravo-Valencia and Karen Warkentin, also of BU, report online March 31 in the Journal of Evolutionary Biology.

Glass frogs aren't exactly obscure species, but until this field project during rainy seasons from 2010 to 2016, female care in the family was unconfirmed.

Female glass frogs may not cuddle their eggs for long, but it's enough to matter, the researchers found. As is common in frogs, the mothers absorb water directly through belly skin into a bladder. Moms pressing against a mass of newly laid eggs caused the protective goo to swell — perhaps by osmosis or peeing — and the mass to quadruple in size. For some of the glass frogs in the study, the youngsters were on their own once mom left. But at least hydration created an unpleasant amount of slime for a predator to bite through. Night-hunting katydids in captivity barely nibbled at a hydrated mass of frog offspring, concentrating instead on an unhydrated clutch. In the field, when researchers removed two dozen moms from clutches in two species, mortality doubled or more to around 80 percent for each species. Predators and dehydration caused the most deaths.

There are still over 100 glass frog species that the team hasn't yet watched in the wild. But the researchers did witness maternal care in 10 of 12 genera. Such a widespread form of maternal care probably evolved in the ancestor of all glass frogs, the researchers propose after analyzing glass frog family trees.

In contrast, prolonged care from glass frog dads — rehydrating eggs as needed and fighting off predators — seems to have arisen independently later, at least twice.

Why females started hanging around



The few hours that a mother Cochranella granulosa glass frog (shown in Panama) huddles over her brood may be brief, but that attention boosts offspring survival.

their eggs at all fascinates Hope Klug, an evolutionary biologist at the University of Tennessee at Chattanooga. In frogs, with eggs mostly fertilized externally, females could easily leave any care to dad. "Parental care is perhaps more common and diverse in animals than we realize," she says. "We just might have to look a little bit harder for it."

Big black hole gets kicked to the curb

Gravitational waves may have delivered push toward deep space

BY ASHLEY YEAGER

A black hole weighing more than a billion suns appears to have gotten the boot toward the outer edges of its galaxy.

Data from the Hubble Space Telescope and other observatories reveal a supermassive black hole zipping away from the center of its galaxy at 7.5 million kilometers per hour. At that rate, it could leave the galaxy for good in 20 million years, says Marco Chiaberge of the Space Telescope Science Institute in Baltimore.

Only gravitational waves — ripples in the fabric of spacetime — could give the black hole such a kick, Chiaberge and colleagues report in the April *Astronomy & Astrophysics*. The work offers some of the best evidence that gravitational waves can kick black holes out of galaxies.

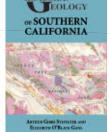
"This is a very nice candidate for a recoiling supermassive black hole," says Francesca Civano, an astrophysicist at the Harvard-Smithsonian Center for Astrophysics. Recoiling black holes form when two big black holes from different galaxies merge, Civano says. If the black holes have different masses and rotate at different rates, the collision can generate gravitational waves more strongly in one direction, booting the merged black hole the other way.

The position of a radiation-gushing supermassive black hole called quasar 3C 186 in its galaxy, about 8 billion lightyears from Earth in the constellation Lynx, tipped off Chiaberge's team to the possibility it had spotted a recoiling black hole. The quasar wasn't at the center of the galaxy, where it typically should be.

The team compared how fast the gas surrounding 3C 186 moves with the speed of star-forming gas in its galaxy. 3C 186's velocity is so great that it must be the result of something forceful, equivalent to 100 million stars exploding. Gravitational waves could provide such a kick.

Hubble images also revealed wisps of stars and gas extending from the galaxy. Such faint tails suggest that it had indeed collided with another galaxy in the past.

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The wide-open spaces of Joshua Tree National Park are ideal for the teddy bear cholla cactus, a beautiful plant that you will regret getting too close to. (33°55.50N, 115°55.77W) —Ivar Midtkandalen photo

JOSHUA TREE NATIONAL PARK

Joshua Tree National Park covers a land area of 1,235 square miles-an area slightly larger than Rhode Island-and nearly 914 square miles are designated wilderness. The park is located in the Little San Bernardino Mountains, part of the eastern Transverse Ranges between the Salton Trough of the Colorado Desert and the Mojave Desert. Geologically, the park's rocks and structures belong to the Mojave Desert.

Much of the north half of the park consists of granite, part of the huge intrusion of magma that formed the batholiths of the Sierra Nevada and Peninsular Ranges when the Farallon Plate subducted beneath the North American Plate in Mesozoic time. Proterozoic granite and metamorphic rocks, intruded by the granite, are also exposed in the park. Metasedimentary rocks, metamorphosed before Cretaceous time, crop out in some less accessible areas. The best place to see Proterozoic rocks is in a few roadcuts between I-10 and the Cottonwood Springs entrance station, where Pinto Gneiss is exposed.

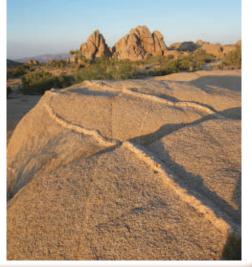
Granite is exposed and accessible in the Wonderland of Rocks, especially in the Jumbo Rocks and White Tank areas. Rock climbers love this 12-square-mile maze of jumbled granite boulders and rock piles, rounded knobs and towers, gentle domes, and smooth cliffs. Look for Arch Rock in White Tank Campground, the Old Woman and Cyclops Rock in Hidden Valley Campground, the Trojan and the Ox along the Hidden Valley Nature Trail, Bread Loaf Rock near Belle Campground, and Skull Rock near Jumbo Rocks Campground.

If you climb some gentle outcrops of granite, you'll notice large, blocky crystals of white or gray potassium feldspar set among minerals grains that are all about the same size. Based on the kind and abundance of minerals, geologists give separate and daunting names to granitic rocks, such as syenogranite, monzogranite, granodiorite, tonalite, and monzonite. Some of them take the name of the place where they are exposed, such as Twentynine Palms quartz monzonite and White Tank monzodiorite. The distinctions among them may be subtle and difficult without careful analysis, especially when cruising at the park's designated speed limits.

If you walk on and around the granitic rocks and through some of the ravines, you'll notice white veins slicing across the granite here and there. These light-colored, fine-grained veins of quartz and feldspar are called aplite dikes, whereas those with large crystals of quartz, feldspar, and mica are pegmatite dikes. They intruded along cracks and joints in the granite when it was cool enough to fracture but still contained some melted rock that could fill and crystallize in those fractures.

Several major faults bound Joshua Tree National Park and are considered active. Strands of the San Andreas fault lie along the southwest edge of the park in Coachella Valley. The Blue Cut fault slices east-west through the center of the park, and the Pinto Mountain fault comes out of Morongo Valley along the north edge of the park. You won't see much of these two faults, because they lie beneath valley fill, but some faults are nicely exposed along the Geology Tour Road and in canyons along the northeast edge of Coachella Valley.

Fine-grained aplite dikes of quartz and feldspar intruded this granite and are more resistant to erosion than the granite. (33°59.12N, 116°00.94W) -Tyson McKinney photo



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Romans, Huns sometimes got along

Along Rome's frontier, nomads and farmers swapped menus

BY BRUCE BOWER

Nomadic warriors and herders known as the Huns are described in historical accounts as having instigated, under Attila's leadership, the fifth century fall of the Roman Empire. But the invaders weren't always so fierce. Sometimes they shared rather than fought with the Romans, new evidence suggests.

Huns and farmers living around the Roman Empire's border in eastern Europe, where the Danube River runs through present-day Hungary, borrowed ways of life from each other during the fifth century, say archaeologist Susanne Hakenbeck of the University of Cambridge and colleagues. Nomadic Huns on the Roman frontier raised relatively small numbers of animals and grew some crops, while border-zone farmers incorporated more meat into what had been a wheat- and vegetable-heavy diet, the scientists report March 22 in *PLOS ONE*.

"Our data show that the dietary strategies of the people on both sides of the Roman frontier were not fundamentally different," Hakenbeck says.

The findings challenge a traditional view of the Huns as marauders who

Nomadic Huns and Roman farmers influenced each other. That finding comes from a study of bones (including this skull elongated from binding) from Roman frontier sites. Binding is thought to have originated among the Huns.

says. No cultivation that can horses Here peop varita SCIENCE NEWS | April 29, 2017

roamed hundreds of kilometers from Central Asia to Europe. There's no evidence of major social upheavals or a

"The dietary

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different."

SUSANNE HAKENBECK

geographically distinctive group of newcomers at the frontier sites, so at least some Huns may have been homegrown, Hakenbeck suggests. Rapidly forming groups of Hun warriors and herders on horseback could have emerged in southeastern Europe not far from the Roman Empire's border, perhaps supplemented by nomadic newcomers from farther east near the Black Sea, she proposes.

Still, geographic origins of the Huns are tough to pin down, says archaeologist Ursula Brosseder of the University of Bonn in Germany. The Huns developed as a political movement that picked up members from various ethnic groups as it spread, she explains. Brosseder suspects the "Hun phenomenon" formed on the grasslands of western Eurasia, a territory that includes regions cited by Hakenbeck. The earliest evidence of Huns in that region dates to about 2,400 years ago.

The new study supports the idea that herding communities adapted flexibly to new environments, sometimes relying only on their livestock and at other times farming to varying extents, Brosseder says. Nomadic herders in Asia probably cultivated millet, a fast-growing cereal that can be used to feed people and horses, Hakenbeck says.

Her group studied skeletons of 234 people buried at five previously excavated sites on or near the Roman frontier. Each site contained evidence of contact with Huns, including bronze artifacts and adult skulls with elongated braincases created by binding the head during childhood. Reasons for this practice are poorly understood. It may have signified affiliation with the Huns or social status of some kind.

Graves at a Roman fort and a nearby cemetery lay on Roman land, about 150 kilometers from the frontier. Another two cemeteries were on the banks of

> the Danube River, directly on the Roman frontier. The researchers suspect these two cemeteries held Romans or a mix of Romans and nomads. A final graveyard fell outside Roman territory, about 150 kilometers east of the border.

> Measurements of ratios of specific forms of carbon, nitrogen and oxygen in teeth and ribs enabled the scientists to identify what types of

plants and how much meat or milk individuals ate during childhood, early adulthood and toward the end of their lives.

Results pointed to considerable consumption of cultivated plants, most likely millet, as well as meat or milk at all five sites, indicating farmers and nomads had influenced each other's diets. Variations on this pattern occurred across sites and among individuals at each site, suggesting that groups and individuals rapidly adjusted how much they farmed or herded as circumstances dictated.

"This mixing and matching was likely a kind of economic insurance policy in violent and unstable times," Hakenbeck says.

Hakenbeck's group also measured another tooth element, strontium, to determine whether individuals at four of the sites had grown up drinking water and eating food in the locales where they were buried. Between 30 and 50 percent of individuals studied at those sites were not locals, Hakenbeck says. The birthplaces of these people remain a mystery.

In many cases, both newcomers and natives to the Roman frontier substantially changed their eating habits over the course of their lives, the researchers find. That fits Hakenbeck's "mix and match" scenario, in which a fluctuating diet aided survival on the Roman Empire's edge.



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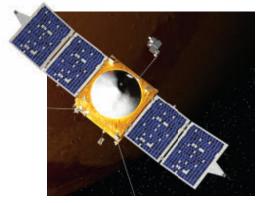
ATOM & COSMOS

Extreme gas loss dried out Mars The Martian atmosphere definitely had more gas in the past.

Data from NASA's MAVEN spacecraft indicate that Mars has lost most of the gas that ever existed in its atmosphere. The results, published in the March 31 *Science*, are the first to quantify how much gas has been lost with time and offer clues to how the Red Planet became a cold, dry place.

Charged particles from the sun constantly bombard Mars. Without a magnetic field to deflect this solar wind, the planet loses about 100 grams of its now thin atmosphere every second (SN: 12/12/15, p. 31). To determine how much atmosphere has been lost during the planet's lifetime, Bruce Jakosky of the University of Colorado Boulder and colleagues measured and compared the abundances of two argon isotopes at different altitudes. Using those measurements and an assumption about the amounts of the isotopes in Mars' early atmosphere, the team calculated that about two-thirds of all of the planet's argon has been ejected into space. Extrapolating from these data, the team estimates that Mars has lost the majority of its atmospheric carbon dioxide.

A thicker atmosphere filled with CO_2 and other greenhouse gases could have insulated early Mars and kept it warm enough for liquid water and possibly life. Losing an extreme amount of gas may explain how the planet morphed from lush and wet to barren and icy, the researchers write. – Ashley Yeager



Over Mars' lifetime, solar wind has expelled much of the planet's atmospheric gas, data from the MAVEN probe (illustrated) suggest.

EARTH & ENVIRONMENT

Thinning ice creates undersea greenhouses in the Arctic

Sea ice skylights formed as Arctic temperatures rise increasingly allow enough sunlight into the waters below to permit phytoplankton blooms, new research suggests. Conditions favorable for blooms were probably rare two decades ago but now extend to about 30 percent of the ice-covered Arctic Ocean in July, scientists report March 29 in *Science Advances*.

Phytoplankton need plenty of light to thrive, so scientists were stunned by the discovery of a sprawling bloom below the normally sun-blocking Arctic ice in July 2011 (*SN*: 7/28/12, p. 17). Satellites can't peek below the ice, so scientists didn't know whether the bloom was an oddity.

Harvard University oceanographer Christopher Horvat and colleagues have now created a computer simulation of sea ice from 1986 to 2015. Warming has thinned the ice, the team found, and increased the prevalence of meltwater pools that allow more light to pass through than bare or snow-covered ice.

Whether blooms, which would alter food webs and soak up more planetwarming carbon dioxide, are more common under the ice remains unclear. The study didn't consider whether there are enough nutrients for budding blooms. – Thomas Sumner

BODY & BRAIN

Food odors entice tired brains SAN FRANCISCO – The nose knows when you're tired.

Sleep deprivation seems to increase the brain's sensitivity to food smells, researchers reported March 27 at the Cognitive Neuroscience Society's annual meeting. That might make snacks more enticing, helping to explain why people who burn the candle at both ends tend to eat more and gain weight.

In a new study, adults who'd had only four hours of sleep inhaled food odors such as those from potato chips and nonfood smells like fir trees while undergoing functional MRI scans. (The scientists controlled food intake during the day.) A few weeks later, the participants repeated the test but after eight hours of sleep.

When tired, people had more brain activity in areas involved in olfaction — the piriform cortex and the orbitofrontal cortex — in response to food smells than when well-rested. That spike wasn't seen for nonfood odors, said Surabhi Bhutani of Northwestern University's medical school in Chicago. Though preliminary, the results fit with previous work showing a link between sleep deprivation and both excessive calorie consumption and weight gain (SN: 8/24/13, p. 18). — Laurel Hamers

BODY & BRAIN

More brain differences seen between girls, boys with ADHD

SAN FRANCISCO – Girls and boys with attention-deficit/hyperactivity disorder don't just behave differently. Parts of their brains look different, too. The cerebellum can be added to that mismatch, researchers reported March 25 at the Cognitive Neuroscience Society's annual meeting.

For boys, ADHD symptoms tend to include poor impulse control and disruptive behavior. Girls more often have difficulty staying focused. These differences are reflected in brain structure: Boys are more likely to show abnormalities in premotor and primary motor circuits, Stewart Mostofsky of Kennedy Krieger Institute in Baltimore has reported.

Now, Mostofsky and colleagues have looked at the cerebellum, which helps coordinate movement. Girls ages 8 to 12 with ADHD showed differences in the volume of various cerebellum regions compared with girls without the condition, MRI scans revealed. A similar comparison of boys showed abnormalities, too. But the types of differences didn't match what's seen between girls. So far, researchers have looked at 18 subjects in each of the four groups but plan to quintuple that number in the coming months.

Differences between boys and girls seem most prominent in areas that control higher-order motor functions. Those circuits help regulate attention and planning versus directing basics like hand-eye coordination, which may help explain why ADHD affects girls' behavior differently than boys'. – Laurel Hamers



TEXAS TECH

UNIVERSITY.

Berto Garicia, Sophmore Computer Engineering major

In high school, Berto Garcia suffered a **concussion** playing football. That led to a science fair project and the creation of a **helmet-and-shoulder pads system that stabilizes the head immediately after impact.** It's a revolutionary concept that has garnered interest from the U.S. Military and national engineering organizations. His **passion for research and discovery** led him to **Texas Tech University** where he is continuing his work on this project and also focusing on his next great idea.

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The Proton Puzzle

A subatomic particle goes through an identity crisis By Emily Conover

uclear physicist Evangeline Downie hadn't planned to study one of the thorniest puzzles of the proton. But when opportunity knocked, Downie couldn't say no. "It's the *proton*," she exclaims. The mysteries that still swirl around this jewel of the subatomic realm were too tantalizing to resist. The plentiful particles make up much of the visible matter in the universe. "We're made of them, and we don't understand them fully," she says.

Many physicists delving deep into the heart of matter in recent decades have been lured to the more exotic and unfamiliar subatomic particles: mesons, neutrinos and the famous Higgs boson — not the humble proton.

But rather than chasing the rarest of the rare, scientists like Downie are painstakingly scrutinizing the proton itself with ever-higher precision. In the process, some of these proton enthusiasts have stumbled upon problems in areas of physics that scientists thought they had figured out.

Surprisingly, some of the particle's most basic characteristics are not fully pinned down. The latest measurements of its radius disagree with one another by a wide margin, for example, a fact that captivated Downie. Likewise, scientists can't yet explain the source of the proton's spin, a basic quantum property. And some physicists have a deep but unconfirmed suspicion that the seemingly eternal particles don't live forever – protons may decay. Such a decay is predicted by theories that unite disparate forces of nature under one grand umbrella. But decay has not yet been witnessed.

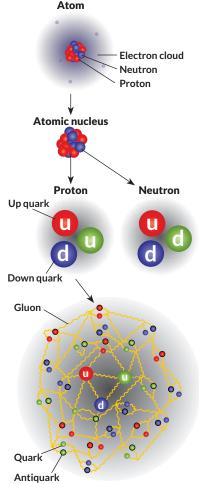
Like the base of a pyramid, the physics of the proton serves as a foundation for much of what scientists know about the behavior of matter. To understand the intricacies of the universe, says Downie, of George Washington University in Washington, D.C., "we have to start with, in a sense, the simplest system."

Sizing things up

For most of the universe's history, protons have been VIPs-very important particles. They formed just millionths of a second after the Big Bang, once the cosmos cooled enough for the positively charged particles to take shape. But protons didn't step into the spotlight until about 100 years ago, when Ernest Rutherford bombarded nitrogen with radioactively produced particles, breaking up the nuclei and releasing protons.

A single proton in concert with a single electron makes up hydrogen - the most plentiful element in the universe. One or more protons are present in the nucleus of every atom. Each element has a unique number of protons, signified by an element's atomic number. In the core of the sun, fusing protons generate heat and light needed for life to flourish. Lone protons are also found as cosmic rays, whizzing through space at breakneck speeds, colliding with Earth's atmosphere and producing showers of other particles, such as electrons, muons and neutrinos.

In short, protons are everywhere. Even minor tweaks to scientists' understanding of the minuscule particle, therefore, could have far-reaching implications. So any nagging questions, however small in scale, can get proton researchers riled up.



A disagreement of a few percent in measurements of the proton's radius has attracted intense interest, for example. Until several years ago, scientists agreed: The proton's radius was about 0.88 femtometers, or 0.88 millionths of a billionth of a meter – about a trillionth the width of a poppy seed.

But that neat picture was upended in the span of a few hours, in May 2010, at the Precision Physics of Simple Atomic Systems conference in Les Houches, France. Two teams of scientists presented new, more precise measurements, unveiling what they thought would be the definitive size of the proton. Instead the figures disagreed by about 4 percent (SN: 7/31/10, p. 7). "We

Protons have issues Three proton conundrums have scientists designing new experiments. Agreement eludes researchers on proton size, spin and stability. Life span	Proton property	Current status	Why do we care?
	Radius	Two kinds of measurements of the proton's radius disagree.	Testing theories of how particles interact requires a precise radius measurement. If the discrepancy persists, it may mean that new, undiscovered particles exist.
	Spin	Scientists can't account for the sources of the proton's known spin.	Understanding the spin would satisfy fundamental scientific curiosity about how the proton works.
	Life span	Despite decades of searching, no one has ever seen a proton decay.	Proton decay would be a sign that three of nature's forces — weak, strong and electromagnetic — were united early in the universe.

Ladder of matter

Protons make up a large part of the universe's visible matter and play an essential role in atomic nuclei. But the building block is still revealing surprises.

Core components

Atoms are made of protons (red) and neutrons (blue), surrounded by a cloud of electrons. The proton number determines the element.

Going inside Protons have two "up" quarks and one "down" guark. Neutrons have two downs and one up.

Deeper dive But protons and neutrons contain much more. Quarkantiquark pairs constantly form and annihilate around the three persistent quarks. Gluons (yellow) hold the quarks together via the strong nuclear force. Quarks have a property called "color charge" - shown here as red, green and blue - which is related to the strong force.

FEATURE | THE PROTON PUZZLE

both expected that we would get the same number, so we were both surprised," says physicist Jan Bernauer of MIT.

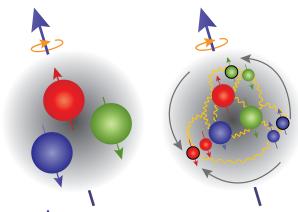
By itself, a slight revision of the proton's radius wouldn't upend physics. But despite extensive efforts, the groups can't explain why they get different numbers. As researchers have eliminated simple explanations for the impasse, they've begun wondering if the mismatch could be the first hint of a breakdown that could shatter accepted tenets of physics.

The two groups each used different methods to size up the proton. In an experiment at the MAMI particle accelerator in Mainz, Germany, Bernauer and colleagues estimated the proton's girth by measuring how much electrons' trajectories were deflected when fired at protons. That test found the expected radius of about 0.88 femtometers (*SN Online: 12/17/10*).

But a team led by physicist Randolf Pohl of the Max Planck Institute of Quantum Optics in Garching, Germany, used a new, more precise method. The researchers created muonic hydrogen, a proton that is accompanied not by an electron but by a heftier cousin — a muon.

In an experiment at the Paul Scherrer Institute in Villigen, Switzerland, Pohl and collaborators used lasers to bump the muons to higher energy levels. The amount of energy required depends on the size of the proton. Because the more massive muon hugs closer to the proton than electrons do, the energy levels of muonic hydrogen are more sensitive to the proton's size than ordinary hydrogen, allowing for measurements 10 times as precise as electron-scattering measurements.

Pohl's results suggested a smaller proton radius, about 0.841 femtometers, a stark difference from the other measurement. Follow-up measurements of muonic deuterium — which has a proton and a neutron in its nucleus — also revealed a smaller than expected size, he and collaborators reported last year in *Science*. Physicists have racked their brains to explain why the two measurements don't agree. Experimental error could be to blame, but no one can pinpoint its source. And the theoretical physics used to calculate the radius from the experimental data seems solid.



A new spin Scientists thought that a proton's spin was due to the three main quarks (left, arrows indicate direction of a quark's spin). Instead, gluons (yellow) and ephemeral pairs of quarks and antiquarks contribute through their spin and motion (gray arrows at right).

Now, more outlandish possibilities are being tossed around. An unexpected new particle that interacts with muons but not electrons could explain the difference (*SN: 2/23/13, p. 8*). That would be revolutionary: Physicists believe that electrons and muons should behave identically in particle interactions. "It's a very sacred principle in theoretical physics," says John Negele, a theoretical particle physicist at MIT. "If there's unambiguous evidence that it's been broken, that's really a fundamental discovery."

But established physics theories die hard. Shaking the foundations of physics, Pohl says, is "what I dream of, but I think that's not going to happen." Instead, he suspects, the discrepancy is more likely to be explained through minor tweaks to the experiments or the theory.

The alluring mystery of the proton radius reeled Downie in. During conversations in the lab with some fellow physicists, she learned of an upcoming experiment that could help settle the issue. The experiment's founders were looking for collaborators, and Downie leaped on the bandwagon. The Muon Proton Scattering Experiment, or MUSE, to take place at the Paul Scherrer Institute beginning in 2018, will scatter both electrons and muons off of protons and compare the results. It offers a way to test whether the two particles behave differently, says Downie, who is now a spokesperson for MUSE.

A host of other experiments are in progress or planning stages. Scientists with the Proton Radius Experiment, or PRad, located at Jefferson Lab in Newport News, Va., hope to improve on Bernauer and colleagues' electron-scattering measurements. PRad researchers are analyzing their data and should have a new number for the proton radius soon.

But for now, the proton's identity crisis, at least regarding its size, remains. That poses problems for ultrasensitive tests of one of physicists' most essential theories. Quantum electrodynamics, or QED, the theory that unites quantum mechanics and Albert Einstein's special theory of relativity, describes the physics of electromagnetism on small scales. Using this theory, scientists can calculate the properties of quantum systems, such as hydrogen atoms, in exquisite detail — and so far the predictions match reality. But such calculations require some input — including the proton's radius. Therefore, to subject the theory to even more stringent tests, gauging the proton's size is a must-do task.

Spin doctors

Even if scientists eventually sort out the proton's size snags, there's much left to understand. Dig deep into the proton's guts, and the seemingly simple particle becomes a kaleidoscope of complexity. Rattling around inside each proton is a trio of particles called quarks: one negatively charged "down" quark and two positively charged "up" quarks. Neutrons, on the flip side, comprise two down quarks and one up quark.

Yet even the quark-trio picture is too simplistic. In addition to the three quarks that are always present, a chaotic swarm of transient particles churns within the proton. Evanescent throngs of additional quarks and their antimatter partners, antiquarks, continually swirl into existence, then annihilate each other. Gluons, the particle "glue" that holds the proton together, careen between particles. Gluons are the messengers of the strong nuclear force, an interaction that causes quarks to fervently attract one another.

As a result of this chaos, the properties of protons — and neutrons as well — are difficult to get a handle on. One property, spin, has taken decades of careful investigation, and it's still not sorted out. Quantum particles almost seem to be whirling at blistering speed, like the Earth rotating about its axis. This spin produces angular momentum — a quality of a rotating object that, for example, keeps a top revolving until friction slows it. The spin also makes protons behave like tiny magnets, because a rotating electric charge produces a magnetic field. This property is the key to the medical imaging procedure called magnetic resonance imaging, or MRI.

But, like nearly everything quantum, there's some weirdness mixed in: There's no actual spinning going on. Because fundamental particles like quarks don't have a finite physical size — as far as scientists know — they can't twirl. Despite the lack of spinning, the particles still behave like they have a spin, which can take on only certain values: integer multiples of 1/2.

Quarks have a spin of 1/2, and gluons a spin of 1. These spins combine to help yield the proton's total spin. In addition, just as the Earth is both spinning about its own axis and orbiting the sun, quarks and gluons may also circle about the proton's center, producing additional angular momentum that can contribute to the proton's total spin.

Somehow, the spin and orbital motion of quarks and gluons

t = 0
Big Bang
t < 10⁻⁶ seconds Quarks and gluons roam freely
t = 10 ⁻⁶ s Protons and neutrons form
t = 10s Protons and neutrons begin to form atomic nuclei
t = 13.8 billion years In today's universe, atoms have formed into stars, planets and intelligent life.
t = 10³⁴ years or later A substantial portion of protons may have decayed.
Cosmic time Protons have been around since the early moments of the universe. If certain theories are correct, the universe may eventually

be devoid of protons.

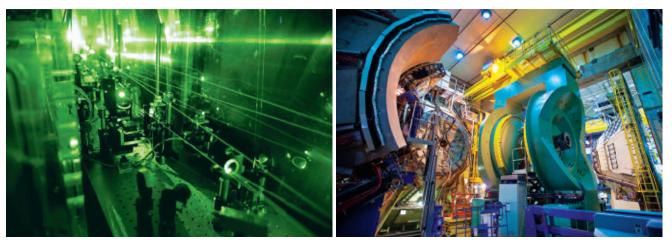
within the proton combine to produce its spin of 1/2. Originally, physicists expected that the explanation would be simple. The only particles that mattered, they thought, were the proton's three main quarks, each with a spin of 1/2. If two of those spins were oriented in opposite directions, they could cancel one another out to produce a total spin of 1/2. But experiments beginning in the 1980s showed that "this picture was very far from true," says theoretical high-energy physicist Juan Rojo of Vrije University Amsterdam. Surprisingly, only a small fraction of the spin seemed to be coming from the quarks, befuddling scientists with what became known as the "spin crisis" (*SN: 9/6/97, p. 158*). Neutron spin was likewise enigmatic.

Scientists' next hunch was that gluons contribute to the proton's spin. "Verifying this hypothesis was very difficult," Rojo says. It required experimental studies at the Relativistic Heavy Ion Collider, RHIC, a particle accelerator at Brookhaven National Laboratory in Upton, N.Y.

In these experiments, scientists collided protons that were polarized: The two protons' spins were either aligned or pointed in opposite directions. Researchers counted the products of those collisions and compared the results for aligned and opposing spins. The results revealed how much of the spin comes from gluons. According to an analysis by Rojo and colleagues, published in *Nuclear*

Physics B in 2014, gluons make up about 35 percent of the proton's spin. Since the quarks make up about 25 percent, that leaves another 40 percent still unaccounted for.

"We have absolutely no idea how the entire spin is made up," says nuclear physicist Elke-Caroline Aschenauer of Brookhaven. "We maybe have understood a small fraction of it." That's because each quark or gluon carries a certain



Proton detectives use equipment that fits on a tabletop – or fills a cavernous room. At the Max Planck Institute of Quantum Optics, researchers use lasers (left) to study proton size. The PHENIX experiment at Brookhaven National Laboratory uses a giant detector (right) to investigate spin.

FEATURE | THE PROTON PUZZLE

fraction of the proton's energy, and the lowest energy quarks and gluons cannot be spotted at RHIC. A proposed collider, called the Electron-Ion Collider (location to be determined), could help scientists investigate the neglected territory.

The Electron-Ion Collider could also allow scientists to map the still-unmeasured orbital motion of quarks and gluons, which may contribute to the proton's spin as well.

An unruly force

Experimental physicists get little help from theoretical physics when attempting to unravel the proton's spin and its other perplexities. "The proton is not something you can calculate from first principles," Aschenauer says. Quantum chromodynamics, or QCD – the theory of the quark-corralling strong force transmitted by gluons – is an unruly beast. It is so complex that scientists can't directly solve the theory's equations.

The difficulty lies with the behavior of the strong force. As long as quarks and their companions stick relatively close, they are happy and can mill about the proton at will. But absence makes the heart grow fonder: The farther apart the quarks get, the more insistently the strong force pulls them back together, containing them within the proton. This behavior explains why no one has found a single quark

in isolation. It also makes the proton's properties especially difficult to calculate. Without accurate theoretical calculations, scientists can't predict what the proton's radius should be, or how the spin should be divvied up.

To simplify the math of the proton, physicists use a technique called lattice QCD, in which they imagine that the world is made of a grid of points in space and time (*SN*: 8/7/04, p. 90). A quark can sit at one point or another in the grid, but not in the spaces in between. Time, likewise, proceeds in jumps. In such a situation, QCD becomes more manageable, though calculations still require powerful supercomputers.

Lattice QCD calculations of the proton's spin are making progress, but there's still plenty of uncertainty. In 2015, theoretical particle and nuclear physicist Keh-Fei Liu and colleagues calculated the spin contributions from the gluons, the quarks and the quarks' angular momentum, reporting the results in *Physical Review D*. By their calculation, about half of the spin comes from the quarks' motion within the proton, about a quarter from the quarks' spin, with the last quarter or so from the gluons. The numbers don't exactly match the experimental measurements, but that's understandable — the lattice QCD numbers are still fuzzy. The calculation relies on various approximations, so it "is not cast in stone," says Liu, of the University of Kentucky in Lexington.

Death of a proton

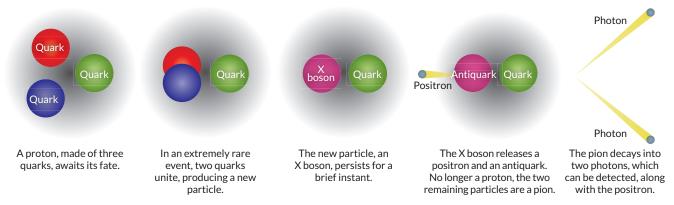
Although protons seem to live forever, scientists have long questioned that immortality. Some popular theories predict that protons decay, disintegrating into other particles over long timescales. Yet despite extensive searches, no hint of this demise has materialized.

> A class of ideas known as grand unified theories predict that protons eventually succumb. These theories unite three of the forces of nature, creating a single framework that could explain electromagnetism, the strong nuclear force and the weak nuclear force, which is responsible for certain types of radioactive decay. (Nature's fourth force, gravity, is

not yet incorporated into these models.) Under such unified theories, the three forces reach equal strengths at extremely high energies. Such energetic conditions were present in the early universe — well before protons formed — just a trillionth of a trillionth of a trillionth of a second after the Big Bang. As the cosmos cooled, those forces would have separated into three different facets that scientists now observe.

"We have a lot of circumstantial evidence that something like unification must be happening," says theoretical highenergy physicist Kaladi Babu of Oklahoma State University in Stillwater. Beyond the appeal of uniting the forces, grand unified theories could explain some curious coincidences of physics, such as the fact that the proton's electric charge precisely balances the electron's charge. Another bonus is that

End of a proton If theories that unite fundamental forces are correct, protons should decay, with average lifetimes longer than the age of the universe. Scientists watch giant tanks of water for the telltale signatures of proton death. One possible type of decay is described below.



The farther apart the quarks get, the more insistently the strong force pulls them back together. the particles in grand unified theories fill out a family tree, with quarks becoming the kin of electrons, for example.

Under these theories, a decaying proton would disintegrate into other particles, such as a positron (the antimatter version of an electron) and a particle called a pion, composed of a quark and an antiquark, which itself eventually decays. If such a grand unified theory is correct and protons do decay, the process must be extremely rare — protons must live a very long time, on average, before they break down. If most protons decayed rapidly, atoms wouldn't stick around long either, and the matter that makes up stars, planets — even human bodies — would be falling apart left and right.

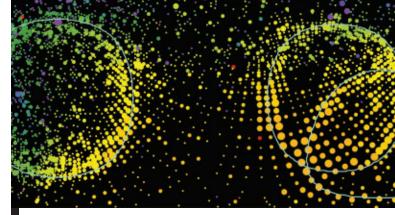
Protons have existed for 13.8 billion years, since just after the Big Bang. So they must live exceedingly long lives, on average. But the particles could perish at even longer timescales. If they do, scientists should be able to monitor many particles at once to see a few protons bite the dust ahead of the curve (*SN*: 12/15/79, p. 405). But searches for decaying protons have so far come up empty.

Still, the search continues. To hunt for decaying protons, scientists go deep underground, for example, to a mine in Hida, Japan. There, at the Super-Kamiokande experiment (*SN: 2/18/17, p. 24*), they monitor a giant tank of water – 50,000 metric tons' worth – waiting for a single proton to wink out of existence. After watching that water tank for nearly two decades, the scientists reported in the Jan. 1 *Physical Review D* that protons must live longer than 1.6×10^{34} years on average, assuming they decay predominantly into a positron and a pion.

Experimental limits on the proton lifetime "are sort of painting the theorists into a corner," says Ed Kearns of Boston University, who searches for proton decay with Super-K. If a new theory predicts a proton lifetime shorter than what Super-K has measured, it's wrong. Physicists must go back to the drawing board until they come up with a theory that agrees with Super-K's proton-decay drought.

Many grand unified theories that remain standing in the wake of Super-K's measurements incorporate supersymmetry, the idea that each known particle has another, more massive partner. In such theories, those new particles are additional pieces in the puzzle, fitting into an even larger family tree of interconnected particles. But theories that rely on supersymmetry may be in trouble. "We would have preferred to see supersymmetry at the Large Hadron Collider by now," Babu says, referring to the particle accelerator located at the European particle physics lab, CERN, in Geneva, which has consistently come up empty in supersymmetry searches since it turned on in 2009 (*SN: 10/1/16, p. 12*).

But supersymmetric particles could simply be too massive for the LHC to find. And some grand unified theories that don't require supersymmetry still remain viable. Versions of these theories predict proton lifetimes within reach of an upcoming generation of experiments. Scientists plan to follow up Super-K with Hyper-K, with an even bigger tank of water. And DUNE, the Deep Underground Neutrino Experiment, planned for



Persnickety protons

Scientists might solve some of their proton dilemmas with new data — for example, by spotting a proton decaying into a positron and two photons, as in the simulated data from the Super-Kamiokande detector above. But plenty more questions await exploration.

- Why are quarks confined within the proton? Scientists observe that quarks don't live on their own, but no one has been able to mathematically demonstrate that they can't.
- How are the quarks and gluons arranged inside the proton? Gluons might be more common on the proton's outskirts than in its center, for example.
- Each quark and gluon carries a certain amount of the proton's energy. How is that energy divvied up?
- Aside from their electric charges, protons and antiprotons appear the same. Do they differ on some level not yet measured?

installation in a former gold mine in Lead, S.D., will use liquid argon to detect protons decaying into particles that the water detectors might miss.

If protons do decay, the universe will become frail in its old age. According to Super-K, sometime well after its 10³⁴ birthday, the cosmos will become a barren sea of light. Stars, planets and life will disappear. If seemingly dependable protons give in, it could spell the death of the universe as we know it.

Although protons may eventually become extinct, proton research isn't going out of style anytime soon. Even if scientists resolve the dilemmas of radius, spin and lifetime, more questions will pile up — it's part of the labyrinthine task of studying quantum particles that multiply in complexity the closer scientists look. These deeper studies are worthwhile, says Downie. The inscrutable proton is "the most fundamental building block of everything, and until we understand that, we can't say we understand anything else."

Explore more

- Randolf Pohl et al. "Laser spectroscopy of muonic deuterium." Science. August 12, 2016.
- Brookhaven National Laboratory. "Spin physics." www.bnl.gov/rhic/spin.asp
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FEATURE



A venomous reef stonefish (*Synanceia* verrucosa) is camouflaged as a rock in the Indian Ocean. Stings from the spines of this species are very painful.

28 SCIENCE NEWS | April 29, 2017

Venomous swimmers have evolved many ways to sting **By Amber Dance**

iologist Leo Smith held an unusual job while an undergraduate student in San Diego. Twice a year, he tagged along on a chartered boat with elderly passengers. The group needed him to identify two particular species of rockfish, the chilipepper rockfish and the California shortspine thornyhead. Once he'd found the red-orange creatures, the passengers would stab themselves in the arms with the fishes' spines.

Doing so, the seniors believed, would relieve their aching arthritic joints. Smith, now at the University of Kansas in Lawrence, didn't think much of the practice at the time, but now he wonders if those passengers were on to something. Though there's no evidence that anything in rockfish venom can alleviate pain — most fish stings are, in fact, quite painful themselves — some scientists suspect fish venom is worth a

look. Studying the way venom molecules from diverse fishes inflict pain might help researchers understand how nerve cells sense pain and lead to novel ways to dull the sensation.

Smith is one of a handful of scientists who are studying fish venoms, and there's plenty to investigate. An estimated 7 to 9 percent of fishes, close to 3,000 species, are venomous, Smith's work suggests. Venomous fishes are found in freshwater and saltwater, including some stingrays, catfishes and stonefishes. Some, such as certain fang blennies, are favor-

ites in home aquariums. Yet stinging fishes haven't gotten the same attention from scientists as snakes and other venomous creatures.

But thanks to Smith's recent work, scientists can now see how venomous fishes fit within a tree of all fishkind. The tree shows that venom arose multiple times throughout history. Understanding which fishes are venomous is the crucial first step to working out the nature of the venoms, Smith says. Researchers are exploring how different fish venoms affect their victims and are discovering extraordinary diversity among fishes' chemical weaponry. The scientists hope the powerful molecules in the venoms might yield insights that could be turned into medicines. One newly described venom appears to act on opioid receptors, perhaps to stupefy its victims. And venom molecules that stall cell division and others that calm inflammation are inspiring new treatment ideas that go beyond pain relief.

Building a tree

While fish-venom studies are rare, fish stings are not. An old estimate says about 40,000 to 50,000 people are stung by fish

each year. But the number is probably much higher, Smith says, since many people don't bother to report their experiences.

The most noticeable effect of a venomous fish sting is immediate pain, ranging from the mild sting of those rockfish from Smith's scouting days to a feeling much more excruciating.

"The most pain that I've ever been in was my first stingray envenomation," says venom researcher Bryan Fry of the University of Queensland in Brisbane, Australia. He was trying to collect a sample from a roughly 11/2-meter-wide smooth stingray when it stabbed him in the thigh. "The pain is immediate and blinding."

Smith's first painful run-in was with a fuzzy dwarf lionfish at a pet store where he worked in his late teens. Later, at the library, he found no reports of that species having venom. In fact, medical records of fish stings documented only about 200 fish species as venomous. The experience helped set his career.

As his research progressed, Smith began building fish family trees to get a better handle on which fish spew venom. He presumed that fish related to known venomous ones could also be venomous. So he checked their anatomy for venom-delivery structures, like grooved spines. He reported

> a partial tree in 2006 and published a more complete version last year in *Integrative and Comparative Biology*. To assemble the latest tree, Smith and colleagues examined eight locations in the genetic instruction books, or genomes, of 388 species of fish, then used a computer program to work out, based on differences and similarities in those genomes, how the animals are probably related. He also examined museum samples of 90 types of fish for spines or fangs and venom glands. Based on what's known about fish diversity, Smith's

lowball estimate is that, of about 35,000 fish species, 2,386 to 2,962 are venomous.

Based on his new tree, Smith estimates that there were 18 distinct instances in which nonvenomous fish evolved a venom apparatus — give or take a few, since venom might have been lost from some groups, or evolved multiple times in others, he says. Jeremy Wright, curator of ichthyology at the New York State Museum in Albany, who has studied venom in catfish family trees, says Smith's methods were sound and the data support the tree. However, Wright's research suggests venom arose separately two or more times in the catfish lineage, while Smith's tree says all stinging catfishes share a single common, venomous ancestor.

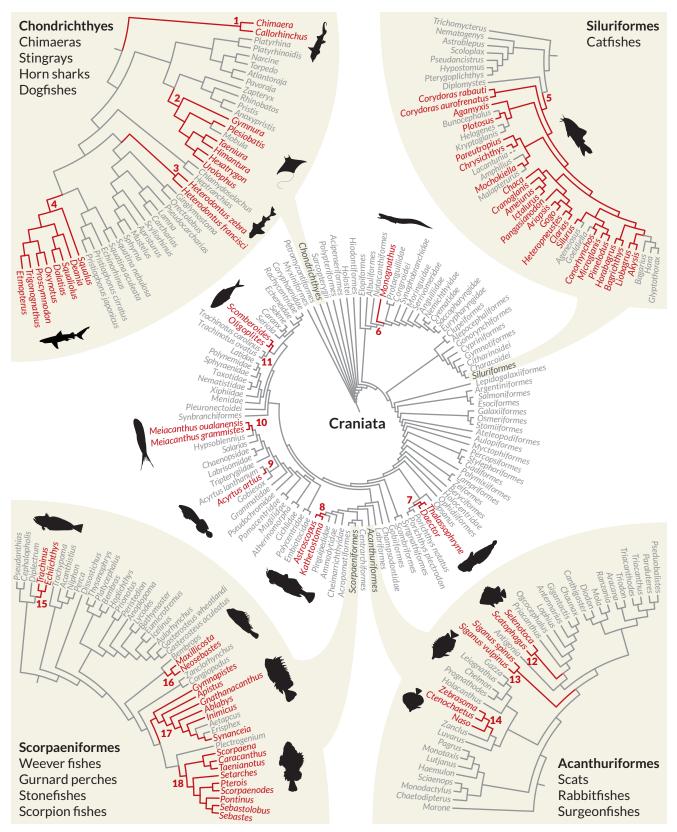
Whether fish venom arose 18 times, or 15, or 20, that's a big contrast to other animals that use venom: In snakes, venom appears to have evolved only once. The same is true for the venom in bees and ants. "To have venom evolve multiple times within a group is extraordinary," says Fry, who's studied a range of venomous critters.

Fish experts say the distinct origins of fish venoms make sense because, unlike snakes, which always use their teeth, fish



The fang blenny *Meiacanthus* grammistes has venom glands in its enlarged lower canine teeth (shown here in a micro-CT scan).

FEATURE | A SEA OF HURT



All in the family Researchers at the University of Kansas used genetic information to develop an evolutionary tree for fishes and greatly expanded the list of suspected venomous ones. In the tree above, the likely branches of venomous creatures are highlighted in red. The scientists estimate that venom evolved independently 18 times (numbered above), many more times than in snakes or bees.

Chemical weaponry Venom taken from nine species of catfish (including striped eel catfish, shown below) was injected into largemouth bass, a typical predator. The venom's effects varied and included loss of color, bleeding, involuntary muscle tightening, loss of balance and even death. SOURCE: J.J. WRIGHT/BMC EVOLUTIONARY BIOLOGY 2009



Venom effect in largemouth bass by catfish species

	Color loss	Muscle jerking	Prolonged muscle spasm	Bleeding	Loss of balance	Death
Columbian shark catfish (Arius jordani)	х		х		Х	
Blue leopard corydoras (Corydoras paleatus)	х					
Günther's catfish (Horabagrus brachysoma)	х		х	х	х	
Bumblebee catfish (Microglanis iheringi)	х			х		
Tadpole madtom (Noturus gyrinus)	х	х		х	х	
Iridescent shark (Pangasius hypophthalmus)		х			х	
Pictus catfish (Pimelodus pictus)	х			х		
Striped eel catfish (Plotosus lineatus)			х			х
Cuckoo catfish (Synodontis multipunctata)	х	х		х		

deliver venom in diverse ways. Spines with venom glands are most commonly found in fins atop the fish's back, but not always. In many venomous catfishes, the pectoral fins contain the barbs and venom glands. Weever fish spines sit on the operculum, a bony flap that protects the gills on the fish's cheeks. In stingrays, the flattened spine protrudes just above the tail. And in fang blennies, the venom glands sit at the base of enlarged lower canines, calling to mind tiny vampires of the sea.

Even within one fish genus, the venom-delivery apparatus can vary. Ichthyologists Jacob Egge, now at Pacific Lutheran University in Tacoma, Wash., and Andrew Simon of the University of Minnesota analyzed pectoral stingers of 26 species of madtom catfish, found in eastern North American freshwater. Some had smooth spines with a venom gland in the shaft, the two reported in 2011. Others had serrated spines, the better to cause injury, with a gland at the shaft and glands spread along the serrations. One species had no venom gland at all.

The effects of venom — from fishes and other creatures vary widely, but in fishes, the goal is usually the same: to stop an attack. For most fish venoms, pain is key, but some cause numbness, too. All affect the cardiovascular system in some way, by lowering blood pressure, for example, which would probably startle and debilitate a predator, Smith says.

In people who have been stung, skin reddening, swelling, itching or temporary localized paralysis might also occur. In some cases, the venom can kill the tissues near the sting site. In rare cases, a combination of low blood pressure, failure of circulation or weak breathing can lead to death.

Just within the catfishes, venom effects differ between species. Wright injected venom from nine different species of catfish into largemouth bass, which are typical predators. "It was clear that it was an uncomfortable experience for them," Wright says of his unlucky subjects. Many venoms caused loss of color and bleeding, some induced jerky muscle contractions or loss of balance, and one simply killed the bass outright, he reported in *BMC Evolutionary Biology* in 2009.

Modus operandi

Why did such diverse venoms and delivery apparatuses evolve so many times in fish? With Smith's comprehensive map of fish venom evolution, scientists can now address that sort of question, says Meg Daly, who studies sea anemone venom at Ohio State University in Columbus. For instance, since most fish use venom for defense, Daly wonders if the evolutionary origins of venoms coincided with times when new predators arrived on the scene.

Venom seems to have arisen often in slow-moving bottom dwellers, which would certainly be vulnerable to predation. "If you're a catfish sitting there sucking on some mud, you need to have some spines," Fry says.

Consider the reef stonefish. It loafs on the floor of the Indian and Pacific oceans, often covered in camouflaging algae, hoping to snatch a passing fish or crustacean. When distressed, the fish raises the 13 spines on its back that are adjacent to venom glands, which hold toxins powerful enough to kill a person.

Though venoms have evolved multiple times across fish species, the toxic blends often converge chemically on a set of similar ways to cause damage. For example, the proteins in many fish venoms act by assembling into large rings that then insert themselves into the membranes of cells. This opens a hole where a cell's innards leak out. When this happens to pain-sensing nerve cells, the body interprets the signal as excruciating discomfort — a good way to distract a predator from chowing down, Fry says.

Other fish venoms share their modes of action with certain venoms from other animals. For example, the venoms

FEATURE | A SEA OF HURT

of stonefishes, snakes and some other organisms contain hyaluronidase, an enzyme that dissolves some of the matrix that supports cells. In that way, the enzyme helps the other venom molecules speed through the victim's tissues.

But still, the multiple evolutions of fish venoms mean that each group of venomous fish probably makes venom components that attack their victims differently. Scientists are just beginning to delve into the specific molecules and actions of different venoms. Fry and collaborators took a stab in a study published February 16 in *Toxins*, extracting and analyzing venom from six types of fishes — dusky flathead, Luderick, mullet, yellowback seabream and two types of stingrays.

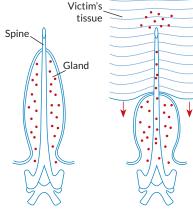
"It was incredibly variable," says study coauthor Nicholas Casewell, a venom biologist at the Liverpool School of Tropical Medicine in England. Injected into a rat, the mullet and seabream toxins caused heart rate to drop slightly, while the other venoms had no effect. All venoms resulted in an initial drop in blood pressure — as is common in human envenomations by fish — but the stingray, mullet and seabream venoms then caused blood pressure to rise.

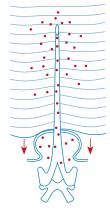
In nerves and muscles growing in a dish, the venoms of stingrays and dusky flatheads blocked muscle twitching, which could potentially mean some moderate level of partial paralysis for a predator, Casewell says. Indeed, paralysis and weakness can occur in people stung by fish. The other fishes' venoms, in contrast, boosted twitching a bit.

Even though the venoms all cause pain, Fry says, these results show that the underlying effects of each venom are a bit different. It's a classic case of evolutionary convergence, in which different evolutionary pathways lead to the same end result in this case, the pain that makes the predator skedaddle.

In a separate study published online March 30 in *Current Biology*, Casewell, Fry and colleagues examined fang blennies. Certain species, found in shallow reefs of the Indian and Pacific

Sharp objects The toadfish *Thalassophryne nattereri* delivers venom via a grooved spine connected to a venom gland at its base (below). As the spine penetrates the victim's tissues, the compression sends the venom (red dots) along the spine and into the tissues. Stingers on other fishes include smooth and barbed spines (at right: top and middle left), spines surrounded by the venom gland (middle right), pectoral spines (lower left, arrow) and fangs (lower right, arrow points to venom gland). SOURCE: M. LOPES-FEREIRA, LZ. GRUND AND C. LIMA/J. OF VEN. ANIM. TOXINS INCL. TROP. DIS. 2014





oceans, use venomous fangs to defend against predators. The researchers were puzzled that fang blenny venom didn't seem to cause pain when injected into a mouse's paw. The venom, it turns out, acts on opioid receptors, where it might work like a sedative. It also lowers blood pressure, probably leaving the victim disoriented or dizzy. The victim is essentially "stoned," Fry says. A predator won't be able to swim away properly, he surmises, or it'll die of something akin to a heroin overdose.

Another group, at the University of Tübingen in Germany, is investigating the venom of the lesser weever fish of the Mediterranean. Graduate student Myriam Fezai was inspired to study the fish by its ability to induce swelling and paralysis in fishermen and tourists in her homeland, Tunisia. The venom also blackens and kills tissues, so she and collaborators wanted to know how it killed cells. The researchers tested the venom on red blood cells in the lab, where it caused the cells to shrink in a form of programmed cell death, Fezai and colleagues reported in *Scientific Reports* in 2016.

The team tested the weever fish venom on cancer cells, too. The cells stopped growing and their mitochondria stopped working properly, triggering apoptosis, a classic mechanism by which cells kick the bucket. Even cells that survived tended to stop dividing regularly. Next, the researchers hope to identify the individual components of the venom involved in the cell killing.

Hurts so good

The hope is that something in weever fish venom can be turned into an anticancer drug. Medicines based on venoms from other animals already exist, including the blood pressure drug captopril (Capoten) from a pit viper. There's even a painkiller, ziconotide (Prialt), developed from the potent venom of a marine cone snail. Sometimes, the same molecules that cause pain can, if applied correctly, also relieve it. Capsaicin,



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the spicy tongue-burning stuff in peppers, is used in a cream to relieve the pain of shingles and other conditions. The molecule desensitizes the pain sensors in nerve cells.

Venoms provide a rich source of potentially useful molecules, says Mandë Holford, a snail venom expert at Hunter College and the American Museum of Natural History in New York City. Evolution has already honed the venoms to precisely interact with their targets. "Every time I read about a new venomous organism, like the fish in Leo [Smith's] work, I get excited because our pot is getting bigger," she says.

Scientists around the world are in the early stages of investigating fish venoms that might combat cancer, control blood pressure or clot blood. In Brazil, researchers studying the venom of the lagoon-dwelling toadfish *Thalassophryne nattereri* found a small protein they named TnP, which has anti-inflammatory abilities. They hope to develop a medicine for multiple sclerosis, a disease in which immune cells cause inflammation and attack the nervous system. In February, the team reported in *PLOS ONE* that in mice with a form of multiple sclerosis, a synthetic version of TnP dampened inflammation, protected and promoted repair of nerves and improved muscle coordination.

Isolating the specific venom ingredient that causes the desired effects, as the Brazilian researchers did with TnP, is the direction several scientists are going in their studies of fish venom. Some are analyzing which genes are uniquely turned on in a fish's venom glands and not activated in nearby fin tissue. Modern mass spectrometry also helps, Holford says, because it allows scientists to analyze the components of even the tiny amount of venom they can extract from a snail or fish.

Unlike snakes, which are easily milked for their venom, collection from fish typically involves clipping the spine off wild specimens and scraping a small bit of venom into a test tube. (The involuntary donor, sent on its way, can typically regrow the spine, like a fingernail, Fry says.) Then things get difficult.

"Fish venom is just horrible ... it has this snotlike consistency," Fry says. "It's easily the most challenging venom that I've had the misfortune to work with." In contrast to venom from other creatures, which often consists of fairly small, stable proteins, fish venom tends to be made of large proteins that fall apart easily once out of the fish. Freeze it, heat it or expose it to certain chemicals, and the proteins fall apart. That's a major disadvantage in the lab, and for medicines, too, Casewell notes. Therefore, he doubts a fish venom could yield the next blockbuster pharmaceutical.

Fry acknowledges that successes such as captopril or ziconotide, in which venom directly leads to a medicine, are quite rare. However, he believes scientists can learn about pain from fish venoms and apply that knowledge to invent novel painkillers. Similarly, Fezai, who started the weever fish project, doesn't think the venom ingredients themselves would be the drug, but some molecule that mimics their actions might be.

The upside of the fragility of fish venoms, though, is that treatment for a fish sting is quite straightforward: running



Killer medicines

Several venoms, examples below, have been repurposed as medicines for human use, most for their effect on blood.

Animal	Drug	Used for
Pitviper	Captopril	High blood pressure control
Pygmy rattlesnake	Eptifibatide	Antiplatelet for heart attack
Saw-scaled viper	Tirofiban	Antiplatelet for heart attack
Medicinal leech	Bivalirudin	Anticoagulant/blood thinner
Cone snail	Ziconotide	Pain relief
Gila monster	Exenatide	Type 2 diabetes control
Lance head snake	Batroxobin	Blood clotting

hot water over the affected body part. That's what Smith did when he was stung by a blue tang — think Dory from *Finding Nemo* — while cleaning his tank at home. About a half an hour under the hot tap stopped the pain by destroying the venom in his finger. But some damage had already been done. About 10 days later, a pea-sized chunk of his finger fell off, dead.

The rockfish, so desired by Smith's copassengers on the San Diego fishing trips, has a milder sting. Those arthritis sufferers weren't risking much. But whether they were really relieving joint pain with a fish venom is an open question. They certainly seemed to think so, Smith says, though as of yet no data support this particular fishy treatment.

But, he notes, the venom of scorpion fish — cousin to rockfish — affects the nervous system, immune system and blood pressure, all of which could, in theory, have some "real" effect on the arthritis. "There's reason to believe that's possible," he speculates.

Explore more

 Han Han et al. "The cardiovascular and neurotoxic effects of the venoms of six bony and cartilaginous fishes." *Toxins*. February 2017.

Amber Dance is a freelance writer based in Los Angeles.



TELEVISION

Drama of Einstein's life unfolds in new series

Albert Einstein was a master of physics, but his talent in personal relationships was decidedly underdeveloped. A new 10-episode series, *Genius*, airing on the National Geographic Channel, focuses on the facets of Einstein's life where he was anything but a virtuoso.

Genius is a dramatization, not a documentary. The series reveals the human side of the famously brainy physicist — through Einstein's numerous romantic liaisons and his reactions to world political events, including two world wars and his departure from Nazi Germany. Unfortunately, although Einstein's personal life reveals insights into his character, *Genius* ends up sacrificing science for the sensational. The first episode, for instance, opens with

a murder followed by a sex scene.

Viewers shouldn't expect to learn much about the science of Einstein's discoveries, at

least based on the first two episodes that were available for review. The explanations are vague enough that those unfamiliar with Einstein's theories will understand little, and those who know them won't learn anything new.

Based on Walter Isaacson's book *Einstein: His Life and Universe*, the television series leapfrogs from one time period to another, contrasting the scientific enthusiasm of the brash young Einstein (played by Johnny Flynn) with the more sedate ruminations of the elder, established physicist (Geoffrey Rush). While time traveling from one period to another, the show plays up Einstein's fascination with time.

The young Einstein is portrayed as a brilliant, willful character. After dropping out of high school, he fails an entrance exam to Zurich Polytechnic. He is finally admitted a year later, in 1896, after additional schooling. There, he skips classes, challenges professors who are reluctant to teach cutting-edge theories and studies mainly on his own.

Meanwhile, the young Einstein's love life makes for surprisingly dramatic vignettes. In one scene, his lover Mileva Marić (Samantha Colley) — a fellow physics student in Zurich who would later become his first wife — realizes Einstein has yet to break things off with his first flame, Marie Winteler

Genius

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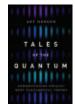
(Shannon Tarbet). Marić smashes a teapot against the wall and then, distraught, berates Einstein for his thoughtlessness.

Despite his smarts, Einstein is not always the hero of his own story. As he plays fast and loose with his lovers' hearts, viewers may find themselves siding with the women. As the show recounts Marić's childhood in Serbia and her struggle to become a physicist when few institutions were willing to educate women, Marić sometimes seems the more impressive member of the pair. (Marić doesn't continue on in physics, after failing her exams and becoming pregnant.) Einstein eventually marries Marić in 1903, then divorces her in 1919, a few years after beginning an affair with his cousin Elsa (Emily Watson), who becomes his second wife.

The older, famous Einstein possesses the same stubborn determination as his younger self. Despite the anti-Semitic sentiment in the run-up to World War II, Einstein, a Jew, initially resists leaving Germany. But circumstances eventually change his mind. In 1922, Einstein's friend, German foreign minister Walther Rathenau, who is also Jewish, is assassinated. And then prominent anti-Semitic scientists, including Nobel laureate Philipp Lenard, denounce Einstein. By 1933, the situation becomes unbearable, and Albert and Elsa leave for the United States.

Overall, *Genius* portrays Einstein as a complicated human, not just a cartoonish brainiac. Those unfamiliar with Einstein's personal life will see the scientist in a new light. But be prepared for an emphasis on drama, sex and love stories, not science. — *Emily Conover*

BOOKSHELF



Tales of the Quantum Art Hobson

This book gives a fresh look at quantum physics from a physicist who explains its validity and believes its

mysteries do not warrant any mystical interpretations. *Oxford Univ.*, \$29.95



A Big Bang in a Little Room

Zeeya Merali A journalist surveys the quirks of cosmology stemming from the Big Bang, including the

prospect of creating other universes, perhaps in a lab. *Basic Books*, \$27.99

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SOCIETY UPDATE

"You see their projects and think: **'These kids are going to change the world.'**"

- DENISE SIGNORELLI, BIOLOGY PROFESSOR AND SOCIETY MEMBER





Denise Signorelli, Biology professor and Society member

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A D V E R T I S E M E N T

FEEDBACK



MARCH 18, 2017

You're a crab, Harry

A translucent crab discovered nearly 20 years ago has finally been identified as a distinct species. Researchers dubbed the crab *Harryplax severus*, after two characters in the popular Harry Potter series, **Helen Thompson** reported in "Crab gets Harry Potter honor" (*SN*: 3/18/17, p. 5). Some online readers continued to riff on the literary theme, suggesting Potterinspired names for other animals.



When are they going to discover the hufflepuffin? MAdScientist72

Or with crabs, the raven-claw. **Quuppie**

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Eau de stinkbug

Stinkbugs accidentally harvested with grapes and fermented during the winemaking process release a pungent stress compound. It takes only three stinkbugs per grape cluster to ruin red wine's taste, **Elizabeth S. Eaton** reported in "Red wine has stinkbug threshold" (SN: 3/18/17, p. 5). "Does contamination of wine by the bugs' stress compound pose any health risk to consumers?" asked **Hal Heaton**. "And does someone really count the number of stinkbugs on each of the huge number of grape bunches picked?"

The hormone emitted by stressed stinkbugs, (E)-2-decenal, is also found in cilantro, says **Elizabeth Tomasino**, a food scientist at Oregon State University in Corvallis who did the research. "It is actually found at much higher concentrations in cilantro than in wine and is not a health risk," **Tomasino** says.

As for counting stinkbugs, there are people who count bugs on the vines, but not by bunch as the researchers did. "What typically occurs is that someone will put a sheet under a plant and beat the leaves to see how many fall out," **Tomasino** says. Another approach involves walking through the vineyard and counting as many bugs as possible in three-minute increments, she says.

Troubled waters

Science journalist Dan Egan's book, The Death and Life of the Great Lakes, chronicles the impacts of global trade, urbanization and climate change on the lakes and communities that depend on them. Invasive species, including zebra and quagga mussels, have been particularly damaging, Cassie Martin wrote in her review "Invaders, climate change threaten Great Lakes" (SN: 3/18/17, p. 30). "I thought that the zebra mussels cleaned up Lake Erie?" asked online reader Robert Stenton. "The Great Lakes are too important economically to let them perish, so as we learn from our mistakes, we will correct the problems."

The billions of invasive zebra mussels that blanket lake beds, boat hulls and water intake pipes didn't clean the once "dead" Lake Erie of pollutants. The lake was revived thanks to the Clean Water Act. "In fact, the mussels do more harm than good," **Martin** says. True, a single adult zebra mussel can filter a liter of water every day, but it also removes the nutrients vital for healthy ecosystems.

Although Lake Erie recovered, it has faced setbacks in recent years. Fertilizer runoff from farms causes huge blooms of toxic blue-green algae. One such bloom left nearly half a million people in Toledo, Ohio, without drinking water for three days in the summer of 2014. Researchers think that booming populations of invasive mussels may contribute to the algae explosions. Mussels don't eat the toxic algae, feeding instead on other plankton that usually help keep the algae in check.

Smell-or-vision

Unlike some of their New World monkey relatives, howler monkeys can see in full color thanks to three types of proteins in their eyes that detect various wavelengths of light. This three-color vision may have evolved thanks to the monkeys' preference for eating bright red young leaves, **Laurel Hamers** reported in "Leaf hue shaped howler monkeys' color vision," (SN: 3/18/17, p. 16).

Online reader **Jan Steinman** wondered if howler monkeys' sense of smell might be compromised by their threecolor vision. "Smell and sight seem to compete for scarce neural resources" in other animals, **Steinman** wrote.

"The jury is out on whether or not some primate species sacrificed sensitive sniffers for enhanced color vision," **Hamers** says. A study published in *PLOS Biology* in 2004 suggested that primates with three-color vision had more nonworking smell-related genes than primates with two-color vision.

But a study a few years later came to a different conclusion: Primates' smell-related genes may have degraded independently of the development of three-color vision, another group of researchers reported in 2010 in *Molecular Biology and Evolution*.

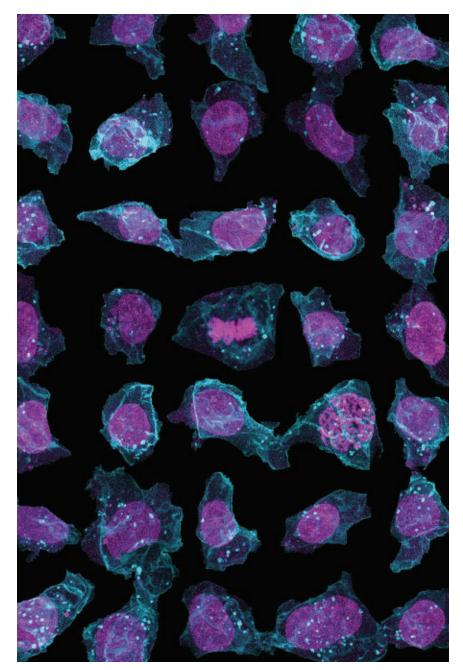
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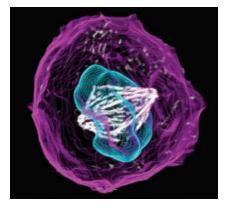
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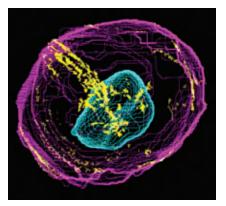




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Variations on a cell

Computers don't have eyes, but they could revolutionize the way scientists visualize cells. Researchers at the Allen Institute for Cell Science in Seattle have devised 3-D representations of cells, compiled by computers that learned where thousands of real cells tuck their component parts.

Most drawings of cells in textbooks come from human interpretations gleaned by looking at just a few dead cells at a time. The Allen Cell Explorer, which premiered online April 5, presents 3-D images of thousands of genetically identical stem cells grown in lab dishes (composite, top), revealing a huge variety of structural differences.

Each cell comes from a skin cell that was reprogrammed into a stem cell. Important proteins were tagged with fluorescent molecules so researchers could keep tabs on the cell membrane (cyan, top), DNA-containing nucleus (magenta, top) and other cell parts.

Using the 3-D images, computer programs learned where the parts are in relation to each other. From those rules, the programs can generate predictive transparent models of a cell's structure (membrane and nucleus colors are switched in bottom images). Microtubules are in white (left) and yellow (right). The new views, which can capture cells at different time points, may offer clues to their inner workings.

Researchers have already learned from the project that stem cells have a definite bottom and top, a proposed structure now confirmed by the combined cell data, says Susanne Rafelski, a cell biologist at the Allen Institute.

The project's tools are available for other researchers to use on various types of cells. Insights gained might lead to a better understanding of human development, cancer, health and diseases.

Old ways of observing cells, Rafelski says, were like trying to get to know a city by looking at a map. The cell explorer is more like a documentary of the lives of its citizens.

— Tina Hesman Saey

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