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MAGAZINE OF THE SOCIETY FOR SCIENCE & THE PUBLIC ■ JUNE 6, 2009

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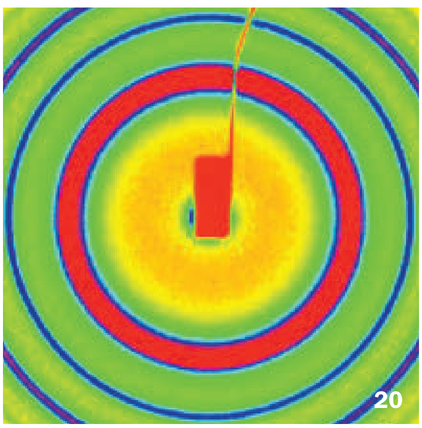

ScienceNews

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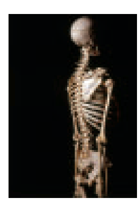

COVER Serotonin's role in the body extends to effects on the human skeleton, shown here in a rear-side view. *Photo: John Davis © Dorling Kindersley*

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FROM THE EDITOR

Adding an 's' to universe, an infinite number of times

More than three centuries ago, the French writer Bernard le Bovier de Fontenelle established himself as one of the first great popularizers of science.

His masterwork, *Conversations on the Plurality of Worlds*, consisted of dialogs with the Marquise, an inquisitive woman to whom he explained the latest findings and speculations of science, with special attention to the prospects for life on the moon or elsewhere in the cosmos.

"It seems to me that nothing could be of greater interest to us than to know how this world we inhabit is made, if there are other worlds which are similar to it, and like it are inhabited too," Fontenelle opined.

Since his day, the issue of the plurality of worlds has occupied great minds and transformed humankind's understanding of nature. From a solar system with a few planets, the known universe grew to a galaxy of billions of stars, and then to an expanding spacetime encompassing billions of galaxies.

Today science is on the cusp of multiplying reality even more grandly, as I recount in an essay in this issue (Page 26). Some cosmologists propose that the known universe is but a speck of space in a cosmic froth of uncountable bubbles — some vastly different from the local universe, but some perhaps sufficiently similar to allow for intelligent inhabitants. By devising mathematical tools for coping with an infinite cosmos, today's pioneers are attempting to determine whether such wild ideas can be verified. If such efforts succeed, they could enlighten humankind's role within existence more profoundly than any scientific advance since Copernicus.

Of course, these ideas are not shared by all experts and are even derided by some. Not all wild ideas in science turn out to be true. But many of the wildest do. And proof of a plurality of universes would extend a long tradition of the human mind's ever-expanding grasp of the vastness of existence. Just as the 20th century's cosmos dwarfed that of earlier times, the 21st's may very well reveal a cosmos of even greater grandeur.

After all, difficulty in imagining an infinite reality does not constitute a logical argument against its truth. As Fontenelle said to the Marquise: "Do we presume to have discovered all things, or to have taken them to the point where we can add nothing? For goodness sake, let's admit that there'll still be something left for future centuries to do." Perhaps the 21st is one of the future centuries he was alluding to.

—Tom Siegfried, Editor in Chief

Scientific Observations

"The pertinence of the phrase 'two cultures' continues; the science kids and the humanities kids, as it were, still sit at different tables in the lunchroom.… Most disturbingly, however, the nagging continued relevance of Snow's phrase should force us to rethink our intended solutions to today's moral concerns, including energy policy, global warming, and genetic engineering." —ROBERT P. CREASE OF STONY BROOK UNIVERSITY, WRITING ABOUT THE 50TH ANNIVERSARY OF C.P. SNOW'S "THE TWO CULTURES" LECTURE, AT PHYSICSWORLD.COM

Science Past | FROM THE ISSUE OF JUNE 6, 1959

A squirrel monkey wears a special molded plastic helmet over leather like the one that protected Monkey Baker, one of two primates blasted into space on May 28, 1959.

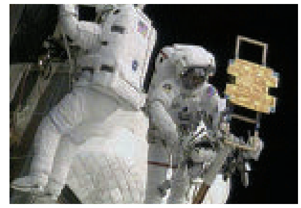
SPACE FLIGHT SUCCEEDS — Two little monkeys, one clad in a space suit and the other lying in a special capsule with her knees drawn up under her, were blasted 300 miles into space on Thursday, May 28, from Cape Canaveral, Fla., the National Aeronautics and Space Administration has revealed. Drama of the experiment was heightened as U.S. Navy frogmen successfully snatched the missile nose cone from shark-infested waters in the Atlantic Ocean. This makes the animals the first monkeys known to have been shot into space and successfully retrieved.… The monkey experiment helps pave the way for "Mr. Mercury," one of the seven men to be chosen by NASA to ride the first manned space capsule in orbit.… Earthbound scientists were able to study the effects of noise, acceleration, deceleration, vibration, rotation and weightlessness upon the two little monkey pioneers as they zoomed into space, then whistled back at 10,000 miles an hour to their Atlantic landing point.

SN Online

www.sciencenews.org

ATOM & COSMOS

Astronauts completed the final space walk to repair the Hubble Space Telescope on May 18 (below). For stories and images visit www.sciencenews.org/HealingHubble



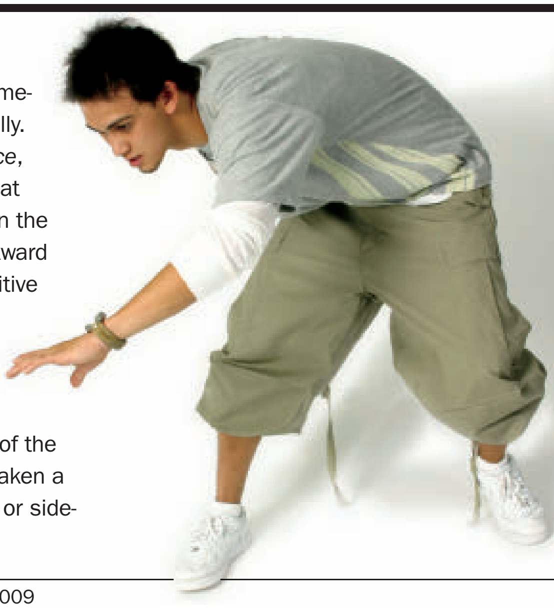
Science Future

June 7–19
High school students compete in the USA Biology Olympiad national finals in Fairfax, Va. See www.cee.org/programs/usabo

July 11–15
American Society for Virology annual meeting in Vancouver, Canada. See www.asv2009.com

September 15
Deadline for the International Science & Engineering Visualization Challenge. Visit www.nsf.gov/news/special_reports

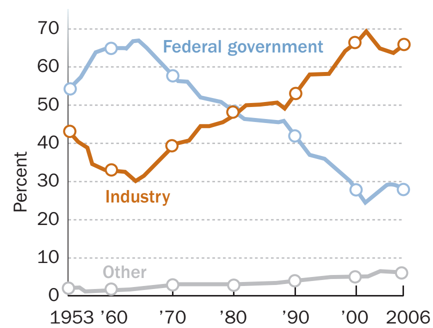
How Bizarre



If you're having trouble with something, take a step back — literally. In the May *Psychological Science*, Severine Koch and colleagues at Radboud University Nijmegen in the Netherlands report that a backward step appears to enhance cognitive control. Participants in a study who were shown a color word in a different hue — such as *blue* shown in red — stated the color instead of the word more quickly if they had taken a step backward, versus forward or sideways, just before the task.

Science Stats | R&D SPENDING

Proportion of national research and development expenditures funded by U.S. government and industry, 1953–2006



SOURCE: SCIENCE & ENGINEERING INDICATORS, 2008

CLOCKWISE FROM TOP LEFT: ©PETER MENZEL/MENZELPHOTO.COM; NASA TV; ERIC FOUGÈRE/VIP IMAGES/CORBIS; *SCIENCE NEWS LETTER*

> “It is fair to say we probably won’t see a lot of solar storms from this cycle.” — DOUGLAS BIESECKER, PAGE 14

(PAGE 14)

In the News

STORY ONE

Scientists find reactions that may have helped to get life started

New chemical tactics create two of RNA’s four basic units

By Solmaz Barazesh

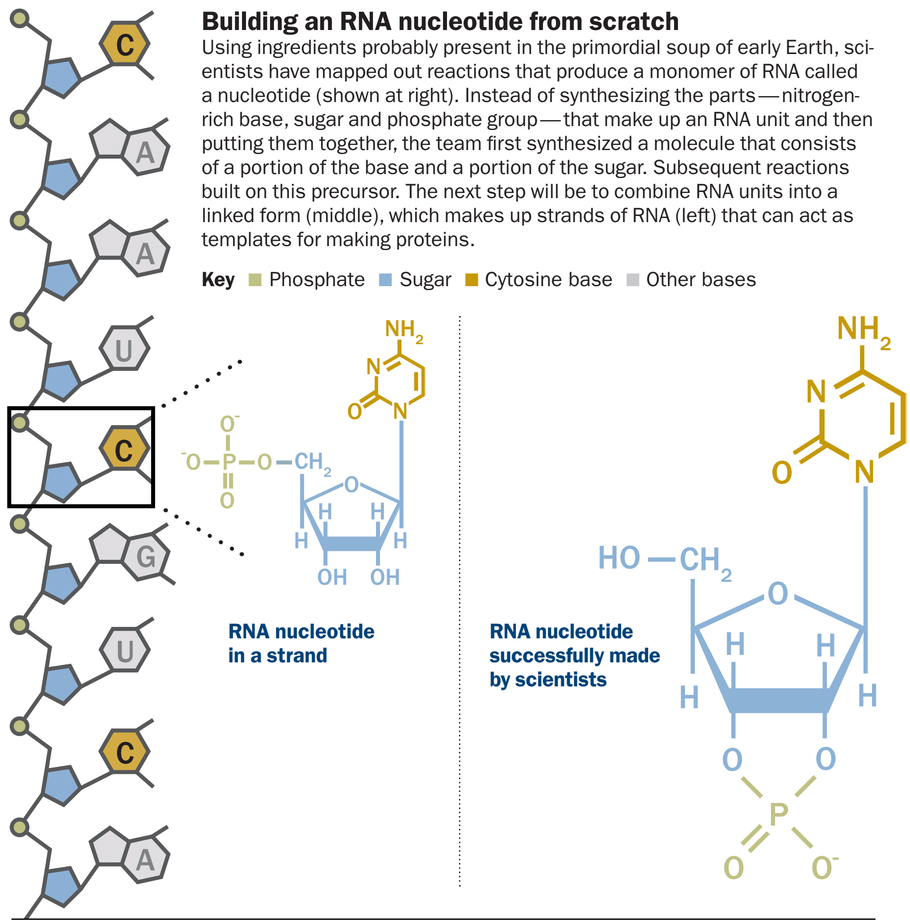
Scientists may have figured out the chemistry that sparked the beginning of life on Earth.

New findings map out a series of simple, efficient reactions that could have formed units of RNA, a close cousin of DNA, from materials available more than 3.85 billion years ago, researchers report May 14 in *Nature*.

“This is a very impressive piece of work — a really excellent analysis,” comments James Ferris of the Rensselaer Polytechnic Institute in Troy, N.Y.

The research supports the idea that RNA-based life-forms were the first life on Earth. Now called the “RNA world” hypothesis, the idea was first proposed some 40 years ago. But scientists hadn’t been able to figure out the chemical reactions that could have created the earliest RNA molecules.

Today, DNA encodes the genetic blueprint for all life — excluding RNA-based viruses, which some consider to be living. RNA usually helps to make protein from DNA, among other tasks. But most scientists think it’s unlikely that DNA was the basis for the first life, says study coauthor John Sutherland of the University of Manchester in England.



Building an RNA nucleotide from scratch
Using ingredients probably present in the primordial soup of early Earth, scientists have mapped out reactions that produce a monomer of RNA called a nucleotide (shown at right). Instead of synthesizing the parts — nitrogen-rich base, sugar and phosphate group — that make up an RNA unit and then putting them together, the team first synthesized a molecule that consists of a portion of the base and a portion of the sugar. Subsequent reactions built on this precursor. The next step will be to combine RNA units into a linked form (middle), which makes up strands of RNA (left) that can act as templates for making proteins.

CHARLES FLOYD

Information-bearing DNA holds the code needed to put proteins together, but proteins catalyze the reactions that produce DNA. It’s a chicken-or-egg problem. Scientists don’t think that DNA and proteins could have come about independently and yet still work together in this way.

It’s more plausible that the first life-forms were based on a molecule that could replicate itself and store genetic information — a molecule such as RNA (*SN: 4/7/01, p. 212*). Proponents of the RNA world speculate that modern DNA and proteins evolved from this RNA-dominated early life, and that RNA in cells today hails from this early time.

RNA molecules are polymers formed from repeating units, or monomers, of three components: a sugar, a nitrogen-rich base and a phosphate group. RNA is made up of four types of these monomers, called nucleotides.

While reactions to make RNA from ancient precursors worked on paper,

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SN Today at **www.sciencenews.org**

the chemistry didn't work in the lab. And some scientists thought that even RNA molecules were too complex to have spontaneously formed in the primordial soup. "We didn't have any convincing synthesis of RNA monomers," Ferris says. Sutherland and colleagues have now shown that the reactions are possible.

In past research, chemists developed each of the components and then tried to put them together to make a complete nucleotide. "But the components are quite stable, and so they wouldn't stick together," Sutherland says. "After 40 years of trying, we decided there had to be a better way of doing this reaction."

The team tried mixing cyanamide and glycolaldehyde, two chemicals probably present in the primordial soup, to make a molecule with a bit of the sugar and the base. The next stages of the reaction built on this molecule, called 2-amino-oxazole, adding the other parts one at a time.

"Basically, we took half a base, added that to half a sugar, added the other piece of base, and so on," Sutherland says. "The key turned out to be the order that the ingredients are added and the way you put them together — like making a soufflé."

Another difference is that the team added the phosphate to the mix earlier than in past experiments. The phosphate group acted as a pH buffer and helped later stages of the reaction occur more quickly and efficiently, the scientists say.

The final result of the reactions was ribocytidine phosphate, one of the four nucleotides in RNA. Shining UV light on the nucleotide converted it to another type, the researchers say. But the last two nucleotides still need figuring out.

"It's related chemistry," Sutherland says. "That's how it must have been in the very beginning — a series of fundamental reactions that could make all four types of RNA monomer."

The starting materials and the conditions of the reaction are consistent with models of the geochemistry of an early Earth, the team says. "The different reactions require different conditions, so we envisage a sequence of geochemical events" allowing the reactions to occur, Sutherland says.

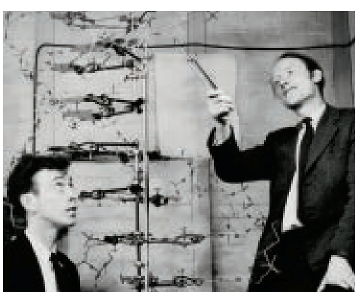
But Ferris points out that this advance is not the whole picture. "It's not as simple as putting compounds in a beaker and mixing it up. It's a series of steps. You still have to stop and purify and then do the next step, and that probably didn't happen in the ancient world."

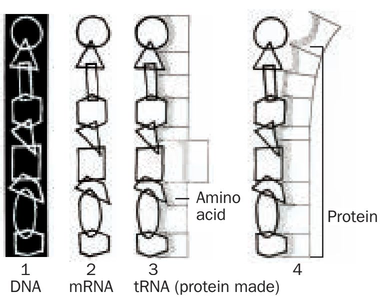
Once all four nucleotides are synthesized, the team will work on stringing them together into a strand of RNA that could act as a template to make proteins.

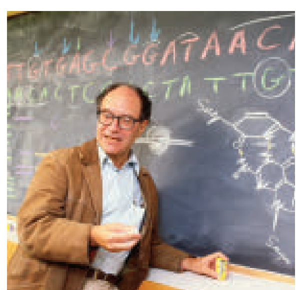
Connecting RNA monomers into polymers is something Ferris works on in his lab. He says that adding an activation group to RNA monomers and mixing a clay mineral into the reaction made the monomers connect into strings of 40 or so units. The activation group, called 1-methyladenine, made joining the RNA monomers more energetically favorable, Ferris explains. The clay mineral, montmorillonite, catalyzed the reaction. Montmorillonite is a derivative of volcanic ash, so it may have been available on early Earth where volcanic eruptions were common, the researchers say. A combination of making the monomers as Sutherland's group showed and stringing them together as Ferris and colleagues described could have made the first RNA strands, Ferris contends.

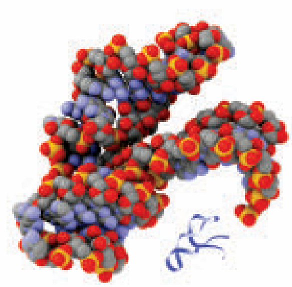
Once RNA polymers were translated into protein, in theory, these proteins could fabricate all the components that make up a cell, setting the stage for evolution to take its course. But exactly how that happened "remains an unanswered question," Sutherland says. ■

Back Story | HISTORY OF A HYPOTHESIS









April 1953
James Watson (left) and Francis Crick discover the structure of DNA, finding it can be replicated. The find set the stage for the discovery of RNA.

May 1953
Stanley Miller and Harold Urey's experiments suggest that amino acids, protein building blocks, spontaneously arose in the young Earth's primordial soup.

1960s
Sydney Brenner, François Jacob and Matthew Meselson show that messenger RNA (above) carries the information required to make proteins.

1967
Carl Woese and, later, Crick and Leslie Orgel independently propose that RNA may have been the earliest repository of genetic information.

1986
Walter Gilbert (shown) coins the phrase "RNA world" for the early Earth environment in which RNA stored information and replicated itself.

1989
Thomas Cech and Sidney Altman share the Nobel for finding that certain RNA molecules, called ribozymes, can cut and join each other—replication.

FROM LEFT: A. BARRINGTON BROWN/PHOTO RESEARCHERS; BETTMANN/CORBIS; LOUIE PSIHOYOS/SCIENCE FACTION/CORBIS; LAGUNA DESIGN/PHOTO RESEARCHERS

The Truth About Paris After Midnight

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I probably shouldn't tell this story, but that's never stopped me before. Curiosity got the best of me during a recent stop in Paris and I found myself strolling through Montmarte toward the Moulin Rouge. Yes, *that* Moulin Rouge. The same cabaret that was famous a hundred years ago for its show-girls and outrageous entertainment. I'd always wanted to see the Can-Can up close, so I headed for the big red windmill.

The show was racy enough to cause a blush or two, but I survived. Then a photo on the wall caught my eye. It was dancer Josephine Baker, drizzled in pearls from head to toe. The inspiration hit me on the walk down the Champs- Elysees.

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Research agencies would get boost from president's proposed budget

Most increases rely on already approved stimulus money

By Janet Raloff

The Obama administration rolled out new details on May 7 about its blueprint for federal spending for fiscal year 2010. And no matter how you cut it, science comes out a big winner. The current proposal is to spend $147.6 billion on research and development during the fiscal year beginning October 1 — $555 million more than Congress enacted for the current fiscal year.

This spending would be supplemented by the already approved American Recovery and Reinvestment Act of 2009, also known as the economic-stimulus package. It directs the government to pump $20 billion into R&D, money to be spent between now and the end of fiscal year 2010, said White House science adviser John Holdren at a press briefing held at the American Association for the Advancement of Science's offices in Washington, D.C. Most of this bonus is being directed into research rather than development.

For instance, the stimulus directs that the National Institutes of Health spend $10 billion on biomedical research and laboratory upgrades or construction. The boost provides another $1 billion to be shared between NIH and the Agency for Healthcare Research and Quality on studies that compare either the effectiveness of different treatments or the effectiveness of one treatment for different populations.

The National Science Foundation, the Energy Department's Office of Science and the National Institute of Standards and Technology together received $5.2 billion from the stimulus package alone. This funding keeps these three agencies on track for a 10-year doubling of their budgets by 2016, Holdren said.

Bottom line: "We in the science and technology community have done better than just about any other constituencies in the budget," Holdren said. But, he added, "We think that's good for the country, not just good for us."

Many science-policy wonks and budget watchers have become almost giddy with what they've seen happening in Washington this year. If Congress approves the president's spending plan, NASA, for instance, would get a 10 percent increase next year.

> "It is an unprecedented year.… There's also been a dramatic shift in research priorities."
>
> ALBERT TEICH
> AAAS

This increase for NASA would include $225.4 million more for space exploration studies and $59.5 million for aeronautics programs. The science budget would lose $4.8 million. These changes are independent of the Recovery and Reinvestment Act.

"It is an unprecedented year," says Albert Teich, director of Science & Policy Programs for AAAS. "There's also been a dramatic shift in research priorities" from those espoused by the Bush White House. Obama is backing climate research, green energy, physical science and engineering research, biomedical studies, and science and math training from prekindergarten through graduate school.

Without the stimulus supplement, spending remains fairly flat from this year to the next for NIH, the Centers for Disease Control and Prevention and the Agency for Healthcare Research and Quality, notes Stacie Propst of Research! America, based in Alexandria, Va. For NIH, next year's projected spending without the stimulus is $30.8 billion, only slightly more than was appropriated for the current year. The increase does not keep up with inflation, so it appears that the administration is using the stimulus funding as a bridge to next year, she says.

"We're concerned," she says, because if baseline budgets don't climb dramatically by 2011, when the stimulus money disappears, "there's going to be drop-off in all of the jobs that the Recovery Act saved."

Teich agrees. The president has said that he plans to begin paying back the deficit as soon as the economy picks up, and the stimulus was sold as a one-shot investment, Teich notes. "So I think we're going to face some very difficult times in coming years — 2011 and 2012." ■

Federal research and development funding

Fiscal year 2010 budget by agency (in millions of dollars)

Agency	FY 2010 proposed	Change from FY 2009	Allocation from Recovery Act
Department of Defense	79,687	–2.4%	300
National Institutes of Health	30,184	1.5%	10,400
NASA	11,439	10.0%	925
Department of Energy	10,740	1.1%	2,446
National Science Foundation	5,312	9.4%	2,900
Department of Agriculture	2,272	–6.2%	176
NOAA	644	–8.0%	1
NIST	637	15.8%	410
U.S. Geological Survey	649	6.2%	74
EPA	619	6.7%	0
Remaining R&D*	5,437	9.6%	703

*Includes departments of Transportation, Veterans Affairs, Education, Homeland Security, Interior (excluding USGS), Commerce (excluding NOAA and NIST), Health and Human Services (excluding NIH), and others. Percent change is not adjusted for inflation.

SOURCE: OFFICE OF SCIENCE & TECHNOLOGY POLICY

“We keep [science’s] mystery and its beauty to ourselves at our peril.”— ELIZABETH MARINCOLA

Intel science fair recognizes top young scientists

Winners investigate bees, nematodes, glowing bacteria

By Rachel Ehrenberg

From left, Li Boynton, Tara Adiseshan and Olivia Schwob each won top honors and a $50,000 scholarship at the Intel International Science and Engineering Fair.

TONY MARABLE

RENO, Nev. — What happens in Reno doesn’t stay in Reno, and some high school students are very pleased about that. On May 15, three top finalists at the Intel International Science and Engineering Fair hit the jackpot, each winning a $50,000 scholarship from the Intel Foundation. Those prizes were part of nearly $4 million in scholarships, tuition grants and scientific trips and equipment awarded at the world’s largest high school science competition.

Olivia Schwob, 16, of Boston won for her experiments that helped the roundworm (or nematode) *Caenorhabditis elegans* learn better. Previous work had shown that the GAP-43 protein is important in learning in humans. Schwob thought this protein might improve learning in the lowly roundworm, so she introduced the *GAP-43* gene into the worm’s DNA. When worms that made the protein received a positive or negative stimulus, they changed their behavior more than those without the protein. The work may help researchers better understand learning disabilities in humans.

Li Boynton, 17, of Houston won a top prize for developing a technique that uses the bioluminescent bacterium *Vibrio fischeri* to detect environmental contaminants. Boynton exposed the bacterium to several pollutants, such as the herbicide atrazine, and correlated the extent of the bacterium’s glow to the level of contaminant exposure. Her analysis could yield a quick and cheap method for detecting pollutants in water.

Tara Adiseshan, 14, of Charlottesville, Va., won for her investigation of the evolutionary relationships between several species of sweat bees and the species of nematodes that live in the bees but do not harm them. Adiseshan determined the genetic coding of a specific gene found in the bees and the nematodes. Then she used these different DNA sequences to build family trees for both groups of organisms. Her analysis revealed that the bees and nematodes had a tight-knit relationship throughout evolutionary history, diverging into new species at the same time.

“With your achievements come responsibilities,” Elizabeth Marincola, president of Society for Science & the Public, which publishes *Science News* and administers the science fair, told the finalists at the May 15 awards ceremony. “The science-initiated must rise to the challenge of becoming science communicators. We keep its mystery and its beauty to ourselves at our peril.”

Other top prizes included the Seaborg SIYSS Award, which is an all expense–paid trip to the Stockholm International Youth Science Seminar in Sweden and entry to the Nobel Prize ceremonies. The award is named in honor of chemist and Nobel laureate Glenn T. Seaborg, who chaired the board of Society for Science & the Public, formerly Science Service. Two students won Seaborgs. Eric Larson, 17, of Eugene, Ore., won for his work on algebraic fusion categories, which have implications for theoretical physics and computer science. Preya Shah, 17, of East Setauket, N.Y., was honored for her development of tumor-targeting drugs that provide a one-two punch. Larson and Shah were also winners of the Intel Science Talent Search in March: Larson won first place and a $100,000 scholarship and Shah won eighth place and a $20,000 scholarship.

Two student teams and 17 individuals won “best of” awards — a $5,000 scholarship, laptop computer and a trip to Geneva to tour the CERN research center — for work in specific disciplines.

“The real end point of the Intel International Science and Engineering Fair is to elevate the recognition of achievement of the younger generation in academic and learning exercises,” said Craig Barrett, then chairman of Intel’s board. “I hope that more young people will look at these students and realize they can be recognized for using their brains. You don’t have to be a quarterback, a basketball player or a baseball player to be recognized by your peers and the public.”

Genes & Cells

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Genetic study links narcolepsy to autoimmunity

Other risk factors probably serve as disease triggers

By Tina Hesman Saey

Scientists have identified a second genetic tie that cements a connection between a disabling sleep disorder and the immune system.

Emmanuel Mignot of Stanford University led a team searching for the genetic causes of narcolepsy. The team reports online May 3 in *Nature Genetics* that several genetic markers associated with narcolepsy map to a gene important for turning the immune system's T cells into microbe killers.

For decades scientists have known that people with narcolepsy are more likely to have a particular version of a gene called *HLA-DQB1*0602*. The gene belongs to the HLA class of genes that make key immune proteins. These proteins present small bits of invading microbes to T cells, much like a handler waves a sweat-laden sock in front of a bloodhound. The proteins help T cells identify, track down and kill the foreign cells. In autoimmune disease, T cells may run amok, mistakenly attacking the body's own healthy cells.

Given the association between narcolepsy and the HLA gene, the lethality of T cells intrigued scientists studying the sleep disorder. Neurons that make a wake-promoting protein called hypocretin die in people who have narcolepsy. Death of the cells means that people can't make enough hypocretin to stay awake, and they experience sudden bouts of sleep during the day and disrupted sleep at night. About one in every 2,000 people in the United States has narcolepsy with cataplexy, a sudden loss of muscle tone that can cause people to collapse.

Neurons that make a wake-promoting protein called hypocretin die in people who have narcolepsy.

That T cells may cause the death of hypocretin-producing cells seemed like a no-brainer to Mignot.

"If you're like me you think, 'Duh, if you've got these associations, it's got to be autoimmune,'" he says. "The problem is no one has been able to prove that." HLA proteins are also found in neurons and other nonimmunity cells, so the death of the hypocretin cells could have had nothing to do with the immune system.

Now, Mignot and his colleagues have found a genetic link between narcolepsy and a gene that encodes the T cell receptor alpha, which interacts with HLA proteins to trigger an immune reaction.

"This solidly positive association provides additional evidence that narcolepsy is an autoimmune disorder," says Masashi Yanagisawa, a neuroscientist at the University of Texas Southwestern Medical Center at Dallas.

The researchers studied 1,830 people who have narcolepsy with cataplexy and 2,164 healthy controls. People with narcolepsy were more likely than healthy people to carry three genetic markers in the area of the genome containing the *T cell receptor alpha* gene.

But the association is not the final piece of the puzzle, Mignot says. Even with all known genetic risk factors, a person has only a 1.5 percent chance of developing narcolepsy, he says. That suggests that there are other genetic and environmental risk factors.

Still the research "is a solid step" toward figuring out how the brain and immune system interact in narcolepsy, says Merrill Mitler of the National Institute of Neurological Disorders and Stroke in Bethesda, Md. "The principles that we're glimpsing because of this finding go well beyond narcolepsy," and may shed light on other autoimmune disorders, he says.

COURTESY OF SIMON TRAGUST, TOBIAS WEIL

Queen gene controls mob

Silencing one gene for a day may weaken the grip a termite queen has on her throne. Or at least let loose a lot of worrisome butting behavior among her subjects. Lab colonies of the termite *Cryptotermes secundus* (worker shown) started acting as if their queen were dead when researchers disabled her *Neofem2* gene, Judith Korb of the University of Osnabrück in Germany and her colleagues report in the May 8 *Science*. Thus *Neofem2* could be the first gene identified in termites that's crucial for queenly domination, Korb says. In the world of termites, honeybees and other ultrasocial creatures, the dominant female does most or all of the reproducing even if her workers still have the capacity. The gene may solve at least part of the puzzle of how the queen keeps them in line —*Susan Milius*

Body & Brain

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Force is strong for blood stem cells, at least in mice, zebrafish embryos

Studies show blood flow and nitric oxide boost production

By Tina Hesman Saey

Blood stem cells grow with the flow.

Two new studies, led by independent groups at Children's Hospital Boston, report that an embryo's heartbeat and blood circulation stimulate the growth of blood stem cells.

The find could be a boon to researchers seeking to make blood stem cells for people with blood cancers, immune system disorders and other diseases that require bone marrow transplants. In people, blood stem cells reside in the bone marrow and constantly replenish blood supply. Only about a third of patients who need bone marrow transplants have matching donors.

"Basically we cannot offer optimal therapy to two-thirds of patients," says Leonard Zon, director of the Stem Cell Research Program at Children's Hospital Boston and a coauthor of one of the new studies, appearing in the May 15 *Cell*.

Scientists can make red and white blood cells from embryonic stem cells easily in the laboratory, but producing blood stem cells, called hematopoietic stem cells, has been much more difficult, Zon says. Now, his group suggests that a little force can boost blood stem cell production in zebrafish embryos.

Reporting online May 13 in *Nature*, a group led by George Daley, director of the Pediatric Stem Cell Transplantation Program at Children's Hospital Boston, demonstrates that blood flow also triggers hematopoietic stem cell production in mouse embryos. Both groups found that nitric oxide plays a role.

Intuitively, scientists might expect that mechanical forces help shape development. But because of experimental difficulties, few biologists have studied this, says Ihor Lemischka of Mount Sinai School of Medicine in New York City. "I think we'll be seeing more of these types of studies," Lemischka says.

Daley's group directly tested the ability of blood flow to turn embryonic stem cells into hematopoietic stem cells. The team placed mouse embryonic stem cells in a centrifuge-like device that mimics shear stress — the frictional force blood creates when it flows over cells — in a mouse's aorta. In early embryos, blood stem cells first form on the floor of the aorta. Later they migrate to the bone marrow.

Embryonic stem cells exposed to the same magnitude of shear stress as found in the mouse aorta produced hematopoietic stem cells. Cells exposed to a different magnitude of stress didn't. A nitric oxide–blocking drug reduced the number of blood stem cells that stress induced. Nitric oxide is a chemical produced naturally in the body that helps regulate blood vessel growth and elasticity.

When the researchers gave the nitric oxide blocker to pregnant mice, mouse embryos also had problems making blood stem cells.

Zon's team used zebrafish embryos, which are transparent, to watch the stem cells develop. The team found that chemicals that increase blood flow in the tails of the embryos also boost activity of the *RUNX1* gene, a master regulator of blood stem cells. Mutant embryos that don't have a heartbeat don't make many hematopoietic stem cells in their tails.

When the researchers gave a nitric oxide–boosting compound to the mutant embryos, however, the embryos produced more blood stem cells. And the nitric oxide blocker inhibited blood stem cell production, the researchers found. Those findings suggest that blood flow may increase nitric oxide levels, which then boost stem cell production, Zon says.

NEWS BRIEFS

Scorpion venom neutralized

The Arizona bark scorpion may be small, but its sting delivers a neurotoxin that can kill or render critically ill a young child. A study in the May 14 *New England Journal of Medicine* finds that an antivenom used in Mexico for such stings neutralizes the toxin, eliminates symptoms and reduces the need for sedation in children who have been stung. Eight of eight critically ill children receiving the antivenom showed no signs of venom in their blood after one hour and recovered within four hours, reports Leslie Boyer of the University of Arizona in Tucson. A sting's effects typically take an average of 16 hours to fade. —*Nathan Seppa*

Misread marks and cancer

Scientists have shed light on how a genetic mutation linked to acute myeloid leukemia may trigger the disease. The problem arises when cells misinterpret chemical tags called epigenetic marks on certain genes, a new study shows. Similar problems probably lie at the heart of other diseases and may represent a new category of diseases, Gang Wang and David Allis of Rockefeller University in New York City and their colleagues report online May 10 in *Nature*.

In some patients with AML, the blood cancer seems to be triggered by a fusion of parts of two proteins, researchers discovered recently. The fused proteins interfere with the cell's ability to regulate epigenetic marks, which act as volume controls, on some genes, the new study shows. This misunderstanding can lead to cancer. —*Tina Hesman Saey*

Life

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To treat, not treat art-covering fungi

Biocides confer resistance to Lascaux cave's microbes

By Sid Perkins

Fungal infestations threaten Stone Age art (shown) in Lascaux cave in France. But new research suggests treating the microbes with biocides has its downsides.

Biocides used in recent years to treat the growth of fungi on the prehistoric-art–festooned walls of France's Lascaux cave have eradicated some populations of human-introduced bacteria and fungi. However, some of those that remain — including some related to known human pathogens — are becoming resistant, researchers report in an upcoming issue of *Naturwissenschaften*.

Human presence has caused problems in Lascaux almost since the cave's discovery in 1940, says Claude Alabouvette of the University of Bourgogne in Dijon, France. Heat from lights that illuminate the art, as well as tourists' body heat, exhalations and left-behind skin cells, has changed the cave's environment drastically.

Earlier this decade, scientists found that black and white fungi had infested parts of the cave and were threatening to cover the art. Recent biocide treatments have halted the spread of fungi in most areas, but their pigments remain.

Alabouvette and colleagues analyzed around a dozen samples from the cave. The tests confirmed that in oft-visited portions, especially those frequented by tourists before the cave was closed to the public in 1963, microbial diversity is high. In some areas, bacteria from the genera *Pseudomonas* and *Ralstonia* — groups that include several microbes that cause disease in humans — make up more than half the organisms in the samples.

Lab tests also hint that two of the *Pseudomonas* species isolated from the Lascaux samples have adapted to survive biocide treatment. Though the cave's microbes aren't a proven threat to human health, they could be in the future, Alabouvette speculates. This find, combined with the fact that biocides break down to form carbon- and nitrogen-containing compounds that microbes could use as nutrients, further concerns the researchers.

"Now we are wondering what is more dangerous, treating or not treating?" Alabouvette says.

Robert J. Koestler, director of the Smithsonian Institution's Museum Conservation Institute in Suitland, Md., thinks treatment is still the best option. If the fungi grow, they will further taint the walls, he says.

Basking sharks go south

When winter comes, many people vacation in the Caribbean. A new report suggests basking sharks have the same idea. Using satellite-based tagging technology, Gregory Skomal of the Massachusetts Division of Marine Fisheries' Martha's Vineyard research station and his colleagues found that the sharks migrate to tropical waters when the weather in their temperate habitats gets cold, some going as far as Brazil. The study, published online May 7 in *Current Biology*, provides the first information on where the sharks hide out for winter, a mystery that has flummoxed marine biologists for years. Why the sharks make the trip is still unknown. "Energetically, it doesn't make sense to swim so far south," Skomal says. Perhaps the tropics provide a good shark nursery with stable temperatures and few predators, the scientists propose. — *Solmaz Barazesh*

FROM TOP: RALPH MORSE/TIME & LIFE PICTURES/GETTY IMAGES; CHRIS GOTSCHALK

Environment

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School-age lead exposures may do more harm than earlier exposures

Levels in 6-year-olds tied to IQ, tissue loss, future criminality

By Janet Raloff

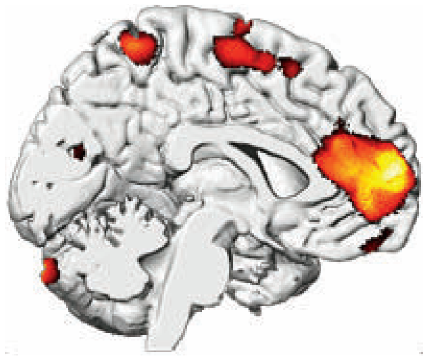
Testing for lead only in infants and toddlers may be a mistake, a new study suggests. Pediatricians routinely test very young children at ages when blood concentrations of the neurotoxic heavy metal tend to be highest. But older children can face significant lead exposures, and lead's ability to lower IQ is much greater for exposures in early school-age children than in toddlers, the new study suggests.

The study, appearing in an upcoming *Environmental Health Perspectives*, also finds that later childhood exposures correlate more strongly than earlier ones with an increased risk of incurring future criminal arrests for violent behavior.

The new data "get at a key concept in environmental health: that there may be some windows of vulnerability — stages of development — that are more vulnerable than others," notes Howard Hu of the University of Michigan in Ann Arbor. If school-age brains are more susceptible to lead toxicity than younger ones, "that's important to know, from a public health perspective," he says. Looking for raised lead levels in older children would be a first step in identifying families that need counseling on reducing sources of lead in and around the home.

Richard Hornung and his colleagues at Cincinnati Children's Hospital Medical Center analyzed data on lead levels and IQ from 462 children. About half of the data were collected from Cincinnati kids in 1979 and the 1980s, the rest from kids in Rochester, N.Y., in the mid-1990s.

Many studies have linked elevated lead exposures in 2-year-olds with a diminished IQ at school age — even when peaks never exceeded the federal action level of 10 micrograms of lead per deciliter of blood. Previous studies, however, hinted that where blood-lead values were available for school-age children, these tracked with IQ better than those from toddlerhood. Hornung's team probed that possibility in two groups of intensively monitored inner-city children.



A new study suggests a brain area involved in planning and reasoning (yellow on composite map) had substantial lead-related reductions in tissue volume.

K. CECIL, C. BRUBAKER, K. DIETRICH (FROM AN UNPUBLISHED STUDY)

The researchers compared IQ at age 6 — about the youngest that intelligence can be reliably assessed — with ratios of lead levels. The team looked at the ratio of the blood level of lead at each age through age 6 to the level at age 2 (for example ages 3 to 2 or 4 to 2). The researchers also compared IQ with the average lead value through age 6 and with a youngster's peak lead value. Far and away, lead ratios at ages 5 and 6 were most predictive of IQ losses, the Cincinnati-based scientists report.

IQ averaged 7 points lower when the age-6 blood-lead value was 50 percent greater than the value at age 2, as compared with when the age-6 value was 50 percent less than at age 2.

Indeed, for children having identical average lifetime blood-lead values, higher ratios at early ages showed a much smaller impact on IQ than elevated ratios at ages 5 and 6, Hornung says.

The Cincinnati group "used a relatively innovative statistical method," says epidemiologist Aimin Chen of Creighton University in Omaha, Neb. In 2005, while working at the National Institute of Environmental Health Sciences, he reported a similar observation: Blood-lead values at age 7 were more predictive than those at age 2 of IQ decrements. But this study wasn't able to point to where the potency of lead seemed to pick up.

The Cincinnati team's new study strengthens this link and suggests that screening 2-year-olds is not enough. "We should expand community screening to school-age kids," Chen says.

Adds Hu, "If there are major differences in vulnerability to lead, we need to understand why."

Kim Cecil, also of Cincinnati Children's Hospital, thinks she's homing in on part of the answer by analyzing magnetic resonance images of now-adult participants of the Cincinnati cohort studied by Hornung's team.

Last year, she and her colleagues linked lead exposures through age 6 in the Cincinnati cohort to reduced tissue volumes in areas of the adult brain — especially regions of the frontal lobe related to judgment, impulsivity and mood. The researchers used magnetic resonance imaging to compare the relative size of brain regions in 157 participants against records of their childhood lead levels.

In a new analysis that she'll be publishing soon, Cecil finds that here, too, the size of affected brain areas — the reduced tissue volume in them — tracked best with lead exposures at ages 5 and 6.

Hornung's team also surveyed data on criminal records for the now-adult Cincinnati participants. In the new *EHP* paper, the team shows that the likelihood that those participants had acquired a juvenile or adult arrest for violent behavior such as assault, rape or homicide correlated best with childhood elevations in lead at ages 5 and 6, notes Kim Dietrich, a coauthor of the study.

Atom & Cosmos

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Dead stars could help astronomers detect subtle ripples in spacetime

Gravitational waves would disrupt pulsar's radio emissions

By Ron Cowen

DENVER — A bunch of dead stars could serve as ready-made recorders for gravitational waves — subtle ripples in spacetime that if discovered would be the crowning achievement of Einstein's theory of general relativity, astronomers propose. Researchers have invested hundreds of millions of dollars to perfect sensitive devices on the ground and launch even more sophisticated experiments in space to detect this cosmic symphony.

The new search technique would instead rely on radio waves generated like clockwork by millisecond pulsars — the collapsed remnants of massive stars that spin about once every one to 10 milliseconds. The speed at which these pulsars rotate enables researchers to measure the timing of the radio waves' arrival at Earth with high accuracy.

Measuring arrival time is critical, says Frederick Jenet of the University of Texas at Brownsville and Texas Southmost College, who presented the proposal on May 2 at an American Physical Society meeting. Colleague Andrea Lommen of Franklin & Marshall College in Lancaster, Pa., reported additional details on May 5.

A gravitational wave passing by the pulsar would warp spacetime, altering the arrival time of the pulsar's radio waves ever so slightly. First the pulses would appear a little earlier, then a little later. The changes in timing would depend on the phase and direction of propagation of the gravitational wave, as well as its distance from the pulsar, Jenet notes.

Low-frequency gravitational waves, produced by the merger of supermassive black holes, would generate the biggest changes in arrival time and therefore be easiest to detect. To detect a general background of such waves, astronomers would need to monitor 20 of the millisecond pulsars for five to 10 years, with the arrival time of the radio waves determined to an accuracy of 100 nanoseconds, Jenet estimates. Recording individual gravitational waves produced when black holes merge would require five pulsars with radio wave arrival times known to 10 nanoseconds, he adds.

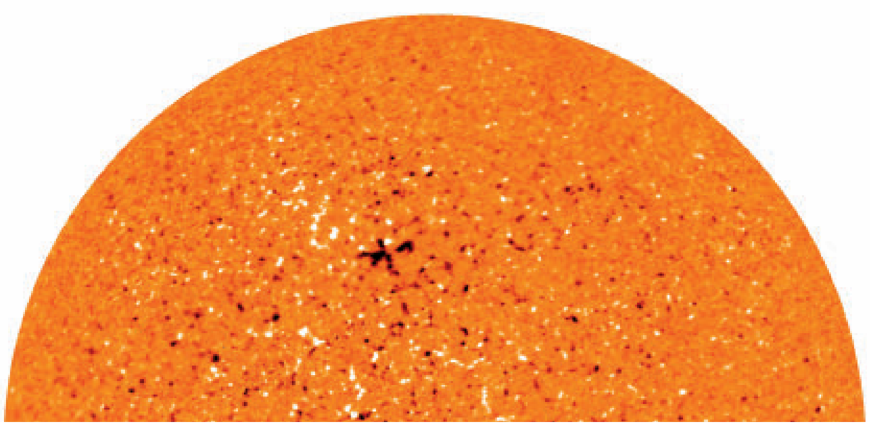
"We currently have about 20 millisecond pulsars, but only five of these can be timed to the needed precision," he notes.

The idea of using pulsars to search for gravitational waves dates back to the late 1970s, Jenet says. "Personally, the romantic notion of building a galactic-scale gravitational wave observatory using exotic stars as part of the instrument itself seems quite appealing," he says.

Using pulsars to search for gravitational waves "is not a crazy idea but a well-established area of research," says Tom Prince of Caltech. The increased sensitivity of radio telescopes and the discovery of additional millisecond pulsars have made the idea practical.

Scientists are currently using several large-scale gravitational wave detectors on Earth, including the twin LIGO detectors. Prince leads an effort to launch a detector called LISA into space sometime in the next decade. LISA will look for high-frequency gravitational waves, while the pulsar method would look for low-frequency waves.

Still, Jenet says, the pulsar method is available now, without the need for new telescopes.



Calm expected from the sun

The sun has entered its weakest cycle of magnetic activity since 1928, meaning fewer solar flares and coronal mass ejections, scientists predicted in a May 8 teleconference. A panel assembled by the National Oceanic and Atmospheric Administration's Space Weather Prediction Center reported that the cycle, which scientists believe began in December 2008, will peak in May 2013. (Cycles usually last about 11 years.) "It's fair to say we probably won't see a whole lot of solar storms from this cycle," Douglas Biesecker of NOAA's Space Environment Center in Boulder, Colo., said at the teleconference. "But a weaker cycle won't lessen the intensity of the storms, just the number of them." Scientists use the number of sunspots, blotches of concentrated magnetic activity on the surface of the sun, as a measure of solar activity. (This May 2009 image shows a quiet sun, with minimal magnetic activity.) The new predictions are based on the cycle's slow start. — *Solmaz Barazesh*

NOAA

Molecules

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Molecule turns red as it breaks

Materials containing it may offer a signal when stressed

By Laura Sanders

Engineers one day may not have to guess when a bridge is about to break. New materials that flush red in response to damage may provide a visible warning sign of trouble to come, scientists report in the May 7 *Nature*.

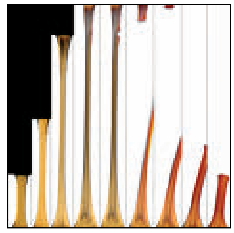
"I think it could be a milestone," says Christoph Weder of Case Western Reserve University in Cleveland and the University of Fribourg in Switzerland.

The materials' chameleon-like abilities are thanks to a small four-ringed molecule called a mechanophore. When the weakest bond in the mechanophore breaks, the molecule takes on a dog-bone shape. The reaction causes the molecule to redden.

"It's a really simple detection method," says study coauthor Nancy Sottos of the Beckman Institute for Advanced Science and Technology at the University of Illinois at Urbana-Champaign.

But it's hard to apply a force to something so small, so Sottos and her colleagues spiked two polymers — a stretchy, soft one and a hard, glassy one — with the molecule.

In the stretchy polymer, the bright red color appeared a few seconds before the material snapped, suggesting the molecules acted as an early indicator that the material had incurred damage. This material also reddened after a few cycles of stretching and relaxing that did not end in breaking. Hard, glasslike beads of the second polymer darkened after squeezing, indicating that the change was triggered by mechanical forces.



A polymer made with a color-changing molecule turns red when stretched and eventually snaps.

D. STEVENSON, A. JEREZ, A. HAMILTON, D. DAVIS

Others have done tricks with color-changing molecules, Weder says, but never before in a solid.

Sottos says the molecule could eventually be used to make products including in-line skate wheels, paints to coat structures such as bridges, or even thin fibers that turn red to signal deformations.

Serotonin: What the Gut feeds the Bones

Chemical messenger plays a surprising role in determining the strength of the skeleton

By Laura Beil

The hip bone is connected to the backbone. The backbone is connected to the neck bone. And lately, scientists have begun to think that all dem bones may be connected to the intestine — at least by biochemical signals. If the current evidence holds up, it means that a chemical better known for influencing the brain may also corrode the internal structure of the skeleton.

Such is the state of research into bone biology: "The more we understand, the more complex it gets," says Clifford Rosen of the Maine Medical Center Research Institute in Scarborough. Rosen is one of a growing number of researchers who think that the brain, intestine and skeleton are conducting an ongoing biochemical negotiation that affects the ebb and flow of tissue building inside bones. One of the chief currencies appears to be serotonin, a neurotransmitter most famous for its role in depression.

The idea that serotonin might be bad news for bones came as a surprise almost a decade ago. And the notion that the intestine hosts a serotonin-bone command center — first described last fall — was more surprising still. "It's thrown the field into a bit of an uproar," says Michael Bliziotes of Oregon Health & Science University in Portland.

By eavesdropping on the crosstalk between the intestine and skeleton, researchers hope to find much-needed ways to help protect bones into old age. More than 300,000 elderly Americans suffer hip fractures each year; one in five die within a year from complications of the injury. Bone-strengthening medications have been hard to come by, largely because bone is simultaneously one of the most simple and most convoluted structures in the body — brilliant and straightforward in engineering, yet owing its construction to an elaborate relationship with internal organs.

It's easy to perceive bones as dense and dead. But on the inside, bones are not hard like blocks of wood, but airy, like sponges. The internal, honeycomb-like scaffolding allows bones to be sturdy without leaving them too heavy. Strength isn't determined by density but by the makeup of the matrix within (in the same way a china plate is denser than a plastic one but less likely to survive a drop on the floor).

Neither are bones dead. Throughout life, bones are constantly remodeling themselves, constructing new tissue in some places, clearing out old bone in others. As with hair or skin, worn bone tissue is constantly replaced with new in what is called bone turnover. Bones generally reach their maximum strength in early adulthood, after which they gradually wear away. After decades of erosion, bone density sometimes dips low enough to qualify as osteoporosis. That disorder occurs largely because, as people age, cells that secrete new bone, called osteoblasts, don't work as robustly as osteoclasts, cells that resorb or break down bone, especially in postmenopausal women. Most treatments for osteoporosis slow the loss of bone; the one drug that can build bone costs thousands of dollars a year per patient and isn't prescribed as a long-term option.

Nutrients and hormones — including vitamin D, calcium and estrogen — are crucial to maintaining a favorable rate of bone turnover. Strength training also tips the balance toward osteoblasts. These aspects of bone biology are clear. But scientists acknowledge that much of the skeleton-building story remains a mystery.

Serotonin is produced in the small intestine (seen right, center in this X-ray image; stomach is upper right) and then carried into bone, where it affects bone formation and density.

GUSTOIMAGES/PHOTO RESEARCHERS

Unexpected connections

The link between serotonin and bones turned up, as scientific discoveries often do, when researchers were looking for something else altogether. In 2000, scientists at Duke University in Durham, N.C., were conducting studies on substance abuse with mice specifically bred to lack certain brain molecules called dopamine transporters, which interact with the neurotransmitter dopamine. The scientists noticed that the mice seemed to have extraordinarily brittle bones. Bliziotes, an endocrinologist who had been collaborating with the Duke team, began to search for a biochemical explanation.

Although they went searching for dopamine transporters in the bones of normal mice, the researchers were astonished to instead find transporter molecules for serotonin, Bliziotes and his colleagues reported in the journal *Bone* in 2001. And the serotonin transporter molecules turned up in all types of bone cells — osteoblasts, osteoclasts and, later work showed, osteocytes, cells derived from osteoblasts. That same year, a Dutch research team studying chicken embryos also discovered a role for the neurotransmitter in bone. "Before 2001, it wasn't known that serotonin had any involvement in bone," Bliziotes says.

In the brain, low levels of available serotonin are thought to contribute to depression. Indeed, the most famous antidepressant in the medicine cabinet — Prozac — works to boost the supply of serotonin available in brain synapses, junctures where neurons communicate. So what was serotonin doing in bones?

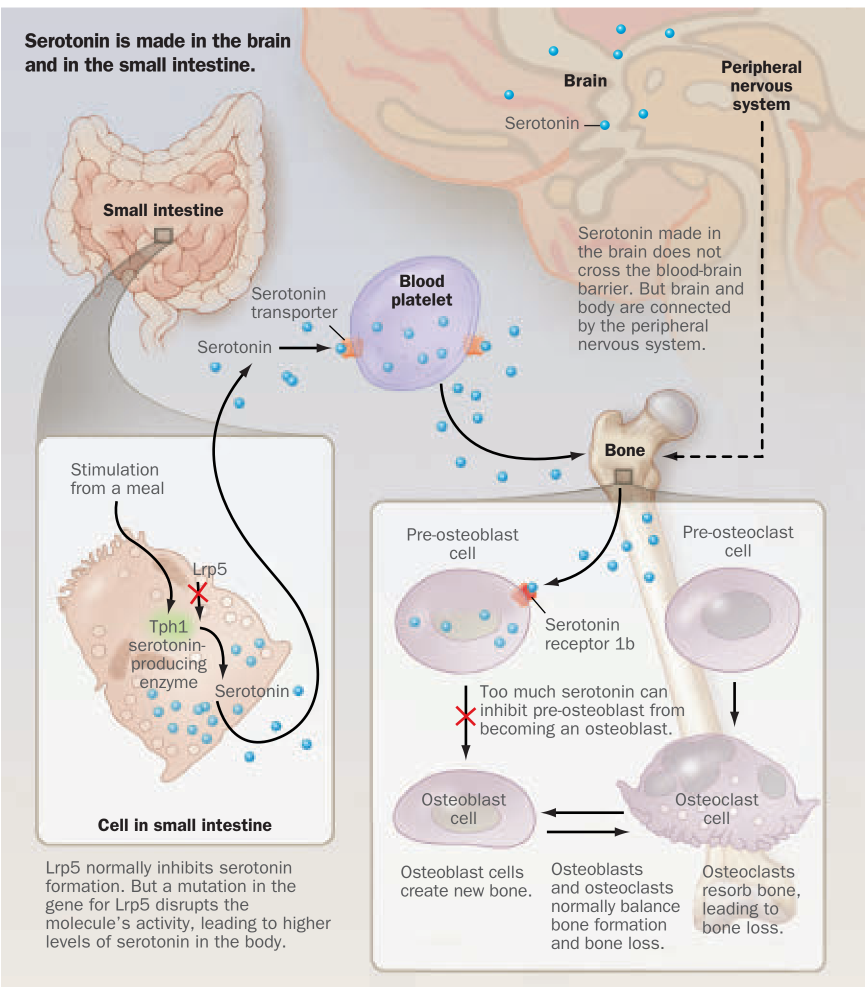
Apparently, making them weaker: Serotonin seems to interfere with the production of the bone-forming osteoblasts. Following the discovery of a serotonin connection to bones, Bliziotes and others began to worry about the more than 8 percent of U.S. adults who take Prozac and related drugs called selective serotonin reuptake inhibitors, or SSRIs, to amplify serotonin. In 2007 in the *Archives of Internal Medicine*, Bliziotes and his colleagues described a study of almost 6,000 older men involved in an osteoporosis investigation. Men taking SSRIs had lower average bone density than those not on the drugs. A related study of postmenopausal women found that bone density declined in those taking SSRIs twice as fast as it did in other women.

"I think the major question right now is — if depressed people are going to be treated with SSRIs, are we subjecting them to risk of fracture?" says Bliziotes. The issue is still under investigation, largely because the studies are difficult to interpret. Among people taking SSRIs, Bliziotes says, "most of them are going to have been put on SSRIs for symptoms of depression. Depression alone has been associated with lower bone density." And people with depression may have weaker bones not from their own physiology but because of lifestyle changes that can accompany the condition, including poor nutrition and low levels of exercise. "We haven't done randomized trials," Bliziotes notes.

To further investigate the role of serotonin, researchers have looked to bone tissue itself to characterize the neurotransmitter's influence over bone cells. These studies have led to a family of proteins called Wnt. (The name comes from a combination of two genes first discovered in fruit flies — *wingless* and

That gut feeling creeps into your bones

Serotonin may be best known for its role in the brain, where it helps regulate mood, learning and sleep. But most of the body's serotonin is made in the gut and never crosses the blood-brain barrier. Eating a meal stimulates the Tph1 enzyme, which makes serotonin in the gut. The signaling molecule Lrp5 can block serotonin production, helping to regulate serotonin levels. Blood platelets move serotonin throughout the body and into bone. Because it binds to serotonin receptor 1b, the neurotransmitter in excess can hinder the formation of new bone cells called osteoblasts. This may lead to lower bone density by upsetting the normal balance between bone formation and loss. In people, genetic mutations in the *Lrp5* gene have been linked to bone density problems.



GRAPHIC BY C. ROSEN MODIFIED AND REPRINTED WITH PERMISSION FROM *THE NEW ENGLAND JOURNAL OF MEDICINE*, 2009; BRAIN IMAGE: N-L/ISTOCKPHOTO

INT — and is pronounced "wint.") Wnt proteins have so many functions that a book about them takes up two volumes. Medical researchers have an intense interest in Wnts because the molecules appear to be involved in cancer, heart disease, obesity and many other conditions. But Wnts also orchestrate basic development and maintenance of body parts.

The fruit fly Wnt proteins have human counterparts, including, of special interest to bone researchers, the signaling protein Lrp5. About a decade ago, researchers found that mice with a mutated form of the gene for Lrp5 had low bone density. In people, mutations in this gene can lead to two distinct effects on bone. One is osteoporosis-pseudoglioma, a rare syndrome that affects children, giving them bones often too fragile even for walking, along with vision problems early in life. A different mutation in the gene produces a condition at the other end of the clinical spectrum: high bone mass syndrome, rendering bones unusually dense and protected against osteoporosis. Looking at the effects of these mutations in people, it became clear that Lrp5 had the power to make or break bone.

"Since the discovery of Lrp5, there has been a tremendous effort to study how it works," says Gerard Karsenty of Columbia University Medical Center. Until last year, most researchers assumed that whatever the role of Lrp5, its importance started and ended in the skeleton. Then in November, Karsenty and his colleagues published a paper in *Cell* that was, in bone research circles, jaw dropping: In experiments with mice, he demonstrated that Lrp5 affects the production of serotonin in the duodenum, the segment of the small intestine where most digestion of food occurs (*SN Online: 11/26/08*).

Despite the neurotransmitter's fame in the brain, 95 percent of the body's serotonin is made in the intestine, from the amino acid tryptophan, which is a component of dietary protein (and lore aside, is no more prevalent in turkey than other meats). After a meal, the intestine turns tryptophan into serotonin, while platelets from the bloodstream ferry serotonin throughout the body. It's an entirely separate circuitry from serotonin production in the brain. Serotonin made in the brain stays in the brain, and the two different sources don't mingle.

Despite serotonin's fame in the brain, 95 percent of the neurotransmitter in the body is made in the intestine.

Karsenty's experiments found that Lrp5 interferes with the production of serotonin in the gut. To arrive at this conclusion, he and his colleagues bred mice with gene mutations known to hamper bone formation. Yet when bone cells from these mice were isolated in laboratory dishes, and thus removed from exposure to serotonin, they grew normally. In short, when not exposed to serotonin, the tissue appeared to be just fine. Similarly, when normal bone cells were exposed to serotonin in the laboratory, their growth slowed. According to these experiments, the problem with bone growth seemed to lie outside of bone cells and not in some faulty bone-building mechanism.

That led Karsenty's team to search for other organs that might affect bone formation. In the *Cell* paper, he and his colleagues reported that Lrp5 acted in the gut, blocking a key enzyme necessary for the conversion of tryptophan to serotonin. When the intestine is awash in Lrp5, less serotonin gets produced, and bones remain stronger. Less Lrp5 means more serotonin, and weaker bones. "This study uncovers an unanticipated molecular mechanism accounting for the Lrp5 regulation of bone formation," the researchers wrote.

Serotonin's long reach

Key questions remain. Among them: How might all this knowledge one day translate into a medical benefit? Other, broader issues go beyond the skeleton. Serotonin isn't present just in the brain, intestine and bones. It works throughout the body, tweaking many different systems, including the cardiovascular system and digestion. "If you turn off the main site of synthesis, what kind of bad effects are you going to have?" says Bliziotes. No one can be sure until the cellular machinery is better understood.

Rosen also wonders how the brain comes into this picture. Although the serotonin in the brain and intestine never meet, evidence suggests that the brain may have other effects on bones. Some of that influence may even act through the digestive system. The hormone leptin suppresses appetite but is also implicated in the regulation of bone mass. And Rosen points to other hints of a brain-bone connection. For example, the rate of new bone formation increases after traumatic head injury.

Rosen isn't surprised that the skeleton would have a connection to the gut. Bones are the body's biggest storehouse for calcium. Bone turnover slows after eating, probably to keep calcium locked in the bones, he says, and increases during fasting. Through serotonin, the intestine may be cueing bones to slow or to rev up turnover based on the body's need for calcium. Ultimately, he believes, scientists may find that bones have a more intimate connection to other organs than anyone first thought. "I think we have just scratched the surface," Rosen says.

For now, scientists are eager to learn more about serotonin and how critical a role it may have in bone structure. More than anything, says researcher Fanxin Long of Washington University Medical School in St. Louis, the new findings are a stark reminder that no organ in the body operates as its own, isolated fiefdom. "It highlights a picture that has become more and more clear," Long says. "Different organs in the body talk to each other." In a language scientists hope to one day fully understand. ■

Laura Beil is a freelance science writer in Cedar Hill, Texas.

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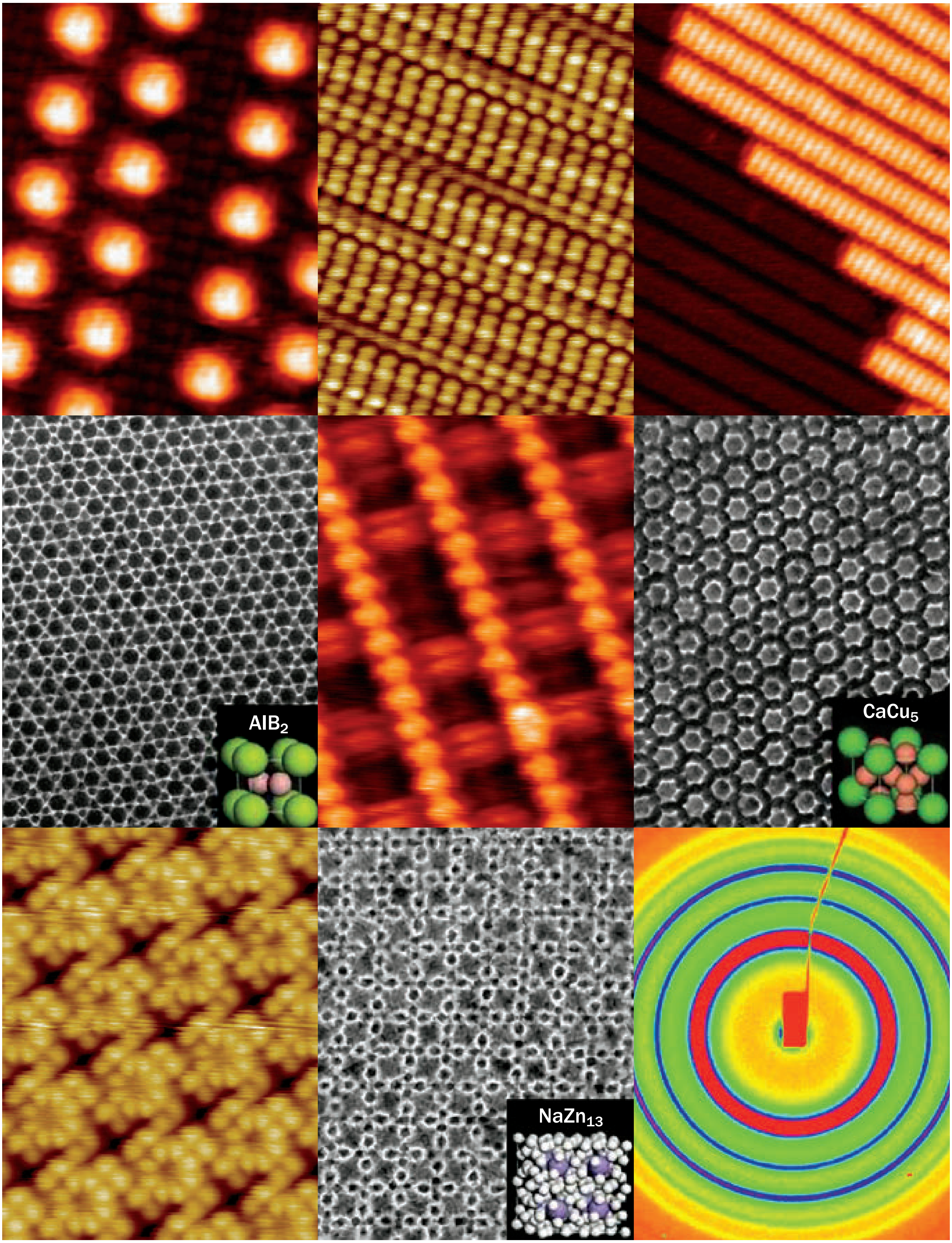
- NIH articles on osteoporosis: health.nih.gov/topic/osteoporosis



AlB_2
$CaCu_5$
$NaZn_{13}$

NANOMAKER'S TOOLKIT

Scientists harness charge, magnetism and even DNA to guide matter's assembly into new materials

By Solmaz Barazesh

When assembling a jigsaw puzzle, just shaking up the box and dumping the pieces in a pile probably isn't the best strategy. The pieces won't fit themselves together by chance. But in the nanoworld, this approach could prove surprisingly fruitful.

It might take the fun out of doing the puzzle, but scientists are now figuring out how to make the pieces move, on their own, into the desired positions for creating new materials. In this case, the puzzle pieces are nanoparticles, tiny collections of atoms smaller than one ten-thousandth of a millimeter across. Properly guided, these particles could assemble into materials useful as conductors or catalysts, with the potential for making smaller computer circuits, better biosensors and more efficient solar panels.

Because nanoparticles are small, a large proportion of their atoms are near the particle's surface. Having fewer neighbors, those relatively unconfined atoms can link in unusual ways, giving materials made of nanoparticles novel properties.

But the same characteristic that makes nanostructures useful — size — also makes working with them no small task. Engineering on the nanoscale is like building a ship in a bottle while wearing mittens.

When properly guided, nanoparticles can arrange themselves into a variety of ordered structures (images show areas nanometers across). Gray images are transmission electron microscope views of nanoparticles steered into ordered structures similar to those naturally achieved by gemstones (illustrated as insets). Brown and orange images show other variations that self-assembly can achieve. One technique uses DNA strands to guide nanoparticles into a cubic structure, revealed by the way X-rays scatter from the array (bottom right).

It would be far cheaper and easier, researchers agree, if nanoparticles could just arrange themselves into nanomaterials — like dropping the pieces of the ship into the bottle and then sitting back to watch the ship build itself. What scientists are working on now is finding the right chemistry — creating just the right conditions so that natural properties such as charge or magnetism direct the pieces of the ship to come together just so, with the mast above the deck and never below or to the side.

This idea, called self-assembly, isn't exactly new. Examples range from the simple separation of oil and vinegar in a bottle of salad dressing to the complex movements of proteins and enzymes — themselves nanosized — reacting in living cells. Scientists have long been inspired by these naturally self-assembling systems. But designing self-assembling systems in the lab, with nanoparticles, presents its own scale of difficulty. And making self-assembled nanomaterials grow large enough to actually be useful is even more challenging.

Previous work on self-assembly set nanoparticles organizing according to size, shape and charge. But the outcomes were not as specific as desired. "It's like trying to build a house by randomly throwing bricks together," says physicist Alexei Tkachenko of the University of Michigan in Ann Arbor. "You get a crude version of a house, but it doesn't look very pretty."

Using different techniques, independent groups of scientists have recently figured out better ways to make the nanoparticles go where they are supposed to go. One group of researchers uses magnetic forces to position particles. Another has figured out how to use DNA to herd nanoparticles into exact conformations. And others can make nanoparticles spread themselves into a thin layer over a surface, changing the properties of the material beneath.

TOP THREE: COURTESY OF CHEN WEI/NATIONAL UNIV. OF SINGAPORE; MIDDLE, FROM LEFT: E. SHEVCHENKO; CHEN WEI; E. SHEVCHENKO; BOTTOM, FROM LEFT: CHEN WEI; E. SHEVCHENKO; O. GANG

Charged to get together

Before self-assembly, scientists used other tricks for making nanoscale impressions. But the tricks have limits.

One technique for making something in the nanoscale is to shrink photolithography, where light serves as a tool for etching intricate circuits onto the tiniest computer chips. A lens focuses ultraviolet light through a stencil to create a pattern on a light-reactive material. This patterned material then stamps its pattern onto a silicon film.

The technique works well — but just setting up to form one specific structure is expensive. And the technique imprints only the surface of the material, making 2-D nanostructures but not 3-D ones such as those required for solar panels.

While still in its early days, the technology of self-assembling systems of nanoparticles is close to building useful, complex, even 3-D materials, researchers believe. "We have some challenges to overcome," says physicist Oleg Gang of the Center for Functional Nanomaterials at the Brookhaven National Laboratory in Upton, N.Y. But "we have the potential to make complicated systems just by mixing up some components."

Some scientists are using nature's self-assembling systems as models for designing their own. "We're trying to mimic nature, where everything is self-organized," Gang explains.

For physicist Elena Shevchenko of Argonne National Laboratory in Illinois, inspiration comes from the structure of opal gemstones. Opals are a naturally occurring nanomaterial, made up of silica nanoparticles that self-assemble into a crystal structure. Shevchenko and her colleagues aimed to build, or "grow," similar crystals from nanoparticles of various materials in the lab.

"Nanoparticles are not identical or uniform in size and shape," says bioengineer John Crocker of the University of Pennsylvania in Philadelphia. "We can take for granted that atoms will crystallize in a certain way. But we don't fully understand how nanoparticles will act in a certain liquid and how they will sit together."

Shevchenko and her colleagues figured out that when certain types of nanoparticles are suspended in liquid, natural electric charges among the particles make them assemble into crystal structures. The scientists figured out how to combine not just one type of nanoparticle but two different types to form the opal-like structures, called binary superlattices. The sizes and concentrations of the nanoparticles determined how they packed together to form crystals.

Evaporating the liquid stabilized the structure, the researchers reported in *Nature* in 2006, when Shevchenko was with Columbia University and IBM. The choice of particles and liquid steered the self-assembly.

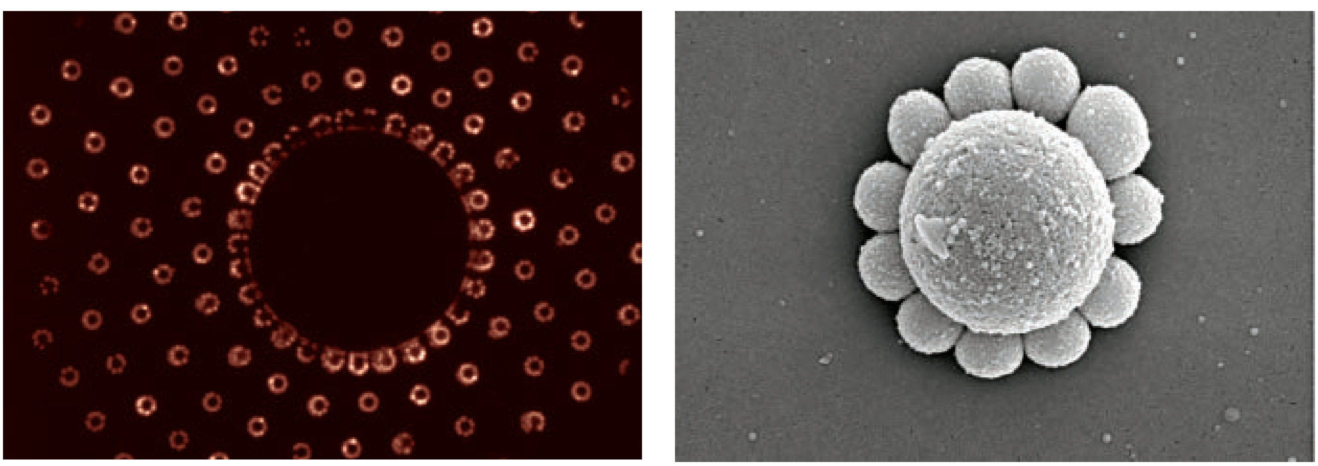
The process successfully created 2-D films of nanocrystals, but adding more types of nanoparticles could allow scientists to precisely tailor the material, and even add a dimension. An alloy of two metals, for example, has properties of both. Similarly, a material made from two or three types of nanoparticles would carry extra properties.

Of course, the same charges that form the nanocrystals also limit the choices for possible structures. The attractive and repulsive forces steered the nanoparticles into only one conformation, but the researchers think that other combinations could be more useful.

So some researchers have come up with a new message about designing useful self-assembling systems, and they're saying it with flowers.

Magnetic beats electric

A team at Duke University in Durham, N.C., created a swirling broth of iron nanoparticles and larger polystyrene beads bouncing around randomly. An applied magnetic field stops the swirling and acts on the iron nanoparticles. Magnetized, the iron helps steer polystyrene beads to line themselves up. Under a microscope, researchers can watch as



Magnetic fields and the right fluid can steer particles to self-assemble. Aided by nanosized iron particles, microsized polystyrene beads embedded with iron follow magnetic forces, and beads left nonmagnetic move in other directions. The result is a flower structure, its center a large bubble trapped in the iron nanoparticle broth (left). At right, a scanning electron microscope image shows the beads after the liquid has been evaporated.

BOTH: RANDALL ERB, B. YELLEN/DUKE UNIV.; RIGHT: *NATURE*, 2009

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the polystyrene particles arrange themselves into flower structures.

Looking down the microscope at the tiny flowers floating in solution "was beyond my wildest imagination," says materials scientist Benjamin Yellen of the Magnetic Nanosystems Group at Duke, who worked on the project. "It wasn't just that the flowers formed, but how reliably they formed. It just turned out that this system worked."

Yellen and his colleagues were the first to apply magnetic forces and manipulate interactions among particles in a liquid. Polystyrene beads embedded with iron could, with help from the iron nanoparticles, follow the magnetic field. The nonmagnetic beads lined up differently. This shift, coupled with interactions among the particles, moved the beads into the flower shapes, the team reported in the Feb. 19 *Nature*.

"The magnetic fields moved the nanoparticles the way we wanted them to move regardless of the charge on the particle," Yellen says.

The polystyrene particles were microsized, large compared with the tiny nanoparticles that Shevchenko and her team steered into structures. But theoretical work suggests that smaller particles can also be manipulated using magnetic forces and similar broths. The technique would allow nanoparticles to form groups called nanoclusters — in this case, nanoclusters of three or more different types of nanoparticles.

Guiding particles into clusters is a way to make materials that have exciting new properties. "It's like making atoms connect to make molecules," Gang explains. Nanoclusters have different properties than their nanoparticles, just as water differs from hydrogen and oxygen.

Follow that DNA

Some researchers have come up with a different strategy to form nanoclusters: using DNA and its system for holding two strands together. "The idea is to use DNA as a smart glue to hold nanoparticles together," Crocker says.

The DNA used for self-assembly is synthetic and does not code for any genes. But these random strands of DNA do have important properties learned from biology. The two strands of DNA in the familiar double helix structure bind together because of attractive forces between the chemical "letters" in the DNA code. Unzipping the helix leaves each strand of DNA open to attach to one nanoparticle, so that each nanoparticle has a DNA tail. Mixed in a liquid, the matching DNA strands bind together again, dragging the nanoparticles with them.

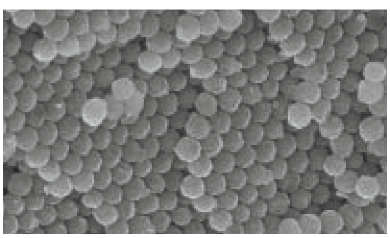
Such DNA shepherds could help in

A toolbox for steering matter to self-assemble at the nanoscale

Scientists interested in making new materials at the nanoscale focus on finding ways to get tiny particles to organize themselves into specific, ordered structures, like bricks building a house. Techniques nature has already employed provide inspiration.

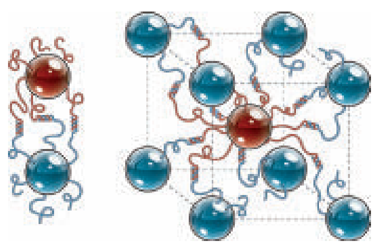
Do as gems do

In the gemstone opal, nanoclusters of silica naturally assemble into a crystal structure (scanning electron micrograph image shown). Work suggests the clusters can be different sizes. Recently, a team found a way to enable other groupings — such as lead-selenium clusters 7.2 nanometers wide with silver clusters 4.2 nanometers wide — to assemble into a similar crystal structure.



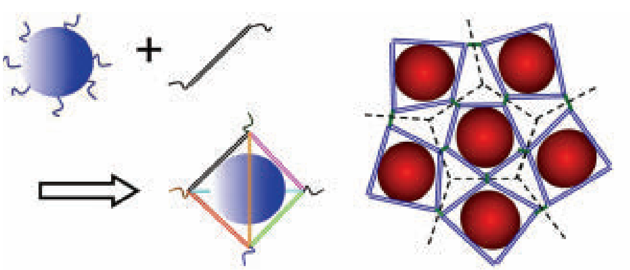
Employ the DNA method

Scientists have attached nanosized spheres of gold (illustrated as red and blue balls) to DNA strands (also illustrated) that naturally want to regroup with companion strands into double helices. The DNA drags the gold nanospheres along for the ride (shown left), enabling the nanospheres to assemble into arrays that have symmetry (shown right is one unit of such an array).



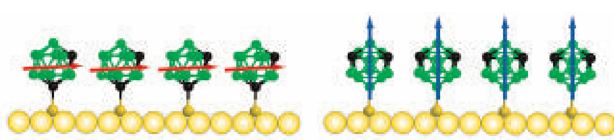
Build DNA cages

Pieces of double-stranded DNA could form the bars of a tetrahedral cage around each nanoparticle. Single DNA strands attached to each bar can connect each unit to fellow strands, forming a regular structure and steering the nanoparticles into that structure.



Cover it in nanoparticles

Layers of molecules called carboranethiols can be manipulated to have different dipole moments (indicated by arrows). A molecule's dipole moment relates to its charge and affects its interactions with other molecules. The carboranethiols can self-assemble into single layers over a regular material, changing the properties of the covered material (two examples shown).



designing complex self-assembling systems, those containing many different components, the researchers say. "We can assign names to the different pieces of the structure. We can tell A to interact with B but not with C," says Gang, a coauthor of several papers on DNA-assisted self-assembly. This level of control could enable the formation of intricately patterned nanomaterials from several different types of nanoparticles.

Making changes in the DNA code that defines how the strands link could make the interactions among nanoparticles stronger or weaker. "It's a recognition system that was developed by nature," Gang says.

Gang's team managed to get nanoparticles to come together but didn't have much control over how the particles organized. So Gang and his colleagues next used DNA to link nanoparticles to a solid surface. Once the nanoparticle is held in place, it's easier to control how it interacts and connects with other nanoparticles, the researchers report in the May *Nature Materials*.

As part of earlier work, Gang's team had optimized the DNA-nanoparticle linkages. Previous researchers had found it difficult to control how many pieces of DNA would attach to each nanoparticle, or exactly where on the nanoparticle the DNA would attach. Some nanoparticles could have two DNA arms, and others could have 10. So instead of forming regular, ordered structures, the nanoparticles stuck together in random clumps.

Reporting in a 2008 *Nature* paper, Gang and colleagues described a technique that links nanoparticles into 3-D crystals. Attaching longer pieces of DNA to spherical nanoparticles of gold helped to make regular crystal structures, the researchers reported. The long DNA pieces wrap around the nanoparticle, enveloping it. Since the DNA surrounds the particle uniformly, the randomness of the DNA attachment doesn't matter.

Although the researchers managed to make small nanoclusters and nanoparticle crystals self-assemble, making larger materials has been "surprisingly difficult," Crocker says. When the crystals assemble, they are floating in water. "We don't want squishy, wet materials," Crocker says, "but when we dry the structure out, the conformation [of the nanoparticles] changes." Filling the gaps between the nanoparticles with a gel or ceramic could be a way to make a solid material, the researchers say.

In the future, researchers hope to be able to use DNA to build cages around nanoparticles, and use the cages as building blocks for a self-assembled system.

The bars of the DNA cages would be made from pieces of double stranded DNA, with short single-stranded DNA sequences at each end. Single-stranded pieces that match would bind together, tying the bars into the cagelike structure. The result is a nanoparticle trapped in a tetrahedral cage with single strands of DNA sticking out at the end of each bar, ready to latch on to the next cage. The symmetrical structure of the cages would prevent the DNA-linked nanoparticles from clumping together at random, says Tkachenko, a coauthor of a paper introducing the idea in the January *Physical Review E*. Stacking the cages could create a material that has a regular arrangement of nanoparticles.

The tablecloth angle

But other researchers think that instead of materials made entirely from nanoparticles, useful materials can be created by placing a layer of nanoparticles over a regular material, like spreading a crisp, white tablecloth over a table.

For Paul Weiss of Pennsylvania State University in University Park and his colleagues, the "tablecloth" is a self-assembling layer of nanosized molecules called carboranes. The layer of carboranes changes the geometry and stability of the material beneath, the researchers report in the March issue of *ACS Nano*. By making a smooth, uniform carborane layer over a surface, "life becomes simpler. We can eliminate differences in the charge or orientation of the molecules beneath," Weiss says.

A carborane molecule is a cage of 10 boron atoms and two carbon atoms, and extra atoms can be attached to the cage. "They're weird molecules," says Weiss. "But we know a lot about them."

Researchers know, for example, how to tweak the chemistry of the molecules to change the properties of the layer. "We can go to town," Weiss says. "We can change the chemical, physical and biological properties of the surface."

In the *ACS Nano* paper, Weiss and his colleagues report enabling types of carboranes called carboranethiols to assemble into a layer attached to a gold surface through sulfur-gold bonds.

The team used two versions of the carboranethiol molecule that differ in the position of a sulfur atom on the cage. Changing this position also altered the orientation of the dipole moment, which is related to a molecule's charge and determines its interaction with water and other molecules.

Changing the dipole moment changes the layer's stability and its relationship with water, the researchers say. One version makes a more stable layer, and the other makes a more hydrophilic layer — one that attracts water and is thus "wettable." Varying the technique builds in different properties.

All of the various tools have their strengths and weaknesses. "We're not competing, these are different strategies," Yellen says. Magnetic fields will work best for making materials from particles of about 100 nanometers across and larger, and DNA-assisted self assembly works better for the tiniest nanoparticles, Yellen explains.

Together, Crocker says, the techniques enable researchers to "build a toolkit that will allow the self-assembly of nearly any material at the nanoscale." ■

Explore more

- John C. Crocker. "Golden handshake." *Nature*. January 31, 2008.
- U.S. Department of Energy nanotechnology primer: www.sc.doe.gov/bes/brochures/files/NSRC_brochure.pdf
- View a nanotechnology information collection from the U.S. National Nanotechnology Initiative website: www.nano.gov

Success in coping with infinity could strengthen case for multiple universes

By Tom Siegfried

Before *ER*, *House* and even *Marcus Welby*, a TV-doctor show called *Ben Casey* opened each week with a hand drawing symbols, as the voice of Sam Jaffe identified them one by one: "Man, Woman, Birth, Death ... Infinity."

Those five symbols supposedly encapsulated what medicine was all about. But they could equally well have summarized the story of the universe. Cosmologists, the scholars of cosmic existence, generally concur that the universe is probably infinite. And they are consumed with understanding the universe's birth, the prospects for its death and whether the presence within it of men and women has anything to do with it all.

Of course, the men and women don't have to be human. Basically any sentient life-form capable of contemplating the cosmos will do. The question is whether life has a starring role in the cosmic drama or is merely an extra, permitted by prevailing conditions but not required to explain them. If the physical laws governing the observable universe reflect mathematical truths, specifying nature's properties without regard to any inhabitants, then life would be the lucky outcome of chance events within a hospitable habitat, not a clue to why the habitat is so hospitable to begin with.

It's not a new debate. Long ago, astronomers argued similarly about the Earth itself — why it orbited so pleasantly around its source of warmth. Perhaps some unknown mathematical law required such a fortuitous location, some savants averred. But it turned out that there was no one law — rather there were lots of planets. People simply populated the one of those planets that offered a congenial environment.

Today many believe that the same principle applies to the congeniality of the universe. There may be no law determining its properties — rather there may be many universes, and life occupies one with congenial conditions. In other words, the properties of the universe that physicists measure are "selected" by the fact that physicists exist to begin with. It's a notion generally known as the anthropic principle, and it evokes intransigent opposition from those who condemn it and unflagging enthusiasm from those who espouse it.

Opponents of anthropic reasoning argue that it cannot be tested, rendering it at best interesting philosophy that doesn't qualify as science. But lately, anthropic advocates have sought ways to calculate values for cosmic characteristics that standard theory cannot explain, suggesting that science may need anthropic reasoning to answer some important questions. Such calculations encounter a major impediment, though: To test whether the universe is the way it is because it's a good place for men and women to be born and die, scientists must learn how to cope with infinity.

Inflation goes on and on

Once defined as everything that exists, the term "universe" now often refers to just one of an infinite number of space-time bubbles.

"What we've all along been calling the universe," says Arizona State University cosmologist Paul Davies, may be "just an infinitesimal fragment in a much larger, more elaborate system for which want of a better word we call the multiverse."

A generation ago, such multiple universes existed only in science fiction, not science textbooks. Nowadays, the multiverse is a hot topic at real-world scientific conferences, including a recent symposium on "Origins" at Arizona State, in Tempe. There Davies and other experts explored the anthropic implications of a multiplicity of universes, which owe their newfound importance to a popular astrophysical theory called inflation.

Among the Origins symposium's speakers was Alan Guth of MIT, who invented the inflation idea in 1980. It explained several mysteries about the Big Bang, the cosmic explosion 13.7 billion years ago marking the birth of today's one known universe.

For a tiny fraction of a second, Guth proposed, the universe expanded exponentially, explaining why the visible cosmos is now so uniform in temperature and structure. That exponential inflation would have stretched spacetime enough to eliminate all but the tiniest lumps in the original amalgamation of matter and energy, resulting in smooth skies today. Inflation would also have provided the impetus for the universe to grow to its current size from its minute origin.

"Inflation explains how the universe got to be so big, which is something we might take for granted, but there isn't really any other theory I know of which comes close to actually explaining it," Guth said at the Arizona conference.

Inflation is driven, Guth explains, by a repulsive form of gravity, generated by an energy field residing in space. As spacetime inflates, some of that field loses its strength — so a local region can expand more gradually, allowing stars and galaxies to develop and stick together. But at the same time, other regions of the inflating field continue to grow exponentially. There is always more inflating material available to spawn new spacetime bubbles — Guth calls them "pocket universes" — and no way for that process to ever stop.

"So once started, inflation goes on literally forever, with pieces of the inflating region breaking off and producing these pocket universes," Guth says. "And if this is right, we would be living in one of these infinity of pocket universes."

Goldilocks bubbles

Most experts today believe that inflation is the best explanation available for the visible universe's appearance and contents. And if it's the right explanation for the one known universe, there must be an infinite number of others.

"The question arises as to whether all these other universes are going to be like ours," says Davies, "or whether they may have different laws and the laws in our universe are in some sense special."

Arguments based on string theory, a favorite candidate (although unsubstantiated by experiment) for explaining all of physical law, suggest that the multiverse encompasses bubbles hosting various sorts of physics. Andrei Linde of Stanford University, another pioneer of inflation theory, noted at the Arizona symposium that string theory predicts the existence of an enormous number of different "vacuum states," or spacetime bubbles with different properties, such as physical constants or particle masses. Of an infinite number of bubbles, Linde says, there could be 10^{500} different varieties. And though any underlying basic law of physics would remain the same, the bubbles could nonetheless exhibit vast physical diversity. "It is the same fundamental law of physics, but different realizations," Linde says.

KATRIN THOMAS/PHOTODISC

Some of those bubbles would not have lasted long enough for life, inflating but then shrinking before any interesting chemistry commenced. Others would expand forever, as seems the case with the bubble that humans occupy. In some, the local laws of physics would have welcomed living things; others would have permitted none of the particles and forces that conspire to build atoms, molecules and metabolic mechanisms. It seems that universes come in all sizes and flavors, with the human bubble being the Goldilocks version, just right for life.

It's not possible, or at least it's very unlikely (*SN: 6/7/08, p. 22*), for any of those other universes to make its presence physically known. So at first glance there is no obvious way to prove that they exist apart from inflation's equations. But in fact, Guth and others argue, applying anthropic reasoning to the multiverse allows calculations of some observable properties of the known universe, otherwise inexplicable. Success in such calculations would validate the assumption that the multiverse is real.

"Whether you like it or not, we may be living in a multiverse — the question is whether or not it will be possible to tell one way or the other," says Alex Vilenkin of Tufts University in Medford, Mass. "Some people complain that this theory is completely untestable. I think it can be tested."

His reasoning is based on the belief that people aren't special. In other words, if the multiverse offers multiple bubbles that permit life to evolve, humans would most likely live in an average bubble. If, for instance, you throw out all the bubbles that wouldn't allow life anyway, and then calculate the average temperature of space in those that remain, humans should measure a cosmic temperature that is not very far off from that average.

But computing that average is not simple enough that a caveman could do it. Even after discarding the bad universes, an infinite number of good ones remain. So calculating the probability of measuring a particular temperature would involve dividing an infinite number of observations by an infinite number of universes. Try it. You can see why it's a problem.

Vilenkin, Guth and others have attempted to circumvent the infinity problem by devising "measures" that permit an estimate for probabilities even in an infinite multiverse. One idea, which looked promising at first, was to define a finite sample of the multiverse, restricted to a limited time period. Just imagine a clock starting up at every point in space and allow the clocks to run until a specified cutoff time. Calculations based on the finite region of space thus monitored could be extrapolated to infinity.

But a cosmos measured in this way would be deceiving. New bubble universes emerge every 10^{-37} seconds; consequently whenever you stopped the clocks, fully half the bubbles would be only 10^{-37} seconds old, and many more would also be very young. This "youngness bias" distorts the calculations, so that most of the universes that did grow old enough for life to evolve would still be much younger than the one that humans occupy. Because the universe cools as it expands, younger universes are hotter, and the most likely temperature of habitable universes in this scenario would be much higher than observed, cosmologist Max Tegmark of MIT has calculated.

So Guth and colleagues are now pursuing a measure of infinite space that largely avoids the youngness bias. Instead of watching the multiverse grow over time, this method (called the scale-factor cutoff) follows the cosmos as it grows by a certain amount of size. This approach still entails some youngness bias, but not very much. And actually, a little youngness is a good thing. For if the average universe age is too old, humans would not be the most likely sentient forms of matter. There would be many, many more Boltzmann brains than people.

Brains in space

Boltzmann brains are named for the 19th century physicist Ludwig Boltzmann, a pioneer in explaining probabilistic processes in physics. In an infinite universe, all things are possible, even random accumulations of atoms that precisely mimic objects that evolved by cause-and-effect processes — such as brains. Somewhere in the cosmos, such a random mix of molecules has produced a brain identical to yours in every respect, neurons in identical configurations, with all your memories and perceptions. If enough matter and energy is around to make them, Boltzmann brains could become quite populous, making them, rather than humans, the typical observers of the cosmos.

It is clear that you are not a Boltzmann brain, though. Close your eyes and clear your mind of all unpleasant thoughts. Then open your eyes, and you see all the same stuff, not the newly randomized world that a Boltzmann brain would see.

If Boltzmann brains dominated the cosmos, humans would be rare, so your very existence implies that the average habitable universe must be young enough to restrain the odds of Boltzmann brain formation. Guth believes the scale-factor cutoff approach may succeed in limiting the likelihood of those Boltzmannesque impostors, as spelled out in a paper by Andrea De Simone of MIT and collaborators (including Guth, Vilenkin and Linde) posted online at arxiv.org/abs/0808.3778.

In any case, the new approach seems to allow calculations relevant to one of the thorniest problems that physicists face today: the amount of energy in the vacuum of space. This "dark energy" exerts a repulsion that drives the universe to expand at an accelerating rate, yet its strength is much less than the best estimates available from standard theory. No known math can specify why the dark energy has the strength that it does.

But a multiverse offers an answer — there is no one right answer. Dark energy's strength would differ from bubble to bubble. Anthropic reasoning suggests, then, that humans should occupy a bubble with something like a typical intensity of dark energy — based on the average dark energy expected for all the bubbles where life would be possible. Using the scale-factor cutoff to evade the infinities in such calculations, Guth, Vilenkin, De Simone and Michael Salem of Tufts show that sure enough, the expected dark energy intensity is rather close to the calculated average, as shown in a paper appearing last year in *Physical Review D*.

"The agreement of this prediction with the measurement is very good," Vilenkin said at the Arizona conference. "So this may be our first evidence that there is indeed a huge multiverse out there."

To be sure, these calculations are still crude. They rely on a rather gross estimate of the number of observers in the multiverse, for example, using the expected number of galaxies as a proxy for people (or other comparable life-forms). But these aren't the only results that point in an anthropic direction. Another group of MIT physicists, in the March issue of *Physical Review D*, analyzes the masses of quarks and ascertains that they lie comfortably in the range to be expected for a universe congenial to complex life.

Still, die-hard opponents remain unconvinced. David Gross, a Nobel laureate and director of the Kavli Institute for Theoretical Physics at the University of California, Santa Barbara, argues passionately against anthropic reasoning every chance he gets.

"Eternal inflation is technically and conceptually shaky," he said in Arizona. And string theory is an unfinished project. "We still don't know what string theory is," he points out.

In the past, Gross notes, apparently unexplained features of physics eventually succumbed to efforts to find a single correct answer, rather than resorting to the anthropic approach. Perhaps, he suggests, some fundamental insight, now missing from conventional theory, will someday show the way to solving nature's riddles with mathematical rigor.

But perhaps that missing insight is merely realizing the need to master the inconveniences of infinity to resolve the cosmic conundrums. In other words, an infinite number of universes could be just what the doctor ordered. ■

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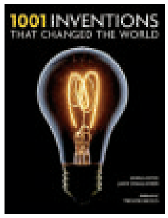
1001 Inventions That Changed the World

Jack Challoner, ed.

Countless inventions, large and small, have played defining roles in human history. But when editor Jack Challoner began to compile a list of these innovations, he wondered if 1,001 might be too many. He quickly realized the number was far too small.

The items that made Challoner's list form a fascinating collection. People use many of them every day yet often take them for granted. Written by a team of more than 50 historians, designers, scientists and anthropologists, the entries in this book tell the stories behind the inventions, from stone tools — appearing about 2.6 million years ago — to the Large Hadron Collider, an atom-smashing particle accelerator that switched on last September.

A quick flip through this hefty book, arranged in roughly chronological order, reveals that many items have been around longer than commonly realized: In 2000 B.C., Egyptian doctors were using anesthesia — compressing a patient's carotid artery to induce loss of consciousness — to limit pain during surgery. The sandwich, though popularized by the Earl of Sandwich in 18th century England, originated in the Middle East, where Hittite soldiers received rations of meat between slices of bread as early as 1000 B.C.



Some of the inventions merely make life easier or more pleasurable, while others can often mean the difference between life and death. From the tea bag to the traffic light, from the paper clip to Prozac, many products are inspired responses to perceived needs. Indeed, Challoner notes, if necessity is the mother of invention, then ingenuity is surely its father. *— Sid Perkins*

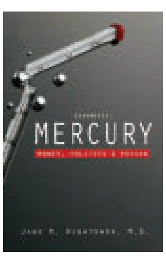
Barron's Educational Series, 2009, 960 p., $35.

Diagnosis: Mercury Money, Politics & Poison

Jane M. Hightower

This is a fish tale, of sorts. It starts when the author, a San Francisco internist, encounters a surprising number of educated professionals with perplexing, nonspecific symptoms: chronic intermittent upset stomachs, headaches, hypertension, fatigue, trouble concentrating and even hair loss.

Hightower eventually traces the symptoms to diets rich in big fish such as tuna and swordfish, the types that accumulate high concentrations of methylmercury. Her cure: Forgo eating fish for up to a year.



In a 2003 paper in *Environmental Health Perspectives,* Hightower first outlined her data from her case reports, as well as her frustration at failing to get regulators and policy makers to accept that current fish advisories may not be keeping people safe.

Now Hightower takes readers along on her eight-year journey of discovery. She describes mercury's extensive use through human history, even as an antiseptic and for other medicinal purposes.

Explains Hightower: "What began as an investigation to help me diagnose mercury-related symptoms in my patients grew into another diagnosis — that of a broken, misused, and abused regulatory system." She charges that the Food and Drug Administration's permissible limit on mercury in fish "is not adequate and not enforced, and it was derived using data that was flawed as well as misrepresented."

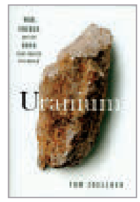
Mercury poisonings can be prevented, this physician ultimately contends, and her book suggests both lifestyle and policy changes to help people safely coexist with this near-ubiquitous toxic constituent of the human environment. *— Janet Raloff*

Island Press, 2009, 307 p., $24.95.

How Women Got Their Curves and Other Just-So Stories: Evolutionary Enigmas

David P. Barash and Judith Eve Lipton

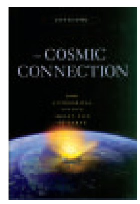
A sociobiologist and a clinical psychiatrist explore why women evolved the way they did. *Columbia Univ., 2009, 224 p., $29.95.*



Uranium: War, Energy, and the Rock That Shaped the World

Tom Zoellner

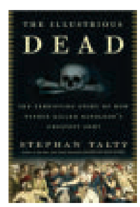
This radioactive substance has offered promise and generated peril throughout history. *Viking, 2009, 337 p., $26.95.*



The Cosmic Connection: How Astronomical Events Impact Life on Earth

Jeff Kanipe

From solar output to supernovas, cosmic events affect Earth's biosphere. *Prometheus Books, 2009, 296 p., $27.98.*



The Illustrious Dead

Stephan Talty

How an eons-old disease — typhus — defeated Napoléon's seemingly unstoppable Great Army. *Crown Publishers, 2009, 336 p., $25.95.*

Crocheting Adventures with Hyperbolic Planes

Daina Taimina

Math and art interweave in this tactile, comprehensible exploration of geometry. *AK Peters, 2009, 148 p., $35.*

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Hormones, milk and fat

I find it difficult to understand why the hormone content of skim milk is greater than that of 2% low-fat milk, which in turn is greater than whole milk ("Scientists find a soup of suspects while probing milk's link to cancer," *SN: 3/28/09, p. 5*). To the extent that 2% and skim milk are produced from whole milk, removing some or essentially all the fat, I would have expected the relation to be reversed. Is there an explanation for why the hormone content of milk increases as fat is removed?

Jerry Kerrisk, Santa Fe, N.M.

The researchers were just as perplexed as the reader about why the data turned out this way. — Janet Raloff

A few questions on the piece about hormone levels in milk: 1. There was no mention of organic versus "conventional." Do you know if that was looked at? 2. Would goat's milk have the same issues as cow's milk? 3. Are there similar levels of hormones present in different types of dairy products, such as yogurt, kefir and cheeses? 4. What about the use of recombinant bovine growth hormone, or rBGH, in dairy cows and its presence in milk?

I would appreciate a more extensive follow-up. This article pretty much left the issues hanging, especially since a food like yogurt has been a human dietary staple for centuries.

Julia Pollock, Sebastopol, Calif.

The research discussed in the article focused only on conventional, store-bought cow's milk, so it did not look at hormone levels in organic or goat's milk products. It also didn't address farmers' use of rBGH.

Earlier work by others has found that little hormone makes it into dairy products like yogurt, cheese, ice cream and butter.

The cancer link to dairy goods, such as it is, appears focused on liquid milk. In fact, a few studies have suggested that consumption of fermented milk products — namely yogurts and cheeses — is associated with a decreased risk of some cancers.

Another possible confounder: Cows that produce a greater volume of milk likely do so because of natural hormonal (including estrogen) differences, researchers note, so breeding for higher-yielding cows may increase — or at least vary — the hormone concentrations present in lactating animals and their milk. However, studies have not yet been done to confirm this. — Janet Raloff

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Dan Arvizu

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Quest for energy efficiency needs public engagement

On April 14, the National Science Board released a draft report called "Building a Sustainable Energy Future," offering advice on how the United States can transition to renewable and clean sources of energy. Dan Arvizu, the cochairman of the board's task force on sustainable energy and director of the National Renewable Energy Laboratory in Golden, Colo., recently talked with staff writer Laura Sanders about U.S. energy policy.

Only about 7 percent of the nation's energy comes from renewable sources. How urgent is it that we increase that?

We really need to be moving very quickly ... we really need to take some dramatic steps so that by 2050 we've substantially eliminated most of the carbon from our energy sources.... The report suggests that unless we change the policies, unless we advance how much innovation is occurring, we're not going to get there very quickly.

Clearly the low-hanging fruit, in my mind, is let's do energy efficiency first. Let's get a lot better about efficiency. That reduces the burden on what the supply needs to look like. And for my money, those cost-effective technologies that are clean and renewable today, it makes sense to use as much of that as we can. We're not promoting one technology over another, but we are saying, "Let's be focused on what our objectives are, and let's be about the business of making that transformation."

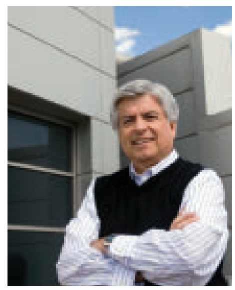
How coordinated is U.S. energy policy both nationally and internationally?

We really don't have a nationally coordinated approach to the science collaboration. It's done agency by agency. So the NSF [National Science Foundation] has one set of operating conditions and set of philosophies, DOD [Department of Defense] has another, Department of Commerce has another, Department of Energy has another, EPA has another. So all the different agencies come at it very, very differently. And quite frankly, the international community is confused, and they say, "Well, who speaks for the United States on this?"... And in fact that's one of the conclusions we drew and one of the recommendations that we made is that we ought to have a coordinating council.

What can we learn from the experiences of other countries?

The rest of the world, in terms of their deployment and implementation, has really passed the U.S. I had the opportunity to testify in front of Congress a number of times last year and kept getting the same question — when is this stuff going to be real?

Well, the fact is that internationally, it's a $150 billion renewable energy industry. Only 10 percent of that is in the U.S. It's primarily driven by Europe and Asia, and they have public policies encouraging it.... So we've got a lot to learn.



NREL/DOE

We really need to take some dramatic steps.... Clearly the low-hanging fruit, in my mind, is let's do energy efficiency first.

The report notes that the government needs to lead by example. How energy-friendly are government buildings?

Not very.... It was just very clear that if the government is going to lead, the first thing we've got to do is practice in our own backyard. If there's a commitment to do it, people will do it.... The good news is that we have control over the government stuff. It's a ripe opportunity, and we really have to take advantage of it.

How important is engaging the public in this transition?

It's probably the most important thing we need to do. Despite the fact that there are all these policies that need to be done, and the R&D needs to be done, the thing that will change those is when the public demands it. It's not just our own behavior, but I think it's our own understanding.... We want politicians who tell us we can have it all without paying for it, and it doesn't cause us to change any behavior, and the politicians are happy to say it. They say, "Oh of course, yeah, you can have it all, and you want a tax cut too?" ... In Denmark, not only can you pay $8 a gallon for gasoline, in addition to that, if you buy a car, they charge you 250 percent tax. So if you buy a car that costs $40,000, it costs you $140,000. That changes your behavior.... I'm not advocating that radical kind of thing, but it shows you how different the mind-set there is than it is here.

Is the transition to a sustainable energy economy going to be painful?

I don't think a lot of people are ready to tell you how painful it's going to be. But the short answer is that it's not easy. It's complex. It takes commitment. It takes national will.

Can we have a better future if we do it? Absolutely.... I know we're not good at preplanning and preventive medicine, but that's what this is. Until people understand that, then they're not going to be able to make the decisions that are necessary. ■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