Math vs. Terror | Enzyme Enigmas | Meet Mr. Lucy

Science News

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MAGAZINE OF THE SOCIETY FOR SCIENCE & THE PUBLIC ■ JULY 17, 2010

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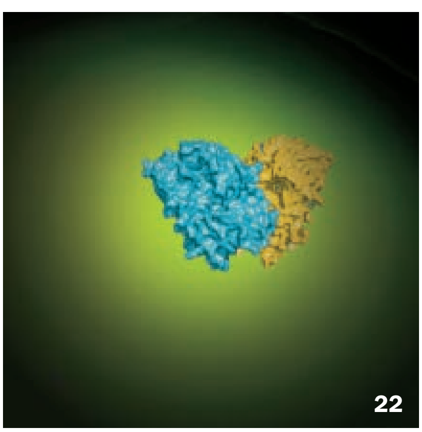
Blind Mice Regain Sight

Your Brain on Snakes

How the fish got its spots

The science of animal patterns and prints



ScienceNews

In The News

Features

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COVER Scientists are learning how animals like the clown triggerfish, *Balistoides conspicillum,* create their colorful patterns. *Photos © Eric Isselée/Dreamstime.com*

ScienceNews
MAGAZINE OF THE SOCIETY FOR SCIENCE & THE PUBLIC

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FROM THE EDITOR

Using math to fight terror could be a good strategy

Old paradigms never die — they just create conundrums for slow learners.

In the print journalism world, for instance, the old paradigm of readers paying for paper with ink on it has been eroded by electronic delivery via various digital devices ranging from laptops to app phones. Sure, many readers still prefer paper, and the best publishers maintain the quality of their traditional physical product. But sustaining economic viability will also require strategies that embrace new media and develop creative methods for delivering credible content in unconventional forms.

In a very similar way, governments seeking to preserve national security can no longer intelligently rely only on the past paradigms of superior military muscle. Enemy forces are no longer restricted to armies supported by political states defined by geography. Threats of deadly punishment do not deter combatants whose strategy often relies on suicide to begin with. Brute force cannot always cope with foes that don't fight by conventional rules of engagement.

Consequently, counterterrorism strategists ought to be interested in adopting some unconventional methods themselves. And, as Laura Sanders describes in this issue (Page 18), some such methods might be rooted in mathematics. In real-life versions of the sort of thing you'd see on the TV show *Numb3rs*, mathematicians have devised ways of analyzing the organization of terrorist cells, identifying key leaders and locating likely sites of hidden weapons caches.

Many of these approaches involve game theory — the science of choosing strategies. Game theory originated in economics and was made famous by the book and movie *A Beautiful Mind*. One of its lessons is that there is rarely only one right strategy in a competitive situation, because your enemy could predict it and choose effective countermeasures. It's almost always better to adopt a "mixed strategy," which means choosing with some element of randomness from among various possible actions.

In other words, game theory says that anyone advocating a one-size-fits-all approach to fighting terrorism (or any other strategic problem) is not too bright. So it makes sense that math should join military might in the antiterror arsenal, both as an additional weapon and as a way of choosing which weapons to use. (And it implies that keeping magazines around is a good idea, too.) *— Tom Siegfried, Editor in Chief*

What's the fastest way to learn a language?

ACT LIKE A BABY.

It's not the advice you'd expect. Learning a new language seems formidable, as we recall from years of combat with grammar and translations in school. Yet infants begin at birth. They communicate at eighteen months and speak the language fluently before they go to school. And they never battle translations or grammar explanations along the way. Born into a veritable language jamboree, children figure out language purely from the sounds, objects and interactions around them. Their senses fire up neural circuits that send the stimuli to different language areas in the brain. Meanings fuse to words. Words string into structures. And language erupts.

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Scientific Observations

"The metrics I see being used by many evaluators are skewed towards outcomes that rely as much on luck as on skill and talent — such as hitting on the right place, time and trend to achieve a top-tier publication. In many professions, one's output is directly proportional to the amount of effort put in. Not so in science.... One solution is to establish more journals (or other formats) in which researchers can quickly and easily publish negative data, solid-but-uncelebrated results, raw data sets, new techniques or experimental set-ups, and even 'scooped' data.... Such 'lower-end' publications should be valued more when the time comes to recruit, fund or promote. We can't all be lucky enough to get *Nature* papers — but many of us make, through persistence and hard work, more humble cumulative contributions that in the long run may well be just as important." — **CELL BIOLOGIST JENNIFER ROHN OF UNIVERSITY COLLEGE LONDON IN A COMMENT POSTED ONLINE JUNE 16 IN *NATURE***

Science Past | FROM THE ISSUE OF JULY 16, 1960

ONE-EYED ROBOT HUNTS OBJECTS LOST IN THE SEA — A one-eyed, swimming robot with powerful claw-like pincers is being developed for hunting and retrieving objects lost in the ocean at depths up to 2,000 feet. Solaris, as the robot is called, has propellers for motion. When its TV eye spots some object on the ocean floor, an image of the object is flashed to a monitoring screen aboard a surface ship, from which operators, by remote control, guide the 500-pound robot to its prey and make it clamp the find in its claw. At a depth of 1,600 feet, Solaris can patrol an area equivalent to 270 football fields.... It is believed the robot could ... be used to recover spent solid-fuel rocket boosters.

Science Future

July 25–29
An international group of animal behavior specialists meets in Williamsburg, Va. See animalbehaviorsociety.org/absmeetings

August 22–26
The fall meeting of the American Chemical Society is held in Boston. See www.acs.org

September 1
Deadline to submit videos for *Science*'s "Dance Your Ph.D." Contest. See submission guidelines at gonzolabs.org/dance

SN Online

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MATH TREK COLUMN
Tidbits of information can tilt probabilities in surprising ways. Read "When intuition and math probably look wrong."

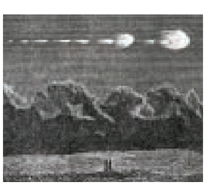
EARTH
If conditions are just right, an airplane can seed clouds to cause a snow shower. See "Planes can trigger snowfall."

BODY & BRAIN
A natural chemical in grapes shown to benefit yeast and animals could help people, too. See "Resveratrol shows activity against insulin resistance and retinal disease."

SCIENCE & THE PUBLIC BLOG
ER visits for drug overdoses are increasing, but not from illegal substances. See "Abuse of pharmaceuticals on the rise."

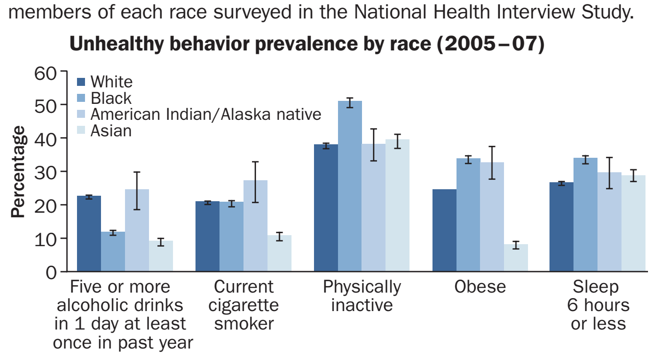
How Bizarre

Walt Whitman's poem "Year of Meteors (1859-60)" has long puzzled astronomers struggling to pin down the inspiration for the "strange huge meteor procession" he references. Previous guesses included the Leonid meteor storms of 1833 or 1858, or an 1859 meteor. But the chance examination of a 19th century painting depicting a meteor event in 1860 prompted researchers at Texas State University in San Marcos to explore an event from that year. Newspaper accounts (illustration shown)and other historical records match Whitman's description exactly, researchers report in the July *Sky & Telescope*.



Science Stats | BAD BEHAVIOR

Physical inactivity was the most common unhealthy behavior reported by members of each race surveyed in the National Health Interview Study.



SOURCE: C.A. SCHOENBORN AND P.F. ADAMS/*VITAL HEALTH STATISTICS* 2010

CLOCKWISE FROM TOP LEFT: LABLIT.COM; JOEL KNAIN; TEXAS STATE UNIVERSITY

“ Our finds provide the earliest secure dates for copper smelting and indicate the existence of different, possibly independent centers of invention of metallurgy. ” —THILO REHREN, PAGE 8

In the News

STORY ONE

New fossil shows Lucy walked tall, discoverers say

But critics contend ‘Big Man’ won’t end locomotion debate

By Bruce Bower

An older guy has sauntered into Lucy’s life, and some researchers believe he stands ready to recast much of what scientists know about the celebrated early hominid and her species.

Excavations in Ethiopia’s Afar region have uncovered a 3.6-million-year-old partial male skeleton of the species *Australopithecus afarensis*. This is the first time since the excavation of Lucy in 1974 that paleoanthropologists have turned up more than isolated pieces of an adult from the species, which lived in East Africa from about 4 million to 3 million years ago. The nearly complete skeleton of an *A. afarensis* child was retrieved from another Ethiopian site in 2000 and described in 2006 after years of fossil preparation (*SN: 9/23/06, p. 195*).

The new fossil’s discoverers consider this a Desi Arnaz moment: As the actor often exclaimed to his wife and costar Lucille Ball, “Lucy, you got some ’splainin’ to do!”

But other researchers are not so convinced that the new fossil changes much of what they already knew about Lucy and her kind.

The fossil’s discoverers, led by anthropologist Yohannes Haile-Selassie of the Cleveland Museum of Natural History, call their new find Kadanuumuu, which means “big man” in the Afar language. Excavations between 2005 and 2008 in a part of Afar called Woranso-Mille — about 48 kilometers north of where Lucy’s 3.2-million-year-old remains were found — yielded fossils from 32 of Big Man’s bones.

Big Man’s long legs, relatively narrow chest and inwardly curving back denote a nearly humanlike gait and ground-based lifestyle, according to a paper published online June 21 in the *Proceedings of the National Academy of Sciences*. At an estimated 5 to 5.5 feet tall, he would have towered over 3.5-foot-tall Lucy, who has often been portrayed as having had a fairly primitive two-legged gait and a penchant for tree climbing.

Big Man’s humanlike shoulder blade differs as much from that of a chimpanzee as it does from a gorilla’s, Haile-Selassie says. The shape of that bone, combined with characteristics of five recovered ribs, suggests to Haile-Selassie’s team that Big Man’s chest was shaped like a human’s. Earlier reconstructions of Lucy’s rib cage had endowed her with a chimplike, funnel-shaped chest.

So despite chimps’ close genetic relationship to people, he says, this new fossil evidence supports the view that chimps have evolved a great deal since their lineage diverged from humans’ roughly 7 million years ago, making them a poor model for ancient hominids.

Big Man’s anatomy bolsters recent analyses of 4.4-million-year-old *Ardipithecus ramidus*, which also challenge traditional views of ancient hominids as chimplike (*SN: 1/16/10, p. 22*).

Estimates of Lucy’s build were based

For the first time since 1974, researchers have unearthed the partial skeleton of an adult *Australopithecus afarensis*.

Y. HAILE-SELASSIE *ET AL.*/*PNAS* 2010

on comparisons to chimps and indicated to some scientists that she lacked the easy, straight-legged stride of modern people. Haile-Selassie and his colleagues suspect that their final reconstruction of Big Man’s anatomy will provide a better

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

model for assessing how Lucy walked.

"Whatever we've been saying about *afarensis* based on Lucy was mostly wrong," Haile-Selassie says. "The skeletal framework to enable efficient two-legged walking was established by the time her species had evolved."

Lucy's legs were short because of her small size, he adds. If Lucy had been as large as Big Man, her legs would have nearly equaled his in length, Haile-Selassie estimates.

Although lacking a skull and teeth, Big Man preserves most of the same skeletal parts as Lucy, as well as a nearly complete shoulder blade and a substantial part of the rib cage.

"This beautiful *afarensis* specimen confirms the unique skeletal shape of this species at a larger size than Lucy, in what appears to be a male," remarks anthropologist Carol Ward of the University of Missouri in Columbia.

A long-standing debate over how well Lucy's kind walked and whether her species spent much time in trees appears unlikely to abate as a result of Big Man's discovery, though. "There's nothing special I can see on this new find that will change anyone's opinion" on how the species navigated the landscape, comments Harvard University anthropologist Daniel Lieberman.

Haile-Selassie's team disagrees. Big Man demonstrates that *A. afarensis* spent most of its time on the ground, the researchers conclude.

"They were good walkers, but we don't know how well they ran," Haile-Selassie says. Big Man's long-legged stride indicates that members of his species could have made the 3.6-million-year-old footprints found more than 30 years ago at Laetoli, Tanzania (*SN Online: 3/22/10*), he adds.

Anthropologist Owen Lovejoy of Kent State University in Ohio, a coauthor of the new paper, regards Big Man as an "excellent runner." Big Man's pelvis supported humanlike hamstring muscles and, as indicated by the Laetoli footprints, his feet had arches, Lovejoy holds.

Big Man's skeleton was discovered in a part of the Afar region of Ethiopia called Woranso-Mille, about 48 kilometers north of the spot where Lucy was found.

Fossil hominid skeletons as complete as Big Man "are few and far between," says anthropologist William Jungers of Stony Brook University in New York. But the new find mostly confirms what was already known about Lucy, he asserts. Lucy's kind, including Big Man, were decent tree climbers, even if they couldn't hang from branches or swing from limb to limb as chimpanzees do, he says.

"Riddle me this," asks Jungers in considering Haile-Selassie's proposal for a ground-dwelling *A. afarensis*. "Where did they sleep? Did they wait for fruit to fall to the ground? Where did they go to escape predators?"

Groups of *A. afarensis* individuals must have devised ground-based strategies to ward off predators, Lovejoy responds. Some big cats would have negotiated trees better than Lucy's kind, he notes.

Jungers also doubts Lovejoy and Haile-Selassie's assertion that a humanlike gait had evolved in *A. afarensis*. Big Man includes only one nearly complete limb bone, from the lower left leg, which makes it difficult to estimate how long his legs were relative to his arms, Jungers contends.

Haile-Selassie doubts additional pieces of Big Man's skeleton will turn up. "If anything more was there, we would have found it by now," he says with a resigned laugh. ■

Back Story | FRAGMENTARY EVIDENCE

Even partial skeletons of *Australopithecus afarensis* have been hard to come by, with only two adult specimens coming to light since the species was named. But paleoanthropologists have collected numerous fragmentary fossils of the species that have added to what's known of Lucy's kind.

LH 4
This adult lower jaw, discovered in 1974 in Laetoli, Tanzania, is the "type specimen" that paleoanthropologists cited to establish *A. afarensis* as a species.

AL 333
This fossil is part of the "First Family" collection, a set of more than 200 teeth and bones that come from at least 13 individuals.

AL 129-1
Unearthed in November 1973, a year before Lucy's discovery, this fossilized knee joint established *A. afarensis* as an upright-walking hominid.

AL 200-1
Found in 1974 by Donald Johanson, one of Lucy's discoverers, this upper jaw shows that *A. afarensis* had apelike teeth.

TOP: CARTESIA, ADAPTED BY E. FELICIANO; BACK STORY (ALL IMAGES): SMITHSONIAN INSTITUTION

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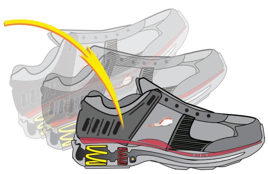

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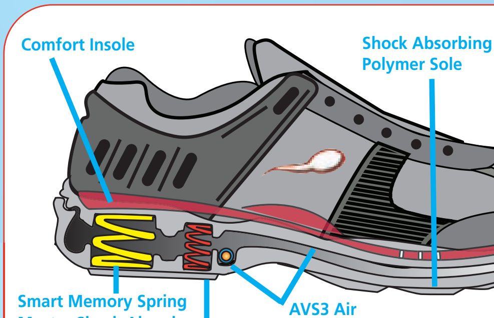

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Humans

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Research tests snakes on the brain

Imaging reveals regions that are active during acts of courage

By Laura Sanders

Researchers can now say what would happen in Samuel L. Jackson's brain if he really confronted snakes on a plane. In a terrifying sequel to the movie, volunteers were persuaded to bring a slithery serpent within centimeters of their heads while lying trapped in a brain scanner.

The experiment, published June 24 in *Neuron*, allowed researchers to watch brain activity as people quelled their fear and brought the snake closer to their heads, offering a glimpse into the courageous brain. Understanding how the brain chooses to overcome fearful impulses may help scientists treat people with phobias, panic disorders or post-traumatic stress disorder.

"This is a breakthrough study that will set the stage for a whole new area of work related to the brain and fear," comments neuroscientist Joseph LeDoux of New York University.

To see what happens in the courageous brain, researchers led by Yadin Dudai of the Weizmann Institute of Science in Rehovot, Israel, enlisted volunteers who admitted to fear of snakes but still agreed to participate.

Dudai and colleagues designed a conveyer belt carrying a large, writhing corn snake strapped by a piece of Velcro to the top of a box. "It's not a poisonous snake," Dudai says, "but for people who fear snakes, it's enough." Each volunteer was confined in an fMRI scanner with the snake behind their heads and were repeatedly given the choice to push a button to bring the snake about 11 centimeters closer or move it 11 centimeters away. A mirror showed the snake's location.

Brain regions active when participants advanced the snake, a move interpreted as courageous, were compared with those that lit up when a subject succumbed to fear and moved the snake away. A region in the front of the brain called the subgenual anterior cingulate cortex, or sgACC, was active with courage but quiet when fear took over. This region may have many functions, including regulating fear.

When the sgACC revved up, the researchers noticed that bodily indicators of fear, such as increased sweating, were reduced. Dudai hypothesizes that this brain region is crucial for directing the body to ignore fear. Stimulating this region might someday help people with phobias overcome their dread.

The new study is "certainly beginning to touch on understanding courage, but it might not necessarily explain all aspects of courage," comments neuroscientist Mohammed Milad of Harvard Medical School. Milad points out that the lab experiment lacks the altruistic components sometimes found in courage — for example, the drive to run into a burning building to save a child.

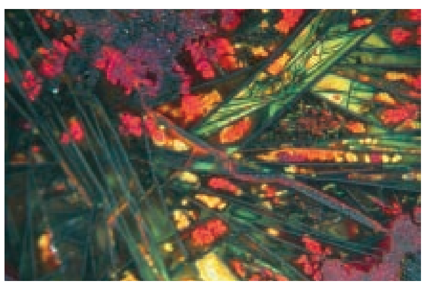
Dating the dawn of copper making

Find may alter views on time, place of metallurgy's origins

By Bruce Bower

An archaeological site in southeastern Europe has shown its metal. This ancient settlement contains the oldest solidly dated evidence of copper making, from 7,000 years ago, and suggests that copper smelting may have been invented in separate parts of Asia and Europe at that time, rather than spreading from one source.

The find extends the known record of copper smelting by about 500 years, a team headed by Miljana Radivojević and Thilo Rehren of University College London reports in an upcoming *Journal of Archaeological Science*. They were joined by Serbian researchers, led by Dušan Šljivar of the National Museum in Belgrade, and German scientists led by Ernst Pernicka of the University of Tübingen.



Copper slag found in Serbia provides the oldest evidence of copper making.

M. RADIVOJEVIĆ

Analyses of material from Serbia's Belovode site have identified pieces of copper slag, residue left after heating separates copper from other ore elements. The raw material came from nearby copper-ore deposits in Serbia or Bulgaria.

"Our finds provide the earliest secure dates for copper smelting and indicate the existence of different, possibly independent centers of invention of metallurgy," Rehren says. Large numbers of copper artifacts have been found at southeastern European sites dating to more than 6,000 years ago, Rehren notes.

His proposal challenges the view that copper smelting spread to Europe after originating in the Middle East's Fertile Crescent or in areas southeast of that region, in today's southern Iran. Archaeologists have dated copper smelting in the Middle East to about 6,500 years ago.

Although Belovode now stands as the oldest copper-smelting site, that status probably won't last, says archaeologist Benjamin Roberts of the British Museum in London. "It's likely we'll see copper-smelting evidence at least contemporary with Belovode from the Fertile Crescent once research programs are in place at well-excavated sites," he predicts.

Atom & Cosmos

"If the masses are different … then the most sacred symmetry of quantum field theory, CPT, is broken." —TOM WEILER

Neutrino data hint at need for revised theories

Nearly massless particles could turn physics on its ear

By Ron Cowen

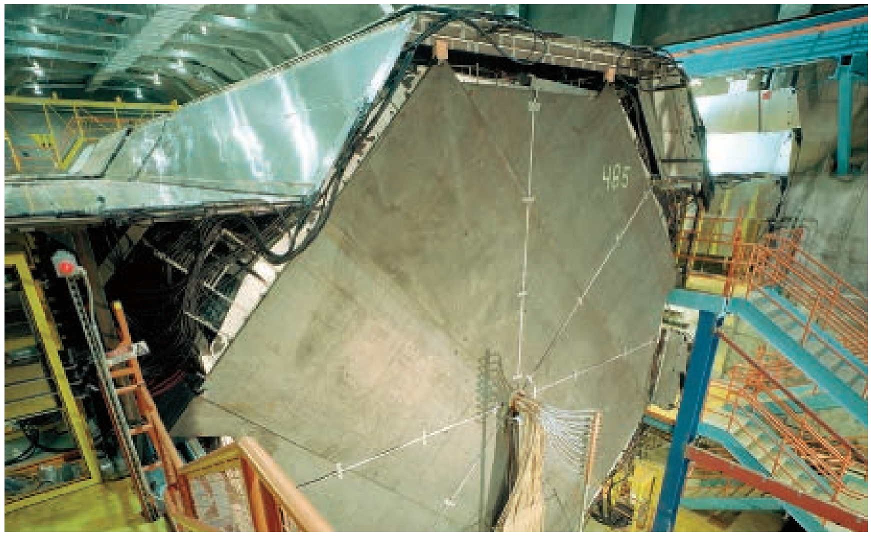
Neutrinos are the big nothings of subatomic physics. Nearly massless and with no electric charge, these ghostly particles interact so weakly with other matter that more than 50 trillion of them pass through a person's body each second.

Yet two new experiments hint that neutrinos may be opening a window on a hidden world of subatomic particles and forces. The findings could end up being statistical flukes. But so far the results, announced June 14 at the Neutrino 2010 conference in Athens, indicate that neutrinos and their antiparticle counterparts, antineutrinos, are not the nearly exact mirror images of each other that current physics supposes them to be.

If confirmed, the results would "indicate a fundamentally new direction in our thinking" about subatomic particles and the origin of matter in the universe, says theorist Rabindra Mohapatra of the University of Maryland in College Park.

The findings may help explain how the universe, believed to have begun with matter and antimatter so perfectly balanced that they would have destroyed each other upon contact, became dominated by matter. The results "could even signal a tiny breakdown of Einstein's theory of special relativity," Mohapatra says.

Current theories of particle physics assume that known forces arise from interactions with neighboring particles and obey special relativity, which holds that the speed of light and the laws of physics are always the same regardless of a particle's speed or rotation. For that to hold true, particles and antiparticles — including neutrinos and their antipartners — must have the same mass, Mohapatra says. But new data from the MINOS (for Main Injector Neutrino Oscillation Search) experiment seem to contradict that notion.



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Data from the MINOS experiment (detector at the Soudan Underground Laboratory in Minnesota shown) hint that neutrinos and antineutrinos might have different masses.

The three known types of neutrinos (electron, muon and tau) transform from one type into another as they travel. During a 735-kilometer journey from Fermilab in Batavia, Ill., to the Soudan Underground Laboratory in Minnesota, about 37 percent of muon antineutrinos disappeared — presumably morphing into another neutrino type — compared with just 19 percent of muon neutrinos, reports MINOS spokesman Robert Plunkett of Fermilab. That difference suggests a difference in mass between antineutrinos and neutrinos — although more data will be needed to confirm the observation. Data collected so far leave a 5 percent chance that the particles weigh the same.

"If the masses are different for neutrinos and antineutrinos, then the most sacred symmetry of quantum field theory, CPT [for charge, parity and time], is broken in the neutrino sector," says Tom Weiler of Vanderbilt University in Nashville.

If particle interactions are thought of as a movie, CPT symmetry requires that whatever physics occurs during the show must be the same when the film is run forward or backward (time), viewed through a mirror (parity) and when replacing each particle by its antiparticle (charge).

If CPT is broken, then a cornerstone of Einstein's special relativity is also violated, Weiler notes.

In a smaller Fermilab study, an experiment called MiniBooNE found a different kind of asymmetry between particles and antiparticles. Over about half a kilometer, muon antineutrinos morphed into electron antineutrinos more often than muon neutrinos became electron neutrinos. That result also requires a mass difference between neutrinos and antineutrinos, Mohapatra says, though others disagree.

There's about a 3 percent chance the MiniBooNE finding is a fluke. But it does match results, later refuted, from an experiment at Los Alamos National Laboratory in New Mexico during the 1990s.

An asymmetry between particles and antiparticles in the standard model of particle physics isn't large enough to account for the MiniBooNE results, notes Fermilab's Boris Kayser. If confirmed, the findings may require a fourth, previously unknown neutrino type, dubbed sterile because it would interact with matter even more weakly than the other three.

Body & Brain

For longer versions of these and other Body & Brain stories, visit **www.sciencenews.org**

Many berries show cancer promise

Common varieties as good as exotic types against rat tumors

By Nathan Seppa

Garden-variety berries provide about the same cancer-fighting punch as more exotic ones, a study of rats with esophageal cancer shows. A separate study finds possible protection against breast cancer.

Cancer biologist Gary Stoner of Ohio State University in Columbus and colleagues tested seven berry types against cancer of the esophagus in rats — black raspberries, red raspberries, blueberries, strawberries, noni berries, açai berries and wolfberries (also called goji berries).

The scientists injected rats with a carcinogenic chemical. Some then got normal food, while others ate a similar chow

Familiar berries fight cancer as effectively as exotic types, research suggests.

of which 5 percent was one of the types of berry in dehydrated form. Nearly all of the rats fed just normal chow developed tumors, but only 60 to 75 percent of the berry-supplemented rats did. The berry-eating rats had about half as many tumors overall, the team reports in the June *Pharmaceutical Research*.

Earlier work by Stoner's group found that black raspberries contain ample amounts of the two cancer-fighting compounds ellagitannin and anthocyanin. But the new work shows that a berry need not have large concentrations of either compound to be a cancer fighter.

In the other study, cancer biologist Ramesh C. Gupta of the University of Louisville School of Medicine in Kentucky and his colleagues used estrogen to induce breast cancer in female rats. Some animals received a diet of 2.5 percent dehydrated blueberries or black raspberries, and others got food without berries. Those getting berries showed less tumor growth, the researchers report in the June *Cancer Prevention Research*.

Practice can be less than perfect

Working memory may limit musicians' sight-reading skill

By Bruce Bower

Here's a harsh piano lesson: Years of tickling the ivories go only so far for those who want to sight-read sheet music fluently, a new study suggests. Aside from those painstaking hours of practice, a memory skill that pianists have little control over may help orchestrate their performance.

Sight-reading is the act of playing sheet music on an instrument with little or no preparation. Any person who practices sight-reading for thousands of hours will get pretty good at it, say study coauthors Elizabeth Meinz of Southern Illinois University Edwardsville and David Hambrick of Michigan State University in East Lansing. But a strong ability to keep different pieces of relevant information in mind while performing a task — known as working memory capacity — aids sight-reading regardless of practice, the psychologists report in a paper published online June 9 in *Psychological Science*. The best sight readers combined strong working memories with decades of piano practice, the researchers found.

Working memory appears to gel early in life and can't be improved much by learning, the study suggests. High scores on working memory tests did not cluster among volunteers who had practiced piano playing and sight-reading the most.

Previous research indicates that working memory capacity varies from one person to another and changes little from childhood to adulthood, the scientists say.

"Practice ... will not always be sufficient to overcome limitations due to a person's basic cognitive abilities," Meinz says.

IQ scores probably relate to sight-reading proficiency as well, because IQ tests tap into working memory capacity, says psychologist Glenn Schellenberg of the University of Toronto Mississauga .

He sees the new findings as a challenge to the influential view, championed by psychologist K. Anders Ericsson of Florida State University in Tallahassee, that expertise in sight-reading or anything else depends on skills acquired through extensive practice. Novices at a particular activity rely on general mental faculties such as working memory, Ericsson argues. But after roughly 10 years of practice at a task such as sight-reading, he suggests, specific mental mechanisms for getting the job done emerge and general-purpose faculties are jettisoned.

Ericsson regards the new study as "not a fair test" of his hypothesis. Most musicians tested by Meinz and Hambrick — including those who had played piano for a long time — were not skilled sight readers, Ericsson asserts. So the study can't address whether differences in working memory capacity limit the performance of expert sight readers, he says.

Working memory capacity shows only a weak relationship to differences in sight-reading skill in the new paper, says psychologist Reinhard Kopiez of Hanover University of Music and Drama in Germany. In a 2008 study of 52 accomplished piano players, Kopiez and a colleague found no link between working memory capacity and sight-reading ability.

DKGILBEY/ISTOCKPHOTO

314 million — Number of people with visual impairments worldwide	**45** million — Number of those people who are totally blind	**85** percent — Portion of visual impairment cases called “avoidable” by the World Health Organization

Gene therapy helps blind mice see

Sight restored in cone cells impaired by retinitis pigmentosa

By Gwyneth Dickey

Researchers have restored sight to blind laboratory mice by using gene therapy. If it works in people, the new treatment may one day allow some with retinitis pigmentosa, an incurable genetic eye disease, to navigate a room, read and drive.

“It’s an excellent study,” says developmental neuroscientist Connie Cepko of Harvard Medical School, who was not involved with the research. “This is conceptually a nice way to try to restore or prolong vision.”

Retinitis pigmentosa causes tunnel vision and night blindness in 2 million people worldwide. It primarily affects rods, light-sensitive cells concentrated in the outer retina that enable night and peripheral vision.

Some patients also lose daylight vision and go blind completely as the color-sensing cone cells of the inner retina slowly degenerate. But the disease doesn’t kill cone cells immediately; it first makes them nonresponsive to light. That means there is a window of time when the cone receptors are still there, but not functioning.

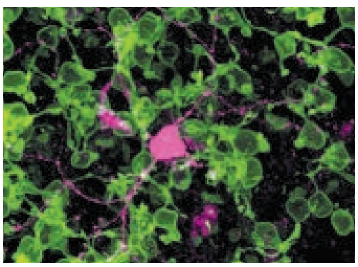
So a team led by scientists at the Friedrich Miescher Institute for Biomedical Research in Basel, Switzerland, attempted to reanimate diseased cone cells in mice. Using a virus already approved for human gene therapy, the researchers inserted a gene from a light-sensitive bacterium, *Natronomonas pharaonis*, into the DNA of cone cells, the team reported online June 24 in *Science*.

The gene is a blueprint for proteins that form passageways in cell membranes. When stimulated by light, those proteins open up and let negatively charged ions into the cell. When inserted and active in the mouse cell membranes, the proteins helped mimic the normal activity of healthy cones.

Not only did the restored cone cells respond to light, but they also sent signals to the brain so the mice could see.

“What was really astounding is that these cells that were blind for a while were still connected to the rest of the circuit,” says neurobiologist Botond Roska, who led the study.

But unlike healthy cone cells, the restored cone cells could not adapt to different light levels. The cells responded best to bright yellow light similar to sunlight at the beach, Roska says. In order for human patients to see in dimmer light, researchers would have to develop special glasses with light-sensing cameras to adjust the intensity of light projected to the patients’ eyes, he says.



Mice cone cells glow green where a therapeutic gene hit its target.

COURTESY OF VOLKER BUSSKAMP AND FMI

After more studies with mice and primates to ensure the treatment’s safety and effectiveness, Roska aims to test it in human patients.

“This is not a treatment for all patients with retinitis pigmentosa,” he says, “but for a subgroup in which the cone receptors are still there.”

His team will also explore how long the therapeutic effects last and whether the gene therapy could have applications for other eye diseases like macular degeneration and retinal damage due to diabetes.

“I have a feeling it will make it into human trials,” says Cepko. “How a person will perceive these signals is hard to say, but it should do at least as well as it did for mice.” ■

NEWS BRIEFS

Stopping platelets at the source

Slowing the production of clot-forming platelets may protect against heart attack and stroke without the risk of excessive bleeding posed by aspirin, scientists say in the June 23 *Science Translational Medicine*. Clots in arteries cause most strokes and heart attacks, but reducing clotting too zealously places a person at risk of bleeding to death. Stephen Hanson of the Oregon Health & Science University in Portland and colleagues used an antibody to limit the outflow of clot-forming platelets from bone marrow in baboons. The antibody inhibits thrombopoietin, a hormone that spurs cells in the bone marrow to make platelets. By keeping platelet levels at the low end of the normal range, the drug substantially limited clot formation without causing excess bleeding. —*Nathan Seppa*

Vitamin may cut lung cancer risk

It might be too soon to start popping supplements, but high levels of vitamin B6 may reduce lung cancer risk, scientists report June 16 in the *Journal of the American Medical Association*. Researchers also note possible benefits from high levels of folate and of the amino acid methionine. Using medical data from more than 380,000 Europeans, an international team calculated that people with vitamin B6 levels in the top quarter of all samples had about half the risk of lung cancer as those with the lowest vitamin B6 levels. A similar benefit was found for methionine. High folate levels seemed to give less protection (and only for smokers). Having stellar levels of all three lowered the risk of lung cancer by a full two-thirds, the scientists calculated. —*Nathan Seppa*

Life

For longer versions of these and other Life stories, visit **www.sciencenews.org**

Warming favors homebody herd

Heading for the hills in spring now strains Yellowstone elk

By Susan Milius

Warming temperatures could help explain why migration isn't such a hot idea anymore for some elk living in and around Yellowstone National Park.

About a third of what's called the Clarks Fork elk herd moves at the end of winter from land around Cody, Wyo., up to grasslands at high elevations in Yellowstone, said ecologist Arthur Middleton of the University of Wyoming in Laramie.

Normally, following the progress of the spring growing season would benefit migrants. But the migratory elk are producing fewer calves compared with the stay-behind part of the herd.

Satellite images show that the annual period when high Yellowstone grasslands are thriving and green with prime nutrition for grazers shrank by 40 percent between 1989 and 2009, Middleton reported June 14.

Climate shifts may hinder the reproductive success of some migratory elk in Yellowstone National Park.

This grassland brownout fits with weather station data showing that over the past 21 years, the average July temperature in the migrants' high-elevation summer range has risen more than 4 degrees Celsius. In contrast, satellite images show little change in the greening of vegetation at lower elk feeding grounds, Middleton and his colleagues propose.

Skimpy food offerings in the high grasslands could help explain why calf production declined by 70 percent among the Clarks Fork migratory elk between 1989 and 2009, Middleton said. Now only about two-thirds of adult Clarks Fork females get pregnant each year, compared with about 90 percent of nonmigratory females in the same herd.

Research has shown that adult male elk seem more vulnerable to wolves in early winter than they used to be, said Douglas Smith, who directs wolf research and management in the park.

Predators also play a role in elk numbers, and Middleton said that migratory elk are likely to be hit harder than sedentary ones. He noted that Yellowstone National Park reports growing numbers of grizzly bears, which prey considerably upon elk calves.

So the elk migration flunks on two counts, Middleton said. It provides neither seasonal food bonanzas nor relief, even temporarily, from predators.

Upslope migrants in similar ecosystems may face similar troubles, Middleton speculated. People tend to concentrate agriculture, with its irrigation and low tolerance for predators, at low altitudes, while parks often end up in the harder-to-develop heights.

Pachyderms prefer picnics sans ants

Six-legged security force protects trees from hungry elephants

By Susan Milius

Ants living in whistling-thorn acacia trees on the African savanna may weigh only 3 milligrams, but they can protect their homes from elephants weighing a billion times more, biologist Jacob Goheen reported June 12.

Some acacia-dwelling ants are known to attack other insects, including some that threaten their hosts' health. Satellite images of Kenya led Goheen, of the University of British Columbia in Canada, and coauthor Todd Palmer of the University of Florida in Gainesville to ask if ants might be effective against much larger foes too.

The team noticed thinning vegetation in the northern part of the Lewa Wildlife Conservancy between 2003 and 2008, a period when elephant populations tripled throughout the reserve. The northern zone doesn't have trees with their own ant militias, but the southern section is about 95 percent ant-defended.

Curious, Goheen and Palmer set up a buffet of acacia branches at an elephant orphanage and found that youngsters there steered clear of anything with ants.

Elephants don't mind acacia thorns but avoid trees that host ants.

The researchers noted a similar preference in wild elephants.

The study raises intriguing questions about how such plant defenses evolved, says ecologist Rob Swihart of Purdue University in West Lafayette, Ind.

FROM TOP: JIM PEACO; R. WINSLOW/ANIMALS ANIMALS

21 Yellowstone wolf population at the end of 1995

171 Yellowstone wolf population in 2007

124 Yellowstone wolf population in 2008

MEETING NOTES

Bats' built-in air conditioning

Plenty of biologists have handled Brazilian free-tailed bats, but none had noticed a feature now revealed by thermal imagery: a heat-radiating stripe on each wing. In images of zones of body heat, these bats (*Tadarida brasiliensis*) look as if they're wearing pale suspenders. After images revealed where to look, Jonathan Reichard of Boston University spotted a narrow, ladderlike array of blood vessels running along the wings of live bats swooping into a roost in Texas. These stripes seem to be a new example of thermal windows, like the blood vessels in a toucan beak, Reichard said June 12. Animals flush these zones with blood to cool down and shunt blood away to avoid chills. Such flexible thermal regulation could aid vigorous fliers like the Brazilian free-tailed bats, which live in warm places but fly high into cold air to forage. In studying museum specimens, Reichard has found radiator stripes only in the family that includes this species. —*Susan Milius*

Wolves eat big in warm times

As droughts and a warming trend grip Yellowstone National Park, wolves have shifted their dining habits. When the predators were reintroduced to Yellowstone in 1995 after a 23-year absence, elk calves were a mainstay of their diet during early winter in the northern range, said Douglas Smith, leader of Yellowstone's wolf project. As winter took its toll on elk, adult males became easier prey. Toward the end of winter, researchers found, bulls made up about a third of wolves' diets. Data from 2004 to 2008, however, show wolves switching from calves to adults earlier in the winter season. On average, wolves were making fewer kills than in previous years, but each elk provided a larger meal. Because elk had less vegetation to eat during recent warm, dry years, the males weren't bulked up to their usual standards by winter, Smith said June 14. The trials of mating season and winter hardship weakened bulls earlier, making them easier prey for wolves. —*Susan Milius*

Genes & Cells

For longer versions of these and other Genes & Cells stories, visit **www.sciencenews.org**

'Vestigial' RNA runs interference

Study suggests pseudogenes influence protein production

By Tina Hesman Saey

Deploying doppelgängers to distract pesky hangers-on isn't reserved for paparazzi-plagued Hollywood heartthrobs. Some genes use look-alikes as decoys to distract mobs of interfering molecules, a new study shows.

The decoys, known as pseudogenes, are defective copies of protein-encoding genes. Many pseudogenes can make RNA copies of the instructions in their DNA but have flaws that prevent that RNA from being converted into proteins.

Because pseudogenes don't sire proteins, most biologists have thought of them as vestigial copies of functioning genes. But a study in the June 24 *Nature* shows that pseudogenes may in fact be important regulators of their protein-encoding twins.

The demonstration that pseudogenes may indeed have a function could transform biology, says study leader Pier Paolo Pandolfi of Beth Israel Deaconess Medical Center in Boston and Harvard Medical School. The finding has already altered the perspectives of people in his lab, he says. "Now we are unable to think the same. It changes the way we do biology on a daily basis."

Pandolfi's group found that RNA from a pseudogene called *PTENP1* draws tiny regulatory molecules called microRNAs away from *PTEN*, a powerful anticancer gene.

> "Now we are unable to think the same. It changes the way we do biology on a daily basis."
> PAOLO PANDOLFI

MicroRNAs are small pieces of RNA that bind messenger RNAs (mRNAs for short), the intermediates between genes and their proteins. MicroRNA binding either causes mRNA to be degraded or blocks protein production. In the case of *PTEN* that could be disastrous, because as the researchers previously discovered, cutting PTEN protein levels by just 20 percent is enough to cause precancerous changes in mice .

That's where *PTENP1* comes in. Pandolfi reasoned that the microRNAs attracted to *PTEN* wouldn't be able to tell gene from pseudogene, and that some microRNAs might go after the mRNA of *PTENP1*, leaving less to block *PTEN*.

When the researchers tested that idea by making more *PTENP1* mRNA in cells, PTEN protein levels rose, indicating that the pseudogene was indeed mopping up microRNAs that would otherwise reduce PTEN production. Removing *PTENP1* from cells had the opposite effect — with nothing to distract the microRNAs, the regulatory molecules latched on to *PTEN* mRNA and suppressed its production of protein.

The researchers also found that tumors from colon cancer patients sometimes lack *PTENP1*, indicating that the pseudogene could help protect against tumors.

It is too early to tell whether the thousands of pseudogenes in the human genome all help regulate their protein-coding siblings, says Frank Furnari, a cancer biologist at the University of California, San Diego. But the finding gives biologists a new type of gene regulation to explore. "For sure we know the importance of microRNAs, and now to have this mechanism by which microRNAs are regulated by what we thought was junk DNA is somewhat surprising and exciting," Furnari says.

Gene tied to autoimmune diseases

Defective enzyme sets B cells loose on the body, study finds

By Tina Hesman Saey

Rare variations in a single gene can lead to a wide variety of autoimmune disorders including diabetes, lupus and rheumatoid arthritis, a new study shows.

The gene in question encodes an enzyme called sialic acid acetylesterase or SIAE, which regulates the activity of the immune system's antibody-producing B cells. About 2 to 3 percent of people with autoimmune disorders have defects in SIAE that allow B cells to run amok and make antibodies that attack the body, a team led by Shiv Pillai of Massachusetts General Hospital and Harvard Medical School report online June 16 in *Nature*. The finding suggests that enhancing the enzyme's activity could help people with autoimmune disorders.

In a study of 13 people with autoimmune disorders, the researchers found that a person with Crohn's disease and one with rheumatoid arthritis had genetic mutations inactivating the enzyme. The team expanded the study and eventually identified genetic variants affecting SIAE in 27 of 923 people with autoimmune diseases and in 17 of 648 healthy people.

Most of the genetic variants found in people with autoimmune disorders disrupted the enzyme's normal function. All but two of the healthy people were found to carry variants that don't interfere with the enzyme's activity.

Whether changes in the enzyme are all that is necessary to trigger autoimmune disease "or if there are more things, we don't know," Pillai says. "I suspect more things. I suspect it's not enough."

Earth

11,000 square km — Size of largest iceberg ever observed

78 square km — Size of largest Northern Hemisphere iceberg ever observed

Texas flood carves canyon in days

Torrent is a model for past megafloods on Earth and Mars

By Sid Perkins

An unexpectedly large canyon carved in just three days by a Texas deluge may help scientists estimate the size of ancient megafloods believed to have sculpted terrain on both Earth and Mars.

In July 2002, record flooding in central Texas caused Canyon Lake, a dammed reservoir about 55 kilometers northeast of San Antonio, to overflow. The water carved a 2.2-kilometer-long canyon downstream of the dam, Caltech geologist Michael P. Lamb and colleague Mark Fonstad, a hydrologist at Texas State University in San Marcos, report online June 20 in *Nature Geoscience*.

Water flowing through the spillway quickly stripped the creek bed of its trees and soil and began chewing into the limestone bedrock below, says Lamb. Over the course of about three days, the torrent carved a canyon that ranged between 40 and 60 meters wide and averaged 7 meters deep over much of its length. Overall, the flood excavated about 460,000 cubic meters of material, almost half of that being rock.

An overflowing Texas reservoir carved a 2.2-kilometer-long canyon in three days.

The torrent was so intense that it plucked large, flat-sided blocks of limestone up to a meter across from the bedrock. During the flood's peak, water flowed through the canyon at a rate that would have filled 20 Olympic-sized pools each minute.

"To be able to document the effects of this event so soon after it occurred, it's an important contribution," says Jim E. O'Connor, a geologist with the U.S. Geological Survey in Portland, Ore.

In the lower half of the canyon, the deluge sculpted streamlined islands of material resembling those found in areas stricken by much larger floods on Earth and presumably on Mars.

The Texas flood "is a potential analog for what we see on Mars," says Alan D. Howard, a geomorphologist at the University of Virginia in Charlottesville who has studied the geology of the Red Planet. The majority of bedrock on Mars is basalt deposited by lava flows, each layer of which would have cracked into large blocks as it cooled, he notes. In a raging flood, these blocks could have been picked up from the Martian terrain and tossed about like the ones in the Texas flood, excavating a lot of material quickly.

"It doesn't take millions of years to create an impressive channel," Howard notes. "Flowing liquid can do a lot of work in a short period of time."

Antarctic shoal breaks the ice

Breakup of a massive berg pinpoints an undersea ridge

By Sid Perkins

During the last couple of decades, scientists poring over satellite images have noticed several large icebergs breaking up as they wafted along a particular stretch of the Antarctic coast. Now, thanks to data gathered in part by an instrument-laden iceberg, the researchers know why: The ice masses were crashing into a previously unreported submarine ridge.

Most icebergs that calve from Antarctica's Ross Ice Shelf are carried by shore-hugging currents past Cape Adare, a section of coast that lies south of New Zealand. That remote stretch of ocean is covered with sea ice about 10 months of the year, says Seelye Martin, an oceanographer at the University of Washington in Seattle. But in October 2005, iceberg B15A — the largest remnant of a 300-meter-thick, Connecticut-sized berg that split off the ice shelf in March 2000 — cleared a path as it bulldozed through the area. Such massive icebergs break free only once every decade or so and can float for years if collisions don't break them into smaller pieces.

Scientists had installed several instruments on B15A in 2003 and 2004 — including a seismometer, a compass and GPS equipment — to monitor the megaberg as it moved north, melted and broke apart (*SN: 5/12/01, p. 298*). Those instruments indicate that in late October 2005, B15A briefly came to a stop, rotated back and forth a few degrees and began cracking up, a splintering also detected by seismometers on shore and by Earth-orbiting satellites.

Sonar surveys revealed a 9-kilometer-long, previously unrecognized undersea ridge where the berg broke up, Martin and colleagues report online June 18 in *Journal of Geophysical Research–Solid Earth*. The shoal, whose peaks lie at a depth of about 215 meters, sits about 25 kilometers off Cape Adare, smack dab in the path of the coast-hugging currents. "This is a big navigational hazard for icebergs," Martin notes. The ridge lies too deep, though, to be a danger to ships that might navigate these mostly ice-bound waters, and many small icebergs have passed over the shoal without incident. ■

RICHARD SEARS

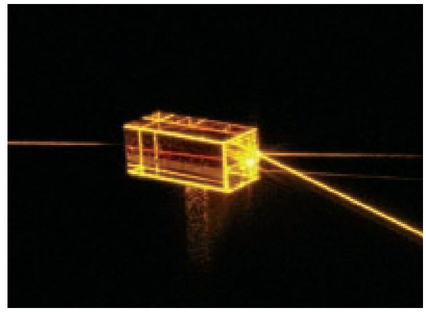
Matter & Energy

17 percent Memory efficiency record for vapor-based quantum systems

69 percent Memory efficiency of new crystal-based quantum system

Solidifying memories made of light

Crystal offers more efficient quantum information storage



A crystal containing praseodymium can store information encoded in light.

MATTHEW SELLARS/AUSTRALIAN NATIONAL UNIVERSITY

By Alexandra Witze

Sun-drenched summer vacations may yield pleasant memories, but physicists have now harnessed light to remember something else: quantum information.

Researchers have coaxed laboratory crystals to capture and release information carried within a light pulse at the highest efficiency yet. The work, reported in the June 24 *Nature*, could lead to new secure communications that exploit weird properties of the quantum world.

"It's quite an important step towards our dream of extending the distances over which we can do quantum communication," says Wolfgang Tittel, a physicist at the University of Calgary in Canada who was not involved in the work.

Until now, researchers have tried to fashion "quantum memories" for light primarily by sending laser beams into a vapor of atoms. The atoms preserve information in the light that can then be read out again, like playing back the data on a DVD. But quantum memories based on vapors are inefficient: The best system so far has 17 percent efficiency (of 100 light particles put in, only 17 make it out). Physicists don't need perfect efficiency, but a system needs at least 50 percent recall to be useful in quantum applications.

Instead of a vapor, the new work uses a solid crystal, in which the atoms are rigidly packed together instead of bouncing around. That control allows a memory efficiency of 69 percent, reports a team led by Morgan Hedges of the Australian National University in Canberra.

It's an impressive breakthrough, says Thierry Chanelière, a physicist at the National Center for Scientific Research in Orsay, France.

As the light pulse enters the crystal, it begins to slow down, its front reaching one end of the crystal and stopping as the rest of the light squeezes itself in to fill the whole crystal. The mostly transparent crystal can absorb one particular color very strongly. Switching on an electric field gradient changes the strongest absorption color in different parts of the crystal, so that one end absorbs strongly at the blue part of the spectrum and the other end toward the red. Quantum information from the light is stored in the oscillations of the crystal's atoms; reversing the electric field gets the atoms to reemit light containing the same information as the original pulse.

The crystal that Hedges and colleagues created is made of praseodymium, a rare earth element, combined with yttrium, silicon and oxygen. The scientists are now beginning to study quantum memories using other rare earth elements, such as europium. Their next goal: to coax the crystal to retain quantum memory for longer than a few microseconds.

Quantum physics takes flying leap

Supercold atoms in free fall may offer clues about gravity

By Laura Sanders

In an experiment that puts the good old-fashioned egg drop to shame, European physicists dropped a small blob of ultracold atoms 120 meters down a shaft. The result: no yolk on their faces.

The researchers created a cloud of about 10,000 ultracold rubidium atoms that fused into a quirky quantum object called a Bose-Einstein condensate, then dropped the stuff off a needle-shaped tower in Bremen, Germany. Since freely falling objects are essentially weightless, the successful drop demonstrates the ability to monitor quantum objects in near-zero gravity. That ability may lead to a deeper understanding of heavy topics such as general relativity, an international team reports in the June 18 *Science*.

The new study is "an impressive technological advance," says MIT physicist Wolfgang Ketterle, who shared a Nobel Prize in 2001 for creating Bose-Einstein condensates, or BECs, in the lab.

One challenge was miniaturizing the jungle of complex equipment usually needed to create a BEC. "These guys fit the equivalent equipment into a 60-by-60 centimeter by 2-meter capsule and sent it down 120 meters and it smashed at the bottom," says physicist Paulo Nussenzveig of the University of São Paulo. "It's really, really amazing."

A camera caught the BEC expanding before the capsule crashed into an 8-meter-deep pit of plastic balls. The atoms' behavior in near-weightlessness largely agreed with theoretical predictions, although tiny stray magnetic perturbations caused the BEC to expand a little less than predicted, the team found.

"This is a modest first step towards something that you can do interesting experiments with," says study coauthor Ernst Rasel of Leibniz Universität Hannover in Germany. Nussenzveig says that studying BECs in microgravity may answer questions about how gravity works on quantum scales.

Technology

30,976 Size of first digital image, in pixels

21.1 million Size of first digital presidential portrait, of Obama, in pixels

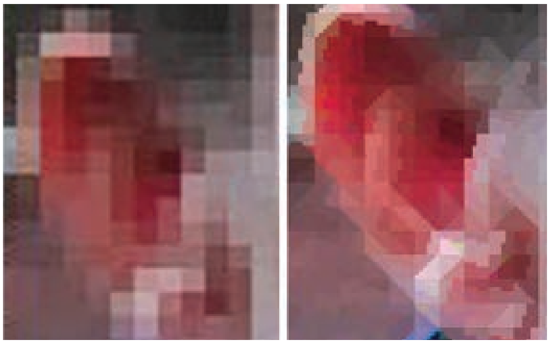
Pixel pioneer offers a better way to scan images than square approach

50 years later, creator of digital photos fixes the early flaws

By Rachel Ehrenberg

Russell Kirsch says he's sorry.

More than 50 years ago, Kirsch took a picture of his infant son and scanned it into a computer. It was the first digital image: a grainy, black-and-white baby picture that literally changed the way people see the world. With it, the smoothness of images captured on film was shattered to bits. Thanks in part to Kirsch, square pixels became the norm, and the world got a little bit rougher around the edges.



In a square-pixel image (left), a close-up of a human ear appears as a blocky stack. Using variably shaped pixels (right), the image reveals a recognizable ear.

At the National Bureau of Standards in Washington, D.C. in the 1950s, Kirsch worked with the first programmable computer in the United States. "The only thing that constrained us was what we imagined," he says. "So there were a lot of things we thought of doing. One of which was, what would happen if computers could see the world the way we see it?"

Their efforts to answer that question would lay the foundations for CT scans, satellite imagery, virtual reality and Facebook.

Kirsch made that first digital image using an apparatus that transformed the picture into the binary language of computers, a grid of zeros and ones. A mere 176 by 176 pixels, the image was built from a fraction of the information in pictures captured with today's digital cameras. Back then, the computer's memory capacity limited the image's size. Today, bits have become so cheap that a person can walk around with thousands of digital baby photos stored on a pocket-sized device that also makes phone calls, browses the Internet and even takes photos itself.

Yet science is still grappling with the limits set by the square pixel.

"Squares was the logical thing to do," Kirsch says. "Of course, the logical thing was not the only possibility ... but we used squares. It was something very foolish that everyone in the world has been suffering from ever since."

Now retired in Portland, Ore., Kirsch recently set out to make amends. Inspired by the mosaic builders of antiquity who constructed scenes of stunning detail with bits of tile, he wrote a program that turns the chunky, clunky squares of a digital image into a smoother picture made of variably shaped pixels.

He applied the program to a more recent picture of his son, now 53 years old, which appears with Kirsch's analysis in the May/June issue of the *Journal of Research of the National Institute of Standards and Technology*.

Scanned in 1957, a picture of Russell Kirsch's son was the first digital image.

"Finally," he says, "at my advanced age of 81, I decided that instead of just complaining about what I did, I ought to do something about it."

His new method assesses a square-pixel picture with masks that are 6 by 6 pixels each, then looks for the best way to divide this larger pixel cleanly into two areas of the greatest contrast. The program tries two different masks over each area. In one, a seam divides the mask into two rough triangles, and in the other a seam creates two rough rectangles. Each mask is then rotated until the program finds the configuration that splits the 6-by-6 area into sections that contrast the most. Then, similar pixels on either side of the seam are fused.

Kirsch's program may find a home in the medical community, he says, where it is standard to feed images such as X-rays into a computer.

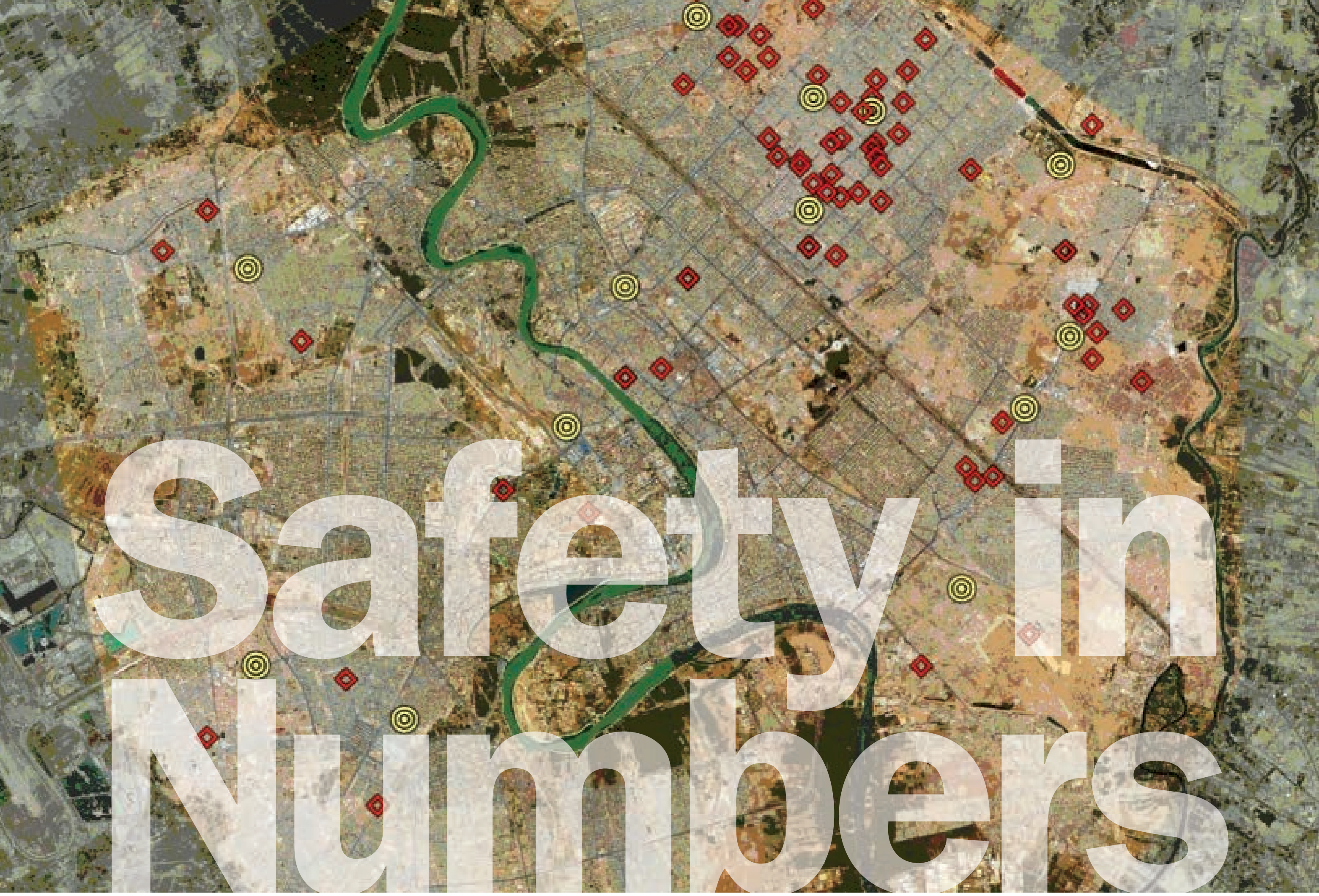
The approach addresses a conundrum that the field of computational photography continues to grapple with, says David Brady, head of Duke University's imaging and spectroscopy program in Durham, N.C. Brady notes that images built from pixels can show incredible detail. "It's fun to talk to kids about this because they don't know what I'm talking about," he says, "but the snow on analog television — a block-based imager can reconstruct that pattern exactly."

Images from real life never look like that, though. Typically, they have several large uniform sections — forehead, red shirt, blue tie. So there's a high probability that one pixel will look the same as the pixel next to it. There's no need to send all those look-alike pixels as single pieces of data; the important information is where things differ.

"In an image, that's an edge," Brady says. "You want to assume smoothness but have a measurement system that's capable of accurately finding where the edges are."

Where Kirsch uses masks to do that, researchers today typically use complex equations to strike the balance between shedding unnecessary information and keeping detail.

IMAGES: NIST



Safety in Numbers

Mathematics offers innovative weapons for fighting terrorism

By Laura Sanders

Mathematicians don't wear capes and tights. They are not more powerful than a locomotive and they can't leap tall buildings in a single bound. But when it comes to protecting people from evildoers, these calculating crusaders could turn out to be super.

On the surface, fighting terrorists with mathematics sounds absurd. Yet some mathematicians and computer scientists are devising equations and algorithms that show real promise as terrorism countermeasures. From simple formulas that focus on mathematical properties underlying terrorist behavior to immense mega-analyses incorporating billions of information bits, mathematics is becoming an increasingly important weapon in the antiterror arsenal.

"The area has exploded, in terms of the types of techniques and technologies," says computer scientist Kathleen Carley of Carnegie Mellon University in Pittsburgh. "There are huge, rapid advances in this area with, of course, some very interesting challenges."

Some researchers, including Carley, are formulating powerful new algorithms that comb through mountains of data and uncover hidden "rules" that govern terrorism behavior. Each tiny electronic crumb — from among billions of cell phone calls, web-browsing records, e-mail messages, credit card receipts and airline manifests — could serve as a microclue to help create a complete picture of a terrorist's life.

Other researchers, instead of using mountains of data, begin with a molehill, seeking simple, pared-down mathematical formulas that might describe the optimal arrangement of a secret terrorist cell, for instance, and provide hints on how to destroy it.

Already, terror-crushing algorithms are proving their mettle. New techniques are untangling the covert organizational structure of terrorist networks. By modeling the internal tugs-of-war between secrecy and the need to communicate, researchers can predict patterns of terror cells' organization. Other mathematical methods may help identify the members of a terrorist cell who are actually calling the shots. And still other numerical techniques can pinpoint concealed weapons caches — a method now being used by two U.S. Army groups to find improvised explosive device stockpiles in Baghdad.

Putting hard numbers to something as nebulous and secretive as terrorism "transforms the science from being

V.S. SUBRAHMANIAN, P. SHAKARIAN, M. SAPINO

A new algorithm uses the location of blasts (red) from improvised explosive devices to deduce the hiding places of weapons caches (yellow) in Baghdad.

kind of a case study, expert-opinion sort of field into a quantitative area," says Alexander Gutfraind, a mathematician at Los Alamos National Laboratory in New Mexico. "If you have a mathematical model that can describe the structure of a terror network — and the model works — then you can predict the future."

Some researchers are convinced of math's merits but face roadblocks in persuading other people that calculations can aid the fight. "These days, the impression I get is that people who ought to support this kind of research don't fully believe that mathematics can be useful," says mathematician Jonathan Farley of Johannes Kepler University Linz in Austria. "And their belief is so extreme that they're not even willing to check it out."

But some of the new methods are beginning to attract attention. Farley, Gutfraind and others belong to the Consortium for Mathematical Methods in Counterterrorism, which promotes math's role in tackling counterterrorism and global security problems. Consortium members share methods and papers, and meet annually to talk about emerging problems in their field, such as how to quantify threats of violence, how to disrupt terror cells and how terrorists arrange themselves into groups.

Connecting the right dots

In the aftermath of the September 11 attacks, a technique called social network analysis was touted as the best way to find terrorist kingpins. Connecting the dots between people called attention to those who were most highly linked — presumably, the most important members of the network. "The idea was to disconnect those social networks, and if you did this, you could inhibit, prevent or moderate the impact of these events — and maybe actually save lives," Carley says. "What we found in the ensuing time is that taking an approach that focuses only on social networks will not work."

Such simple maps can miss crucial features of terrorist networks. "The person with the most links is not necessarily the most important person," Farley says.

Carley's research group and others have begun to find that people who have roles in multiple groups — called interstitial members — are some of the most important. Interstitial members communicate between groups and relay information, a position critical to operations going as planned. A new technique called fuzzy grouping, which allows people to be assigned to multiple groups simultaneously, better describes how these people fit into networks, Carley says.

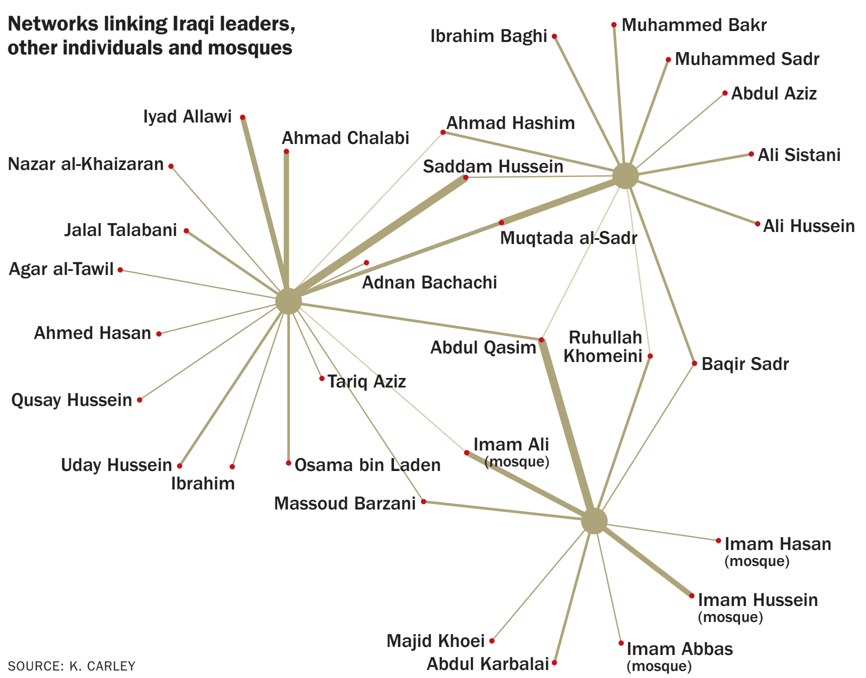
Another important attribute is exclusivity. Some members of a network have specialized training and so are in high demand for certain jobs. People who know how to launder money or fly an airplane, for instance, have a high exclusivity measure. Accounting for exclusivity measures and adopting fuzzy grouping techniques can lead to more nuanced descriptions of covert networks.

Putting terrorists into groups or assigning exclusivity measures is a matter of collecting and assessing the right pieces of data. "The data is coming from a wide variety of sources, things like open-source text, crowd-sourced information off the Web, anything you can basically imagine," says Carley. "The million dollar question is, can we drill down and find the network relevant to the problem?"

Ideally, drilling down through this aggregation of data will reveal trails. "We link together the who, the what, the where, the why, the how, and we use all of these things in a dynamic complex configuration," Carley says. Once specific trails are identified, complex grouping algorithms may be able to decipher unexpected locations for groups to meet, for instance.

Piecing together trails and anticipating behaviors of any single person is a challenge, and guessing the next move of clandestine groups such as Al Qaeda seems nearly impossible. But because terrorists rarely work in isolation, they are susceptible to what computer scientist V.S. Subrahmanian of the University of Maryland in College Park calls the "bureaucracy effect." Because of sluggish coordination, terrorist

Linked up A type of network arrangement called fuzzy group clustering pinpoints people who belong to two distinct groups simultaneously, such as Saddam Hussein. Models suggest that such "interstitial" members are likely to be the key coordinators of a terrorist mission.



SOURCE: K. CARLEY

organizations' behavior is constrained, he says. "Large organizations, even if they are terrorist organizations, may not have the ability to make radical changes in their behavior without taking time to do so, and that makes them a little more predictable," he says.

A particularly rich source for data on behavioral patterns is news articles, Subrahmanian says. He and colleagues have begun testing a new algorithm that identifies and extracts keywords, such as "abduction," "suicide bombing" and "hostage" from news databases. The team aims to have the program ultimately extract over 700 variables accurately and automatically. These word frequencies could then be combined with other data to form "rules" about groups' behaviors. One such rule is that Lebanon-based Hezbollah, regarded by many, including the U.S. government, as a terrorist group, attacks Israel less often during Lebanon's election years, the team found, probably in an effort to garner public support at home.

Subrahmanian is exploring how to not just predict terrorist group behavior but to actually change it. With a grant from the Air Force Office of Scientific Research, he and his colleagues have developed a tool called the policy analytics generation engine. "The goal is to take the same kinds of data and turn it backwards," he says. "Rather than saying, 'Here's my data and here are the behaviors I've learned and here are my forecasts for what this group will do in the third quarter of 2010,' can we go the other way?"

Changing one key factor might make a big impact, Subrahmanian says. For instance, the rule about Hezbollah suggests that the political pressure of an election year keeps attacks low. Finding ways to dial up Hezbollah's political involvement in Lebanon might lead to fewer attacks on Israel. The idea is to identify the critical factors, and then figure out the constellation of forces that influence those factors, Subrahmanian says.

Calculated risks

In a more concrete example of counterterrorism, Subrahmanian and his team have devised a new algorithm that predicts where caches of improvised explosive devices might be hidden. The algorithm was designed to discern a fine line: Stockpiled weapons kept too close to attack locations run a high risk of being blown up or targeted in military sweeps. The weapons also couldn't be too far away, because transporting explosives long distances heightens the risk of being caught. These dueling considerations push weapons caches into doughnut-shaped rings of ideal locales.

Researchers fed the program the locations of seven months of attack data and weapons caches found in Baghdad. Then the program was asked to find the best cache locations for the next 14 months of attack data. The algorithm pinpointed the weapons caches' locations to within about 0.7 kilometers — less than half a mile — of actual caches discovered by U.S. forces. The work, done with graduate student (and U.S. Army Captain) Paulo Shakarian and Maria Luisa Sapino of the University of Turin in Italy, will appear in an upcoming *ACM Transactions on Intelligent Systems and Technology*.

"We view this as not being a predictor of where attacks will occur," Subrahmanian says, "but rather, preventing those attacks from occurring." U.S. Army officials have begun using Subrahmanian's program in Baghdad.

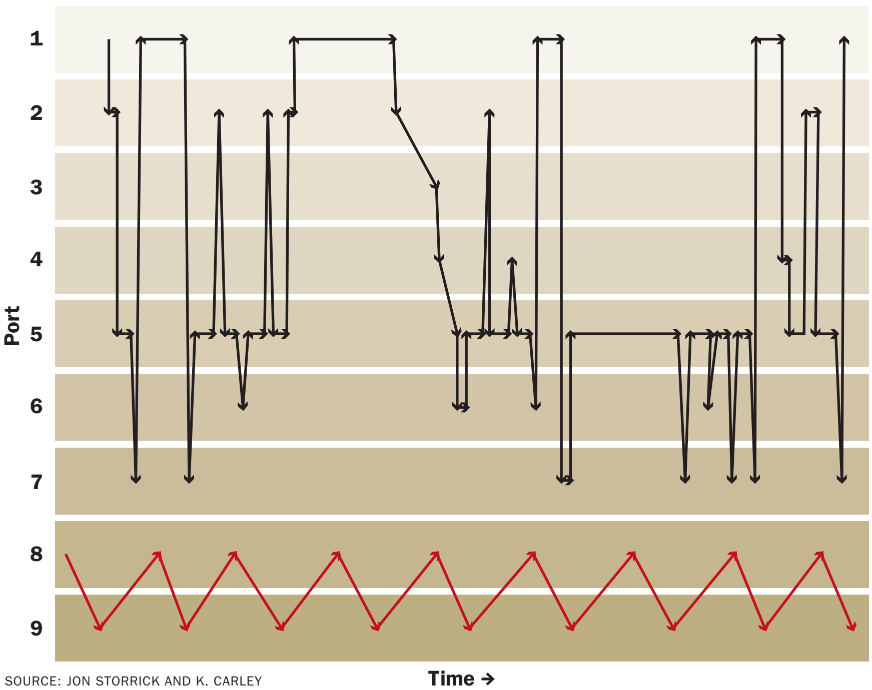
Since these results will soon be published for everyone — including terrorists — to see, the researchers also figured out how the ideal cache location would change if terrorists know that computer scientists can predict their hiding places. In an unpublished follow-up study, Subrahmanian and colleagues found that this situation would probably push the caches outside of the doughnut-shaped comfort zone, both farther from and closer to the attack sites.

Building the perfect cell

Applying principles from game theory — the mathematical study of strategic interactions — is also useful for studying the structure of terrorist cells. Using a version called cooperative game theory, Roy Lindelauf of Tilburg University in

Terrorist trails Two suspicious ships sail between ports (numbered), forming trails that can be analyzed for insight into terrorist activities. One ship's trail (red line) has a very predictable pattern. The other ship's trail (black line) isn't as tidy, but still offers some useful clues. Every time the ship leaves Port 1, it goes somewhere for a quick trip and eventually ends up at Port 5.

Ship travel between ports



SOURCE: JON STORRICK AND K. CARLEY

the Netherlands and his colleagues have come up with a description of a resilient cell.

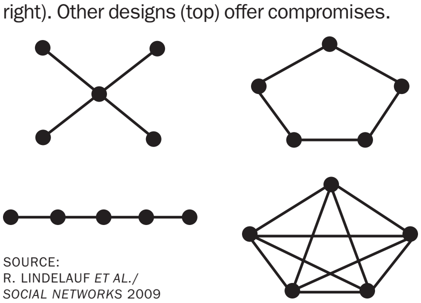
"We imagined we were the terrorists and we wanted to set up our organization," Lindelauf says. "How do these guys operate? What kinds of organizational structures do they use? How do they prevent being destroyed by governmental organizations?"

It turns out that like choosing a good spot for a weapons cache, setting up an effective terrorist cell requires compromises. The desire to remain secret prompts organizations to let as few people as possible in on the important details. If everyone knows everything, each person is a walking security risk. If just one person were captured and spilled the beans, he or she would be able to take down the entire organization single-handedly. "In a criminal organization, the people you know represent a threat," Lindelauf says.

On the other hand, the fewer people involved, the harder it is to get anything accomplished. "These kinds of organizations are bargaining with themselves," Lindelauf says. "We combine this bargaining model with network analysis, and then use that to create new mathematical techniques to predict the structure of terror organizations."

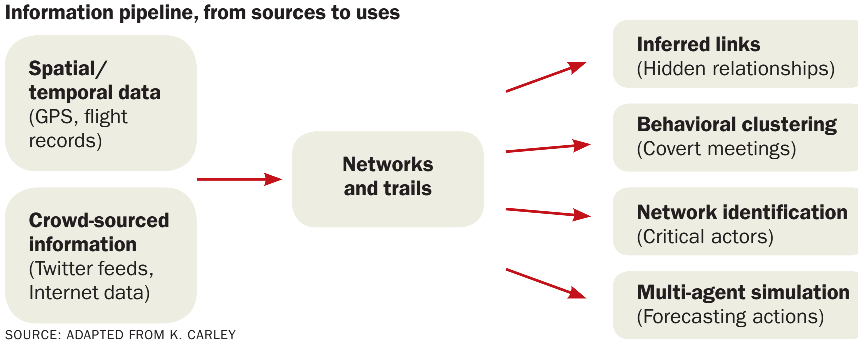
Lindelauf and colleagues analyzed graphs in which each person was a dot, or node, with links from node to node representing communication between people. This communication could be

Terror cell trade-off Dots representing terrorists and their relationships (lines) show how terrorist cells can be structured to balance the need for communication with the risk of betrayal. In the bottom left network, secrecy comes at the expense of information flow. When members can easily coordinate, secrecy is lessened (bottom right). Other designs (top) offer compromises.



SOURCE: R. LINDELAUF *ET AL.*/ *SOCIAL NETWORKS* 2009

Information pipeline, from sources to uses



SOURCE: ADAPTED FROM K. CARLEY

Putting the pieces together Mathematicians are using bits of data (left) to assemble trails and networks, which ultimately can be used to forecast the behavior of terrorists (right).

anything from smuggling weapons or fake documents to selecting targets to something as simple as a telephone call. The team found that the ideal organizational structure changes as the threat of being discovered increases. Diagrams of the structures can range from stars and reinforced rings to reinforced wheels and even reinforced windmill shapes.

"We can predict structures that resemble organization structures that we observe in reality," Lindelauf says. In the study, which appeared in *Social Networks* in May 2009, the authors acknowledge that their analysis omits some complexities, but say that even a basic understanding of network-shaping forces is important.

In a paper currently under review, the Lindelauf team has extended the network analysis to figure out what happens to the optimum network shapes when cell members are attacked. "The surprising result," Lindelauf says, "is that organizations that adopt such a structure are pretty good at withstanding attacks." These organizations will be destroyed only if massive attacks bring down most of the key players, he says. "And that's clearly not what we're doing right now."

Farley is taking a different approach to the same question of defining a perfect terrorist cell. Like Lindelauf, Farley begins with a pared-down, tidy version of reality — a small number of variables that he can work with. "I'm coming up with simple models with few assumptions and I'm openly admitting that they could be wrong," he says. "I'm not saying forget about data. I'm just saying that our assumptions are all laid out. They're simple and they're clear."

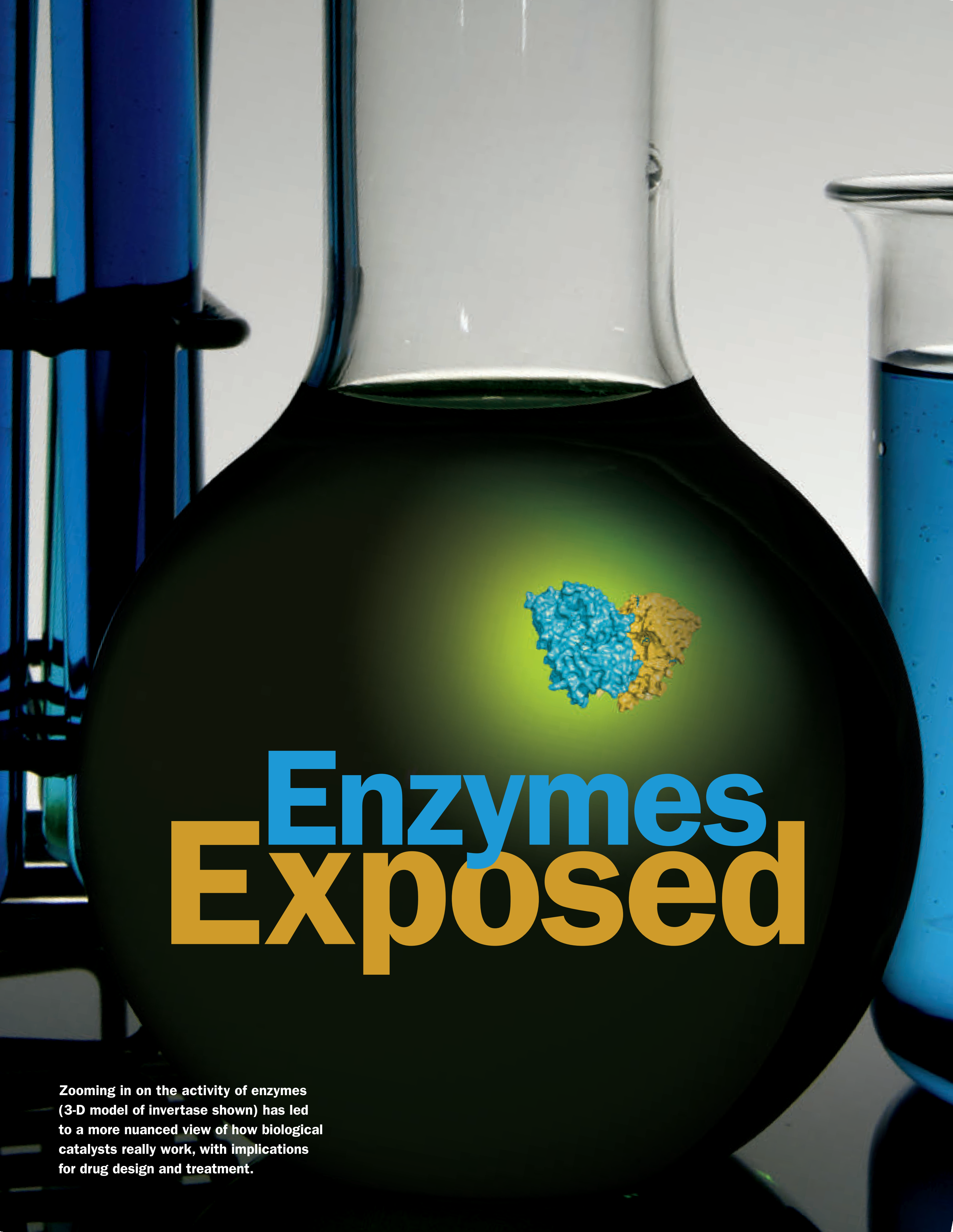
Using a branch of mathematics called lattice theory, Farley relies on the basic hierarchical nature of terrorist networks to figure out the most stable arrangement of leaders and followers. By assuming that the leaders and followers are spread out in a particular arrangement, Farley has come up with several structures for terror cells that can't be easily destroyed. In certain cases, destroying links in the network would result in the network splitting into two smaller — and still functional — networks, rather than a complete collapse, Farley's studies show.

It remains to be seen whether the models and algorithms that work so well in the lab will also work in the messy, complex real world. Subrahmanian is quick to point out that the best way to get at these hard problems will be an amalgam of many different approaches.

"There's got to be a collaboration between multiple disciplines — computer science, social scientists, mathematicians — in jointly trying to address this," he says. "There's still a long way to go here in translating the behaviors that are being learned to policy," he cautions. "But we believe this stuff is going to be useful." ■

Explore more

- The Consortium for Mathematical Methods in Counterterrorism website: www.rit.edu/cos/math/cmmc
- University of Maryland LCCD group: www.umiacs.umd.edu/research/LCCD



Enzymes Exposed

Zooming in on the activity of enzymes (3-D model of invertase shown) has led to a more nuanced view of how biological catalysts really work, with implications for drug design and treatment.

Clearer views of the cell's movers and shakers threaten a century-old mainstay of biology

By Lisa Grossman

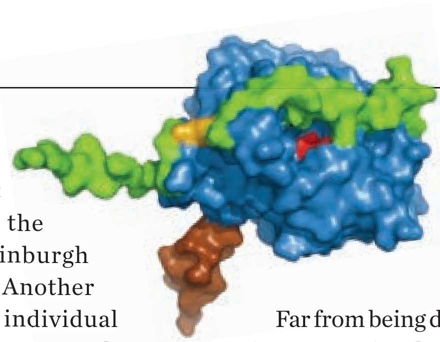
In some ways, cells are a lot like cities. Maps of a cell's innards depict thoroughfares linking factories that build large molecules to post offices where those molecules are packaged up and shipped out, for example. The cell's denizens — proteins and other molecules — shuttle around busy cellular byways like people on the street, meeting up, interacting and keeping the whole enterprise going.

But anyone who has ever been delayed on the way to an important meeting knows something about cities that biochemists are just beginning to learn about cells: Maps don't capture a lot of details — traffic, closed roads, a downed tree — that can drastically slow a journey.

For almost a century, biologists trying to describe cells' inner workings have assumed that the differences between map and street didn't matter. That has been especially true for studies of the cell's go-to, workhorse proteins called enzymes, which orchestrate the majority of the chemical reactions necessary for life. A revered textbook formula that describes how these crucial molecular catalysts speed up reactions, the Michaelis-Menten equation, assumes that enzymes don't usually get stuck in traffic. Enzymes are supposed to meet other molecules at regular intervals and do their transactions at a constant speed, more like workers on an assembly line than urban pedestrians.

In most laboratory experiments, researchers make sure that molecules can move freely and interact often, so the classic formula seems to work well. But lab experiments don't reflect the inner lives of cells. And the differences could dethrone the venerable equation.

Because of the crowds, in a cell it's more difficult for enzymes to find their partner molecules than it is in a test tube, biophysicist Ramon Grima of the University of Edinburgh recently showed. Another study noted that individual cells can have different numbers of enzymes — even when the cells are otherwise identical. Combined, the new results could mean models of enzyme kinetics based on the Michaelis-Menten equation are wrong.



Shape-shifting enzymes like CalB are revealing the role of form in reaction speeds.

"It's a system that people thought they had understood for 100 years," says enzymologist Kerstin Blank of Radboud University in Nijmegen, the Netherlands. "Now we get some new information that, a little bit, turns everything upside down."

When scientists model the chemistry in a cell, Michaelis-Menten is the default equation for enzymes. "It has a broad impact," Grima says. "Given any biochemical pathway, you'll always find that at the backbone of the pathway you will have a few enzymes. When you're modeling that enzyme, you will naturally assume a Michaelis-Menten equation for it."

By zooming in to the street view, scientists hope that they can draw a more accurate map of the cellular city. Experimental methods for watching enzymes in cells aren't yet good enough to see how important variations in these chemical reaction speeds actually are. But if it turns out that the Michaelis-Menten equation doesn't accurately predict how fast enzymes work in living cells, it could change everything from introductory biochemistry classes to strategies for cancer treatments.

Far from being discouraged about having to rewrite their textbooks, though, scientists are now dreaming about how to use this newfound knowledge to engineer new drugs or biofuels. "Ultimately," says Nathan Price of the University of Illinois at Urbana-Champaign, "you want to understand those processes so you can control them."

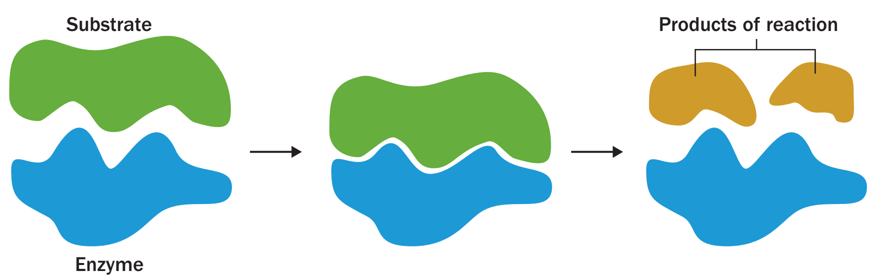
Shape-shifting enzymes

Enzymes make the cellular city run on time. Reactions that would take more than 300 years unassisted can take about a second when an enzyme steps in. By embracing a specific partner molecule, called the substrate, and morphing it into something new, enzymes enable everything from transcribing DNA to digesting food to generating light in fireflies. So understanding how enzymes work is crucial for understanding how cells work — and for manipulating them.

When Leonor Michaelis and Maud Menten published their now-famous paper in *Biochemische Zeitschrift* in 1913, watching an individual enzyme at work was impossible. To figure out how quickly enzymes help transform neighboring molecules from one form to another, the duo had to make do with analyzing test tubes full of billions of molecules.

Michaelis and Menten focused on the enzyme invertase, which helps break down sucrose, ordinary table sugar. If

Lowering the energy Enzymes make reactions in the body go, and go fast, by permitting them to proceed with less energy input than would otherwise be needed. The substrate molecule is held by weak forces, such as hydrogen bonds, in a suitably shaped active pocket in the enzyme. This facilitates the conversion of substrate into products, which are then released without using up the enzyme.



FACING PAGE: PHOTO: PEDRO SALAVERRÍA/SHUTTERSTOCK; MOLECULE: M. ALVARO-BENITO *ET AL./J. BIOL. CHEM.* 2010;
PHOTO ILLUSTRATION: T. DUBÉ; THIS PAGE, FROM TOP: K. BLANK, PYMOL; T. DUBÉ

they could have somehow seen exactly what was happening in their test tubes, Michaelis and Menten would have seen the enzyme embrace a sugar molecule (fitting part of it neatly into a cleft) and then breaking it in two. The resulting simple sugars, fructose and glucose, go on to become energy sources for the cell, and the enzyme sits and waits for a new sucrose molecule to come around.

Michaelis and Menten found that the time it takes to transform a spoonful of sucrose to glucose and fructose depends on how much sucrose there was to begin with. The more sucrose, they showed, the faster the reaction — up to a point. After that, the reaction went at a steady pace.

Biologists explained this phenomenon by picturing enzymes and their partners fitting together like a lock and key. Each type of enzyme generally works with only one type of partner, and the two shape themselves to fit together perfectly. But each enzyme can couple with only one partner at a time. When all the enzymes are busy, new partners have to wait for an enzyme to free up.

Researchers were more or less satisfied with that picture for the next 85 years, and plugged in the Michaelis-Menten formula to determine reaction rates in cells. As far as most lab experiments went, it worked.

But in 1998, Sunney Xie, now of Harvard University, and colleagues used a fluorescent marker to watch a single molecule of the enzyme cholesterol oxidase as it met and morphed its partners one at a time. The researchers noticed something strange: The enzyme didn't always work at the same speed.

"If you had simple chemical reactions, you'd expect these times [between one reaction and the next] to be constant," Blank says of Xie's work. "These times are not constant."

The speeds didn't vary randomly, either. The enzyme seemed to work quickly for several partner molecules in a row, slow down for the next several molecules, then speed up again. If one reaction took a particularly short time, the next one was more likely to go quickly as well, as if the enzyme could remember how long it spent on the last reaction it performed.

In 1998 in *Science*, Xie proposed that the enzyme was flip-flopping between many different shapes, each of which did the same job at a different speed.

"For many years we just thought that the substrate fits in the enzyme with this lock-and-key mechanism. That's what we all learned at school," Blank says. "It's basically not true."

> **"We just thought that the substrate fits in the enzyme with this lock-and-key mechanism.... It's basically not true."**
>
> KERSTIN BLANK

The leading hypothesis posits that one shape fits best with the partner molecule and so works more efficiently, but takes more energy to maintain, Blank says. Other shapes may not work as well, but are more energetically relaxed. Scientists think that the enzyme chugs along in a high-energy shape for as long as it can, but inevitably slouches into a couch-potato shape. It stays slouched until a new burst of energy, perhaps from temperature changes in its environment or from random fluctuations, kicks it back into high-efficiency mode.

"The enzyme molecule, like us, works hard for a while and then slows down," Xie says.

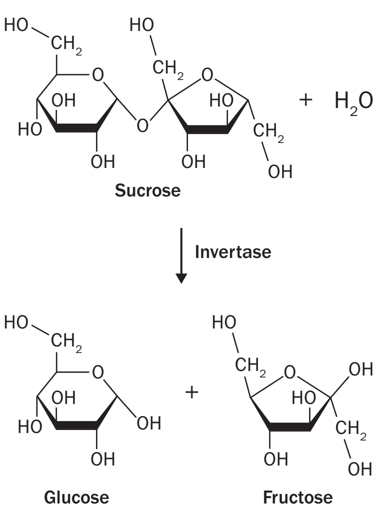
Microscopes still aren't sensitive enough to take snapshots of these shape-shifting enzymes in action, but a decade of research backs up Xie's idea. In one particularly illustrative case, Blank and her colleagues recently found that when they tug on part of the enzyme CalB using an atomic force microscope, the enzyme works faster. Pulling the enzyme may open it up, like pulling on a tab in a pop-up book, changing the enzyme's shape and ability to catalyze reactions.

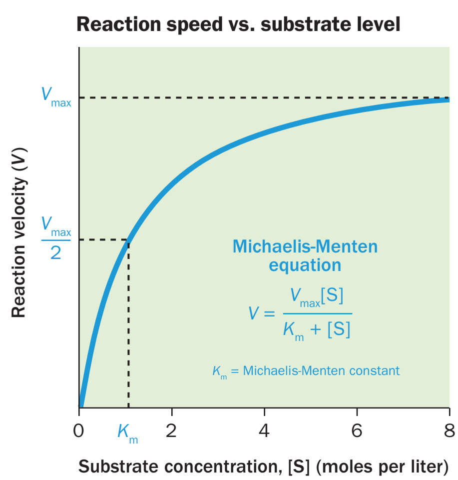
The ease with which the body absorbs medication and digests food may depend on how much time an enzyme spends in each shape. Blank suggests that shape-shifting enzymes could even drive evolution, if a genetic mutation were to enable a helpful enzyme to stay in a more efficient shape for a longer time.

These shifting reaction rates should shift the outcome of the Michaelis-Menten equation, too. Initially, the scientific community reacted with confusion: If Michaelis-Menten was wrong, why had all the experiments so far worked?

"When Sunney began these researches in the late '90s, people said, 'Gee, if you have these fluctuating rates, how come we almost always see Michaelis-Menten

Sweet biochemistry Leonor Michaelis and Maud Menten's classic work on the speed of enzymatic reactions was based on studies of the conversion of table sugar, or sucrose, into two simpler sugars, glucose and fructose, by the invertase enzyme (left). Michaelis and Menten found that the reaction rate rises with the concentration of sucrose before leveling off at a maximum, shown in graph (right). These studies led to their long-used equation for determining reaction rates.





SOURCE: ENCYCLOPÆDIA BRITANNICA, INC.

kinetics? Something must be wrong with your experiment,'" recalls Attila Szabo of the National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Md.

In 2005, Xie resolved the paradox. He and his colleagues found a partner molecule that let off a burst of fluorescence after reacting with an enzyme. The researchers watched the molecular fireworks show for roughly 20,000 reaction cycles, about 40 times more reactions than were captured in the 1998 studies.

The enzyme was still wiggling and shifting its efficiency every few reactions, the researchers found. But given enough reaction cycles, the differences averaged out. "Enzymes seem to have a changing personality," Xie says. "But in spite of that, the Michaelis-Menten equation still holds."

The biochemistry community seemed to breathe a sigh of relief. The 2006 issue of *Nature Chemical Biology* where Xie's paper appeared also included a commentary titled, "Michaelis-Menten is dead; long live Michaelis-Menten!"

Back-alley trysts

Yet, as Xie and others predicted, still another challenge to the classic equation has been brewing. Recent studies of individual cells suggest that while some of the basic assumptions behind Michaelis-Menten may work in the lab, they don't always work for real cells.

"In test tubes, you have a very artificial environment," says Grima, who has explored the basic question of how reactions actually happen in cells.

Cells have a few obvious differences from test tubes. For one thing, cells are crowded. Just the largest molecules inside take up between 5 and 40 percent of the physical volume of a cell. What free space remains is found in tiny compartments that range from about 50 nanometers to just a few micrometers on a side. Enzymes themselves may be between a few and a hundred nanometers long. Some enzyme-assisted reactions can take place only inside the nucleus or other cellular organelles. Inside real cells, liaisons between enzymes and their partners may be relegated to the back alleys, where only a few individual molecules can fit at a time.

This means that it's not always easy for enzymes and their partners to find each other. Biologists have shown that cells have what are called active transport networks, filaments that molecules can slide along to travel between meeting places. If enzymes can't meet locally, they have to take public transport.

If reactions inside cells are like back-alley trysts, reactions inside test tubes are like square dances in a big hall. With such a large space to move around and researchers constantly mixing the solution, every enzyme is almost guaranteed to dance with every potential partner.

These differences ought to influence how quickly enzyme-aided reactions go, Grima reasoned. There should be some big departures from the Michaelis-Menten equation inside real cells.

In 2009, Grima used mathematical models and computer simulations to show that two basic assumptions behind the Michaelis-Menten equation throw its predictions off in real cells. First, he considered the number of molecules interacting. In a test tube, billions of molecules could come together. But in a cell, only 10 to 100 may meet at any given time.

Accounting for this and other "noise" in a cell, Grima's model suggests that enzyme reactions in real cells proceed as much as 20 percent slower than Michaelis-Menten predicts. Next, he considered active transport. If partners must ride intracellular subway lines to meet up with their enzymes, Grima found, Michaelis-Menten may overshoot the real reaction rate in a cell by as much as several hundred percent.

A faster reaction rate translates into more reaction products from the same amount of enzyme. For drug designers, miscalculating the amount of product throws off the prediction of how much enzyme should be added to begin with. To explore such implications, Grima ran his simulations for a made-up drug that works by binding to an enzyme before the enzyme's proper partner can

Flip-flopping forms As an enzyme (blue) shifts its shape, its fit with a substrate molecule (green) shifts too, changing the enzyme's ability to drive a reaction. Frequent changes in form translate into more variability in reaction rate than the Michaelis-Menten equation takes into account. But the average reaction rate, it turns out, is in line with the equation.

T. DUBÉ

reach it, a phenomenon called enzyme inhibition. In the case Grima studied, the amount of the drug needed to effectively combat the theoretical disease was seven times higher than the amount predicted by Michaelis-Menten.

"When I computed those estimates for drug dosages, that's when I had the 'aha!' moment," Grima says. "That's when I thought, oh wow, these things may be actually important."

Population effects

Price and Pan-Jun Kim of the University of Illinois at Urbana-Champaign think their results, like Grima's, could have important implications for drug development. Even if Michaelis-Menten does work for one particular cell, variations between cells can pose another threat to the equation — and to the efficacy of drugs designed using it.

"Any enzyme in a chemical soup has a potential chance to catalyze substrates anywhere else in the chemical soup," Kim says. This was the case in Xie's single-enzyme studies: Thousands of partner molecules floated past a solitary enzyme, and each one had an equal chance of reacting with it. But in real cells, each enzyme usually meets only with the partners that happen to live with it.

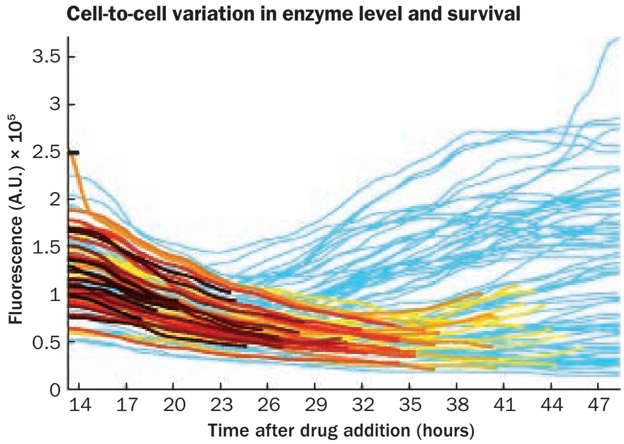
And different cells may make different numbers of any particular enzyme, even when the cells are genetically identical. A 2008 study in *Science* showed that this difference can literally mean life or death for a cell: Tumor cells that survived treatment with chemotherapy were shown to make more molecules of a particular enzyme than cells that succumbed to the drug, hinting that the enzyme might play a role in drug resistance.

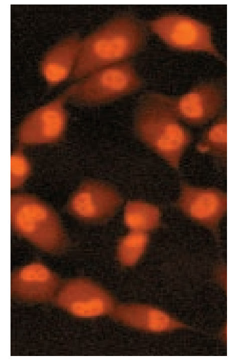
This variation could also mean that even if one cell follows the Michaelis-Menten equation, large groups of cells taken all together might not, Kim says. And drugs designed using equations that ignore the differences between cells could therefore be less effective.

"Even in an ideal situation where the Michaelis-Menten equation might be working well inside a single cell, it is still unavoidable to witness its breakdown at a population of cells," Kim says.

Kim and Price showed mathematically that using the Michaelis-Menten equation to calculate how fast a large group of cells will perform a reaction gives a different answer than averaging the reaction speeds of each individual cell. By comparing the old equation with new data on single cells, the researchers found that the standard predictions for how fast enzymes work can be off by about 25 percent.

"When we first started this we thought, oh, this looks interesting, but maybe it's negligible. Turns out they have pretty huge effects," Price says. "For any scenario where we know protein copy number varies between cells, which looks to be common, you'd be off."





Life or death Differences in enzyme levels among individual cells were tracked using a red fluorescent marker (right). Human tumor cells (at left, each line represents one cell) that withstood a dose of the anticancer drug camptothecin made more of the DDX5 enzyme (as measured by fluorescence level), while enzyme levels dropped in the cells eventually killed by the treatment. Blue lines mark cells that survived treatment. Other colors show cells that died, with the darker colors corresponding to earlier cell death.

COHEN *ET AL.*/*SCIENCE* 2008

Enzyme engineering

Understanding how the differences within and among cells change reaction rates can also eventually let scientists engineer better enzymes. Most of Price's research focuses on building computational models of metabolic networks in cells, which means that he is concerned with what the cell eats and excretes. Ultimately, he says, better models will mean better control.

"You could have an organism that eats something toxic and spits out a biofuel, or something like this," Price says. "You could convert compounds that are either cheap and abundant, or deleterious, and make them into something valuable and useful and good for the environment."

Not everyone is convinced that the Michaelis-Menten equation is really doomed, however. When Grima presents his results at conferences, "a lot of people get enthusiastic, and a lot get defensive."

A major problem is that the new models don't have experimental data backing them up.

"I wouldn't consider a few theoretical papers as a substantial claim unless it's backed up by experiments," Xie comments. "That's my experimentalist prejudice."

Grima acknowledges that this is a weakness of his argument. "At this point, what is limiting its more wide acceptance is combined theoretical and experimental studies," he says. "Nobody has done a study in which they do a model, make predictions and then test them, all at one go. This would be the killer."

Such an experiment may be around the corner. At the moment, there are limited techniques for getting quantitative data on individual molecules inside a cell without killing the cell in the process. But several groups — including Xie's — are developing more. A recent review paper in *Trends in Biotechnology* heralds single-cell analyses as a new frontier that will transform differences between cells "from a source of noise to a source of new discoveries."

Even if future observations of the location and concentration of enzymes vindicate Michaelis and Menten, though, many scientists think that the emerging street-level details of the cellular city will continue to challenge traditional ideas.

"Any reaction occurring inside the cell will be impacted by these conditions, but we don't know exactly how," Grima says. "We're probably sitting on top of the iceberg." ■

Lisa Grossman is a writer in Seattle.

Explore more

- Daojing Wang and Steven Bodovitz. "Single cell analysis: the new frontier in 'omics.'" *Trends in Biotechnology*, June 2010.

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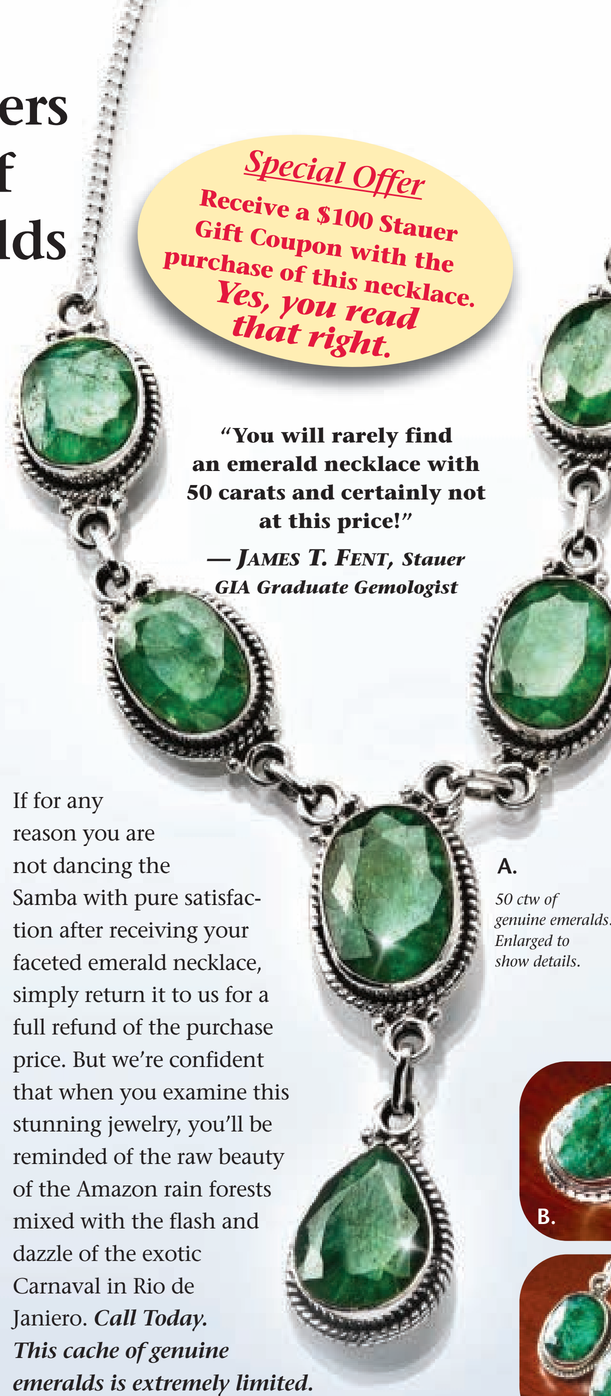

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— *JAMES T. FENT, Stauer GIA Graduate Gemologist*

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All patterns great and small

Researchers uncover the origins of creatures' stripes and spots

By Tina Hesman Saey

How the leopard got its spots and the zebra its stripes might not be just-so stories much longer. Biologists are beginning to pinpoint the molecular mechanisms animals use to deck themselves out with colorful swirls, stripes, spots and dots.

Insects, fish and mammals may have different tricks. Butterflies and fruit flies, for instance, paint their wing decorations on top of underlying patterns, such as wing veins. Fish may similarly arrange their colored scales according to a "prepattern" but probably decorate their fins according to mathematical principles laid out on a blank slate. And mammals' beauty marks may arise like those of fish — or via an entirely different mechanism.

British mathematician Alan Turing was one of the first scientists to explain how color patterns might form. In a 1952 paper, he envisioned patterns as self-assembling products of molecular reactions created as two chemicals spread across a uniform surface. Turing's mathematical models could replicate any pattern found in nature, and scientists soon began hunting for the chemicals responsible for painting butterfly wings and tiger stripes.

But "Turing has led biologists astray," charges Fred Nijhout, a developmental physiologist at Duke University in Durham, N.C. "Mathematically it's completely correct, and there are some physical systems in which it can occur," he says. Turing formulated his theory before the modern era of molecular genetics, though, and biological systems don't always work the way his models predict.

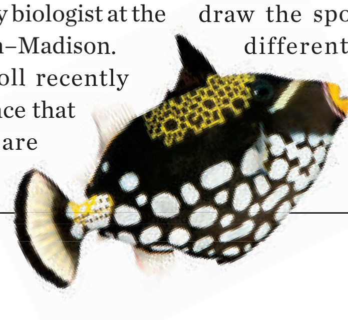
For one thing, skin, scales and fur aren't the blank canvases upon which Turing envisioned color patterns painting themselves. "Sometimes biology is a bit uncooperative because it uses more components than models tell us are necessary," says Sean B. Carroll, a developmental and evolutionary biologist at the University of Wisconsin–Madison.

A team led by Carroll recently found molecular evidence that preexisting patterns are important in directing color patterns to form. The researchers studied a species of fruit fly called *Drosophila guttifera*, which sports 16 black spots and four gray shadows on each wing. The black spots develop where wing veins cross, while the shadows form in the spaces between veins.

The mechanism that creates these spots and shadows piggybacks on a system that lays out the wing veins and other body parts, Carroll's team reported in the April 22 *Nature*.

Every time scientists found a fly with a new black spot on its wing, the spot always appeared in the place where a new sensory organ had formed, or where wing veins made a new junction. Flies that lacked certain wing veins or sensory organs were also missing spots.

Molecular detective work revealed that a protein called Wingless helps draw the spots. Wingless has many different jobs during fruit fly development, including properly orienting the fly's body segments, directing where legs and



FROM TOP: TRIGGERMOUSE/ISTOCKPHOTO; GLOBALP/ISTOCKPHOTO; GLOBALP/ISTOCKPHOTO wings will grow, and helping set up part of the digestive system. At some point in evolution, Carroll says, an ancestor of *D. guttifera* and some related fly species co-opted the Wingless system to create color patterns.

The hijacking was accomplished by inserting a new switch into the DNA control panel that governs activity of a pigment-producing gene. Wherever Wingless helps build sensory organs on the wing, the switch flips on pigment production, and a spot or shadow appears.

Carroll doesn't claim to have solved the riddle of all animal patterns with this new work. "I'm happy we planted a flag on polka-dotted wings," he says, "but there's a whole world of color patterning left to understand."

Still, the mechanism might also occur in other insects. Nijhout says that butterflies, for instance, might use Wingless to create stripes on their wings, since the protein is made in the same places where bands of color later appear. A similar mechanism may paint the eyelike spots on some butterfly wings, using proteins called Distal-less and Notch instead of Wingless.

Just because Turing's models fail to predict how insects decorate their wings doesn't mean he was completely wrong about all aspects of animal patterning, scientists say. In vertebrates, including fish and mammals, pigment cells may self-organize into patterns the way Turing's interacting chemicals do.

Animals such as fish, tigers and zebras don't seem to position their spots and stripes over any particular body structures. And the pattern can be slightly different from one side of the animal to the other. Such clues suggest that pigment cells, which are born in one part of the body and migrate to their eventual location on the skin, assemble themselves into patterns according to a Turing-like mechanism.

"Mathematically, the cellular behaviors [in these animals] meet the behavior of the Turing predictions," says David Parichy, a developmental and evolutionary biologist at the University of Washington in Seattle. Still, he says, "it's quite clear that you need some type of a prepattern there to orient the cells."

Parichy's work in zebrafish supports the idea that multiple mechanisms are in play. He studies the way zebrafish form multicolored stripes along their bodies and on their fins. Along with colleague Jessica Turner, Parichy found that delaying the development of yellow pigment cells as fish transitioned from larvae to adults could cause their tail stripes to switch from horizontal to vertical. Some unknown factor, which the researchers are investigating now, must orient pigment cells in the right direction. And once pigment cells begin migrating, something has to tell them where to settle down.

"There's a whole world of color patterning left to understand."

SEAN B. CARROLL

One protein Parichy's group knows to be involved in making fish patterns is called basonuclin-2, which helps keep pigment cells healthy and allows the stripes to form. Fish that lack basonuclin-2 in their skin also lack stripes, the researchers reported last year in *PLoS Genetics*. "If the pigment cells are paints, the basonuclin-2 is essentially priming the canvas to receive these paints," Parichy says.

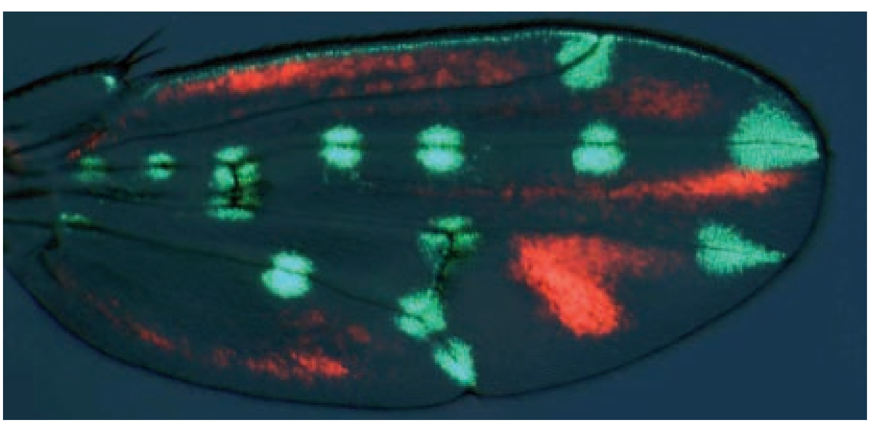
Until his team discovered basonuclin-2's role in the skin, all of the other proteins known to affect stripe development were found in the pigment cells themselves. So fish may deploy a combination of prepatterning along with a Turing-like mechanism to create their stripes, Parichy says.

With mammals, it remains to be seen if the Turing mechanism alone is at work. Insects and fish are easier to work with in the lab than large cats like tigers or leopards, so scientists know much more about smaller creatures. For now, no genetic evidence indicates mammals might make patterns differently, or that leopard spots are fundamentally different from butterfly dots.

One day, research into color patterns could help illuminate wider questions about the animal world, says Parichy. For instance, pigment patterns are tied to animal behavior, such as mating signals, and can reflect the state of an animal's health. Studying the relatively simple regulation of color patterns could give biologists clues to how organisms change and adapt other body parts.

And the research raises questions such as how the Wingless prepattern is laid out, what draws the blueprints for that pattern's prepattern, and so on. It could be an infinite loop that will take many years of colorful research to understand. ■

Glowing gene expression The wing of a young genetically modified fruit fly (*Drosophila guttifera*) displays underlying genetic activity where spots (green) and shadows (red) will form.



T. WERNER *ET AL.*/*NATURE* 2010

Explore more

- H.F. Nijhout. "Molecular and physiological basis of colour pattern formation." *Advances in Insect Physiology.* 2010.

Pandora's Seed: The Unforeseen Cost of Civilization

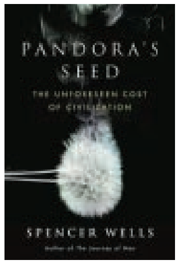
Spencer Wells

At first glance, it's hard to see the downside of being civilized. Compared with Stone Age living, an office job doesn't look too shabby. Throw in the Internet, leisure time and dessert, and all this culture looks like a win-win.

But there's a catch, says Wells, an anthropological geneticist. Civilization grew out of a gradual switch 10,000 years ago from hunting and gathering to farming, and, he says, "more food produced more people." The result is a planet with 6.8 billion human grazers.

The rise of farming meant that adults' leading health threat, trauma, gave way to infection over the past several millennia as animal domestication and city living spread disease. Now humans enter a new phase of threats, also tied to agriculture. Wheat, rice and corn supply more than half the calories consumed by people worldwide, and high-carbohydrate, processed foods have spawned epidemics of obesity, type 2 diabetes and heart disease. Exacerbated by a sedentary lifestyle, the modern diet represents "a profound shift in the causes of disease," Wells writes. "More and more, we are causing our own deaths."

Wells isn't advocating a return to hunting and gathering. He points out



that farming settlements fostered common language and innovation, and these positive trends continue. Farming took thousands of years to spread, he notes, but the industrial revolution needed only a few generations. The information age is even faster.

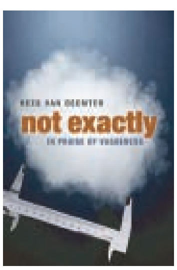
But Wells wonders whether technological advances can solve today's health and environmental problems — if gene research will counteract disease and if nuclear or renewable energy will make up for oil shortages. And then there's climate change and species loss. "It is time," Wells writes, "to take stock and realize that with great desires come great consequences." — *Nathan Seppa*

Random House, 2010, 230 p., $26.

Not Exactly: In Praise of Vagueness

Kees van Deemter

Politicians and salesmen aren't the only people who use — or even rely on — vague language. Never mind that much of the world can be measured in



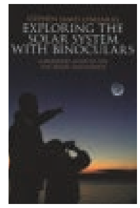
neatly defined units such as centimeters, milligrams and degrees, writes van Deemter, a computer scientist. Most people have little sense of those units, so vagueness permeates speech and ideas, from describing a person as "tall" to the weather as "chilly."

Van Deemter argues that vagueness is not only the norm, but can even be useful. The imprecision of "chilly," for example, quickly conveys a comparison and judgment that isn't necessarily captured by a precise temperature reading.

Much of the book surveys vagueness in unexpected places, like mathematics and the study of logic. Chapters explore the sorites paradox (which concerns the question of how many stones make a heap) and physicists' quest to define the meter in increasingly precise terms. But forget eliminating imprecision, van Deemter contends. Like original sin, he writes, vagueness is "a stain that can be diminished but never removed."

Besides being inevitable, vagueness can be essential. Engineers developing artificial intelligence, for example, know the importance of building in fuzzy logic. "If we were to build a robot that can communicate, how precise would we like it to be when it speaks to us?" asks van Deemter. Such questions are intriguing, though at times the book's philosophical wanderings become overly complex. The author makes a strong central argument, though: In a world of shades of gray, vagueness can be a virtue. — *Sid Perkins*

Oxford Univ. Press, 2010, 341 p., $29.95.



Exploring the Solar System with Binoculars

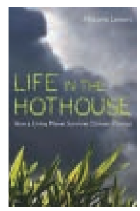
Stephen James O'Meara

Backyard observers can make the most of basic tools. *Cambridge Univ. Press, 2010, 156 p., $29.99.*

Super Structures: The Science of Bridges, Buildings, Dams, and Other Feats of Engineering

Mark Denny

Structures stand, soar and collapse based on fundamental physics principles. *Johns Hopkins Univ. Press, 2010, 266 p., $30.*



Life in the Hothouse: How a Living Planet Survives Climate Change

Melanie Lenart

A scientist explains how the planet adjusts to warming. *Univ. of Arizona Press, 2010, 236 p., $22.95.*

Remembering Smell: A Memoir of Losing–and Discovering–the Primal Sense

Bonnie Blodgett

The author's experience with anosmia leads her to explore the biology and cultural context of smell. *Houghton Mifflin Harcourt, 2010, 256 p., $24.*

Explaining Research: How to Reach Key Audiences to Advance Your Work

Dennis Meredith

Scientists can use new and traditional media to communicate findings to the public. *Oxford Univ. Press, 2010, 357 p., $35.*

Engineering irritation

The article "Engineering a cooler Earth" (*SN: 6/5/10, p. 16*) was incredibly irritating. The solution to global warming is not technology of the type presented, but population and pollution control. You need to start talking about that. The longer we see the problem in technical terms, the less likely we are to even talk about the real solutions. (How many articles have you had recently discussing limiting population — that's science, isn't it?) Suppose we dump a bunch of chemicals in the biosphere and it cuts global temperatures a bit or holds them steady. Is that the kind of outcome we want so we can dump ever more CO_2 into the atmosphere and add a billion or two more people?

Bill Amborn, West Linn, Ore.

Your article on geoengineering raised, but did not fully explore, the crucially important question of the impact of the cloud-brightening scheme on rainfall over land. Three studies have been made, by three separate groups, using three different and well-regarded models. One by Jones *et al* (2009) seeded a small fraction of suitable maritime clouds and reported significant reductions of rainfall over northern South America. Another, Rasch *et al* (2009), seeded an intermediate fraction, found no rainfall reduction in this area, and no significant rainfall reduction over land. A third, to be published by Bala *et al,* seeded all suitable clouds and found no rainfall reduction anywhere over land. They provided a plausible physical/meteorological explanation for this result. No categoric statement can currently be made as to whether or not the cloud-brightening scheme would reduce rainfall significantly anywhere over land.

John Latham, National Center for Atmospheric Research, Boulder, Colo.
Stephen Salter, University of Edinburgh, Scotland

ET, phone where?

It seems from your article "Can you hear me now?" (*SN: 4/24/10, p. 22*) that most searches for ET communications have assumed that we were looking for a deliberate signal — that we assumed ET was trying to phone us. But seriously, why should he? It would be horribly foolish to assume that ET politics resembled ours, but the allocation of resources according to priorities is a necessary preoccupation of life from the single cell on up. Yelling into the void by any of the methods described would use power that would likely be needed elsewhere. (Are we doing it on purpose?) Only the searches for leakage from ET power generation are likely to turn up anything, and they will be difficult to sort out from natural causes.

Nancy Parker, Caldwell, Idaho

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Robert Russell

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Nutrition society president says eat less, move more

Physician Robert Russell became president of the American Society for Nutrition earlier this year. A policy consultant to the National Institutes of Heath, Russell spent a quarter century with the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University in Medford, Mass., most recently as its director. He has authored hundreds of papers on nutrition science, many in the fields of vitamins, food-derived antioxidants and gastrointestinal disease. Science News *senior editor Janet Raloff spoke with him about today's most prominent nutrition issues.*

What's the biggest issue facing the nutrition community today?
It's got to be obesity. But it's a medical issue as much as a nutritional one because obesity can play a role in so many diseases, from cancer and diabetes to arthritis, stroke, cardiovascular disease — almost every chronic disease of aging.

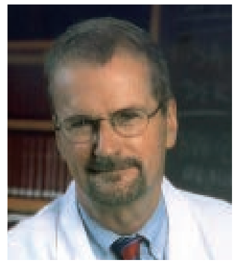
The public is aware of obesity's risks because they hear about it almost every day on the news. Unfortunately, that awareness has not translated into major behavioral change for the vast majority of the overweight population. We used to think that just getting the word out and providing education would be all that's needed to change things, but we've been learning that it's not all that's needed. We also need to involve communities, families, schools — many, many actors — in order to really catalyze effective behavioral change.

Is this because we're working against our biology?
Essentially. Evolutionarily, our bodies developed to make very efficient use of energy. Particularly in storing calories that we don't need to use right away. Now that our lifestyles are dominated by computers and television viewing, people are becoming increasingly sedentary. And this energy-use efficiency, which is built into our genes, is no longer so necessary.

So we have to change food habits — working against the way our bodies have been programmed.

To do that in ways that will be effective, we need to understand the biochemical and molecular mechanisms that are involved. We need to better understand all aspects of appetite regulation and aspects of energy metabolism by muscle and fat cells. You've probably been reading about the body's brown fat, which is far more metabolically active than white fat. But we really don't understand the mechanisms that control the activity of brown fat in burning energy.

Another big data gap: behavior. We don't have enough research to know what really drives the behavior to eat or make specific food choices. There can be a host of drivers — culture, genetics, family issues, economics, community factors. We now have to understand their relative roles.



TUFTS UNIVERSITY

The public is aware of obesity's risks.... Unfortunately, that awareness has not translated into major behavioral change.

The federal government's most recent dietary guidelines included a chapter on exercise. Is that something ASN wants to put on the dietary radar screen as well?
Definitely.... Another one of those data gaps is understanding what drives the behavior to exercise — or not. And that's important because it's half of the equation that explains obesity, which reflects a mismatch between energy in and energy used.

What other issues need more attention?
With the demographic changes in our country — our graying population — we have to investigate more closely the relationships between nutrition and chronic diseases of aging. For instance, inflammation now is thought to be the common denominator in many chronic diseases. We're also learning that obesity is related to chronic inflammation.

Nutritionists have been interested for many years in trying to modulate inflammation through antioxidants. But research has shown that in trials using fairly high doses of single antioxidants, or small combinations of them, that they don't work. In fact, they can become harmful prooxidants.

So now we have to learn more about finding optimal combinations of different antioxidants, rather than looking to prescribe just one or two.

Diet can also be related to cognition in aging. We have a lot of clues that food can be very important in preventing or slowing cognitive decline through nutrients such as omega-3 fatty acids, for example, and the B vitamins, such as B12. These need to be explored more.

Finally, we have to realize that because of genetic differences, the dietary recommendations that work for me might not be right for you. Although we don't have all of the scientific data that we need, it's becoming clear that increasingly we may need to begin tailoring recommendations, based on the individual's genetic makeup. ■

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NASA scientists looked to nature for a solution to eye protection which led them to their studies on how eagles can simultaneously distinguish their prey from their surroundings with utmost precision, while

Who Better to Know About the Best UV Eye Protection than America's Astronauts?

"I have worn the EAGLE EYES® brand for years and depend upon their superb capabilities in UV eye protection, glare reduction and vision-enhancement."

— WALTER CUNNINGHAM, APOLLO-7 ASTRONAUT

protecting their eyes from sunlight. NASA scientists independently replicated this same technology into Eagle Eyes® **Apollo Gold™** optical sunglasses, serious sun-protection that offers **12 distinct performance levels** in a single lens. Eagle Eyes® **Apollo Gold™** patented, polarized lens technology was tested to enhance vision while protecting from the sun's harmful UVA, UVB radiation and blue-light.

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