SCIENCE NEWS

THE WEEKLY NEWSMAGAZINE OF SCIENCE

FEBRUARY 16, 2008 PAGES 97-112 VOL. 173, NO. 7

obesity's link to cancer

entering america, step by step

early bats flew sans sonar

distant galaxies magnified

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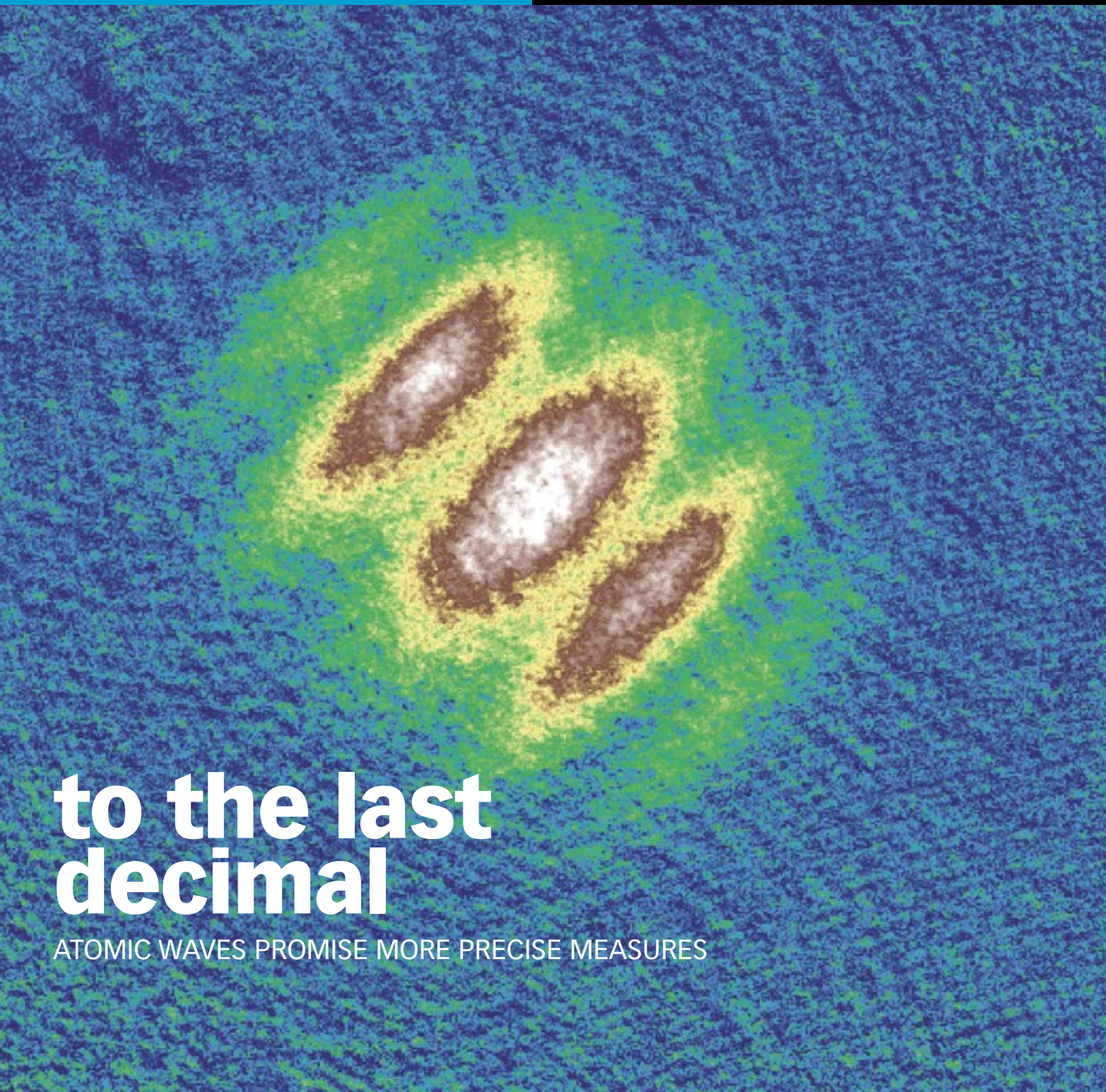

to the last decimal

ATOMIC WAVES PROMISE MORE PRECISE MEASURES

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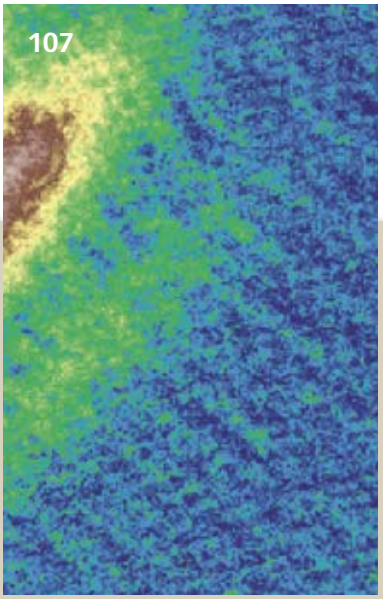

Features

This Week

THIS WEEK ONLINE
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MathTrek Artworks express beauty of mathematics.

Of Note

Departments

Cover An interference pattern of light and dark reveals minute differences in the paths taken by two atom waves. Atom interferometry could be a tool for steering airplanes on precise courses, discovering oil and minerals, or answering fundamental questions about the universe.
(Trey Porto, NIST) Page 107

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Flying Deaf?

Earliest bats probably didn't echolocate

Fossils of a cardinal-sized creature recently unearthed in western Wyoming suggest that primitive bats developed the ability to fly before they could track their prey with biological sonar.

More than one-fifth of living mammal species are bats, and most of those use echolocation to track prey or avoid obstacles. The fossil record of these delicate-boned creatures is sparse, but analyses hint that even the earliest known bats—those flitting through the skies between 54 million and 50 million years ago—could echolocate, says Nancy B. Simmons, a vertebrate paleontologist at the American Museum of Natural History in New York City. In fact, of the six bat species previously known from that era and with enough remains to analyze, all apparently were sonar capable, she notes. Evidence includes a large cochlea, or inner ear, that enabled the bats to detect the echoes of their high-pitched squeaks.

Paleontologists have long debated whether bats' ability to fly preceded, followed, or evolved in tandem with their ability to echolocate. Now, in the Feb. 14 *Nature*, Simmons and her colleagues describe the almost complete fossils of a creature that suggests the "flight-first" hypothesis is correct.

The ancient bat, dubbed *Onychonycteris finneyi*, had a 30-centimeter-wingspan and lived in what is now western Wyoming about 52.5 million years ago, says Simmons. *Onychonycteris*, which means "clawed bat" in Greek, refers to the creature's most distinctive feature: It has claws on all five digits of its forelimbs, whereas all living bats and previously studied fossil bats have claws on no more than two digits. The name *finneyi* honors the fossil collector who excavated the specimens, says Simmons.

O. finneyi's wings were relatively short and broad compared with those of other bats, and the outermost portion of the wing membrane—the part stretched between the bat's fingers—was relatively small. Modern species that are built similarly have an unusual flying style, alternately gliding and fluttering their wings, says Simmons. This undulating mode of flight saves energy at most flight speeds and may replicate the evolutionary bridge between gliding and full-fledged flapping, she and her colleagues speculate.

Also, the researchers note, *O. finneyi*'s legs are relatively longer than those of any known bats, and the ratio of its forelimb length to its hindlimb length approaches that of nonflying arboreal mammals such as sloths and lemurs.

Together, these traits—numerous claws, unbatlike limb proportions, and a presumably clumsy flying style—suggest that *O. finneyi* represents the most primitive known lineage of bats. Although *O. finneyi* clearly could fly, the bat's cochlea was small, a sign that the creature couldn't echolocate. That inability suggests that the evolutionary predecessors of bats also could not echolocate, the researchers note.

FREQUENT FLYER **Although many aspects of the fossils of *Onychonycteris finneyi* suggest that the ancient bat could fly, the size and structure of its inner ear indicate that the creature couldn't echolocate.**

ROYAL ONTARIO MUSEUM

"This is a really big find, a huge piece of the [evolutionary] puzzle," says Emma C. Teeling, a paleontologist at University College Dublin. Not only do these fossils answer the age-old question of whether flight and echolocation developed separately, but they also provide hints about what protobats may have looked like, she says.

"To find something in the fossil record that isn't a full-fledged bat is great," says Suzanne Hand, a vertebrate paleontologist at the University of New South Wales in Sydney, Australia. However, she adds, *O. finneyi* may simply represent an evolutionary experiment, one newfound bat lineage among the many that were flapping about at the time. —SID PERKINS

Animal Origins

Genome reveals early complexity

A microscopic spermlike organism contained many of the same tools for cell-to-cell communication found in animals today, two new reports find.

Analysis of DNA from a choanoflagellate, the closest known living nonanimal relative of animals, allows scientists to infer the genetic starter kit possessed by the first animal, the studies suggest.

"It blows open doors for future research," says Nicole King, coauthor on both papers, published this week in *Science* and *Nature*.

Over 600 million years ago, the single-celled choanoflagellates (Latin for "bearing a collar and a whiptail") branched off from the same ancestor that gave rise to animals. Studies of their genetic makeup allow scientists to deduce which genes evolved before or after the transition to multicellular forms.

Developmental biologist Sean Carroll of the University of Wisconsin–Madison says King's work helps answer key questions: "How sophisticated was the genetic toolkit at the dawn of animal origins?" he says.

In the last decade, genomes from flies, mice, and humans have revealed unexpected similarity. On the other hand, the decoded genomes of single-celled organisms like yeast, paramecia, and giardia are much simpler than animal genomes. Although also single-celled, choanoflagellates have twice as many genes as yeast.

The wee creature's DNA contains as many sequences that code for proteins per gene as animals' genes do. And a number of those genes coded for proteins involved in vital processes in animals.

But choanoflagellates do little but swim and eat. They may not even have sex. They don't have specialized membranes. Yet they have loads of genes used by animals to create characteristic body membranes. Although mainly solitary, they have genes for signaling other cells.

King, a biologist at the University of California, Berkeley, and collaborators from Berkeley and nine other institutions, say that the flagellates used these genes in other roles before they were "hijacked" for different functions in the lineage leading to animals. This "co-option" is analogous to using a cell phone to tell time. For example, genes encoding proteins that help cells stick together in modern animals may correspond to genes for proteins used by choanoflagellates to attach to the seafloor. Similarly, genes responsible for immune reactions in animals might have been used by choanoflagellates to help recognize the bacteria they eat.

Among the surprises in the flagellates'

genes was a complete set of phosphotyrosine (pTyr) signaling molecules, known to regulate communication inside and between animal cells. But many of the *pTyr* genes occurred in combinations not seen in animals. "It highlights how little we know about their biology," says King.

Some collared flagellates form colonies. One hypothesis holds that multicellular organisms arose when single-celled organisms began living in groups to protect themselves against predators or to buffer against environmental extremes. To this end, one of the colonial species is being sequenced by the Joint Genome Institute in Berkeley to see if cell-signaling genes facilitate interaction between individuals. —AMY MAXMEN

Going the Distance

Galaxies may hail from early universe

Using a cosmic magnifying glass to peer into the deepest reaches of space, two teams of astronomers have discovered tiny galaxies that may be among the most distant known. Images suggest that one of the galaxies is so remote that the light now reaching Earth left this starlit body when the 13.7-billion-year-old universe was only about 700 million years old.

The discoveries are important, notes Tim Heckman of Johns Hopkins University in Baltimore, because they probe a special time in the universe, when the cosmos changed from a place filled with neutral gas to a place ionized by the emergence of the first substantial population of stars and black holes. Studies of distant galaxies help pinpoint when that critical era happened.

All of the galaxies are so small that even the keen eye of the Hubble Space Telescope couldn't have spotted them without nature providing a gravitational assist. According to Einstein's theory of general relativity, a massive foreground body acts like a lens, bending and magnifying light from a more remote galaxy that lies along the same line of sight to Earth.

That's why Garth Illingworth and Rychard Bouwens of the University of California, Santa Cruz and their colleagues went hunting for distant galaxies around a nearby cluster of galaxies called Abell 1689.

The cluster's gravity distorts images of background galaxies, bending them into arcs and magnifying their brightness. One of these galaxies proved especially intriguing because it appeared bright at several infrared wavelengths recorded by Hubble but disappeared in visible light.

That's a sign that the galaxy, dubbed A1689-zD1, is both extraordinarily distant and youthful. The data also indicate that the galaxy forms stars at a rate equivalent to five suns a year, typical of the small galaxies thought to be common in the early universe, says Bouwens.

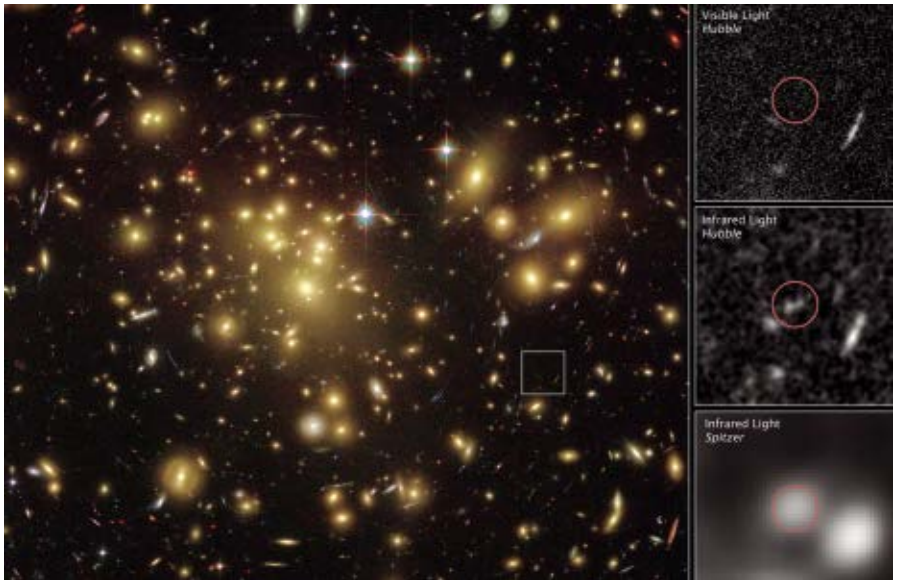
The researchers don't have a spectrum for the galaxy and therefore can't be sure of its distance, but they calculate in an upcoming *Astrophysical Journal* paper that the galaxy most likely lies 13 billion light-years from Earth and has a redshift of 7.6. That redshift signifies that cosmic expansion has stretched the wavelengths emitted by the galaxy by a factor of 8.6.

"The reason we are excited about this [galaxy] is that we can look at it in great detail because of the factor of 10 gravitational amplification by the foreground cluster," Bouwens says. A1689-zD1 is the brightest known galaxy that's likely to be extremely distant, his team notes.

The Hubble images show several dense clumps, each containing hundreds of millions of stars. Follow-up images, taken at longer infrared wavelengths with NASA's Spitzer Space Telescope, provide additional evidence that the galaxy is remote and also yield a more accurate measurement of the galaxy's mass.

"It looks pretty convincing" that A1689-zD1 is remote, but proof may require spectra taken by Hubble's proposed successor, the James Webb Space Telescope, Heckman says.

In searching for distant galaxies, a second team, which includes Richard Ellis and Johan Richard of the California Institute of Technology in Pasadena, also surveyed several galaxy clusters. The team found evidence of six distant galaxies, which may lie between 12.9 billion and 13.1 billion light-years from Earth, Richard reported this week at an astrophysics meeting at the Aspen Center for Physics in Colorado. Because the galaxies don't appear as bright—the clusters magnify them by a factor of only two to four—astronomers have less information about these faint bodies than about A1689-zD1, Richard notes. —RON COWEN



L. BRADLEY & H. FORD/JHU, BOUWENS & ILLINGWORTH/UCSC, NASA, ESA

LONG AGO, FAR AWAY **Gravity of the cluster Abell 1689 acts as a gravitational lens, bending into arcs and magnifying the light from remote background galaxies. One galaxy appears so remote that it doesn't show up in visible light (top, right) but only in the infrared (middle and bottom, right).**

Drug Running

Bust nets suspects in counterfeit antimalaria trade

Over the past decade, researchers have documented the sale of fake antimalaria tablets in Southeast Asia. A new report traces the source of some of these drugs to southern China, and police there have located an illicit drug "factory" and arrested multiple suspects accused of trafficking the pills. Authorities in Burma (Myanmar) have also nabbed two suspects.

The busts mark the first time that the World Health Organization (WHO) has teamed with Interpol and physicians, pharmacists, and scientists working in Southeast Asia to analyze and track packages of antimalaria pills. The investigators found that many fake tablets, which have been linked to deaths, were visual mimics of legitimate pills

made and packaged by the Chinese company Guilin Pharmaceutical. In 2006, the investigators informed the Chinese government.

In addition to making arrests, Chinese police seized 24,000 packets of counterfeit artesunate pills. Artesunate is made from sweet wormwood leaves. When combined with another drug, it has a remarkable success rate against malaria (*SN: 2/7/04, p. 94; 6/16/07, p. 381*).

The illicit factory in Yunnan province in southern China has been "found, searched and shut down," says John Newton, intellectual property rights program manager at Interpol in Lyon, France.

The action may have disrupted the trafficking of some fake pills in Burma, Thailand, and parts of Laos, the international team reports in the February *PLoS Medicine*. But there may be another southbound traffic route supplying Vietnam, Cambodia, and southern Laos.

Fake artesunate first cropped up in Southeast Asia in 1999, says study coauthor Paul Newton, an infectious disease physician at the University of Oxford and the Wellcome Trust who works in Laos. Since then, he and others have documented cases in which malaria patients died after receiving counterfeit pills. That work ultimately triggered a secret meeting with WHO and Interpol in Manila, Philippines, in 2005.

The ensuing investigation revealed a highly sophisticated enterprise, Paul Newton says, with holograms on packages designed to look like Guilin products. Pollen was also detected on some pills from plants in southern China, leading to talks with Chinese officials.

"This is a tour de force combining many disciplines," says David Sullivan, an infectious disease physician at Johns Hopkins University in Baltimore. "Pharmaceutical counterfeiting is usually tough to track. It took a team effort [that] can now be duplicated elsewhere."

In developing countries, many prescription drugs are obtained over the counter with little regulation. "Two surveys that our group has done suggested that one-third to one-half of artesunate bought [in Southeast Asia] is counterfeit," Paul Newton says.

Some of the fake pills collected in the new investigation showed traces of active artesunate or related compounds. Such amounts invite the development of resistant malaria strains and can shorten the useful life span of a drug, says Terrie Taylor, an osteopath at Michigan State University in East Lansing and scientific director of the Blantyre Malaria Project in Malawi.

To date, no tests have established any resistance to artesunate, Sullivan says.

Meanwhile, fake medication "can diminish faith in the drug," Sullivan says. Some of the fake pills contained banned pharmaceuticals, including one known carcinogen.

Taylor notes that drug subsidies for antimalaria pills would bring down their prices and put some counterfeiters out of business by hurting profitability.

This year, Interpol plans to investigate whether fake drugs are moving from Asia to Africa, says John Newton. —NATHAN SEPPA

L. ALLEN/HARVARD-SMITHSONIAN CENTER FOR ASTROPHYSICS; JPL-CALTECH/NASA

Where stars are born

Some 300 young stars shine through the dust in this infrared portrait of the main cloud of a nearby star-forming region called Rho Ophiuchi. (When viewed in visible light, the stars remain hidden in the dust.) In this false-color rendition, red indicates stars only a few hundred thousand years old, so young they still reside within the cocoons of dust and gas from which they grew. Nested inside those cocoons are disks of material from which planets may coalesce. Blue stars are only slightly older but have shed their cocoons. The stars concentrate within the cloud's densest, coldest, and darkest patches; they heat adjacent dust, depicted in white. Diffuse pink indicates carbon-rich dust. NASA released the image, taken by the Spitzer Space Telescope, on Feb. 11. —RON COWEN

Swell, a Pain Lesson

Gut microbes needed for immune development

Bacteria in your belly can be a pain in the neck, knee, or *tuchus*. Beneficial microbes that live in the colon are responsible for developing immune system responses that lead to inflammation and pain, a new study in mice shows.

People and animals host hundreds of different bacteria and microbes in their large intestines. Generally, the microbes are friends, helping to digest food and even ensuring that our intestines develop correctly.

Now, a group of researchers in Brazil has shown that our bacterial buddies help our immune systems acquire the ability to cause swelling and pain.

The news may sound like a classic case of "With friends like these ... ," but the results actually show that bacteria and other microbes that normally live in our intestines are helping protect us, says Arthur Ouwehand, a microbiologist at the University of Turku in Finland.

"When you read this paper, you might get the idea that microbes are bad, because you get more inflammation and pain," he says.

But pain and swelling are the correct responses to a wound or infection, he points out. Inflammation and tenderness signal that something is wrong and that the immune system is on the job to correct the problem. The discomfort encourages a person or animal to treat the injured area more carefully.

"We have to see this all as a defense mechanism," says Ouwehand, who was not involved in the new study. "Not reacting is actually potentially dangerous." The study was published Feb. 12 in the *Proceedings of the National Academy of Sciences*.

Researchers led by Mauro Teixeira, an immunologist at the Federal University of Minas Gerais in Belo Horizonte, Brazil, raised mice in a sterile environment so that the mice had no bacteria in their intestines. They injected the footpads of the so-called germfree mice and of conventionally raised mice with carrageenan, a gelatin-like substance extracted from red seaweed.

Mice with normal bacteria in their guts developed tender paws when injected with the irritant. The sore feet are the result of the way the immune system normally reacts to injury. White blood cells invade the injured area and a flood of inflammatory proteins, called cytokines, cause swelling and eventually pain.

The germfree mice had 52 percent less

swelling when injected with carrageenan. The mice also delayed production or made lower levels of certain cytokines at the wound area, and white blood cells in the germfree mice were sluggish in responding to the injury. Introducing intestinal bacteria in the mice later improved the reaction.

Newborn human babies don't have any intestinal microbes. The bacteria that infants acquire help their immune systems mature and adapt to the environment, and prepare to fight infections, Teixeira says.

The result implies that changing the mix of intestinal microbes might relieve pain in people with inflammatory diseases such as Crohn's disease and eczema. Such therapies are far away, Teixeira says.

"We don't know how long or how much you need to change your microbiota in order to change your pain," he says.

The new research "shows how profound an effect microbes have on your immune system and your entire health," Ouwehand says. —TINA HESMAN SAEY

Don't like it hot

As climate change raises seawater temperatures, king penguin populations could shrink, say researchers. Since 1999, implanted ID tags like those for dogs have let researchers monitor bird family life on the Crozet Archipelago in the Indian Ocean. Warmer water means less food. Chick survival declined during seasons with higher surface water temperatures, reports Yvon Le Maho of CNRS in Strasbourg, France. In winter, adult king penguins leave chicks to fast for months while parents swim away to replenish their strength in food-rich waters near Antarctic ice. The team found that adult populations eventually declined after winters with unseasonably warm waters. A 0.26°C warming of seawater can reduce adult survival 9 percent, the researchers will report in the Feb. 19 *Proceedings of the National Academy of Sciences*. —SUSAN MILIUS

New World Stopover

People may have entered the Americas in stages

Think of it as the ultimate travel delay. Asian migrants first reached the northwestern edge of the Americas as early as 40,000 years ago but then had to wait at least 20,000 years before heading south into the continent's heart, a new genetic analysis finds.

Until now, many researchers had assumed that multiple waves of migrants rapidly settled the New World some time after 16,000 years ago.

The reason for the holdup: Two massive ice sheets on what is now Alaska blocked entry into North America from Beringia, a once-habitable region that today lies submerged in the Bering Strait. Melting of those glaciers yielded a coastal and an inland passage south by 16,000 years ago.

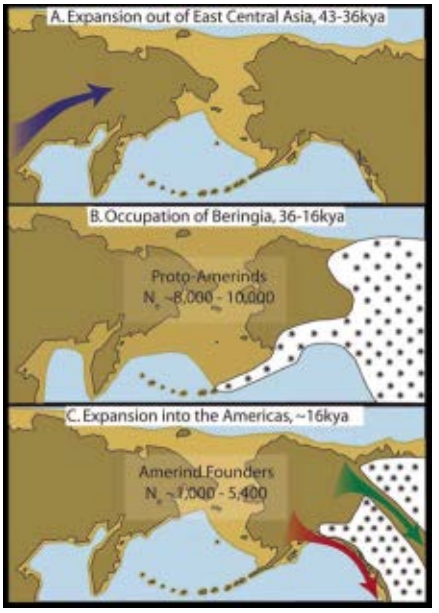
Between 1,000 and 5,400 people rapidly moved through those routes and settled the New World, propose anthropologist Connie J. Mulligan of the University of Florida in Gainesville and her colleagues. Previous DNA-based studies had estimated that no more than 100 individuals initially settled the Americas.

Stone Age travelers likely left a harsh environment in what is now eastern Asia and crossed the land bridge looking for greener pastures. They eventually reached Beringia, which was exposed during the last glacial maximum and contained grasslands and abundant large animals from around 36,000 to 16,000 years ago.

"Beringia wasn't paradise, but the new settlers survived," Mulligan says. "When the North American ice sheets started to melt and passage into the New World opened, we think they left Beringia to go to a better place."

Her team used new methods to assess DNA sequences obtained from eastern Asian and Native American populations.

An initial analysis, based on identifying the kinds and frequencies of mutations in mitochondrial genomes of 77 people, allowed the scientists to construct an evolutionary tree showing which sequences arose first and which came later. They then used a computer model to estimate the number of individuals who were mating and contributing to the gene pool at each branch in the tree.



STEP-BY-STEP **Maps labeled A, B, and C depict each phase of the new three-step colonization model for the peopling of the Americas. Light-brown areas are exposed seafloor and dark-brown areas are current land. The phrase *kya* indicates thousands of years. *Amerinds* are early Americans.**

This technique re-creates changes in an ancient population's size over time, rather than taking a genetic snapshot of population size at one time, as do most studies.

The scientists also combined evidence from mitochondrial DNA—which is passed solely from mothers to their children—and nuclear DNA, which contains genes from both parents, to estimate the size of the group that initially settled Beringia and the timing of its arrival from Asia.

Several hundred Asians started their trek to Beringia roughly 43,000 years ago, the researchers report in the February *PLoS ONE*. The population grew rapidly and peaked to several thousand by 36,000 years ago. The population was stable for about 20,000 years, and then swelled after migrating further south, the investigators conclude.

"What's most surprising is the long period of population stability in Beringia, especially with no archaeological evidence for such an occupation," Mulligan says. She and her coworkers suspect that, since Beringia now lies underwater, ancient sites of the first Americans are submerged as well.

"The idea that people were stuck in Beringia for a long time is obvious in retrospect, but it has never been promulgated," remarks anthropologist Henry C. Harpending of the University of Utah in Salt Lake City. —BRUCE BOWER

LE MAHO; A. KITCHEN, M. MIYAMOTO, MULLIGAN

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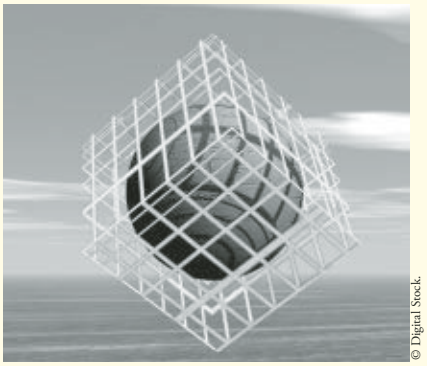
Professor Michael Starbird is a distinguished and highly popular teacher with an uncommon talent for making the wonders of mathematics clear to nonmathematicians. He is Professor of Mathematics and a Distinguished Teaching Professor at The University of Texas at Austin. Professor Starbird has won several teaching awards, most recently the 2007 Mathematical Association of America Deborah and Franklin Tepper Haimo National Award for Distinguished College or University Teaching of Mathematics, which is limited to three recipients annually from the 27,000 members of the MAA.



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WEIGHTY EVIDENCE

The link between obesity, metabolic hormones, and tumors brings the promise of new targets for cancer therapies

BY LAURA BEIL

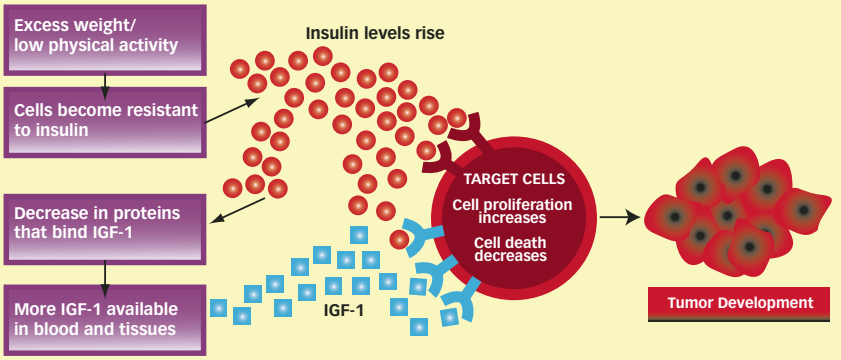
Living large can mean dying large, as familiar reminders about obesity's link to cardiovascular disease and diabetes repeatedly emphasize. But those warnings often overshadow another threat from obesity: cancer. Excess weight accounts for 14 percent of cancer deaths in men, and 20 percent in women, researchers estimate. Among all preventable cancer risk factors, only smoking claims more lives.

Obesity's link to cancer should come as no surprise. Signs of that relationship began to emerge 2 decades ago. In the late 1980s, laboratory researchers found connections between cancer and insulin—one of the major hormones that responds to obesity.

While the findings got little attention then, today at least a half-dozen companies are developing cancer drugs that interfere with the hormone's cousin—insulinlike growth factor 1 (IGF-1).

"We've been working on this for 20 years," says Derek LeRoith of the Mount Sinai School of Medicine in New York City. Yet until recently, "nobody ever bought into it." After all, even if a tumor does need insulin, the rest of the body does too. The early research was seen as hardly relevant for disease treatment.

Not so today. If clinical trials find that dampening IGF-1 shrinks tumors in cancer patients, scientists will have not only a new kind of cancer drug but also a new source of insight into the interplay between body weight, metabolism, and cancer. In 2003, a study in the *New England Journal of Medicine* estimated that if the U.S. population were of a healthier weight, "90,000 deaths due to cancer could be prevented each year." That number may not fall for generations, as obesity rates among even the youngest Americans continue to soar.



INSULIN HIGH TIDE — The observed link between obesity and cancer may be explained by the growth-promoting activities of insulin and IGF-1. One theory posits that excess weight sets off a biochemical cascade that increases insulin and, in turn, IGF-1 levels. Both hormones may activate IGF-1 receptors on cells, which can spur cell growth and inhibit cell death pathways that usually protect against tumor development.

HEAVY HORMONES Lower weight and more physical activity can affect the production of insulin, the hormone that allows the body to soak up fuel. After a meal, food is broken down into glucose, which is the body's main source of energy. Insulin triggers cells to take up and use glucose. As a person gains excess weight, the cells can become resistant to insulin's actions. To compensate, the pancreas begins to produce more insulin, but it can't stay in overdrive indefinitely. Eventually, insulin production will fall and blood glucose levels rise in some people.

The potent hormone IGF-1 and the related IGF-2 are very similar to insulin, helping support rapidly dividing cells, especially during childhood and adolescence. IGF-1 is a powerful driver of cell growth and body size: A toy poodle is a standard poodle with a faulty IGF-1 system.

The link between these insulinlike hormones and obesity is less clear than the connection between insulin and obesity. Although insulin and IGF-1 have individual parking places, or receptors, on a cell, some experiments suggest that at high enough levels, insulin starts to trespass on the IGF-1 receptor, LeRoith says.

In the late 1980s, laboratory researchers demonstrated that IGF-1 might have a role in cancer. Tumor cells were found to contain the IGF-1 receptor. In 1989, experiments with mice showed that blocking the receptor with an antibody could stop tumor growth. Researchers also found that mice bred to lack IGF-1 receptors in all their tissues were born tiny, thereby establishing the hormone's significance in growth. More important for cancer research, cells taken from the miniature mice lacking IGF-1 receptors could not be transformed into tumor cells.

"A cancer cell has to have the IGF-1 receptor," says Renato Baserga of the Kimmel Cancer Center at Thomas Jefferson University in Philadelphia, one of the field's pioneers. "If not, it cannot grow."

At first, results like these were puzzling. Unlike cancer genes that encode other proteins and start down the path to cancer after mutating, the IGF-1 receptor gene wasn't altered in tumors. Also, IGF-1 receptors show up in normal tissues throughout the body. The hormone itself is such a basic substance for animal life that even flies produce it. It was hard to imagine that a normal receptor found in normal cells could have anything to do with cancer.

Then scientists had an idea. Malignant cells may be overly dependent on IGF-1 receptors, on a scale far surpassing the dependence of normal cells. A tumor is like a car—a gas-guzzling Hummer—with a stuck accelerator and no brakes. Even if IGF-1 doesn't spark the

E. ROELL/SOURCE: NATURE REVIEWS CANCER, 2004

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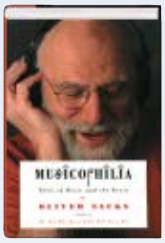

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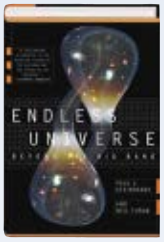

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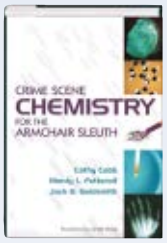

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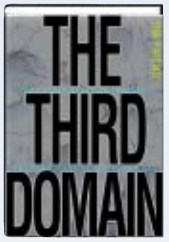

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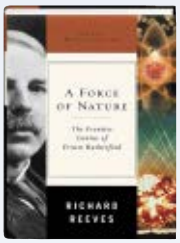

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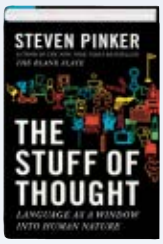

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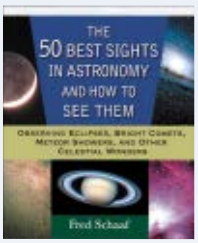

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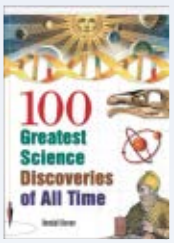

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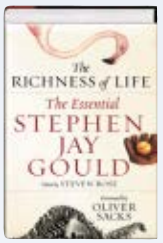

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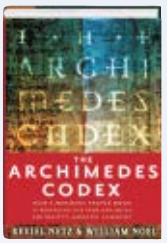

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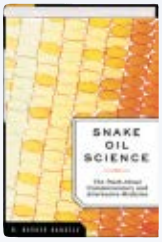

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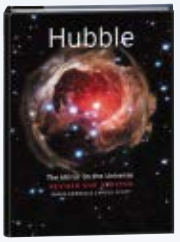

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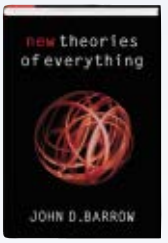

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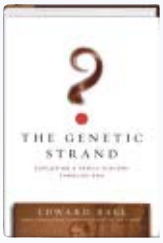

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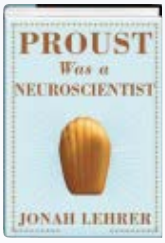

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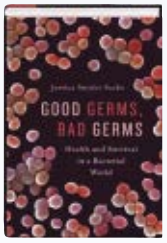

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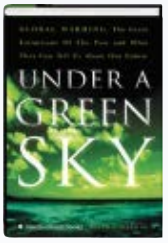

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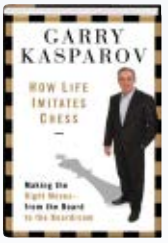

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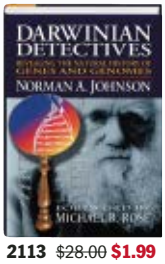

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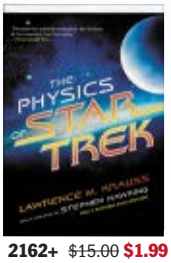

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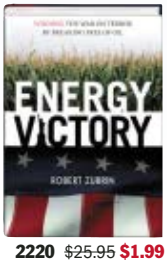

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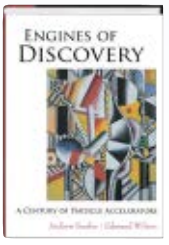

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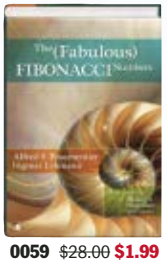

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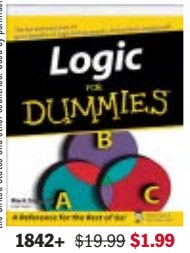

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ignition, the hormone keeps the gas tank full. Block IGF-1, according to this line of thinking, and the tumor suddenly finds itself running on empty.

FUELING CANCER Still, this notion might have stalled without two other developments. First, epidemiological studies began to find links between cancer and the insulin-IGF axis in people. Then, the entire field of cancer treatment underwent a transformation.

"What got people's attention was the epidemiologic data," says Doug Yee of the University of Minnesota Cancer Center in Minneapolis. In 1998, researchers reported in the journal *Science* that the risk of prostate cancer among men with the highest circulating levels of IGF-1 was four times as great as the risk among men with the lowest IGF-1 levels. Similar findings quickly followed in breast, colon, and other cancers.

So far, colon cancer has the most consistent association with insulin and IGF-1 levels, says Edward Giovannucci of the Harvard School of Public Health, a coauthor of the 1998 *Science* study. In 1999, he and his colleagues reported that colon cancer rates were more than twice as high among men who had the highest levels of IGF-1 as they were among men with the lowest IGF-1 levels.

Such findings fit with global patterns of the disease. "If you look at the rates of colon cancer across the world, populations where you expect people to have low insulin invariably have low rates of colon cancer," Giovannucci says. Physical activity and reduced calorie intake can lower insulin levels; populations with more sedentary jobs and calorie-dense diets have higher rates of obesity and higher insulin levels.

"Once you become economically developed, colon cancer rates go up," Giovannucci says. Also, the risks for colon cancer read largely like a list of red flags for type 2 diabetes. Diabetes itself is a risk factor for colon cancer.

Scientists are quick to point out that a higher insulin level isn't the only chemical change that can occur with obesity. Levels of hormones that cause inflammation also rise, as do sex hormones, which can be produced in fat tissue. These and other changes in the body could themselves drive cancer. Or all these fluctuations could work in concert to feed malignancies.

And it might be not only the IGF-1 of middle age that matters, but also the IGF-1 production that orchestrates development early in life. Studies have suggested that babies born at the highest birth weights—and children experiencing early growth spurts—have a greater risk of cancer as adults.

While epidemiologists gathered evidence for a relationship between insulin and cancer, a second, unrelated advance gave the insulin-cancer connection new life: treatment success using antibodies that can attach to precise targets. Antibody-based drugs are large molecules that take the parking space so its rightful owner can't use it. Herceptin, an antibody-based breast cancer treatment, came on the market in 1998, followed by others. Targeted antibodies were suddenly more than theory.

"I think once people got more comfortable making these drugs, the floodgates opened," says Yee. And when pharmaceutical companies started casting for other promising targets for antibody development, the IGF-1 receptor suddenly looked attractive.

"They turned around and said, 'You know, there's this IGF receptor,'" says LeRoith of Mount Sinai. Drug development didn't happen, and perhaps couldn't have, until epidemiology and the technology caught up with the laboratory evidence.

BROAD TARGET Nonetheless, an antibody that interferes with IGF-1 in people raises concerns. Although the full role of IGF-1 in adult tissues is still being worked out, rapidly growing tissues such as those in bone marrow and the intestine might become innocent by-standers of chemotherapy.

"You're going to hit a receptor that's present on every cell in the body, except the liver," LeRoith says.

Also, in a case of molecular friendly fire, the drug might hit unintended targets. Because the insulin receptor and the IGF-1 receptor are cousins—they are actually more than 70 percent alike—some drugmakers worry about the possibility of accidentally interfering with the insulin receptor and making a cancer patient diabetic.

As an endocrinologist, LeRoith isn't as disturbed by these scenarios as some of his colleagues may be. He believes chemotherapy-induced diabetes would be only temporary, and treatable. In the larger picture, it would not be as grave a threat as the cancer itself. Also, he says, chemotherapies already on the market cripple rapidly growing cells in the intestine, bone, and elsewhere. While these drugs do cause notorious side effects, the complications are generally accepted as the price of disease treatment.

So far, though, the experimental drugs haven't caused major problems in early tests. Results of the first human-safety studies are starting to appear, most just in the past few months. The results are encouraging enough that companies are easing into larger studies.

> "We have one patient … who really has had honestly one of the best responses I've seen in 20 years."
>
> — RAZELLE KURZROCK, UNIV. OF TEXAS

"This was a target that was on everybody's radar screen, but nobody jumped so strongly at it," says Kapil Dhingra of Roche Pharmaceuticals in Nutley, N.J.

They have now. In October, at the International Conference on Molecular Targets and Cancer Therapeutics, researchers from Roche described a study of 34 patients with advanced tumors who received infusions of an experimental drug designed to target the action of IGF-1. Disease in nine patients stabilized. The most common side effects were fatigue, weight loss, and anorexia—complaints that are also often found in patients with advanced cancer. Subjects' blood sugar levels appeared to remain stable.

The trial was designed to test the safety, and not the effectiveness, of the drug. But the researchers noted that it seemed to have a remarkable result in one of the study participants with Ewing's sarcoma, a cancer of children and young adults that Yee in Minnesota had long ago identified as feeding heavily off IGF-1.

"We have a patient, a young woman in her 20s, who really has had honestly one of the best responses I've seen in 20 years," says Razelle Kurzrock of the University of Texas M.D. Anderson Cancer Center in Houston. "When you see something like that in cancer, you've usually hit the molecular target."

Within 6 weeks, the woman's tumor melted away. The results were promising enough that Roche plans to test more patients.

The antibody-based drug that appears to be the farthest along in testing comes from Pfizer Inc., which has moved beyond safety studies into tests that gauge its effectiveness on cancer. Last summer, during a meeting of the American Society of Clinical Oncology, company researchers described results of a trial involving 70 patients with advanced lung cancer. About 46 percent of patients who received the drug in combination with standard chemotherapy improved, compared with 32 percent of those who did not get the anti-IGF-1 drug. Twenty percent of the patients getting the treatment experienced a jump in blood-glucose levels, implying some interaction with insulin. Later this year, the company hopes to report the effects of treatment on patient survival.

Other companies are also working on antitumor antibodies or on smaller molecules that will block the IGF-1 receptor. In the end, researchers say, the drugs may have a role in combination with standard treatments, and trials will probably also find that some tumors are more dependent than others on IGF-1.

"It's not realistic to think that any one target is going to hit all of them," says Kurzrock. Still, she says, "I would say this is going to be a good molecule." If so, a line of research almost lost to the past could one day benefit cancer patients of the future. ■

Laura Beil is a freelance writer in Texas.

EXTREME MEASURES

Atom interferometry's precision could make it the Swiss Army knife of physics

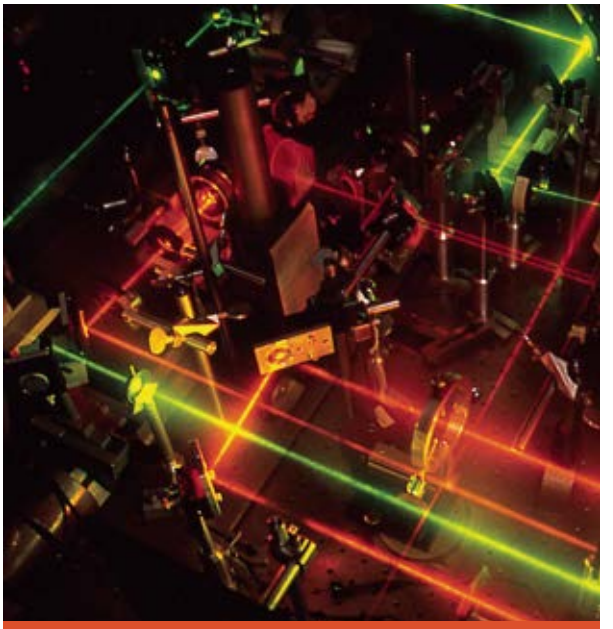
BY EWEN CALLAWAY

In spring 2010, the military plans to embark on a road trip across the country to test a new way of navigating. Instead of taking a path marked by a dog-eared road atlas, a compass, or even global positioning satellites, the vehicle will follow one mapped by super-cold cesium atoms.

This cross-country trek will be a field test for the Defense Department's Precision Inertial Navigation Systems program to navigate by measuring the Earth's rotation using atoms that behave like waves. The vehicle won't drive blind, but the machine guiding it could make such a feat possible. And someday the new system could also improve the accuracy of gyroscope navigation in airplanes 200-fold, says Air Force Lt. Col. Jay Lowell, who is leading the project.

The atoms' direction-finding powers come from a technique called atom interferometry. Once a lab curiosity, atom interferometry is now becoming the Swiss Army knife of physics. It has the potential to steer airplanes and submarines, uncover buried caches of oil and diamonds, and perhaps hunt down cave-dwelling terrorists. The technology is also helping scientists probe the very nature of the universe, from detecting theoretical waves of gravity sent out by exploding stars to measuring deviations in the strength of gravity at super-close distances. Physicists are even rallying to put an atom interferometer in orbit to test theories like Einstein's general relativity with unparalleled exactness.

"In the last 10 years, atom interferometry has gone from inventions and demonstrations into precision measurement tools," says physicist Alex Cronin, an expert on the technique at the University of Arizona in Tucson.



COOL WAVES — Lasers chill atoms to a few millionths of a degree above absolute zero. At this temperature, they act more like waves than particles.

R. RATHE/NIST

THE PATH LESS TRAVELED At its heart, atom interferometry is similar to light interferometry, a 200-year-old technique that itself improved the accuracy of many measurements.

Shine a light through a half-silvered glass plate and half the waves pass through, while half bounce off at an angle. A couple of regular mirrors can reflect the two beams back together. If one wave travels a little bit further than the other, the recombined waves will be slightly out of sync. With visible light, this effect produces a pattern of white-and-black stripes: white stripes correspond to areas where the waves line up and black stripes to where they cancel each other out. Physicists use this effect—called an interference pattern—to calculate differences in the distance each beam travels.

During the late 1800s, two American physicists, Albert Michelson and Edward Morley, used a light interferometer to try to detect the "luminiferous ether," then thought to occupy all space. Just as sound consists of vibrations in air, light was supposedly a vibration of the ether, scientists thought. If so, the apparent direction of Earth's motion through the ether would alter the velocities of light beams taking different paths. However, Michelson and Morley's experiment found no such difference, casting doubt on the ether's existence.

Classical physics explains the interference of light waves just fine. Atom interferometry, however, hinges on the bizarre behavior of atoms predicted by quantum mechanics, the math that describes how matter works at sub-microscopic scales. Just as waves of light can sometimes act like particles called photons, atoms can be coaxed into showing off their inner waves. In this condition, an atom can exist in two or more places at once, called a superposition. "It's just weird and you finally end up saying this is a very weird theory," says physicist David Pritchard, a pioneer in the field who works at the Massachusetts Institute of Technology.

One advantage of using atoms for interferometry is their tiny wavelengths. In the 1920s, French physicist Louis-Victor de Broglie proposed that a particle could behave as a wave, and the wavelength would be determined by the particle's speed and mass; the heavier and faster the particle, the shorter its wavelength. Shortly thereafter, experiments proved de Broglie right. The atoms used in interferometry have wavelengths around a hundredth of a nanometer, while the wavelength of visible light measures from 400 to 700 nanometers. Atom waves split into two paths can be used to detect much smaller differences than light. If the path an atom takes varies by even a thousandth of a nanometer (a picometer) an atom interferometer can spot the difference, Cronin says.

Another benefit of atoms is the breadth of their physical characteristics, which include mass, magnetic sensitivity, and ability to hold an electric charge. And atoms feel the pull of gravity. If light interferometry is an old wooden meter stick, then atom interferometry is a modern tape measure, scale, and voltmeter rolled into one.

Yet these beneficial traits also make atoms tough to observe as

waves, Cronin says. Atoms flitting about at room temperature tend to bump into one another. To better detect the waves, physicists cool the atoms to a few millionths of a degree above absolute zero—the temperature at which all atomic motion virtually stops—and manipulate them to fly in the same direction.

HITTING PAY DIRT The first atom interferometers were developed in the early 1990s by four independent teams working in Germany and the United States. Initial applications, such as exacting measurements of the Earth's gravity and rotation, were obvious, says Pritchard, whose MIT lab developed one of the first atom interferometers. "When we made it, we certainly had a pretty good list of things we wanted to do," he says. "What I think was a little surprising to me was the rapidity with which the precision developed."

Many researchers, including Pritchard, credit Mark Kasevich, a Stanford University physicist, with pushing the frontiers of atom interferometry, especially its more practical uses. "Mark's a very good scientist, but he's an off-the-scale good engineer," Pritchard says.

Kasevich's lab is using an atom interferometer to sense tiny fluctuations in the Earth's gravity. High school physics students learn that every second an object is in free fall, it speeds up another 9.8 meters per second. This isn't exactly true, says Kasevich. The acceleration from gravity gets smaller the further you are from the Earth's center. The difference in gravity—the gravity gradient—between sea level and the top of Mount Everest is about 0.3 percent.

On the Earth's surface, gravity's acceleration changes depending on the composition of the rock (or other substance) beneath it. "Anytime you have missing dirt, you can ask if you can find the gravity gradient," Kasevich says. It's a task perfect for an atom interferometer. "One of the killer applications is using it to find oil and minerals," he says.

One hundred thousand metric tonnes of oil buried a kilometer underground will decrease the effect of gravity by a few hundred thousandths of a percent compared with the surrounding rock—small enough for an atom interferometer to detect. The international mining company BHP Billiton has used conventional gravity gradiometry to hunt for diamonds in Australia and Canada's Northwest Territories. Atom interferometry could make these searches even more accurate, Kasevich says.

Oil reserves and diamond caches aren't the only buried structures that atom interferometers could find, says Lowell, program manager for atom interferometry applications at the Defense Advanced Research Projects Agency (DARPA), an arm of the military that supports speculative research. DARPA will fund about $5 million in atom interferometry work this year, Lowell says.

Underground bunkers or even caves might someday be detected with an atom interferometer.

Better navigation may be the most immediate commercial application for atom interferometry. GPS can't reach every nook and cranny of the Earth—deep underwater, for instance—and planes need to have a way of navigating that doesn't count on spotty satellite signals. Today, most jumbo jets have navigation systems that measure the change in the Earth's rotation relative to a fixed point. But these gyroscopes lose about 1 kilometer of accuracy every hour. The military's atom interferometry system aims to cut the loss to 5 m every hour, Lowell says. The cross-country road trip planned for 2010 will test this accuracy by comparing the measurements of an onboard atom interferometer to known landmarks.

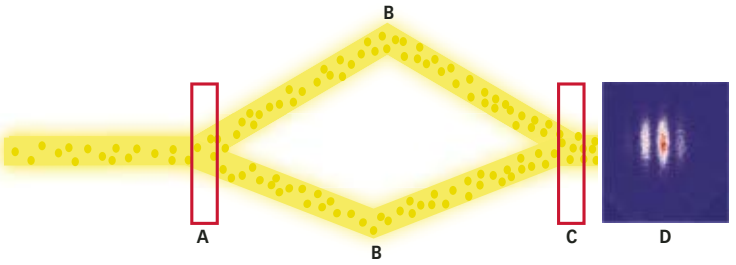
Such precision has become routine in lab experiments, but building an interferometer that can take the bumps of an airplane or helicopter ride demands changes to lab models, Lowell says. "We have systems that are now smaller and more compact and work with the flip of a switch, instead of a system that takes up massive chunks of tabletops and a rack of equipment, and takes armies of grad students to keep operating," he says.

> "Whenever you … extend your ability to see, you're going to stumble onto something new."
>
> — STEVEN CHU, DIRECTOR, LAWRENCE BERKELEY NATIONAL LABORATORY

A CONSTANT STRUGGLE On a sprawling 20-by-20-foot table at the National Institute of Standards and Technology (NIST) in Gaithersburg, Md., physicist Kris Helmerson shows off an instrument that does in fact demand an army of graduate students.

On one end of the gigantic table, the eerie glow of an orange laser dances around a dozen little lenses and mirrors set at different angles and orientations. The laser will chill sodium atoms to a hair above absolute zero. In this state, hundreds of thousands of atoms together act like one big wave, called a Bose-Einstein condensate.

Just creating the condensate earned Nobel prizes in 2001 for the three physicists who accomplished the feat in 1995. Helmerson, who works in NIST's Advanced Measurement Laboratory, uses atom interferometry to measure more esoteric properties of Bose-Einstein condensates. In 2000, for instance, he and colleague Bill Phillips put a kind of sound wave, called a soliton, into their condensate. And in 2006, the team created a whirlpool-like vortex out of a condensate.



STEERING ATOMS' PATHS — The pulse of a laser splits (A) supercooled atoms onto two different paths. A second pulse (B) steers them on a collision course so that they converge (C). If their paths differ by even a thousandth of a nanometer (picometer), the atoms create an interference pattern (D).

Less exotic pursuits keep other atom interferometers busy. The most common experiments are measurements of physical constants, the numbers describing gravity, electricity, and other forces that make the universe tick. Over the past two centuries, light interferometry refined these figures, and atom measurements will do the same, says physicist Steven Chu, director of the Lawrence Berkeley National Laboratory in California.

Chu, whose lab is based at Stanford, has shown that atom interferometry can achieve the same precision as conventional methods in measuring the acceleration due to gravity on Earth. With technological improvements, atom interferometry could do even better.

Atom interferometry could also refine another measure of gravity—the constant that describes the gravitational tug between any two objects, which physicists call "big G." Currently, G's value is known only to one part in 10,000. That's equivalent to knowing the length of 100 meters (roughly a football field) down to a centimeter—not very precise by the usual standards for fundamental constants of nature. "It's kind of embarrassing," Cronin says.

In a paper in the Feb. 8 *Physical Review Letters*, a team of Italian physicists suggests that atom interferometry could improve the precision of G by at least a factor of 10. In another paper, the same team used atom interferometry to measure gravity between objects separated by a few millionths of a meter. Such measurements could reveal a breakdown in Newton's laws of gravity, which could have implications for theories suggesting the existence of extra dimensions of space.

Adding an extra digit or two to constants like G may sound like

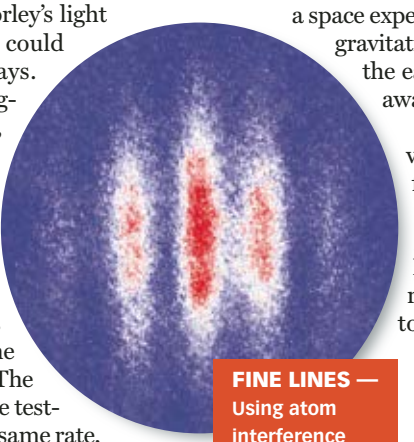
E. ROELL

the scientific equivalent of dotting i's and crossing t's, but physicists like Chu think otherwise. "It's not chasing after the last digits," he says. "It's chasing after the first digit of something radically new." Better telescope measurements of celestial orbits buttressed Newton's theory of gravity, and Einstein's theory of special relativity explained the results of Michelson and Morley's light experiments. Likewise, atom interferometry could augur the next scientific revolution, Chu says. "Whenever you make something orders of magnitude better and extend your ability to see, you're going to stumble onto something new."

COLLIDING FRONTIERS A basement physics laboratory at Stanford might produce such a discovery. Kasevich's team is nearly finished building the world's biggest atom interferometer, a 10 m deep well. Several factors determine an interferometer's precision, but the distance the atoms can travel is a big part of it. The first experiments planned for the device include testing whether objects of different mass fall at the same rate, echoing Galileo's legendary experiment at the leaning tower of Pisa. Kasevich plans to toss two different kinds of rubidium atoms down his interferometer. The atoms differ slightly in mass because one contains more neutrons than the other.

Even with his giant interferometer set to begin experiments in 6 months, Kasevich is thinking bigger. A planned underground laboratory in the abandoned Homestake gold mine in Lead, S.D., has the physicist licking his lips. "We've been brainstorming about what we can do if we have a kilometer rather than 10 meters," he says.

Yet all interferometers on Earth, however deep, suffer from environmental noise, such as ocean tides and earthquakes. Physicists go to great extremes to shield their instruments from these effects, but as precision increases, environmental noise eventually drowns out results. "For the ultimate in precision we would like to consider space," says Savas Dimopoulos, a theoretical physicist at Stanford who hopes to use atom interferometry to detect gravitational waves radiating from pairs of black holes and other binary systems. He's working with Kasevich to perform the experiments on Earth, but a space experiment offers an even better chance to see the gravitational waves, which could provide a glimpse of the early universe. Any launch is at least a decade away, Dimopoulos says.



NIST

FINE LINES — Using atom interference patterns, physicists can make excruciatingly sensitive measurements of gravity and other forces.

While atom interferometry probes the universe with growing meticulousness, another frontier of physics is taking a different approach to unlocking its secrets. Deep below ground crossing Switzerland's border with France, an army of physicists and engineers is readying the world's largest particle accelerator, the Large Hadron Collider (LHC), for a planned summer startup. With the LHC, physicists will smash protons together at speeds within a sliver of the speed of light, hoping to find new forms of matter.

These two approaches—precision and high energy—overlap in the questions they can answer, Dimopoulos says. For instance, the LHC could detect what are called supersymmetric particles—sparticles—that he and other physicists have proposed lurk beside the quarks, neutrinos, and other elementary particles that fill the universe. Atom interferometry, by measuring the charge on an atom's electrons with great sensitivity, could support the existence of those supersymmetric particles. "In the end we are looking for a new theory," he says. "This one theory has the same consequences at high energy and high precision." ■

OF NOTE

NEUROSCIENCE

More evidence that flies sleep like people

A common brain chemical is enough to keep a fruit fly up at night. Scientists know that the chemical, a neurotransmitter called GABA, is important for the human sleep cycle. But a new study is the first to show the chemical also controls whether a *Drosophila melanogaster* nods off or tosses and turns all night.

The research, published in the Feb. 1 *Nature Neuroscience*, shows that a receptor for GABA controls whether fruit flies fall asleep, just as it does in humans. But the receptor, found in cells that control wakefulness, doesn't influence whether the fruit flies stay asleep or determine how long they slumber, says Leslie Griffith, a neuroscientist at Brandeis University in Waltham, Mass.

Fruit flies with mutations in the GABA receptor, which is encoded by a gene called *Rdl*, fell asleep faster than normal fruit flies. An epilepsy drug called carbamazepine has the opposite effect, keeping fruit flies awake. A common side effect of carbamazepine is insomnia.

GABA receptors form channels that help generate electric currents in some brain cells, enabling communication between neurons. The mutation in the *Rdl* GABA receptor causes the channel to stay open, blocking wake signals and giving Mr. Sandman more time to work his magic. Carbamazepine works like a quick-reset button, closing the channel and allowing the cell to fire messages quickly.

The discovery may lead to better drugs for people with certain types of insomnia, Griffith says. —TINA HESMAN SAEY

ZOOLOGY

Bird fads weaken sexual selection

Every year, there's a new fashion pick for the hot male. With lark buntings, that is.

A study of style among birds adds new dimensions to the understanding of how female taste drives the evolution of male charms. This process of sexual selection can lead to outrageous male ornaments, but only if females swoon over the same traits over many generations.

Something different goes on with sex appeal among lark buntings (*Calamospiza melanocorys*) in Colorado's Pawnee National Grassland, says Bruce Lyon of the University of California, Santa Cruz. He and Alexis Chaine of the CNRS Experimental Ecology Station at Moulis, France, tracked the characteristics of Colorado male birds who found mates. Trends certainly did appear in size and looks but varied by year, the researchers report in the

OF NOTE

Jan. 25 *Science*. In 2000, for example, big white wing patches were in. In 2002, it was small patches.

Fickle as the shifts sound, they might be important, says Lyon. More of a particular year's hot-male traits than expected by chance turned up in the dads that successfully raised chicks that year. Lyon suggests that either the traits themselves, or something linked to them, tells females who's the right fellow for a particular year's conditions.

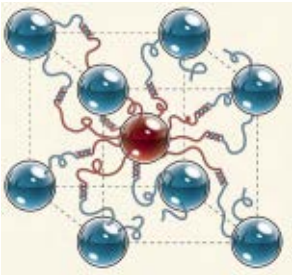
As for sexual selection, Lyon says the various strong trends in particular years had pretty much canceled out each other's effects by the end of five years. Flip-flops in taste, he says, might help explain what keeps variety within a species. —SUSAN MILIUS

NANOTECHNOLOGY

Nanocrystal

Using DNA as a sort of Velcro, two separate teams of scientists have created what may be the first nanomaterials that assemble themselves into ordered 3-D structures. The techniques may enable the creation of crystals with novel properties.

Using the propensity of DNA's chemical bases to bind to their ideal complements—A with T, C with G—researchers had previously put DNA to work to self-assemble into orderly 2-D arrangements or chaotic 3-D lumps.



FREE TO ASSEMBLE DNA strands link gold nanospheres in ordered arrangements to create a new type of crystal.

To create the first true 3-D materials from nanoscale components, each team attached single strands of DNA to gold spheres about 10 nanometers across. The scientists used two different DNA sequences to create two distinct batches of nanospheres. The DNA sequences were chosen so that, when the two batches were mixed, the unattached ends from one batch would latch only on to the ends in the other batch.

After repeated cycles of heating and cooling, the nanospheres found their most stable configurations, interlocking into a 3-D lattice of spheres linked by DNA and resembling a web of mattress springs. Its arrangement mirrored that of atoms in a crystal—but on scales 50 or 60 times as large. The results appear in two papers in the Jan. 31 *Nature* and one in an upcoming *Journal of the American Chemical Society*.

"This is really a new form of matter," says Chad Mirkin of Northwestern University in Evanston, Ill., who led one of the teams. The structures also leave plenty of space between spheres, points out Oleg Gang of Brookhaven National Laboratory in Upton, N.Y., who led the other team. This space leaves room for custom designing crystals with new magnetic or catalytic properties—and maybe unusual lenses such as those envisioned for invisibility cloaks. —DAVIDE CASTELVECCHI

SCIENCE & SOCIETY

Heed your elders, survive a tsunami

An oral tradition passed down among islanders in the South Pacific—"run to high ground after an earthquake"—saved many lives during a tsunami last year and illustrates the benefits that community-based education and awareness programs can provide, scientists say.

On April 2, 2007, a magnitude-8.1 temblor struck about 50 kilometers (km) south of the New Georgia Islands, northeast of Australia. A tsunami spawned by that quake damaged or destroyed more than 6,000 buildings in 300 communities and killed 52 people, says Hermann M. Fritz, a civil engineer at the Georgia Institute of Technology in Savannah. Less than 5 minutes after the ground stopped shaking, a wave 5 meters (m) tall swept more than 100 m inland on Simbo Island, completely destroying the village of Tapurai.

Because elderly residents of Tapurai had experienced a smaller temblor and tsunami in 1959, they often warned young villagers to immediately seek high ground in case of a quake. As a result, says Fritz, only 7 of the community's 241 residents died in last year's disaster.

A telling counterexample to Tapurai's success comes from the Peruvian fishing village of Lagunilla, whose residents didn't know to run for the hills after a quake. After a magnitude-8.0 temblor struck about 60 km offshore last August, a tsunami killed 43 percent of the village's residents, even though the wave there was half the size of Tapurai's, high ground was closer, and warning time was longer.

Oral tradition can serve as an effective early-warning system for tsunamis, Fritz and colleague Nikos Kalligeris of the Technical University of Crete in Chania, Greece, propose in the Jan. 16 *Geophysical Research Letters*. "Knowing what to do is what saves lives," Fritz says. —SID PERKINS

BIOMEDICINE

Caffeine intake tied to miscarriage

Pregnant women who consume two or more cups of coffee per day face a higher miscarriage risk than women who avoid caffeine, a study finds.

In the late 1990s, researchers at the Kaiser Foundation Research Institute in Oakland, Calif., interviewed 1,063 women less than 15 weeks pregnant. Of these, some consumed no caffeinated beverages during pregnancy, some consumed at least 200 milligrams (mg) of caffeine daily, and the rest consumed less. The average cup of coffee contains about 75 to 135 mg of caffeine, while tea and soft drinks aren't as potent.

Women ingesting 200 mg of caffeine or more per day in any form were roughly twice as likely to miscarry during the first 20 weeks of pregnancy as were those getting no caffeine. Women consuming less caffeine faced no increased risk. The report will appear in the March *American Journal of Obstetrics & Gynecology*.

The scientists accounted for age, race, education, household income, marital status, smoking status, alcohol consumption, hot-tub use, and differences in morning sickness—a factor seldom included in studies of this type.

Nausea might lead some women to change their caffeine intake during pregnancy, so the researchers focused only on women who maintained their caffeine-use patterns during pregnancy.

Some scientists have also wondered whether women with nausea represented a healthier-pregnancy group, since morning sickness stems from potent hormones that ostensibly would help a fetus develop. By eliminating the morning-sickness variable, the new study establishes an effect by caffeine, says study coauthor De-Kun Li, an epidemiologist at Kaiser.

Caffeine alters normal cell functions and reduces blood flow to the fetus. But beyond that—and that it can pass through the placental barrier—its effects on a fetus remain poorly understood. —NATHAN SEPPA

NATURE

Books

A selection of new and notable books of scientific interest

HANDBOOK TO LIFE IN THE AZTEC WORLD

MANUEL AGUILAR-MORENO

King Cuauhtémoc, the last Aztec emperor, was defeated by the Spanish Army in 1521. After the conquest, monastic orders arrived in Mexico and the remaining native peoples were baptized into the Christian faith. Despite the death and destruction inflicted by the conquistadors, the cultural exchange between the Aztecs and Spaniards has provided historians with enough evidence to explore for centuries. Gathering the results of archaeological discoveries and scholarly research into a single volume, this handbook covers Aztec history, arts, political systems, class structure, science, types of human sacrifice, and more. Naturalistic details were woven into each aspect of Aztec society. City avenues were arranged to trace the movement of the sun. Buildings in capital cities were designed according to astronomical alignments. Even the word for city, *altepetl*, incorporates nature; it means "water-producing mountain." Aguilar-Moreno also elucidates the complicated Aztec calendar system. Of note, in the 365-day calendar, the "five useless and unlucky days" correlate in the Christian calendar to Feb.9–13. ***Oxford Univ., 2007, 440 p., b&w photos and illus., paperback, $25.00.***

THE THIEF AT THE END OF THE WORLD: Rubber, Power, and the Seeds of Empire

JOE JACKSON

When Henry Wickham heard about a kind of tree that produced strong and durable rubber, he ventured into Amazonian jungles in search of it. Rubber was craved during the Victorian era, and Wickham hoped his expedition would make him a wealthy man. He found the rubber trees and smuggled 70,000 of the seeds into England. Wickham's seeds were planted throughout the British Empire. Within a few years, they produced trees that yielded rubber used in everything from trains to baby bottles. Wickham himself never reaped a financial benefit from the rubber boom. His story is one of shattered patriotism and industrial greed. Jackson, a former investigative reporter, combed through botanical archives and private letters, and trekked through South America to produce a thorough account of what may be the first case of biopiracy in the modern era. ***Viking, 2008, 413 p., b&w photos, hardcover, $27.95.***

PLAN B 3.0: Mobilizing to Save Civilization

LESTER R. BROWN

As president of Earth Policy Institute in Washington, D.C., Brown has been analyzing the interaction between environmental and economic trends for decades. In this book, the third in a series, he proposes three actions needed to stabilize the climate: raise energy efficiency, develop renewable sources of energy, and expand Earth's tree cover. These goals will not be met by what Brown calls Plan A—that is, business as usual. Some of the suggestions in Brown's Plan B are as simple as replacing incandescent bulbs with fluorescent bulbs. Retrofitting existing buildings can cut energy use by 20 to 50 percent he writes. Brown praises big-picture thinking that recognizes the need to move away from fossil fuels as much as possible. He encourages individuals to make change at the local level and to persuade their elected representatives to support environmental initiatives. "Saving civilization is not a spectator sport," writes Brown. Remaining true to its theme, *Plan B 3.0* can be downloaded free of charge from the Earth Policy Institute Web site (*earthpolicy.org*). ***Norton, 2008, 398 p., paperback, $16.95.***

THE LITTLE BOOK OF PANDEMICS

PETER MOORE

Hypochondriacs and germophobes may want to look for a less terrifying bedtime read—perhaps something by Stephen King. Moore's breezy catalog of pestilence features the world's most notorious killers, such as Ebola, anthrax, and smallpox. The book also highlights dozens of lesser-known infections. For instance, English sweating sickness, a mysterious, swift-killing disease, appeared in 15th- and 16th-century England and then vanished. Scientists still don't know what caused it. Rift Valley fever, a mosquito-borne virus that hit Sudan recently, can lead to hemorrhaging and seizures and kills one out of a hundred. Moore devotes a few pages to each of 50 infectious diseases, describing their origins, symptoms, and treatments (if there are any). He also rates every infection on the basis of how fast it spreads and how likely its victims are to survive. ***Collins, 2007, 144 p., paperback, $14.95.***

RED PROMETHEUS: Engineering and Dictatorship in East Germany, 1945–1990

DOLORES L. AUGUSTINE

The effect of government on science might be most transparent when research is conducted under a dictatorship. Technological progress was an ideal in East Germany during the Cold War. Engineers and scientists, however, often clashed with government officials regarding its goal. By the 1960s, socialist leaders strove to win a technological race with the West. Secret police penetrated the "technical intelligentsia" in order to ensure loyalty to the socialist system above all else. In researching her book, Augustine delved into the vast archives that have opened since the fall of the communist regime. She examined official reports and interviewed former East German engineers and scientists to provide a picture of research in East German industry and, more generally, in the communist Eastern Bloc. ***MIT Press, 2008, 381 p., b&w photos, hardcover, $40.00.***

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LETTERS

Inert placebo?

Regarding "Getting the Red Out" (*SN: 1/19/08, p. 35*): While drug companies wish to market their products, my attention is drawn to the fact that 1 in 8 of the control group of psoriasis patients was cured by placebo effect. Who will investigate the process therein? Is there a market for it?

CARSON BARNES, LOMA MAR, CALIF.

*A potent placebo effect, even of 12 percent, isn't unheard of in medical studies. To find out more about the placebo effect and efforts to capitalize on it, see "Medicinal Mimicry: Sometimes, placebos work—but how?" (*SN: 2/3/01, p. 74*) and "Intrinsic Remedies for Pain: Placebo effect may take various paths in brain" (*SN: 1/21/06, p. 37*).* —NATHAN SEPPA

Time of death

"Struck from above" (*SN: 1/5/08, p. 14*) suggested yet a second possibility leading to the decline or extinction of the mammoths in the region of the apparent iron micrometeorite-shower impact, which drove the metallic particles into the sides of the fossil tusks examined. That same shower of high-velocity metallic particles found in the tusks probably perforated the skin and soft tissues of the mammoths, causing extensive hemorrhaging and more or less immediate, widespread death rather than having "rendered much of northern Alaska inhospitable for decades."

CARL B. MANKINEN, JACKSONVILLE, FLA.

This study focuses on the mammoth tusks, but a skull of a Siberian bison shows signs of bone growth after similar particles became embedded in it, suggesting the creature survived the event. Because the outer layers of tusk material are already dead (essentially, a tusk is a big tooth), it's impossible to tell whether the mammoths survived the event. —SID PERKINS

Survival of the bravest

There is little mystery why some female fishing spiders are so aggressive that they eat their suitors before mating can take place ("Not So Spineless," *SN: 1/5/08, p. 10*). It would take a very bold male to court a female knowing he is going to be lunch. To maintain such inherited aggressive behavior in the female, one only has to assume that both sexes inherit the same aggressive trait.

ROBERT STENTON, CINCINNATI, OHIO

The Best Reason to Stop Global Warming Is Growing Up Fast!

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Television and film star Eva La Rue with her daughter Kaya

Photographed by Jay Silverman © 2007

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