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Just Say No to Antibiotic Resistance

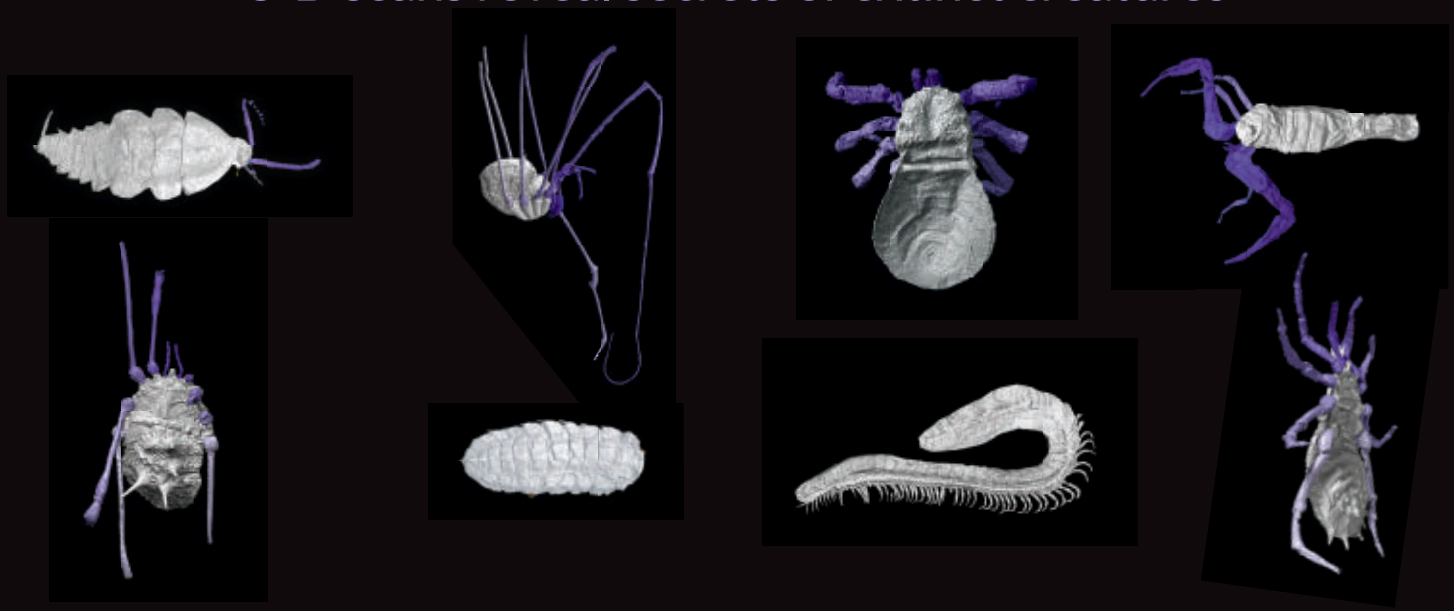
Laser-Controlled Memories

Pyramid Puzzle Re-solved

Icy Tectonics on Europa

BRINGING FOSSILS TO LIFE

3-D scans reveal secrets of extinct creatures



We found our most important watch in a soldier's pocket

It's the summer of 1944 and a weathered U.S. sergeant is walking in Rome only days after the Allied Liberation. There is a joyous mood in the streets and this tough soldier wants to remember this day. He's only weeks away from returning home. He finds an interesting timepiece in a store just off the Via Veneto and he decides to splurge a little on this memento. He loved the way it felt in his hand, and the complex movement inside the case intrigued him. He really liked the hunter's back that opened to a secret compartment. He thought that he could squeeze a picture of his wife and new daughter in the case back. He wrote home that now he could count the hours until he returned to the States. This watch went on to survive some harrowing flights in a B-24 bomber and somehow made it back to the U.S. Besides the Purple Heart and the Bronze Star, my father cherished this watch because it was a reminder of the best part of the war for anysoldier—the homecoming.

He nicknamed the watch *Ritorno* for homecoming, and the rare heirloom is now valued at $42,000 according to *The Complete Guide to Watches*. But to our family, it is just a reminder that nothing is more beautiful than the smile of a healthy returning GI.

The hunter's back

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COVER By reconstructing fossils using X-ray scans, researchers are able to take a closer look at these varied and fascinating extinct creatures. *Russell Garwood; © The Trustees of the Natural History Museum, London 2014; National Museum of Natural History, France*

CLOCKWISE FROM TOP: CDC; COURTESY OF C. PAINTING/UNIV. OF AUCKLAND; TED STRYK/GALILEO PROJECT/JPL/NASA

Thoughtful approach to antibiotic resistance

I spent a good chunk of last week in a hospital where my mother was undergoing surgery, so I had a chance to see, firsthand, some of the double-checking that doctors and nurses use to avoid making simple mistakes. They repeatedly asked my mom her name, her date of birth, what surgery she was there for and which side of her body doctors were supposed to operate on. All went well, but the experience reminded me of Atul Gawande's 2007 *New Yorker* article (and 2009 book) about how using checklists could improve medical outcomes. Gawande discussed a list designed to combat the spread of bacterial infections in intensive care units. First was a reminder for doctors to wash their hands with soap — a low-tech, common sense approach similar to asking a patient whether her right or left side is slated for surgery. That same approach may help ebb the tide of antibiotic resistance.

As biomedical writer Nathan Seppa describes on Page 22, some strains of staph, strep, salmonella, gonorrhea and other pathogens now routinely evade antimicrobial drugs, leading to some 23,000 U.S. deaths each year. One way to deal with the problem is simple but counterintuitive: use fewer antibiotics. Reducing unnecessary use, Seppa explains, will help keep the drugs effective for longer. Antimicrobial stewardship programs that encourage more strategic prescribing of antibiotics and remind doctors (and patients) of appropriate uses are on the rise. Changing how people think about antibiotics is already showing promise in reducing antibiotic use and costs. It may also help with the problem of resistance.

It's doubtful, however, that any single strategy will be enough. As game theory demonstrates, multiple strategies usually give you the best chance of winning. We'll need a slew of approaches, from thoughtful prescription guidelines, to the rollout of new antibiotics, to radical new ways of treating infection (perhaps by modulating signaling between bacterial cells, or by recruiting other microbes to assist in our defense). And, of course, there's good old hand washing. Even as more cutting-edge strategies are developed, one can be implemented now: seeing antibiotics as a valuable, and vulnerable, resource and using them accordingly. That should improve everyone's outcome. — *Eva Emerson, Editor in Chief*

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Customer service: member@societyforscience.org
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SANDY SCHAFFER

NEW

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Excerpt from the October 10, 1964, *Science News Letter*

50 YEARS AGO

Warren Commission Report

A new way to fight crime, called neutron activation analysis, uses penetrating neutron radiation to help catch a criminal from only a speck of evidence. The Warren Commission included the results of a neutron activation analysis test of Lee Harvey Oswald in their recent assassination study. The tests, however, could not prove that Lee Harvey Oswald fired the rifle.... Activation analysis may replace the old chemical "paraffin test" that law enforcement officials have found unreliable....

UPDATE: Even high-tech methods such as neutron activation analysis can't distinguish the type of weapon fired, says Michael Martinez of the Scientific Working Group for Gunshot Residue. Tests can only determine whether a person has fired a gun, held a discharged weapon or was close to a gun when it went off. Neutron activation analysis and paraffin testing have been supplanted by a combination of scanning electron microscopy and energy-dispersive X-ray spectrometry.

Big male giraffe weevils (top) can lose out to smaller males (middle) that sneak underneath to mate with females (bottom). Dots of paint help researchers identify individual weevils.

SAY WHAT?

Brazil nut effect *BRUH-zil nuht ih-fekt*\ n.

The phenomenon in which a mixture's larger objects, such as the Brazil nuts in a can of mixed nuts, rise to the top when the mix is shaken vertically. Some scientists think that smaller nuts slip into the spaces under the larger ones during each shake.

Researchers are now using the Brazil nut effect to explain mysteries in space. Scientists report October 1 in the *Monthly Notices of the Royal Astronomical Society* that the effect could account for why only big boulders dot the surfaces of asteroids. The researchers calculate that asteroid-quakes and impacts from smaller space rocks could jostle an asteroid enough to cause larger rocks to rise to the surface. — *Thomas Sumner*

Large boulders speckle the surface of the asteroid Itokawa.

FROM TOP: COURTESY OF C. PAINTING/UNIV. OF AUCKLAND; COURTESY OF JAXA

Watch a video of male giraffe weevils battling it out at **bit.ly/SN_weevils**

IT'S ALIVE

Sneaky little giraffe weevils beat big rivals

You might think a male giraffe weevil, or a male anything for that matter, would object to a rival creeping between his legs when he's mating.

But creeping sneaks get away with outrageous stunts among New Zealand's giraffe weevils (*Lasiorhynchus barbicornis*). Christina Painting at the University of Auckland remembers the first big male weevil she watched, an 80-millimeter bruiser standing possessively over a female for more than an hour. "He moved away — I guess to have a rest — and I realized the whole time there had been a tiny, tiny male underneath him waiting for the opportunity to mate."

A sneaker can hide even while he mates. "He'll rotate himself around and tuck his long [snout] underneath the female," Painting says. "Often they quite happily keep mating" when a big male arrives and repeatedly fumbles to get into position himself. "The big male can't figure out what's going on," she says.

Only small guys resort to funny business, but they don't have much choice. Male giraffe weevils joust with fishing-pole–like snouts that can grow as long as the rest of their bodies. In a fair fight, a 40-millimeter-plus weapon would leave the smallest males' 7 millimeters ridiculously out-snouted.

Underendowed males of a variety of species, from dung beetles to salmon, procreate via sneakery. But biologists usually treat them as "these subordinate little things," Painting says. Among giraffe weevils, however, "I found very quickly that males of all sizes — it doesn't matter how small you are — will fight." Little weevils just don't pick dumb fights with giants.

Overall, guile can compensate for lack of size. Sneakers mate about as often as big jousters do, Painting and Gregory Holwell, also at Auckland, report August 24 in *Behavioral Ecology*.

All this fighting and male drama fails to stir an obvious reaction from female weevils. Even while mating, the female's attention seems focused on boring into a tree's bark with her tiny, sharp jaws to create a hole for her egg. "There's no courtship," Painting says, and females hardly ever reject a male's advances.

But the female's role in giraffe weevil sex shouldn't be overlooked. Females stow incoming sperm in a hard-cased storage organ. Whether sperm from sneaky or super-snouted males ends up actually fertilizing her eggs remains to be seen. And so does whether the females are making that final choice themselves. — *Susan Milius*

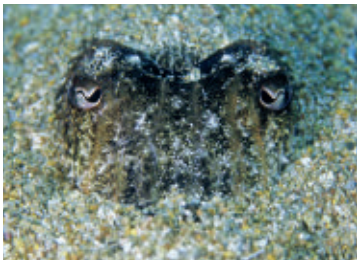
HOW BIZARRE

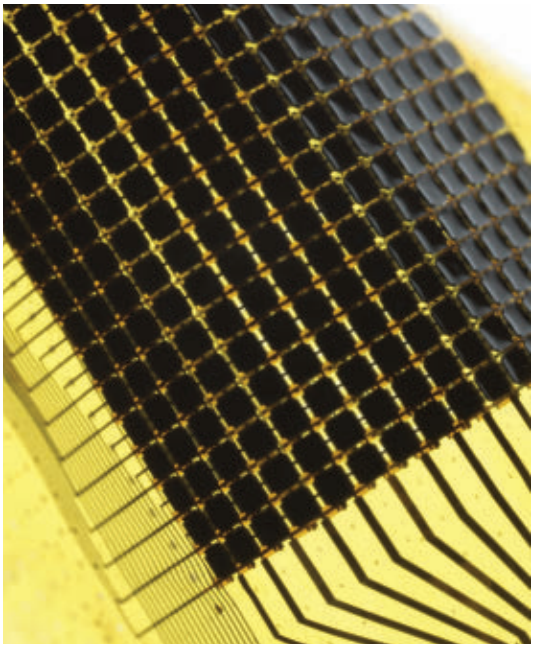
Nature-inspired camouflage

Scientists have swiped the secrets of certain sea creatures' cloaking skills to create a camouflaging material that responds to light.

Some cephalopods such as cuttlefish can mimic colors and patterns in their environment using three-layered skin. Each layer has a role: light-detecting cells at the skin's lower surface trigger muscle cells in the middle to adjust pigment cells at the top.

Now researchers led by materials scientist John Rogers at the University of Illinois at Urbana-Champaign have copied that format using silicon and a polymer. A bottom layer of photodetectors senses light and sends weak electrical currents to actuators in the middle. These tiny devices convert the electrical signal to heat, which prompts a chemical in the top layer to change color. The researchers say the thin, flexible material could be useful in everything from military camouflage to wallpaper. The results appear September 9 in the *Proceedings of the National Academy of Sciences*. — *Beth Mole*

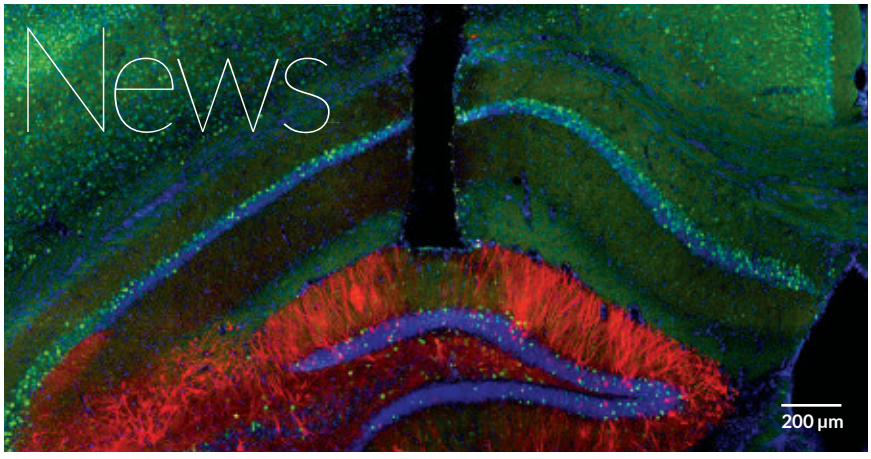




By mimicking the skin of camouflaging cephalopods like cuttlefish (left), scientists created a thin, flexible material that can copy light patterns in the environment.

FROM LEFT: FRANCO BANFI/SCIENCE SOURCE; J. ROGERS/UNIV. OF ILLINOIS AT URBANA-CHAMPAIGN

Watch a video of the cephalopod-based camouflage in action at **bit.ly/SN_camo**



A mouse's unpleasant memory can be turned into a pleasant one, or vice versa, when nerve cells (red) storing the memory in the brain are activated with light while the mouse experiences something new. The black region (center) contains a light-delivering optical fiber.

BODY & BRAIN

Laser light rewrites memories in mice

Nerve cells in the hippocampus help modify recollections

BY LAURA SANDERS

With a burst of light, scientists can change good mouse memories into bad ones, and bad ones into good. The results, published August 27 in *Nature*, underscore that memories are not written in stone and bring scientists closer to understanding how nerve cells in the brain create and store memories.

The study provides a "much more precise handle on some of the steps of memory formation than we've had before," says neuroscientist Richard Morris of the University of Edinburgh. One day, such knowledge may lead to treatments for people who struggle with unwanted negative memories.

The results are the latest in the effort to manipulate mouse memories with optogenetics, a technique that uses light to control specific nerve cells in the brain. In earlier experiments, scientists made mice afraid of a harmless room, layering fearful memories onto previously neutral experiences (*SN: 8/24/13, p. 18; SN: 4/21/12, p. 10*).

In the new work, MIT scientists led by Susumu Tonegawa go further by transforming a once-negative memory into a pleasant one and a once-positive memory into a bad one. The team exposed male mice to either of two distinct situations: Some received small electric shocks while others spent time with females. A molecular trick marked neurons that stored the memory of the experience so that the cells, and the memory they evoked, could be later activated with laser light piped through tiny optical fibers embedded in the brain. The targeted neurons were located in the hippocampus or the amygdala, two brain structures involved in memory.

After tagging these memories, the researchers reactivated them with a flash of the light. In a completely new environment, the mice could choose whether to have the laser stimulate their brain by walking into a certain area — a decision that allowed the scientists to determine whether the stimulation, and thus the memory, was pleasant or not. Mice with memories of being shocked spent less time getting stimulated than did mice with positive memories of spending time in the company of a female, the team found.

> "We can go inside the brain, tweak the circuit and achieve something that otherwise we'd need drugs or ... behavioral therapy to get."
>
> **ROGER REDONDO**

In the next step, the researchers changed the positive or negative experience of a memory. They did this by calling up the memory with light while each mouse experienced the opposite situation, says study coauthor Roger Redondo. For example, the team used light to evoke the memory of a shock while the animal was in the company of females, causing the negative memory to be diluted with a more positive one.

After the memory switch, the mice were again put in a different environment. Those that had their good memories sullied chose to stimulate themselves less with the laser. Meanwhile, mice that had their nasty memories made more pleasant went for the laser more often. And back in the room where they had received shocks, these mice acted less frightened, spending less time frozen in fear.

The memory switch seems to be driven by cells in the hippocampus, not in the amygdala, the team found.

Emotional memory switching isn't a new concept, Redondo says. The same thing happens when a person experiences a terrible meal at a formerly beloved restaurant. And a similar process might underlie exposure therapy for posttraumatic stress disorder, in which a person recalls a traumatic experience in the hopes of forming new, less upsetting associations. What makes the laser technique different is that it switches memories quickly and without returning to the scene of the event, he says.

"We know the circuit so well that we can go inside the brain, tweak the circuit and achieve something that otherwise we'd need drugs or weeks and hours of behavioral therapy to get," Redondo says.

Tonegawa points out, however, that the technology doesn't yet exist to enable a similar switch in people. "It's not something we can do next week or next year," he says. But he's hopeful that the research might ultimately help people with traumatic memories. ■

R. REDONDO

A sequence of images shows how a Senegal bichir moves on land. The fish plants a fin on the ground, and the tail and rear of the body curve from one side to the other, pushing forward. That push drives the fish "shoulder" upward and forward as if the fin were a crutch.

LIFE & EVOLUTION

Fish reared out of water give clues to land transition

Terrestrial environment altered animals' development

BY SUSAN MILIUS

The deft wrigglings of fish forced to grow up on land could offer a glimpse of how ancient vertebrates started to make the big move out of the sea.

The modern Senegal bichir (*Polypterus senegalus*) normally swims in African rivers. But the elongated fish possesses both gills and lungs and can walk on land if it has to. And that's what Emily Standen forced bichirs to do for much of their youth.

While working at McGill University in Montreal, she created tanks with special bottoms that let only a few millimeters of water seep across the surface where the fish would move. Grocery-store produce aisles provided additional inspiration for the tanks' design. ("We need misters, lettuce misters!" she realized.) For eight months, the tanks housed crowds of roughly 7- to 8-centimeter-long young fish, which used their fins and tails to walk around the bottom looking for food.

As the fish matured, certain bones in their shoulder regions began developing differently than in bichirs that grew up swimming. The skeletal changes matched what scientists have seen in fossils of early animals transitioning to life on land, says Standen, now at the University of Ottawa. The land-reared fish also moved in ways that should be more land friendly than water-reared fish forced as adults to walk, Standen and her colleagues say August 27 in *Nature*.

Young fish raised to walk, not swim, developed a longer and more strongly attached clavicle bone in their chests. The change marks a step toward a skeleton that could bear weight instead of relying on support from water. Also, the gill area enlarged a little and bone connections loosened slightly at the back of the head, both small advances toward a flexible neck. (Fish in water can dart stiff-necked at food from above, below or elsewhere, but having a bendy neck helps terrestrial feeding.)

Land-reared bichirs were also better than water-baby ones at reducing drag in walking. Landlings kept the front stepping fin close to their bodies, gaining a little extra height when their "shoulders" rose upward and forward, as if the fin were a crutch. The close-in fin hoisted more bichir body temporarily into the air, leaving less to rub along the ground.

Bichirs don't belong to the broad group of lobe-finned fishes that gave rise to land-dwelling vertebrates. But the fish are near relatives. The changes observed in the land-reared bichirs suggest how some of those early fishes might have moved, Standen says.

The speed with which the fish in the experiment changed — within one generation that grew up in bizarre circumstances — raises the possibility that some developmental quirk might also have given ancient fish a little head start in adapting to life out of water.

This developmental plasticity, as it's called, has triggered interest among evolutionary biologists in recent years, says Armin Moczek of Indiana University in Bloomington. Changing environments can reorchestrate the genes an organism already has and reveal new forms without mutations. A role for plasticity in such a major evolutionary event as marine vertebrates' colonization of land would be a big deal, he says.

Still, showing that a modern fish has the flexibility to cope with land doesn't prove that ancestral fish had it. But, he adds, this experiment "raises the possibility that preexisting developmental plasticity provided the first baby step." ■

FROM TOP: ANTOINE MORIN; TOM BENSON/FLICKR (CC BY-NC-ND 2.0)

Watch a video of a fish walking at **bit.ly/SN_bichir**

LIFE & EVOLUTION

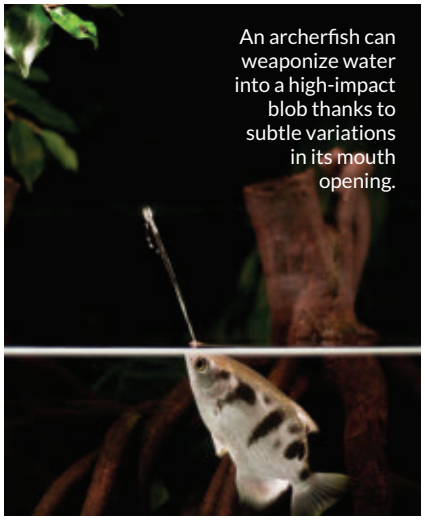
Archerfish mouth reveals spit secret

Shooting gobs of water at prey requires rapid oral acrobatics

BY SUSAN MILIUS

When archerfish hunt by precision spitting water into the air, they do a lot more with their mouths than put their lips together and blow.

If a *Toxotes* archerfish can't jump high enough to snatch an insect off an overhanging leaf, the fish spits water upward that knocks the prey off its perch. In a quirk that puts extra punch into the water blast, the fish fires the trailing end of a water stream faster than the water released at the beginning.



An archerfish can weaponize water into a high-impact blob thanks to subtle variations in its mouth opening.

Archerfish in the lab have revealed that they tailor the extra punch to the height of their target, says physiologist Stefan Schuster of the University of Bayreuth in Germany. The fish blasted several of his hypotheses about how they manage their sophisticated spitting. But high-speed videos of the target shooters finally linked water speed control to split-second changes in the fish's mouth openings, Schuster and Bayreuth colleague Peggy Gerullis report in the Sept. 22 *Current Biology*.

Human-made fluid spitters, such as the nozzles in ink-jet printers, don't have refinements such as variable-size openings, says Alberto Vailati of the University of Milan. He has also studied archerfish and says the new findings suggest the potential for some fish-based technological innovations.

Spit speed matters to archerfish because the variation produces a stream with a fat glob of water at the front that maximizes wallop on the target. (The glob forms when the faster water toward the end of the stream catches up with the slower spit at the leading edge.)

A 2012 paper indicated that fish shooting at a nearby target could time their spit so that the water glob forms shortly before the stream smacks prey. Schuster and Gerullis now report that the fish orchestrate glob formation right before impact regardless of the distance to the target.

Pondering how fish managed to form globs at the proper distance, the team tested for additives such as fish mucus, which can change water viscosity. "After very much effort, the result is absolutely zero," Schuster says. The archerfish use slime on their scales but not in their spit.

Researchers also checked to see if the

BODY & BRAIN

Nose cells offer knee cartilage fix

Patches grown from nasal tissue perform well in goats

BY NATHAN SEPPA

Cartilage-making cells in the nose seem to produce a worthy stand-in for the cartilage lost at the tips of bones in damaged knee joints, a study in goats suggests.

Patches of cartilage grown from snippets of nasal tissue worked so well when implanted into the goats that a small group of people with knee injuries have now undergone the treatment with their own nasal cartilage, researchers report August 27 in *Science Translational Medicine*. While full results aren't yet available, "the patients are doing extremely well," says study coauthor Ivan Martin, a bioengineer at the University Hospital Basel in Switzerland.

Replacing the glossy hyaline cartilage that coats the ends of bones has been an elusive goal with a long learning curve. The trick is to get cartilage-making cells called chondrocytes to grow replacement patches.

Chondrocytes or cartilage generated from knee-joint chondrocytes in labs have produced mixed results when implanted into injured knees. Similarly inconsistent results have been found with a common surgery called microfracture, in which a surgeon drills tiny holes into the ends of the bones where cartilage has been worn off or lost to injury. Marrow cells that leak out have stem cell–like properties that can form cartilage caps, but the cartilage is inferior to the smooth hyaline cartilage that normally caps the ends of bones (*SN: 8/11/12, p. 22*).

The nasal passages also contain hyaline cartilage. So Martin and colleagues removed chondrocyte-containing cartilage from goats' noses, grew it in dishes for four weeks and then used the newly grown patches to repair knee cartilage damage at the ends of the animals' femurs. Six months later, the nasal-origin patches held up better than others grown from joint chondrocytes.

The nasal chondrocytes formed higher-quality patches than the joint chondrocytes. The scientists noted that a family of genes called *Hox*, which are important in development, behave differently in the nasal chondrocytes than in the joints. Martin says the research team plans further tests to determine whether this unusual *Hox* profile has a direct role in the performance of the nasal chondrocytes.

Triggering tissue growth can be useful, but too much cell growth would be a concern. In the goats, Martin says, the injury defects were "sufficiently filled but never overfilled" by the cartilage patches, with no signs of aberrant growth.

INGO RISCHAWY/SCHUSTER LAB/UNIV. OF BAYREUTH

Watch a video of a fish spitting at **bit.ly/SN_archerfish**

fish were making head movements that might adjust for different heights. Again the answer was apparently not.

Training an archerfish to perform for a high-speed camera took about a year, Schuster says. Getting fish to spurt water at targets is the easy part, but he also needed them to spit only from the small zone where the cameras focused and to ignore the glaring lights.

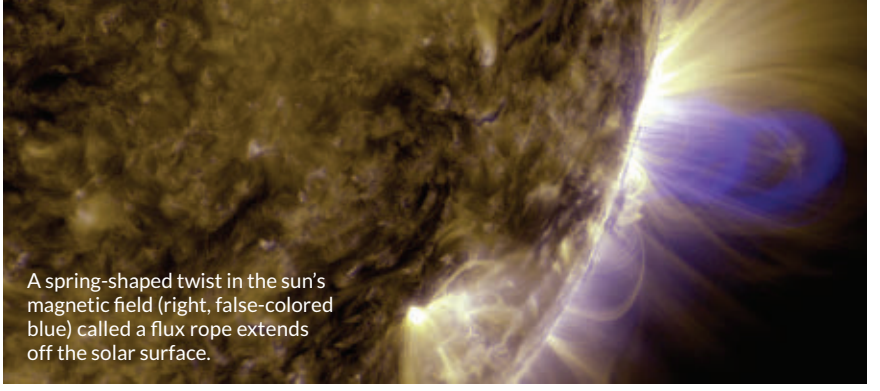
Videos of fish faces and the streams they were spitting revealed complex mouth motions. Opening and closing speeds, for example, changed depending on the height of the target. Plus, he saw evidence of continuous shaping of the water stream as the shot varied in cross section.

Now Schuster is interested in how the demands of nuanced spitting may have influenced the considerable cognitive powers of archerfish. The new research, he says, means that archerfish need to be added to the club of animals that use tools. The fish aren't just appropriating an object (water, in this case) to do a job; they're also modifying it to improve its function. ■

Ming Pei, a cell biologist who studies cartilage regrowth at West Virginia University in Morgantown, calls the series of tests described in the study impressive. It's key that the nasal chondrocytes could grow well and produce cartilage, he says. "These nasal chondrocytes look like stem cells," Pei says. "They're a promising source for cartilage regeneration."

The patches also seem to bind well to existing cartilage tissue at the edge of the injury sites, Martin says. Magnetic resonance images of the human patients show no clear difference between the new and old cartilage, suggesting that hyaline cartilage derived from different parts of the body can integrate.

The researchers have now treated their 10th patient and will assess the group's knee health in a year. They also plan to investigate the method in animals with injuries that have degenerated into inflammatory osteoarthritis in the joint. ■



A spring-shaped twist in the sun's magnetic field (right, false-colored blue) called a flux rope extends off the solar surface.

SDO/GSFC/NASA

ATOM & COSMOS

Plasma corkscrews produce new twist

Latest observation extends debate over solar eruptions

BY THOMAS SUMNER

A twist on the sun is throwing solar scientists for a loop.

For the first time, researchers have watched the sun's magnetic field force plasma into a spring-shaped curl during a powerful solar eruption known as a coronal mass ejection, or CME. The new observations contradict previous research suggesting that the twisted plasma structures are precursors of CMEs, which can disable satellites and disrupt air travel when directed toward Earth. The new findings appear August 28 in *Astrophysical Journal Letters*.

Understanding whether the magnetic curls trigger CMEs or are caused by them could help solar scientists spot impending solar storms well in advance, says astrophysicist Angelos Vourlidas of the U.S. Naval Research Laboratory in Washington, D.C., who was not involved with the new study. "A reconciled theory would potentially allow us to see the early stages of a CME and issue warnings days instead of hours before it reaches Earth," he says.

Scientists monitor the sun's invisible magnetic field by watching how it steers glowing solar plasma. In the aura of plasma that surrounds the sun, called the corona, the field can bend into large loops of plasma more than 10 times as wide as Earth. When two loops cross paths, they can spiral around each other into a coil-shaped structure known as a flux rope.

Plasma physicists have produced two competing hypotheses to explain the formation of the spring-shaped structures and their connection to CMEs. The debate boils down to whether ropes form before or during these solar eruptions.

In the first hypothesis, the rope forms before a solar eruption. After drifting for hours or days, the rope suddenly kinks like an overtwisted phone cord, pushing solar material outward as a CME.

In the second idea, CMEs instead erupt when the ends of magnetic loops somehow disconnect from the sun's surface. As the CME's blob of solar material bursts outward, the severed loops connect to one another, forming a flux rope.

The first hypothesis gained credence in July 2012 when NASA's Earth-orbiting Solar Dynamics Observatory satellite spotted a flux rope form and float around for eight hours before it kinked and appeared to trigger a CME. The event seemed to settle the debate.

But in November 2013, the probe recorded the birth of another flux rope that supported the second explanation. The rope formed during an ongoing CME when severed magnetic loops fused together into a slinky-shaped spiral. Solar physicist Hongqiang Song of Shandong University in Weihai, China, who led the analysis, says that the eruption's location on the sun's edge, when viewed from the probe's perspective, allowed researchers to clearly see the plasma outlining the rope.

Song says his team's finding demonstrates that neither theory can completely explain the relationship between CMEs and flux ropes, which complicates efforts to improve solar storm prediction. "We still have a long way to answer why, when and where solar outbursts will take place," he says. ■

Watch a video of a solar eruption at **bit.ly/SN_sun**

Drifting ice slabs periodically refresh the surface of Jupiter's frozen moon Europa. This frigid world is the only known place aside from Earth home to active plate tectonics.

ATOM & COSMOS

Plate tectonics spotted on Europa

Shifting landscape on Jupiter's moon is first outside Earth

BY THOMAS SUMNER

Plate tectonics churns the icy exterior of Jupiter's moon Europa, researchers report September 7 in *Nature Geoscience*. The finding marks the first evidence of plate tectonics beyond Earth.

"Earth is not unique — we've found another body in the solar system with plate tectonics," says planetary scientist Simon Kattenhorn of the University of Idaho in Moscow. "This tells us that this process can happen on more than just rocky planets like Earth."

Previous observations have seen surface reshaping, such as volcanic activity, on other planetary bodies including Saturn's moon Titan (*SN: 1/25/14, p. 14*). However, Kattenhorn says, Europa is the first found with a patchwork of drifting tectonic plates.

The rising and sinking ice slabs on Europa's surface may provide a mechanism for nutrients to move from the moon's surface to its subsurface ocean, Kattenhorn argues. Such transport would bolster the likelihood that this ocean hosts life. Astrobiologist Britney Schmidt of Georgia Tech in Atlanta says the mechanism is "very exciting for Europa's chances for supporting life."

Though the moon formed over 4 billion years ago, at the same time as the rest of the solar system, Europa's icy surface is surprisingly young. Based on the moon's small number of impact craters, scientists estimate Europa's surface to be just 40 million to 90 million years old. Dark bands crisscross the moon where warm, fresh ice wells up to the frigid surface, but a mystery remained: Where is the old material?

Two years ago, Kattenhorn and coauthor Louise Prockter of Johns Hopkins University Applied Physics Laboratory in Laurel, Md., spotted something odd as they scoured a Louisiana-sized portion of Europa mapped by NASA's Galileo spacecraft in 1998. In the moon's northern hemisphere, a 20,000-square-kilometer hunk of landscape was missing. Like a torn photograph placed so that the pieces overlap, Europa's crisscrossing surface fractures didn't properly line up.

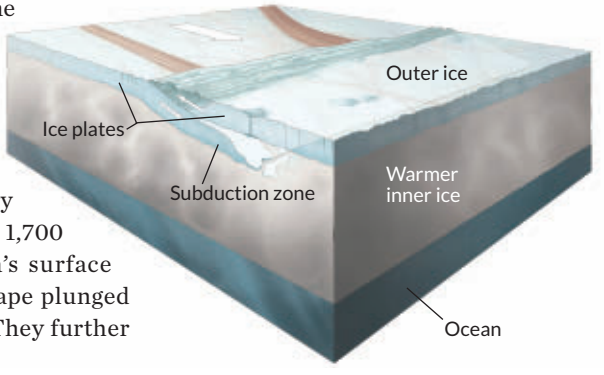
The researchers propose that this discrepancy marks where two massive ice slabs smashed together, with one sinking under the other and blending into the moon's warmer interior ice. The action resembles a subduction zone on Earth, where one slab of crust — or tectonic plate — slides beneath another. Studying the maps, Kattenhorn and Prockter trace the boundary between the ice slabs over 1,700 kilometers along Europa's surface where the missing landscape plunged into the moon's interior. They further suggest that Europa's entire surface is broken into a network of rigid segments analogous to Earth's tectonic plates.

"The subduction rate on Europa could be very similar to what we have on Earth," Kattenhorn says. Because of Europa's small size, that rate could mean the surface recycles itself in less than 90 million years. "That's exciting," he says, "because it means we now have a mechanism that explains the young surface."

This churning could benefit any possible life in Europa's subsurface ocean, Kattenhorn says. As radiation from Jupiter bombards the moon's surface, energy-packed organic nutrients may form from simpler chemicals. The tectonic activity offers a way for these surface nutrients to plunge down into the liquid water tucked under Europa's thick ice shell.

Schmidt says that the finding comes at an opportune time. Europa Clipper, a proposed NASA mission to the frozen moon, recently entered its early design stages in hopes of a 2022 launch.

"Everything we've discovered about Europa makes it more and more Earth-like and exciting for the potential of life beyond our planet," she says. "This research shows we need to go back to Europa and we should go back soon." ■



Crushed ice Where two ice slabs, analogous to Earth's tectonic plates, collide on Europa, one slab dives under the other, forming a subduction zone. The sinking ice fuses with the warmer inner ice shell surrounding the moon's subsurface ocean.

FROM TOP: TED STRYK/GALILEO PROJECT/JPL/NASA; NOAH KROESE/I.NK

BODY & BRAIN

Rabies hijacks cell transport system

Scientists get first good look at how virus races up neurons

BY MEGHAN ROSEN

The rabies virus may take the express train to the brain.

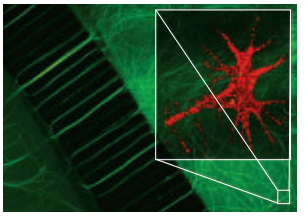
To race up long nerve cells that stretch through the body, the virus hijacks a transporter protein and hits the gas, researchers report August 28 in *PLOS Pathogens*.

The new work "is very promising," says virologist Monique Lafon of the Pasteur Institute in Paris, and could give researchers another target in their search for therapies against rabies infections.

With a fatality rate near 100 percent when untreated — higher than Ebola — rabies stands among the most deadly diseases in the world. The virus lurks in the saliva of infected animals and passes to humans most commonly through a bite. Then it steals up the nerves and into the brain, killing cells and often triggering bizarre behaviors, such as hyperactivity and a fear of water.

A vaccine can block the infection, but only if given to patients before or soon after a rabid animal's bite. Once the virus creeps into the nerves, it's pretty much unstoppable, Lafon says. "We need to find antivirals that can block the progression of the virus."

Scientists knew that the virus hitchhiked up nerve cells instead of cruising through the bloodstream, but until now no one had been able to get a good look at this long-distance travel, says Harvard virologist Silvia Piccinotti.



A nerve cell protein (inset, red) resides throughout the splayed tip of a mouse nerve and ferries the rabies virus (inset, green dots) up cells' long extensions.

By adopting a microfluidics technique used in physics and engineering, the scientists were able to mimic on a silicone chamber the movement of virus particles in the body. After growing mouse nerve cells on the penny-sized chamber, neurobiologists Shani Gluska and Eran Perlson of Tel Aviv University in Israel and colleagues infected the neurons with rabies. Then the team tracked the viruses' journey through the long, skinny mouse cells, as well as the paths of proteins known to latch onto the virus.

One such protein, called p75NTR, normally carries molecules important for nerve cell survival. But when p75NTR traveled with the virus, the protein shuttled the disease-causing particles up nerves even faster than usual, the team found. "Rabies virus kidnaps and manipulates the cells' transport machinery," Perlson says.

The virus rides with p75NTR in little acidic bubbles and somehow forces the protein to speed up. The virus has other methods it uses to travel along nerve cells, but p75NTR seems to be the rapid transit system for rabies, Perlson says.

Future antivirals could target p75NTR, Lafon notes, as well as other cellular proteins the rabies virus exploits. ■

ERAN PERLSON AND COLLEAGUES

BODY & BRAIN

Treatment may aid babies with autism

Changing how parents interact with children shows promise

BY LAURA SANDERS

Changing how parents talk to, play with and feed babies in their first year of life may reduce the symptoms of autism, a small preliminary study suggests.

Although many children with autism aren't diagnosed until age 4 or later, researchers are finding ways to detect the signs of the disorder in younger children, even in the first few months of life (*SN Online: 11/6/13*). The trouble is that good treatments for infants don't yet exist.

"We don't just want to identify kids with autism and then make parents wait for a really long time to get intervention," says psychologist Annette Estes of the University of Washington in Seattle. Though preliminary, the study, published September 12 in the *Journal of Autism and Developmental Disorders*, is a step toward developing early, effective treatments, she says.

A behavior-based therapy called the Early Start Denver Model, which focuses on teaching children with autism ways to communicate and learn, has already shown promise in toddlers between 18 and 30 months old. In the new work, scientists asked if a modified version of the therapy helped even younger children.

Sally Rogers of the University of California, Davis MIND Institute in Sacramento and colleagues tried the technique on 6- to 15-month-olds who had shown signs of autism. These infants seemed more interested in objects than in people, showed strong fixation on objects and didn't try to communicate with caregivers as much as typical babies do.

Over 12 weeks, the researchers taught the parents techniques to engage their babies. Compared with four babies who had shown similar autism signs but whose parents declined the therapy, seven treated babies scored better on learning and language measures at age 3. Three of the four untreated babies received an autism diagnosis at age 3, compared with two of the seven treated children.

Because the study did not randomly assign infants to treatment, the researchers can't say whether the therapy helped. "These data do not prove that this intervention either prevented autism or changed the course," Rogers said in a news briefing.

Still, child psychiatrist Fred Volkmar of Yale University says the results are encouraging. "I don't want to oversell this study, but this is one now of several studies that are showing promising results with treatment" in young children. ■

HUMANS & SOCIETY

DNA illuminates Siberian immigration

First North American Arctic culture vanished, study suggests

BY BRUCE BOWER

North America's Arctic regions were settled around 5,000 years ago by people from Siberia who eventually created a culture that lasted for nearly 4,000 years before suddenly disappearing, a new genetic study suggests.

This founding Arctic culture vanished either shortly before or after the arrival of another genetically distinct crowd of Siberians. That later band of immigrants spread their Thule culture across Alaska, northern Canada and Greenland and served as the ancestors of present-day Inuits, says a team led by paleogeneticists Maanasa Raghavan and Eske Willerslev, both of the University of Copenhagen.

Neither the Thule nor the earlier Arctic colonists, who created tools and figurines typical of what's called Dorset culture by around 3,000 years ago, display a genetic connection to current Native American groups living south of the Arctic, the scientists report in the Aug. 29 *Science*.

Those Native Americans descended from an even earlier group of Siberians that traveled to North America at least 12,000 years ago but didn't settle in the Arctic, the investigators propose.

While their North American populations may have overlapped for only a few generations, members of the Dorset and Thule cultures shared genetic similarities that point to a common, founding population in Siberia. That group existed before anyone reached Arctic North America, Raghavan says.

New genetic evidence also challenges a prevailing view that a remnant population of Dorset descendants survived into the early 20th century, until they died from a disease introduced by European whalers. The Sadlermiut people, inhabitants of two islands in Canada's Hudson Bay who perished in 1903, display evidence only of ancestry to modern Inuits, Raghavan says. Sadlermiut culture developed over generations of living in isolation from other Inuit groups, in her view.

"The real mystery is therefore why the Dorset disappeared so completely ... after they and their [New World] ancestors had survived successfully in the Eastern Arctic for around 3,500 years," writes anthropologist Robert Park of the University of Waterloo in Canada, in a commentary in the same issue of *Science*.

Radiocarbon dates from ancient campsites indicate that Dorset and Thule peoples coexisted in the New World for as many as 150 years, says anthropologist and study coauthor William Fitzhugh of the Smithsonian Institution in Washington, D.C. Dorset people were no match for bow-and-arrow-equipped members of large, well-organized Thule communities capable of hunting walruses and large whales, Fitzhugh holds. Dorset folk were either pushed out or annihilated by the newcomers, he suspects.

Alaskans who made wooden dolls such as this one 400 to 500 years ago descended from members of the Thule culture, which arrived in the New World over 1,000 years ago.

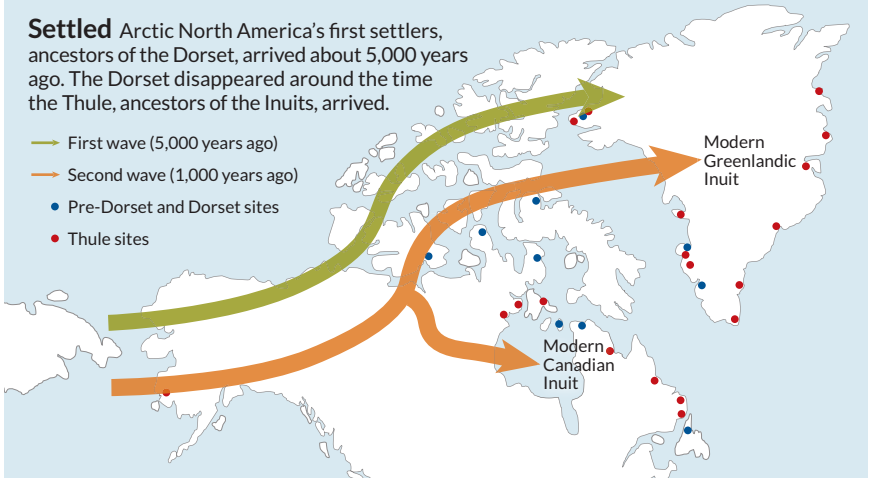
Park disagrees. No evidence exists that Dorset people uprooted entire villages or retreated to less desirable locations near the end of their run, he says. Radiocarbon dates in the Arctic may be off by decades or centuries, he adds. Dorset people were gone before the Thule arrived, Park suspects, for unknown reasons.

Willerslev's team extracted mitochondrial DNA from preserved bones, teeth and hair of 154 ancient individuals excavated in Arctic Siberia, Alaska, Canada and Greenland. Data from complete mitochondrial genomes came from 26 samples. Comparisons of mitochondrial DNA sequences allow researchers to trace people's maternal ancestry.

Ancient samples included mitochondrial DNA previously obtained from 4,000-year-old hairs from a Greenland man (*SN: 3/13/10, p. 5*) and the 24,000-year-old arm bone of a Siberian boy (*SN: 12/28/13, p. 16*).

The researchers also analyzed nearly complete mitochondrial genomes from modern Arctic residents: two Native Americans in western Canada, an Inuit in Greenland, an Aleutian Islander and two Siberians.

Ancient Thule people showed no genetic relationship to 34 later Scandinavians from southern Greenland. That argues against mating between the Thule and Vikings who reached Greenland around 1,000 years ago. ■



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EARTH & ENVIRONMENT

Sea trash defies ocean boundaries

Plastic garbage swirls around globe, obscuring its sources

BY BETH MOLE

Math may help scientists figure out who is responsible for massive tracts of trash in the oceans — and the culprits may not be the obvious suspects.

Using mathematical simulations of ocean currents, researchers at the University of New South Wales in Sydney show that plastic garbage may take circuitous cruises before joining huge patches of floating debris in distant oceans. The study, published in the September *Chaos*, bucks a common assumption that coasts closest to the litter are responsible for the plastic, which can be deadly to sea life. The new calculations redefine ocean borders and offer a way to help identify the countries dumping the most debris.

"This is an important step if you want to get to a point where we can say, 'The U.S. is responsible for X percent' " of the pollution, says oceanographer Erik van Sebille, one of the study's coauthors.

At least five giant masses of floating rubbish exist around the world, including the great Pacific garbage patch. The patches are areas with high concentrations of trash — mostly tiny bits of plastic particles degraded from larger pieces of litter such as water bottles. The bits amass within ocean vortices, driven by wind and ocean currents. Because of the patches' tiny pieces and constant swirling, researchers have trouble tracking and sourcing the flotsam.

Van Sebille and colleagues used ocean simulations run on a supercomputer to estimate how millions of plastic bits would flow off land and move within and between the world's oceans over a period of about a year. The team then looked for common patterns and links between ocean regions to predict where trash from a certain coast would end up.

The researchers found surprising routes for the trash. Garbage flung toward the Indian Ocean from southern Australia could end up in the Pacific, van Sebille says. And litter that sets sail off eastern South Africa may anchor in the Atlantic rather than the Indian Ocean. What makes identifying polluters especially complicated, van Sebille says, is that trash doesn't always stay in a garbage patch. A piece of litter can join one clump of rubbish, then later break free and make its way to one in another ocean.

Most researchers wouldn't have guessed that debris in one ocean can come from another, says Kara Lavender Law, an oceanographer at the Sea Education Association in Woods Hole, Mass.

These unexpected paths suggest the oceans' borders need to be redrawn, van Sebille says. Lines on maps are somewhat arbitrary. By seeing how ocean circulation and winds move particles from region to region — or keep them out — scientists can get a better sense of each ocean's true boundaries. ■

BODY & BRAIN

Magnets diagnose malaria in minutes

Tabletop device detects metallic excrement of blood parasites

BY NSIKAN AKPAN

Magnets might soon reveal brewing malaria infections long before symptoms appear. In mice, magnetic sensors take mere minutes to spot otherwise imperceptible levels of the parasitic blood infection, scientists report August 31 in *Nature Medicine*.

"With malaria, a few days can be the difference between life and death," says coauthor Peter Preiser, a parasitologist at Nanyang Technological University in Singapore. "If confirmed in humans, our technique could detect disease roughly two to four days earlier."

Infecting an estimated 207 million people worldwide, malaria is currently diagnosed in one of two ways. Splashing a few blood droplets on a dipstick can yield a color-coded answer in 15 minutes. These rapid tests can ensure early treatment; however, they miss about one of six cases in patients with low levels of the parasite. In the second method, expert eyes supply greater accuracy by spotting the parasites under a microscope, but this technique requires training, equipment and time.

207 million
Malaria cases globally (2012 estimate)

In the new study, researchers harnessed magnetic sensors to diagnose malaria infections in five minutes with even better accuracy than routine microscopy. Researchers detected parasites in mouse blood as low as one-fifth the levels perceptible with microscopes. Similar sensitivity in human samples would allow detection before symptoms appear, upping the odds of successful treatment.

"When diagnosis comes too late, it often leads to hospitalization," says Preiser.

The device relies on the inherent magnetism in the iron-containing protein hemoglobin in red blood cells. In the bloodstream, malaria parasites invade and gorge on hemoglobin, converting it into tiny crystallites called hemozoin, says micromechanist Weng Kung Peng of the Singapore-MIT Alliance for Research and Technology in Singapore. Hemozoin boosts the red blood cells' magnetization, revealing the presence of parasites, says Peng, a coauthor of the study.

The gadget is innovative because of its microelectronics and because it tracks natural nanoparticles, says Hakho Lee, a biomedical engineer at Harvard University who wasn't involved with the study.

The new device, which draws its inspiration from nuclear magnetic resonance machines, could fit in a shoebox. The next challenges will be to test the technique in humans and to make the device even smaller, says MIT biomedical engineer and coauthor Jongyoon Han. ■

The heavy stone blocks ancient Egyptians used to build the pyramids thousands of years ago could have been rolled along the ground like makeshift wheels.

MATH & TECHNOLOGY

Another pyramid solution proposed

Stones could have been rolled on wooden dowels, physicists say

BY MEGHAN ROSEN

Egypt's pyramid construction plans could have included a little rock and roll.

Ancient Egyptians might have rolled giant bricklike stones to pyramid building sites by strapping wooden rods to each rock, researchers suggest in a paper posted August 14 at arXiv.org.

The method offers a new take on a Herculean task that has long puzzled people. The rolling hypothesis could even dodge potential complications with the leading theory: that Egyptians slid blocks along slippery paths.

Physicist Daniel Bonn of the University of Amsterdam, who has studied the mechanics of the sliding technique, thinks the rolling method could probably work. "Technically, I think what they're proposing is possible. But technically, a lot of things are possible."

Over 4,000 years ago, ancient Egyptians hefted more than 2 million limestone blocks into place to build the Great Pyramid of Giza. Each massive stone was on average about 1.3 by 1.3 by 0.7 meters and weighed 2,500 kilograms — as much as a Chevy Tahoe. Egyptians hauled each of these blocks a kilometer or more from quarries to the construction site. Many researchers think workers loaded the blocks onto sleds and pulled them along a sort of Slip'N Slide, a ramp slickened with wet clay or cattle fat.

Some evidence supports the theory: Scientists have found the remains of ramps built out of sand, clay and fist-sized chunks of limestone, and traces of fat in soil near the pyramids. What's more, ancient tomb and temple drawings depict Egyptians transporting enormous statues on sleds.

But while watching a TV special in which archaeologists used the sled method to construct a small-scale pyramid, physicist Joseph West of Indiana State University in Terre Haute had a new idea.

"I thought, well gosh, why don't they just try rolling the things?" he says. Strapping wooden rods to four faces of a block, he thought, would turn it into a kind of rough wheel. "It should be a lot easier to roll than a square," he remembers thinking.

He and two students tested the idea by lashing three wooden dowels to four sides of 30-kilogram limestone or concrete blocks, turning each block's square cross section into a dodecagon.

Then the team rolled the block by placing it on a rope on the ground, like a spool of thread lying on its side. By wrapping one end of the rope around the block and pulling, the team could roll the makeshift wheel over grass, gravel and hard-packed dirt.

Rolling didn't require much effort, the team found. The researchers needed about the same amount of force to keep the block rolling as people using the slippery road method needed to keep the sleds sliding.

Block rolling isn't a completely new idea. Engineers had previously devised related techniques but didn't collect force data.

Although West hasn't tested a scaled-up version of his method, he thinks it has some potential advantages over sleds. Workers wouldn't have had to carry water or fat to lube up the roadways ahead of the sleds, for one. And rolling the blocks may have caused less road damage than sleds, he suggests.

After strapping wooden dowels to four faces of a concrete block, researchers rolled the clunky cuboid stone over dirt, grass and gravel.

Instead of attaching wooden dowels to the blocks, Egyptians would have had to use thick posts about 30 centimeters in diameter — about the size of masts used on ships in the Nile, West points out.

At this point, the rolling theory is pure speculation, says Richard Redding, an archaeologist at the University of Michigan in Ann Arbor. "People see the pyramids as a great mystery," he says. "They're always coming up with new ideas about how they're built." ■

FROM TOP: STEVENALLAN/ISTOCKHOTO; J. WEST *ET AL*/ARXIV.ORG 2014

LIFE & EVOLUTION

Bats hunt frogs by echolocation

Male túngara frogs make easy prey for fringe-lipped bats, thanks to echolocation, scientists report August 27 in the *Journal of Experimental Biology*. The bats' sonar spies the amphibians' ballooning vocal sac (shown), turning a sexual display into an invitation for lunch. Researchers placed 10 wild fringe-lipped bats into enclosures with two lifelike rubber imitations of male túngaras. Both frogs played mating calls, but only one had a billowing vocal sac. The bats always attacked the frog sporting the puffing sac. Shutting off the lights didn't stop bats from successfully hunting. Bats became flummoxed, however, when a plastic cup covered the fake frog's vocal sac, indicating that the hunt requires echolocation. An ultrasonic microphone detected the sound waves of the bats' echolocation chirps. The bats emitted at least two sonar bursts after each of the frog's croaks, which overlapped with the sac's expansion and deflation. Constant sac movement was the giveaway, says coauthor Wouter Halfwerk of the Smithsonian Tropical Research Institute in Panama. The bats build a mental scene with the contrasting echoes, spotting the moving vocal sac among static ground clutter, Halfwerk says. — *Nsikan Akpan*

BODY & BRAIN

Electrical pulses to the brain may bring memory gains

Zaps to the head can enhance people's memory by coaxing brain regions to work more cooperatively. A technique called transcranial magnetic stimulation, or TMS, helped healthy people recall words paired with faces, Joel Voss of Northwestern University and colleagues report in the Aug. 29 *Science*. In TMS, an electromagnetic coil placed on the head produces small electrical currents that stimulate nerve cells close to the brain's surface. A logical location for applying such stimulation would be the hippocampus, a structure important for memory. But the hippocampus is buried too deeply in the brain to be reached with TMS. The team instead turned to a spot near the

ADAM DUNN

top left surface of the brain's wrinkly outer layer that's known to work with the hippocampus. Sixteen healthy subjects received stimulation at the location for 20 minutes for five days. About a day after their last stimulation, participants saw pictures of faces paired with spoken words. About a minute after first learning the pairs, participants who had received stimulation remembered which word went with each face better than those receiving no stimulation. — *Laura Sanders*

High-dose flu shot benefits elderly

Compared with standard vaccination, a beefed-up flu shot better protects older adults, researchers report in the Aug. 14 *New England Journal of Medicine*. The elderly are at higher risk of flu because immunity wanes with age. In 2009, a "high-dose" flu shot for people age 65 and older was approved. To find out whether the vaccine translates into fewer flu cases, researchers randomly assigned over 30,000 elderly people in the United States and Canada to get the high-dose or standard flu shot. Scientists at vaccine maker Sanofi Pasteur, which funded the study, tabulated who got sick during the subsequent flu season. Lab tests confirmed that about 1.9 percent of people getting the standard vaccination and 1.4 percent of those getting the heftier shot developed the flu. The stronger shot contains more flu protein than the other one. — *Nathan Seppa*

GENES & CELLS

Gut bacteria curb food allergies

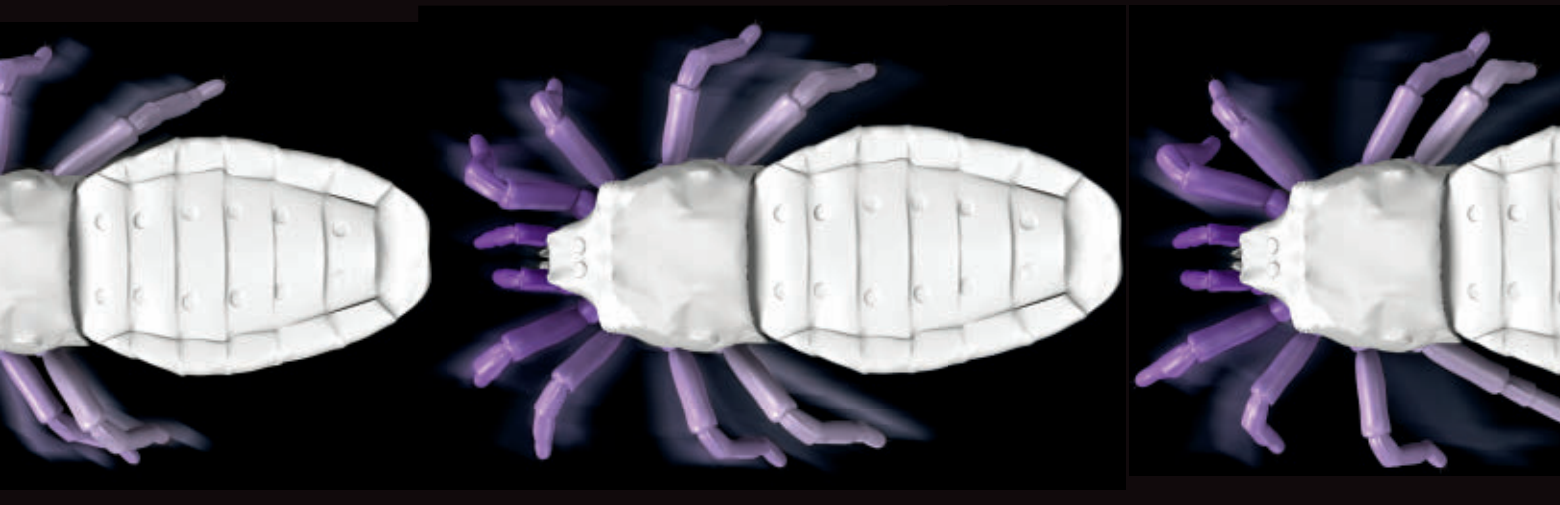
Peanuts can drive people's immune systems nuts, but microbes could offer some protection. Mice harboring *Clostridia* bacteria in their guts are less sensitive to the legumes than mice without the microbes, researchers report August 25 in the *Proceedings of the National Academy of Sciences*. Cathryn Nagler of the University of Chicago and colleagues treated mice with antibiotics to wipe out the animals' gut bacteria, and then triggered an allergy-like response to peanut particles. Peanuts revved up the germ-free animals' immune systems, but mice with normal gut bacteria didn't have the bad reaction. Giving germ-free mice a dose of *Clostridia* made the animals more like mice with normal gut flora. The microbes encourage mouse cells to make mucus that helps seal the intestines, keeping food particles from slipping into the bloodstream and riling up the immune system. Humans also harbor *Clostridia*, so boosting these bacteria's numbers with probiotics may help prevent or treat food allergies in people, the team suggests. — *Meghan Rosen*

ATOM & COSMOS

Milky Way's place in space mapped

The Milky Way is part of a much vaster galactic network than previously thought. The galaxy drifts in a stream of galaxies on the outskirts of a newly identified collection of galaxy clusters, each of which contains hundreds to thousands of galaxies. This supercluster, named Laniakea, holds the mass of 100 million billion suns in a region that spans 520 million light-years. R. Brent Tully of the University of Hawaii and colleagues sifted through data on the positions and velocities of over 8,000 galaxies to get a fresh look at the Milky Way's place in space. After accounting for motion caused by the universe's expansion, the team created a 3-D view of how gravity molds the galaxy's cosmic neighborhood. The work, published in the Sept. 4 *Nature*, reveals Laniakea's boundaries and web-like framework. The Milky Way lies along one of the lines of that web, in a tributary feeding one of many galactic rivers. Those streams converge in a gravitational valley roughly 200 million light-years away near two massive galaxy clusters. Their combined gravity appears to be drawing in other galaxies and clusters within Laniakea, including the Milky Way. — *Christopher Crockett*

VIRTUALLY THERE



Paleontologists are using 3-D scanning to resurrect ancient animals on-screen and learn how they lived **By Alexandra Witze**

On a paleontologist's computer screen, this arachnid moves as it did 410 million years ago.

All Rachel Racicot wanted to do was look at a fossil. As a paleontology graduate student at San Diego State University, Racicot had scheduled some time with a local hospital's CT scanner. She was going to examine a 3-million-year-old porpoise jaw.

But when the day came to slide the fossil into the scanner, the hospital put her on hold. A stabbing victim needed the CT machine. Paleontology would have to wait.

For Racicot and her colleagues, such temporary setbacks are a small price to pay. In the last few years, cutting-edge CT scans and other novel techniques have dramatically altered how paleontologists visualize and study ancient life. Detailed images provided by the improved technologies are allowing researchers to build digital three-dimensional reconstructions of prehistoric plants and animals like never before.

This field is called virtual paleontology. It has become much more than a source for nifty images of cool fossils; it reveals fundamental new insights about past life.

Once Racicot finally snared the scanner for her fossil, the resulting images revealed a porpoise unlike any known today. Elsewhere, scientists using animation software have digitally reactivated an ancient predatory arachnid that walked the planet hundreds of millions of years ago. Other teams have used three-dimensional CT scans to explore extraordinary detail preserved in fossilized plant seeds, allowing scientists to reconstruct new histories of how plant groups evolved and spread over time.

"We're now getting down to resolutions that no one ever imagined," says paleontologist Imran Rahman of the University of Bristol in England.

R. GARWOOD AND J. DUNLOP/*JOURNAL OF PALEONTOLOGY* 2014

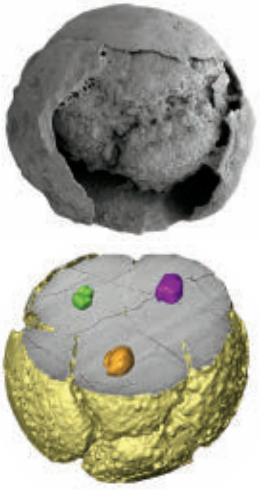
"Sometimes we know much more about the fossils than about the living animals they are related to."

Rahman and colleagues reviewed the field's promise in June in *Trends in Ecology & Evolution*.

Paleontologists have been trying to build 3-D visualizations of fossils since the early 20th century, when William Sollas of the University of Oxford perfected a technique for grinding through a fossil sequentially. Sollas would grind away for a fraction of a millimeter, then stop and photograph the exposed fossil in exquisite detail. By repeating this process time and again — sometimes through hundreds of layers — Sollas eventually built a slice-by-slice encyclopedia of a given fossil, which he could then reconstruct as a 3-D wax model.

But his method destroyed the fossil and took a lot of time. By the 1980s, paleontologists had taken to zapping fossils in machines such as CT scanners, which send X-rays through an object to build up a three-dimensional picture of what's hidden inside. In recent years, that technology has improved enough for scientists to extract tantalizing information about fossils.

In most cases, an ordinary CT scanner will do. Researchers typically take a rock to their local hospital or university CT laboratory and adjust the settings until the X-rays penetrate at just the right energies to reveal the form encased in the rock. In more complicated cases, such as when the fossil and the rock surrounding it look stubbornly similar, the scientists might take the rock to a more sophisticated machine.



Synchrotron scans of a fossil from China's Doushantuo formation (top) yield a 3-D image (bottom) showing three nuclei, indicating the fossil is not from an animal or embryo, but a protist.

Virtual dissection

Paleontologist John Cunningham, also at the University of Bristol, regularly packs up his most precious fossils and flies with them to the Swiss Light Source in Villigen, Switzerland. That machine is a synchrotron, which accelerates electrons to nearly the speed of light. The accelerated electrons emit radiation including X-rays, which are usually used to explore questions in physics, materials science and chemistry. Unlike CT scanners, which use X-rays over a range of wavelengths, synchrotrons can produce X-rays of a single wavelength. That level of control allows scientists to manipulate the scan far more precisely and coax out detail from even the most stubborn structures hidden within rock.

Cunningham has used the Swiss synchrotron to explore some of paleontology's most controversial fossils: millimeter-sized blobs in 570-million-year-old rocks from the Doushantuo formation in southern China. Some scientists think the blobs represent embryos of some of the oldest known animals in the fossil record, which if true would be an astonishing witness to the earliest evolution of animals. But nobody could see past the surface.

Using the super-sharp insight of the synchrotron X-rays, Cunningham's team virtually dissected the blobs, revealing structures within. Those structures, some as small as a thousandth of a millimeter across, may be the nuclei of ancient cells. If so, they show that the fossil creatures had been developing differently than would be expected from early animals, and probably belong instead to a group known as protists.

The work, reported in 2011 in *Science*, underscored the power of synchrotron imaging for studying complicated fossils. Cunningham is now looking at slightly younger fossils, embryos from about 542 million years ago — just after a diversity of animals spilled forth in the evolutionary burst known as the Cambrian explosion. The synchrotron images reveal details about how the embryos developed: One of them "might look like a worm curled up and about to hatch, or something with spines around its mouth," Cunningham says. By piecing together different fossils that represent the various stages as these embryos developed, he and his colleagues are building a more complete picture of how early animals might have been related to one another.

Rahman has been using CT scans to work out the digestive systems of ancient echinoderms, a group of marine animals including starfish and sea urchins. Searching the literature, he found mostly century-old information on the digestive systems of a modern group of echinoderms. That drove him to start scanning as many echinoderms as possible, to try to build up a database of information on how the modern and ancient groups might relate to one another.

Rahman's scans revealed the first known digestive tract in ancient echinoderms. It looks

In 1904, William Sollas devised a method of grinding through a fossil layer by layer (top) to build up a 3-D wax reconstruction, such as the model of the vertebrate *Palaeospondylus* (below).

FROM TOP: T. HULDTGREN ET AL/SCIENCE 2011; J. CUNNINGHAM ET AL/TRENDS IN ECOLOGY & EVOLUTION 2014

Even an ancient fossil as fragile as a daddy longlegs can be visualized in exquisite detail.

remarkably similar to the guts of modern echinoderms. "Instead of this idea of things starting out simple and becoming incredibly complex, almost from the very beginning of the appearance of these different organisms, they have been rather complex," he says.

Ancient versus modern life

Sometimes the scans show more than just never-before-seen details: They help paleontologists reconstruct major evolutionary changes from the past. Rahman's scans revealed that the earliest echinoderms had a body plan that was bilaterally symmetrical, where one side mirrors the other. Modern echinoderms, such as the five-pointed starfish, are fivefold symmetric. If their ancestors displayed a twofold symmetry, Rahman says, the creatures must have undergone some significant changes in body design over the last half-billion years. "You can see that in the fossil record," he says.

Such insights wouldn't have been possible without the exceptional detail coming from computer scans. The discoveries are more than just pretty pictures — they divulge fundamental differences between ancient and modern life, allowing biologists to better understand how organisms evolved.

"In the past paleontologists may have been guilty of coming up with ideas that we weren't really able to test," Rahman says. "With these new modeling and imaging approaches, we can go about testing some of these hypotheses and try to unlock the secrets of the history of life."

Russell Garwood is taking this challenge to the extreme. A paleontologist at the University of Manchester in England, Garwood specializes in arthropods, the invertebrate animals that thrived on land well before creatures with a spine ever crawled out of the sea. He has studied fossils from the Rhynie Chert, a famous rock formation from northern Scotland. Silica-rich water from a hot spring infiltrated an ancient terrestrial ecosystem there and then mineralized, preserving plants and animals in extraordinary detail.

Garwood chose a 410-million-year-old fossil of a creature called a trigonotarbid, which despite being just a couple of millimeters long was one of the first predators to ever stalk on land. Garwood didn't use X-rays to probe the fossil, because it is so similar to the rock encasing it that even synchrotron beams can't tease it out. Instead, he used old-school techniques, studying thin sections of rock containing the fossil to develop 3-D maps. He transferred his maps of the animal's leg fragments to computer-graphics software similar to that used to animate movie characters.

"Each joint within the leg has only the range of motion available to it that we think the original creature had," Garwood says. "You can then work out how we think it walked." He calculated the creature's center of mass and then compared its possible motion to living arachnids.

The result: an extinct arachnid, resurrected and walking around on Garwood's computer screen. His calculations suggest that it moved pretty much like modern spiders and could scuttle relatively fast. Its mouth parts — including a filtering plate where it might have predigested food — indicate that it fed on other animals, so "we can say they were probably running down their prey," Garwood says. This tiny terror adds to the understanding of what the ancient Rhynie Chert landscape looked like and how its inhabitants interacted.

"The more work like this we do, the more complete picture we have of the fossil record," Garwood says. For instance, he and his colleagues have figured out something new about a 305-million-year-old daddy longlegs. The fossil was preserved within an iron-rich mineral called siderite, which often precipitates out around dying organisms in coal-rich rocks. The animal becomes entombed in siderite and, after its body rots away, leaves behind a hole reflecting its shape.

Garwood and colleagues used a CT scanner to obtain exquisite detail on the daddy longlegs fossil. They discovered a pair of structures on its side, which they argue might be a second pair of eyes.

Larger than life

The ancient arachnid *Eophrynus* pops into virtual reality when its fossil (top) is given dimension in a computer reconstruction (middle) and printed on a 3-D printer (bottom).

FROM TOP: R. GARWOOD, NATIONAL MUSEUM OF NATURAL HISTORY, FRANCE; I. RAHMAN *ET AL/ EVO. EDU. OUTREACH* 2012; I. RAHMAN *ET AL/EVO. EDU. OUTREACH* 2012; I. RAHMAN

Virtual digging CT scanning can take a single fossil (at left, a shark tooth embedded in rock) and, using X-rays to differentiate between the fossil and the encasing rock, extract virtual cross-sectional slices (center) of the remains. Adding lights, color and perspective renders the fossil into a three-dimensional view (right).

Shark tooth fossil | CT slices | Ready for 3-D glasses

Modern daddy longlegs have only one pair of eyes, but spiders have multiple pairs aimed in different directions. The ancient daddy longlegs could have had eyes on both its front and its sides before losing the side pair in evolutionary history, the team wrote in May in *Current Biology*.

An aquatic lifestyle

Computer scans and reconstructions are helpful not only for probing tiny animals, but also for shedding light on bigger creatures. For instance, Racicot uses 3-D scans to explore the evolution of whales, dolphins and porpoises. Unlike most marine animals, whales once lived on land and moved into the sea starting about 50 million years ago. Somewhere along the way, dolphins and porpoises also evolved the ability to use echolocation to find their way around the deep. That meant major evolutionary changes to their skulls.

"Their heads are just really weird," says Racicot, who is now with Howard University in Washington, D.C. "They committed totally to an aquatic lifestyle." For example, the noses of toothed whales moved from the fronts of their faces to the top of the skull to form a blowhole. They also developed a lump of specialized fat tissue atop the head, known as the melon, which helps the animals focus and direct sound to bounce off nearby fish.

Three-dimensional fossil scans help expose those differences as the animals evolved, Racicot says. "If you scan it, then you basically have a copy of it forever, and you can reconstruct things like the brain, the little holes and areas that are important in different ways."

In San Diego, she finally managed to scan the skull and other parts of a 3-million-year-old porpoise that had been unearthed at a construction site. Ever since the fossil's discovery in 1990, paleontologists had noticed the animal's odd protruding lower jaw.

The CT scans allowed Racicot to see that the sensory canals in the porpoise's jaw extended the entire length of the bone. The only modern animals that have this sort of structure are skimmer birds and a kind of fish known as a halfbeak, she says. Both of those feed by using sensory canals in their jaws to sense nearby prey and then snap down their dinner as they skim above or through the water. Similarly, the extinct porpoise may have used its pointy chin to root through the soft sand on the seafloor, sensing the vibration of small animals and then eating them. In the March 31 *Current Biology*, Racicot and her colleagues dubbed the animal *Semirostrum*, since the upper part of its jaw, or rostrum, is so much shorter than its elongated lower part.

It's not clear when or why *Semirostrum* eventually went extinct, although changing sea levels

Slicing and dicing Unlike older forms of analysis, which destroy the fossil and can take weeks to do, nondestructive, high-resolution scanning has become a go-to method for paleontologists interested in revealing hidden anatomies of ancient organisms. SOURCE: J.A. CUNNINGHAM *ET AL/TRENDS IN ECOL. & EVOL.* 2014; I. RAHMAN AND S. SMITH/*J. PALEO.* 2014

Technique	Data collected	Destructive?	Resolution	Scan time
Serial grinding	Optical images of exposed surfaces	Yes	10 µm	Days to weeks
Micro-CT	X-ray attenuation images	No	1 µm	Minutes to hours
Synchrotron-based tomography	X-ray attenuation images	No	200 nm	Minutes
MRI	Distribution of light elements	No	10 µm	Minutes to days
Laser scanning	Surface images	No	50 µm	Minutes to hours

R. ABEL *ET AL/PALAEONTOLOGIA ELECTRONICA* 2012

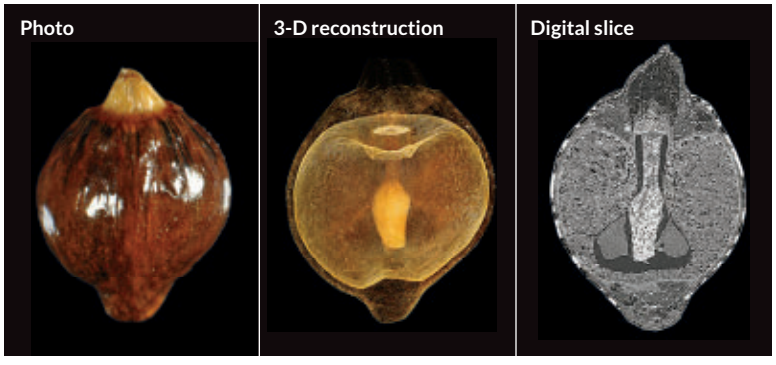
Peculiar porpoise Computerized scans of a now-extinct porpoise called *Semirostrum* reveal the sensory organs (middle, red) embedded in its unusually long lower jaw. The animal may have used the organs to sense prey as it rooted through seafloor sediments.

may have played a role by shrinking the animals' available habitat. Modern porpoises also find their food in seafloor sediment, but they don't have the extra sensory organs in their jaws that *Semirostrum* appears to have had millions of years ago. "It's pretty obvious that this animal was extremely specialized compared to any of the modern porpoises that we see," Racicot says.

Botanical surprises

The same is true for many ancient plants revealed through 3-D computer scanning. Paleobotanists have long used microscopes to devise detailed pictures of the surface of plant fossils. But X-rays can penetrate inside to expose crucial structures such as the stamen or pollen-bearing organ. In a comparison of different flowers from the Cretaceous period, from 145 million to 66 million years ago, paleobotanist Else Marie Friis of the Swedish Museum of Natural History in Stockholm and her colleagues described a range of botanical surprises. For one, X-ray scans revealed that a single fragmentary fossil from western Portugal was actually the oldest known flower from the group that today includes water lilies. And scans of rare Swedish flower bud fossils confirm that they had an unusual number of stamens hidden inside, Friis' team reports in the July *Journal of Paleontology*.

Seeds of discovery
A grain-of-paradise (*Aframomum melegueta*) seed (photographed, at left) is scanned and made into a 3-D volume rendering on the computer (middle). At right is a single digital slice through the seed. Botanists use these images to explore the evolutionary relationships among plants.



Selena Smith, a paleobotanist at the University of Michigan in Ann Arbor, uses X-ray imaging to explore the evolutionary history of banana and ginger plants from the order Zingiberales through their fossilized seeds. "Seeds have an amazing amount of information in them, even more than flowers for some groups," she says. How the seed coating is put together, which parts are thicker than others and how many cells and layers are in different parts of different seeds are the kind of details that help botanists trace the relationships among various plants.

Smith has been studying a part of the seed called an operculum, a little lid through which a germinating plant must push to escape the seed. The shape of the operculum varies dramatically among the banana and ginger plants, helping Smith place the seeds in their proper places on the evolutionary tree. Surprisingly, she says, botanists know relatively little about modern banana and ginger seeds, so she is scanning many of them as well.

As scanning technologies and computer software get more sophisticated, 3-D reconstructions will probably gain in popularity among paleontologists. Some are already copying fossils using 3-D printers so that they can touch specimens they once only dreamed of handling. Rahman says the applications he has seen are striking.

"The technology has been taken in directions no one really anticipated." ■

Explore more

- I.A. Rahman *et al.* "Virtual fossils: a new resource for science communication in paleontology." *Evolution: Education and Outreach*. March 2012.
- J.A. Cunningham *et al.* "A virtual world of paleontology." *Trends in Ecology & Evolution*. June 2014.
- Palaeontologica Electronica: http://palaeo-electronica.org

FROM TOP: R. RACICOT *ET AL*/*CURRENT BIOLOGY* 2014; S. SMITH/UNIVERSITY OF MICHIGAN

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LOW-TECH Bacteria BATTLE

To fight antibiotic resistance, doctors need to change the way they prescribe

By Nathan Seppa

Clostridium difficile (shown) is common in hospitals and is hard to treat.

"It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them...."
Alexander Fleming, discoverer of penicillin, in his 1945 Nobel Prize lecture

Fleming's remarks were spot-on. Since the heady days of penicillin's discovery, an overuse of antibiotics has spawned bacterial resistance to the drugs and threatened to erase decades of success. Every prescription that misses the mark or throws excess drugs at a bacterium gives bystander bacteria a good look at those antibiotics and a head start in resisting their effects, as Fleming noted.

Some microbes are changing faster than antimicrobials can kill them. As a result, it's once again possible to get a bacterial or fungal infection for which there is no sure cure. That's how roughly 23,000 people die in the United States each year.

As hopes fade that new antibiotics will save the day, many treatment centers are taking a surprisingly low-tech approach: They are changing the behavior of prescribing physicians. The goal of this tactic, called antimicrobial stewardship, is to curb antibiotic resistance by speeding diagnoses, getting the most appropriate drug to each patient, limiting intravenous drug delivery and avoiding use of broad-spectrum antibiotics — scattershot drugs that hit more than one kind of microbe. Evidence shows that antimicrobial stewardship can shorten a patient's hospital stay and lower drug expenses. Fighting resistance may not be futile.

Antimicrobial stewardship requires an agile response from institutions that are not known for changing quickly. But it mainly demands human investment: training, diligence and doctors' agreement to abide by guidelines and relinquish some control over prescribing. Consumers also have to do their part. The days of demanding antibiotics at the doctor's office may soon be history.

It won't be easy. Ending antibiotic resistance, or even getting the upper hand, will take more than antimicrobial stewardship: It will demand the relentless use of infection-control measures such as hand-washing and "gowning and gloving" in hospitals and clinics. Pharmaceutical companies will need to develop new antibiotics. Plus, doctors will need prompt access to top-line diagnostics to identify ever-changing microbes (see sidebar, Page 25), the high-tech piece of the puzzle.

In the early antibiotic era following World War II, a stream of drugs from Big Pharma kept bacteria at bay. But the pipeline is running dry. "Pharma is not producing antibiotics at a rate that allows us to stay ahead of the problem," says physician Scott Flanders of the University of Michigan in Ann Arbor. There's not much profit in creating drugs if bacteria are just going to outsmart them. The deck seems stacked against a supply-side solution.

Some new drugs are likely to get approved in coming years, but prescribing behavior will have to change to take advantage of them, says physician Dennis Maki of the University of Wisconsin–Madison. "The development of new antibiotics without having mechanisms to ensure their appropriate use is much like supplying your alcoholic patients with a finer brandy."

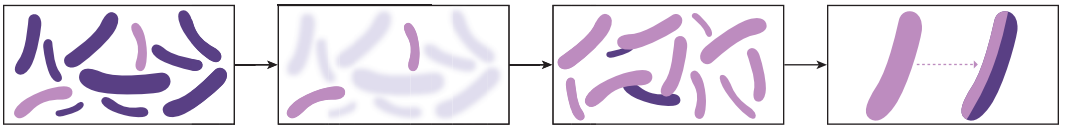
Antibiotic overload

Well-known bacteria such as *Staphylococcus*, *Streptococcus*, *Escherichia coli*, *Salmonella* and *Neisseria gonorrhoeae* are increasingly dodging the effects of drugs as are other less-known but dangerous microbes, the World Health Organization

55.7
percent
Fraction of U.S. hospital patients who got antibiotics in 2010

CDC

Resistance grows Antibiotic resistance is a selection process by which microbes become impervious to drugs built to kill them. SOURCE: CDC



reported in April. Antibiotic resistance frequently shows up in patients with tuberculosis, pneumonia, wounds and urinary tract infections.

Resistant infections send doctors searching for another pill that will work. More than half of patients discharged from U.S. hospitals received antibiotics during their stay in 2010, the U.S. Centers for Disease Control and Prevention estimated in a report released in 2014. The report suggests that antibiotic prescriptions for some ailments could be cut by more than one-third with key interventions.

"Our goal is not in any way to limit necessary antibiotic use," says study coauthor Arjun Srinivasan, a CDC physician. "We are seeking to improve the use of antibiotics so they remain effective for patients who need them down the road."

The kind of controlled use CDC is aiming for would logically start in hospitals, especially in the intensive care unit — resistance central. Patients who land in the ICU are already in trouble, and doctors tend to medicate them thoroughly. ICU patients have the highest antibiotic use in hospitals, says Nick Daneman, an infectious disease physician at the University of Toronto.

Those patients also have the highest resistance rates, he says. For example, bloodstream infections in patients, which can trigger a lethal condition called sepsis, were traceable to multidrug-resistant pathogens in 23 percent of patients analyzed at nine hospitals in the southeastern United States, according to a report in the March 18 *PLOS ONE*.

Antibiotics taken unnecessarily are not harmless, says physician Jeffrey Linder of Harvard Medical School. He points to *Clostridium difficile* as an example of what can go wrong. *C. diff*, for short, is a bacterium that can establish itself in the gut and cause debilitating diarrhea when it overgrows. Good microbes that dwell in the intestines normally suppress levels of *C. diff*, but the microbe circulates in hospitals and strikes patients who are on antibiotics that have wiped out some of those protective gut bacteria. When *C. diff* takes hold, it's hard to treat (*SN Online: 10/4/13*).

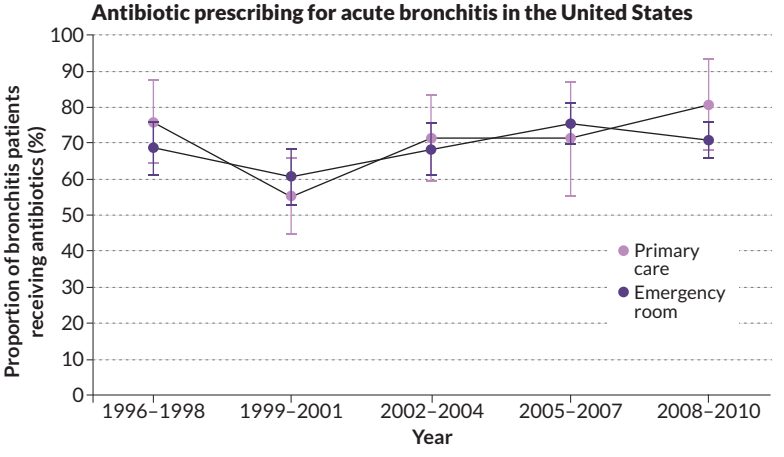
To illustrate, physician Timothy Sullivan of Mount Sinai Hospital in New York City describes a recent case of *C. diff* in August's *JAMA Internal Medicine*: A woman in her 80s with diabetes arrived at a hospital emergency room with an infected cut on her arm. She got three antibiotics and treatment for the wound. A soft tissue infection required surgery to remove dead tissue. She stayed in the hospital and received broad-spectrum antibiotics for three weeks as the surgical site healed. The day after her antibiotics were stopped, she developed a *C. diff* infection, with diarrhea, fever, dropping blood pressure and signs of kidney failure. Despite best efforts, she died.

People entering a hospital with an indeterminate-but-serious infection often get antibiotics immediately because, if the infection really is bacterial, the patient might die without the drugs, Flanders says.

CDC recommends a stewardship review of prescriptions within 48 hours after the first dose by an impartial source, such as an infectious disease doctor or pharmacist. More than second-guessing the prescribing doctors, these audits offer a chance to fine-tune the treatment if the diagnosis has changed, says Daneman.

He and his colleagues conducted a study of critical care patients in which they intervened as

Stubbornly high Even though most acute bronchitis is caused by viruses, the percentage of U.S. patients treated with antibiotics remains in the range of 55 to 80 percent, according to a national sampling. SOURCE: M.L. BARNETT AND J.A. LINDER/*JAMA* 2014



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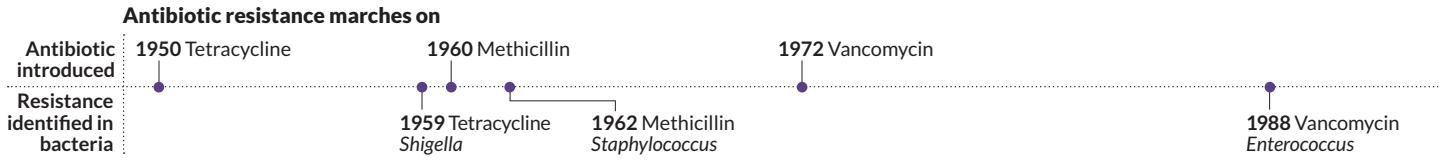


Give and take
This sampling of four antibiotics and subsequent resistance to them shows how quickly resistance emerges as antibiotics are introduced.
SOURCE: CDC

necessary three days after the first dose of antibiotics and again at day 10. The diagnosis for many patients had changed. A stewardship pharmacist spoke with the doctors attending the patient regarding antibiotic use. Doctors accepted 82 percent of those recommendations. As a result, broad-spectrum antibiotics use at the large hospital was reduced from earlier rates and, most importantly, ICU cases of *C. diff* originating in the hospital decreased. The study appeared in *Infection Control and Hospital Epidemiology* in 2012.

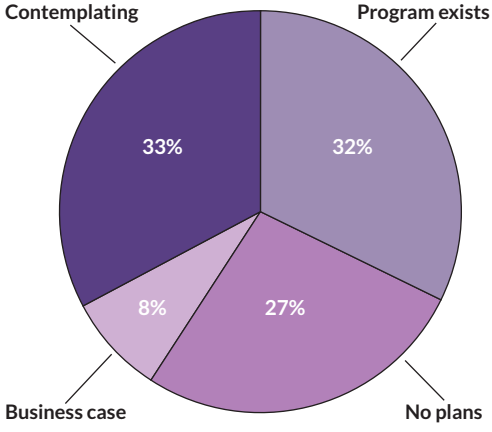
At Blount Memorial Hospital in Maryville, Tenn., pharmacist Brad Crane evaluates prescriptions and recommends changes. Prescribers accepted more than 90 percent of 977 recommendations made by Crane and colleagues in the first two years of the hospital's stewardship program. Antimicrobial costs per patient have dropped from an average of about $29 to $22 per day, a sign of more efficient use of the drugs. Crane says the results show that stewardship can work at community hospitals, not merely at large facilities affiliated with universities. He reported early findings at a medical meeting in 2013.

Blount Memorial Hospital uses a strategy typical of stewardship programs. The aim is to steer doctors away from intravenous drugs, since IV lines can get infected, and discourage broad-spectrum antibiotics in favor of narrowly focused drugs.

"We tend to use antibiotics too long and at too-high doses," says Neil Fishman, an infectious disease doctor at the University of Pennsylvania.

Coming around
Antimicrobial stewardship is a work in progress. This 2011 survey of hospitals in Ontario, Canada, showed that about a third had a protocol in place, just over 40 percent were working up a business case for implementation or were discussing the idea, and more than one-quarter had yet to act.
SOURCE: P. REDDY *ET AL/PUBLIC HEALTH ONTARIO, ID WEEK* 2013

Antimicrobial stewardship programs in Ontario, 2011



Antibiotic stewardship can improve quality of care and cut costs, he says, so it's not difficult to convince hospital administrators of the programs' value. Flanders notes that hospitals are increasingly judged on how many hospital-origin infections they have. Any program that lowers that number is welcome, he says.

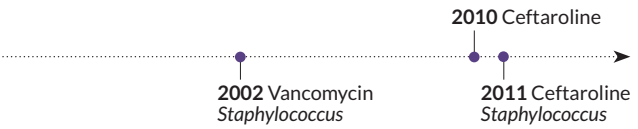
Outpatient clinics

Hospitalized patients are typically quite sick and many have bacterial infections. In those cases, the stewardship challenge is to determine the correct antibiotic. The question facing doctors in outpatient clinics is often different: "Does this patient need any antibiotic at all?" says Ralph Gonzales, a physician at the University of California, San Francisco.

Outpatients walk in under their own power, often with nondescript symptoms they have researched on the Internet. Some ask for drugs up front. Bronchitis is a common complaint, and antibiotics typically don't help because more than 90 percent of the time the illness is caused by a virus, says Linder, the Harvard physician. With or without drugs, he says, "it's gone by day 20." Even so, more than half of U.S. patients with bronchitis are prescribed antibiotics. "There's this magical thinking that an antibiotic prescription will treat a viral infection."

To test whether stewardship interventions can clean up prescribing in clinics, Gonzales and his colleagues enlisted 33 clinics in central Pennsylvania for a study. Eleven received a large poster for the examination room showing low-to-high likelihood of a patient having bacterial pneumonia — which would merit antibiotics — or a viral ailment. Eleven other clinics received decision-making guidelines electronically that doctors and nurses could consult when diagnosing respiratory infections. The last 11 clinics got neither.

Over six months, rates of antibiotic prescribing dropped from 80 percent to 68 percent in clinics showing the posters and from 74 percent to 61 percent in those getting computerized guidance. Prescriptions were largely unchanged in the control group, where about three-fourths of patients got antibiotics for respiratory infections, the researchers reported in 2013 in *JAMA Internal Medicine*.



While that reduction might seem modest, Gonzales says, "across the population that accounts for a lot."

Doctors' chief concern when testing a patient with a respiratory ailment is pneumonia, he says. The electronic guidance helps them sort that out, he says, providing details on symptoms that point to pneumonia and away from myriad other respiratory ailments.

The posters help them counsel patients. Adults coming in with a cough-related illness often are in some kind of denial, Gonzales says. "I tell them this drug could do more harm than good, and they say, 'That's OK, I'll take my chances.'" He adds, "[The poster] helps to provide some collective norms about proper antibiotic use."

Going a step further, some researchers have asked prescribers to sign and post a commitment letter about antibiotic use in the exam room. Jason Doctor, a psychologist at the University of Southern California in Los Angeles, tested the effect of a letter stating that antibiotics can make bacteria more resistant and that getting them needlessly can cause problems.

"This was a powerful motivator," he says. Having the letter visible in 14 exam rooms coincided with an average drop in inappropriate prescribing from 44 percent to 34 percent. The key was getting the doctors to sign and post the letter. It made them more accountable, Doctor says. "Precommitment ties you to the mast." The report appeared in *JAMA Internal Medicine* in March.

Prescriptions in doctors' offices are harder to track than in hospitals. But prescribers doled out antibiotics for sore throats in about 60 percent of adult cases between 1997 and 2010 in the United States, even though only about 10 percent of sore throats in adults are due to strep bacteria and require the drugs. In clinics, doctors face pressure "to appease the patient" even when an antibiotic isn't needed, says Ohio State University pharmacist Debra Goff.

There are other pressures, too. "It takes a minute to write a script," Fishman says. "It takes 15 minutes to not write one, to provide education."

And even when strep throat is correctly diagnosed, Linder says, some doctors treat it with the broad-spectrum antibiotic azithromycin, sold as Z-Pak, to which *Streptococcus pyogenes* has shown resistance. Use of penicillin, to which *S. pyogenes* has never been resistant, "has dwindled off," he says. Z-Pak requires a shorter course than penicillin. People and doctors have this perception that newer is better, Linder says. "Z-Pak sounds cool."

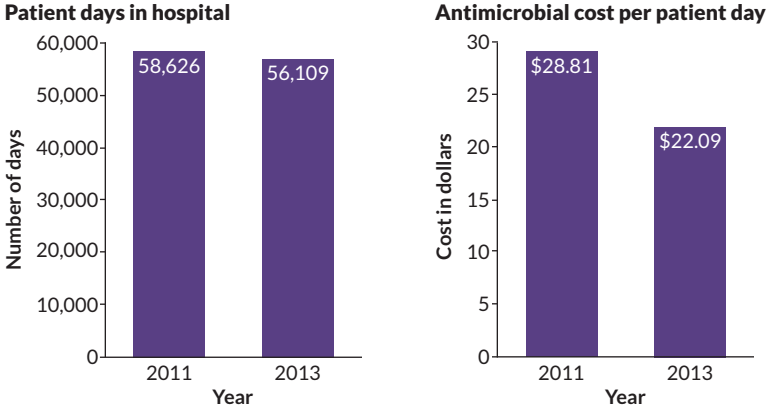
Turning the Titanic

Antibiotics deserve a big share of the credit for improved health care in the 20th century, but now their sporadic failure risks sabotaging those gains. Hospitals have changed from healing centers to risky stopovers where

Delays matter

A fast, accurate diagnosis can aid antimicrobial stewardship by curbing the drug-bug mismatches that add to resistance:

- **Polymerase chain reaction (PCR).** *Staphylococcus aureus* hangs out innocently in most people, but it can also cause infection and gain resistance to the antibiotic methicillin. Ohio State University pharmacist Debra Goff and her colleagues tested 74 people at OSU Medical Center in 2008 using standard *S. aureus* diagnostics, which took about three days. In 2009, the researchers repeated the test on 82 patients, using PCR after the initial blood culture, to amplify the bacteria's DNA and discern within an hour if a patient had methicillin-resistant *S. aureus*. Those patients got the right meds 1.7 days sooner on average than the 2008 group, the scientists reported in *Clinical Infectious Diseases* in 2010. "We saved $21,000 per episode of staph," Goff says.
- **Mass spectrometry.** Researchers at Houston Methodist Hospital analyzed 265 patients with gram-negative bacteria infections. Patients treated before the researchers had mass spec, a rapid chemical analysis, waited more than 80 hours to get optimal antibiotic therapy. When mass spec was available, patients received the correct drug within 30 hours, as reported in the *Journal of Infection* in September. Only 9 percent of patients aided by mass spec died compared with 21 percent who got the slower diagnosis.
- **Procalcitonin test**. This peptide appears in the blood during bacterial infections, which can lead to sepsis, a lethal condition. At Mercy Medical Center in Des Moines, Iowa, researchers checked procalcitonin levels in 35 patients with suspected sepsis or pneumonia. Those patients, on average, needed only 10 days of treatment versus 14 days in a similar group that didn't get the test, according to a 2013 report.
- **Rapid antigen detection test**. A quick test to distinguish strep throat from a viral sore throat is available in many clinics. It can rule out strep — and the need for antibiotics — in about 10 minutes. The test has the most utility in children, who are more prone to strep than adults. — *Nathan Seppa*



One hospital's progress At a community hospital in eastern Tennessee, an antimicrobial stewardship program instituted in 2011 has been followed by lower antimicrobial costs per day. Overall, the total days patients spent in the hospital, including those unaffected by stewardship decisions, declined modestly.

SOURCE: B.J. CRANE/BLOUNT MEMORIAL HOSPITAL

one is advised to get in and get out before catching a superbug. Not even Alexander Fleming could have predicted that.

The medical community was caught off guard. "We used to consider antibiotics as all value-added, not harmful at all," says Sara Cosgrove, an infectious disease physician at Johns Hopkins Hospital in Baltimore. "Nobody really believed it would get to this point."

It will take more than antimicrobial stewardship programs to reverse the trend. Resistance is a global phenomenon with antibiotics sold over the counter in many countries. In Mexico, Gonzales and his colleagues found that about half of 101 insured individuals who visited a family medicine clinic with a respiratory ailment were already on antibiotics, 20 of whom were self-treating. When interviewed, many mistakenly thought common cold remedies were antibiotics.

Ultimately, patients need to know better, Linder says, but he can sympathize with them. People often take a half-day off work to go to a clinic with a respiratory infection. "I spend 10 minutes with them, tell them there are no drugs and that they'll be sick for two weeks. It's all very unsatisfying," he says. "No wonder the prescriptions get written a lot."

Creative approaches might work. Gonzales and his colleagues used computer screens at kiosks in hospital emergency rooms to quiz people, in English or Spanish, on what they know about antibiotics. Of 686 people coming in with respiratory infections, only 22 percent initially doubted they needed antibiotics. That fraction rose to 49 percent after using the kiosk, the scientists reported in *Patient Education and Counseling* in 2011.

The key to establishing the value of such antimicrobial stewardship programs, whether aimed at doctors or patients, will be to show they actually slow or stop resistance. These data are just starting to trickle in. Daneman and his colleagues pored over 24 studies of stewardship programs and found that after being in place for more than six months, many showed a reduction in resistance, particularly in ICUs. The rate of decrease varied among microbes. And last month, at a microbiology meeting in Washington, researchers at New York Hospital Queens in Flushing, N.Y., reported reduced rates of multidrug-resistant *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *Staphylococcus aureus* after two years of a stewardship program. The hospital is also seeing fewer readmissions within 30 days for infections, physician Nishant Prasad said.

Antimicrobial stewardship, widely applied, could curb resistance at the source, Fishman says. But wide-scale adoption will take time.

"We're turning the Titanic," Linder says. Even so, a 2012 survey by the Children's Hospital Association found that 31 of 43 hospitals surveyed either had a stewardship program in place or were planning one. A nationwide survey of doctors found that about half worked in facilities with formal programs in place, and more than 90 percent were using some form of stewardship techniques. And a California survey revealed that half of hospitals there had a stewardship program and another 30 percent planned one.

The Obama administration appears ready to push the issue. At a July meeting of the President's Council of Advisors on Science and Technology, panel cochair Eric Lander raised the possibility of requiring hospitals to have a stewardship program to receive Medicaid and Medicare reimbursement. "We believe that having an antibiotic stewardship program is a reasonable expectation," he said.

This kind of hammer is necessary, says Fishman, otherwise some doctors could continue to dish out drugs without regard for their macro effect on the microbe population.

"This really is a 'tragedy of the commons,'" says Jason Doctor, the psychologist, referring to the classic tale of farmers overgrazing their animals on community land until it was lost to use. "Clinicians are using the public 'space' to prescribe big antibiotics. The potential harm to the greater good is devastating. We're going to really be in trouble if we don't manage this issue." ■

"We're going to really be in trouble if we don't manage this issue."

JASON DOCTOR

Explore more

■ S. Flanders and S. Saint. "Why does antimicrobial overuse in hospitalized patients persist?" *JAMA Internal Medicine*. May 2014.

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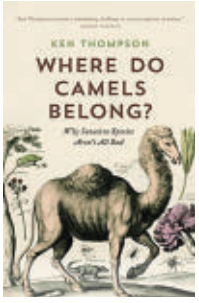


BOOKSHELF

Where Do Camels Belong?

Ken Thompson

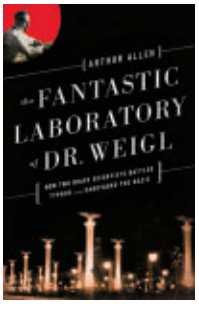
Invasive species are the outlaws of the ecological world. They move in and muck up ecosystems, sap natural resources and muscle out respectable natives. The U.S. government spends billions of dollars each year to combat these rowdy aliens, and yet they keep on coming.

But many nonnatives get a bum rap, says Thompson, an ecologist at the University of Sheffield in England. In his engrossing book, he examines the evidence for the accusations leveled against these outsider species and finds that most don't deserve the bad press.

More often than not, Thompson argues, invaders' greatest crime is moving in after human activities have made ecosystems unsuitable for natives. Even the most disparaged offenders can bring unexpected benefits to new neighborhoods. Zebra mussels, the pipe-clogging scourge of the Great Lakes, also act as an important food source for local waterfowl and fish, for example.

And eradication efforts can do more environmental damage than the invasives. Dousing hillsides in herbicide or bringing in another species to police previously introduced plants and animals can harm natives and nonnatives alike. Neither tactic worked on spotted knapweed, which has spread across the continental United States since it arrived in the late 1800s. In fact, the European flies introduced to control knapweed made a tasty snack for local deer mice. As the rodent population boomed, the mice gobbled up native plant seeds with gusto, preventing them from taking root. Knapweed, which can coexist fairly peacefully with its native neighbors, continues to bloom despite the flies.

Thompson isn't claiming that all invaders are upstanding citizens: Guam would be better off without brown tree snakes, for instance, and Australia could do without cane toads. But deforestation, dam building and other types of meddling have irrevocably changed ecosystems. Before putting the blame on nonnatives and taking costly measures to oust them, he says, it pays to figure out if they're guilty as charged. —*Allison Bohac*
Greystone Books, $17.95



BOOKSHELF

The Fantastic Laboratory of Dr. Weigl

Arthur Allen

The bacteria that cause typhus rely on the body louse to spread. Because lice thrive wherever people are crammed together under unsanitary conditions, typhus became a threat to armies and refugees alike during World War II. As a result, Nazi Germany "whipped itself into a typhus terror," writes science journalist Allen.

That fear sets the stage for Allen's book, which tells the intertwining stories of two scientists who fought on separate fronts to develop typhus vaccines and thwart the Nazis.

Before World War II, Polish biologist Rudolf Weigl had used lice to grow typhus bacteria, which are difficult to cultivate in vitro, and developed the first effective vaccine using the parasites' blood-bloated guts. After invading Poland, the Nazis pressed Weigl to produce the vaccine for the German army. A kind of Oskar Schindler of science, Weigl, a Christian, found a spot in his lab for many educated Poles needing protection. Thus, a prized job in Nazi-occupied Poland became louse feeder. Every day hundreds of Poles came to Weigl's lab and strapped matchboxes filled with body lice to their legs so the parasites could gorge on human blood.

One of Weigl's assistants during the vaccine's development was Ludwik Fleck, who was Jewish. An immunologist by training, Fleck became known for his philosophical theory of "thought collectives," which holds that no matter how objective scientists try to be, they cannot escape certain cultural tendencies.

A most perverse outcome of the Nazi thought collective, of course, was its *Geomedizin*, which defined disease in racial and cultural terms and classified typhus as a Jewish plague. Sealing off Jews in ghettos on the pretense of containing the disease became a self-fulfilling prophecy, resulting in a typhus epidemic that killed thousands. Weigl's vaccine became the most coveted item on the black market.

During the war, Fleck was condemned to concentration camps, where Nazi physicians tasked him with producing a typhus vaccine — using humans rather than lice as reservoirs. Fleck quietly resisted the Nazis, becoming a master of sabotage and using complicated sleights of hand to defy his oppressors. "The most important experiment being conducted in these laboratories, one could say, was the one that showed how easy it was to conduct bad science with a straight face," Allen writes.

Allen's vivid depictions of the scientific community before and during the war and the treacherous parallel paths Weigl and Fleck traversed — gleaned in part from interviews with Holocaust survivors — are stirring. Considering all the energy channeled into mere survival, Allen's book makes you wonder what pinnacles of research might have been achieved by now, if not for the march of war.
—*Laura Fisher Kaiser*
W.W. Norton & Co., $26.95

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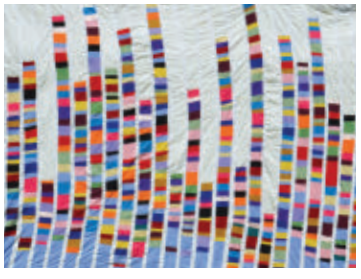
Science-inspired sewing



Longtime reader **Mary Dreyer** created a quilt (shown) based on a graph of the microbial communities found on shoes and smartphones that appeared in "Germs you carry around" (*SN: 3/24/12, p. 4*). The quilt's design, which included a citation for the study, took second prize at the Albemarle County Fair in Virginia this summer.

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The great asteroid grab

NASA plans to nab an asteroid and bring it into orbit around the moon. The mission is billed as a stepping stone to Mars, but critics question whether redirecting space rocks will help put humans on the Red Planet. ***Meghan Rosen*** *detailed the debate in "A rocky road to Mars"* (SN: 8/23/14, p. 22).

Responses to the Asteroid Redirect Mission ranged from enthusiastic ("Bring it home, NASA," urged **Stuart Pullinger** on Facebook) to lukewarm. Many people agreed that the plan was at best a compromise. "Sure, ARM was not what President Obama initially had in mind when he challenged NASA to send astronauts to an asteroid, but, given the problems of long-duration human spaceflight existing at present, it is the next best thing," wrote **Paul Scutts**. And some people saw the potential benefits of the endeavor: "I think the Asteroid Redirect Mission is an excellent idea," wrote **James Van Zandt**. "To properly exploit asteroids, or to plan defenses against asteroid strikes, we need to know much more about them."

Not everyone was excited about the plan. "It bothers me that the USA doesn't do more with its space programs, but it also doesn't help that NASA does so much these days beyond space travel," wrote **Nas**. Other comments were less kind, like this response from **damead**: "NASA is fiddling while Earth burns. The space agency is crazy not just because it's taking on such a wacko project, but because it couldn't pick a worse time to frivolously waste limited and irreplaceable resources." In an e-mail, **Don Griffiths** wondered if the agency still has the right stuff to put people in space. "NASA's constructive days are just about over in terms of future exploits. Regretfully, I agree that it's time to defund NASA in favor of private enterprise pointing the way of future growth in space."

Taking stock of stress

Money trouble, responsibility overload and health problems all topped the chart of common concerns in "Survey catalogs what is stressing out Americans" (SN: 8/23/14, p. 5).

Readers weighed in on the particular issues that keep them up at night. "Surprised that formatting references for journals is not in the list," tweeted **Sylvain Deville**. While commenting on the story, **Purple-Stater** had a moment of self-reflection: "I find it strange that politics isn't on the list. Fanatical politics is about the only thing that bothers me on a regular basis. I guess that makes me pretty lucky overall."

Looking at the results, **Dan Midgett** made an observation: "Just noticed that the percentage for women is higher on every category except 'problems with friends.' " Commenter **johnay** suggested an underlying cause for the differences between men and women: "These are self-reported factors, so there could be a cultural under-reporting bias among males."

Human impressions

In "Romanian cave holds some of the oldest human footprints" (SN: 8/23/14, p. 20), ***Bruce Bower*** *reported that fossilized tracks discovered in 1965 were left behind by* Homo sapiens *as long as 36,500 years ago.*

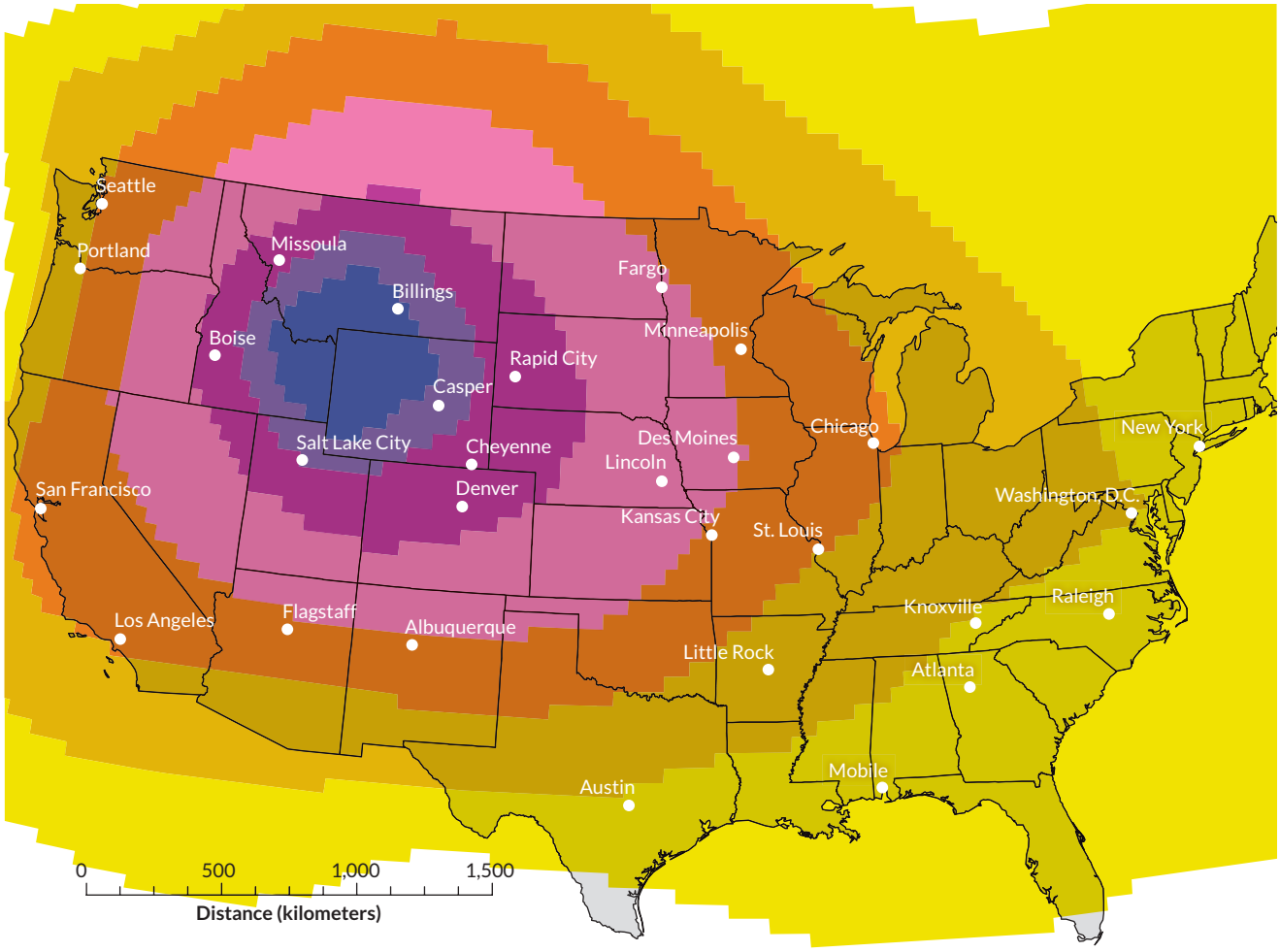
"In the article, you mention that most of the footprints in the cave have been destroyed. How did that happen?" asked **Henry Jones** in an e-mail.

Since 1965, visitors and cave explorers have trampled many of the prints, says anthropologist **David Webb** of Pennsylvania's Kutztown University. A gate recently installed across the cave's entrance now restricts access to a small number of tourists and scientists.

Correction

"A rocky road to Mars" (*SN: 8/23/14, p. 22*) said that Apollo 11 "landed three American astronauts on the moon." **Lee Helms** and **Eric E. Sporrer** pointed out that only Neil Armstrong and Buzz Aldrin touched down on the lunar surface, while Michael Collins remained in orbit aboard the command module Columbia.

M. CARSON



Forecast: Cloudy, 100% chance of ash

A new simulation illustrates the explosiveness of the volcano that lurks beneath Yellowstone National Park in Wyoming. Around 640,000 years ago, the volcano blew its top and coated North America with roughly 1,000 cubic kilometers of ash, enough to fill Lake Erie twice over. A simulation of the eruption described August 27 in *Geochemistry, Geophysics, Geosystems* reveals that a similar outburst today would bury Billings, Mont., in more than a meter (about 40 inches) of volcanic glass shards and pulverized rock. Even New York and Atlanta would receive dustings several millimeters thick as winds whisked ash through the darkened atmosphere for days.

Researchers used simulation software called Ash3d that forecasts ash fall by applying global wind patterns to data from historical eruptions. Ash3d churns out results several times faster than previous simulators and is the first program to incorporate the physics of how ash particles clump within a cloud. While geologists say Yellowstone will likely never erupt again, scientists around the world use Ash3d daily to predict the potential fallout from restless volcanoes — including Bárðarbunga, the Icelandic volcano that began erupting in late August. — *Thomas Sumner*

A country buried in ash
In the extremely rare chance that the Yellowstone volcano erupts, ash accumulations would vary from over 1,000 millimeters in areas near the volcano (blue) to a dusting on the East Coast (yellow). An inch equals roughly 25 millimeters.

Ash thickness (millimeters)
- 1–3
- 3–10
- 10–30
- 30–100
- 100–300
- 300–1,000
- >1,000

The Bárðarbunga volcano in Iceland erupts on September 4. The eruption has produced spectacular lava flows but not much ash.

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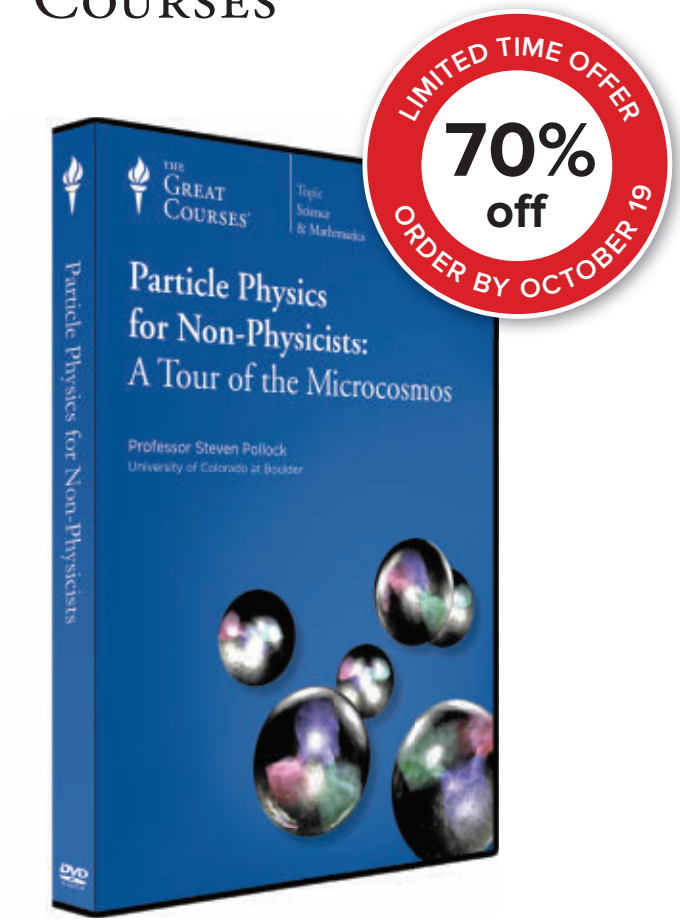

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