SN
SCIENCE NEWS MAGAZINE
SOCIETY FOR SCIENCE & THE PUBLIC
NOVEMBER 14, 2015

Earth's Fascinating Boring Billion

The Brain's Memory Holes

Gene Edits Go Big in Pigs

Quantum Computing With Silicon

Bloody BRILLIANT

How blood fuels, and sometimes drives, the brain's activity

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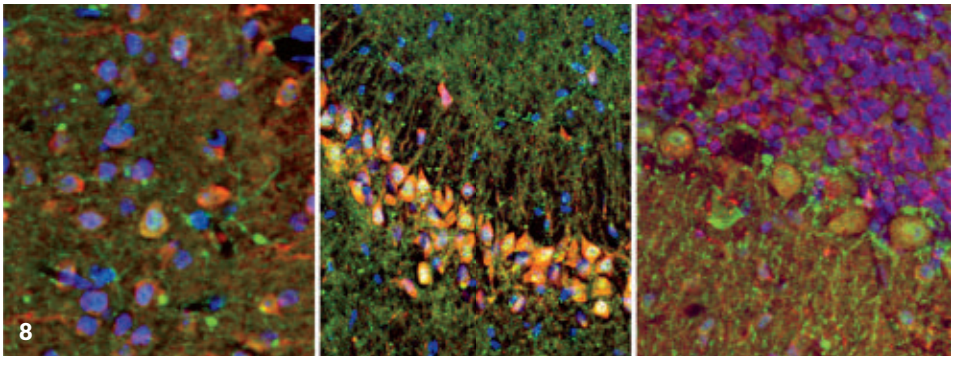

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COVER Blood in the vessels that envelop the brain, shown in a plasticized specimen, may do more than once thought. *Aad van Vliet/© 2-BBB Medicines B.V. 2015*

CLOCKWISE FROM TOP: NICOLLE RAGER FULLER; VAUGHAN LEIBERUM/FLICKR (CC BY 2.0); S. PALIDA *ET AL*

Scientists find the intrigue in Earth's dullest times

Earth's history is not so long that scientists can easily ignore large bits of it, much less a billion years — nearly a quarter of the planet's existence. But geologists have traditionally found little of interest in the time from 1.8 billion to 800 million years ago, dubbed the "boring billion." More dynamic periods have stolen scientists' attention, leaving this era relatively unexplored.

Now, new methods, coupled with new attitudes, are revising ideas about the boring billion, Thomas Sumner reports on Page 18. And that's transforming the uninteresting into the intriguing, leading scientists to ponder why the climate was so unusually stable during this period, for example, and what chain of events later jazzed things up. Scientists now say oxygen levels might have been even lower than has been thought. And evolution, presumed to have stalled given the dearth of oxygen during the boring billion, actually might have been quietly percolating the whole time.

Many biologists now argue that the boring billion was an important time in the evolution of early eukaryotes, the intricate life-forms that gave rise to the first animals. That's because, just about 260 million years after the era's end, the Cambrian explosion produced a riot of complex animals.

Recasting the boring billion as a thrill ride for life underscores how sometimes our own assumptions limit our knowledge. Looking at something carefully, with better tools or perhaps a fresh perspective, can reveal processes once hidden. We just can't see it until we look in the right way.

Laura Sanders' story on Page 22, for instance, will make you think of blood in an entirely new light. Instead of just responding to brain cells' demands for fuel, blood itself appears to sometimes command those cells. Blood can be seen as a key information-carrying medium in the body, ferrying chemical data and instructions throughout the circulatory system. Blood and brain are locked in a surprisingly dynamic give-and-take. It's yet another example of the complexity that awaits whenever we can look past our old beliefs about how things work. — *Eva Emerson, Editor in Chief*

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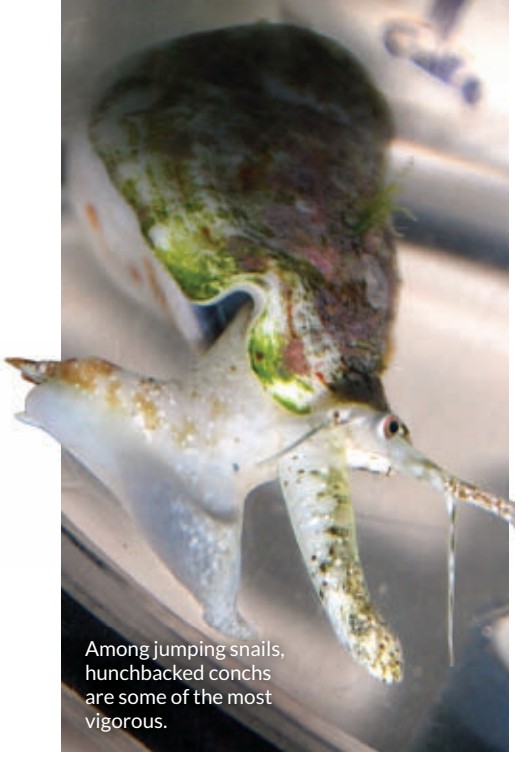
Excerpt from the November 13, 1965, issue of *Science News Letter*

50 YEARS AGO

Dog brain transplanted

Dog brains have been successfully transplanted for the first time in medical history. Dr. Robert J. White and his team of scientists at Cleveland Metropolitan General Hospital ... believe this accomplishment has opened the way to treatment of brain tumors, cancerous growths and a better knowledge of the cause and treatment of multiple sclerosis. The transplant ... acted as a second brain in the animal's neck.

UPDATE: In 1970, White transplanted a rhesus monkey's head onto a decapitated body, but the animal did not survive long. The problem of how to reconnect severed spinal cords remains a major hurdle to brain transplantation. In 2013, an Italian neuroscientist proposed a full head transplant, but many neuroscientists consider the idea technically and ethically out of bounds. Recently, special glues have shown promise in fusing severed nerve tissues. Most of today's above-the-neck transplant research focuses on faces rather than brains or heads.



Among jumping snails, hunchbacked conchs are some of the most vigorous.

IT'S ALIVE

Great jumping conchs

A whiff of danger makes hunchbacked conchs so jumpy they actually jump.

"A very peculiar movement for a snail," says Sjannie Lefevre of the University of Oslo in Norway.

Admittedly, the motion of *Gibberulus gibberulus gibbosus* is less boing-boing and more kerflop-kerflop. But each push-off can send the small, striped conchs in Australia's Great Barrier Reef several centimeters above the sea bottom and almost a body length (3 or 4 centimeters) forward. They can keep at it too, jumping as many as 100 times in three to five minutes.

The sea snails save their jumping for

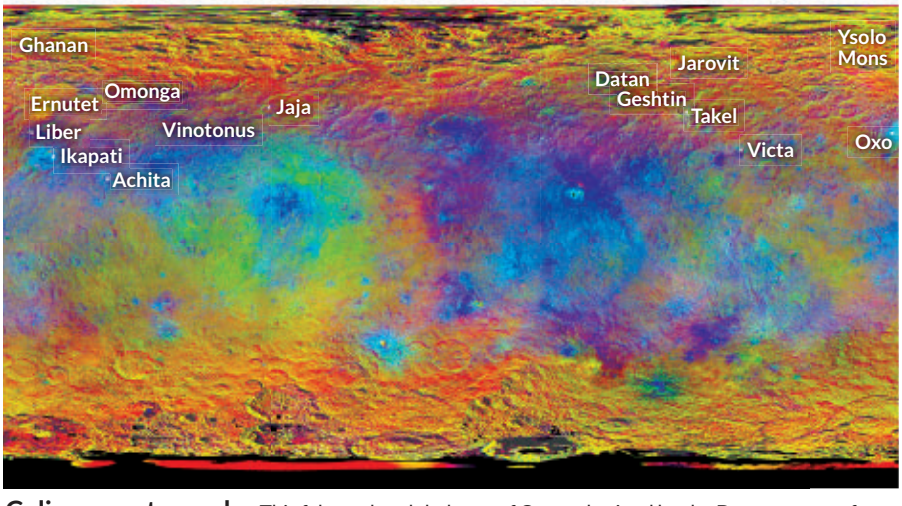
THE NAME GAME

Ceres' peaks and craters get harvest-focused names

Tubers, maize and eggplants are finally getting astronomical recognition — actually, it's the deities that look after the crops and the celebrations of their harvest. In September, 15 craters and mountains on the dwarf planet Ceres were officially named after various spirits and celebrations of things that grow, befitting a world named after the Roman goddess of agriculture.

The International Astronomical Union officially recognized a crater in the north as Takel, a Malaysian goddess of tubers. The Mayan god Ghanan now watches over not just maize but a crater near Ceres' north pole. And an Albanian festival that marks the first day of the eggplant harvest marks the mountain Ysolo Mons.

With no liquid water on the airless Ceres, gathering an assortment of divine beings is probably the only way to get anything to grow there. — *Christopher Crockett*



Culinary cartography This false-color global map of Ceres obtained by the Dawn spacecraft highlights the dwarf planet's newly named features and its changing mineral composition. Red marks areas that strongly reflect infrared light and blue regions reflect shorter wavelengths.

FROM TOP: S. LEFEVRE/UNIV. OF OSLO; JPL-CALTECH/NASA, UCLA, MPS, DLR, IDA

Watch conchs in action at **bit.ly/SN_jumpingconchs**

conch emergencies, such as when they detect dissolved body odor from the deadly cone snail *Conus marmoreus*. Cone snails glide rather than jump. But if a cone snail gets close enough, it harpoons the conch with a long, venom-delivering proboscis that is as agile as an elephant's trunk. Then it reels in the paralyzed conch like a fish on the line.

Such threats favor epic jumping in spite of the conch circulatory system, which looks inefficient at first glance. Unlike vertebrates, which sluice their blood through vessels in a closed, recirculating system, conchs and other snails pump blood away from the heart in arteries that just — end. Blood floods outward, spreading and washing over organs to deliver oxygen and nutrients. The blood then seeps back into veins that channel it eventually to the heart for another spurt.

When a conch jumps, this spurt-and-leak circulation supplies tissues with four to six times the oxygen delivered when the snail just chills, Lefevre and colleagues report in the Oct. 1 *Journal of Experimental Biology*.

In one measure of athletics, the kerflopping conch outperformed some agile, darting reef fishes. As researchers pushed water temperatures to 38° Celsius, the conch kept jumping. And its circulatory system still comfortably delivered ample oxygen. This kind of heat is less comfortable for many reef fishes, Lefevre says. "They'd be dead." — *Susan Milius*

FROM LEFT: VAUGHAN LEIBERUM/FLICKR (CC BY 2.0); J. LAMSDELL/YALE UNIV.

SCIENCE STATS

Elephants' secret weapon against cancer

Elephants' genetic instruction books include a hefty chapter on fighting cancer.

The massive mammals have about 20 copies of *TP53*, a gene that codes for a potent tumor-blocking protein, researchers analyzing elephant DNA report October 8 in *JAMA*. Humans have just one copy of *TP53*.

More gene copies mean fewer cancer deaths

	Elephants	Humans
Cancer death rate	4.8%	11 to 25%
Copies of *TP53* gene	~20	1

SOURCE: L.M. ABEGGLEN *ET AL*/JAMA 2015

An extra dose (or 19) of the anti-cancer gene may explain why elephants have unusually low cancer rates, say Joshua Schiffman, a pediatric oncologist at the University of Utah in Salt Lake City, and colleagues.

Schiffman's team pored over 14 years of animal autopsy data from the San Diego Zoo and a separate database with detailed information on 644 elephant deaths. From these data, the team calculated that just 4.8 percent of elephants die of cancer. For humans, that number runs between 11 and 25 percent depending on cancer type and population.

Elephants' extra genes could help keep defective cells from morphing into tumors, the researchers suggest. — *Meghan Rosen*

THE -EST

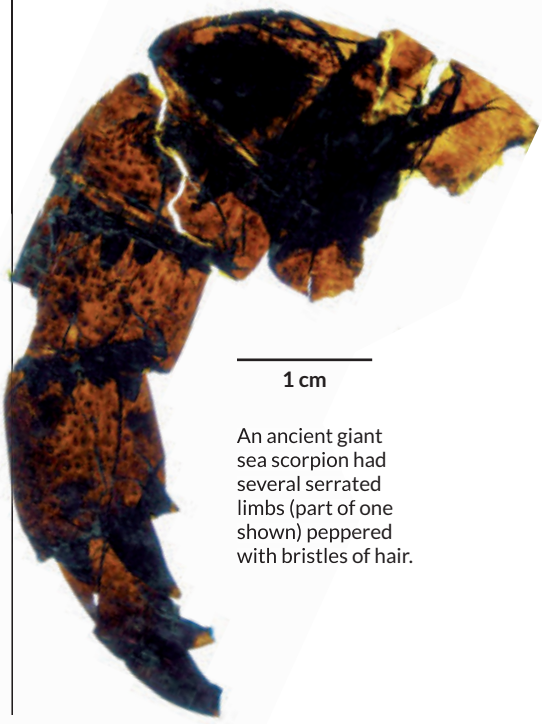
Earliest sea scorpion discovered in Iowa

Giant scorpions may have terrorized the seas some 460 million years ago.

A newly discovered species of sea scorpion, *Pentecopterus decorahensis,* stretched up to 1.7 meters long — almost as long as a twin-sized bed. Scientists unearthed more than 150 fragmentary remnants of the arthropod from the sandy shale of an impact crater in what is now Iowa.

The sea predator may have used its forelimbs to capture prey and its paddlelike hind limbs to swim or dig, Yale University paleobiologist James Lamsdell and colleagues report September 1 in *BMC Evolutionary Biology*. Pressed between layers of rock for hundreds of millions of years, the specimens lay so well preserved that researchers could make out very fine hairs bristling from the scorpion's underside.

Pentecopterus is the earliest sea scorpion yet discovered, edging out the previous record holder by some 9 million years. — *Meghan Rosen*



An ancient giant sea scorpion had several serrated limbs (part of one shown) peppered with bristles of hair.

GENES & CELLS

Gene editing put to the test in pigs

Method could make organs safe for human transplants

BY TINA HESMAN SAEY

Recently developed methods for editing genes could make pig organs safe for human transplant.

Pig organs have not been used for transplants partly because they carry viruses that could infect people. Researchers now report online October 11 in *Science* that they have used a powerful gene-editing tool to simultaneously disable 62 of the viruses.

Pig cells contain multiple copies of embedded viruses called porcine endogenous retroviruses, or PERVs. Such viruses copy and paste themselves into pig DNA. If the retroviruses infected a person during or after a transplant, they could disrupt important human genes, leading to cancer or other diseases.

CRISPR/Cas9, as the gene-editing method is known, has been used to edit DNA in monkeys and in laboratory animals (*SN: 3/8/14, p. 7*). Cas9 is a DNA-cutting enzyme. It works in association with pieces of RNA that chemically match with a target on DNA to guide the enzyme to specific cutting spots. When Cas9 cuts DNA, the cell tries to repair the breach either by pasting the cut ends together again or by copying unbroken DNA from a twin gene. Tying together broken ends can result in mistakes that disable the gene, the goal of this technique.

Usually, researchers target single genes. But doing that would disable only one PERV. "We wanted to get rid of all of them," says George Church, a geneticist at Harvard Medical School. Church and geneticist Luhan Yang in Church's lab headed the project. They theorized that since the retroviruses are identical, all of them could be eliminated in one fell swoop with the same guide RNAs.

Yang and colleagues designed two guide RNAs that target the *pol* gene of the retroviruses for cutting. That gene encodes a polymerase enzyme necessary for the retrovirus to replicate itself.

At first, the experiment didn't work at all, Yang says. The problem may have been that the researchers put in too much of the cutting enzyme, dicing up the DNA and leading cells to launch a suicide program.

Yang and colleagues designed a more tunable system. They inserted DNA-editing genes, engineered to turn on only when researchers added the antibiotic doxycycline, into pig cells. In that experiment, a maximum of 37 percent of retrovirus *pol* genes showed signs of editing 17 days after the team gave the signal for editing to begin.

But the efficiency of editing wasn't uniform. The team sorted out cells that had been edited with what looked like 37 percent efficiency. When the team examined the cells individually, they found that the cells fell into one of two camps. Either about 10 percent of the virus genes were edited, or 97 to 100 percent were. Cells in which all or nearly all of the *pol* genes were revised carried only 16 to 20 types of edits — mostly cases in which little bits of DNA had been snipped out. That pattern indicates that as Cas9 sliced genes, the cells often repaired the damage by copying a previously edited *pol* gene.

"It's very cool," says Jennifer Doudna, a molecular biologist at the University of California, Berkeley and one of the researchers who first developed the CRISPR/Cas9 system as a gene-editing tool. Such a chain reaction "just underscores the efficiency of the system."

With the Harvard group's discovery, researchers now know that bulk editing is possible. Making pig organs safe for transplant is just one possible medical application. Other applications, such as fixing mutations in human germline cells (eggs and sperm) or in embryos, have been controversial (*SN: 5/30/15, p. 16*).

While developing pig organs for human transplant seems to be a good use of the technology, Doudna says scientists need to give serious consideration to how and when to apply CRISPR/Cas9. Human germline editing is one case that deserves particular thought and debate. "We as scientists should take a step back and say, 'Should we really go there?' " she said October 9 in Baltimore at the annual meeting of the American Society of Human Genetics.

In the new experiments, Yang and colleagues also measured how often pig cells transmit PERVs to human cells grown in the same lab dish. Normally, about 1,000 pig retroviruses are found in a group of 1,000 human cells. (Because they are measuring in bulk, the researchers can't tell how many viruses invade each human cell.) Edited pig cells passed along 1,000 times fewer retroviruses — probably zero viruses, Yang says — than did unedited cells. The researchers suspect that the low level of PERVs detected in human cells grown with edited pig cells are actually human viruses that are very similar to the pig viruses.

> "We as scientists should take a step back and say, 'Should we really go there?' "
>
> **JENNIFER DOUDNA**

That doesn't mean pigs will be an immediate source of transplant organs. There are still other genes in pigs that could cause organs to be rejected if transplanted into humans. It's only a matter of time until those genes are altered to be more people-friendly, too, the researchers predict. They need to apply the technique to produce whole animals that lack retroviruses and other troublesome genes. "If we can do 62, we can do 20 more," Church says.

About 2 million people worldwide are waiting for transplants, Church says. He and Yang cofounded a company called eGenesis to engineer pigs to produce transplant organs. The researchers aren't worried that the public will reject genetically engineered pig organs. "Human life is at stake," Yang says. "I would think the public would be very accepting if it is proven safe and effective." ■

MATTER & ENERGY

Quantum computing goes old school

Engineers modify silicon transistors to perform basic logic tasks

BY ANDREW GRANT

Silicon transistors have been converted into the basic components of a quantum computer.

With modified versions of transistors used in smartphones, tablets and desktop computers, engineers have built the first quantum logic gate in silicon for performing quantum computations. The gate, described in the Oct. 15 *Nature*, uses the value of one quantum bit within a transistor to determine whether to change the value of a quantum bit in another transistor. The researchers say they have demonstrated all the fundamental components needed to build a silicon-based quantum computer, which could swiftly perform tasks like factoring large numbers and searching huge datasets.

Other researchers say that while the silicon work is an impressive physics feat, engineers pursuing alternate quantum computing platforms are farther along and years ago demonstrated gates that manipulate two quantum bits, or qubits. But silicon research has a built-in advantage, says study leader Andrew Dzurak, an electrical engineer at the University of New South Wales in Sydney. There's a global manufacturing infrastructure for printing tiny electronic components onto silicon, allowing engineers to more cheaply and easily test — and ultimately produce — their creations.

Traditional computers perform calculations with binary bits: Different voltages of electricity surging through silicon chips correspond to 0s or 1s. Those bits get manipulated when they pass through logic gates made of transistors. For example, an AND gate outputs a 1 when two incoming bits are both 1; otherwise it produces a 0. Computers perform such operations in response to every keystroke, mouse click and screen touch.

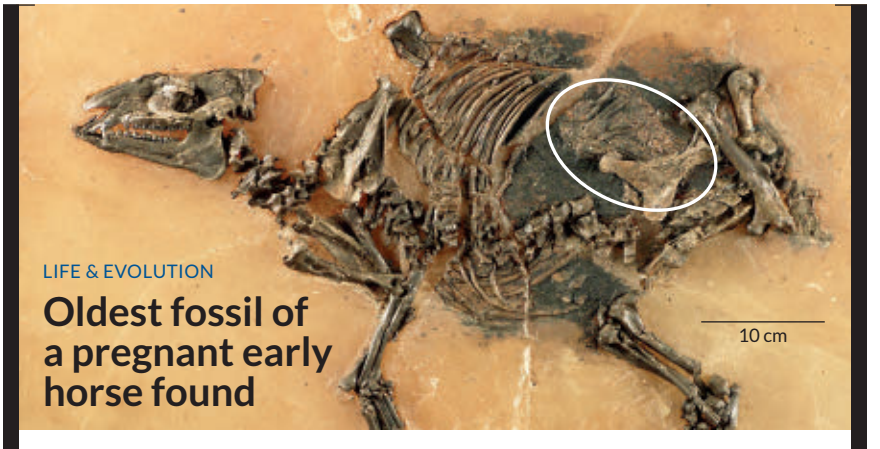
Quantum computers would work on a similar principle, but qubits would be encoded in delicate properties such as an electron's spin. Qubits can be 0, 1 or a blend of both simultaneously, a phenomenon called superposition that enables quantum computers to perform certain calculations more efficiently.

Dzurak's team modified silicon transistors to hold single electrons and then placed two transistors close together at temperatures just above absolute zero. Microwave pulses and magnetic fields coaxed the two electrons serving as qubits to interact. Two-qubit logic gates flipped the spin of one electron if the other electron had a particular spin. "It's state-of-the-art control of silicon qubits," says Chris Monroe, a physicist at the Joint Quantum Institute at the University of Maryland in College Park.

Dzurak says the next step is scaling up the technology to integrate several gates and multiple qubits. "You can build up any calculation you want with a combination of one- and two-qubit gates," he says.

Monroe says to hold off on the hype. He works on a competing platform that uses ions as qubits and was part of a group that demonstrated two-qubit gates with ions in 1995. So silicon is way behind. Monroe adds that dirt and other surface aberrations quickly interfere with electron spins, an issue that should worsen as the computer is scaled up in size and the number of qubits increases. "I don't really consider silicon competition," he says.

Building any quantum computer remains a tremendous challenge due to the fragility of those quantum superposition states. Monroe admits silicon has one giant leg up on the competition: "Our systems are so much cleaner, but we don't have the infrastructure to print a chip with a million atoms on it." ■



LIFE & EVOLUTION

Oldest fossil of a pregnant early horse found

A confluence of unlikely events led to the exquisite preservation of the oldest fossil of a primitive pregnant horse ever discovered.

Some 48 million years ago, an equoid mare (*Eurohippus messelensis*) and her almost fully gestated fetus fell into an ancient lake in Germany. The lake had just the right mix of bacteria to preserve evidence of soft tissue from the tiny mare's uterus and placenta. The unusually detailed fossil (shown above, with the fetus circled) provides a window into the evolution of modern placental reproductive systems, researchers report October 7 in *PLOS ONE*.

The fossil's reproductive tract looks much like that found in horses today, the researchers say. The placenta is only loosely attached to the uterine wall, allowing a mare to stand and move soon after birth without the risk of excess bleeding. The fossil's reproductive anatomy is so advanced that it must have taken a long time to develop. It could have arisen during the Mesozoic era, as early as 250 million years ago, says study coauthor Christine Aurich, a reproductive veterinarian at the University of Veterinary Medicine in Vienna. — *Natasha Gilbert*

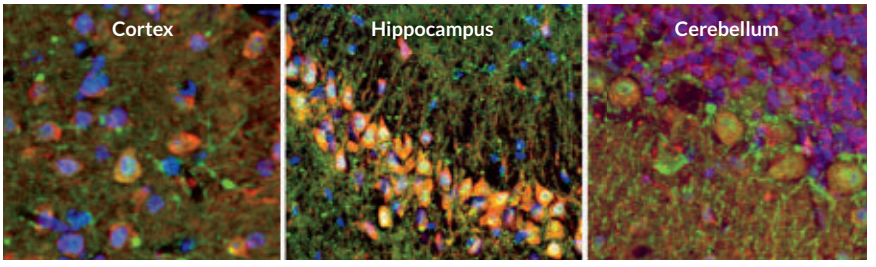
J.L. FRANZEN *ET AL*/*PLOS ONE* 2015, SVEN TRÄNKNER/SENCKENBERG FORSCHUNGSINSTITUT FRANKFURT (PHOTO)

BODY & BRAIN

Nets full of holes snag memories

Mesh that wraps nerve cells may store long-term info

BY LAURA SANDERS



Durable nets (green) wrap around nerve cells throughout this adult mouse brain (three different regions shown). Holes in these nets store long-term memories, a new study suggests. Nerve cells are marked by red; cell nuclei are blue.

Tough, stable nets that swaddle nerve cells may be the ultimate memory catchers. These structures, called perineuronal nets, may store long-term memories, scientists reported October 19.

"This is clearly a novel idea and it does, at first glance, look a bit way out," said neuroscientist Eric Kandel of Columbia University. But there are good reasons to suspect that perineuronal nets hold memories, he said.

The idea, presented by neuroscientist Sakina Palida of the University of California, San Diego, offers an explanation for how the brain can hold memories for decades. "Up to this point, we still don't understand how we maintain memories in our brains for up to our entire lifetimes," she said. A deeper understanding of how memories last may ultimately point to treatments for memory-stealing disorders like Alzheimer's disease.

Synapses — connections between nerve cells — hold memory information. But the proteins involved in this process are created and destroyed rapidly — a fluid situation that, like a game of telephone, could distort the memory. "The majority of these proteins turn over on the scale of a few hours to a few days," Palida said.

But some of the sturdy proteins and carbohydrates that knit together to form perineuronal nets may last a lifetime.

Palida's colleague Varda Lev-Ram, also of UC San Diego, fed mice food containing a heavy form of nitrogen, allowing the researchers to study the life span of newly created net proteins. In some cases, the net proteins lasted for 180 days.

But these net components didn't cover the entire nerve cell; they weren't found at synapses. Other experiments revealed that newly formed synapses burn holes in the net, producing enzymes that chew through the net's fibers. The pattern of these holes stores memories, the team proposes. "The information is encoded in what is left behind," Palida said.

Mice lacking a protein that punches holes in the net showed long-term memory problems. With a diminished ability to change their perineuronal nets, mice were worse at remembering a fear signal.

Perineuronal nets might also help hold memories on a shorter timescale, said MIT neuroscientist Susumu Tonegawa. Perineuronal nets might provide support to nerve cell connections in the days after a memory is first formed.

Perineuronal nets swaddle nerve cells across the brain, the researchers found, not just in select areas, as previous experiments have suggested. ■

BODY & BRAIN

Signs of Huntington's appear in youth

Adult-onset disorder may affect children's brain development

BY LAURA SANDERS

Huntington's disease usually appears in middle age but actually begins long before then, a new study suggests. The rogue protein that causes the disease seems to cause trouble as the brain is built.

Huntington's is a devastating inherited disorder marked by uncontrollable movements, emotional impairment and psychiatric illness. Symptoms usually appear in a person's 40s as nerve cells deteriorate in a part of the brain called the striatum. But changes in the brain's wiring show up decades earlier, Jessica Lee of the University of Iowa reported October 18.

With functional MRI, Lee and colleagues scanned the brains of 26 children ages 6 to 18 who had inherited genetic instructions for a dangerous version of the huntingtin protein. These kids will go on to develop Huntington's. The brain scans were done while the kids rested quietly, allowing the researchers to see coordination among different brain areas.

Compared with 36 kids who had the usual versions of the huntingtin protein, the children who will get Huntington's had differences in how the striatum connects with other parts of the brain.

Some of these connections, such as those involved in movement and emotions, were weaker in the kids who will develop Huntington's. A different connection involved in thinking skills was actually stronger.

Researchers don't yet know if these brain changes result in any behavioral changes. All of the children fell within the normal range on a series of movement and brain tests, though subtle differences may exist, Lee suspects.

The results illustrate the importance of timing, said psychiatrist Jay Giedd of the University of California, San Diego. Genes can have profoundly different effects early and later in life, he said.

Lee said she hopes her work will help clarify the huntingtin protein's role in brain development, which may ultimately help guide gene therapy treatments. ■

S. PALIDA ET AL

MEETING NOTES

Multitaskers do worse on tasks that require focus

Teens like high-tech gadgets so much that they often use them all at once. Although these multitaskers might think they are boosting their ability to attend to multiple activities, they are probably impairing their ability to focus, cognitive scientist Mona Moisala of the University of Helsinki reported October 18.

Moisala and colleagues asked 149 adolescents and young adults, ages 13 to 24, how frequently they juggle multiple forms of media and whether they play video games daily. Each participant had to focus attention on sentences (some logical, some illogical) under three conditions: without any distractions, while listening to distracting sounds and while both listening to a sentence and reading another sentence.

Using functional MRI to track brain activity, the researchers found that daily gaming had no effect on participants' ability to focus. Those who often juggle multiple forms of electronic media, however, had more trouble paying attention. Those who scored higher on multitasking performed lower overall, even when they weren't being distracted. Brain images showed that the multitaskers also had a higher level of activity in the right prefrontal cortex, an area of the brain implicated in controlling attention and inhibiting actions. — *Susan Gaidos*

Sex influences ability to read crowd's emotions

Whether you assess a crowd as an angry mob or happy partygoers depends on both you and whom you're looking at, a new study suggests. Emotions and sex influence how well people evaluate the collective mood of a crowd, Hee Yeon Im of Harvard Medical School reported October 19.

When shown images of faces in a crowd, participants were better at identifying happy female crowds than happy male crowds, and better at spotting angry male crowds than angry female crowds, Im and her colleagues found. What's more, female happy faces were judged to be happier than an equally happy male group, and angry male crowds were judged to be angrier than angry females, suggesting that the sex of the people in the crowd colors how a person perceives emotion. A viewer's anxiety also plays into the assessment. People who had more anxious traits were faster to assess a crowd than less anxious people, though this speed came with a cost: Anxious people made more mistakes in distinguishing a happy crowd from an angry one.

Overall, humans are quite good at assessing the mood of a group, Im said, but people's abilities vary. Teasing apart the factors that influence crowd recognition might offer insight into disorders in which people have trouble recognizing emotions. — *Laura Sanders*

High-fat diet's negative effect on memory may fade

Eating a high-fat diet as a youngster can affect learning and memory during adulthood, studies have shown. But new findings suggest that such diets may not have long-lasting effects. Rats fed a high-fat diet for a year recovered their ability to navigate their surroundings.

Neuroscientist Erica Underwood of the University of Texas at Dallas tested the spatial memory of rats fed a high-fat diet immediately after weaning, for either 12 weeks or more than 52 weeks. Rats were put in a chamber-filled box that held Lego-like toys. Once rats became familiar with the box, the toys were moved to new chambers. Later, rats were put back in the box; those that ate high-fat foods for 12 weeks appeared confused and had difficulty finding the toys. But rats that ate high-fat foods for a year performed as well as those fed a normal diet. Underwood repeated the experiment, posing additional spatial memory tests to new rats. The findings were the same: Over the long-term, rats on high-fat diets recovered their ability to learn and remember.

Studies of brain cells revealed that rats on the long-term high-fat diet showed reduced excitability in nerve cells from the hippocampus, the same detrimental effects seen in rats on the short-term high-fat diet.

"The physiology that should create a dumber animal is there, but not the behavior," said Lucien Thompson of UT Dallas, who oversaw the study.

Underwood and Thompson speculate that some other part of the brain may be compensating for this reduction in neural response. — *Susan Gaidos*

Reading faces In a study of how people read the emotions of crowds, participants thought that female crowds (left, outlined in red) looked happier than equally happy males, and that angry male crowds (right, outlined in blue) looked angrier than similarly angry females.

H.Y. IM

EARTH & ENVIRONMENT

Skin soaks up toxic air pollutants

Lungs may not be main entry into body for some phthalates

BY JANET RALOFF

For some toxic air pollutants, more can get into the body through the skin than via breathing, new human data indicate.

Earlier work had suggested that semivolatile compounds — those that move through air in both the gas and condensed phases — pass through skin relatively slowly. "But if the whole body is exposed, then even low rates of exposure can deliver what turns out to be nontrivial amounts of these chemicals," says John Kissel of the University of Washington in Seattle.

Semivolatile phthalates, used as solvents and building blocks for plastics, are one worrisome group of chemicals. Studies have linked prenatal phthalate exposure to gonadal and cognitive changes in babies and young children (*SN Online: 7/1/09*; *SN: 6/4/05, p. 355*).

A new Danish study exposed six men to two semivolatile phthalates during two six-hour stints. Diethyl phthalate, or DEP, is a common ingredient in cosmetics, perfumes and personal-care products such as shampoos. Di-*n*-butyl phthalate, or DnBP, is found in cosmetics, too. It's also an industrial solvent and an ingredient in adhesives, antifoaming agents, plastics and lubricants.

Air exposures to phthalates were high but below limits set for industrial workers. To control for inhalation exposures, participants wore a hood on one day, so they could breathe relatively clean air. To maximize skin contact with air, each man wore only shorts.

Inhalation and skin transport delivered roughly equal amounts of DEP into the blood and urine. For DnBP, "dermal exposures were about 80 percent as big as inhalation's," says indoor-air chemist Charles Weschler of Rutgers University in Piscataway, N.J. Weschler and colleagues report the data in the October *Environmental Health Perspectives*.

Computations show that with another 30 to 40 hours of exposure, "dermal absorption could be five to six times higher than inhalation," Weschler says.

The data may help explain high phthalate levels seen in babies treated in neonatal intensive care units (*SN: 8/13/05, p. 109*), where phthalate-based tubing and plastics have been widely used.

In another study, Glenn Morrison of Missouri University of Science and Technology in Rolla exposed himself to the same conditions as in the Danish trial. But unlike the mostly bare-skinned men, Morrison wore clean clothes for one exposure and for another he wore clothes left in phthalate-tainted air for nine days.

On June 10 in the *Journal of Exposure Science and Environmental Epidemiology*, Morrison and Weschler's group reported that freshly laundered clothes reduced his dermal uptake of airborne phthalates compared with the average uptake in the earlier trial. Wearing togs seasoned by exposure to room air increased exposure over the bare-skinned conditions. Clean clothes appear to work as a sink, Kissel explains, soaking up the air pollutants before they can reach the skin. ■

HUMANS & SOCIETY

Hunter-gatherers may get less sleep

But foragers don't appear to suffer from insomnia, study finds

BY CHRIS SAMORAY

People in the postindustrial world don't always get a sound night's sleep. But they appear to sleep about as much as hunter-gatherers do in Africa and South America, a new study finds.

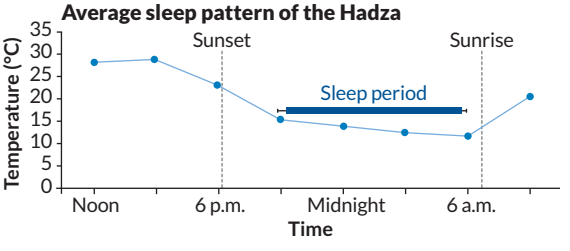
"It's absolutely clear that they don't sleep more than we do," says UCLA sleep scientist Jerome Siegel. In fact, hunter-gatherers may even sleep a little less.

Recommended nightly sleep for adults is seven to nine hours; a 2013 Gallup poll showed that Americans get an average of 6.8 hours. On most nights, members of three hunter-gatherer groups — the Hadza of Tanzania, the San of Namibia and the Tsimane of Bolivia — sleep 5.7 to 7.1 hours, Siegel and colleagues report in the Nov. 2 *Current Biology*.

The group gathered over 1,000 days' worth of data from 94 hunter-gatherers who wore watches that collected sleep data. Typically, people fell asleep several hours after sunset with falling ambient temperatures and awoke before dawn as temperatures reached a low.

Only 1.5 to 2.5 percent of participants reported having insomnia more than once a year; chronic insomnia rates in postindustrial societies are 10 to 30 percent. Siegel says that studying sleep in more natural environments, outside of the lab, and in many different populations may help scientists better understand problems such as insomnia.

Anthropologist Carol Worthman of Emory University in Atlanta welcomes the study. "We've been studying sleep in one small slice of humanity living under particular postindustrial conditions and making assumptions," she says. "Just on the descriptive level, we are incredibly interested in seeing this [study] because there's a complete lack of data." ■



Bedtime Hunter-gatherer sleep patterns are tied to temperature, new research shows. Among the Hadza in Tanzania, for instance, people fall asleep as ambient temperature drops and wake up when temperature hits its lowest point of the day. SOURCE: G. YETISH *ET AL*/*CURRENT BIOLOGY* 2015

GENES & CELLS

DNA tags differ in gay, straight men

Epigenetic changes may reflect sexual preference, study finds

BY TINA HESMAN SAEY

A molecular test claims to distinguish homosexual from heterosexual men.

Chemical modifications to DNA known as epigenetic tags, which change gene activity without altering the gene itself, differ between gay and straight men, researchers from UCLA reported October 8. Patterns in one type of these changes, called DNA methylation, in pairs of twins in which one brother is gay and the other straight distinguish one group from the other about 67 percent of the time, computational geneticist Tuck Ngun and colleagues say.

> "None of us see homosexuality as a disorder or something to be fixed."
>
> TUCK NGUN

The work already has provoked controversy. Some scientists question its methodology, and others worry about how the research could be used. Some are concerned that it could be misinterpreted as one step in an effort to "cure" homosexuality. Nothing could be further from the researchers' intentions, say Ngun and Eric Vilain, the geneticist who heads the research group. "None of us see homosexuality as a disorder or something to be fixed," Ngun said. "We're just interested in what makes us tick."

Previous studies have found tentative genetic links to male sexual orientation, but no "gay gene" or genes. Sexuality does seem to have origins early in life, maybe stemming from cues in the womb. For instance, for each biological older brother a man has, the small likelihood of being homosexual rises by 33 percent. That finding could indicate that some condition in the womb sets epigenetic marks, which later influence sexual orientation.

Epigenetic marks have been shown in rodents to influence behaviors such as maternal care and drug addiction (*SN: 5/24/08, p. 14*). Whether these marks are involved in human behavior is a matter of debate, said human geneticist Peng Jin of Emory University.

Ngun and colleagues measured DNA methylation levels in the saliva of 37 pairs of identical twins in which one twin self-identified as gay and the other as heterosexual. After analyzing methylation data from half of the twins, a computer algorithm could use nine spots in the genome to identify the gay men in the remaining sets of twins 64 percent of the time.

Further analysis included 10 twin pairs in which both were gay. The algorithm had to find spots that differed in the mixed orientation twins but were the same in the gay twins. That left five sites that could identify 67 percent of gay twins in the test group.

Some of those regions may be involved in controlling activity of two genes: *CIITA*, which regulates activity of some immune system genes, and *KIF1A*, which is involved in the transport of communication molecules in the brain.

Scientists question whether the finding will hold up in larger groups of unrelated people. And the algorithm hasn't been tested on other datasets, raising concerns about its validity. Jin doubts that a study of less than 100 men has the statistical power to predict sexual orientation.

He also questions whether saliva really reflects what's happening in the brain where behavior is controlled. Cells in saliva can change dramatically depending on what a person eats and other factors.

Vilain agrees that the study has limitations. Ideally, researchers would track DNA methylation changes in the brain from fetal stages on, but such research is not ethical in humans.

Vilain said the work has no clinical application. It's just a statistical measure that epigenetic marks differ between men of opposite sexual orientations. The study can't determine whether the epigenetic tags are a determining factor or a result of differing experiences, he said. ■

MEETING NOTES

Genetic diversity grows in U.S.

The American melting pot is more flavorful than ever.

Except for a dip in the 1940s, genetic diversity in the United States has been increasing every decade since 1920, Amir Kermany of AncestryDNA in San Francisco reported October 9.

Americans are increasingly crossing ethnic lines when choosing a mate, Kermany and colleagues found after analyzing DNA from more than 800,000 AncestryDNA customers born in the United States between 1920 and 2010. The team looked for genetic variants characteristic of heritage from six continents. People born more recently are more genetically diverse — carrying ancestry from more than one ethnic group or continent — than their parents and grandparents. — *Tina Hesman Saey*

Microbes may disclose colon cancer mutations

Microbes can reveal which mutations colon cancers carry.

By examining bacteria growing alongside 44 colon cancer tumors and 44 healthy tissue samples, researchers determined that particular mixes of microbes are associated with both the number and type of DNA mutations the cancer carries.

Tumors with more mutations had a more diverse mix of bacteria than did tumors with few mutations, reported Ran Blekhman of the University of Minnesota, Twin Cities on October 9. And certain bacteria were more likely to be found next to cancer cells carrying specific mutations. For instance, *Fusobacterium* was associated with tumors harboring mutations in the *APC* gene, Blekhman and colleagues found. Microbe analysis predicted with 70 to 80 percent accuracy when researchers would find mutations in five of 11 genes examined. — *Tina Hesman Saey*

ATOM & COSMOS

Milky Way may harbor primeval stars

Astronomers dig through cosmic pollution to find stellar fossils

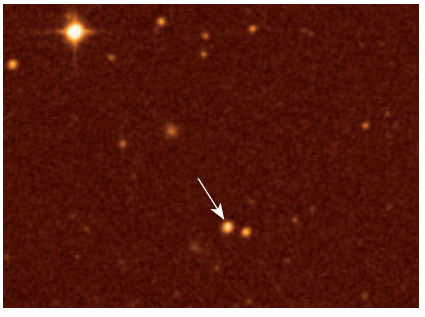
BY CHRISTOPHER CROCKETT

They're hiding among us. Some of the first stars to appear in the universe might still be lurking in the Milky Way, masked by nearly 13 billion years of cosmic pollution.

Computer simulations indicate that relatively lightweight first-generation stars might be scattered throughout the galaxy. Observations have yet to turn up any, but that's because exposure to interstellar dust and gas make the few remaining first stars look younger than they are, Jarrett Johnson, an astronomer at Los Alamos National Laboratory in New Mexico, suggests in the Nov. 1 *Monthly Notices of the Royal Astronomical Society*.

The first stars were made of hydrogen and helium; they came on the scene before later generations of stars forged nearly all the heavier elements. While astronomers have found stars in the Milky Way with just traces of heavier atoms, pristine samples remain elusive.

Johnson calculated how the slow, steady rain of interstellar detritus might change the makeup of any aboriginal stars. Starlight would push back on some dust, he finds, but gas would be undeterred. The polluted star would end up with a relative abundance of gas elements (such as carbon and oxygen) whereas those locked away in dust (such as titanium and iron) would be mostly missing.



Some Milky Way stars already believed to be ancient, such as HE 0107-5240 (arrow), may be even older first-generation stars in disguise.

Although the calculations make several assumptions, such as how interstellar chemistry has changed over the age of the universe, "we have to start somewhere and this is a really good effort," says MIT astronomer Anna Frebel.

There probably aren't that many very old stars left, so astronomers will have to spend years combing through the galaxy for that perfect specimen. Recent calculations indicate that researchers need to look at about 20 million Milky Way stars before knowing if any primordial stars are still around.

Frebel and others have found several stars that roughly resemble Johnson's predictions for the blend of elements. But observed candidates are relatively abundant in titanium, she notes, whereas the calculations suggest that polluted first-generation stars should have very little. ■

HUMANS & SOCIETY

DNA illuminates reverse migration

Ancient genome points to Eurasian ancestry in Africa

BY BRUCE BOWER

DNA from a man who lived about 4,500 years ago in what's now Ethiopia has illuminated a surprisingly influential migration of Eurasians into Africa 1,500 years after his death.

That back-to-Africa trek occurred some 3,000 years ago and left a substantial genetic imprint on populations now living in sub-Saharan Africa, say University of Cambridge evolutionary biologist Marcos Gallego Llorente and colleagues. The genome, the first map of ancient human DNA from Africa, helped to determine that a population closely related to Europe's first farmers later made major inroads in Africa, the researchers report online October 8 in *Science*.

The DNA was extracted from a skeleton found in Ethiopia's Mota Cave and radiocarbon dated to about 4,500 years ago. The genome provides a reference for estimating what African DNA looked like shortly before Eurasians showed up. The DNA also shines light on Africans' genetic makeup before speakers of an early Bantu language spread from West Africa into central and southern regions some 3,000 years ago. The Bantu expansion reshaped Africa's population genetics and may have helped spread Eurasian gene variants, the researchers suspect.

The study was inspired by an analysis of DNA from modern populations suggesting that Europeans or West Asians reached East Africa about 3,000 years ago and passed on genetic variants that populations in all three regions now share (*SN Online: 5/16/13*). Geneticist Joseph Pickrell, now at the New York Genome Center in New York City, led that effort. "It's quite plausible that a population related to early Neolithic farmers of Europe migrated into eastern Africa sometime after 4,500 years ago," he says.

Other comparisons among modern populations show genetic contributions from Eurasians in East and West Africa, says Pontus Skoglund, a Harvard geneticist. But armed with the first ancient African genome as a baseline from a time before migration into Africa, Llorente's team finds a "very surprising" contribution of Eurasian ancestry — even in Central Africa's Mbuti people, a pygmy group, Skoglund says.

About 6 percent of Mbuti DNA comes from Eurasians, the study finds. West Africa's Yoruba people carry a 7 percent genetic contribution from Eurasians. That figure reaches 18.5 percent in South African groups and is as high as 47 percent in East African populations.

"My guess is that these [Eurasians] were farmers who left the Near East [in or around Turkey] and perhaps colonized the Arabian Peninsula before migrating into East Africa," speculates study coauthor Ron Pinhasi, an archaeologist at University College Dublin. ■

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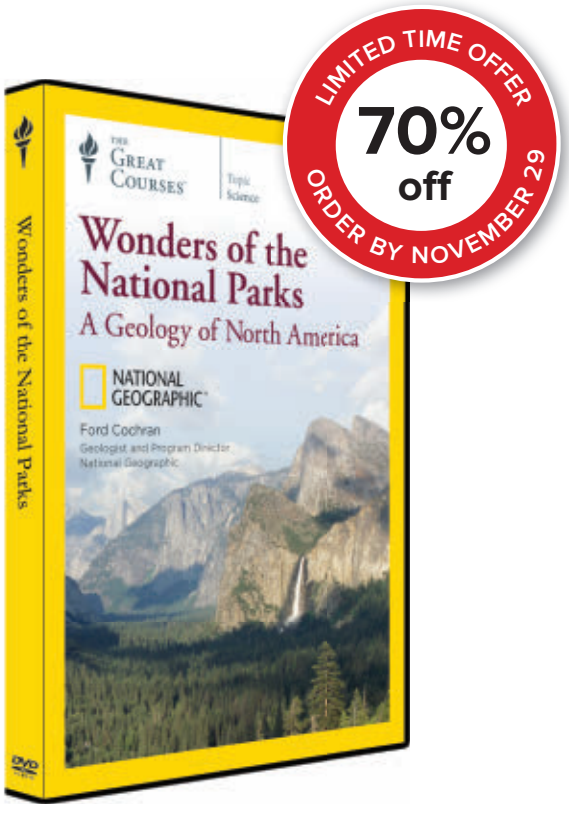

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BODY & BRAIN

Daily pill prevents HIV infections

Other options for preexposure prophylaxis in development

BY LAURA BEIL

After a decade of controversy and halting progress, preexposure prophylaxis may finally be about to take its place in the vanguard of AIDS prevention.

In September, for the first time, the World Health Organization expanded the population recommended for this option, which involves taking daily doses of antiviral medication. If a person is exposed to HIV, the drugs should defeat the virus before it establishes a foothold.

Previously, preexposure prophylaxis, or PrEP, was reserved only for those deemed at high risk, such as couples in which one partner is infected or men who have sex with men. But in the updated guidelines, WHO officials now say that anyone "at significant risk" should take the drugs. The HIV prevention advocacy group AVAC called the change a "potentially profound development" that stands to greatly expand PrEP among adolescents and young women. About 380,000 women ages 15 to 24 become infected every year, mostly in sub-Saharan Africa.

The recommendation follows the release of two studies that reported some of the highest success rates so far using the drug Truvada, which contains the antiviral drugs tenofovir and emtricitabine (*SN: 12/18/10, p. 16*), as a daily preventative. Early next year, clinical trials on antimicrobial vaginal rings will be completed, and studies of long-acting antiretroviral injections are under way.

Public health officials hope that PrEP will one day be viewed like birth control — a prevention strategy with enough approaches for men and women to choose the method best suited for their lives.

"It is a really exciting time," says Meredith Clark, who heads preclinical activities at CONRAD, a nonprofit based in Arlington, Va., that focuses on contraception and HIV prevention. "A lot is happening. A lot is changing."

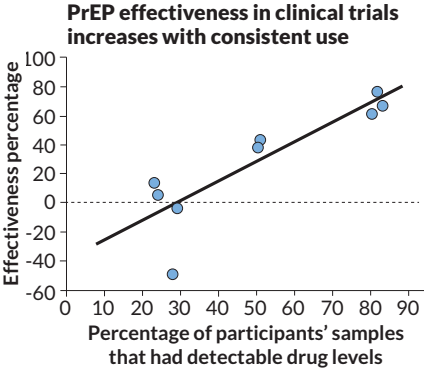
The outlook was not always so rosy. Early in the epidemic, doctors hypothesized that it would be possible to prevent infections with PrEP, which interferes with viral replication. But many early studies were abandoned before they even got off the ground, as they grew beset with allegations of unethical behavior, fears of drug resistance and other problems. Other early studies yielded lukewarm results, in large part because study participants did not use the drugs consistently. Researchers have also fielded social opposition — the president of one well-known AIDS nonprofit referred to Truvada as a "party drug" that would encourage risky behavior and discourage the use of condoms. (The drug does not protect against other sexually transmitted infections and is not a substitute for condoms.)

At the same time, some PrEP studies began to show remarkable effectiveness. The U.S. Food and Drug Administration approved Truvada in 2012, but its effectiveness outside the carefully controlled and monitored world of clinical trials was unclear. In September, researchers from Kaiser Permanente reported in *Clinical Infectious Diseases* that after more than two years, no new infections occurred among 657 people in San Francisco who were instructed to take the drug daily.

"It adds really compelling data that prophylaxis can work," says study coauthor Jonathan Volk, an infectious disease physician at Kaiser. A similar study from the United Kingdom, with support from Truvada manufacturer Gilead Sciences, compared 275 men who received PrEP for a year with 269 who were told to wait a year before receiving it. During that time, 20 men who were deferred became infected compared with three offered PrEP — an 86 percent reduction in risk. Those results appeared in September in *The Lancet*.

The challenge is that the drug doesn't work if it stays in the bottle. Pills carry the potential for stigma, since they are among the same medicines used to treat HIV. Addressing those concerns, a vaginal ring under investigation might increase adherence and offer discreet prevention. Two large studies, The Ring Study and the ASPIRE study, are being conducted by the nonprofit International Partnership for Microbicides and the Microbicide Trials Network, which is funded by the National Institutes of Health. Those

Use as directed The results of tenofovir-based preexposure prophylaxis, or PrEP, studies (dots) have been mixed. But as adherence across studies increases, so does the drug's effectiveness in preventing HIV. SOURCE: SALIM S. ABDOOL KARIM/CAPRISA, AVAC REPORT 2013



Pick and choose Taking a daily pill may not be the best HIV-prevention strategy for everyone, so researchers are investigating alternative PrEP delivery methods. SOURCE: IPM, MTN, NIH

	Active ingredients	FDA approval status	Advantages	Disadvantages
Oral Truvada	Tenofovir and emtricitabine	Approved	■ Highly studied ■ Proven effective	■ Requires daily adherence ■ Can be difficult to keep discreet
Vaginal ring	Dapivirine	Not approved, in Phase 3 trials	■ Offers greater privacy ■ Ease of adherence	■ True effectiveness unknown
Long-acting injections	Rilpivirine and cabotegravir	Not approved, in Phase 2 trials	■ Does not require daily adherence ■ Offers greater privacy for both men and women	■ Potential for the development of drug resistance ■ If side effects occur, cannot remove the drug immediately

E. OTWELL

studies have enrolled over 4,000 women in sub-Saharan Africa. The ring contains the antiviral dapivirine and lasts for a month. Also under development is a rectal microbicide containing tenofovir, which would be used only as necessary.

It's not clear how well a topical microbicide would work. Studies have been weak or inconsistent. One study of a vaginal gel microbicide, published in 2010, found that women who used the product before and after sex had a reduced risk of infection of about 40 percent overall (*SN: 8/14/10, p. 9*). Effectiveness would have been higher if women had used it consistently, says Clark, from CONRAD, which was one of the study sponsors.

She points out that some people have not been keen on PrEP because they weren't convinced it would work. "Now that we have success stories, it will change how people view it, and adopt it," she says.

In addition to microbicides, two long-acting injectable antiviral agents (rilpivirine and cabotegravir) are under development. Those products may also eliminate the need for daily use and offer protection that is easy to keep private. Ian McGowan of the University of Pittsburgh, who is principal investigator of the Microbicide Trials Network, has two main concerns about this approach. "These products have very long half-lives, which would complicate the management of any side effects that might occur," he says. "Also, during periods when there were low drug levels, there's a real risk that anyone acquiring HIV infection would develop antiviral resistance."

Until more PrEP methods are on the market, public health officials will work to make antiviral tablets available to those at greatest risk. Right now, the number of people outside North America who take PrEP "is horribly small," says Peter Godfrey-Faussett, science adviser to UNAIDS, a global health agency that is part of the United Nations. "I think we've established beyond any reasonable doubt that a daily pill form is absolutely proven now to work, providing you take it," he says. "The challenge now is to make this new exciting tool available in the settings where it is needed." ■

S. XING AND X-J. WU

Recently excavated human teeth (shown) support the idea that *Homo sapiens* arrived in southern China more than 80,000 years ago, tens of thousands of years before Stone Age people entered Europe.

HUMANS & SOCIETY

Before Europe, humans went to Asia

People reached China by 80,000 years ago, fossil teeth suggest

BY BRUCE BOWER

Modern humans reached southern China at least 35,000 years before setting foot in Europe, new fossil finds suggest.

These discoveries provide the best evidence to date that *Homo sapiens* took its first major strides out of Africa deep in the Stone Age and headed east, staying within relatively warm regions similar to those of its East African homeland.

Excavations in southern China's Fuyan Cave produced 47 human teeth dating to between 80,000 and 120,000 years ago, paleoanthropologists report October 14 in *Nature*. The presence of Neandertals in Europe may have helped deter humans' migration to that continent until around 45,000 years ago, when Neandertal populations started to shrink, says a team led by Wu Liu and Xiu-jie Wu of the Chinese Academy of Sciences in Beijing and María Martinón-Torres of University College London.

An early *H. sapiens* presence in China challenges the idea that modern humans moved eastward out of Africa about 60,000 years ago. It now appears more likely that *H. sapiens* left the continent as early as 120,000 years ago, dispersing east and south, from the Arabian Peninsula or the eastern Mediterranean, archaeologist Robin Dennell of the University of Exeter in England writes in *Nature*.

A hominid lower jaw previously found in southern China's Zhiren Cave dates to between 55,000 and 110,000 years ago. Researchers disagree about whether that find comes from a modern human or *Homo erectus*, a hominid with far older roots in East Asia.

It's not yet clear whether the human teeth from Fuyan Cave represent a variant of *H. sapiens* that included jaw bones such as the one from Zhiren Cave, says paleoanthropologist Erik Trinkaus of Washington University in St. Louis. Trinkaus, who coauthored a report on the Zhiren Cave find (*SN: 8/25/12, p. 22*), suspects ancient humans interbred with other *Homo* species on the way to East Asia. As a result, those populations would have displayed some unusual physical traits once they reached China.

Until now, the oldest well-accepted *H. sapiens* remains in East Asia, dating to 50,000 to 60,000 years ago, came from northern Laos (*SN: 5/19/12, p. 14*). Aside from the Fuyan Cave discoveries, the earliest Chinese *H. sapiens* fossils date to about 40,000 years ago.

Liu and his colleagues dated a stalagmite that formed just above fossil-bearing soil to about 80,000 years ago. That estimate rests on measurements of two radioactive decay products in the stalagmite. Animal bones found with the *H. sapiens* teeth, including remains of predatory cats, have previously been dated at other sites to no more than around 120,000 years ago.

All 47 modern human teeth from Fuyan Cave are relatively small, much like teeth of European *H. sapiens* from later in the Stone Age and present-day people, the researchers say. Fuyan teeth are shaped more like those of living human populations than like teeth of Neandertals or Asian *H. erectus*. ■

LIFE & EVOLUTION

Diet of *Dimetrodon* reconsidered

Extinct reptilelike predator ate sharks, other aquatic prey

The ancient amphibian *Diplocaulus* probably served as a prime food source for *Dimetrodon*, which chomped bites out of the aquatic animals' snouts, as shown in this *Diplocaulus* fossil.

BY MEGHAN ROSEN

Dimetrodon chowed down on sharks and amphibians like a prehistoric Pac-Man.

Rather than dining on plant eaters, the reptilelike carnivore ate mainly aquatic animals, chomping big bites out of amphibians' heads as they peeped up out of their burrows, paleontologist Robert Bakker reported October 14.

"It's cool and exciting because it's completely different from what people thought," said Stephen Hobe, a paleontology student at Carthage College in Kenosha, Wis.

Dimetrodon, one of the first big land predators, was the size of a small crocodile, with a snub nose, sharp teeth and a towering fin on its back. The creature lived about 280 million years ago — some 50 million years before the dinosaurs.

Bakker and colleagues have spent 11 years cataloging the bones and teeth in a *Dimetrodon*-laden fossil pit near Seymour, Texas. The pit, nearly the length of two football fields, includes ancient ponds and floodplains. Bakker's team has dug up 39 *Dimetrodon* specimens, but only one each of *Edaphosaurus* and *Diadectes* — large herbivores thought to be prime *Dimetrodon* cuisine.

That's not nearly enough food to sustain such a large population of predators, said project member Christopher Flis, a paleontologist at the Whiteside Museum of Natural History in Seymour. Other animals must have made up the difference, he said.

The team unearthed the remains of 134 small sharks and the dismembered skulls of 88 *Diplocaulus*, an amphibian with a bulky, boomerang-shaped head. The researchers found loads of *Dimetrodon* teeth buried amid the chewed-up bones.

The predator probably used its teeth to pull amphibians out of the ground — like a gardener yanking up carrots. ■

LIFE & EVOLUTION

Hunting implicated in Ice Age die-off

Warming didn't wipe out mammoths, study of tusks suggests

BY MEGHAN ROSEN

The story of the woolly mammoth's demise might be written in tusks.

Human hunters, not climate change, killed off the Ice Age mammals, a new chemical analysis of youngsters' tusks suggests.

If the preliminary results hold up, they'll "help convince more and more people that hunting was the main driver of extinction — or at least that climate change wasn't," said paleontologist Michael Cherney on October 15.

The extinction of the mammoths has sparked debate for decades, said paleontologist Roger Wood of Stockton University in Galloway, N.J. But Cherney tackled the question with a new approach, Wood said, and "it's let him come to a seemingly very clear conclusion."

Siberian mammoths bit the dust some 10,000 years ago after the last glacial period ended. Some researchers think hunters finished the animals off — people migrated to the mammoths' turf about when they went extinct, said Cherney, of the University of Michigan in Ann Arbor. Others argue that a warming climate wiped out the beasts. Higher temperatures could have shriveled up the plants that mammoths ate (*SN: 3/22/14, p. 13*).

But Ice Age animals had gone through warming periods before, "and none of those were associated with a big extinction," said David Polly, a paleontologist at Indiana University in Bloomington.

One recent analysis tied extinction to abrupt temperature spikes, which would have given animals little time to adapt and could have made them more vulnerable to hunting (*SN: 8/22/15, p. 9*).

Cherney realized that climate changes might leave a mark on young mammoths' bodies. Living tissues have both heavy and light versions of nitrogen. The ratio of heavy to light nitrogen drops as juveniles wean from their mothers' milk, but babies nurse longer than usual if they're stressed by lack of food, Cherney said.

To figure out weaning ages, Cherney reasoned, he could analyze nitrogen levels — because the chemicals were deposited in mammoths' tusks as they added new growth each year. He sampled tusks of about a dozen Siberian mammoths that lived 10,000 to 40,000 years ago.

Weaning age ping-ponged up and down as temperatures changed, Cherney and Michigan colleague Daniel Fisher found. During the last glacial maximum, the coldest period before the Ice Age ended, mammoths weaned at around 7 years old. But as temperatures climbed, weaning age dropped to around age 4.

The results suggest that low temperatures were more stressful for mammoths than warmer weather. And that doesn't fit the idea that a warming climate snuffed out the megafauna, Cherney said.

Hunting, which can force animals to mature faster, probably caused mammoths to wean early, he said.

Evolutionary biologist Alan Cooper of the University of Adelaide in Australia isn't convinced. Heavy nitrogen levels in the environment bounce around. And 10,000 to 20,000 years ago, heavy nitrogen suddenly dropped, which may partially explain the changing nitrogen levels Cherney found, Cooper cautioned. ■

COURTESY OF R. BAKKER

See how researchers estimated weaning age at **bit.ly/SN_mammothtusks**

LIFE & EVOLUTION

Brightest glowworms get the guys

In the animal world, females usually aren't the ones that show off for potential suitors. But for a species of glowworm in Finland, the females that glow the brightest are not only the most fertile, but they may also be the most pursued by mates, researchers report in the October *Biology Letters*.

In the nocturnal *Lampyris noctiluca*, the wingless females use a green glow to attract flying males. Researchers set LED traps and found that males preferred brighter traps, suggesting that males are more attracted to the brightest females. The team also found that females with bigger glowing structures laid more eggs.

Since males can't accurately judge a female's size in the dark, the glow could be the first indication of a healthy mate, the scientists say. — *Chris Samoray*

A female glowworm with the brightest glow is more likely to attract a mate and lay more eggs, a new study finds.

BODY & BRAIN

Cancer drug's effectiveness inflated in animal studies

Researchers investigating how well the chemotherapy drug sunitinib works against various types of cancer have overestimated the drug's effectiveness by an average of 45 percent, an analysis shows.

Valerie Henderson of McGill University in Montreal and colleagues reexamined data from 158 experiments involving 2,716 animals, mostly mice. Researchers who conducted the original experiments tended to publish only those in which sunitinib shrunk tumors. Not publishing negative findings led to an 11 percent overestimate of the drug's ability to shrink brain tumors called high-grade gliomas, Henderson and colleagues report October 13 in *eLife*. Sunitinib's breast cancer–fighting ability was inflated by 52 percent, the team found.

Study results were also biased by not "blinding" studies to keep researchers from knowing which animals got the experimental drug.

Failure to reproduce findings from animal studies has been a major stumbling block for drug researchers (*SN: 1/24/15, p. 20*). — *Tina Hesman Saey*

ATOM & COSMOS

White dwarf upsets planetary system, consumes evidence

At least one poor planet — or possibly over half a dozen — is becoming a snack for the core of a dead star. A white dwarf dubbed WD 1145+017, in the constellation Virgo, hosts an orbiting trail of rocky debris, researchers report in the Oct. 22 *Nature*. The detritus might be all that remains of a dying solar system.

The debris cloud, detected by the Kepler space telescope, gave itself away by repeatedly blocking some starlight. Researchers also observed traces of heavy elements such as aluminum, silicon and nickel on the white dwarf. Ordinarily, these elements would sink into the star quickly and disappear, so the atoms are probably raining down on the white dwarf as the planets break apart.

The presence of heavy elements in this and other white dwarfs suggests that these dead stars periodically enjoy a planetary snack (*SN: 9/24/11, p. 10*). — *Christopher Crockett*

ATOM & COSMOS

Comet carries alcohol, sugar

Like a roving interplanetary cocktail bar, a comet is carting around booze and sugar. The aptly named Comet Lovejoy contains ethanol and the simple sugar glycolaldehyde, researchers report October 23 in *Science Advances*. This is the first time that these complex organic molecules have been detected on a comet.

Ethanol and glycolaldehyde have been found around young stars where planets are forming (*SN: 5/2/15, p. 10*). Finding these molecules on a comet — a frozen time capsule from the birth of the solar system — suggests that they are preserved from the sun's formative years. While comets probably didn't play a major role in delivering water and organics to the young Earth (*SN: 5/16/15, p. 18*), they have a lot in common with the icy asteroids that did.

Comet C/2014 Q2 (Lovejoy) is a visitor from the Oort cloud, a shell of frozen debris enveloping the solar system. The comet was visible to the unaided eye during its closest approach to the sun in January 2015. Its unusual brightness made it a good hunting ground for molecules. Nicolas Biver, a planetary scientist at the Paris Observatory in Meudon, France, and colleagues used a radio telescope in the Spanish Sierra Nevada to observe Lovejoy. Ethanol and glycolaldehyde are two of 21 molecules detected streaming from the comet. The other molecules, such as carbon monoxide and a host of organics, have been seen previously in other comets. — *Christopher Crockett*

Comet Lovejoy (shown) carries ethanol and the simple sugar glycolaldehyde.

EARTH'S (Not So Boring) BORING BILLION

When the planet's oxygen was scarce, animals may have emerged under the radar

By Thomas Sumner

Earth's long history starts with an epic preamble: A collision with a Mars-sized space rock rips into the young planet and jettisons debris that forms the moon. Over the next few billion years, plot twists abound. The oceans form. Life appears. Solar-powered microbes breathe oxygen into the air. Colossal environmental shifts reshape the planet's surface and drive the evolution of early life.

After this wild youth of rapid change, things slowed down. About 1.8 billion years ago, the climate stabilized. Oxygen levels steadied. Evolution seemingly stalled. For around a billion years, not a lot changed on planet Earth. Scientists called this interval the dullest time in Earth's history. It came to be known as the "boring billion."

Dullsville Earth's environment stagnated around 1.8 billion years ago. The breakup of the Nuna supercontinent, illustrated here during its disassembly 1.38 billion years ago, should have triggered an ice age but didn't.

NICOLLE RAGER FULLER

But scientists are taking a fresh look at the boring billion and coming up with very different, downright fascinating, alternatives. Recent work recasts the era as a possibly pivotal (and definitely contentious) chapter in the story of life, which took a new twist not long after, with the introduction of animals.

Some geochemists say that recent measurements of the boring billion's oxygen-poor environment offer an even stronger argument that conditions forestalled the evolution of animals until after the era ended and oxygen levels rose, around 800 million years ago. Biologists counter that even with shockingly little oxygen, animals could have emerged and persevered. New experiments on modern sea sponges support that theory. Instead of a slowdown, biologists say, this period was the time of some of the most important evolutionary stepping-stones between simple life and modern animals. Some scientists even propose that the emerging animals deserve credit for boosting oxygen levels and bringing the boring billion to an end. Rather than environmental conditions, they say, life was calling the shots.

Uncovering what shook Earth out of its monotonous midlife will reveal why complex life emerged, contends Timothy Lyons, a geochemist at the University of California, Riverside. It might even reveal what could support or hinder the

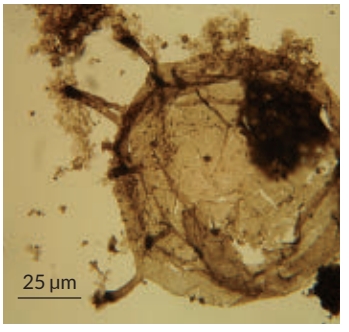
emergence of creatures on faraway worlds.

"For a long time, the boring billion was commonly thought to be remarkably unremarkable," Lyons says. "But it's a critical chapter in the history of life on Earth, and there are basic questions we don't understand."

A breath of fresh air

The planet's first whiff of oxygen came more than 3.2 billion years ago, following the evolution of the earliest photosynthetic microbes, cyanobacteria (*SN Online: 9/8/15*). These bacteria churn out oxygen into the environment. When the microscopic critters die, however, their remains decay and consume oxygen. Normally the life and death of a cyanobacterium would result in no net oxygen gain. Luckily for oxygen-loving life, accumulating sediments can bury the decaying organic matter under the seafloor and halt the drawdown of oxygen.

Before the boring billion, around 2.4 billion to 2.3 billion years ago, cyanobacteria flooded Earth's atmosphere with oxygen (*SN: 10/10/09, p. 11*). This oxygen rise, nicknamed the Great Oxidation Event, permanently altered the planet's chemical portfolio and purged the surface of nearly all oxygen-intolerant life.



This roughly 1.4-billion-year-old fossil is probably from an early eukaryote, which preceded animals.

The breath of oxygen ultimately spurred the evolution of complex life-forms called eukaryotes, with distinct cell nuclei and organelles. Early eukaryotes — the forebears of animals and plants — appeared at the start of the boring billion, 1.8 billion years ago. During their first few hundred million years, single- and multicelled eukaryotes eked out a marginal existence while bacteria and archaea unequivocally ruled Earth's ecosystem (*SN: 12/31/11, p. 12*).

For decades, many scientists blamed the boring billion's lack of eukaryote expansion and evolution, as evident in the fossil record, on low levels of oxygen. Today, oxygen makes up about one-fifth of Earth's atmosphere; early studies pegged the boring billion as having 1 to 40 percent of modern oxygen concentrations. That made sense because most of the boring billion took place during the Mesoproterozoic era, when the rate of burial of decaying organic carbon matter under marine sediments flatlined. Oxygen production and consumption roughly canceled each other out.

Low oxygen isn't the boring billion's only defining feature — its changeless nature stands in marked contrast to the two dynamic eras that came before and after: the Paleoproterozoic and the Neoproterozoic. During those geologic bookends, wild swings in organic carbon burial were the norm. Similarly, while the Paleoproterozoic and Neoproterozoic included titanic freeze-overs of the planet, no great glaciations chilled the boring billion. As far as scientists can tell, warm and stable climate reigned for hundreds of millions of years.

The very stability of the boring billion left it overshadowed, scientifically, by its more lively neighboring eras, which have long seized the attention of researchers, says Linda Kah, a geologist at the University of Tennessee in Knoxville. "It's easier to get funding if you go for the exciting spots," she says. "You either want the Neoproterozoic when animals evolved or you want to go to the oldest, because the oldest is always cool."

But on closer inspection, scientists are now finding the boring billion's characteristic stability — unprecedented and unrepeated in Earth's history — much harder to explain than the environmental shifts that punctuate other time periods.

"There's no shortage of ways to stabilize the carbon cycle and oxygen levels," says Yale geochemist Noah Planavsky. But for a lot of these stabilizing mechanisms, things get too stable. It becomes "difficult to imagine how you'd move on. We can imagine scenarios where we're stuck in a boring system indefinitely," he says. And that clearly didn't happen.

Information from the time remains sparse, however, prompting new inquiries into what conditions were like for life 1.8 billion to 800 million years ago. So far, findings from these studies reveal a surprisingly suffocating world.

Chemical clues

Investigating ancient environments requires some clever chemical detective work. Because there is no ancient air or seawater remaining from billions of years ago, researchers hunt for evidence of primordial conditions embedded inside rocks.

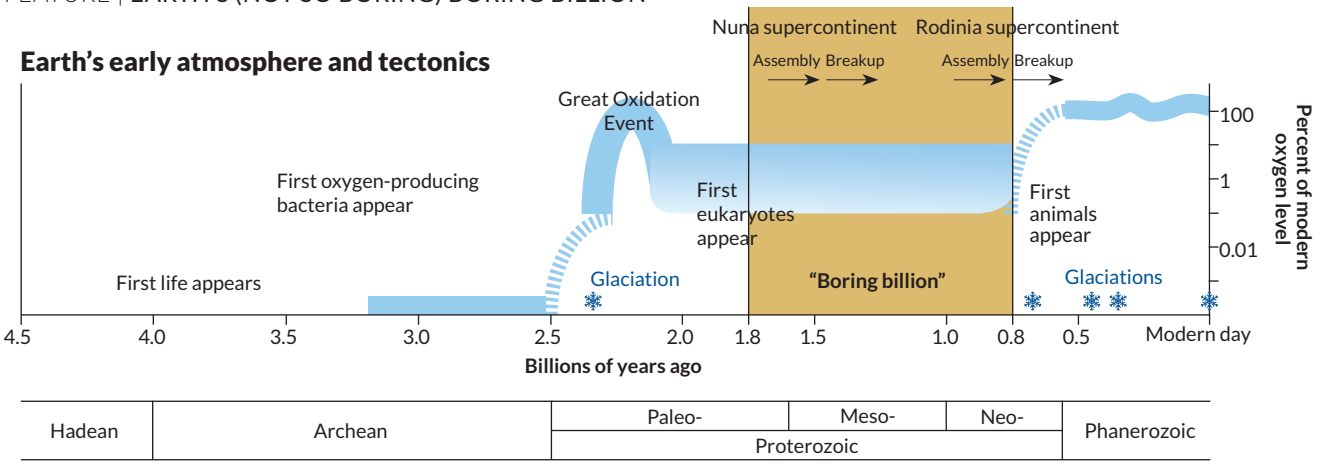
Last year, Planavsky, Lyons and colleagues presented a new way to track oxygen during the boring billion. Scouring the chemical contents of marine sedimentary rocks laid down during the interval, the researchers found that oxygen levels were much lower than anyone had thought. While previous estimates predicted boring billion oxygen levels as high as 40 percent of modern concentrations, the new work suggests levels were only a few thousandths of that.

Planavsky and colleagues looked for signs that bacteria in ancient soils oxidized significant quantities of manganese atoms for energy, something that can happen only when oxygen levels are above about 0.1 percent of modern day.

These microbes lived on land, but the researchers hunted for evidence of manganese oxidation in what were once ancient shorelines. The chemical clues traveled from land to sea after the oxidized manganese in turn oxidized chromium atoms in the soil, leaving a telltale mark. Some varieties of chromium oxidize more readily than others. (The extra mass in chromium-53 makes it oxidize disproportionately more frequently than its lighter sibling chromium-52). Once oxidized, the chromium atoms could dissolve in water and wash into the ocean via streams. Any chromium imbalance created in the soil would ultimately be buried on the ocean floor.

After analyzing sedimentary rocks from the boring billion, the researchers reported last year in *Science* that no such

A. KNOLL/HARVARD UNIV.



Storied history Life and oxygen on Earth have remained tightly entangled for billions of years. Following a rise known as the Great Oxidation Event, oxygen levels (blue) seemingly steadied for roughly a billion years, though precise data about much of the interval are lacking. During this time span, Earth remained warm with no glaciations (marked by snowflakes), despite supercontinent formation and breakup.

SOURCES: T.W. LYONS, C.T. REINHARD AND N.J. PLANAVSKY/*NATURE* 2014; N.J. PLANAVSKY *ET AL/ANNUAL SHORT COURSE VOLUME OF THE PALEONTOLOGICAL SOCIETY* 2015

chromium-53 surplus existed (*SN: 11/29/14, p. 14*). Oxygen levels during the boring billion must have been lower than the 0.1 percent threshold for manganese oxidation, the researchers argue.

"Oxygen was a lot lower than anyone imagined," Lyons says, possibly low enough to prohibit the evolution of animals.

Oxygen forms the ozone layer in the atmosphere, but if oxygen levels were as low as Planavsky estimates, the ozone layer would have been razor thin, says Penn State geoscientist James Kasting. Such scant ozone makes the boring billion's lack of ice ages harder to account for, he says. At the start of the Mesoproterozoic, the sun shined about 85 percent as brightly as it does today (*SN: 5/4/13, p. 30*). With that much less warmth from the sun, keeping the planet hot enough to curtail ice ages would require an intense greenhouse effect to trap Earth's heat. But carbon dioxide concentrations alone weren't high enough at the time to explain the above-freezing conditions, Kasting says.

Deep-sea microbes can produce methane that helps lock in Earth's warmth, but the dearth of oxygen poses a problem: Methane degrades in ultraviolet light; if the ozone layer barely existed, as Kasting says, that methane wouldn't stand a chance.

But greenhouse warming must have been in play because, tectonically, the boring billion wasn't boring. Supercontinent formations and breakups expose new rock to the atmosphere. The new rock pulls carbon dioxide from the air, triggering ice ages. Yet in the middle of the boring billion, between 1.6 billion to 1.3 billion years ago, a supercontinent called Nuna assembled and broke up without causing any icing over. That lack of freezing temperatures suggests that the impact of plate tectonics on the planet's climate "isn't as strong as we had thought," says Yale geoscientist David Evans. He suspects that, during the boring billion, living things influenced the environment and kept the planet warm.

Just how much life altered the environment, and just how strongly the environment controlled life, remains hard to suss out, Evans says. Some biologists propose that life did more than affect temperatures; it also triggered chemical and climatic changes that brought an end to the boring billion. Even paltry oxygen levels, those scientists contend, can't stop the unending march of evolution.

Shallow breaths

Scientists have long assumed that animals could appear only once oxygen levels rose to about 6 to 10 percent of modern concentrations. Animals munch on other life-forms for energy. Obtaining and digesting food requires lots of oxygen. The low-oxygen conditions of the boring billion predicted by Planavsky and colleagues, therefore, seems an animal no-go.

At first glance, the fossil record appears to support that notion. The first fossilized animals, sponges, don't appear until around 650 million years ago, coincident with a proposed rise in atmospheric oxygen. But fossils aren't a perfect record, and other lines of evidence hint that animals originated tens of millions of years earlier, during the boring billion's closing chapters.

Pinpointing when animals could have evolved, based on atmospheric conditions alone, is difficult because estimates of early animals' oxygen needs are speculative. After millions of years of adaptation, no early animals are alive today to testify. Instead of guessing how ancient animals might have lived, geobiologists Daniel Mills and Donald Canfield of the University of Southern Denmark in Odense and colleagues tested a modern analog: the sea sponge. Their finding challenges the view that low oxygen levels during the boring billion prohibited the evolution of animals, Mills and Canfield wrote last year in *BioEssays*.

Mills' team studied the bread crumb sponge (*Halichondria panicea*). The animal was not selected for its hardiness. In fact, the sponge has no special adaptations for low-oxygen life and typically lives in highly oxygenated shallow waters. Mills chose the sponge out of convenience: Bread crumb sponges are

J. HIRSHFELD

common in the fjord near his university's marine biology lab.

Mills dunked the yellowy globs into special water tanks. Slowly and in stages, he trimmed back the oxygen levels in the water while monitoring each sponge's health. As oxygen levels plummeted, the sponges seemed unfazed. They thrived in water containing as little as 0.5 to 4 percent of modern oxygen levels, Mills and colleagues reported last year in *Proceedings of the National Academy of Sciences*. Some animals, it seems, don't require that much oxygen after all.

"If we were to go back in time to the Mesoproterozoic, we'd suffocate and die if we stepped outside the time machine," Mills says. "But that doesn't mean that no animals could have survived in those conditions."

"Oxygen was a lot lower than anyone imagined."
TIMOTHY LYONS

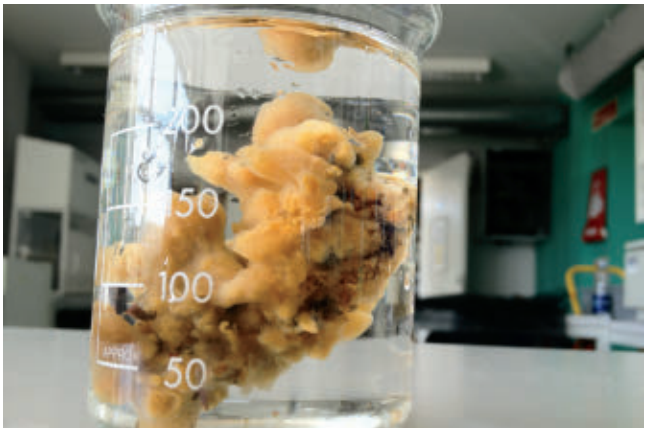
While the sea sponge wasn't tested under the skimpy 0.1 percent of modern oxygen conditions later predicted by Planavsky and colleagues, oxygen levels probably weren't that low everywhere, Mills says. Pockets of oxygenated water, called oxygen oases, may have formed near clusters of oxygen-producing microbes. Small animals may have emerged in these havens and lived isolated lives until the global oxygen supply spiked after the boring billion, he proposes.

In this scenario, animals emerged after clearing an evolutionary hurdle, suggests Harvard paleontologist Andrew Knoll. Animals and other complex life have more intricate cell biology than early eukaryotes. The evolution of these sophisticated systems may have taken a relatively long time and wouldn't be evident in the fossil record, he says.

"Animals had to be preceded by important events at the level of how cells are structured, how the genes are organized," Knoll says. "That level of evolution, which doesn't leave a particularly sexy fossil record, happened during the boring billion."

Which came first?

Some scientists, including Nicholas Butterfield, a paleontologist at the University of Cambridge, go further, saying that the first animals might have been responsible for the environmental changes at the end of the boring billion.



D. MILLS/UNIV. OF SOUTHERN DENMARK

This bread crumb sponge survived suffocating waters, suggesting that some animals require much less oxygen to function than once thought.

In August, at the Goldschmidt Conference in Prague, Butterfield argued that early sea sponges altered the composition of Earth's seawater. Sponges can filter hundreds of liters of water per day, sifting out organic carbon that would decay and reduce oxygen levels in the process. The result, Butterfield proposes, is that early animals indirectly increased the oxygen available in Earth's oceans and helped pull the planet out of the boring billion.

"When you invent animals, they have an enormous impact on the chemistry and quality of the surrounding water," Butterfield says. "It was a long run-up time, but once animals evolved, bingo, away you go."

Many scientists, however, are unconvinced that animals emerged in the boring billion's tough environment. In June, at the Astrobiology Science Conference in Chicago, geochemist Dalton Hardisty, who works with Lyons at the University of California, Riverside, proposed that conditions would have been much harsher for animals than previously thought. Measuring chemical traces in rock layers from the boring billion, Hardisty discovered that low-oxygen water from the ocean depths often mixed with surface water. This mixing may have prevented oxygen oases from lingering long enough to support early animals.

The deep water may have also brought something deadly along with it: hydrogen sulfide produced by deep-sea microbes. Hydrogen sulfide is usually toxic to animals and could have made the shallow ocean inhospitable to complex life, Hardisty says.

Lyons likes to take the conversation to more out-there questions. Whether an evolutionary speed bump or a poisonous environment, identifying what postponed the emergence of animals is crucial to understanding the challenges faced by life on other worlds, he says. The boring billion preceded the Cambrian explosion of animal diversity, around 542 million years ago.

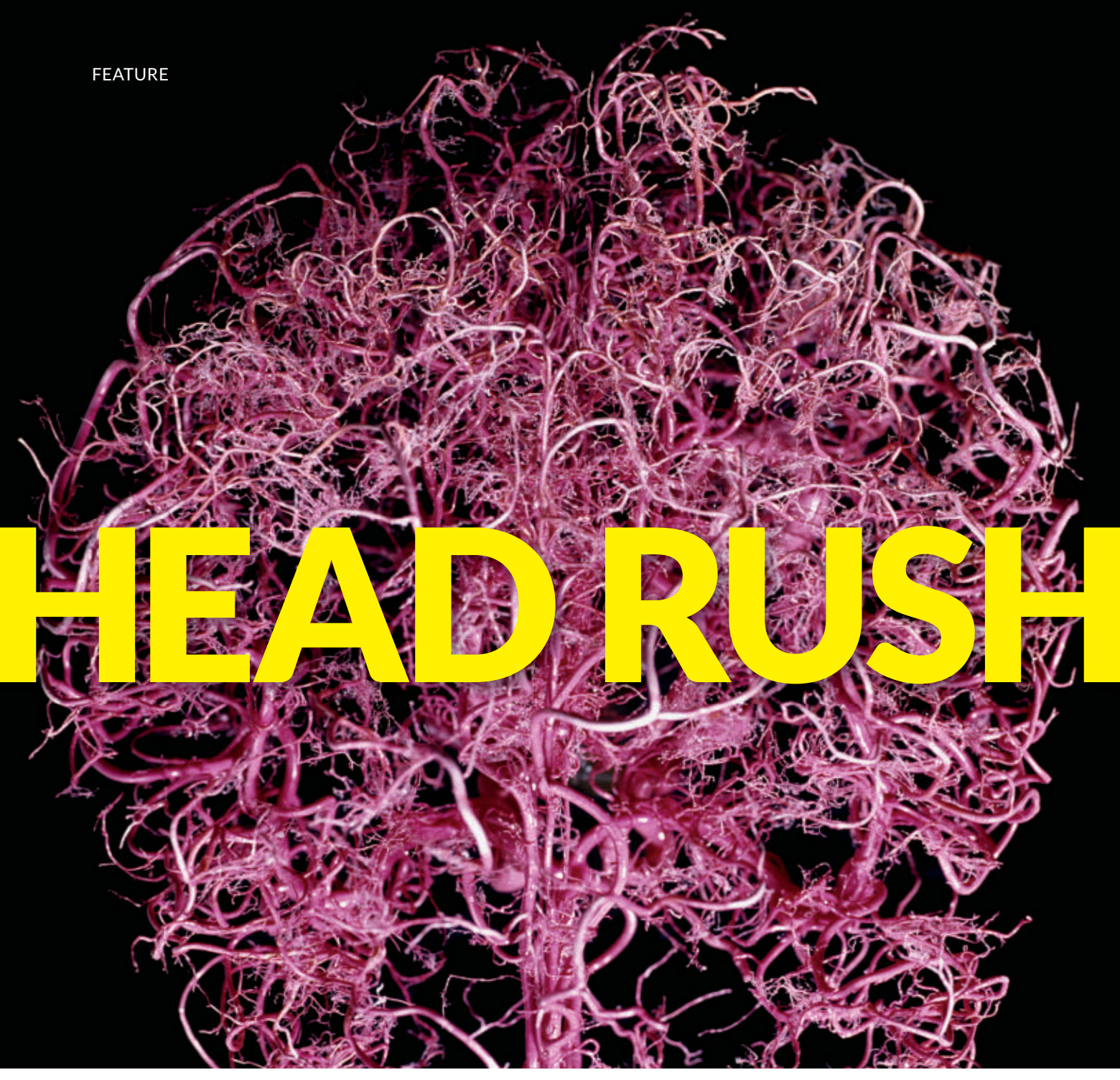
Learning what broke the boring billion's cycle of monotony will illuminate whether sophisticated life could be common in the universe, or just a fluke, he says. As new telescopes catch glimpses of exoplanet atmospheres, understanding how Earth's ancient air interacted with early life will help astrobiologists postulate what sort of life-forms may cling to distant planets.

For now, the boring billion will continue to be a hotbed of research into the interplay between life and the environment, not exactly boring.

"I'd actually be delighted to keep calling it the boring billion, but always with a wink," Lyons says. "Scientifically, there's nothing boring about it, and I love the irony in that. I'd never change the name." ■

Explore more

- Timothy W. Lyons *et al.* "The rise of oxygen in Earth's early ocean and atmosphere." *Nature.* February 20, 2014.



HEAD RUSH

Blood exerts a powerful influence on the brain

By Laura Sanders

Blood tells a story about the body it inhabits. As it pumps through vessels, delivering nutrients and oxygen, the ruby red liquid picks up information. Hormones carried by blood can hint at how hungry a person is, or how scared, or how sleepy. Other messages in the blood can warn of heart disease or announce a pregnancy. Immune molecules can reveal an infection.

When it comes to the brain, blood also seems to be more than a traveling storyteller. In some cases, the blood may be writing the script.

A well-fed brain is crucial to survival. Blood ebbs and flows within the brain, moving into active areas in response to the brain's demands for fuel. Now scientists have found clues that blood may have an even more direct and powerful influence. Early experiments suggest that, instead of being at the beck and call of nerve cells, blood can actually control them. This role reversal hints at an underappreciated layer of

Blood vessels run through the brain delivering oxygen and nutrients — and maybe even commands — to nerve cells.

RALPH HUTCHINGS/VISUALS UNLIMITED, INC.

complexity — a layer that may turn out to be vital to how the brain works.

The give-and-take between brain and blood appears to change with age and with illness, researchers are finding. Just as babies aren't born walking, their developing brain cells have to learn how to call for blood. And a range of age-related disorders, including Alzheimer's disease, have been linked to dropped calls between blood and brain, a silence that may leave patches of brain unable to do their jobs.

This line of research is expanding scientists' view of what makes the brain tick, and the implications for human health are enormous. Diabetes, multiple sclerosis and hypertension — diseases that harm blood vessels elsewhere in the body — may afflict the brain too. What's more, common drugs that tinker with blood flow, including statins, anti-inflammatories and even Viagra, may affect how the brain operates.

In Vancouver this summer, neuroscientist and biomedical engineer Elizabeth Hillman of Columbia University attended a meeting devoted to blood flow in the brain. Though the field is full of unanswered questions, "there was a palpable sense we were getting somewhere," Hillman says.

Flow control

When nerve cells, or neurons, are active, they call for more blood by somehow signaling to nearby vessels. The vessels respond by widening and allowing more blood to flow. This blood beckoning forms the basis of a brain-scanning technique called functional MRI, which measures blood flow as a proxy for neural activity.

When delivering fuel such as glucose and oxygen to hungry neurons, blood first pumps into large arteries that run along the outside of the brain. It then plunges inward through smaller vessels called arterioles before squeezing down into capillaries so thin that red blood cells must travel single file.

Textbooks about the brain often point to star-shaped cells called astrocytes as the middlemen that carry the message — "more blood, please" — from neurons to arterioles. Astrocytes (*SN: 8/22/15, p. 18*) are often found tangled up with both neurons and blood vessels, a perfect spot for a go-between.

But the idea that astrocytes complete the connection between neurons and larger blood vessels may be too simple. Much still remains mysterious about this neuron-to-blood messaging. There's no consensus yet on how neurons come up with the request, which molecules carry the signal or which cells respond to it, though scientists are turning up plenty of suspects.

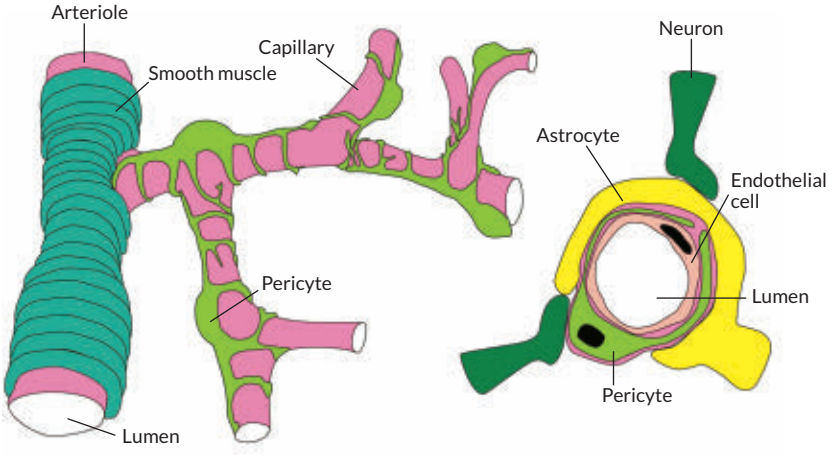
Neuroscientist David Attwell of University College London and colleagues have started focusing on cells called pericytes, which dot the outside of capillaries throughout the body. Pericytes, best known in the brain for their role in forming the blood-brain barrier, also have a hand in delivering blood by controlling capillaries, Attwell and colleagues proposed last year in *Nature*. Capillaries were larger and let more blood flow in places where pericytes resided, suggesting that the cells could control the floodgates, the team found.

That idea is controversial. Neuroscientists Robert Hill and Jaime Grutzendler of Yale University and colleagues published a paper in July in *Neuron* claiming that pericytes cannot dish out blood. Pericytes lack actin, a contractile protein that would be needed to squeeze or relax vessels, the researchers argue. Smooth muscle cells that line vessels larger than capillaries control blood flow, they say.

Then there are the endothelial cells, which may also help regulate blood flow. Unlike astrocytes and pericytes, which live outside of vessels, endothelial cells are stitched into the very fabric of blood vessels large and small. As the innermost layer of all the blood vessels in the body, endothelial cells are perfectly poised to detect chemical signals from their surroundings and carry ultrafast messages along vessels, Hillman says.

When Hillman and her colleagues damaged the endothelial cells lining an artery on the surface of

The squeeze The cells in and around the brain's blood vessels somehow carry messages that change blood flow. Scientists are scrutinizing the role of astrocytes, smooth muscle cells, pericytes and endothelial cells, which surround the lumen, the channel where blood flows.



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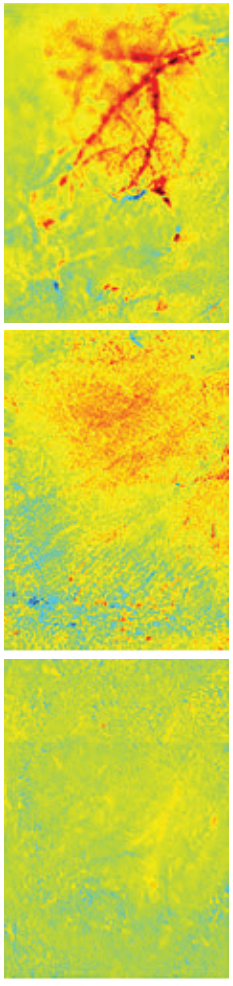


Feed me Blood rich in hemoglobin (red) rushes into a patch of brain in an adult rat after its paw is stimulated (top panel). In adolescents, the signal is just beginning to emerge (middle). In newborn rats, when neurons call for blood, the request goes unanswered (bottom panel).

a rat's brain, blood no longer responded to busy neurons. Vast networks of endothelial cells may carry messages lightning-quick from neurons that need fuel to distant large arteries that can supply it. Those results, published in 2014 in the *Journal of the American Heart Association*, suggest that the same system that regulates blood flow in the rest of the body might also apply to the brain. "The real irony is that [people thought] there was somehow this divide" between body and brain, Hillman says.

Newborn brains can't do it

As Attwell and others try to work out how neurons call for blood, other research is showing that this skill is not part of a newborn's repertoire — and maybe for good reason. In the days and weeks after birth, the communication wires between blood vessels and neurons are put down with precise specifications, recent studies suggest. The fact that this system takes time to grow helps explain why young babies' brains give off funny results during an fMRI scan. Instead of sparking an influx of blood, neural activity in a baby's brain can cause what looks like blood leaving the area.

"There's a whole bunch of odd goings-on in the very young brain," Hillman says. These puzzling negative signals hint that the infant brain has its own surprising way of operating.

In very young rats, active neurons can't call blood for nutrients, Hillman and colleagues reported in the *Proceedings of the National Academy of Sciences* in 2013. "If the neurons are trying desperately to fire in response to the stimulus, but they simply don't get the energy they need to do it, they have to stop. That's what it looks like to us," she says. "It looks like they give up."

A pause may be its own kind of signaling, perhaps laying the groundwork for a fully functioning adult brain. As the rats grew up, their neurons' hunger cries were answered. Blood flooded the area soon after neurons fired, the team found.

This interaction between neuron and blood can lead to more blood delivered not just by turning up the flow, but also by creating new pipes, a different study reveals. Neurons that respond to whisker twitches in young mice could actually trigger new blood vessels to form, neuroscientist Chenghua Gu of Harvard University and colleagues found. When the researchers plucked a whisker so that its corresponding neurons were deprived of input, neurons sensitive to that whisker remained silent. Those inert neurons had fewer nearby blood vessels than neurons that were handling incoming information normally, Gu and colleagues reported in 2014 in *Neuron*. But if the scientists flicked a whisker, sparking lots of activity in the associated neurons, blood vessels sprouted new branches and delivered blood to the active cells. In the growing brain, neurons are literally drawing blood to themselves, the results suggest. "You're building more roads," Gu says.

The results make sense to Hillman. "If you were building a city, you wouldn't put in all the sewers and all the electronics before the houses are built," she says. "You let the houses get built, and then you provide each house with what it needs."

It's not clear exactly how the young neurons will vessels into existence, but Gu has an idea. She thinks that the low-oxygen state that results from the neurons cranking away without fuel might be the key signal. While it might sound alarming to think of patches of starving neurons within babies' brains, that desperate state might be the impetus for blood vessel growth. If so, the recent findings might ultimately point to optimal dosages of oxygen for young babies born in distress. Too much might interfere with blood vessel formation, Hillman says.

Blood takes the wheel

Beyond keeping neurons well fed, blood may actually tell neurons when to fire. Kind of like gasoline oozing out of a car's gas tank and taking the wheel.

The idea isn't as crazy as it sounds, says neuroscientist Christopher Moore of Brown University. In 2008, he and colleague Rosa Cao laid out their "hemo-neural hypothesis" in the *Journal of Neurophysiology*. The gist is that blood may influence the behavior of neurons in a way that goes beyond just providing energy to already active cells.

"The blood has exquisite access to where we stand," Moore says. Replete with hormones, sugar and other signals, the blood contains an accurate readout of what the body needs. It makes sense that this complex system would be able to influence its neural neighbors. "It would be amazingly stunning if there was a neuron-to-vascular effect and no vascular-to-neuron effect," he says.

In the last few years, he and his group have caught glimpses of that reversed effect. In Moore's lab, neuroscientist Tyler Brown led projects to change blood flow by tweaking the size of vessels. A slight dilation or constriction of vessels reliably changes the behavior of nearby neurons. The team used optogenetics (*SN: 1/30/10, p. 18*) to squeeze blood vessels by activating

M. KOZBERG *ET AL/PNAS* 2013

endothelial or smooth muscle cells that were genetically modified to respond to light. Tweaking the vessels caused some nearby neurons to dial their behavior up or down, the team reported last year in Washington, D.C., at the annual meeting of the Society for Neuroscience.

Figuring out the details of these blood-to-neuron commands will take a long time, Moore says. "We still don't know how a neuron being active draws a blood vessel, and people have been working on that forever."

Talking about blood directing the brain is odd in the context of the normal working brain, says Hillman. "Does the blood somehow make decisions for the brain?" she asks. But for catastrophic events like strokes, the concept is obviously true. "When you think about it in terms of diseases and disorders, it makes a lot of sense."

Scientists are starting to investigate blood flow troubles in dementia, suspicious that cognitive problems may stem from lost conversations between neurons and blood. Abnormal blood flow in the brain is present in the five major forms of dementia, including Alzheimer's disease and dementia with Lewy bodies. This idea isn't new: In the early 1900s, Alois Alzheimer suggested that problems in the circulatory system might trigger the memory-robbing disease now named for him.

Other disorders, such as diabetes, might harm the brain by damaging blood vessels. Many scientists attribute the mental fuzziness that can accompany diabetes to neuron damage from excess glucose. But maybe faulty lines between unresponsive blood vessels and neurons are to blame, Hillman says.

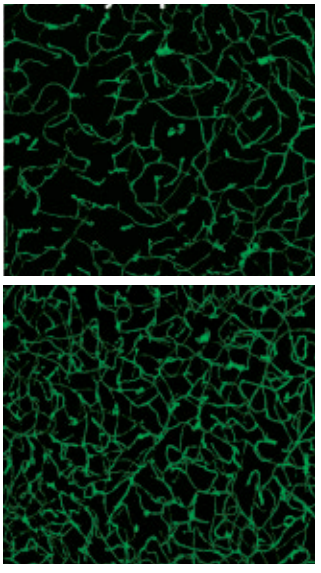
Common drugs that influence blood flow may also have unanticipated effects on the brain. In addition to statins, drugs such as Viagra, blood pressure drugs and even anti-inflammatories may unintentionally change how the brain operates. These drugs may be dampening the brain's ability to call for blood when it needs it, Hillman says. "That could have a long-term effect that I don't think anybody is thinking about right now."

There's also the possibility that some blood-modulating drugs may have beneficial brain effects. Blood vessel–clearing statins, for instance, may help protect memory in people with Alzheimer's disease.

Statin treatment improved the memory of middle-aged mice engineered so their brains produce gobs of sticky amyloid-beta, the protein that piles up in people with Alzheimer's. Three months on the statin simvastatin restored short- and long-term memory in these mice, neuroscientist Edith Hamel of McGill University in Montreal and colleagues reported in 2012.

Compared with mice that didn't get the treatment, the mice on statins also had healthier blood vessels in their brains that seemed more responsive to changes in neuron activity. Though the idea remains controversial, a similar effect may happen in people. Several studies have linked statins taken in early old age to lower rates of Alzheimer's later on.

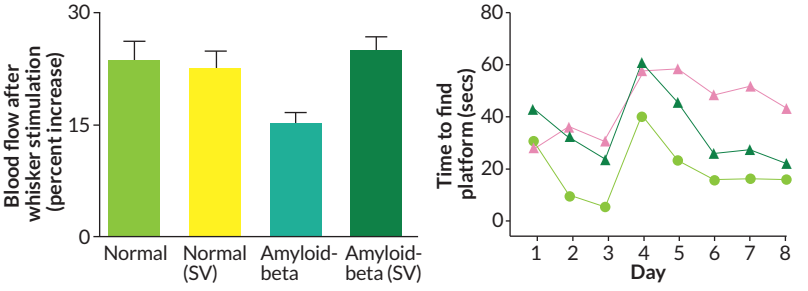
Because it's so easy to get drugs into the bloodstream, the promise of changing the brain by changing the blood is great. And these early hints of how blood vessels and neurons work together are bringing scientists closer to that alluring goal. Though there is still much to learn, one thing is already clear: Together, the blood and brain are telling a compelling story. ■



B. LACOSTE/HARVARD MEDICAL SCHOOL

Stimulating growth
Blood vessel networks branched less and were shorter in the brains of mice that had no sensory stimulation (top). In the brains of mice that got many whisker flicks (bottom), vessels were more plentiful.

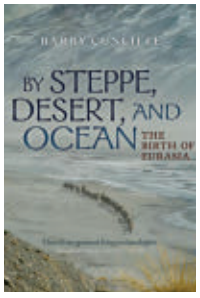
Statins improve memory in Alzheimer's-like mice



Protecting memory
Among adult mice engineered to show signs of Alzheimer's (teal and dark green, left), blood flow responded more readily to neural signals in those receiving a statin drug (SV) than those receiving no drug. The statin-treated mice (dark green line, right) also found a previously visited hidden platform faster than mice receiving no statins (pink). Light green shows normal mice with no signs of Alzheimer's. SOURCE: XIN-KANG TONG *ET AL/J. NEUROSCI.* 2012

Explore more

- Baptiste Lacoste *et al.* "Sensory-related neural activity regulates the structure of vascular networks in the cerebral cortex." *Neuron.* September 3, 2014.



By Steppe, Desert, and Ocean
Barry Cunliffe
OXFORD UNIV., $49.95

BOOKSHELF

Early globalization on display in history of Eurasian civilization

Today's globalized, interconnected, in-your-face world has a complex backstory. In *By Steppe, Desert, and Ocean*, archaeologist Barry Cunliffe unravels events in Eurasia between 12,000 and 700 years ago, a pivotal stretch of time that witnessed a transformation of the first farmers into seagoing traders who created the first global networks.

It's a fascinating tale of survival, ingenuity, power, greed, cooperation and brutality. Scheming characters on the TV show *Empire* have nothing on the Mongol empire, a band of nomadic horsemen that conquered much of Eurasia during the 1200s. This empire's ruling family held its vast domain together for three generations before internal rivalries tore the realm apart.

Cunliffe uses the archaeological record to identify developments that forced widespread social changes in the ancient world. He sees those transitions as driven by several key forces: geography, climate shifts, population growth and humans' intense need to acquire goods and knowledge.

Consider the transition from foraging to farming. Rising temperatures triggered cultivation in two regions: West Asia's Fertile Crescent and China. To the west, farming started nearly 12,000 years ago and spread rapidly through open geographic corridors to South Asia and Europe by 7,000 years ago. In the east, plant cultivation spread throughout much of China between 11,000 and 8,000 years ago. But mountains, deserts and forests deterred agriculture's advance into Southeast and Central Asia. Food surpluses in West and East Asian farming regions set the stage for political states to emerge.

Then it was off to the civilizational races, especially with the introduction of horseback riding roughly 6,000 years ago in Central Asia. Herding communities there became long-distance travelers, trading goods with states to the west, east and south.

Starting around 2,900 years ago, Central Asian nomadic societies grew in size and complexity, leading to expanded trade across the continent's midsection. Ascending Chinese and Roman empires accelerated the growth of trade networks across previously unbreachable deserts and oceans. Finally, warlike nomads such as the Mongols conquered sedentary societies throughout Eurasia until the nomad-run empires fell apart largely from internal discord. Societies then turned to long-distance ocean trade, opening the way to European contacts with the Americas and beyond.

In tracing the rise of Eurasian civilization, Cunliffe makes clear that history is much more than just one thing after another. As migrations and conquests pile up in the book, it becomes apparent that a dizzying array of forces interacted to produce the modern world. — *Bruce Bower*

On the Wing
David E. Alexander
OXFORD UNIV., $29.95

BOOKSHELF

On the Wing chronicles origins of flying animals

The Wright Brothers powered their way into the air at Kitty Hawk, N.C., a little more than a century ago. Like millions of humans before and since, they were inspired by myriad creatures that first took to the air eons earlier.

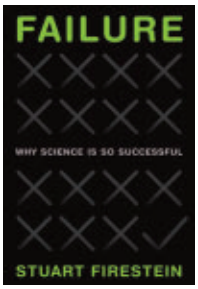
In *On the Wing*, biomechanicist David E. Alexander reviews in detail the evolution of the four groups of animals that preceded humans into the skies. The four — insects, birds, bats and the dinosaur-era reptiles known as pterosaurs — have a lot in common, Alexander notes.

The fossil record suggests that each group evolved the ability to fly just once. They all fly (or flew) by flapping their wings, but their ancestors' first aerial excursions were probably short glides from elevated perches, either to chase prey or to escape a predator. And all fliers must keenly sense obstacles or potential landing sites at a distance, the better to avoid crashing at high (and possibly fatal) speed. That need typically translates into acute vision, Alexander writes, but bats have made do with echolocation.

Yet great differences emerge among the groups: Insects, which took to the air more than 350 million years ago, didn't give up a pair of legs to gain their wings, while birds, bats and pterosaurs did. Another contrast: Although paleontologists have discovered fossils that chronicle the gradual evolution of birds, Alexander writes, the earliest flying members of the other groups are, for now, frustratingly absent from the fossil record.

The rules of aerodynamics apply across these groups despite great disparities in size. Evolution sculpted the animals, and their wings, accordingly. Pterosaurs, the largest creatures ever to fly, had wingspans comparable to a single-engine Cessna aircraft's; the smallest fliers are millimeter-sized insects called thrips.

In addition to the true fliers, Alexander explores the variety of creatures that merely glide ("flying" squirrels, anyone?) and those with ancestors that once flew, such as fleas, bedbugs and ostriches. These sidelights add entertaining and informative insights into the story of flight.
— *Sid Perkins*



Failure
Stuart Firestein
OXFORD UNIV., $21.95

BOOKSHELF

Failure explores the upsides of mistakes

Failure is nothing to disparage — at least in research. Indeed, it's one of the principal "engines that propel science forward," argues Stuart Firestein in the provocative new book *Failure*. A biologist at Columbia University, Firestein has experienced his share of failures. And as long as they are not due to sloppiness, ineptitude or taking on tasks beyond one's capabilities, he says, failures in science are not a reason to apologize. They might even be something to shoot for.

Firestein quickly makes a compelling case that fear of failure constrains imagination. Meanwhile, scientists unafraid of failure can consider a whole universe of testable explanations — even if adequate tools don't yet exist to undertake those tests.

Many failures initially appeared to be successes. Consider Newton's claim that time and space were fixed and absolute. This idea held for centuries until Einstein, whose ideas about relativity would conflict with — and win out over — Newton's approach to explaining gravity (*SN: 10/17/15, p. 16*).

Some misinterpretations of data survived even longer. It wasn't until the early 1600s that William Harvey overturned the pneumatic theory of blood proposed by Erasistratus around 250 B.C. and by Galen some 400 years later. The two early physicians thought the body's arteries circulated a vital energetic force acquired from air. Although Galen, Erasistratus and their followers mapped out human anatomy well, "they were mostly wrong about how it all worked," Firestein observes. But that's common in science, he asserts: Measurements and data tend to precede understanding.

Firestein views science as the endless quest for answers. But any success by a good researcher will be short-lived, he says. It just serves as a point of departure for more quests, most of which could fail and probably will. In fact, no theory can hold up unless it could have been wrong and was shown not to be. So, Firestein argues, science "is trustworthy precisely because it can fail." The problem, he says, is that researchers have done a poor job of educating the public and policy makers that failure is the strength of science, not its Achilles' heel. — *Janet Raloff*

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Cooking up a win at Broadcom MASTERS

SAN JOSE, CALIF. — Annie Ostojic knows how to cook up good science. The 13-year-old from Munster, Ind., spent two years designing a better shape for the home microwave oven. What she eventually created is an award-winning appliance that cooks food all the way through, with no cold spots.

Ostojic won the $25,000 Samueli Foundation prize for her project, her overall scientific skills and ability to work with others. She was honored October 6 at the fifth annual Broadcom MASTERS competition. Nine other students also took home cash prizes or money to attend science, technology, engineering and mathematics (STEM) summer programs.

MASTERS stands for Math, Applied Science, Technology and Engineering for Rising Stars. The Broadcom Foundation sponsors the event. The Foundation's mission is to inspire and enable young people to pursue careers in STEM. The program was created by Society for Science & the Public, which publishes *Science News* and *Science News for Students*.

Middle school students qualify for Broadcom MASTERS by placing in the top 10 percent of an affiliated science fair. Thirty finalists then present their projects, take on team challenges and work together to solve problems. Ostojic and her peers spent three days competing in challenges held around the San Francisco Bay Area. Teams identified invertebrates in bay-bottom mud, built bridges and designed their own computers. They also toured Google, Lucasfilm and NASA's Ames Research Center.

Ostojic studied how microwaves cook by using an infrared camera to watch marshmallows and cheese cubes melt. Last year, she designed a large microwaveable cup that cooked food more thoroughly with less energy. This year, she knew she needed to make her idea more practical by tackling the microwave itself. "I've always been a person to think outside the box, but this time I had to literally think inside the box," she says.

Annie Ostojic and Maximilian Du work on a team challenge at the Broadcom MASTERS in California.

Ostojic concentrated on designing a cavity that would refocus lost corner energy toward the center turntable of the machine while also mitigating hot spots. The young engineer lined the microwave with reflective materials to redirect heat toward the oven's center. Aluminum foil worked best, she found. She also rounded the rectangular cavity, helping minimize energy loss in the corners.

Ostojic has applied for a patent for her microwave design, but she is already moving on to new projects and intends to become a mechanical engineer.

"You always have unanswered questions" in research, she says. "No matter what, you're going to find some sort of new angle that's going to be interesting." This encourages you, she says, to "just keep going."

Cocompetitor Sebastian Mellen won the $10,000 Marconi/Samueli Award for Innovation for his smartphone app, Mathsuite, which does a range of algebra calculations. The 14-year-old from San Diego says he was inspired to create the app after watching teachers and students struggle with math.

Eight other finalists earned awards in four STEM categories (see list). The first- and second-place awards come with $3,500 and $2,500, respectively, to help winners attend a STEM-oriented program. — *Bethany Brookshire*

STEM Awards for Science

FIRST PLACE **Maximilian Du,** 13, Eagle Hill Middle School, Manlius, N.Y.

SECOND PLACE **Hannah O. Cevasco**, 14, St. Charles School, San Carlos, Calif.

STEM Awards for Technology

FIRST PLACE **Manasa (Hari) Bhimaraju**, 11, John F. Kennedy Middle School, Cupertino, Calif.

SECOND PLACE **Anusha Zaman**, 14, Glasgow Middle School, Baton Rouge, La.

STEM Awards for Engineering

FIRST PLACE **Avery P. Clowes**, 13, Oak Meadow School, Bolton, Mass.

SECOND PLACE **Soyoun Choi**, 16, Viera Charter School, Melbourne, Fla.

STEM Awards for Math

FIRST PLACE **David Yue**, 14, Rice Middle School, Plano, Texas.

SECOND PLACE **Madison A. Toonder**, 14, Florida Virtual School, St. Augustine, Fla.

LINDA DOANE PHOTOGRAPHY/SSP

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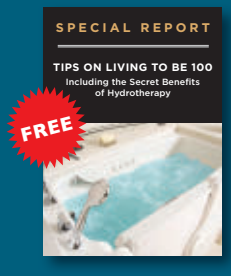

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SOCIAL MEDIA

Octopus intimacy

Readers weighed in on Twitter and Facebook about a previously unknown method of octopus mating: The animals match up their arms eight to eight, Susan Milius reported in "When octopuses dance beak to beak" (*SN: 9/19/15, p. 4*).

"It looks, um, complicated! #scienceiscool #mothernaturerocks #tentacleseverywhere."
@NSUnews

"Heaven, I'm in heaven, and we're dancing beak to beak."
Joseph Charneskie

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Quantum loopholes

A new experiment convincingly shows that locality doesn't apply in the quantum realm, ***Andrew Grant*** *reported in "Physicists verify quantum spookiness" (*SN: 9/19/15, p. 12*). Locality, he wrote, is the idea "that an event on Earth can't immediately influence what happens on Mars." The new study showed particles were coordinated when they were 1.3 kilometers apart.*

Reader **Paul Bendt** took issue with using the word "influence" to describe how entangled particles interact. "None of the experiments with entanglement demonstrate instantaneous influence at a distance, but only that two simultaneous, faraway events can be correlated," he wrote in an e-mail. "The word 'influence' implies that entanglement could be used to create a faster-than-light communication system. This is not correct."

Bendt is spot-on, **Grant** says. "The researchers showed that an experimenter who knows the spin of electron A has a much better than expected chance of predicting the spin of A's entangled partner, B — even if B were located on Mars," he says. The words "immediately influence" may have led some readers to think that measuring A changes B instantly, but that's not the case. Someone on Mars would have to talk to the experimenter on Earth or make a separate measurement to determine the spin of B, **Grant** says. There is no opportunity for faster-than-light communication.

Magnetic shield for Mars

Thomas Sumner *shined a light on the paradoxical past of the Earth's magnetic field in "Mystery at the center of the Earth" (*SN: 9/19/15, p. 18*). This powerful shield protects the planet from harmful solar particles and makes life on Earth possible.*

One reader wondered about the mechanics of beefing up Earth's magnetic field — or creating a new one. "Would it be possible to put solar-powered magnetic field–generating satellites in orbit around Earth to augment its magnetic field during solar storms?" **Jay Boylan** asked in an e-mail. "Or perhaps to create a magnetic field for Mars?"

This would be a logistical and technical nightmare, **Sumner** says. To cover Earth with a magnetic field as strong as it has now — or to create one on Mars — would take an astronomical number of these satellites somehow evenly distributed around the planet without crashing into one another, he says. That's assuming the orbiters provided enough electricity, even at night. Even then, the satellites wouldn't be able to re-create Earth's substantial shield, but would instead have their own individual magnetic fields. "That wouldn't offer much protection," **Sumner** says.

Science as art

Modern science embodies beautiful ideas, a truth author Frank Wilczek came to through his training as a physicist, ***Tom Siegfried*** *wrote in his review of Wilczek's recent book,* A Beautiful Question (*"Nobel laureate finds beauty in science and science in beauty,"* SN: 9/19/15, p. 29).

Reader **Tom Klebold** remembered his aha! moment linking science and beauty. "One of the most memorable moments of my life happened in a lecture hall, watching a gifted physics professor derive Maxwell's equations," he wrote in an e-mail. "The beauty of the mathematics as presented by the instructor was both transcendental and inescapable."

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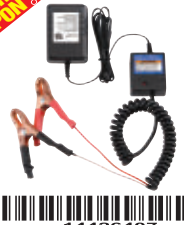

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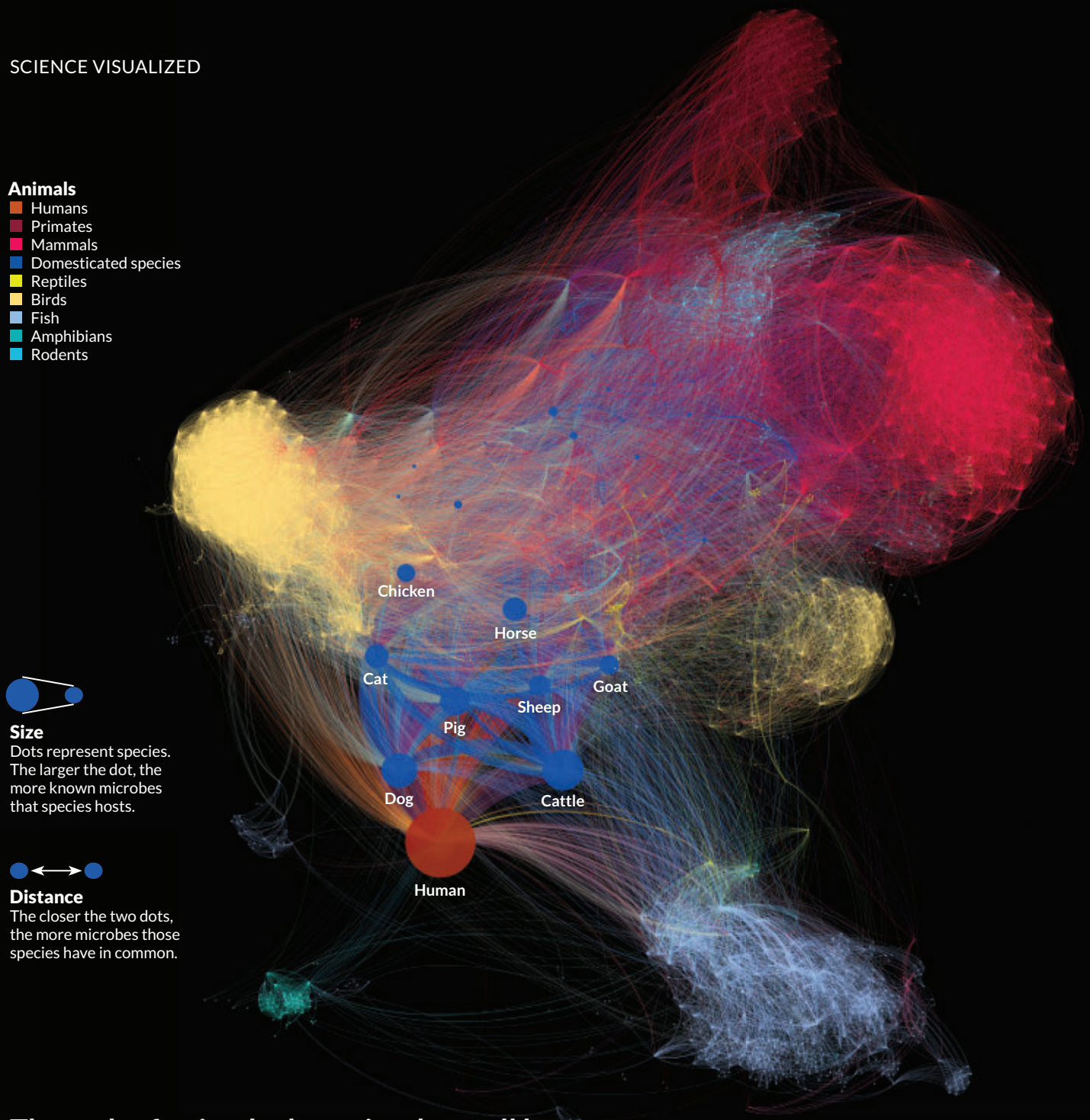

The web of animals that microbes call home

At least 233 species of bacteria, viruses and more live on or inside both humans and dogs.

That's one finding from a study that matched animals with their known microbes and drew connections between species with similar microbial crews. The above diagram, published September 15 in *Scientific Data*, is a social network of species that resembles a vibrant tangle of yarn.

Each dot is an animal species; the creatures are clumped into colored groups such as light blue for fish and yellow for birds. Humans have the largest dot because they host at least 1,600 different microbes. The distance between dots and the lines connecting them indicate that many human microbes also reside in dogs, pigs and cattle.

Domesticated animals live beside humans, so the microbial overlap isn't surprising, says study coauthor Maya Wardeh, a computational biologist at the University of Liverpool in England. Yet humans share microbes with fish and fall victim to *Cryptosporidium fayeri*, a diarrhea-inducing parasite that also infects the eastern gray kangaroo.

Wardeh and colleagues say that scientists can use the information to study how various diseases originate and jump between species. — *Meghan Rosen*

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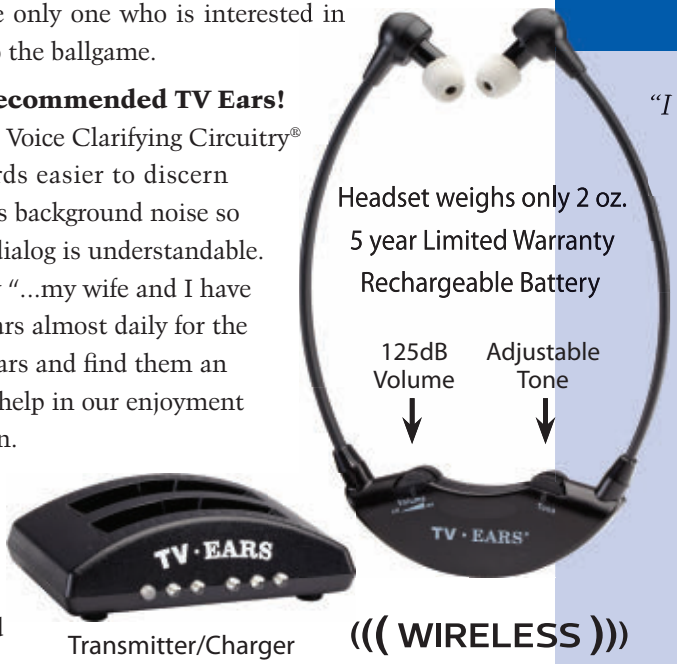

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