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SCEENCE SCEENC

toxicity conundrum feathered drug factories extinctions down under maine lobsters vs. whales

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DOES IT MAKE PEOPLE FAT?

THE WEEKLY NEWSMAGAZINE OF SCIENCE

SCIENCE NEWS JANUARY 20, 2007 VOL. 171, NO. 3

Features

- **40 Counterintuitive Toxicity** Increasingly, scientists are finding that they can't predict a poison's low-dose effects by Janet Raloff
- **43 Weighing In on City Planning** Could smart urban design keep people fit and trim? by Ben Harder

This Week

- **35 Engineered hens lay drugs** by Christen Brownlee
- 35 Triple-quasar system may signal galaxy mergers by Ron Cowen
- 36 Ephemeral *Pfiesteria* compound surfaces by Aimee Cunningham
- **36** Lost chromosome tips linked to heart problems by Nathan Seppa
- **37** Less lobstering could mean fewer whale deaths by Susan Milius
- **38 Early people at fault in Australian extinctions** by Sid Perkins
- **38 Coercion aids treatment of eating disorders** by Bruce Bower



Of Note

- 45 Mercury pollution settles in hot spots Nanoparticles find tumors, form clumps
- **46** Of penguins' range and climate change

2006: Hottest year in U.S. history

Salmonella illnesses traced to pet rodents

Gene variant shapes beta-blocker's effectiveness

Departments

- 47 Books
- 47 Letters

Cover Metropolitan Atlanta, often called a poster child for urban sprawl, has undergone rapid geographical expansion as its population has burgeoned to about 5 million. Studies suggest that urban sprawl contributes to physical inactivity and obesity. (Getty Images) Page 43

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SCIENCE NEWS This Week

Golden Eggs Engineered hens lay drugs

Scottish scientists have genetically engineered hens that can not only produce useful drugs in their eggs but also reliably pass on this characteristic to new generations of

QUOTE

You could perhaps

change the flavor

FRANÇOIS POTHIER,

[of eggs] or add

interesting for

Laval University

something

health."

chickens. Successfully combining these two traits represents a first for researchers aiming to transform animals into living drug factories, the scientists say.

Certain proteins can counteract a variety of medical conditions, from anemia to diabetes to cancer. While some of these protein drugs are relatively simple to make in the lab, others are difficult, time-consuming, or expensive to produce.

Since animals naturally make thousands of proteins, researchers have sought to harness this innate capability. Over the past several years, scientists have engineered cows, sheep, and other mammals to produce protein drugs.

However, these animals have several drawbacks, says Simon Lillico of the Roslin Institute outside Edinburgh. Most of the engineered animals are large, expensive to house and feed, and take years to mature enough to produce the desired proteins. Furthermore, these animals can't stay healthy while making compounds toxic to mammalian cells—a trait many medicines require.

Some researchers have suggested that chickens—with their small sizes, low maintenance needs, and quick generation times—could produce protein drugs in their eggs. But Lillico notes that previous attempts to engineer drug-producing chickens have run into problems. For example, in some engineered hens, drugmaking capability fades with each generation.

Lillico and his colleagues, led by the Roslin Institute's Helen Sang, took a new approach. They constructed drug-coding genes that would insert themselves into the gene that all chickens carry for making the egg-white component ovalbumin.

The team worked with two synthetic genes that code for different protein drugs: an antibody called miR24, which has shown promise against melanoma, and a protein called human interferon-beta-Ia, which is already used to treat multiple sclerosis. The researchers employed viruses to ferry both genes into cells in young chick embryos inside unhatched eggs.

When the eggs hatched, the researchers selected the male chicks that carried the altered gene. When the team later bred these roosters with normal hens, half the female offspring laid eggs containing both protein drugs in their whites, the researchers report in an upcoming *Proceedings of the National Academy of Sciences.* The researchers continue to screen for male offspring carrying the genes and to breed them with normal hens. They now have five generations of drug-producing birds, Lillico says.

The newly engineered chickens "could pave the way to something very interesting," says animal sciences professor François Pothier of Laval University in Quebec City, who has engineered pigs to produce useful proteins in their semen. Pothier points out that before chickens roost in pharmaceutical factories, the researchers in Scotland have many hurdles to overcome, such as increas-

ing the small amounts of the two drugs present in the hens' egg whites.

However, Pothier notes that once the scientists perfect their technique, it might be possible to introduce a variety of useful proteins that would improve eggs' food value.

"You can imagine that eventually, not only could you modify the content of an egg for therapeutics, but you could perhaps change the flavor or add something interesting for health," such as vitamins or heart-healthy fatty acids, Pothier says. —C. BROWNLEE

A Cosmic Pas de Trois

Triple-quasar system may signal galaxy mergers

Astronomers have discovered the first example of a trio of quasars, the brilliant beacons of light that seem to be fueled by supermassive black holes at the centers of galaxies. The triplet adds to earlier evidence that supermassive black holes and galaxies grow in lockstep.

George Djorgovski of the California Institute of Technology in Pasadena and his colleagues began their study by examining a distant quasar called LBQS 1429-008. Another team had found the quasar in 1989 and soon after detected a nearby spot that could have been either a companion quasar or a cosmic mirage. According to Einstein's general theory of relativity, the gravity of a massive foreground galaxy can act as a lens, splitting the light from a background body, such as a quasar, into two or more images.

In the new work, Djorgovski's team analyzed images of the quasar and its surroundings taken at two telescopes. The images revealed a second, even fainter potential companion to LBQS 1429-008.

The team initially proposed that both of the nearby spots were optical illusions generated by the gravity of a foreground galaxy. But the researchers couldn't find any such galaxy. Computer modeling revealed that gravitational lensing couldn't plausibly account for the brightness and geometry of the three quasar images.



TRIPLE PLAY The first example of a trio of quasars (arrows) resides about 10.5 billion lightyears from Earth. The quasars arose when the universe was about one-fifth its current age.

SCIENCE NEWS This Week

Instead, the triple images almost certainly represent three distinct but closely spaced quasars about 10.5 billion lightyears from Earth, Djorgovski reported last week at a meeting of the American Astronomical Society in Seattle. Scientists have occasionally found two quasars in the same vicinity, he notes, but "to find three is unprecedented."

At the Seattle meeting, theorist Fred Rasio of Northwestern University in Evanston, Ill., described new simulations of the interactions of three closely spaced supermassive black holes. His team finds that when a third black hole meets up with two already orbiting each other, one of the trio tends to get kicked out of the system while the other two orbit more closely, hastening their eventual merger.

Of the three black holes powering the quasars in Djorgovski's study, two will probably coalesce in about 100 million years, Rasio says.

The tight grouping of these three quasars indicates that their host galaxies must be in the early stages of merging, Djorgovski suggests. He notes that the separation among the quasars, about 100,000 light-years, is a distance typical of interacting galaxies.

Galaxy mergers are less common today than during the early era from which the triplet quasars hail—about 3 billion years after the Big Bang. Since than, the expansion of the universe has pushed galaxies farther apart.

Over the past few years, astronomers have accumulated evidence that the mass of stars surrounding a galaxy's center is always about 1,000 times the mass of the galaxy's supermassive black hole (*SN: 1/22/05, p. 56*). If two of the three galaxies ultimately merged, that interaction would funnel gas to the central black holes, increasing their girth, says Rasio. This would enhance quasar activity, which in turn would influence the star-formation rate in the galaxy's core. —R. COWEN

Fish Killer Caught?

Ephemeral *Pfiesteria* compound surfaces

A team of researchers claims to have found an elusive algal toxin implicated in massive fish kills along the Mid-Atlantic coast in the 1990s. They say that the compound's characteristics explain why it has been so difficult to track down. Other researchers, however, remain skeptical.

The hunt for a toxic product of the single-celled alga *Pfiesteria piscicida* dates to the early 1990s, when researchers laid the blame for fish kills in North Carolina waters on the organism (*SN: 9/27/97, p. 202*). Moreover, scientists who worked with the alga in the laboratory reported headaches and rashes. Public safety concerns led Maryland officials to temporarily limit access to certain Chesapeake Bay waterways in 1997 after a fish kill occurred there.

Not all scientists agreed that a toxic agent secreted by that alga was responsible for the fish deaths. Some researchers blamed a fungal disease first described in the 1980s (*SN: 10/10/98, p. 231*), while two research groups independently reported that they couldn't find evidence that *Pfiesteria shumwayae*, the other named *Pfiesteria species*, makes a toxin (*SN: 8/10/02, p. 84*). One of those teams proposed that the alga eats away fish skin.



CHEMICAL CAPTURED The alga *Pfiesteria piscicida*, shown here in a scanning electron micrograph, was blamed for fish kills in the 1990s. Researchers say that they've found the toxic compound produced by the alga.

A different group now reports a structure for the chemical that it says is responsible for the toxicity. Peter D. R. Moeller, an organic chemist with the National Oceanic and Atmospheric Administration's Hollings Marine Laboratory in Charleston, S.C., and his colleagues describe their data online for an upcoming *Environmental Science* \mathfrak{S} *Technology*.

From work that used five analytical methods, the researchers propose that the toxin's structure contains a carbon chain interrupted by a sulfur-copper-sulfur segment. They found that the compound, when energized by light, produces free radicals, which are highly reactive chemical species with unpaired electrons.

As the compound generates free radicals, it decomposes, Moeller says, so it remains active only for several days. This could explain why the toxin has been so elusive. "It's destroying itself. That's why you can't find it after the fact," Moeller says.

Various environmental cues are necessary to start the compound on its free radical-generating path, he adds. The researchers found that light, high heat, and changes in pH can set off the compound. Other environmental conditions could also contribute, Moeller says, adding that the researchers won't know more "until we test this in the wild."

But the new evidence has left others unconvinced of the compound's structure and toxicity. Robert E. Gawley, an organic chemist at the University of Arkansas in Fayetteville who has searched for the toxin, says that the characterization report is incomplete and doesn't meet "the standards of a rigorous structural proof."

William B. Tolman, an inorganic chemist at the University of Minnesota in Minneapolis, says that the evidence for coppersulfur bonds is weak. The reported distance between the copper and sulfur atoms is too long for the proposed structure, he says.

Tolman also notes that while the researchers provide proof that free radicals are present, "whether or not the free radicals are responsible for the toxicity is not clear." -A. CUNNINGHAM

Coming to a Bad End Lost chromosome tips linked to heart problems

The prime risk factors for heart disease are well known—obesity, smoking, elevated cholesterol, and high blood pressure. Yet many people with these warning signs develop heart problems, while others don't. This observation indicates that yet-unrecognized factors must also influence risk.

A new study finds that the sequencerepeating sections of DNA called telomeres, which protect the ends of chromosomes, might play a role. Middle-aged men with long telomeres are only half as likely to develop heart disease as are men of the same age with short telomeres, researchers report in the Jan. 13 *Lancet*.

Telomeres buffer chromosomes' tips much as plastic caps preserve the ends of shoelaces. But telomeres get shorter with each successive division of a cell, and tooshort telomeres ultimately leave a cell unable to replicate.

In the new study, Nilesh J. Samani, a cardiologist at the University of Leicester in England, and his colleagues assessed telomere length in the white blood cells of Scottish men entering a trial of the cholesterollowering statin drug pravastatin (Pravachol). The 6,595 participants averaged 55 years old, and all had elevated blood concentrations of low-density lipoprotein (LDL), the bad cholesterol. Researchers randomly assigned them to receive pravastatin or a placebo.

Over the next 5 years, 484 of the men developed heart disease. Samani and his cohorts identified 1,058 other study participants who matched those men in age and smoking status but who remained free of heart problems.

The researchers found that among the men getting the placebo, those with short telomeres were roughly twice as likely to develop heart disease as men with long telomeres were.

The statin drug seemed to remove this distinction. Regardless of their telomeres' lengths, men taking pravastatin developed heart disease at the same rate.

Among the men with long telomeres, receiving the drug didn't affect heart disease incidence.

Short telomeres "may provide an explanation for unexplained heart problems," Samani says. But he cautions that this study offers only an association between telomere length and heart disease, not proof that long telomeres are protective.

Past research has linked chronic inflammation to heart disease (*SN*: *6*/*4*/*05*, *p. 365*). Shortened telomeres in white blood cells might induce those immune cells to trigger inflammation, surmise Ioakim Spyridopoulos and Stefanie Dimmeler of the University of Frankfurt in Germany, also writing in the Jan. 13 *Lancet*. They suggest that short telomeres might also prevent nascent blood vessel cells from fending off atherosclerosis, a major form of heart disease.

Stress, obesity, and insulin resistance may shorten an individual's telomeres (*SN*: 12/4/04, p. 355; 6/11/05, p. 381). Other lines of research suggest that shortened telomeres might result from the accumulation of free radicals, which are reactive oxygen or nitrogen molecules that can damage cells.

Heart disease will ultimately involve "more variables than we know, and telomeres may be one of them," says Kathleen Collins, a molecular biologist at the University of California, Berkeley. —N. SEPPA

Saving Whales the Easy Way?

Less lobstering could mean fewer deaths



Atlantic right whale (above), entangled in lobster gear, lie on the beach. The same whale was photographed 7 months earlier (right) already snarled in the gear, which is one of the main perils to the highly endangered species. Only 350 right whales remain in the population, which isn't increasing despite the ban on killing whales.

whales dying as a result of getting tangled in lobster gear.

To create this better world, the lobster fleet should shorten its season and set out fewer traps, suggest biologists led by Ransom Myers of Dalhousie University in Halifax, Nova Scotia. The drop in effort shouldn't undermine profits, they say, because the Canadian lobster fishery just across the border is thriving despite restrictions.

U.S. regulations permit lobster harvesting year round, while the Canadian season runs from the end of November through May. Overall, the U.S. fleet catches a third more lobsters but expends disproportionately more resources doing it.

For a given lobster harvest, the U.S. fishery uses 13 times as many traps as the Canadians do, the researchers say. Because tending extra traps requires more fuel and bait, a shorter, more efficient fishing effort could be as profitable, the team argues. In the Jan. 9 *Current Biology*, the biologists suggest a 6-month season and a 90 percent reduction in the several million traps currently permitted.

Although there's no rule regarding season, U.S. lobster boats traditionally take almost all their catch during the 6 months of summer and fall, says lobster biologist Carl Wilson of the Maine Department of Marine Resources in West Boothbay Harbor. As for reducing the number of traps, "it's an interesting idea, but the devil is in the details," he says.

Limitations on the lobster fleet would be good news for the North Atlantic right whale, says coauthor Boris Worm, also of Dalhousie. The large, slow-moving, coastal whales have virtually vanished from the Atlantic coast of Europe. Only some 350 right whales remain along the North American coast.

For 70 years, laws have banned killing of the North Atlantic right whale, yet the population isn't increasing, unlike that of a sister species, the South Atlantic right whale.

The northern whale might be stuck in a bad neighborhood—with heavy ship traffic, near-shore fisheries, and pollution—Worm says. "It has been called the urban whale," he notes. Computer modeling has indicated that in such dire circumstances, losing even two or three adult females could send the already depleted population into a downward spiral.

According to previous studies, the top killers of right whales are ships that run into them and fishery rigging—often lobster gear—that accidentally entangles them.

Because migrating right whales travel through the Gulf of Maine in spring and fall, reducing the area's lobster traps at those times would make the passage safer, says Worm.

The plan doesn't impress Patrice McCarron of the Maine Lobstermen's Association

A controversial new study argues that the U.S. lobster fishery in the Gulf of Maine could have the better of two worlds: less work to make the same profit and fewer

SCIENCE NEWS This Week

in Kennebunk. Regulations already require some low-tangle gear, and rules for more such gear are under consideration. Also, McCarron says, lobster-trap tenders don't see any whales, so changing the industry "will not have any benefit to whales."

Worm notes that migrating whales are difficult to spot and that scientists have incomplete information about routes. —S. MILIUS

Going Under Down Under

Early people at fault in Australian extinctions

A lengthy, newly compiled fossil record of Australian mammals bolsters the notion that humanity's arrival on the island continent led to the extinction of many large creatures there. Archaeological evidence suggests that people arrived in northern and western Australia about 50,000 years ago (*SN: 3/15/03, p. 173*). By 5,000 years later, about 90 percent of the continent's mammals larger than a house cat had gone extinct, says Gavin J. Prideaux, a paleontologist at the Western Australian Museum in Perth. Casualties of that era include several species of kangaroos and wombats as well as marsupials that filled the ecological niches elsewhere populated by lions, hyenas, hippos, and tapirs.

By unearthing and cataloging specimens from a group of fossil-rich caves about 300 kilometers southeast of Adelaide, Prideaux and his colleagues assembled a nearly complete record of the past 500,000 years. Most of the 62 species of nonflying mammals on the list fell into the caverns via sinkholes, but some remains were brought in by owls that roosted there.

Scientists had compiled a long-term climate record for southeastern Australia by analyzing the caves' stalactites. Those structures formed and grew when rainfall was plentiful but not during dry spells.

During most of the past 500,000 years, the number and diversity of mammal fossils found in the Australian caves decreased only during intervals when the local climate was dry. When moisture returned, so did the animals. The only exception is the die-off of mammals between 50,000 and 45,000 years ago, the team reports in the January *Geology*.

Those extinctions occurred at least 25,000 years before the most recent ice age began. "The climate was stable then, and mammals really shouldn't have been going extinct," says coauthor Richard G. Roberts, a geochemist at the University of Wollongong in Australia. "The only thing that's new during that period is people," he adds.

Scientists are debating how people might have caused the extinctions. Some researchers argue that the new inhabitants drastically altered Australian ecosystems by burning the landscape (SN: 7/23/05, p. 61). However, large species may have died off gradually when people preyed on the mammals' offspring faster than the animals reproduced, says Roberts.

The fossil record compiled by Prideaux and his colleagues shows that "the mammal fauna was resilient through time, despite climate fluctuations," says David W. Steadman, a paleontologist at the University of Florida in Gainesville. Changes in mammal populations during times of climate change "were nothing like those that occurred after people showed up," he notes.

"To think climate caused these extinctions is [now] untenable," comments Gifford H. Miller, a geologist at the University of Colorado at Boulder. —S. PERKINS

Starved for Assistance Coercion finds a place in the treatment of two eating disorders

any people with serious eating disorders seek mental-health care only after they are pressured into it by concerned clinicians, family, friends, and employers. Although these cases make psychiatrists uncomfortable, a new study suggests that coercion plays a valuable role in jumpstarting participation in the treatment of eating disorders.

A team of psychiatrists studied people with eating disorders who had denied a need for treatment when they were admitted to a hospital clinic. Nearly half changed their minds and acknowledged the necessity of treatment within 2 weeks of being hospitalized, reports Angela S. Guarda of Johns Hopkins Hospital in Baltimore.

The predominantly female patients included many with anorexia nervosa and bulimia nervosa. In the former disorder, a person typically loses weight through starvation and exercise. People with bulimia alternate food-eating binges with induced vomiting.

The new study, published in the January *American Journal of Psychiatry*, focused on 139 patients admitted to a Johns Hopkins treatment program for eating disorders between January 2000 and February 2003. Patients ranged in age from 15 to 35. The program concentrates on establishing proper eating habits, restoring weight, and developing healthy attitudes toward food and personal appearance.

Each patient completed a 13-item questionnaire upon entering the program and again after 2 weeks of treatment. The questionnaire asked patients whether they needed hospitalization, whether they were coerced to join the program, and what their perceptions were of the hospital-admission process.

Of the 139 patients, 46 said at first that they were being coerced and didn't need hospitalization. Of that number, 20 switched after 2 weeks of treatment to saying that hospitalization had been justified.

The participants who changed their minds consisted of 14 of 34 anorexia patients and 6 of 12 bulimia patients.

Anorexia patients, who are often grossly underweight, reported more perceived coercion and less satisfaction with the admissions process than the bulimia patients did.

Guarda suspects that as these patients are tracked for longer periods during and after hospitalization, even more of them will switch to endorsing the treatment. The Johns Hopkins program lasts an average of 6 weeks. Although the participants weren't legally bound to stay in the treatment program, none left during the first 2 weeks. Among those who had felt coerced, their willingness to stay "illustrates the ambivalence towards treatment that characterizes eating disorders," Guarda says.

"Many patients with anorexia nervosa remain untreated because no one pressured them into seeking treatment, and a significant proportion of them die," Guarda says. "The rest often lead isolated and very impaired lives."

It's compassionate to coerce individuals with eating disorders into treatment aimed at altering their potentially fatal pursuit of weight loss and thinness, comments psychiatrist Arnold E. Andersen of the University of lowa Hospitals and Clinics in lowa City. —B. BOWER

First in Freedom

Learn how and why our American forefathers risked all in 48 fascinating lectures in audio and video formats

hen colonists on the eastern fringes of a new continent converted Enlightenment thought first into action, then into government, it rocked the world.

Why and how they did it is the subject of Professor Peter C. Mancall's 48 lectures. He brings to life the revolutionaries who were caught up in the debates over rights and power, liberties and empire. It is a story of immense importance and rich discoveries.

The American Revolution did not occur only from 1775–83. It began when British colonists first questioned the intrusions of Great Britain into their economic progress and civil lives. It erupted into armed conflict in 1775, but it did not end with the peace treaty of 1783. The Americans had yet to craft a government that brought into being new ways for citizens to relate to their government and for government to relate to the nation.

Independence—Just a Start

In achieving freedom the colonists traded one set of problems for another. The young nation could not pay its debts, craft an effective foreign policy, or forestall armed tax revolt from its western settlements. European monarchies expected imminent collapse.

Instead, 55 men from 13 sovereign states gathered to create a constitution for establishing a national government. The debate raged, but in the end, owing to a pledge to add a list of guaranteed liberties, the United States Constitution became the supreme law of the land.

About Your Professor

Dr. Peter C. Mancall is a Professor of History and Anthropology at the University of Southern California and Director of the USC-Huntington Early Modern Studies Institute. He has received

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COUNTERINTUITIVE TOXICITY

Increasingly, scientists are finding that they can't predict a poison's low-dose effects

BY JANET RALOFF

or decades, researchers largely assumed that a poison's effects increase as the dose rises and diminish as it falls. However, scientists are increasingly documenting unexpected effects sometimes disproportionately adverse, sometimes beneficial—at extremely low doses of radiation and toxic chemicals.

Consider the environmentally ubiquitous plastic-softening agent, di-2-ethylhexyl phthalate (DEHP). A German team recently found that in newborn male rats, the lowest DEHP doses tested suppressed the brain activity of an enzyme critical for male development. This was a surprise because higher DEHP doses stimulated that enzyme's action.

Anderson J.M. Andrade and his colleagues at Charité University Medical School in Berlin note that the enzyme's suppressive action would have been missed if they had done what most toxicologists do—project low-dose impacts from high-dose tests. The low dose that suppressed aromatase in the rodents was comparable to exposures occurring in the general human population, Andrade's team reports in the Oct. 29, 2006 *Toxicology*.

Other toxic agents have unexpectedly beneficial effects. X-rays and gamma radiation are well-recognized carcinogens. Data collected over decades have shown that exposures to 1 gray (Gy)—the dose from perhaps 100 computerized tomography scans—typically increase an individual's lifetime risk of cancer by 5 percent. However, a growing body of animal data now indicates that lower radiation exposures can defend against cancer-inducing biological changes.

"The little dose is turning on some kind of protective mechanisms so that when a big dose comes along, it's not as damaging," says radiation biologist J. Leslie Redpath of the University of California, Irvine. Conceptually, it's analogous to a vaccine.

Many such effects have been overlooked because researchers prematurely stopped probing for biological impacts as soon as they identified dosage levels of a poison that appear benign, says toxicologist Edward J. Calabrese of the University of Massachusetts–Amherst. Poisons can have a variety of effects at both high and low doses—whether they trigger release of a hormone, switch a gene on or off, or stimulate cell growth. Indeed, Calabrese told *Science News*, that he has seen the same low dose of a chemical have beneficial effects on one tissue and detrimental effects on another.

He and others worry that if researchers don't begin regularly probing the effects of these agents at very low doses, scientists will continue to miss important health impacts—both bad and good of pollutants, drugs, and other agents.

ANOMALY OR NORM? Regulatory agencies don't require scientists to evaluate a poison at exposures below that at which no harm is apparent. This dose is referred to as the NOAEL, for "no observable adverse-effects level".

Calabrese has campaigned relentlessly over the past 15 years to draw attention to biological effects that occur below a NOAEL. These include nonlinear effects, such as a toxicity that initially decreases as concentration goes down but eventually increases, producing a U-shaped curve. In a related class of nonlinear effects, called hormesis, a compound at high doses has an inhibitory and generally toxic—effect on some biological process but the opposite effect at certain low doses. Unlike many other toxicologists, Calabrese uses the term *hormesis* to cover most nonlinear lowdose effects.

Radiation offers one of the best examples of hormesis in its narrower definition. At the Environmental Mutagen Society meeting last September in Vancouver, British Columbia, Redpath reported that cells exposed to no more than 0.1 Gy of radiation were less likely to spawn tumors than were cells receiving either far higher doses or no radiation.

In another study, Brenda E. Rodgers of Texas Tech University in Lubbock gave mice a small dose of radiation by caging them

"Conceptually, [low-dose radiation] is analogous to a vaccine."

— J. LESLIE REDPATH, UNIVERSITY OF CALIFORNIA, IRVINE in a Ukrainian forest roughly 1.5 kilometers from where the Chernobyl nuclear accident occurred 18 years earlier. Depending on their location, it took between 10 and 45 days for each mouse to receive a dose of 0.1 Gy.

A day after an animal had reached that dose, it was moved to a nearby lab and quickly bombarded with 1.5 Gy. Blood tests showed that the lab radiation produced only half as many chromosome breaks—an indicator of damage that could lead to cancer—in these animals as it did in mice without the

earlier low-dose exposure.

A low dose of radiation can reduce damage even if it comes after a larger dose, says Tanya K. Day of Flinders University in Bedford Park, Australia. In one study, her team gave mice a 1-Gy dose of radiation. Four hours later, some mice received a second, far smaller dose. Rodents getting both doses developed only half as many DNA inversions—a particular type of cellular damage—as did mice getting just the first dose, and often fewer inversions than did mice receiving no radiation at all.

Day reported her findings in June at the International Hormesis Society meeting in Amherst, Mass.

Calabrese's team reviewed hundreds of toxicology papers that document a biological effect below the NOAEL for chemical poisons. He terms all these effects as instances of hormesis, although only about 5 percent of the articles did. The rest described the results as inexplicable or as evidence of some type of nonlinear toxicity.

To determine how commonly trace exposures trigger unanticipated biological impacts, Calabrese's team has analyzed databases of biological responses to potentially toxic chemicals, each throughout a broad range of doses. In their most recent study,

GRAND UNIFICATION OF A 2 PHOTON UNIVERSE

A Complete Grand Unified Theory

With elegant simplicity, the author has resolved the wave/particle duality paradox by combining single wave-propertied photons and single particle-propertied photons to construct precise diagrams of all the standard model-entities in physics (proton, antiproton, quark, antiquark, gluon, bosons, etc.). Thereafter, detailed reaction diagrams illustrate their step-by-step synthesis, as well as their photon constituents and spatial arrangement.

Also, for the first time, the unique photon units which generate each of the necessary forces

(strong, weak, electromagnetic) to accomplish the above steps of synthesis are identified and diagramed as to their photon constituents and spatial structure. For example, the unit generating the strong force, the gluon/antigluon meson, is identified and diagramed; as are detailed sequences showing how the meson organizes respective quarks and antiquarks into protons, neutrons and their antiparticles; as well as diagrams demonstrating how and what each antiproton and antineutron is thereafter converted into.

Unique Understandings Presented

- The two unique photon structures which are dark energy and dark matter.
- How the construction of a "double-quark" unit between elements is the universal fusion mechanism splicing together lighter elements into heavier ones.
- How General Relativity Theory and Quantum Mechanics are reconciled.
- How each of the forces (strong, weak, electromagnetic) is a minute fractional unit of the gravity force.
- A 55 dimension model of the Universe; consisting of 5 phases of 11 dimensions each.
- The "Singularity"; and how the Universe emerged and evolved from it.
- Why the Universe is closed; and when and by what method it will remerge with the Singularity.
- The origin and structure of the two types of gravitons; and how they direct the evolvement of the Universe; as well as the method by which they created from their substance the two respective types of photons.
- The 7 epochal stages and processes in which all of the elements and the solar system were formed.
- How the proton and neutron decay process is caused by an unstable gluon/antigluon meson in each.
- The cause of earth evolving differently than the other planets.
- How an unusual photon charge structure permits the display of magnetism in elements such as the ferromagnetic.
- What " C^2 " in E = MC² is; and how it is the key to processes leading to Grand Unification!

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described in the December 2006 *Toxicological Sciences*, Calabrese and his colleagues analyzed data showing how cell proliferation in 13 different yeast strains responded to various doses of 2,189 potential anticancer drugs.

Almost 80 percent of the drugs exhibited a NOAEL, the team found. Among these, the group further looked for reports of biological effects triggered by doses even lower than that level. The authors had expected that 25 percent of these drugs, just by chance, would exhibit activity above that seen with no exposure. In fact, 60 percent did.

The effects observed at those low doses were modest, perhaps 60 percent higher or lower than those that occur in the absence of any exposure, Calabrese notes. He acknowledges that such changes might not always have clinical significance.

These findings and earlier analyses by his group, Calabrese says, show that measurable biological effects at low doses appear to be more the norm than an anomaly.

Indeed, even pollutants that don't have a NOAEL may have nonlinear effects at low doses, notes Bernard Weiss of the University of Rochester (N.Y.) School of Medicine and Dentistry. For example, the drop in a child's IQ for each 1 microgram per deciliter of lead in the blood is much higher at concentrations below 10 μ g/dl than at concentrations above that value (*SN*: 5/5/01, p. 277).

So, Weiss concludes, toxicity estimates based on high-dose measurements greatly underestimate low-dose harm.

HOW DOES IT WORK? Scientists have recently begun to discover mechanisms to explain hormesis and other nonlinear dose responses. For instance, Rodgers has been looking at what genes are preferentially turned on or off in the mice exposed to Chernobyl radiation. Compared with unexposed mice, those caged in the Ukraine forest had 600 to 1,200 genes whose activity had been altered.

"We expected to see an increase in the expression of genes involved in DNA repair," Rodgers says. "What we found instead was an increase in the expression of genes that respond to oxidative stress—such as free radicals."

Another explanation of hormesis was suggested in 2000 by researchers working with human-cancer cells exposed to epigallocatechin gallate (EGCG), the principal cancer-fighting ingredient in green tea. The team showed that although high-dose exposures of EGCG inhibited cell growth, low doses stimulated cell proliferation. D. James Morré of Purdue University in West Lafayette, Ind., says that his team several years ago found a unique enzyme on cell surfaces that appeared to be "a molecular target for chemical hormesis."

The group subsequently determined that this enzyme can bind to various substances, in addition to EGCG, and alter their cellular effects. Those responses disappeared when the enzyme was inactive.

Some scientists have suggested additional processes that play a role in hormesis. In an upcoming issue of the *International Journal of Low Radiation*, Bobby R. Scott of the Lovelace Respiratory Research Institute in Albuquerque, N.M., and his colleagues report that low doses of radiation induce mild oxidative stress in cells, activating a high-efficiency form of DNA repair and stimulating the immune system. This stress also "activates a special apoptosis [cell suicide] process"—one that culls genetically unstable cells, he says.

Scott suggests that these same processes probably work to counteract chemical poisons.

IMPLICATIONS Although most toxicologists today agree that hormesis occurs—a big change from a decade ago—some argue that Calabrese and his team greatly overstate its frequency. A major portion of this controversy hinges on differences in the use of the term *hormesis*.

"I totally believe that [nonlinear] low-dose responses occur frequently," says Kristina A. Thayer of the National Institute of Environmental Health Sciences in Research Triangle Park, N.C. "In fact, I have no problem accepting that most of the time they might be stimulatory."

However, she says that Calabrese equates stimulatory low-dose effects with benefits when there's no reason to expect that they would necessarily be beneficial. Her research with the plastic-softening agent bisphenol A, a hormone-mimicking agent, illustrates a detrimental effect of low-dose stimulation similar to what Andrade found for DEHP.

Among toxic agents that show positive biologic effects at low doses, Calabrese sees the possibility for better drug design. For example, he says, current treatments for dementia provide tiny doses of drugs that at high doses would be toxic. For instance, he says, "every Alzheimer's drug on the market today acts via hormetic [low-dose] activities."

Even though a hormetic treatment may show only a small effect, Calabrese proposes that several treatments might be put together to achieve a therapeutic benefit.

"I believe hormesis is real, [but] is fundamentally difficult—and expensive—to demonstrate."

YALE SCHOOL OF

MEDICINE

Scott suggests a related therapeutic application of hormesis that uses small doses of radiation to trigger immunological and cell-death processes. However, cancer cells are "reluctant" to undergo programmed death, Scott notes. Because certain compounds such as resveratrol, a polyphenol in grapes (*SN: 11/4/06, 293*)—sensitize cancer cells to radiation, Scott envisions pretreating people with such compounds and following this up with a hormetic dose of radiation. "For lung cancer," he says, "perhaps just low-dose diagnostic X rays would do."

Beyond new medical applications, information gleaned from research into low-dose exposures might help fine-tune regulation of chemicals. Scientists may find that many pollutants aren't as toxic at low doses as has been assumed,

Calabrese says. "You can imagine why industry loves hormesis," Weiss says. It suggests pollution may not need to be cleaned up as thoroughly as regulations have been asking for.

Calabrese counters, however, that if traces of certain pollutants are not as dangerous as earlier estimates had suggested, why not investigate whether some regulations are unduly strict?

Indeed, proving that some low-dose exposures are "of no regulatory concern could make a qualitative difference in regulations," observes economist Lester B. Lave of Carnegie Mellon University in Pittsburgh. However, he adds that to justify changing guidelines for regulations, far more research would be needed.

For instance, there has been much discussion suggesting that low doses of chemicals—even pollutants—might rev up immunity in a beneficial way. However, because many people have compromised immune systems, Lave says that before raising the acceptable environmental limits of a pollutant, "I'd want to know if we see a [beneficial] hormetic response in those people, or babies with undeveloped immune systems, or the elderly." Moreover, he says, effects at low doses tend to be subtle, so "I'd want to see them documented in humans, not just animals"—and to know at precisely what dose they turn detrimental.

Jonathan Borak, a toxicologist at the Yale School of Medicine in New Haven, Conn., agrees that it's too early for hormesis or other nonlinear low dose–effects data to be "practically relevant" for altering regulatory or health policy.

Although "I believe hormesis is real, it is fundamentally difficult and expensive—to demonstrate," Borak says. Looking for relatively small low-dose effects could quadruple the cost of toxicology studies, he estimates, underscoring "practical and economic reasons why today almost nobody looks for them."

WEIGHING IN ON CITY Planning

Could smart urban design keep people fit and trim?

BY BEN HARDER

awrence Frank is no couch potato. Taking full advantage of his city's compact design, the Vancouver, British Columbia, resident often bikes to work and walks to stores, restaurants, and museums. That activity helps him stay fit and trim. But Frank hasn't always found his penchant for self-propulsion to be practical. He previously lived in Atlanta, where the city's sprawling layout thwarted his desire to be physically active as he went about his daily business. problems with urban sprawl, a loose term for humanmade landscapes characterized by a low density of buildings, dependence on automobiles, and a separation of residential and commercial areas. Frank proposes that sprawl discourages physical activity, but some researchers suggest that people who don't care to exercise choose suburban life. Besides working to settle that disagreement, researchers are looking at facets of urban design that may shortchange health.

As scientists investigate the relationship between sprawl and obesity, a compact style of city development sometimes called smart growth might become a tool in the fight for the nation's health. However, University of Toronto economist Matthew Turner charges that "a lot of people out there don't like urban sprawl, and those people are trying to hijack the obesity epidemic to further the smart-growth agenda [and] change how cities look."



TIGHT FIT — Densely built urban areas such as Vancouver's downtown may encourage pedestrian traffic and promote physical activity. In contrast, cities of low density, where people depend on cars to get to stores and other facilities, seem to favor obesity.

"There was not much to walk to," says Frank, a professor of urban planning at the University of British Columbia. For example, he recalls that there was only one decent restaurant within walking distance of his old home. Many restaurants and other businesses in Atlanta cluster in strip malls that stand apart from residential areas.

In Vancouver, by contrast, Frank's neighborhood contains dozens of eateries, and he often strolls to and from dinner. "I'm more active here," he says.

The glaring difference between the two cities' landscapes figures in Frank's professional life as well as in his personal one. Frank is part of an emerging area of cross-disciplinary science that's examining the relationship between the shapes of our cities and the shapes of our bodies.

He and other researchers have evidence that associates health

STUDYING SPREAD For decades, housing and population growth in U.S. suburban areas have outpaced those in city centers. Shifts in commuting patterns reflect the trend toward people residing at a sizable distance from where they work, shop, and play. According to U.S. Census data, the average commute lengthened from 22.4 minutes to 25.1 minutes between 1990 and 2000, and the proportion of workers walking or biking to work dropped by one-quarter.

A few communities buck the national trend. For example, Frank says, "there is a great deal of new development in Atlanta that is walkable."

"That said, the overall trend is not in this direction in that region or most others," he adds. Even "Vancouver is embarking on a massive road-building program that threatens [to create] sprawl in the developing parts of this region."

In September 2003, two major studies linked sprawl and obesity. Since those reports, researchers in fields as disparate as epidemiology and economics have generated a spate of similarly themed studies. In the first of the 2003 reports, researchers analyzed data from a nationwide survey in which each of some 200,000 people reported his or her residential address, physical activity, body mass, height, and other health variables. Residents of sprawling cities and "We're the only ones that have tried to distinguish between causation and sorting ... and we find that it's sorting," he says. "The available facts do not support the conclusion that sprawling neighborhoods cause weight gain."

counties tended to weigh more, walk less, and have higher blood pressure than did people living in compact communities, concluded urban planner Reid Ewing and his colleagues at the University of Maryland at College Park's National Center for Smart Growth Research and Education.

In the second study, health psychologist James Sallis of San Diego State University and his colleagues reported that residents of "highwalkability" neighborhoods, which have closely packed residences and a mix of housing and businesses, tended to walk more and were less likely to be obese than residents of low-walkability neighborhoods.

In 2004, Frank and his colleagues produced additional connections among urban form, activity, and obesity. The data on more than 10,500 people in the Atlanta area indicated that the more time a person spends in a car, the more obese he or she tends to be. But the more time people spend walking, the less obese they are.

Frank's team, like the other groups, found that areas with interspersed homes, shops, and offices had fewer obese residents than did homogeneous residential areas whose residents were of a similar age, income, and education. Furthermore, neighborhoods with greater residential density and street plans that facilitate walking from place to place showed below-average rates of obesity.

The magnitude of the effect wasn't trivial: A typical white male living in a compact, mixed-use community weighs about 4.5 kilograms (10 pounds) less than a similar man in a diffuse subdivision containing nothing but homes, Frank and his colleagues reported.

So far, the dozen strong studies that have probed the relationships among the urban environment, people's activity, and obesity have all agreed, says Ewing. "Sprawling places have heavier people," he says. "There is evidence of an association between the built environment and obesity."

CAUSE OR COINCIDENCE The evidence

for a relationship between physical activity, body weight, and the environmental characteristics called urban form "looks compelling," adds Ross Brownson, an epidemiologist at St. Louis University School of Public Health in Missouri.

But Brownson, Ewing, and others caution that these associations don't prove that sprawl causes laziness or weight gain. Most of the studies provide only a snapshot of different people at a single time. Such studies can't prove that living amid sprawl leads to inactivity; it may also be that inactive people choose to inhabit areas where driving is the easiest way to get around.

In other words, people with different health habits and different propensities to gain weight may sort themselves into different kinds of neighborhoods.

That's what Turner suggests is going on. Turner conducted a study that tracked people over time, as some of them moved from one neighborhood to another. He and his collaborators found no change in weight associated with moving from a sprawling locale to a dense one, or vice versa.



OBESITY CITY — Infrared satellite images show the rapid geographical expansion of metropolitan Atlanta. Built areas, such as roads and buildings, appear bluish-white against the red backdrop of areas dominated by trees and plants.

Turner's team analyzed data collected over 6 years on more than 5,000 young adults living across the United States. Most of the volunteers moved at least once during the study. The researchers compared individuals' weights before and after they moved between communities with different degrees of sprawl.

To measure sprawl, they used satellite images to calculate the average distance between residential buildings. They also determined the average density of nonresidential establishments such as churches and shops in each volunteer's zip code.

"We're estimating the effect [of sprawl on weight] to be zero or very close to zero," Turner says. Any weight gain attributable to sprawl, he says, is at most "a couple of ounces."

The authors released the study as a working paper on Oct. 30, 2006.

Other researchers challenge some of the study's analytical methods, particularly the way in which Turner's team assessed sprawl and mixed use. For example, Sallis says, "They assumed that [churches and retail businesses] were equally dispersed around the zip code." The study may therefore have inaccurately estimated volunteers' access to walkable destinations, he says.

Sallis also argues that it could take many years for significant weight gain to develop after a person moves between dissimilar neighborhoods. Moreover, the study didn't assess whether volunteers' degree of physical activity changed when they moved, a measure that would hint at impending changes in weight.

Still, Sallis says, Turner's longitudinal approach to the issue is "definitely an advance. We've been wanting studies like this for some time."

Ewing has also completed a prospective study using a similar set of data, but he declined to discuss his results with *Science News* before the study's publication.

Obesity is not the urban environment's only nor even necessarily its most likely—potential health effect, says physician Deborah Cohen, a health researcher at the RAND Corporation in Santa Monica, Calif. If a neighborhood's design

were to make people less active, they might eat less to avoid obesity but still miss out on other health benefits of physical activity, notes Cohen.

"Physical activity is independently important for health, [and] urban form is important for physical activity," she says.

In 2004, Cohen and Roland Sturm of RAND asked more than 8,000 residents of 38 U.S. communities to list their health problems. The researchers also assessed the degree of sprawl in each resident's community.

"People reported more complaints—more health problems when they lived in more sprawling areas," Cohen says. The excess of physical problems such as arthritis linked to sprawl was comparable to the change that would occur if the entire population suddenly aged by 4 years, Cohen and Sturm concluded.

SETTING AND SORTING Frank's latest findings could split the ideological difference. By surveying people in a variety of neighborhoods, he learned that people who are less inclined to be active

tend to live in less pedestrian-friendly locales—evidence that people are sorting themselves. But he also found that, no matter how much people like or dislike being active, they are more active when they live in compact, walkable areas than when they live in sprawling neighborhoods.

His study, he says, "demonstrates that both preferences and the

neighborhood in which people live impact their behavior." He described the findings at a conference in Atlanta on Jan. 19 and reports them in an upcoming *Social Science and Medicine*.

The people most at the mercy of sprawl, Ewing suggests, are those who have limited access to healthy foods and who don't recognize the importance of fitness.

Children are another group that could be disproportionately affected by urban design, Frank says.

In two recent studies, Cohen and her collaborators examined the relationship between adolescent girls' physical activity and specific aspects of the urban environment. Girls who live near parks and recreational facilities are more physically active than those whose neighborhoods contain no such spaces, the researchers found.

They selected a middle school in each of six metropolitan areas throughout the country. From among the female students attending the schools, the team randomly selected 1,556 sixth graders.

In one study, the researchers used maps and government records

THE DISCONNECT — A community's so-called network efficiency influences its walkability. In an efficient network, such as in the gridlike Atlanta neighborhood at left, pedestrians can walk relatively directly between any two points. The maze of cul-de-sacs at right, also in Atlanta, forms an inefficient network.

to locate public parks. On average, 3.5 parks lay within a 1-mile radius of each volunteer's home. That figure varied from about six parks in Minneapolis to about one park in Tucson.

The researchers outfitted the girls with pedometerlike devices called accelerometers, which record motion and can be used to measure the intensity of physical activity. Each volunteer wore her

accelerometer for 6 consecutive days. During that time, the girls performed, on average, the metabolic equivalent of 611 minutes of vigorous physical activity.

The researchers conservatively estimated that each park within a halfmile of home contributed an extra 17.2 minutes of vigorous activity per girl over the course of the study. The team reports its findings in the November 2006 *Pediatrics*.

"Neighborhood parks

are particularly important for adolescents who are too young to drive," says Diane Catellier, a statistician at the University of North Carolina at Chapel Hill who collaborated with Cohen on that study.

In the other study, reported in a 2006 supplement to the *Journal of Physical Activity and Health*, Cohen's team used data on the same girls to show that living in proximity to one's school is also associated with increased levels of physical activity.

"The overarching message is that the built environment is an enabler or a disabler of active transportation—of walking," Frank says. ■



ENVIRONMENT Mercury pollution settles in hot spots

Mercury in the environment tends to accumulate in certain geographical areas, new research suggests.

In a pair of related studies, David C. Evers of the BioDiversity Research Institute in Gorham, Maine, and his colleagues analyzed mercury concentrations in yellow perch and common loons in the northern United States and southern Canada. Those species provide indicators of ecosystems' overall exposure to the contaminant, say the researchers.

The team identified five "hot spots" where perch and loon populations showed heavy mercury contamination. These are the Androscoggin and Kennebec rivers in Maine, the Merrimack River that runs through Massachusetts and New Hampshire, the Adirondack Mountains in New York, and central Nova Scotia.

Typically, mercury enters the atmosphere from coal-burning power plants. The researchers determined that an ecosystem's proximity to such sources had a greater effect on mercury pollution than past studies had indicated.

Air currents, rainfall patterns, and topography also conspire to deliver mercury to the hot spots, Evers and his colleagues report in the January *BioScience*. —B.H.

BIOMEDICINE Nanoparticles find tumors, form clumps

Newly designed nanoparticles could have dual benefits for fighting cancer. Not only do these tiny particles home in on tumors, but they also stick together once they enter tumors' blood vessels. The particles could eventually be a means to choke off the blood vessels that deliver nutrients to tumors or to ferry cancer-killing drugs, researchers report.

In the past several years, scientists have designed several types of cancer-seeking nanoparticles by coating bits of iron with molecules that stick to proteins found only in tumors. Choosing an even tighter target, Erkki Ruoslahti of the Burnham Institute for Medical Research in Santa Barbara, Calif., and his colleagues covered iron nanoparticles with a peptide they designed to adhere to proteins found only in tumor blood vessels.

The researchers injected these nanoparticles into mice that had been implanted with human-breast tumors. After gathering inside tumors, the particles clumped and blocked about 20 percent of each tumor's blood vessels. Adorned with the iron clumps, the tumors became easily visible in magnetic resonance images, Ruoslahti's team reports in the Jan. 16 *Proceedings of the National Academy of Sciences*.

OF Note

The team is currently working to improve the particles' cancer-fighting abilities by increasing their potential to block blood vessels and by designing hollow nanoparticles that can also deliver chemotherapy drugs. —C.B.

PALEONTOLOGY Of penguins' range and climate change

Variations in the range of Adélie penguins along one section of Antarctica's coast during the past 45,000 years are a keen indicator of climate change there, a new study suggests.

Adélie penguins thrive only at sites with ice-free terrain, an abundant marine-food supply, and access to open water during

nesting season, which starts each October, says Steven D. Emslie, a paleontologist at the University of North Carolina in Wilmington. To determine when such conditions occurred along the Ross Sea area of Antarctica, he and his colleagues carbon-dated Adélie bones, feathers, and eggshells from 21 active and abandoned nesting sites in that region.

At a penguin rookery on Cape Hickey, a site near the present-day edge

of the Ross ice shelf, the scientists found samples dating back 27,000 to 43,000 years, a hint that during that period, as today, the Ross Sea was open water during the penguin-breeding season, says Emslie.

By contrast, a gap in the Adélie fossil record between 27,000 and 13,000 years ago at all sites along the Ross Sea that have been analyzed chronicles the northward advance of the Ross ice shelf during that period, Emslie and his colleagues argue in the January *Geology*.

Adélie penguins fully recolonized the Ross Sea coast only 8,000 years ago, after the most recent ice age ended, following the retreat of the ice shelf to near its present location. More-recent gaps in the fossil record at most sites in the area—one between 5,000 and 4,000 years ago, and another between 2,000 and 1,100 years ago—indicate periods when ocean conditions weren't favorable for penguin breeding and the climate was substantially cooler than it is now, the researchers speculate. -S.P.

CLIMATE 2006: Hottest year in U.S. history

Preliminary analysis of weather data gathered from more than 1,200 sites across the continental United States indicates that last year was the warmest on record.

The average temperature for 2006 was 12.8°C (55°F), National Oceanic and Atmospheric Administration (NOAA) scientists reported on the agency's website Jan. 9. That's about 1.2°C above the average temperature for the 20th century and 0.04°C warmer than the previous yearly record, set in 1998, says Richard Heim, a meteorologist at NOAA's National Climatic Data Center in Asheville, N.C.

That year began during the strongest El Niño ever recorded (*SN: 12/11/99, p. 374*). Changes in weather patterns during El Niños typically warm winter temperatures

across much of North America.

The latest El Niño began around the end of September, says Heim. Despite a frigid start to December in many areas, five states had their warmest Decembers ever, and no state measured below-average temperatures for that month. "Mother Nature fooled all of us and gave us a warm spell," he notes.

With temperatures above average from October through December, the

nation's home-energy consumption was about 13.5 percent lower than it would have been if temperatures had been normal, the NOAA scientists estimate. —S.P.

INFECTIOUS DISEASES Salmonella illnesses traced to pet rodents

Hamsters and other pet rodents are probably underappreciated spreaders of salmonella bacteria, researchers say. A recent outbreak investigation linked 15 of 22 infections caused by *Salmonella enterica* of a type called Typhimurium to the act of handling an infected rodent or to having contact with a person who'd handled such an animal.

Salmonella is most commonly a food-

borne illness but has, on occasion, been linked to pets, including turtles.

The investigation began in August 2004, when researchers identified an antibiotic-resistant strain of Typhimurium in eight hamsters from a pet distributor in Minnesota. Minneapolis-based Stephen Swanson of the Epidemic Intelligence Service, a division of the Centers for Disease Control and Prevention, led the effort.

Swanson's team compared the genetic pattern of the hamster's bacterial strain with genetic patterns of bacteria obtained from sick people and recorded in a national database. The researchers identified 28 people in various states who had contracted virtually identical Typhimurium during a 10month period. The team interviewed 22 of those patients to find out whether they'd had contact with rodents. Thirteen reported direct contact with pet rodents, while two had contact with pet owners who'd fallen ill.

Further investigation revealed that one patient's pet mouse harbored the outbreak strain, and that several hamsters from pet stores where other patients had shopped also had the drug-resistant bug.

Swanson's team reports its findings in the Jan. 4 *New England Journal of Medicine*. —B.H.

BIOMEDICINE

Gene variant shapes beta-blocker's effectiveness

A medication widely used for heart failure may be most effective in people who have a common variant of a particular gene, a laboratory study suggests. Genetic testing for the variant could potentially identify patients who are most likely to benefit from the drug carvedilol, the researchers say.

Beta-blocking drugs such as carvedilol reduce the heart's workload by blocking beta-adrenergic receptors on cells. This can protect hearts that don't pump efficiently, such as those in people with heart failure. The primary beta-adrenergic receptor comes in several forms, the most common of which are arg389 and gly389. The majority of people have the arg389 variant.

To investigate the significance of these genetic differences, Stefan Engelhardt and his colleagues at the University of Würzburg, Germany, tested three betablockers, including carvedilol, on heart cells from rats that had either the arg389 or gly389 variant.

Carvedilol blocked the receptor more effectively in cells that contained the arg389 variant than in cells that contained gly389, the researchers report in the January *Journal of Clinical Investigation*. The effects of the two other beta-blockers didn't depend on the form of the receptor. —B.H.



CLIMATE SENSOR By dating the remains of Adélie penguins, which thrive only in certain conditions, scientists can tell when penguin-friendly climate conditions prevailed in a region.

Books

A selection of new and notable books of scientific interest

MEDICAL APARTHEID: The Dark History of Medical Experimentation on Black Americans from Colonial Times to the Present

HARRIET A. WASHINGTON

Beginning in colonial times, blacks were seen as property that could be experimented upon and dis-



posed of at will by slave owners and unscrupulous medical practitioners. Much of the early research performed on blacks, especially by southern doctors, was done to outline the perceived fundamental biological differences between blacks and whites, which were viewed as two separate species. Washington

outlines white fascination in the early 19th century with black anatomy and skin color. She details the infamous Tuskegee syphilis study as well as the use of nonconsenting black prisoners, children, and medical patients in experiments examining the effects of radiation, contraceptive techniques, and bioterrorism agents. Finally, Washington examines current racial inequities in access to medical care, testing, and advanced treatments. She offers recommendations for combating the widespread mistrust between the medical community and African Americans. Doubleday, 2006, 501 p., b&w plates, hardcover, \$27.95.

SAXONS, VIKINGS, AND CELTS: The Genetic Roots of Britain and Ireland BRYAN SYKES

Sykes, the founder of an organization that sequences individuals' DNA so they can explore



their roots, here recounts the genetic history of the people of the British Isles. At the forefront of what he calls genetic history, Sykes has participated in archaeological research throughout Great Britain. By sampling the DNA of more than 10,000 volunteers from Britain, Ireland, and the United States, Sykes has attempted to

solve the mystery of who the British Isles' first inhabitants were and how they arrived. His book explores the traditional accounts passed on in England and Ireland and uses the DNA evidence to sort fact from fiction. Sykes looks to modern DNA evidence to sort the genetic legacies of the Vikings, Romans, Saxons, Celts, and other groups. *Norton, 2006, 306 p., b&w plates, hardcover, \$26.95.*

EXPLORATOPIA

PAT MURPHY, ELLEN MACAULAY, AND THE STAFF OF THE EXPLORATORIUM

Located in San Francisco, the Exploratorium is a world-renowned science center full of interactive exhibits. Murphy, a 20-year employee of the center, and her colleagues bring its educational and exploratory spirit to this book. More than 400 experiments encourage young people to take a close look at themselves and the world around them. Readers explore why two eyes are better than one, how the



folds of the outer ear help a person locate the source of a sound, and how to improve memory. Other fanciful experiments include mummifying a hot dog, making a rocket launcher, and building a 20foot-high tower out of paper and tape. The authors explore the principles of physics

behind roller coasters, optical illusions, lenses, and magnets. Throughout, they include tools for exploration and tips for becoming a better observer. *Little, Brown, 2006, 373 p., color images, hardcover, \$29.99.*

DEATH BY BLACK HOLE: And Other Cosmic Quandaries NEIL DEGRASSE TYSON

In this collection of more than 40 essays taken from *Natural History* magazine, Tyson, director of the Hayden Planetarium at the American Museum of Natural History in New York City, shares his



affection for the oddities of our universe. He traces the history of astrophysics, explores the possibility of life on other planets, and introduces the idea of antimatter. The essays are collected into seven separate sections ranging from "The Nature of Knowledge" to "Science and God." In the former section, Tyson explains how

people discovered our solar system's planets and what their continued exploration can reveal about the past and future of Earth. In the section titled "When the Universe Turns Bad," the author enumerates the many ways in which life as we know it could end, such as by asteroid collisions and "death by black hole." *Norton, 2007, 384 p., hardcover, \$24.95.*

DREAMING IN CODE: Two Dozen Programmers, Three Years, 4,732 Bugs, and One Quest for Transcendent Software SCOTT ROSENBERG

Our modern lives rely on the proper functioning of billions of lines of software code to run everything from laptops to on-board automobile computers to the latest toasters and toys. It can be a daunting responsibility for programmers to create software that serves a unique function and that works con-



sistently. Rosenberg, journalist and cofounder of Salon.com, gives an inside view of the evolving process of software development. Why is it so hard to get computers to think like people? Why are bugs a persistent problem in computer programs? Rosenberg surveys the history of programming suc-

cesses and programming failures. Rosenberg spent 3 years following a group of programmers working on software for a personal-information-management program called Chandler. The author recounts the many advances and missteps that the innovative programmers made as they tried to reconcile human behavior with a computer's operation. *Crown, 2007, 400 p., hardcover, \$25.95.*

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LETTERS

Sea tales

In "Dashing Rogues" (*SN: 11/18/06, p. 328*) on rogue waves, you make no mention of the use of satellite data, which is ideal for this sort of study. Two projects, in particular, are of great relevance: the European Union's MaxWave study and the subsequent WaveAtlas project. The former, with just 3 weeks' data, identified 10 rogue waves above 25 meters in height. WaveAtlas aims to prepare a worldwide atlas of rogue waves.

STORM DUNLOP, EAST WITTERING, WEST SUSSEX, ENGLAND

Your excellent report brought to memory a huge-wave event when I was in the crew of the aircraft carrier USS *Enterprise* in December 1945. Midway in the Atlantic Ocean, we encountered waves that broke at least 50 feet higher than the flight deck. I lashed myself to the handrail behind the superstructure to prevent being washed overboard.

GLEN D. CARTER, HILLSBORO, ORE.

The article didn't mention the counterpart to rogue waves, rogue troughs. Not much is known of these. If a ship is positioned where a rogue trough occurs, the ship falls in and is gone without a trace. JOHN SINK, COSTA MESA, CALIF.

Sorry, wrong number

"Ancient Gene Yield: New methods retrieve Neandertal's DNA" (*SN: 11/18/06, p. 323*) reads: "... a huge chunk of Neandertal DNA, covering more than 1 million of the roughly 3 million paired chemical constituents of an individual's genetic makeup." That 3 million should be 3 billion.

HEATHER TRUMBOWER,

UCSC GENOME BIOINFORMATICS GROUP, SANTA CRUZ, CALIF.

Way outside the box

It would seem difficult to distinguish between the repulsive force that dark energy proposes and the regular gravitational pull of ordinary matter ("Dark Fingerprints: Hubble sheds light on cosmic expansion," *SN: 11/18/06, p. 323*). Somehow, the idea of multiple universes surrounding our universe, embodying the known laws of physics and providing the gravitational pull, is easier for me to accept than a mysterious dark energy nobody can explain.

VERN SHELLMAN, DENVER, COLO.

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EMR Chart



This chart includes all known ranges of EMR including: gamma rays, X-rays, ultraviolet light, visible light, infrared, microwaves, radio waves (ULF, VLF, LF, MF, HF, long, short, HAM, VHF, UHF, SHF, EHF), cosmic microwave background radiation and brain waves, all organized by octaves. The audio frequency spectrum is also included. Descriptions are included for all ranges and properties of EMR, including reflection, refraction, LASER, television, gravity waves, emission and absorption. There is also a chart of SI unit prefixes ranging from yocto to yotta. All items are placed on the graph using custom programmed formulas. Great chart on a difficult subject! Size: 24" X 36," Laminated Order#EMR - 1020, Cost \$19.95

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