Early Galaxies | Dark Matter Before the Dawn | Desert Maze

Science News

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MAGAZINE OF THE SOCIETY FOR SCIENCE & THE PUBLIC ■ JANUARY 12, 2013

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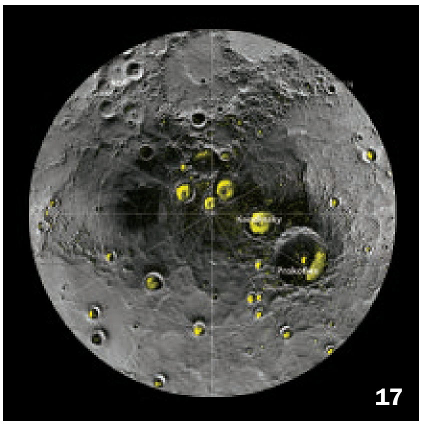

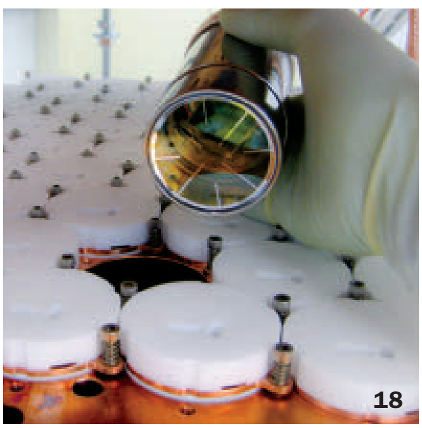

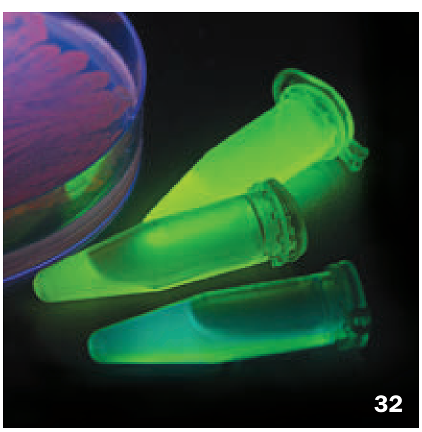

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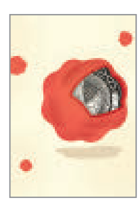

COVER Synthetic biology promises to revolutionize the biotechnology industry by turning living cells into machines. *Harry Campbell*

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FROM THE EDITOR

Engineers take on the messy world of biology


PHILIP CHANNING

Biology is a tricky business. Living cells are complex and unpredictable, and the tools of genetic engineering are nowhere near as precise and reliable as those of, say, an electrical engineer. Enzymes that splice DNA don't always yield the same results; isolating and moving a functional gene from one bacterial species to another can take years. While biologists have made huge advances in their ability to purposefully tweak the genetic instructions of bacteria, viruses and other organisms, many of the field's early expectations have yet to be fulfilled.

Enter synthetic biology, a still-emerging branch of genetic engineering that seeks to bring a true engineer's perspective to the messiness of molecular biology. The idea is that such an approach will enable scientists to design new life-forms to do useful work on an industrial scale. As Alexandra Witze reports on Page 22, a number of synthetic biology pioneers are in fact electrical engineers, having migrated from the world of silicon to that of DNA. People like MIT's Tom Knight worked on the pre-Internet ARPANET — and are now convinced that synthetic biology will lead to an equivalent revolution. "This is not just — oh, we're going to go build something that's able to make pieces of DNA better," Knight says. "We're going to go create a technology infrastructure in the same way that the semiconductor infrastructure was developed." He and others see bioengineers poised to make dramatic advances, much as computer developers did decades ago.

The work also has the potential to reveal more about life itself: Designing and building the first synthetic cells may lead scientists to understand exactly which of an organism's many genes are essential, what's known as the minimum genome.

This story comes with a few caveats. Besides a microbe that produces a hard-to-make precursor of an antimalarial drug, synthetic biology has so far had few commercial successes. Research in biofuels, an early goal, has yet to yield much. Standardizing biology may prove more difficult than working with semiconductors. And unlike computers, the most ambitious aims of the field — for improving health, the environment, agriculture — may be largely invisible to most people, who probably wouldn't notice if their medicine was churned out by designer bacteria. Then there are the ethical questions, and whether synthetic biologists will overcome the public queasiness about engineering life that genetic engineers have struggled with for decades. *— Eva Emerson, Editor in Chief*

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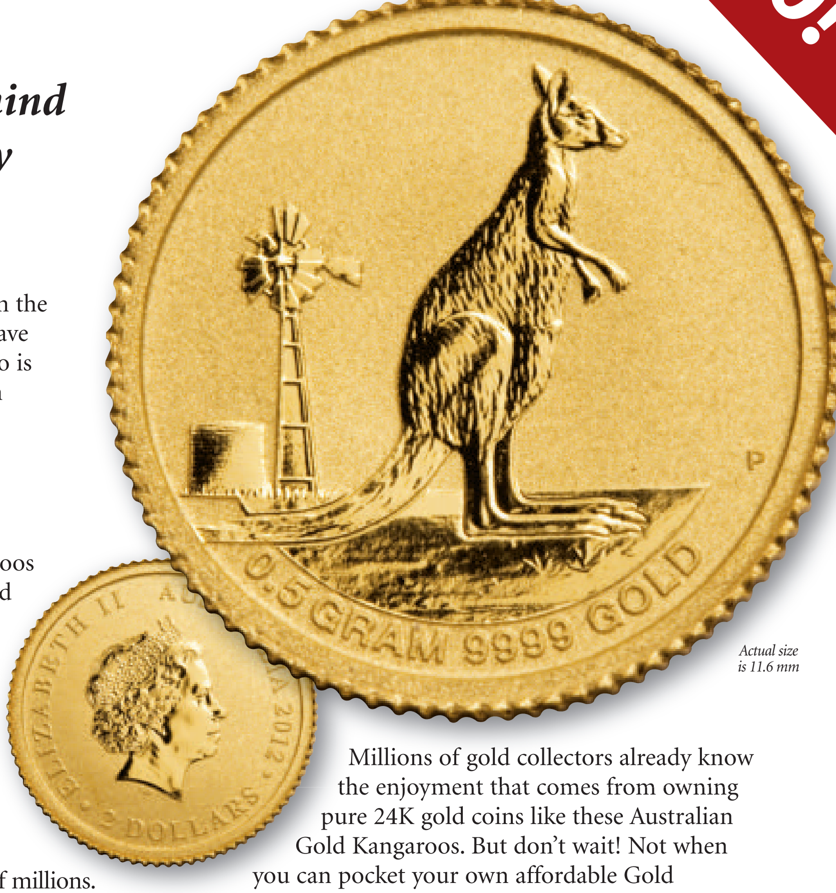

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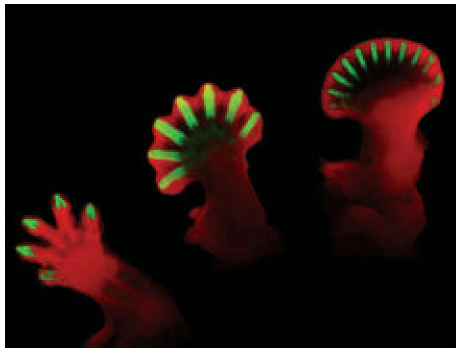

Turing pattern *TER-ihng PAH-tern*\\ *n.*
Repeating patterns that may form when chemicals activate or inhibit one another as they diffuse through a system, such as tiger stripes or leopard spots. Such patterns — named for mathematician Alan Turing, who theorized the phenomenon — may help explain the number of fingers and toes an animal has. An international team found that mice with fewer working *Hox* genes were born with narrower spaces between their fingers and toes and had more, thinner digits per paw than normal mice (shown). Simulations of the possible actions of activators and inhibitors indicate that this limb development probably follows a Turing pattern, the researchers report in the Dec. 14 *Science*. — *Erin Wayman*

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ATOM & COSMOS
Listen to a recording of electromagnetic disturbances called chorus waves in “Extraterrestrial chorus heard in radiation belts.”

Curiosity sends back results of its first full analysis of Martian soil, including signs of carbon. See “Mars rover deploys final instrument.”

ON THE SCENE BLOG
Scientists compete for best short sell in “Cell biologists hone elevator pitches.”

SCIENCE & THE PUBLIC BLOG
Janet Raloff reports on looking for life under glaciers in “Antarctic test of novel ice drill poised to begin.”

Science Past | FROM THE ISSUE OF JANUARY 12, 1963

DAILY SCIENCE NEWSPAPER SEEN NECESSARY SOON — The increase in scientific research will make necessary a daily newspaper devoted to science in a short time if predictions made by Prof. Derek J. de Solla Price of Yale University to the American Association for the Advancement of Science are fulfilled. In the next decade there will be as many scientific papers published as have appeared in the total history of the world until now, he foresees. The number of scientists will increase prodigiously and as the population doubles, the scientific manpower and literature will increase ten times with every doubling of the population.

Science Future

February 11
Earliest launch date for the Landsat Data Continuity Mission, the next generation in the U.S. Earth-observing satellite program. See bit.ly/SFlandsat

February 12
Learn about the animal world in the New York Academy of Science’s program “Lust and Love in the Animal Kingdom” in New York City. See bit.ly/SFlust

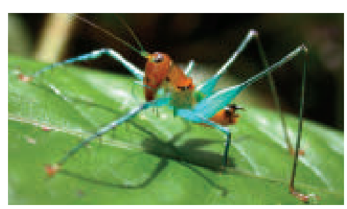
Introducing | GAGA FOR FERNS

Botanists have named two new species of fern in honor of singer-songwriter Lady Gaga. *Gaga germanotta* combines the musician’s stage and family names, and *Gaga monstraparva* refers to Gaga fans, known as “little monsters.” Both fern species probably arose when ancestors mated outside their own species. Another 17 fern species will be reclassified into the newly formed *Gaga* genus, Fay-Wei Li of Duke University and colleagues report in the October–December *Systematic Botany*. In all *Gaga* ferns, DNA bases line up in a G-A-G-A string at a particular spot, which is different from other ferns. And when the fern spores start growing (far left), the young plants resemble Gaga’s light green outfit (shown) at the 2010 Grammy Awards. — *Susan Milius*

Science Stats | BUG COUNT

Entomologists have completed the most comprehensive survey of arthropods ever. Scientists collected thousands of insects, spiders and their relatives (katydid, below) from ground level to treetops in a patch of Panama rainforest. Scaling up, the team estimates that the Manhattan-sized forest holds 25,000 arthropod species. Earth’s tropics may have about 6 million.

SOURCE: Y. BASSETT *ET AL*/*SCIENCE* 2012



129,494
Total specimens identified

6,144
Total species found

3,279
Beetle species found

270:1
Ratio of arthropod to mammal species

2 years
Time to collect specimens

8 years
Time to identify species

CLOCKWISE FROM TOP LEFT: L. QUINTANA, R. SHETH, M. ROS AND J. SHARPE; J. RALOFF; © MAURICE LEPONCE; FERN: PRYER LAB/DUKE UNIV.; GAGA: MATT SAYLES/AP

“For the family, it's very important to know if someone will recover or not.” —MÉLANIE BOLY, PAGE 8

In the News

STORY ONE

Clutch of distant galaxies reveals infant universe

Hubble captures cosmic structure first taking shape

By Alexandra Witze

The deepest look yet into the universe has identified seven galaxies that appear as they were when the universe was less than 4 percent of its current age.

NASA, ESA, R. ELLIS, UDF 2012 TEAM

Peering into the far reaches of the universe, astronomers have spotted seven galaxies so distant that they appear as they did less than 600 million years after the Big Bang.

Finding so many primordial galaxies allows scientists to pin down crucial questions about the newborn universe, such as when light from early stars and galaxies first penetrated the early cosmic gloom. “It's the scientific study of Genesis,” says Avi Loeb, a Harvard astronomer who was not involved in the work.

The discovery comes from the hard-working Hubble Space Telescope, which in August and September spent more than 100 hours staring deeply into a small patch of sky. That region, in the southern constellation Fornax, is the same one that was targeted in 2009 for a long-duration exposure known as the Hubble Ultra Deep Field.

Astronomers led by Caltech's Richard Ellis looked there again, but for longer exposure times and with an additional filter that's sensitive to the faint, red light of faraway galaxies. The new census, to appear in an upcoming *Astrophysical Journal Letters*, includes seven galaxies at great distances — including one that might be the record-breaker of them all, seen as it was just 380 million years after the Big Bang.

Because the cosmos has been expanding since the Big Bang, 13.7 billion years ago, light from these very distant objects has only now arrived at Earth — and so they appear as they did during the universe's infancy. The distance to such faraway objects is usually stated in terms of redshift; the higher the redshift, the more distant the object.

The seven galaxies described by Ellis and his team all have redshifts higher than 8.5. One of them may even be as high as redshift 11.9, Ellis says. That galaxy, named UDFj-39546284, was spotted earlier by other astronomers who pegged it at a redshift of 10.5 (*SN Online: 1/26/11*). Hubble data suggest it may be even more distant, Ellis says.

Another recent Hubble survey also found a handful of faraway galaxies with redshifts possibly in the range of 8.5 to 10. That survey is called CLASH, for the Cluster Lensing and Supernova Survey with Hubble. It looks for distant objects whose light has been bent and magnified by the gravitational influence of galaxies lying in the line of sight between the faraway objects and observers on Earth or in orbit around it. This effect boosts the light of dim objects,

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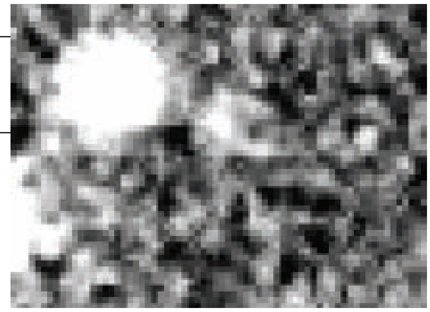
making them easier to see.

In November, astronomers with CLASH announced finding a galaxy with a redshift of 10.8 in the constellation Camelopardalis. In September, CLASH reported a redshift-9.6 galaxy in the constellation Leo. “Broadly speaking, their results are consistent with ours,” says James Dunlop, an astronomer at the University of Edinburgh who works with Ellis.

More important than any record-breaker, says Ellis, is what a census of distant galaxies can say about how and when the early universe lit up (see Back Story).

About 400,000 years after the Big Bang, hydrogen gas formed throughout the newborn universe. But not until some 200 million years later did those clouds of hydrogen grow dense enough to gravitationally collapse and ignite fusion in the hearts of the first stars. (Back then the universe was much hotter and denser than today, because it was smaller.)

At some point, there were enough stars to start assembling together into the first galaxies. Without a clear picture of the early universe, astronomers haven’t been able to figure out the exact timescale of how those galaxies came together — whether it happened quickly or was a long, drawn-out process.



One of seven distant galaxies recently captured by the Hubble telescope is seen as it was when the universe was less than 600 million years old.

The new findings indicate that it might have been gradual, Ellis says. Hubble found enough early galaxies, spread out over different redshifts, to suggest that they formed slowly. “Cosmic dawn was probably not a single dramatic event,” he says.

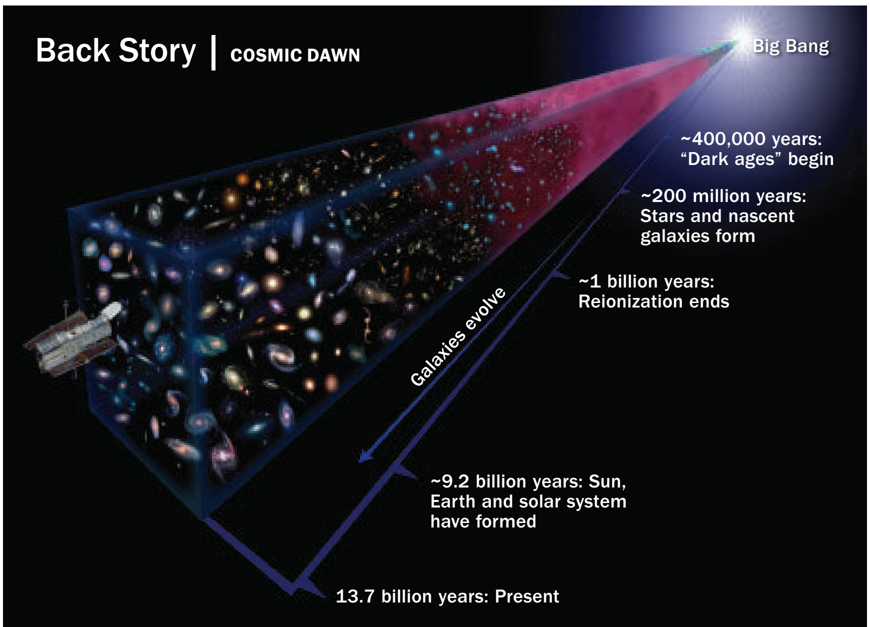
Not all astronomers think the new census is the final word on the early universe, though.

Rogier Windhorst, an astronomer at Arizona State University in Tempe, says he’s surprised the new survey found only seven galaxies. “We ought to be able to see a number of these galaxies, and Hubble only sees a handful,” he says. More may be lurking in the data, hidden by the bright lights of other, closer stars or galaxies, Windhorst suggests.

Any lingering questions may have to wait until the 2018 launch of the James Webb Space Telescope, the successor to Hubble that is designed to look in infrared wavelengths for the dim light of even more distant galaxies. “We confidently predict there are many galaxies beyond this,” Ellis says. The Webb telescope should see objects with a redshift of 20 or even higher.

John Grunsfeld, an astronaut who has visited Hubble several times to upgrade its components, says the new images have a profound meaning that extends beyond their scientific value. “These are baby pictures of the universe,” says Grunsfeld, who is now NASA’s associate administrator for science. “We always wonder where we came from and where we’re going, and Hubble is providing answers to both those questions.” ■

Back Story | COSMIC DAWN



The universe might have begun with a bang, but it remained dark for quite some time. A bleak period known as the cosmic “dark ages” stretched from about 400,000 years to 200 million years after the Big Bang. During this period the universe was filled with neutral hydrogen gas, which rendered everything murky and opaque. When the first stars ignited, they released ultraviolet radiation that essentially burned off the hydrogen fog. At first, individual stars cleared pockets within the fog; later, more stars began to form and collect into galaxies, clearing larger pockets of space until the entire universe was transparent. Astronomers call this process “cosmic reionization.” Soon stars also began forging heavier chemical elements, like carbon and iron, in their hearts. When the stars blew up and died, they spewed those elements into interstellar space, there to be incorporated into planets and people. —*Alexandra Witze*

FROM TOP: NASA, ESA, R. ELLIS, UDF 2012 TEAM; NASA, ESA, A. FEILD

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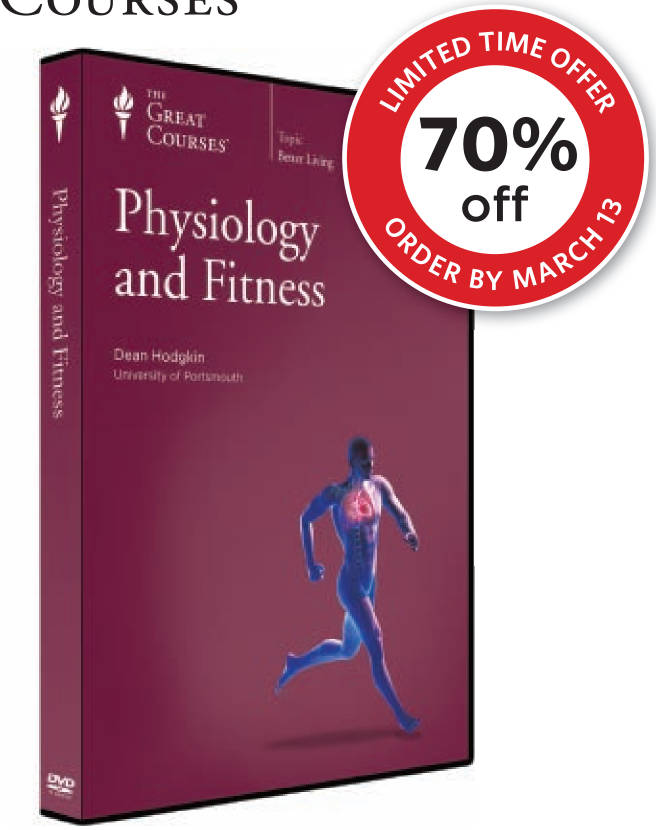

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Health & Illness

"It's a very promising tool for prognosis." —MÉLANIE BOLY

Smoking hurts teen girls' bones

Growth in density lags for those who use cigarettes

By Nathan Seppa

High school might be a bit early to start thinking about bone loss and osteoporosis, but a new study finds that teenage girls who smoke may put themselves on a trajectory to accrue less bone mineral than those who don't light up.

Osteoporosis is a loss of bone density that predisposes people to fractures and leaves many elderly people — particularly women — hunched over. While bones regenerate and remodel nonstop over a lifetime, the teen years are crucial to developing a strong, dense skeleton.

"This age group is when you should gain about 50 percent of your bone accrual," says study coauthor Lorah Dorn, a developmental psychologist and pediatric nurse practitioner at Cincinnati Children's Hospital Medical Center.

5.2 percent

Fraction of U.S. middle school students who smoked, 2009

Dorn and her colleagues recruited 262 healthy girls ages 11 to 17. Each girl filled out confidential questionnaires about her nutritional habits and lifestyle and returned for three yearly visits to undergo bone density tests. Girls who reported smoking regularly showed nearly flat rates of bone density growth in the lower vertebrae and a decline in bone density at the hips. Nonsmokers showed normal, steadily rising bone density in both regions, the authors report online December 4 in the *Journal of Adolescent Health*.

"These girls are on different trajectories all the way across adolescence," Dorn says. The analysis accounted for differences between smokers and nonsmokers in race, weight, calcium intake, physical activity and vitamin D level.

The results concur with studies in adults, says Kenneth Ward, a psychologist at the University of Memphis School of Public Health in Tennessee. A 2001 review by Ward and colleague Robert Klesges of adults' bone density estimated that smoking increased the risk of a vertebral fracture by 13 percent and hip fracture by 31 percent in women.

Sound test predicts coma outcome

Improved auditory response in early days a positive sign

By Tanya Lewis

A coma patient's chances of waking up could be predicted by changes in the brain's ability to discriminate sounds.

Recovery from coma has been linked to auditory function before, but it wasn't clear whether function depended on the time of assessment. Whereas previous studies tested patients several days or weeks after comas set in, a new study looks at the first 48 hours. At this early, critical stage, comatose brains can still distinguish different sound patterns. How this ability changes can predict whether a coma patient will ultimately regain consciousness, researchers report.

"It's a very promising tool for prognosis," says neurologist Mélanie Boly of the Belgian National Fund for Scientific Research, who was not involved with the study. "For the family, it's very important to know if someone will recover or not."

A team led by neuroscientist Marzia De Lucia of the University of Lausanne in Switzerland studied 30 coma patients who had experienced cardiac arrest that deprived their brains of oxygen. All the patients underwent therapeutic hypothermia, a standard treatment to minimize brain damage, in which their bodies were cooled to 33° Celsius for 24 hours.

The researchers played sounds for the patients and recorded their brain activity using scalp electrodes — once in hypothermic conditions during the first 24 hours of coma, and again a day later at body temperature. The sounds were a series of pure tones interspersed with tones of different pitch, duration or location. Brain signals revealed how well patients could discriminate the sounds, compared with five healthy subjects.

All the patients whose discrimination improved by the second day of testing survived and awoke from their comas within three months. By contrast, 55 percent of those whose sound discrimination deteriorated by the second day did not survive. The results were reported online November 12 in *Brain*.

Psychophysiologist Geert van Boxtel of Tilburg University in the Netherlands found it surprising that "irrespective of outcome, at the first recording, all of the patients showed signs of auditory discrimination."

This, De Lucia says, suggests that residual auditory function itself does not predict recovery; it's the progression of function over time that is crucial.

The study couldn't distinguish whether auditory function initially was preserved due to the hypothermia treatment or was related merely to the early stage of coma. But the scientists speculate that the hypothermic conditions may have reduced distracting neural jabber, making it easier for the patients' brains to register distinct sounds.

De Lucia and her colleagues are now running a follow-up study with 120 coma patients, to see whether the results can be replicated in a bigger population. "This test could give information about patients who will survive during the first two days of coma, when doctors can still make decisions about treatment," De Lucia says. ■

Humans

"The element of surprise was crucial to the experience of Nazca labyrinth walking." —CLIVE RUGGLES

Silver's route to Europe traced

Tests of English coins reveal how New World riches flowed

By Alexandra Witze

Chemical studies of old English coins are helping unravel a centuries-old mystery: What happened to all the silver that Spaniards extracted from the New World?

Silver from Mexican mines started being used in English coins around the mid-1550s, researchers report online November 6 in *Geology*. But silver from the legendary Potosí mines, in what is now Bolivia, didn't show up until nearly a century later.

The new study adds hard data to theories linking the transatlantic influx of silver to price inflation across Europe from about 1515 to 1650.

The composition of copper and lead that appears along with gold and silver betrays the precious metals' origins. Anne-Marie Desaulty and Francis Albarède of the École Normale Supérieure in Lyon, France, looked at these chemical fingerprints in 15 English coins, dated between 1317 and 1640 (one shown from the reign of Elizabeth I).

Lead in coins from before the reign of Mary I, which began in 1553, showed that the ore was at least 220 million years old, suggesting it came from rocks in central Europe or England. Lead in later coins showed a higher contribution of silver younger than 50 million years old — suggesting it came from the mines of Mexico.

The coins show very little hint of Potosí silver. That's surprising, Desaulty says, because the Potosí mines were churning out far more silver at the time than Mexico was.

Geography may explain this: It was easier to ship Mexican silver east to Europe. Potosí silver went west, from Lima to Acapulco and onward to markets in China.

Scholars already knew of this westward trade route, which probably didn't become really important until the early 17th century, says John Munro, an economist at the University of Toronto.

Lines in sand may be labyrinth

Desert drawings perhaps a deliberate path left by Nazca

By Bruce Bower

Famous line drawings etched into Peru's Nazca desert plateau around 1,500 years ago are enduring puzzles. At least one of them is also a labyrinth, researchers say.

Archaeoastronomer Clive Ruggles of the University of Leicester in England discovered the labyrinth — a single path leading to and from an earthen mound, with a series of disorienting twists and turns along its flat, 4.4-kilometer-long course — by walking it himself. From the ground, little of the labyrinth is visible, even while ambling through it. From the air, it's difficult to recognize the array of landscape lines as a connected entity.

In the December *Antiquity*, Ruggles and archaeologist Nicholas Saunders of the University of Bristol in England describe and map what they regard as a carefully planned labyrinth from the ancient Nazca (sometimes spelled Nasca) culture. Nazca civilization flourished in southern coastal Peru from around 2,100 to 1,300 years ago.

"This labyrinth was meant to be walked, not seen," Ruggles says. "The element of surprise was crucial to the experience of Nazca labyrinth walking."

Ruggles and Saunders reconstructed the path's course in several small sections that had been washed away by rains. Fieldwork from 2007 to 2011 resulted in a map of the entire labyrinth. It probably took around one hour for a walker to complete the journey.

There's no way to know how the labyrinth was used, Ruggles says. Shamans or pilgrims could have walked the tricky trail on spiritual journeys. Or the path might have been reserved for Nazca gods.

Ruggles and Saunders' contention that Nazca labyrinths were made to be strolled through while staying mostly hidden from view "is novel and well-argued," says archaeoastronomer Anthony Aveni of Colgate University in Hamilton, N.Y.

An aerial view shows part of what researchers regard as a massive labyrinth, including a spiral pathway (red box), etched onto a Peruvian desert floor around 1,500 years ago by members of the Nazca culture.

FROM TOP: THOMAS BRETON, ENS LYON; © C. RUGGLES

Science & Society

What goes wrong when talks fail

Nonlinear analysis finds vulnerabilities in negotiations

By Rachel Ehrenberg

Peace talks can be a frustratingly precarious process. Often negotiations seem to be moving forward, then one side sabotages the process by turning to violence. A new way of simulating how groups make decisions combines social psychology and nonlinear mathematics, revealing how forces may unexpectedly conspire to send negotiations off the rails.

The approach captures the unpredictability of group decision making and might be used to foresee which members of a jury, legislature or corporate board will support a policy, or if consensus is even possible. It may also help explain how Burhanuddin Rabbani, a key figure in negotiations between the Afghan government and the Taliban, ended up the victim of a suicide bomber in September 2011.

Many methods for assessing how negotiations unfold assume a linear, relatively predictable relationship between the group members' opinions, their influence on each other and the outcome of the negotiations. These methods can work well for small groups, said policy analyst Hilton Root of George Mason University in Arlington, Va. "But," he said, "there's a lot you can't do with them."

This approach revealed Afghan High Peace Council chairman Rabbani's key position in the middle.

To capture the turns and twists that often occur in real-world negotiations, University of Washington physicist Michael Gabbay developed an approach that allows for a traditional linear discussion path but also incorporates nonlinear dynamics, where outcomes can be unpredictable and driven by a seemingly random variable, such as who gets to talk first.

Simulating the behavior of decision makers with this technique can suggest tactics — such as not having everyone talk to everyone at the same time — that might make reaching consensus easier, Gabbay reported December 6.

To put the new approach to use, key negotiators are identified and each is assigned a place on a spectrum that reflects some quality relevant to the negotiations. With the goal of determining how the Afghan government and insurgent leaders might reach agreement, the spectrum was hawk on one end, dove on the other. Experts were surveyed as stand-ins for political leaders and asked whether they agreed with statements such as "a strong emir with power concentrated in his hands is needed to rule Afghanistan."

The position each player has on the spectrum can shift subject to the player's natural inclinations, the influence of the group and the force of new information. When applied to the Afghan situation, this approach revealed Afghan High Peace Council chairman Rabbani's key position in the middle. He wasn't an extreme hawk, nor an extreme dove.

Then the players and forces are expressed mathematically and run through a computer simulation, yielding a graph of the possible trajectories of the negotiations. In the Afghan example, such an analysis suggested that Taliban-affiliated actors supported the goal of seizing central state power. Rabbani's position suggested he could have succeeded in reaching out to all groups and pushing for peace talks, which would not have aligned with Taliban goals. This may explain Rabbani's assassination, Gabbay said. ■

MEETING NOTES

Winning the arms race with spam

Spammers are tricky adversaries: If e-mail spam filters seek out words like "enlargement" then spammers switch up their approach. "Spam changes a lot — it starts looking more like ham," said Richard Colbaugh on December 5. Now Colbaugh and Kristin Glass, both of Sandia National Laboratories in Albuquerque, have created a one-two punch that anticipates new tactics and makes antispam programs less predictable. Training filters, for example, to look for bits of ham mixed with spam, such as several nonspammy words, will help detect even cleverly disguised spam. And instead of using one superior filter all the time, spam fighters should mix up their weaponry. Keeping several filters on hand can keep spammers from deducing and evading antispam tactics.
—Rachel Ehrenberg

When paid sick leave pays

Paid sick leave is an HR dilemma. The policy can keep an infection from spreading and limit medical costs, but it also lowers productivity, especially when employees intent on playing hooky abuse it. Computer simulations of how an epidemic might spread through Miami suggest that paid sick leave usually pays off. It typically curtails a disease's spread and minimizes health costs without crippling work output, Achla Marathe of Virginia Tech reported December 5. But if a company offers more days than infections usually last and employees are both highly productive and dishonest about being sick, then paid sick leave does little good.
—Rachel Ehrenberg

Wanted: pals for power brokers

Shared interests a big factor for applicants at elite firms

By Bruce Bower

Big-time investment banks, law firms and management consulting companies choose new workers much as they would choose friends or dates, zeroing in on shared leisure activities, life experiences and personality styles, a new study finds.

These elite firms recruit Ivy League students assumed to have basic job skills and then select those who jibe with the organization's culture and personality, says sociologist Lauren Rivera of Northwestern University in Evanston, Ill.

Similarities in hobbies and outside interests have been proposed as keys to acceptance into exclusive groups for more than a century. In the December *American Sociological Review*, Rivera provides a systematic look at how this effect influences the hiring process.

"I was surprised at the power of shared culture in hiring decisions made by these employers," Rivera says.

Rivera's findings underscore how values and activities of one's social class that are typically taken for granted can be deliberately used to segregate people into different workplaces, says Harvard University sociologist Michèle Lamont.

From 2006 to 2008, Rivera interviewed 120 professionals involved in hiring applicants for entry-level jobs at banking, legal and consulting firms. She also attended recruitment events, spoke with interviewers after they had met with applicants and sat in on hiring committees' deliberations at one company over nine months from 2006 to 2007.

All recruits were assumed to have enough "intellectual firepower" to learn how to be good bankers, lawyers and consultants. But Rivera says that once interviews started, other factors appeared to outweigh job qualifications.

Most interviewers used a simple hiring criterion that many called "the airplane test." As one investment banker put it, "Would I want to be stuck in an airport in Minneapolis in a snowstorm with them?"

Participants said that they had fought hardest to hire real-life applicants with whom they had felt a deep connection, typically because of shared interests or personality traits.

As a result, evaluators described their own and others' firms as having distinct personalities. Companies ranged from "sporty" and "scrappy" to "egghead" and "country club." One outfit even specialized in hiring people with drab personalities.

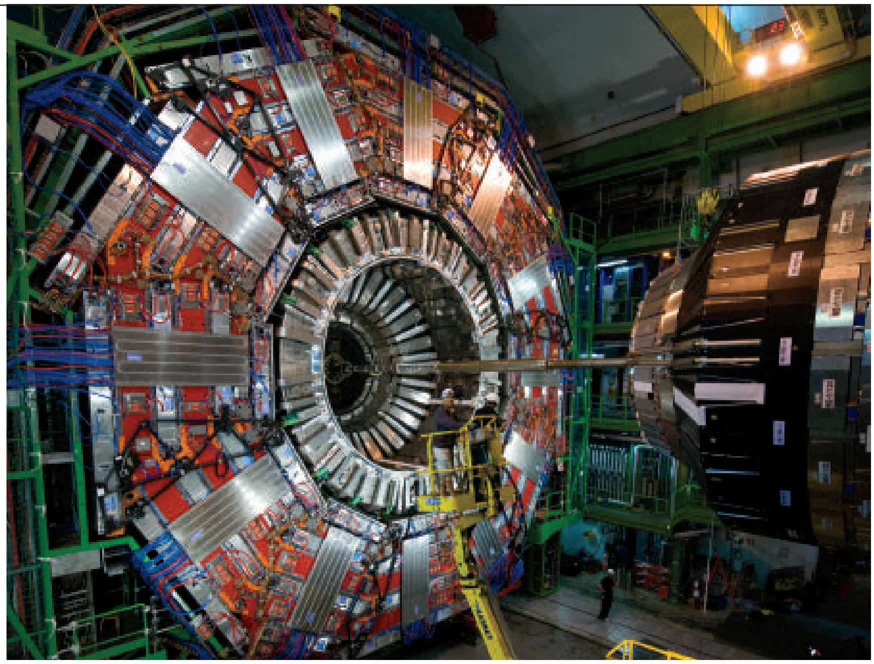
Matter & Energy

"This is one of the most interesting unexpected effects we've observed at the LHC." —GUNTHER ROLAND

Smashups spark odd behavior in matter at LHC

Particles' coordinated motion puzzles theorists

By Andrew Grant



The Compact Muon Solenoid experiment (shown before closure) at the Large Hadron Collider has recorded coordinated movements in the debris of lead-proton collisions that may yield insights about how matter behaves under extreme conditions.

Strangely behaving subatomic particles at the world's most powerful particle accelerator could lead to fresh insight into how matter behaves at the smallest scales and highest energies.

Ordinarily, the Large Hadron Collider near Geneva sends protons hurtling into each other at velocities approaching the speed of light. But for several hours in September, the machine collided protons into lead nuclei — tightly packed bundles of 82 protons and 126 neutrons. It was merely a test run, designed to calibrate instruments for future experiments.

But when physicists with the Compact Muon Solenoid collaboration analyzed the data, they quickly saw that something was amiss. When a proton and a lead nucleus collide, they shatter into smaller particles that jet out in all directions. The movement of each piece of shrapnel should be almost random; the direction of one particle should provide no clue to that of any other. Yet during these collisions, the particles' directions tended to correspond to one another. Even particles located far from each other seemed to be coordinating their paths.

"This is one of the most interesting unexpected effects we've observed at the LHC," says Gunther Roland, an MIT physicist and member of the CMS team. The team describes the odd behavior in an upcoming *Physics Letters B* without trying to explain why the particles behaved as they did. But Roland notes that other physicists have come up with a few ideas.

One possibility is that the enormous heat and density in the collision zone actually liquefied the tiny bits of matter. Physicists first observed a liquid-like exotic state of matter, known as quark-gluon plasma, in 2005 when they slammed gold nuclei together at the Relativistic Heavy Ion Collider at Brookhaven National Laboratory in New York. Because quark-gluon plasma behaves like a liquid, it flows; the observed effect at the LHC could be the result of particles emerging from the outer edge of the plasma as it cools.

Physicists Raju Venugopalan and Kevin Dusling from Brookhaven present an alternative: The particles are actually influencing the movement of each other. If true, this theory would be a manifestation of quantum mechanics, the strange laws of physics that reign at the smallest of scales. The physicists argue that gluons, tiny particles that hold protons together, can form fields when moving near the speed of light. These fields allow gluons within multiple protons to interact and influence each other. In essence, Venugopalan and Dusling claim that under the right conditions certain particles can stop behaving like individual pieces of matter and act more like a coordinated posse.

Berndt Mueller, a Duke University physicist who is not on the CMS team, says he favors the quark-gluon plasma theory because it is the simpler one. But either suggestion, if proven correct, would help physicists better understand the strange rules that dictate how matter works under the most extreme conditions. Physicists want to learn more about quark-gluon plasma because they believe all matter was in this state a few millionths of a second after the Big Bang.

Both explanations have holes. Roland notes that proton-lead collisions should not generate the extreme conditions necessary to produce quark-gluon plasma. And Venugopalan and Dusling's prediction, while theoretically possible, has never been experimentally verified.

This mystery may find a quick resolution. This month the LHC will again slam protons into lead nuclei, this time for several weeks. Those experiments should provide the team with up to 100,000 times more data to determine which, if any, explanation holds up. ■

Mind & Brain

2.5 million Number of neurons included in simulation of the human brain

Protein takes destructive path

Parkinson's-linked clumps wind through brain, kill cells

By Laura Sanders

The insidious spread of an abnormal protein may be behind Parkinson's disease, a study in mice suggests. A harmful version of the protein crawls through the brains of healthy mice, killing brain cells and impairing the animals' balance and coordination, researchers report in the Nov. 16 *Science*.

"I really think that this model will increase our ability to come up with Parkinson's disease therapies," says study coauthor Virginia Lee of the University of Pennsylvania Perelman School of Medicine in Philadelphia.

The new study targets a hallmark of Parkinson's disease, clumps of a protein called alpha-synuclein. The clumps, called Lewy bodies, pile up inside nerve cells in the brain and cause trouble, particularly in cells that make dopamine, which helps control movement. Death of these dopamine-producing cells leads to the characteristic tremors and muscle rigidity seen in people with Parkinson's.

Lee and her team injected molecules of alpha-synuclein into the brains of healthy mice. After 30 days, the protein had spread to connected brain regions, suggesting that rogue alpha-synuclein moves from cell to cell. Months later, the spreading was even more extensive.

> "I really think that this model will increase our ability to come up with Parkinson's disease therapies."
> VIRGINIA LEE

Alpha-synuclein appeared to colonize several areas of the brain, but the protein was abundant in nerve cells that make dopamine. After six months, Lewy bodies were found inside these cells. As a result, fewer cells survived, and the ones that did churned out less dopamine.

"The real thing here, the novelty, is that the aggregate form can spread from one brain region to another and one cell to another, and cause cell death and disease," says neuroscientist Patrik Brundin of the Van Andel Research Institute in Grand Rapids, Mich.

The mice had subtle deficits six months after the injection: They were worse at balancing on a turning rod and couldn't cling to a wire cage for as long as those injected with saline.

Scientists don't know whether such cell-to-cell transmission happens in people. But some clues come from the brain of a woman with Parkinson's who received fetal cell transplants in an effort to replenish her missing neurons. Fourteen years after the procedure, Lewy bodies were found in these previously healthy transplanted cells, raising the possibility that alpha-synuclein had spread there from the rest of her brain.

Model brain mimics human quirks

Computer simulation turns decisions into plans for action

By Laura Sanders

A new computer simulation of the brain can count, remember and gamble. And the system, called Spaun, performs these tasks in a way that's eerily similar to how people do.

Short for Semantic Pointer Architecture Unified Network, Spaun is a crude approximation of the human brain. But scientists hope that the program and efforts like it could be a proving ground to test new ideas.

What distinguishes Spaun from other attempts to construct a realistic model of the human brain is that it actually does something, says computational neuroscientist Christian Machens of the Champalimaud Centre for the Unknown in Lisbon, Portugal. At the end of an intense computational session, Spaun spits out instructions for a behavior, such as how to reproduce a number it's been shown.

Spaun was cobbled together from bits and pieces of knowledge gleaned from years of basic brain research. The behavior of 2.5 million nerve cells in parts of the brain important for vision, memory, reasoning and other tasks forms the basis of the new system, says Chris Eliasmith of the University of Waterloo in Canada, coauthor of the study, which appears in the Nov. 30 *Science*.

Input takes the form of written or typed characters, which Spaun "sees" with its vision system. The incoming information flows through the system, bouncing to and from various brain areas as it gets compressed into a manageable task. Then, Spaun makes a decision about what to do. Finally, the decision gets expanded into action — it generates precise instructions on how to write out an answer. Because of the size and complexity of the system, the process is slow — in Spaun's world, one second of work takes over two real hours of computations.

After Spaun was assembled, scientists threw eight tasks at it, some of which resembled IQ test puzzlers, like a complete-the-pattern quiz. Spaun was also asked to reason, memorize and even gamble. As Spaun worked through these jobs, some curiously human quirks emerged. Just like human volunteers, Spaun was better at remembering the first and last number in a series. Also like people, Spaun took longer to count to higher numbers. "That's the kind of thing we couldn't program in," Eliasmith says.

Genes & Cells

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Gut bacteria may affect arteries

Antioxidant-making microbes appear to stabilize plaques

By Tina Hesman Saey

Though atherosclerosis is an artery problem, microscopic denizens of the intestines may have a surprising role in how the disease plays out.

A new study suggests that different mixes of intestinal microbes help determine whether people will have heart attacks or strokes brought on by breakaway plaque from the arteries. Compared with healthy people, heart disease patients who have had strokes or other complications of atherosclerosis carry fewer microbes that make anti-inflammatory and antioxidant compounds. These patients also have more bacteria that produce inflammation-triggering molecules, researchers report online December 4 in *Nature Communications*. Inflammation is thought to promote cardiovascular disease.

The findings could explain why people with higher levels of antioxidant molecules like beta-carotene and lycopene in their body fat have a lower risk of developing heart disease, but simply feeding people dietary supplements containing the compounds doesn't help. It may be that a lifelong, intimate association with antioxidant-producing microbes helps some people stave off some of the worst consequences of hardened arteries.

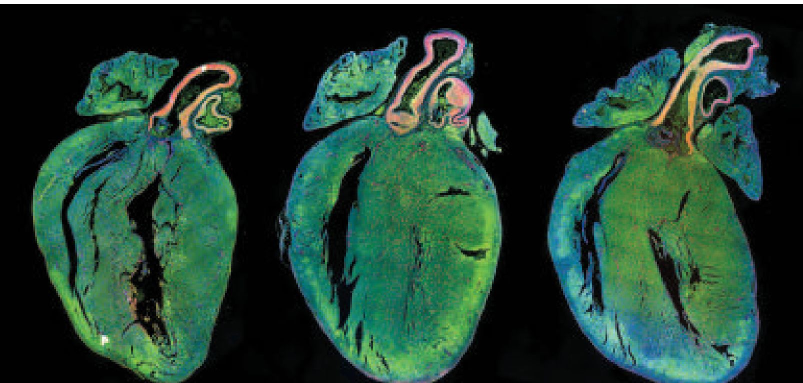
Nearly everyone develops atherosclerosis with age. But some people are more susceptible than others to strokes and heart attacks, even though their arteries are no more blocked than the next person's, says study coauthor Fredrik Bäckhed, a microbiologist at the University of Gothenburg in Sweden. The difference stems from the stability of the plaque that builds up inside blood vessels, stiffening and narrowing the vessels. When bits and pieces of plaque break off, they can block the flow of blood to the heart or brain and cause a heart attack or stroke.

To determine whether intestinal bacteria play a role in causing plaque to break away, Bäckhed and colleagues examined the microbial mixes in the feces of 13 healthy people and in 12 people with atherosclerosis who had experienced mild strokes, clogged blood vessels in the brain or temporary blindness due to plaques blocking blood vessels of the eye.

Most people have one of three major types of bacterial communities inhabiting their intestines. Stroke patients in the new study tended to fall into the category characterized by *Ruminococcus* bacteria. They also had more *Collinsella* bacteria species. In addition, bacteria in the guts of stroke patients carried more genes for making peptidoglycan, a component of bacterial cell walls that can set off inflammation.

Healthy people's feces were rich in *Eubacterium*, *Roseburia* and *Bacteroides* species. They also tended to have more *Clostridium* bacteria. Those bacteria often carry genes involved in making an anti-inflammatory molecule called butyrate. And healthy people's microbes carry lots of genes for making other inflammation-reducing substances such as lycopene and beta-carotene, the researchers found.

"This is a tour de force of bioinformatics," says Stanley Hazen, a cardiologist at the Cleveland Clinic who led previous work linking a person's microbes to heart disease risk. The findings need to be replicated in larger groups of people, he says, but he will be excited to see studies that determine exactly what the bacteria are doing to promote health or disease.



Mending broken hearts

When it comes to the heart, some old cells can become new again, especially with some special prodding. Small genetic molecules called microRNAs that help control protein production can stimulate adult heart cells to replicate, Mauro Giacca of the International Centre for Genetic Engineering and Biotechnology in Trieste, Italy, and colleagues report. The researchers treated hearts in newborn rats with a control treatment (left) or with two human microRNAs (middle and right). The hearts treated with the human microRNAs have more new muscle cells than the control and have heart tissue (green and blue) that is thicker and healthier. Mice given one of the two microRNAs after a heart attack made a nearly full recovery, the team reports online December 5 in *Nature*. Similar harnessing of the heart's own regenerative ability may one day help heal heart attack damage in people. —*Tina Hesman Saey*

A. EULALIO *ET AL*/*NATURE* 2012

Earth

5–6 million years Estimated age of Grand Canyon based on age of washed-out gravel

70 million years Proposed age of Grand Canyon based on rock chemistry

Grand Canyon's age pushed back

Rock erosion pegs ancient chasm at 70 million years old

By Alexandra Witze

Rock of ages it may be, but the Grand Canyon's age itself is under fire. New work suggests the iconic chasm was already in place 70 million years ago — making it far older than commonly believed.

By most geologists' definition, the Grand Canyon proper emerged between 5 million and 6 million years ago, as the Colorado River flowed across and eroded its way through layer after layer of rock. Evidence for this age comes from, among other things, great piles of washed-out gravel at the canyon's western end that appeared around that time.

But the new study, reported online November 29 in *Science*, looks instead at the chemistry of rocks exposed throughout the canyon. Rocks get cooler as erosion strips away the material above them. That cooling is chemically preserved in several ways, including in helium levels within the mineral apatite.

"When the apatite is hot, the helium simply diffuses out of the crystal; when the apatite is cold, helium is completely retained," says study leader Rebecca Flowers of the University of Colorado Boulder. So by measuring the helium in the rock, scientists can tell when the rock went from hot to cold as it moved closer to the Earth's surface, or as the Earth's surface moved closer to the rock as the canyon was carved, she says.

Flowers and Kenneth Farley of Caltech looked at helium in apatite crystals throughout the canyon, including how the element was distributed within the crystals. The scientists concluded that some ancient river must have carved out a chasm roughly the shape and size of the Grand Canyon by around 70 million years ago.

Not everyone is convinced by the new findings, which build on earlier work from the same research team. Karl Karlstrom, a geologist at the University of New Mexico, says that there must have been canyons throughout the area 70 million years ago, but most geological evidence supports the modern canyon — what visitors see today when standing at the rim — appearing only in the last 5 million to 6 million years.

"The question is, how come we don't know the shape of all the landscapes that eroded away to make this spectacular thing we see today?" Karlstrom says. "That's a hard thing to tell." ■

Life

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Fishing may exert evolutionary pressure on largemouth bass

Fish most vulnerable to anglers are also the best dads

By Susan Milius

The same qualities that make a largemouth bass an easy mark for anglers make him a successful dad. So recreational fishers, a new study suggests, may be accidental forces of evolution, selecting against the best in male fish parenting.

"Does that mean that bass populations are imminently in danger of becoming too hard to catch and at the same time totally inefficient at reproducing? Not really," says study coauthor David P. Philipp of the Illinois Natural History Survey. "Does it mean that we are impacting populations of bass in ways that we never envisioned and don't understand well at all? Most certainly."

Among the prized sports fish *Micropterus salmoides*, it's the dads that do the child care. They go for weeks without food to guard their nests from predators or to swim protectively nearby as tiny fry start exploring the big wet world.

In a study of fish dads in experimental ponds, largemouth bass from a lineage known to be an easy target for anglers proved more diligent at babysitting than did hard-to-catch males, says coauthor David Sutter, a fisheries ecologist at the University of Illinois at Urbana-Champaign. Fish that were swift to strike at lures that anglers jiggled in the water also readily attacked nest intruders.

Such good parenting paid off: Those easy-mark males tended to raise more youngsters than hard-to-catch males in the same ponds, Sutter and his colleagues report in the Dec. 18 *Proceedings of the National Academy of Sciences*.

Large body size also inclined males to reproductive success, or fitness, in the experiments. But Sutter says that vulnerability to anglers by itself was linked with both good parenting and reproductive fitness.

The new study is the first experimental evidence for this link between vulnerability and reproductive fitness, says conservation geneticist Fred Allendorf of the University of Montana in Missoula, who wasn't part of the study. Finding such a connection marks a crucial step in figuring out how anglers might affect the evolution of traits in the fish population.

David O. Conover of Stony Brook University in New York welcomes the study for showing that recreational fishing can be a potent evolutionary force. The study also shows that such practices can act not just on physical traits but also on fish behavior, adds Conover, who has studied commercial-style fishing practices as forces of evolution on fish size.

Over time evolutionary pressure from fishing can change the remaining population. The harvest of largemouth bass, especially males fidgeting over their nests, "favors more docile males that are, in the process, less willing or effective in defending their offspring," Philipp concludes.

BISSELL/ISTOCKPHOTO

Fishing may unintentionally pressure largemouth bass to evolve into harder-to-catch fish that aren't very diligent parents, a new study suggests.

The study builds on a string of experiments using two fish lineages that researchers bred for opposite reactions to anglers. One bass group became extremely gullible to angler ploys and the other grew extra wary. Parents pass these tendencies on to their offspring, Philipp and his colleagues reported in 2009.

To see what inheriting vulnerability (or not) might mean for fish, Sutter stocked four gullible and four wary male bass in each of six lab ponds, along with wild female bass and predatory bluegills. At the end of the breeding season, Sutter used genetic markers to identify the parents of 1,189 of the bass offspring. The highly vulnerable males had sired about 62 percent of the next generation, and a statistical analysis uncovered the links between catchability and parenting.

Many states let anglers fish during the spawning period, when touchy, hyperprotective dads may be especially vulnerable, Philipp notes. Whether that's a good idea has been debated at length.

Closing fisheries during spawning time is only one of several ways managers might soften the evolutionary pressures created by recreational and commercial harvest, says fish ecologist Jim Kitchell of the University of Wisconsin–Madison. Tweaking the legal limits on fish size might change pressures toward slower growth or smaller body size.

"From my perspective, the implications of this work go far beyond bass management," Allendorf says. Managers of other species, in the sea or on land, would do well to consider the possibility that harvesting can bring fast evolutionary changes that may turn the enterprise unsustainable. ■

Atom & Cosmos

"It's like you've got a bunch of people with shovels, reworking the surface." —DAVID PAIGE

Voyager enters uncharted territory

New frontier may be last before probe hits interstellar space

By Tanya Lewis

On its way out of the solar system, the Voyager 1 spacecraft has encountered a "magnetic highway" of charged particles — a hint that the probe may not have far to go before reaching interstellar space.

This highway lies where the sun's magnetic field and the interstellar magnetic field meet. Particles blown by the solar wind are speeding outward, while particles from cosmic rays generated outside the solar system are racing inward.

"This was a major unexpected result," Voyager scientist Stamatios Krimigis of the Johns Hopkins University Applied Physics Laboratory said in a December 3 teleconference.

Voyager 1 and 2 were launched 16 days apart in 1977 and are the most distant human-made objects in the universe. Voyager 1 is now more than 123 times as far from Earth as the planet is from the sun, and Voyager 2 is about 101 times as far away from Earth.

The magnetic highway may be the outermost region Voyager 1 will encounter before it leaves the bubble of charged particles that envelops the solar system. Though scientists suspect the crossing will occur soon, the exact time is unknown. "It could take several more months; it could take several years," said Voyager project scientist Edward Stone of Caltech.

Voyager 1 first encountered the magnetic highway July 28, as the sun's particle wind dropped away abruptly and the magnetic field ramped up in strength. After drifting in and out of the region several times, the spacecraft finally entered for good August 25.

"Voyager 1 has entered a new region, never before sampled by humanity," said space scientist David McComas of the Southwest Research Institute in San Antonio. Models of the edge of the solar system failed to foresee the highway region, but after the earliest clues came in July, McComas and a colleague published a study in the Oct. 10 *Astrophysical Journal* explaining how it could exist.

So what will the Voyager probes encounter once they finally do leave the solar system? "We think we will find a magnetic field oriented more in a north-south direction, and we've detected radio waves of a few kilohertz," says Stone, "but we could well be quite surprised once we get out of the bubble."

First rock from the sun has ice

Mercury's water probably came on asteroids or comets

By Tanya Lewis

NASA's MESSENGER spacecraft has found the strongest evidence yet of frozen water — and carbon-rich material — on the planet closest to the sun.

While Mercury itself couldn't support life, the findings provide clues about how water and other vital ingredients may have ended up on Earth, perhaps delivered by comets or asteroids. "Studying this stuff elsewhere in the solar system is really relevant for the origin of life," says UCLA planetary scientist David Paige.

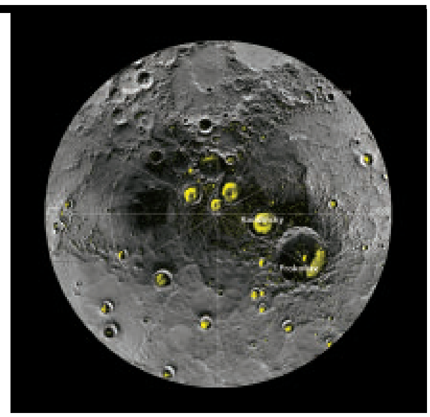
He and other scientists describe the findings in three studies published online November 29 in *Science*.

In the early 1990s, Earth-based radar measurements hinted at the presence of ice when they showed mysterious bright spots near Mercury's poles. The new studies reveal that the spots are indeed water ice. Darker areas may be carbon-rich material blanketing the ice and insulating it from the sun.

"The combination of results has presented a beautiful case for water ice with hydrocarbon infusion," says Ann Sprague, a planetary scientist at the University of Arizona.

New observations of Mercury's northern polar regions come from MESSENGER's laser altimeter, which maps the planet's topography and measures how reflective the surface is. Simulations of Mercury's surface temperatures match the laser measurements. Inside shadowy, steep-walled craters temperatures are below –173° Celsius, so frozen water can exist. Bright areas coincide with regions predicted to be cold enough for ice to be stable, while the dark areas coincide with warmer regions thought to harbor ice only beneath the surface.

Scientists think the water and carbon-rich material probably arrived via comets and asteroids, in a constant pummeling that should have mixed up the top layers of the crust. "It's like you've got a bunch of people with shovels, reworking the surface," says Paige. The fact that the bright and dark spots have not yet been mixed in suggests that the spots formed fairly recently, in geologic terms.



New data from NASA's MESSENGER spacecraft reveal bright spots (shown in yellow) near the north pole of Mercury that are almost certainly ice.

NASA, JHUAPL, CARNEGIE INSTITUTION OF WASHINGTON, NATIONAL ASTRONOMY AND IONOSPHERE CENTER, ARECIBO OBSERVATORY

Light in the dark

Scientists may be on the brink of identifying a mysterious form of matter

By Tom Siegfried

For decades, astronomers have grappled with their inability to decipher the universe's darkest secret: the identity of most of its matter.

It's not the same stuff as the ordinary atomic variety of matter common on Earth. Atoms or their parts — such as protons and neutrons — make up less than 17 percent of the mass in the cosmos. All the rest is "dark" — invisible to eyes and telescopes, its presence deduced by its gravitational tug on stars and galaxies (*SN: 8/28/10, p. 22*). This mystery matter apparently consists of tiny particles of some exotic species, but efforts to trap them (in underground detectors) or make them (in particle accelerators) have produced frustrating results: Some experiments find hints of such particles; others find nothing.

Yet despite the frustration, physicists offer a message of hope. With a deluge of new data already in hand, and more precise probes in the works, learning the identity of dark matter may just be a matter of time.

"My feeling," says theoretical physicist Katherine Freese, "is that we're on the edge of discovering it."

> "I'm predicting that one of the anomalies is right and we'll know pretty soon."
> KATHERINE FREESE

By discovering it, she means directly detecting the existence of dark matter particles, determining their species and mass and then, ideally, figuring out how they fit into physicists' broader theories of matter and energy. And as it turns out, the latest twists in the dark matter plot suggest that those particles might not fit where most experts had expected.

Two problems, one particle

Dark matter does have to fit in somehow, though. While its existence has been established only indirectly, few experts now doubt its presence throughout the cosmos. It was first inferred 80 years ago, when Caltech astronomer Fritz Zwicky noticed that clusters of galaxies behave oddly — the speeds of galaxies moving within a cluster cannot be explained by the gravity of the visible mass.

Later, astronomers found that the outer edges of most galaxies rotate much more rapidly than they ought to, if galaxies contain only visible matter. Extra unseen matter was needed to explain those observations, unless the law of gravity had somehow been repealed for long distances (a prospect seriously entertained by some researchers but dismissed by most experts). Further compelling evidence for dark matter came in 2006, when observations of colliding galaxies showed that ordinary matter did not track with the gravity of the collision debris.

As recently as a couple of decades ago, many astronomers suspected that dark matter might be ordinary matter clumped into lightless spheres — massive compact objects whimsically dubbed MACHOs. Such balls of darkness might be "failed stars" known as brown dwarfs, or possibly black holes. But various studies showed that MACHOs couldn't provide enough mass to explain the galactic spin rates. More likely, each galaxy is embedded in a cloud of massive subatomic particles, invisible because they don't interact with light.

For that matter, they don't interact with much of anything — hence their designation as weakly interacting massive particles, or WIMPs. If they exist, billions of these particles pass through you every second, but only about one per minute makes an impact on even a single atom in your body.

Enthusiasm for WIMPs as dark matter candidates was bolstered by theorists' attempts to unite matter, gravity and other forces in a single mathematical package. Those physicists proposed that each fundamental particle of matter, and each basic force-carrying particle, had a "superparticle" cousin. Such particles would be more massive than their ordinary partners, perhaps just the right mass to explain the dark matter in space.

Here was one of science's favorite coincidences: a possible solution for one mystery also offering an explanation for another great mystery. With two independent excuses for believing in WIMPs, scientists and funding agencies deemed it worthwhile to conduct experiments to search for them.

One such search strategy was proposed in the 1980s by Freese and collaborators Andrzej Drukier and David Spergel. If galaxies lived in a massive cloud (known as a halo) of WIMPs, each star within a galaxy (and each planet) would constantly smash into those WIMPs as the galaxy rotated. The sun, for instance, travels along a spiral arm of the Milky Way toward the constellation Cygnus, plowing through the swarm of WIMPs in its path the way a car windshield splatters mosquitoes.

Despite the reluctance of WIMPs to interact with ordinary matter, some few would, thus making it possible to record their presence with sensitive detectors. But windshields splatter more than mosquitoes. All sorts of gnats and moths and other bugs get flattened as well, their identities undecipherable from the smudges on the glass. In the same way, other subatomic particles, such as those produced by natural radioactivity, could fool the WIMP detectors. Freese and colleagues realized, though, that those other collisions occur at random. Collisions with WIMPs would be at a peak in June, as the Earth moved in the same direction as the sun toward Cygnus, but at a minimum in December, when the Earth was revolving around the sun in the opposite direction. (Fewer mosquitoes hit your windshield when you're backing up than when you're driving forward.)

Sure enough, when an experiment named DAMA, buried deep under an Italian mountain, looked for signs of such collisions, it found more in the summer than winter. But that finding was met with skepticism when other experiments failed to confirm it. More recently, an experiment called CoGeNT, in a Minnesota mine, did find hints of a summer-winter difference (*SN: 6/4/11, p. 10*). But another detector (CDMS II), operating in the same Minnesota mine, has found no sign of WIMPs. And yet another experiment in the Italian lab (XENON100) also sees nothing. Analysis of 13 months of data "has yielded no evidence for dark matter interactions," the XENON100 team recently reported in *Physical Review Letters*.

Dark reconciliation

Despite the apparent inconsistencies among current experiments, Freese, of the University of Michigan, believes evidence for WIMPs will emerge in the next few years.

"There are anomalous results, and they obviously can't all be right. But I'm predicting that one of the anomalies is right and we'll know pretty soon," she said at a recent symposium in Raleigh, N.C., sponsored by the Council for the Advancement of Science Writing.

At first glance, the experiments seem hard to reconcile: Those finding nothing seem to suggest that the searches reporting signs of WIMPs must be wrong. But upon further review, the evidence against WIMPs is not indisputable. For one thing, Freese points out, each experiment uses a different material to detect the WIMPs, so comparisons can be tricky. And other theoretical issues come into play when comparing one experiment with another, Freese says, such as whether the likelihood of a WIMP collision depends on the spin of the atomic nucleus it collides with.

Besides all that, current experiments are pushing the limit of their sensitivity. That's turning out to be an especially crucial problem — made worse by the realization that WIMPs might not possess the amount of mass that the detectors were designed to look for.

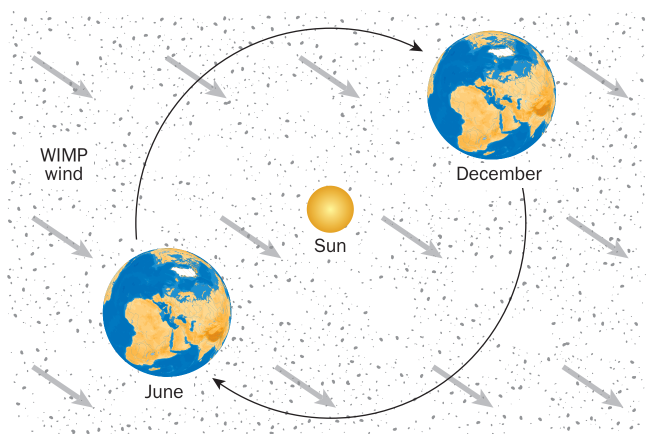
In 1998 the first supposed WIMP sighting, by the DAMA experiment, suggested a WIMP weighing in at about 60 proton masses, based on collisions recorded with iodine atoms in the detector's sodium iodide crystals. When other experiments found no sign of WIMPs, many physicists dismissed the DAMA results. But further data collected by the more advanced DAMA/LIBRA experiment continue to show the June-December difference — and with a new twist: Analyzing collisions with sodium rather than iodine suggests a much lighter WIMP, perhaps of only five to 10 proton masses.

That's not what scientists had expected. Although once considered a possibility, such low masses had supposedly been ruled out by particle accelerator searches.

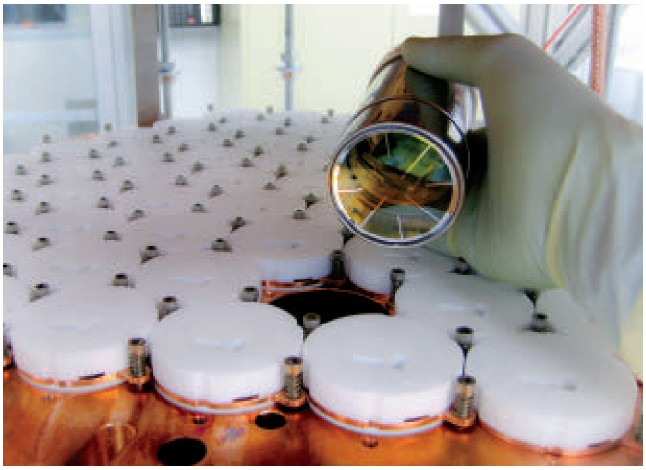
"The idea that this region is back is really a surprise," Freese says. "The experiments were really designed for the higher-mass region, not this low-mass region."

With the realization that WIMPs might have relatively low

WIMP wind As the solar system moves along a spiral arm of the Milky Way toward the constellation Cygnus, it may pass through a halo of dark matter particles. The resulting "WIMP wind" will appear strongest in June, as the Earth and sun travel together toward Cygnus.



GEOATLAS/GRAPHI-OGRE, ADAPTED BY T. DUBÉ



Part of the LUX detector, these tubes are designed to sense photons produced when dark matter particles collide with a xenon nucleus. The experiment is set to start this year.

masses, it may be possible to reconcile the incompatibilities among current WIMP-hunting detectors. "It has become clear that the breadth of possibilities for light WIMPs is much larger than previously appreciated," theorist Dan Hooper of Fermilab and colleagues write in a recent paper. But low-mass WIMPs live on the fringe of what current experiments were designed to find. Establishing the existence of dark matter WIMPs for sure will require more sensitive detectors, or novel detector strategies.

One experiment expected to provide more sensitivity than previous searches will use a combination of liquid and gaseous xenon in a detector called LUX. It is scheduled to begin collecting data this year at a depth of 1.5 kilometers in the Sanford Underground Research Facility (formerly the Homestake Mine) in South Dakota. Another promising approach is now being tested at the South Pole by a collaboration known as DM-Ice. It would use sodium iodide crystals, the same material used in the Italian DAMA/LIBRA experiment. Placing the detector more than 2 kilometers deep in Antarctic ice would shield it from most of the impostor particles. And because it is in the Southern Hemisphere, the peak WIMP rate would be expected in winter rather than summer, a check on whether it is the season, rather than the Earth's direction of travel, that accounts for the Italian results.

Still, just counting more hits than expected isn't proof that the colliding particles arrive from the direction of Cygnus. A WIMP striking an atomic nucleus sends it recoiling in the opposite direction of the WIMP's arrival path. But current detectors measure WIMP impact by recording signals such as flashes of light or a slight increase in temperature, obtaining no information about direction.

With a little help from biology, though, a future detector might be able to track the path of the recoiling nucleus. Freese and collaborators, including Harvard geneticist George Church, recently proposed a detector using single strands of the genetic molecule DNA hanging from a gold target. If the strands of DNA are strategically positioned, they will be sliced by a gold nucleus as it flies away after a WIMP impact (*SN: 12/1/12, p. 9*). If the order of the DNA building blocks (abbreviated A, T, C and G) is known, the pieces can be put back together to determine the path of the recoiling nucleus, kind of like reassembling the pages of a book that had been cut at a specific angle by scissors.

SUSY steps aside

If these new experiments establish low-mass WIMPs as the dark matter, scientists will no doubt celebrate the confirmation that WIMPs exist. But they will probably want to invite Alanis Morissette to the ceremony to sing "isn't it ironic." For if WIMPs turn out to have a low mass, one of the main motivations for seeking them so enthusiastically in the first place will have been a mirage.

All along, most experts assumed that WIMPs would be the superpartner of an ordinary particle, as described by a theoretical framework known as supersymmetry (affectionately called SUSY for short). When accelerator experiments failed to find low-mass superpartners, dark matter hunters jumped to the conclusion that WIMPs must have higher masses. But WIMPs do not have to be superpartners. Any particle that interacts weakly with ordinary matter would do.

Designing experiments to search for superpartner WIMPs may have led physicists astray, and may explain why the current results are so confusing. New detectors, designed without the constraint of faith in SUSY, may have better luck pursuing more speculative possibilities.

"You remove one restriction from your theory," Freese says, "and a whole new world opens up."

It wouldn't be the first time that scientists have let their theories mislead the interpretation of observations. Ancient astronomers didn't realize that the rotation of stars around the sky at night was observational evidence of the Earth's spin — the reigning theory held that the Earth was motionless. Albert Michelson thought his experiment to detect the ether had failed — the prevailing theory that light required an ethereal medium blinded him to his discovery that the ether didn't exist.

Theory is nevertheless important, of course, in guiding the design of experiments and in interpreting their results. But, as Darwin's friend Thomas Henry Huxley once pointed out, sometimes a beautiful theory is slain by an ugly experimental fact. It's the law of the scientific jungle. So someday soon, scientists may have to sacrifice the beauty of SUSY to the cause of identifying the dark matter. Whatever the bulk of cosmic mass is made of, sooner or later earthbound scientists are going to figure it out. ■

Tom Siegfried is the former editor in chief of Science News *and serves as treasurer of the Council for the Advancement of Science Writing.*

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FACTORY OF LIFE

Synthetic biologists reinvent nature with parts, circuits

By Alexandra Witze

Quietly, on the top floor of a nondescript commercial building overlooking Boston Harbor, the future is being born.

Rows of young scientists tap intently in front of computer monitors, their concentration unbroken even as the occasional plane from Logan Airport buzzes by. State-of-the-art lab equipment hums away in the background. This office, in Boston's Marine Industrial Park, is what California's Silicon Valley was four decades ago — the vanguard of an industry that will change your life.

Just as researchers from Stanford provided the brains behind the semiconductor revolution, so are MIT and Harvard fueling the next big transformation. Students and faculty cross the Charles River not to build computer chips, but to re-engineer life itself.

Take Reshma Shetty, one of the young minds at work in the eighth-floor biological production facility. After receiving her doctorate at MIT in 2008, she, like many new graduates, decided she wanted to make her mark on the world. She got together with four colleagues, including her Ph.D. adviser Tom Knight, to establish a company that aims "to make biology easy to engineer."

Place an order with Ginkgo BioWorks and its researchers will make an organism to do whatever you want. Need to suck carbon dioxide out of the atmosphere? They can engineer the insides of a bacterium to do just that. Want clean, biologically based fuels to replace petroleum taken from the ground? Company scientists will design a microbe to poop those out.

Ginkgo is, in essence, a 21st century factory of life. The researchers working there specialize in synthetic biology, a field that seeks to build living things from the ground up. After envisioning what they want new organisms to do, Ginkgo biologists actually grow vials full of redesigned cells. "We're going from the place we used to be, in doing science and studying the natural world, to a place where we're now going to be able to engineer and manipulate it," says Shetty.

Synthetic biology was born a little more than a decade ago, an offshoot of traditional genetic engineering but distinct in its ambitions, precision and mind-set. Instead of randomly tweaking the genetic blueprints of living organisms and then working backward to identify a cell with a desirable trait, the new field offered the power of designing and building cells with novel functions. Its pioneers dreamed of making armies of organisms that could produce alternative fuels, churn out drugs to battle disease or fill every stomach on the planet by squeezing more food out of each crop acre.

Now, synthetic biologists have laid the groundwork for that radical new future, by building biology's version of Silicon Valley. One research team has created a new and more complex set of biological building blocks that snap together like Legos, bringing large-scale production of engineered organisms closer to reality. Other scientists have hooked those parts up in a complex living analog of an electrical circuit and programmed it, much like programming a computer. Researchers are now writing code to make cells do things never before thought possible, like hunt down and kill cancer cells.

"This is not just — oh, we're going to go build something that's able to make pieces of DNA better," says Knight, one of the field's top visionaries. "This is — we're going to go create a technology infrastructure in the same way that the semiconductor infrastructure was developed."

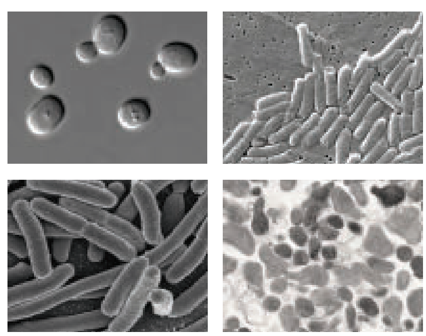
From scratch

In its early years, synthetic biology had a less practical, more daring public image. In part that was because of the involvement of J. Craig Venter, the motorcycle-riding, globe-hopping, high-profile iconoclast of modern biology. In the 1990s he led a private effort to decipher the human genetic instruction manual, or genome, that competed with a publicly funded effort. More recently, he sailed his yacht around the world, scooping up water samples every 200 nautical miles to see what microbes were there.

Venter also decided that he wanted to synthesize a living organism from scratch. Such a feat would involve stitching together a creature's entire genome. DNA's double helix is made of chains of paired molecules abbreviated as A, T, G and C; long stretches of these letters make up genes, the basic units of heredity. Genes contain the information needed to make proteins, which perform the lion's share of work in a cell.

Commercial biotechnology companies can easily synthesize short strands

Little big players To carry out their synthetic feats, biologists typically turn to microbes that have short genetic instruction books and reproduce quickly. Organisms worthy of note include, clockwise from top left, *Saccharomyces cerevisiae*, *Salmonella*, *Mycoplasma genitalium* and *Escherichia coli*.



OPPOSITE PAGE: HARRY CAMPBELL; THIS PAGE, CLOCKWISE FROM TOP LEFT: MASUR/WIKIMEDIA COMMONS; JANICE HANEY CARR/CDC; SPL/SCIENCE SOURCE; ELAPIED/WIKIMEDIA COMMONS of DNA, but putting those together into a full genome is an entirely different matter. So Venter turned to a set of bacteria known as *Mycoplasma*, which have some of the shortest known genomes (one species has just 580,000 pairs of genetic letters, compared with the 3 billion pairs in the human genome).

Venter's team took commercially made strands of DNA, then joined them together in his lab using reactive enzymes. After many such steps, the scientists succeeded in fabricating the genome of one *Mycoplasma* species. The team then inserted the synthetic genome into a second species (which had had its own DNA removed), booting it up. The resulting organism, dubbed "Synthia," essentially cribbed lab-made DNA to run itself (*SN: 6/19/10, p. 5*).

Headlines predictably exploded. Life had been made from scratch — sort of. Many synthetic biologists weren't nearly as excited about Venter's achievement as the media suggested. These critics point out that his group had simply built an organism to run off a program that already existed in nature; the team didn't engineer Synthia to do anything new. The crucial difference in today's synthetic biology, scientists say, is the ability to customize organisms from the start.

"We're at the beginning of being able to design life in the way that we want," says Pamela Silver, a biologist at Harvard Medical School and Harvard's Wyss Institute for Biologically Inspired Engineering.

By design

Engineering new forms of life starts with setting up a biological assembly line, the living equivalent of a transportation innovation. Synthetic biologists aim to reinvent biology in the same way Henry Ford revolutionized automobile manufacturing. Instead of installing standardized spark plugs or carburetors as a car moves down the line, the scientists tuck brand-new biological parts into the body of a bacterium.

To do so, researchers first have to identify distinct, easily defined parts within a cell — biological versions of wheels, hoods, dashboards, engines and so on. Such parts need to be useful in any design, like a power steering pump that works on both a Taurus and a Focus. The parts also need to be standardized so that those made at one factory work with those made at another.

Drew Endy, a synthetic biology pioneer at Stanford, likes to tell the story of William Sellers, who in 1864 argued for the standardization of nuts and bolts so that a wrench made in Wilkes-Barre would fit a nut made in Nashville. Until then mechanics had been working with custom-built hardware. In a lecture at Philadelphia's Franklin Institute, Sellers called for the country to adopt his new screw design. The standardized, easily measurable shape of its threads would also apply to nuts and bolts, allowing industry to develop a cheap and profitable way to mass manufacture machine shop hardware. Industry agreed, and within just a few years the Sellers screw took off.

Similarly, scientists are now compiling their own list of biological parts like the Sellers screw. Most parts are stretches of genetic material, much shorter than a gene, that trigger some particular process to turn on or off. A part known as a promoter, for instance, starts the conversion of DNA information into its counterpart, the RNA molecule, while a terminator part stops the action. Many of the parts are proteins known as transcription factors, which hook onto DNA to help control how cells work and respond to their environment.

Scientists make parts by building a stretch of DNA or RNA known to perform a desired job, then adding a standardized string of letters at the beginning and the end to identify it as a part. They then insert the whole thing into a circular strand of DNA until they need it. In 2003, MIT biologists started keeping a formal inventory of these biological parts. Many are added by students who spend summers working on a synthetic biology competition, the International Genetically Engineered Machine contest, or iGEM (see Page 32). Today the list of parts tops 20,000.

Even that roster is too small for some.

T.S. MOON *ET AL*/*NATURE* 2012, ADAPTED BY E. FELICIANO

Building complexity

Redesigning organisms to do people's bidding requires biological parts that can mix and match to create genetic circuits. Like electrical circuits, these genetic versions perform a useful task or computation and can be combined into more complex systems.

Biological parts

Protein-coding sequences are stretches of DNA that hold the recipe for building a protein.

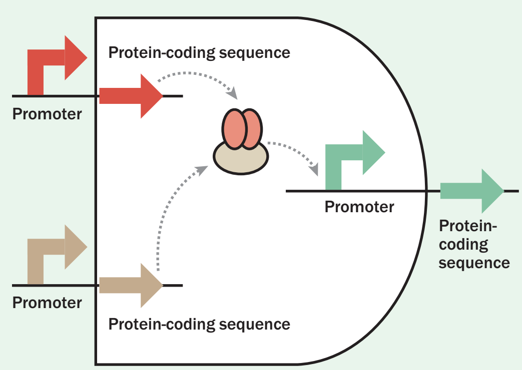
Promoters turn on the process that creates a counterpart RNA molecule from DNA, and ultimately a protein.

Terminators turn off the process that creates a counterpart RNA molecule from DNA.

Protein domains are portions of a protein sequence that can act independently. The domains may influence a protein's functions and characteristics.

Plasmids are rings of DNA molecules that can be copied independently from chromosomal DNA.

In this circuit, two promoters turn on the transcription of two protein-coding sequences. The resulting products need to join together before another promoter can turn on another sequence, leading to an output product. The circuit is only on when both of the promoters are active.



In his office at Boston University, bioengineer James Collins practically bounces in his chair as he complains about the quality and quantity of most parts. "We just don't have enough parts to do what we'd like," he says. "If you survey the original parts out there, we usually use only a dozen or so."

Collins wants more. Most synthetic transcription factors are designed after versions found in bacteria like *Escherichia coli*. Collins' team recently looked instead at yeast cells. Yeast are more complex than bacteria; if engineers could build more parts inspired by yeast, they could use those to create more advanced designs. Working with colleagues including MIT's Timothy Lu, Collins developed a system to make new transcription factors, and made 19 new ones to start with. "Instead of relying on this small number of things arrived at in nature, we now have a very nice platform that allows you to ramp up and create transcription factors by design, in large numbers," Collins says. The work appeared last August in *Cell*.

Cells wired up

Once synthetic biologists have enough parts to work with, the next question is what to do with them. Here, bioengineers take their cue from electrical engineers. Individual biological parts are like the transistors, resistors and capacitors that electrical engineers connect together with wires to create a circuit through which current flows. Circuits can then be connected together on a semiconductor chip to perform computing tasks.

Biologists first reported making synthetic genetic circuits in 2000, when two *E. coli* papers appeared in the same issue of *Nature*. In one, a team led by Collins announced the first artificial toggle switch in bacteria; the scientists designed two promoters to interact and drive gene activity if prompted by one molecular signal, and to stop when prompted again.

In the second paper, Stanislas Leibler and Michael Elowitz, then at Princeton, described a synthetic timing switch, in which three genes inhibited one another in sequence, their activity cycling regularly.

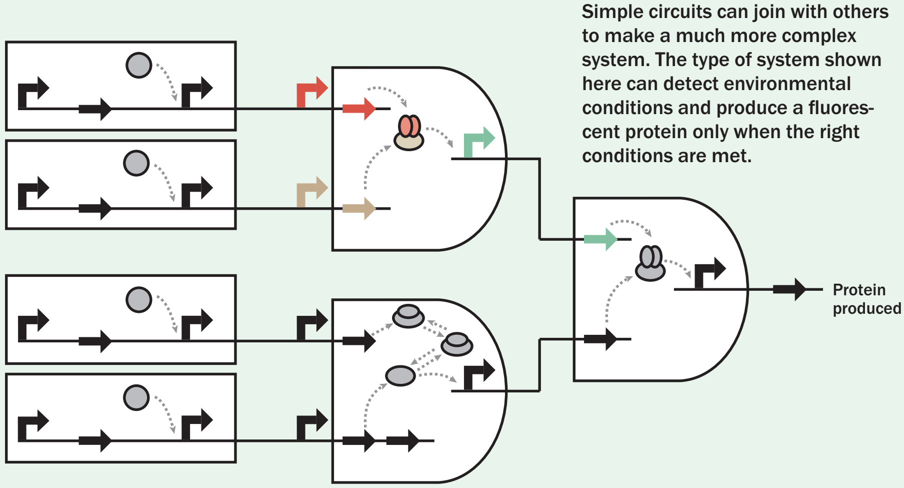
These first papers were necessarily clumsy attempts to emulate what nature does effortlessly. But with genetic circuits that accomplished particular tasks, researchers could go one step further: They could connect those circuits with other components, just as electrical engineers do on a computer chip, and program the whole contraption to perform an even more elaborate job.

Across the Charles River from Ginkgo, on the second floor of a gleaming biotechnology building, sits one major hub where biological parts are being turned into sophisticated machinery. This is MIT's synthetic biology center. Being MIT, it is full of engineers with novel and creative ways to think about programming — even when that programming involves DNA-based circuits rather than electrical ones.

One such tinkerer is Christopher Voigt, whose round face and easygoing manner belie the fact that he commands living organisms to do his bidding. Voigt, a former computer programmer, got into synthetic biology because he saw it as the last frontier. "Being able to write a language that programs *E. coli* to perform a set of operations is the most challenging

Solving hunger

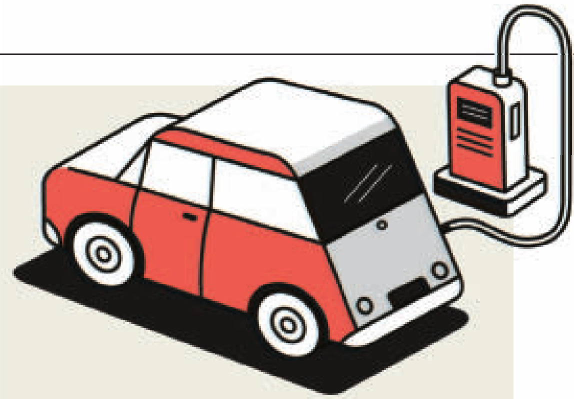
Synthetic biology may help farmers feed more people. For millennia, crops have been bred with an eye toward improved harvests. Later, genetic manipulations upped plant yields and made crops more resilient against drought and other hazards. Now, scientists are looking at tweaking photosynthesis. "You don't need to increase the biomass of plants by that much to solve the food problems across the world," says Harvard's Pamela Silver. One idea is that new enzymes could boost the amount of energy that plants can extract from the sun. Another suggests there might be a totally different way to pull usable carbon from the atmosphere. In the April 2012 *Applied and Environmental Microbiology*, Silver and colleagues reported engineering a bacterium to churn out up to 200 percent of its initial cellular mass as sugar. The work could be used to develop plants that produce more food per harvest.



Simple circuits can join with others to make a much more complex system. The type of system shown here can detect environmental conditions and produce a fluorescent protein only when the right conditions are met.

HARRY CAMPBELL

Making energy



An early hope for synthetic biology was that it could wean society off fossil fuels. Engineering microbes to churn out hydrocarbons would presumably be a lot cleaner and more climate-friendly than extracting and burning coal and oil. Since 2000, the U.S. Department of Energy has poured millions of dollars into funding synthetic biology biofuels research, such as new types of algae to secrete biodiesel or other engineered fuels that don't have to be pumped from the ground. So far, progress has been limited.

problem," he says.

At first, it wasn't clear that the dream of programming life would be possible. For most of the 2000s, synthetic biology fought a reputation as being not much more than a bag of parlor tricks. Students working on iGEM teams designed cute proof-of-principle projects, like engineering *E. coli* to darken in "bacterial photographs" or to smell like wintergreen or banana. It seemed that scientists were connecting and reconnecting biological parts, but not in any kind of profound or truly useful way.

That paradigm is now beginning to shift, Voigt says, as researchers develop more reliable parts and, crucially, many more ways in which to wire them together. Instead of using the same few parts and circuits over and over again, programmers like him now have far more sophisticated designs. "We're getting to an inflection point," he says. "Finally."

Last year, for instance, Voigt's research group reported re-creating the main pathway through which bacteria convert atmospheric nitrogen to ammonia. By replacing natural parts with synthetic ones, the scientists essentially adapted the genetic programming guiding the job. The system involved 94 biological parts — a scale of engineering unheard of until recently, Voigt says.

Going one step further to original design, Voigt and his colleagues recently built the largest synthetic genetic circuit to date, described in *Nature* in November. It involves four sensors, each of which can detect a particular input from the environment. One sensor may detect oxygen levels in a cell, for example, while a second sniffs for glucose. Combining those inputs and others prompts the cell to decide whether to take a particular action.

Voigt and his colleagues hope to use these types of circuits in industrial fermentation vats, so that bacteria inside the vats can sense multiple ways in which the environment changes and adjust activity accordingly. "Some of the very basic circuits are already used in biotechnology, to turn on the production of protein as much as you possibly can," says Voigt. "But if you're trying to make materials or chemicals like natural products, that requires a lot more sophistication in terms of timing when things happen."

Put enough circuits together and program them in the right way, and synthetic biology may soon become a lot more personal. Just as the earliest clunky computers eventually gave way to the iPhone in your back pocket, designer cells might one day become an everyday part of your life. They might even course through your veins — if Ron Weiss has his way.

Weiss works just down the hallway from Voigt at MIT. He began his graduate student career in typical fashion, using computer programs to simulate biological changes in a developing embryo. But then something clicked in his brain. "I remember the day when I thought, let me flip this around," he says. "Let's look at what I know in computing and understand how I can program biology." Then his advisers told him he was too close to getting his Ph.D. to start going down such crazy paths.

Weiss wasn't going to drop his doctoral quest, but he walked over to Knight's office and asked to join the budding synthetic biology research group there instead. After many 16-hour days teaching himself how to string together DNA, Weiss changed his focus from engineering to synthetic biology.

Now, in a sort of biological hit job,

Treating patients

One of the most obvious goals of synthetic biology is to make people healthier. Engineering new drugs, or designing cells that can target disease inside the body, has been a goal of the field from the start. An early success involved creating a bioengineered version of a drug to fight malaria. Researchers managed to engineer a species of yeast to produce large amounts of a chemical precursor to the antimalarial drug artemisinin, typically harvested from the wormwood tree of east Asia. The pharmaceutical company Sanofi is now working to bring the process to market. In another take on better health, engineered human cells could locate and eliminate cancerous cells by tricking the evildoers into committing suicide. Though the technique has been demonstrated in a lab dish, it is still far from tackling cancer in real human patients.

BOTH: HARRY CAMPBELL

Weiss' team has engineered assassin cells to track down and annihilate cancerous cells. The scientists, including Yaakov Benenson formerly of Harvard and now at ETH Zürich, programmed a synthetic circuit that can sense levels of chemicals often found in cancer cells. The circuit also includes a kill switch, a synthetic version of a gene carrying information that can make other cells commit suicide.

Cells carrying this circuit search for cells that are turning cancerous. Once there, the assassin cells flip the kill switch and cause the cancerous ones to off themselves.

In a 2011 *Science* paper, Weiss' team showed that this killer circuit could work in human cells in a lab dish. But there's a long way to go before it could treat cancer in people. Scientists need to find a way to deliver the assassin payload into the body. "We need something like a virus that would go into cells and then compute whether each cell is cancerous or not," Weiss says. His team is now working to harness a virus that could be used to test the idea in mice. If it works, doctors might eventually be able to inject assassin circuitry into a person suffering from cancer.

Weiss also has his eye on fighting several other important diseases. Diabetes, for instance, can require a person to regularly inject insulin, but Weiss thinks that engineered cells might be able to do that job from within the body. In early theoretical work, his team showed how synthetic gene circuits could steer stem cells to develop into insulin-producing cells. Adding synthetic switches could nudge the insulin production process in one direction or another as needed, the team reported last July in *PLOS Computational Biology*. The cells could reproduce over and over again, and then die when no longer needed.

Reviews give green light, encourage caution

Engineering life is not the sort of thing you can do quietly.

Ever since biologists first started piecing together genetic components, ethicists have pondered the implications. Could an artificial form of life turn out to have unexpected consequences, like invading the environment or otherwise running amok? And what about bioterrorists who might want to get their hands on synthetic bugs and put them to nefarious uses?

A March 2012 report from Friends of the Earth, the International Center for Technology Assessment, and the ETC Group — nongovernment organizations that have worked against genetically modified organisms, among other causes — calls synthetic biology "an extreme form of genetic engineering" that is "developing rapidly with little oversight or regulation despite carrying vast uncertainty." Not since the 1990s' birth of nanotechnology, the engineering of the very small, has a new technology elicited such ire.

Nearly every major safety review of synthetic biology, though, has given the field a cautious green light. A 2010 government review, requested by President Obama after Craig Venter booted up a cell with a synthetic genome, suggested there was no need to create a new government body to oversee synthetic biology research. Rather, the report's authors promoted the idea of "prudent vigilance" — paying attention to what's happening in the field without regulating it out of existence from the start. "With these unprecedented achievements comes an obligation to consider carefully both the promise and potential perils that they could realize," the report said.

The Woodrow Wilson International Center for Scholars in Washington, D.C., has also started a scorecard for tracking public discussions about synthetic biology. An update last July found that many U.S. federal agencies had begun taking steps to learn more about the field, as recommended by the presidential report. Still, the center says, more work is needed. *—Alexandra Witze*

Picking up the pace

A medical breakthrough was, in fact, one of synthetic biology's first major industrial successes: a bioengineered version of artemisinin, a malaria-fighting drug that once had to be laboriously and expensively harvested from the wormwood tree of east Asia. In 2006, researchers from the University of California, Berkeley and Amyris Biotechnologies in Emeryville, Calif., reported that they had engineered baker's yeast to churn out a crucial precursor to the drug. The scientists teamed up with the pharmaceutical company Sanofi to scale up the process and make the drug in its laboratories. Sanofi is in the early stages of shipping the first commercial artemisinin made using synthetic biology.

Researchers haven't been as successful with another of synthetic biology's lofty original goals — to help solve the energy crisis. One early and much-touted promise was that scientists could insert synthetic genes into an organism's DNA to make it secrete biodiesel or other petroleum alternatives. Some companies, including Ginkgo, are still working on this challenge. But many of the highest profile projects, like those that engineered algae to pump out biofuels, simply haven't panned out. In most cases, fuel made by synthetically altered organisms can't compete economically with regular petroleum products.

Most synthetic biologists see this setback as a bump in the road rather than a major derailment for the field. Harvard's Silver, for instance, has shifted from working on synthetic biology approaches for clean-burning hydrogen fuel to new ways to re-engineer photosynthesis within plants.

Once a molecular biologist, Silver shifted to synthetic biology in the early 2000s so that she could tackle scientific questions no one else could. "The idea of building with biology struck me as very exciting," she says. Today she oversees one of the largest and most productive synthetic biology research teams, a warren of lab benches and graduate students on Harvard Med's campus in Boston. Among other efforts, she has developed synthetic genetic counting devices, to keep track of exposures to things like radiation within a cell.

For Silver, synthetic biology is all about accelerating the pace of practical advances. "Biology needs to move faster so that people cheer when something great happens," she says.

Though it may still lag behind some scientists' ambitions, there's no question the field is progressing rapidly. Time and again, researchers have invented new methods for assembling synthetic parts and genetic circuits cheaper, faster and more easily than before.

In 2009, scientists working for Venter came up with a new way of stitching together different biological parts by using DNA strands with overlapping letter sequences on their ends. Biologists can easily add the matching sequences to any parts they want to link, then stir in some enzymes and, voilà, assembly. The method, invented by Daniel Gibson, has caught on quickly because it lets scientists patch together more than a dozen DNA strands at once. Just a year after its invention, Gibson assembly inspired a devotional YouTube video from an iGEM student team. Today it is used in nearly every synthetic biology lab.

And at Harvard, biologist George Church devised a technique that makes multiple changes to an organism's genome at a time. MAGE (for multiplex automated genomic engineering) is like a genetics editor on speed; it zips through, finding and tweaking DNA automatically

Many electrical engineers, including Ginkgo BioWorks' Tom Knight, have moved to the field of synthetic biology.

so that researchers can add various synthetic components at once and test what they do. In 2011, Church and colleagues founded a company, Warp Drive Bio in Cambridge, to use a version of this superfast technique to hunt for potential new drugs in natural compounds.

The market for synthetic biology products is still quite small, and one of Church's earlier start-ups failed after trying to do too much too fast. But he and other visionaries are convinced that synthetic biology will be big. Huge, in fact — as huge as the Internet.

And they should know. Several scientists pushing the field forward today are former electrical engineers who helped develop key components of what became the Internet, such as its ARPANET predecessor.

"The Internet disrupted the world — it was unleashing a completely different aspect of nature," says MIT's Randy Rettberg, a former engineer at Sun Microsystems who now runs the iGEM competition. So, too, will synthetic biology, by telling biological matter precisely how to behave. "First we had the industrial revolution, then we had the network revolution," says Rettberg, "and now we have the matter revolution."

Rettberg thinks that synthetic biology's full impact, like that of the Internet, will take decades to emerge. "We're only about 10 years into it; it took about 25 years from ARPANET until you had the beginning of the World Wide Web," he says. "And although the Internet took a very long time, its impact was dramatically bigger than everybody but the visionaries imagined."

It's hard not to get caught up in Rettberg's enthusiasm as he bustles about the iGEM offices in Cambridge, proudly introducing students who help box up test tubes full of biological parts and mail them out to competitors. This is a man who charted out the final phase of his scientific career on graph paper to see if he had enough time left to learn something completely new. Then he taught himself synthetic biology.

As did Rettberg's longtime friend Knight, also a former electrical engineer. Knight now spends most of his time at Ginkgo's offices, where his business card reads simply "DNA Hacker." As automated machines whir in lab space across the hall, testing what freshly engineered organisms can do, Knight dreams up new designs for Ginkgo to try. Just as he once dreamed up what would become some of the first single-user computer workstations.

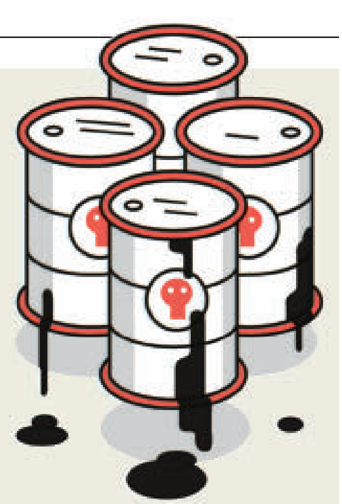
"I knew this was the exciting thing to go do," he says. "What does it take to make the next Intel? I am actually interested in making that work." ■

Explore more

- George Church and Ed Regis. *Regenesis: How Synthetic Biology Will Reinvent Nature and Ourselves*. Basic Books, 2012 (see Page 30).
- Rob Carlson. *Biology is Technology: The Promise, Peril, and New Business of Engineering Life*. Harvard Univ. Press, 2010.

Cleaning up

Microbes are already used at oil spill sites, eating petroleum components and converting them into less hazardous by-products. Designing synthetic versions that can do the job quicker, and perhaps break down more stubborn pollutants such as pesticides and radioactive waste, would be a logical next step. Researchers at Spain's National Center for Biotechnology have designed circuits capable of redirecting microbes to feast on industrial chemicals instead of sugar.



FROM TOP: HARRY CAMPBELL; FRANCIS LEE

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Regenesis: How Synthetic Biology Will Reinvent Nature and Ourselves

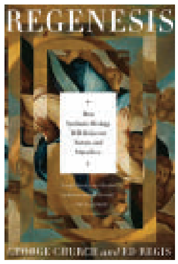
George Church and Ed Regis

Reading the first book penned by Church, a Harvard biologist and polymath, is like falling down a rabbit hole straight into his fermenting brain.

Church's wide-ranging career includes developing novel methods for reading the genetic instruction manual, or genome, of creatures from bacteria to humans. Now he focuses on synthesizing those instructions from scratch. Church doesn't just think that the new field of synthetic biology (see Page 22) will change your life. He claims it will also change your world and notion of your place within it.

Why not, after all, synthesize a Neandertal? Church and his coauthor explore the Neandertal genome and how modern humans could be used as a template to re-create one — should society be willing to accept building a Neandertal child in the laboratory. Or how about pushing into transhumanism, the concept that genes could be engineered to give people mental or physical capabilities well beyond their ordinary means?

Such philosophical musings are tethered to reality by long passages describing the gory details of how molecular and cellular systems work. Church also explains everything and then some about many of his inventions, such as



"multiplex automated genome engineering," which breaks apart DNA and mutates small sections of it to test for the evolutionarily fittest versions. This is not a book for the biologically faint of heart.

But it is a dizzying survey of how scientists have unearthed the secrets of living organisms and are now using that information to revamp life itself. Whether that information will be used to build a Neandertal remains to be seen. — *Alexandra Witze*

Basic Books, 2012, 284 p., $28

Hallucinations

Oliver Sacks

Just before a migraine, *New York Times* blogger Siri Hustvedt had an amiable encounter with a tiny pink man and an equally tiny pink ox. The odd pair wandered around her bedroom a bit before vanishing. "I have often wished they would return," she writes, "but they never have."

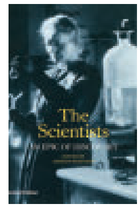
Hustvedt's story is just one of the case studies that Sacks, a neurologist, recounts in

this charmingly bizarre compilation of strange sensory experiences. Hallucinations tend to be viewed as a sign of an unsound mind (*SN: 4/7/12, p. 22*). Far more often, Sacks contends, the causes are mundane: migraine auras, fevers, injuries, grief, drugs — prescription and otherwise — and even falling asleep or waking up. Seeing, hearing, smelling or feeling things that aren't there, he says, is a normal part of the human condition.

Sacks uses first person accounts to explore how the brain builds perception from sensory information, and what can happen when that process breaks down. In one tale, an exhausted cyclist mistakes a motor home for a UFO during a long-distance race. In another, a microbiologist infected with the nerve-damaging herpes simplex virus catches the phantom whiff of a fishy odor for an entire year. A musician taking medication for Parkinson's disease attempts to play musical scores on his piano before hallucinatory notes skitter off the page.

Sacks' writing can be on the dry side, but this works to his advantage here. When the human brain can conjure miniature pink oxen out of thin air, a little clinical language helps keep things grounded in reality. — *Allison Bohac*

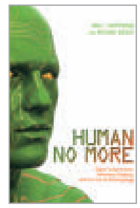
Alfred A. Knopf, 2012, 326 p., $26.95



The Scientists

Andrew Robinson, ed.

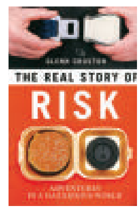
Short biographies of scientists through the ages, from Copernicus to Watson and Crick, illustrate where new ideas and discoveries come from. *Thames & Hudson, 2012, 304 p., $45*



Human No More

Neil L. Whitehead and Michael Wesch, eds.

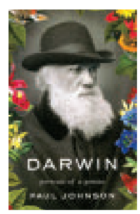
Online worlds are redefining what it means to be human, according to the authors of these anthropological essays on digital culture. *Univ. Press of Colorado, 2012, 243 p., $75*



The Real Story of Risk

Glenn Croston

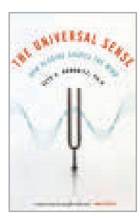
A biologist explores why humans are poor at judging risk — fearing rare shark attacks, for example, more than common heart attacks. *Prometheus, 2012, 276 p., $19*



Darwin: Portrait of a Genius

Paul Johnson

A historian celebrates Charles Darwin's triumphs and analyzes his weaknesses in the latest biography of the naturalist. *Viking, 2012, 164 p., $25.95*



The Universal Sense

Seth S. Horowitz

This review of the science of hearing considers how people have learned to create and control music, sonic weapons and other noises. *Bloomsbury, 2012, 305 p., $25*

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Early puberty's cause

Regarding "Early arrival" (*SN: 12/1/12, p. 26*): In 1960 I left the Ohio Valley of grass- and corn-fed cows to teach in the Los Angeles area. When I arrived, I found that eighth- and ninth-grade girls looked physically like 25-year-old women in Ohio. I asked the other teachers what was going on. They all responded, "beef growth hormones." If researchers would track earlier puberty in preteen girls alongside the use of growth hormones in cattle, they would most likely find matching graphs. Is this another horror of fast food such as hormone-laden hamburgers?
Irene Baron, Zanesville, Ohio

Meat and dairy products from animals given growth-promoting hormones has long been a concern among parents and physicians, but the relationship can be difficult to study (for example, children who consume a lot of meat and dairy may also be overweight). One of the more recent studies, which followed 7,500 children in Hong Kong, was published in the Sept. 1 Pediatrics*. It did not find that the onset of puberty was associated with the consumption of cow's milk. —Laura Beil*

Symbolic illogic

As soon as I saw the → in the editor's letter (*SN: 12/15/12, p. 2*), I thought of the Pioneer message plaque designed by Carl Sagan. The first time I saw that placard and the discussion of the message it purportedly contained, I questioned the symbolism. An arrow is an anthropomorphic symbol that could only be understood by one familiar with the history of human weaponry. When I imagined another race trying to "read" the symbolism, I thought they would be more likely to interpret the arrow as a rocket surface-blast and assume the flight, indicated on the plaque, was directed away from the spacecraft and toward the third rock from the sun.
David Adams, Aiken, S.C.

Up a tree

Is it really surprising that *A. afarensis* could climb trees ("Fossil puts Lucy's kind up a tree," *SN: 12/1/12, p. 16*)? Or that children were more adept or did it more often than adults? Just because we evolved to walk upright doesn't mean we can't climb trees, just as the fact that we came out of the oceans several hundred million years ago doesn't mean we don't like to take a swim now and then.
Wayne Harris-Wyrick, Oklahoma City, Okla.

Researchers studying A. afarensis *don't see climbing and upright walking as mutually exclusive. The question is whether Lucy's kind evolved to spend much of its time in the trees as a survival strategy rather than for occasional forays. This long-standing debate shows no signs of dimming. —Bruce Bower*

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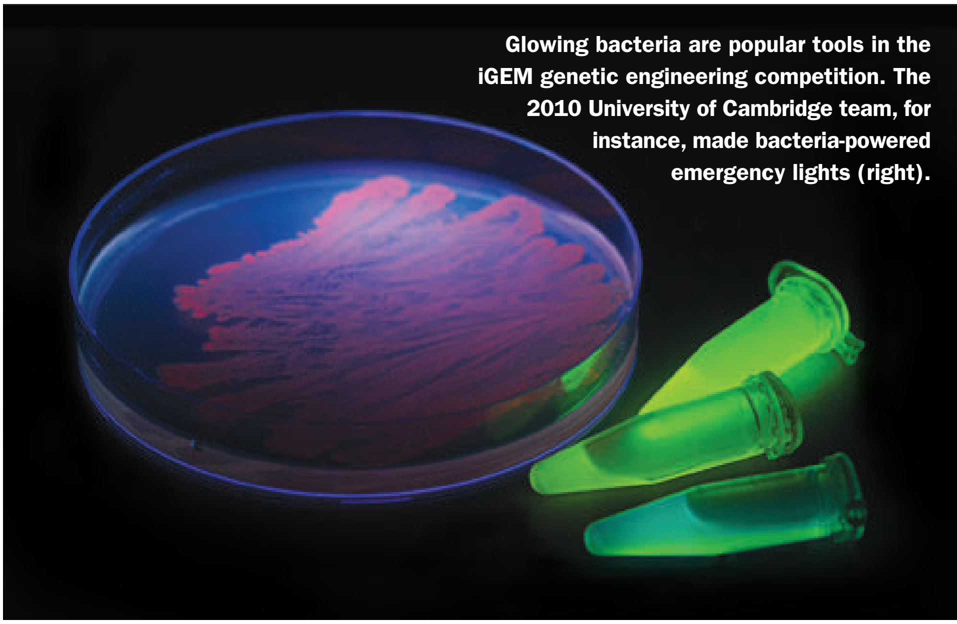

Glowing bacteria are popular tools in the iGEM genetic engineering competition. The 2010 University of Cambridge team, for instance, made bacteria-powered emergency lights (right).

Contest brings out the biohackers

Mix one part enthusiasm, two parts engineering and three parts biology — and you've got a recipe for do-it-yourself genetic engineering.

Every November, college kids from Michigan to Munich descend on MIT, eager to show off their biohacking skills. In the International Genetically Engineered Machine (iGEM) competition, teams battle one another to build the coolest synthetically altered organisms. If you want to create a microbe that will sniff out and destroy contaminants in mining waste ponds, or a cell that will produce drugs right in your body, iGEM is for you.

Pioneers of synthetic biology (see story, Page 22) founded iGEM in 2003 to get young scientists thinking about the field's possibilities. What began as a small winter project at MIT has expanded to 191 collegiate teams, plus divisions for high schoolers and entrepreneurs. "The thing the world needs is more excited engineers," says Randy Rettberg, an iGEM founder and its current director.

Each spring, organizers at iGEM's Cambridge, Mass., headquarters FedEx out kits containing about 1,500 biological "parts." Most of those parts are engineered fragments of genetic material that can be put into bacteria to make them do a particular task — make more of a specific protein, say, or turn off gene activity. Students can use the provided parts or build their own. "We say iGEM isn't easy, but iGEM is worth it," Rettberg says.

At many universities, iGEM teams have achieved a sort of rock-star legacy, with the same students signing up year after year. Others have to start from scratch. In 2012, for instance, the University of Colorado Boulder fielded its first iGEM team.

Boulder team leader Joe Rokicki and his crew read paper after paper, brainstormed possible projects and settled on a bacterial night-light. They managed to clone six genes involved in light production in the bacterium *Aliivibrio fischeri* — but ran out of time to make those genes do anything significant.

"We've been so invested in this every day," says team member Max Jacobs. "But," adds Simon Greenberg, a bit wistfully, "we're at the whim of the cells." The Colorado team didn't advance past regional semifinals.

This year's overall iGEM champion: the University of Groningen from the Netherlands. Its Food Warden sticker uses engineered *Bacillus subtilis* to sense rotten meat and turn yellow or purple as an alarm. — *Alexandra Witze*

A not-too-rotten idea

Students from the University of Groningen triumphed in the 2012 iGEM competition by creating a prototype sticker (below) to signal food spoilage. The Food Warden sticker uses bacteria engineered to activate a pigment-producing gene when substances made by rotting meat are present. The sensor might help reduce food waste by determining when meat is actually starting to go bad instead of relying on an arbitrary "use by" date. Of 338 people surveyed by the research team, two-thirds said that they would pay a few cents extra for such a product in their food packaging, even though it contains genetically modified organisms.

TOP (ALL): FERNÁN FEDERICI; BOTTOM: UNIV. OF GRONINGEN IGEM TEAM