15 WAYS TO EXPOSE CREATIONIST NONSENSE

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Building Better Drugs from Sugars

SUPERSYMMETRY in atomic nuclei

ARTIFICIAL HEARTS and the alternatives

A NOSE THAT "SEES"

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july 2002

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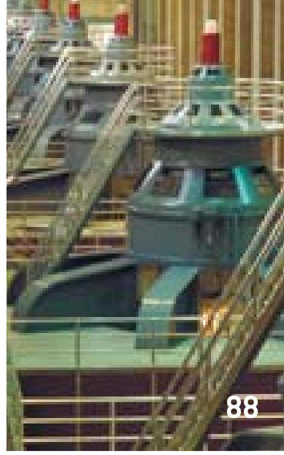

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SA Perspectives

Bad Science and False Facts

Preaching to the converted is unrewarding, so why should *Scientific American* publish an article about the errors of creationism [*see page 78*]? Surely this magazine's readers don't need to be convinced. Unfortunately, skepticism of evolution is more rampant than might be supposed. A Gallup poll from 1999 and a National Science Board poll from 2000 both revealed that close to half the American public rejects evolution. Inadequate education plays a part in this—confidence in evolution grows with schooling—but clearly a lot of remedial tutoring is in order: the NSB also determined that only about half the population recognized the statement "The earliest humans lived at the same time as the dinosaurs" as false.

With respect to evolution and science education, this year has already had a mixed record. The state legislatures of Mississippi and Georgia considered bills that would have undermined the teaching of evolution (thankfully, the bills died in committee). The Cobb County Board of Education in Georgia voted to insert into new science textbooks a notice that evolution is "just one of several theories" about the diversity of life on earth. As of this writing, the Ohio Board of Education is still deciding whether to give equal time to the creationist ideas known as intelligent design.

Ideas deserve a fair hearing, but fairness shouldn't be an excuse for letting rejected, inadequate ideas persist. Intelligent design and other variants of creationism lack credible support and don't mesh with the naturalistic fabric of all other science. They don't deserve to be taught as legitimate scientific alternatives to evolution any more than flat-earth cosmology does.

Unfortunately, creationism's allies set up smoke screens. For example, writing in the *Washington Times,* Senator Rick Santorum of Pennsylvania claimed that the federal education bill signed into law this year contained a provision that "where topics are taught that may generate controversy (such as biological evolution), the curriculum should help students to understand the full range of scientific views that exist." But biologist Kenneth R. Miller of Brown University has pointed out that the law says no such thing—the "Santorum amendment" was removed before the bill was signed.

Addressing the Ohio education board, two prominent advocates of intelligent-design theory, Jonathan Wells and Stephen C. Meyer, submitted a bibliography of 44 peer-reviewed papers that they said "challenge" evolutionary explanations for life's origins. Sleuthing by the National Center for Science Education revealed, however, that this list is less than it seems. The NCSE attempted to contact all the authors of those papers and heard from 26 of them, representing 34 of the 44 publications. None of those authors agreed that their work contradicted evolution, and most insisted that their work actually supported it (the complete story can be found at www.ncseweb.org).

Readers of *Scientific American* are well placed to expose ignorance and combat antiscientific thought. We hope that this article, and a new resource center for defending evolution at www.sciam.com, will assist them in doing so.

MATT COLLINS

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FEATURED THIS MONTH

Visit www.sciam.com/explorations/
to find these recent additions to the site:

LOST IN SPACE

A series of bad budgeting decisions over the past few decades has left NASA in a serious bind. Both the space shuttle and the International Space Station are facing severe cutbacks, forcing NASA to reallocate funds from unmanned missions that would probably yield greater scientific returns. Can the agency that took us to the moon get back on track?


NASA

Secrets of the Stradivarius

With a tone that is at once brilliant and sonorous, the violins created by Antonio Stradivari in the 17th and 18th centuries stand alone. For years, instrument makers and scientists have studied the extraordinary violins, hoping to uncover their secrets. Now one investigator believes that reproduction of that legendary sound is within reach. The key, expounds Joseph Nagyvary of Texas A&M University in an interview with SCIENTIFIC AMERICAN, lies in the chemistry.

ASK THE EXPERTS

What is synesthesia?
Thomas J. Palmeri, Randolph B. Blake and René Marois of Vanderbilt University explain.
www.sciam.com/askexpert/

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Letters

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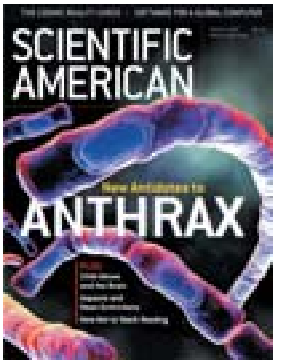
A FAVORITE TOPIC of many letter writers for the March issue was reading—specifically, "How Should Reading Be Taught?" by Keith Rayner, Barbara R. Foorman, Charles A. Perfetti, David Pesetsky and Mark S. Seidenberg. One flaw with phonetics as a teaching tool, pointed out George Chudolij of Massachusetts, is that "unfortunately, the English language is not 100 percent phonetic, which contributes to confusion. I say revamp the written spelling of the language and eliminate unnecessary letters. Thus, there would not be any 'x's or 'c's. The 'a' as in 'father' would remain the same; 'a' as in 'fat' would be written with an umlaut, as German does today for this very purpose. 'Enough' would be 'enuf,' and so on." Sumthing tu pander äs yu reed tha leters an tha nekst tu payjez.



MORE REFLECTIONS ON READING

"How Should Reading Be Taught?" gives information about a problem that has been solved in many schools. As an elementary school principal, I work with teachers to be sure we teach reading in ways that blend the necessary mastery of phonics (word study) with the enjoyment of literature. Several current approaches, widely used for at least 10 years, combine phonics with literature. For example, one of the "blocks" in the "four blocks" approach is the study of phonics. The other blocks are guided reading, independent reading, and writing.

A second approach, "guided reading," developed out of the Reading Recovery program at Ohio State University, includes phonics. The teacher frequently assesses each child and teaches the student using eight- to 10-page single-story books selected to be at precisely the student's current reading level. This article too narrowly refers to guided reading as a whole-language approach that neglects phonics.

JANE J. SHARP
Finley Road Elementary School
Rock Hill, S.C.

I thought your article was very well researched and was a true representation of the many experiences I have had in teachers college classes and in my work as both a student teacher and teacher. My reading professors did not teach us how to provide direct instruction in phonics; they sincerely believed that linguistic concepts would be "absorbed" by the students as they were exposed to a "literature-rich" classroom experience. Fortunately, we are entering an era in which it is recognized that a balance between the two philosophies is necessary as well as possible.

ELAINE R. MALONE
Lincoln, Neb.

WORLDWIDE-COMPUTER WOES

The idea of a superfast global operating system wherein some unknown person's file fragments are stored on my computer is wonderful ["The Worldwide Computer," by David P. Anderson and John Kubiatowicz]. But as America drowns in litigation and the definition of a "right" becomes ever more clouded, the prevailing impetus is to *build* walls around my computer, not tear them down.

JOSH LACEY
Los Angeles

The authors failed to address the bandwidth needs of such a global network. Although installation of high-bandwidth residential service is growing exponentially, most providers anticipate—and base their pricing structure on—idle bandwidth time, which the authors' system would use. This is why my residential DSL service costs $40 a month, whereas commercial service, with comparable bandwidth, runs about 10 times that amount.

A closed-network environment, in which bandwidth and hardware are more

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easily managed, is where technology holds enormous promise. Imagine harnessing (and selling) the power of an entire university or corporate campus. Such a setting would be the perfect incubator for the quantity and quality of applications needed to take advantage of this technology.

ANDY JELAGIN
Network Administrator
Kaleidoscope Imaging/Brandscope Design
Chicago

GENOME RIGHTS

I read with interest Gary Stix's account of a mock patent dispute over the DNA of the fictional Salvador Dolly [Staking Claims]. As a professional sculptor, I was immediately struck that Dolly's attorneys failed to approach the case from the correct basis: this is clearly not an issue of patent law but of copyright law. A person's genome is nothing more than a unique expression of information. And expression, whether it is artistic or genetic, is protected by copyright.

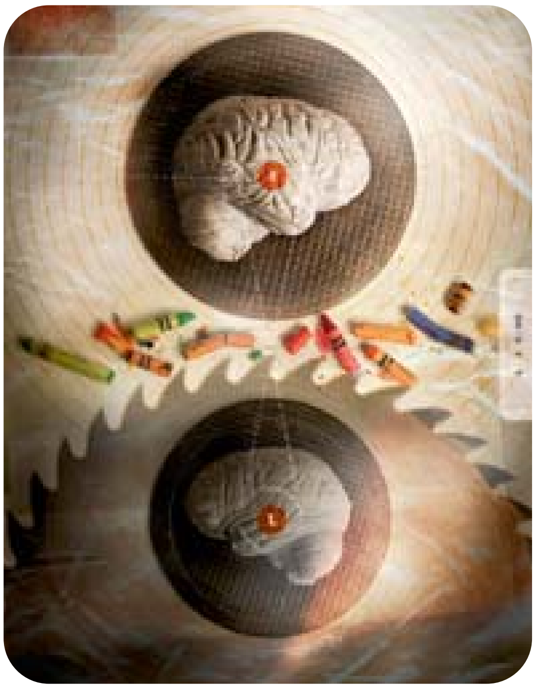
As the sole originator and holder of his genome, Dolly can demand payment for every copy or "excerpt" made by a company. With polymerase chain reaction, or PCR, replication, that could amount to quite a sum. These royalties would be payable, under current law, for 70 years beyond Dolly's death.

CHRISTOPHER PARDELL
Fallbrook, Calif.

ABUSE AND HEALING

As a clinical social worker who treats adult survivors of child abuse, I was grateful for your article and the author's years of research on the effects of childhood trauma on the brain ["Scars That Won't Heal: The Neurobiology of Child Abuse," by Martin H. Teicher]. I must, however, take strong exception to the title and to repeated statements that this research shows that the "developing mind may never truly heal" and that the damage is "irrevocable" or "hardwired."

There are *no data reported* to say that such harm to the brain is irreversible. Indeed, the analogy of "software" and "hardware" is especially flawed, because the brain is an evolving organ; new cells, new connections, changes in its chemistry continue into old age. For example, many people have been able to recover full function after stroke destroyed critical areas of their brain. Studies have shown that brain-function changes after therapy for depression are similar whether the treatment is medication or talk therapy.



EARLY ABUSE, research shows, leads to indelible changes in a youngster's developing brain.

Psychotherapists such as myself see most of our clients gain dramatic and meaningful reductions in the problematic symptoms and behaviors caused by childhood abuse. Although full recovery may take years, it is irresponsible to take away this hope based on an absence of data.

MICHELLE SALOIS
University City, Mo.

TEICHER REPLIES: I celebrate your spirit of hope, but I stand by what I've written. Through therapy, individuals can adapt to and compensate for these experiences. But there is no evidence to suggest that structural (as opposed to functional) alterations in the brain are reversible through therapy. Studies on the effects of antidepressant medications and psychotherapy show alterations in metabolism and blood flow but do not show any changes in gross anatomy. It is most unlikely that an adult with 40 percent reductions in the size of his or her corpus callosum could have this region regrow through any known form of treatment. Individuals often recover function after stroke, to use your example, through compensatory processes, but the destroyed regions remain destroyed. I have in fact examined brain function in individuals with a history of childhood maltreatment who, through therapy, have made an apparent full clinical recovery, but their brains functioned quite differently than normal in the recall of neutral versus disturbing memories.

As you've indicated, patients can respond dramatically to certain forms of therapy, although other sequelae, such as borderline personality disorder, can be much more intractable. I have not received a single letter from a patient indicating that this article caused him or her to lose hope; I have received many letters from individuals thanking me for helping to explain why their condition has endured so long despite therapy. The best hope for adaptation or functional recovery is with early intervention when the brain is more plastic. There is, however, a pressing need for better treatments and a crucial need for the prevention of childhood abuse.

BOUNCING BABY UNIVERSES

"Been There, Done That," by George Musser [News Scan], suggests that instead of a singular universe started by a big bang, we live in one of two parallel universes that repeatedly bounce off each other like a ball connected to a paddle by a rubber band. Fascinating idea, but it needs a catchy name. How about the Big Boing?

STAN BENJAMIN
Garrett Park, Md.

STUART BRADFORD

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50, 100 & 150 Years Ago
FROM SCIENTIFIC AMERICAN

Subversion Suspicion ▪ Consciousness Data ▪ Social Revolution

JULY 1952

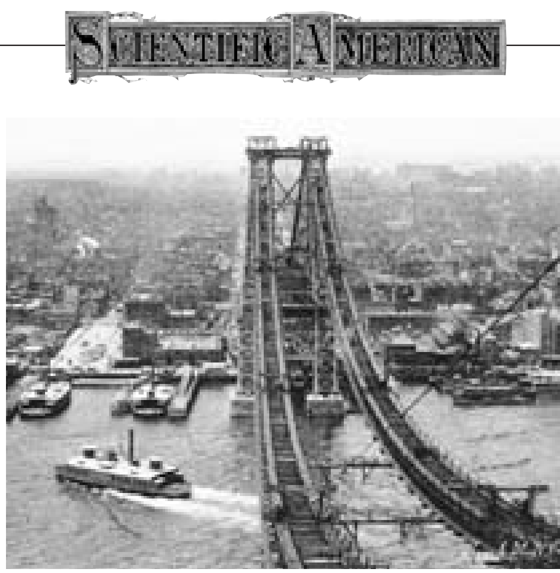
RED SCARE—"U.S. scientists have been running into trouble getting permission to travel abroad. The most recent publicized case being that of Linus Pauling, head of the Department of Chemistry and Chemical Engineering at the California Institute of Technology. Pauling had planned to attend a conference of the Royal Society of London on protein structure. He said a State Department official told him that the decision had been made 'because of suspicion that I was a Communist and because my anti-Communist statements had not been sufficiently strong.' Pauling had declared that he was not a Communist and had pointed out that his resonance theory of chemical combination had been attacked in the Soviet Union. He has reapplied for a passport and sent a letter to President Truman."

JULY 1902

THE LONGEST BRIDGE—"The last of the strands has now been completed on the four great cables which will support the massive roadway of the new East River Bridge between Brooklyn and Manhattan [*see illustration*]. Each cable is 2,985 feet in length from anchorage to anchorage. The horizontal distance from saddle to saddle across the main span is 1,600 feet. The cables have an average breaking strength of 225,000 pounds per square inch; a truly marvelous result, and one which places these cables far ahead in point of tensile strength of any other structural material yet used in bridge building." [*Editors' note: The Williamsburg Bridge, which opened on December 19, 1903, was the longest suspension bridge in the world until 1924.*]

RADIO ASTRONOMY—"M. Charles Nordmann [*sic*] gives an account of experiments at the Mont Blanc observatory to determine whether waves of an electro-magnetic nature are given off by the sun. He used a horizontal mast wire 550 feet long which was laid along the Bossons glacier upon wood insulating supports so that the sun's rays would fall directly upon it. Nordmann used a coherer which was placed in a vessel of mercury. The experiment was repeated several times on the 19th of September during fine weather, but no deflection of the galvanometer could be obtained. This seems to prove that the sun does not emit such electro-magnetic waves, or in the contrary case such waves are absorbed by the sun's or earth's atmosphere." [*Editors' note: Successful experiments by Karl Jansky in 1931 are considered the beginning of radio astronomy.*]

THE END OF SCIENCE—"President Minot, of the American Association for the Advancement of Science, stated that consciousness is at once the oldest problem of philosophy and the youngest problem of science. Consciousness ought to be regarded as a biological phenomenon, which the biologist has to investigate in order to increase the data concerning it. The biologist can often tell why a given function is performed, but how the function exists he can tell very imperfectly. It is more important to seek additional positive knowledge than to hunt for ultimate interpretations. Correct, intelligent, exhaustive observation is our goal. When we reach it, human science will be complete."



BUILDING the world's longest suspension bridge, 1902

JULY 1852

THE SEWING REVOLUTION—"In 1847 there was not a solitary machine of the sewing machine kind in active operation, in our whole country, if in the world. There are now, we believe, about five hundred. We expect them to create a social revolution, for a good housewife will sew a fine shirt, by one of these little machines, in a single hour. The time thus saved to wives, tailors, and seamstresses is of incalculable importance. Young ladies will have more time to devote to ornamental work (it would be better for them all if they did more of it). We suppose that, in a few years, we shall all be wearing shirts, coats, trousers, boots, and shoes—the whole habiliments of the genus *Homo*—stitched and completed by the Sewing Machine."

MARKED FISH—"The Scotch commissaries of fisheries have been adopting an ingenious device for learning the migrations of the salmon. They have marked a large number of fish, hatched from spawn, deposited last year in the river Tweed, by placing around them a belt or ring of india rubber numbered and dated. All fishermen, taking such marked fish, are desired to take note of the weight, the place and date of capture, and various other particulars named in the directions. The idea is a novel and amusing one."

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news SCAN

INFOTECH

Who's Who

CAN DIGITAL TECHNOLOGY REALLY PREVENT IDENTITY THEFT? BY PAUL WALLICH

Every year scam artists reportedly create some 700,000 false identities—enough to fill a virtual San Francisco. That estimate is conservative, insists Norman A. Willox, Jr., of the National Fraud Center, a consulting firm. It's based on the number of fake credit cards, bank accounts, driver's licenses and other supposed proofs of identity that are being uncovered. Data from the U.S. General Accounting Office suggest that identity fraud has been increasing by roughly 50 percent a year since 1999. And despite corporate and government moves toward universal IDs, the quest for absolute proof that you are who you say you are appears quixotic.

Creating a false identity is easy, especially if you start with a real one. A few visits to Web-based public directories (or local libraries and records offices) can yield addresses and phone numbers past and present, date of birth, employers, mother's maiden name and similar vital personal data. Add an illegitimately obtained Social Security or credit-card number, and an impostor has almost as solid a case for claiming to be someone as the real person does. Criminal information brokers even package up complete identities for sale, according to Willox.

In a society in which people regularly do business without meeting face to face, a system that bases trust on a few dozen bytes of lightly guarded data is fundamentally insecure. Federal estimates of losses from identity fraud are well up in the billions of dollars a year, and those whose names or numbers are used as a basis for fake identities may spend several years and thousands of dollars trying to clear their records. Some have even been arrested and imprisoned for crimes committed by their doppelgängers. The rapid expansion of global trade, Willox says, is at risk.

The rise in identity theft, coupled with the current climate of fear about terrorism, has led organizations ranging from database builder Oracle to the American Association of Motor Vehicle Administrators to propose the development of tamperproof IDs that would positively verify everyone's identity for purposes as diverse as opening a bank account or getting on an airplane. Besides the usual name, address, birth date and ID number, proposed computer-readable identity cards could also contain biometric data such as fingerprints or iris scans to make falsification impossible—assuming that it was issued to the right person in the first place.

But in addition to the obvious civil-liberties implications of an ID that could be used to track every commercial or government trans-

FAKE IDs are not always so easy to spot.

AUTHENTICITY VIA DATABASES

New "knowledge-based" techniques may be a means for better identity verification. Putting our surveillance society to good use, these algorithms match purported identifying information against dozens of databases, including some to which a scammer would, it is hoped, have no access. An impostor might be able to match a few items in a legitimate dossier but not the entire file. This knowledge-based approach can be more than 99.9 percent accurate. Still, there will always be a need for manual overrides in case the information about a real person doesn't match what's in the databases. Studies have shown, for example, that 30 percent of credit reports contain significant errors.

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action, an ostensibly perfect token of identity could reduce security rather than enhance it. One problem, says Lauren Weinstein, moderator of the Internet-based Privacy Forum, is that you shouldn't confuse proof of identity with proof of trustworthiness. The FBI and CIA knew exactly who Robert Hanssen and Aldrich Ames were, for example, but that didn't help stop their espionage. Similarly, Weinstein argues, relying on a "frequent traveler card" for airline security could lead to relaxed vigilance just when it's most needed.

Tamperproof ID would be a "high-value target," Weinstein explains. Given how often criminals dupe or suborn the officials who issue birth certificates or driver's licenses (and how many false identities are already in place), even 99.9 percent accuracy would give thousands of fake people a government imprimatur. Biometric certification of dubious identities could make life even worse for victims of identity fraud—today as a last resort you can cancel all your accounts and even get a new Social Security number, "but how do you cancel your fingerprints?" Weinstein points out.

Bruce Schneier of Counterpane Internet Security in Cupertino, Calif., suggests that instead of spending more resources on a holy grail of perfect identification, governments and businesses should accept that ID failures will occur and make reporting identity fraud as easy as reporting a single lost or stolen credit card. "Give the liability to the person who can fix the problem," Schneier says, noting that consumers rather than information vendors now bear the costs of correcting the damage done when ID data are stolen or falsified. In such a regime, more limited forms of identification—each suited to a small range of transactions—might turn out to be more cost-effective and secure than a single overarching digital persona.

FAST FACTS: STEALING A LIFE

In only about 20 percent of cases is the method of identity theft known. Of those, the most common are:

Relationship through victim: 52.5%

Stolen or lost wallet/purse: 34.4%

Mail theft/false address change filed: 13.4%

Compromised records: 6.9%

Burglary: 3.6%

Internet solicitation/purchase: 2.4%

SOURCE: General Accounting Office, March 2002. Total exceeds 100 percent because some victims reported that multiple methods were used.

WEAPONS

Ground below Zero

ARE BUNKER-BUSTING NUCLEAR WARHEADS A VIABLE OPTION? **BY DAVID APPELL**

A **joint report** of the U.S. Departments of Defense and Energy estimates that more than 10,000 potential hardened and deeply buried targets worldwide contain crucial infrastructure and possibly chemical or biological weapons. Although many of these targets are vulnerable to conventional weapons, hundreds are fortified below 25 to 100 meters of concrete. Nuclear weapons are the only sure means to defeat these strongholds, some defense analysts say, calling for a new generation of weapon: a low-yield, earth-penetrating warhead that would deliver a knockout blast without releasing plumes of deadly radioactivity. But such weapons, various physicists argue, are not technically feasible.

NUCLEAR BLAST for underground bunkers would be much smaller than this 1962 detonation of 104 kilotons at 195 meters deep, but critics say a similar "Roman candle" effect would occur.

U.S. DEPARTMENT OF ENERGY

"Earth-penetrating weapons cannot penetrate deeply enough to contain the nuclear explosion and will necessarily produce an especially intense and deadly radioactive fallout," concludes Robert W. Nelson of the Program on Science and Global Security at Princeton University. In a paper to appear this summer in the journal *Science and Global Security,* Nelson calculates that a one-kiloton, earth-penetrating "mini nuke" used in an urban environment such as Baghdad would spread a lethal dose of radioactive fallout over several square kilometers and result in tens of thousands of civilian fatalities. Regardless of its impact velocity or its construction material, no missile can penetrate reinforced concrete more than about four times its length, Nelson calculates, a number supported by data he received from Sandia National Laboratories via the Freedom of Information Act.

Penetration through rock or soil is more variable—and more controversial. Gregory H. Canavan, a senior scientist at Los Alamos National Laboratory, believes that Nelson's equations show that depth-to-length penetration of 30 is possible in dirt; Nelson denies

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that they are applicable in that domain. Robert L. Peurifoy, who in the 1970s managed design work for a penetrator option for the Pershing II missile at Sandia, agrees with Nelson. "You can't stick a penetrator into dense earth more than 40 feet or so," Peurifoy states. "It comes down to the strength of materials."

DANGEROUS SEARCHES in bunkers, such as this one presumably used by the Taliban, is one reason some are calling for the nuclear option.

Even if a missile could burrow deeply, the explosiveness needed to ensure a bunker's destruction may be too much to keep buried. Working in weapons designers' favor is the fact that exploding a weapon in the ground instead of the air increases its equivalent yield by about an order of magnitude, because rocks transmit energy much better than an air-rock interface does. Even so, Nelson argues, the yield would have to be at least three kilotons, about one seventh that of the Hiroshima bomb, to destroy a structure 100 meters down. Such an explosion would not be contained; rather it would produce a crater nearly 160 meters wide and 30 meters deep. Cratering would in fact happen for any yield—"at minimum, an earth penetrator creates an open crater or shaft, allowing release of hot plasma and radioactive material in a 'Roman candle' type of explosion," according to Nelson. Dose rates could exceed 100 rads an hour (acute radiation sickness begins to occur at total dosages between 100 and 200 rads); most of the exposure would come within the first few hours, leaving little time for evacuation.

Similar conclusions have been reached independently by Peurifoy, physicist Sidney D. Drell of Stanford University and geophysicist Raymond Jeanloz of the University of California at Berkeley. In a March *Los Angeles Times* commentary, the trio wrote that "even a one-kiloton warhead detonated at a depth of 20 feet would eject about one million cubic feet of radioactive debris from a crater about the size of ground zero at the World Trade Center."

U.S. administrators are understandably reluctant to be specific about military capabilities in this novel realm. "Whatever depth you go to, you're just basically setting a target for the enemy to put its sensitive facilities deeper," says Jim Danneskiold, public affairs officer at Los Alamos. But what is clear is that high-ranking officials have been thinking for years about the nuclear option for the attack of underground bunkers. In a white paper published in 2000, Stephen M. Younger, then associate laboratory director for nuclear weapons at Los Alamos and now director of the Defense Threat Reduction Agency, argued for the retention of a small number of nuclear weapons to undermine enemy confidence in the survival of hardened bunkers.

"In my opinion the issue is not, 'Can you fully contain the fallout from a nuclear explosion?' I don't believe that you can, realistically," Younger states. "However, if circumstances force you to consider the use of a nuclear weapon, then you should use the minimum destructive force required to achieve that military objective." He disagrees with Nelson's opinion, published last year in the *Journal of the Federation of American Scientists,* that underground nuclear testing would be required to develop low-yield weapons.

The fiscal year 2003 budget includes a request by the National Nuclear Security Administration for $15 million for each of the next three years to undertake a feasibility and cost study into a "robust nuclear earth penetrator." The study will determine whether existing weapons in the U.S. stockpile can be modified to take on this different mission. Moreover, the 2003 Defense Authorization Act passed by the House of Representatives in May allows the national labs to conduct research on, but not develop, a low-yield earth-penetrating nuclear weapon. It also requests the National Academy of Sciences to study the collateral effects of such weapons.

Doubts in the government persist, however. In a February letter to President George W. Bush, 76 members of the House expressed "deep concern" about "the development of a new generation of low-yield nuclear weapons and the resumption of underground nuclear testing." At a time when the common euphemism for the site of the worst terrorist attack on U.S. soil is borrowed from Hiroshima, Americans might want to think carefully about the feasibility of a nuclear attack without nuclear consequences.

David Appell is based in Gilford, N.H.

BLAST FROM THE PAST

The U.S. already has a nuclear weapon that can burrow into the ground. The B61-7—modified into an earth-penetrating nuclear weapon and called the B61-11—was introduced in 1997. Its yield is believed to be between 0.3 and 340 kilotons (the actual figure is classified), and it can dig through 100 meters of solid rock, according to a former Pentagon official quoted in the *Washington Post* in June 2000. What is needed now, he continued, was something "that can threaten a bunker tunneled under 300 meters of granite without killing the surrounding civilian population." The development of such weapons would run the risk of squashing ongoing efforts to reduce nuclear weapons and could require the resumption of underground nuclear testing.

The unclassified "Report to Congress on the Defeat of Hard and Deeply Buried Targets," by the U.S. Departments of Defense and Energy, was made available last December by the Physicians for Social Responsibility and Nuclear Watch New Mexico (www.nukewatch.org/important_documents.html#hdbt).

ADAM BUTLER *AP Photo*

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PSYCHOLOGY

Inner Turmoil

PRESCRIPTION PRIVILEGES MAKE SOME PSYCHOLOGISTS ANXIOUS BY CHRISTINE SOARES

Intending to ease consumer access to mental health care, New Mexico legislators in March passed a law allowing psychologists to prescribe psychotropic medications, such as antidepressants. The state's action, the first in the nation, has the blessing of the American Psychological Association (APA), which considers prescriptive authority a logical extension of psychologists' role as health care providers. But powerful groups, including the American Medical Association, oppose the idea and have a surprising source of support: psychologists themselves, some of whom call it a radical experiment and fear that the most likely victim will be the science of psychology. "I am concerned that nonmedically trained people as legitimate prescribers of drugs will not be accepted by the American public," says psychologist Gerald C. Davison of the University of Southern California.

The APA has spent more than $1 million to help state psychological associations develop and lobby for such prescription privileges—or "RxP"—legislation. The version endorsed by the APA would license doctoral-level psychologists to independently prescribe psychotropic drugs after completing 300 hours of classroom instruction in neuroscience, physiology and pharmacology, followed by four months' supervised treatment of 100 patients. Critics say that is not nearly enough compared with other prescribers, such as M.D. psychiatrists or nurse practitioners who have at least six years' medical education and clinical experience.

Neither Davison nor most other RxP opponents doubt the efficacy of medications. Their greatest objection is to the notion of turning psychology into a prescribing profession.

In a field that has struggled long and hard to prove that mind, mood and behavior can be studied empirically, the past decade, Davison says, has seen "exciting developments" that demonstrate the validity of various psychotherapeutic interventions and the psychosocial-behavioral models on which they are based. "The timing *is* peculiar to abandon psychological science or to convert it to a medical science," explains Elaine M. Heiby of the University of Hawaii, who chairs a committee of the 1,000-member American Association of Applied and Preventive Psychology that is concerned about the medicalization of psychology. "Making sure that practicing psychologists are giving patients interventions based on the best available *psychological* science should be the APA's priority," argues Emory University's Scott Lilienfeld, president of the Society for a Science of Clinical Psychology (SSCP).

More than any philosophical betrayal of psychology, RxP opponents fear that the movement will undermine the science they love. They believe that if prescriptive authority becomes the norm, biomedical requirements will inevitably seep into the psychology curriculum, at the expense of traditional psychological science and methodology. Lilienfeld feels that many clinical psychologists already receive inadequate training in fundamentals such as research design and evaluation.

RxP opponents charge the APA with pushing its prescription-privileges agenda without adequately assessing support for it in the field. The 300-member SSCP is the only group within the APA to have taken a formal stance against prescription privileges.

The APA has scheduled 30 minutes at its meeting in August for an RxP debate, but its leadership believes it already has an accurate sense of support for its RxP policy. "Except for this small vocal minority, we have just not gotten a lot of groundswell against this from members," remarks APA president Philip G. Zimbardo of Stanford University.

With prescription privileges now a reality in one state, some RxP opponents concede that it may be too late. Still, hoping to rouse their colleagues, they were to have held an anti-RxP symposium on June 9 at the annual meeting of the American Psychological Society (APS). Whereas half of the APA's members are practicing psychologists, the 15,000

THE WRITE STUFF for psychologists?

TOMMY FLYNN *Photonica*

PSYCHOLOGY'S BATTLE LINES

- This year four states besides New Mexico—Georgia, Hawaii, Illinois and Tennessee—have pending legislation for psychologist prescription privileges.
- Over the past decade 14 state legislatures have considered such laws.
- A total of 31 state psychology associations have task forces dedicated to developing and lobbying for prescription-privileges legislation.
- In 1998 Guam gave psychologists limited prescriptive authority.
- Between 1991 and 1997 a U.S. Department of Defense psychopharmacology demonstration project involving two to four years' training produced 10 military psychologists who can write prescriptions.

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members of the APS are predominantly academics and researchers. The APS, which has taken no position on prescription privileges, declined to comment on the controversy because it centers on practitioners and, according to a spokesperson, would thus be inappropriate for the organization to address.

"Boy, they couldn't be more wrong," counters a disappointed Davison. "If they don't see this issue as germane to science and education in psychology, they've got their heads where the sun don't shine."

Christine Soares is based in New York City.

ACOUSTICS

Orbital Shouting

NOISE BECOMES A CONCERN ON THE INTERNATIONAL SPACE STATION **BY JAMES OBERG**

In space, no one can hear you scream—because, in the case of the International Space Station (ISS), your voice would be drowned out. Fans, compressors, motors, transformers, pumps and other gear create a literally deafening cacophony hazardous to the health and well-being of the crew. At a NASA quarterly review of the space station program in early February, the noise situation was rated as "bad"—and it's getting worse as more equipment goes up.

NOISY EQUIPMENT in the Russian service module limits astronaut duties there to two hours at a stretch.

NASA

For years, station designers were aware that noise could be troublesome, but more serious problems demanded their attention. "Noise was one of those issues that never seemed to get much respect," NASA acoustics engineer Jerry Goodman told a space engineers seminar in Houston last year.

"Our primary concern is the Russian service module,'" says Michael E. Engle, the acoustics integration manager for the ISS. Under severe financial constraints, the Russians did not give a high priority to the sound issue. (The Mir space station was also known to be noisy.) In the service module, Engle remarks, "the continuous noise levels there are in the 70- to 72-decibel [dB] range"—akin to standing next to a freeway. By comparison, U.S. Navy standards limit continuous exposure to shipboard noise above 60 dB. Astronauts have been limited to working less than two hours at a time in the Russian module. Noise tapers off from the service module through the Russian FGB module to the U.S. lab module at the other end, where levels have been measured between 55 and 62 dB. The U.S. end may be "the only relatively quiet work place," an internal NASA report noted. But noise levels are creeping up there, too: in April the arrival of one device "about doubled the acoustic energy," the report stated.

Engle says that crew members' hearing loss was the top concern: "They are not in any danger of permanent hearing loss"—just a temporary reduction. Of four U.S. astronauts who have served on long-term missions, according to Engle, one lost some hearing but recovered. Another issue is diminished communications: on the second long-term mission to the ISS, crew members "recalled saying 'What?' a lot to each other," Engle recounts. One American complained that the hazard alarms didn't seem loud enough against the background noise.

Mitigation efforts to date have not helped much. In a January meeting convened in Houston to discuss noise issues, Boeing official Charles R. DuSold explained how the use of noise-canceling and noise-reducing headsets was "not acceptable," proving to be too uncomfortable for the astronauts over long periods. ("I don't think they wear them a whole lot," Engle admits.) Existing audio hardware can probably reduce noise locally, DuSold continued, but only at the expense of higher noise levels elsewhere in the modules, and "it would likely be an extremely expensive option." He was also pessimistic about the practicality of retrofitting equipment already in orbit. Besides, sometimes the supposed fixes with add-on mufflers and acoustic mats have damaged equipment or blocked air

DECIBEL DISTRACTIONS

"Logging acoustic data on Medical Equipment Computer. Numbers are roughly 61–63 dB [decibels] around our sleep locations, 75 in work areas and central post, and 80–85 around the noisiest equipment.... Noise is a distraction, but bearable."

—Log entry of Commander Bill Shepherd on the International Space Station, November 24, 2000

Library: 40 dB

Large office: 50 dB

Normal conversation: 45 to 60 dB

Vacuum cleaner: 75 dB

Food processor: 80 to 90 dB

Shouting in the ear: 110 dB

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cooling, leading to overheated components.

According to Engle, NASA is now encouraging builders to design quieter hardware from the start. In the past, such calls for countermeasures before flight—such as muffling material, baffles and mounting brackets that do not transmit acoustic energy—were ignored to control costs. But early awareness and tough standards can ameliorate the problem. For example, a Russian depressurization pump initially produced 100 dB, but after it was retrofitted on the ground with four isolation mounts ($13.95 each), it generated 60 dB.

"It would have been nice to fix this problem before we flew," Engle concedes. But now that the challenges of lofting the ISS have been met, reducing noise has moved to very near the top of the priority list, he states. Mark Geyer, director of ISS program integration, concurs and adds that "it's still a difficult thing to solve." At least for the next several years, it seems, ISS crew members will frequently be saying, "What?"

James Oberg, based in Dickinson, Tex., is a consultant and writer on space sciences.

ENVIRONMENT

A Case of the Vapors

GROUND TOXINS DIFFUSING INTO HOMES PROVE HARD TO ASSESS **BY REBECCA RENNER**

Denver, the mile-high city, has a deep-down problem. Underneath a neighborhood in the southeastern part of town lies a groundwater plume contaminated with chlorinated solvents. Such contamination is not unusual; chlorinated organic solvents, many of them dry-cleaning and degreasing agents, are among the most common and troublesome groundwater contaminants in the U.S. But in Denver, potentially harmful concentrations of these volatile compounds—all suspected carcinogens—have accumulated in houses by moving up through the soil and foundations, in a phenomenon known as vapor intrusion.

Denver's case, which has led to the installation of fans and venting systems in more than 350 homes, is at the heart of a vigorous national debate among environmental scientists about the prevalence and significance of this problem. Federal and state site managers are charging that the U.S. Environmental Protection Agency's assessments, which are based on theoretical modeling, substantially underestimate the amount of contamination in houses.

Vapor intrusion is still a new concern for regulators, and evaluating this pollution pathway is a can of worms. Directly measuring the levels is usually not the best way to do it, explains environmental consultant Christopher VanCantfort, because indoor air changes so frequently. Worse, many houses already have background levels of chlorinated organic solvents—emitted by household air fresheners, paints and glues—that exceed health guidelines, says Lance Wallace, an EPA research scientist.

Indoor measurement difficulties are one of the reasons modeling is the most widely accepted approach for evaluating vapor intrusion. But the popular model is complex and, some claim, misused. The method, developed in 1991 by Shell chemical engineers Paul Johnson and Robbie Ettinger, breaks down volatile intrusion into several steps. First, contaminants volatilize out of groundwater. Then they diffuse through soil toward a building. Once near the foundation, the lower internal pressure sucks the contaminants into the building through cracks and other openings.

Johnson and Ettinger's model is good, but it is complicated to use. A contaminated-site manager needs to plug in much information about the soil and its subsurface structure. "Most of the model inputs are things that you

TOXIN released into groundwater by an old factory in Denver has led to elevated indoor readings of a solvent called 1,1 DCE. (Numbers are in micrograms per cubic meter.) Denver's dry soils and highly fractured bedrock make it easier for vapors to migrate upward.

SAMUEL VELASCO; SOURCE: HENRY SCHUVER, EPA/OSW/PSPD/CAPB, REGIONAL RISK ASSESSORS TRAINING AND CONFERENCE, MAY 24, 2001

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don't usually measure in a site assessment," says Johnson, who is now at Arizona State University. "My experience is that model misuse is a significant problem among regulators, industry and consultants," he concludes. For example, roughly half a dozen states currently list levels of chlorinated solvents in groundwater that could cause vapor intrusion problems in houses. But the levels are "all over the map," VanCantfort observes. The reason for the discrepancies, which can be as high as 1,000-fold, is that states use slightly different variations of the same model and different default values for important factors, such as soil type and soil moisture.

But others question whether it is even possible to come up with the right numbers to plug in: VanCantfort notes that the model has not been adequately field-tested. Michigan's Environmental Science Board expressed similar unease. "With this model, it's all too possible to decide that a site is safe when in fact it's risky, or risky when in fact it is safe," VanCantfort insists.

Vapor intrusion may also be coming in for intense scrutiny because the hazard can result in tough cleanup numbers. "Most people believe that drinking-water standards are the most stringent standards for groundwater," explains Paul Locke, a scientist with the Massachusetts Department of Environmental Protection. "But in reality, vapor infiltration for chlorinated hydrocarbons" requires stricter control. More communities may be getting the vapors unless regulators devise a better way to evaluate contaminated sites.

Rebecca Renner is based in Williamsport, Pa.

VAPOR INTRUSION: HOW BAD?

"We don't know the national extent of this problem," says EPA environmental scientist Henry Schuver. "But circumstantial evidence suggests it's big." Schuver is working to revise the EPA's guidelines on vapor intrusion. Chlorinated solvent trichloroethylene (TCE), a degreasing agent, is ranked among the top 20 pollutants at Superfund sites, according to the Agency for Toxic Substances and Disease Registry, indicating that many contaminated sites could potentially have a vapor infiltration problem.

CHEMISTRY

Filtering in Reverse

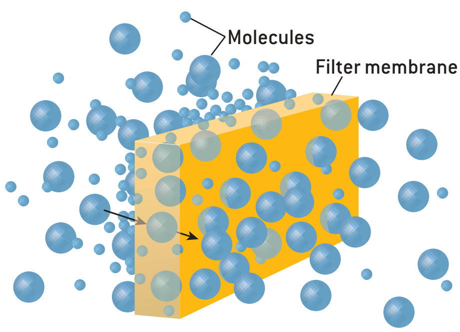
MEMBRANES THAT PASS THE BIG STUFF THROUGH **BY STEVEN ASHLEY**

Filters block the big particles and allow the finer substances through, right? Not necessarily—some filters work in the opposite way. A team of chemical engineers and materials researchers has discovered a method to markedly improve these so-called reverse-selective membranes in a unexpected manner: by adding nonporous filler materials. Rather than stopping up the filter holes, though, the additives enhance the membrane's permeability to large molecules.

This result stems from how these unusual gas filters operate, according to team leader Ingo Pinnau of Membrane Technology and Research in Menlo Park, Calif. A reverse-selective membrane first allows compounds to dissolve directly into its matrix; then the molecules diffuse to the other side. Because larger molecules condense into a liquid more readily, they generally tend to dissolve more quickly than smaller constituents. As a result, the proportion of large molecules to small ones can increase on the other side of the membrane. The separation efficiency is limited, however, because large molecules diffuse more slowly through the matrix of the membrane.

A few years ago Pinnau and several collaborators decided to try to speed up the diffusion rate of the larger molecules. They modified a class of inherently reverse-selective polymers—so-called substituted polyacetylenes—by adding fused silica (nanosize sand particles). Mixing in hard particles would normally have little effect: the spaghetti-like polymer chains would merely wrap around the particles. But the bulky chains of substituted polyacetylenes are rigid and behave more like dry fusilli macaroni. The fused silica particles serve as spacers to open up the already loosely packed polyacetylene chains. The resulting wide-open structure permits larger molecules to diffuse through faster, making the composite membrane twice as effective as previous versions.

Pinnau believes that in the future, high-performance membranes could separate unwanted hydrocarbons from methane—a feat that could make the exploitation of vast untapped natural gas deposits considerably more economical.



REVERSE-SELECTIVE FILTER allows molecules to dissolve into its matrix and then diffuse across. Larger molecules mix in faster, so more get to the other side.

MATT COLLINS

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BY THE NUMBERS

Filling the Pipeline

ARE THERE ENOUGH PH.D.S IN SCIENCE AND ENGINEERING? BY RODGER DOYLE

The 2002 edition of *Science and Engineering Indicators,* published by the National Science Board, paints a remarkable picture of American knowledge workers at the beginning of the second millennium. It shows that there are about 10.5 million college-educated people in the U.S. with a science or engineering degree and that American universities are producing new scientists and engineers at an unprecedented rate of well over half a million a year.

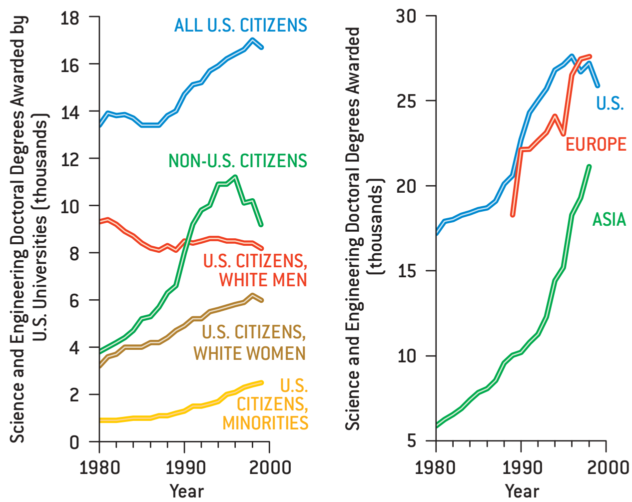
The report also reveals a potential weak spot: the supply of doctorates in science and engineering. Ph.D.s in these disciplines have been a key element in making the U.S. the world's leader in high-tech exports during the past several decades. American universities awarded a rising number of S&E doctorates through 1996, but since then, the number has decreased, primarily because of the decline in degrees earned by noncitizens, who have been increasingly drawn to universities in China, South Korea and Taiwan. The number of doctoral degrees granted to U.S. citizens has apparently stopped growing and shows signs of leveling off at about 16,000 to 17,000 annually, probably not enough to meet recruitment needs over the coming decade.

Underlying the plateau is the failure in recent decades of white American males to enter S&E doctoral programs. For reasons that are not clear, white men since the early 1980s have found higher education (including S&E programs) less appealing than before [see "Men, Women and College"; By the Numbers, October 1999]. White women and minorities have been increasingly attracted to S&E doctoral programs, as have African- and Hispanic-Americans, but these two minority groups, unlike Asian-Americans, are underrepresented.

About a third of S&E Ph.D.s now working in the U.S. are foreign-born and might, if conditions in their homelands improve, opt to return, thus causing a potentially severe shortage in the U.S. This possibility, together with the flattening in the supply of doctorates to American citizens and the rapidly growing number of doctorates awarded in Europe and Asia, is a cause for concern, although it does not necessarily portend a greatly diminished capacity of the U.S. to compete in world markets. Nevertheless, it would be sound public policy for the federal government to promote the creation of more doctorates in specialties in which there is underemployment, such as computer science and nanotechnology.

A successful effort to steer members of underrepresented minorities—blacks and Hispanics—into needed specialties and to bring them to a level proportionate to their population in the U.S. would add about 2,800 new S&E doctorates a year. A similar effort to increase the participation of non-Hispanic white men would yield somewhat smaller returns: if they got Ph.D.s at the same rate as in 1980, about 1,700 to 1,800 would be added annually.

Rodger Doyle can be reached at rdoyle2@adelphia.net



SOURCE: Science and Engineering Indicators, 2002. *National Science Board, National Science Foundation, Arlington, Va., 2002. Europe includes Germany, France and the U.K. only. Asia includes China, India, Japan, Korea and Taiwan only.*

RODGER DOYLE

SCIENCE BY DEGREES

Science and engineering degrees granted by U.S. universities in 2000:

ALL DEGREES	**542,032**
DOCTORAL DEGREES	**25,744**
Biological sciences and life sciences	4,867
Physical sciences and science technology	4,018
Agriculture and natural resources	1,181
Computer and information science	777
Mathematics	1,106
Psychology	4,310
Social sciences	4,095
Engineering	5,390
MASTER'S DEGREES	**88,143**
Biological sciences and life sciences	6,198
Physical sciences and science technology	4,841
Agriculture and natural resources	4,375
Computer and information science	14,264
Mathematics	3,412
Psychology	14,465
Social sciences	14,066
Engineering	26,522
BACHELOR'S DEGREES	**428,145**
Biological sciences and life sciences	63,532
Physical sciences and science technology	18,385
Agriculture and natural resources	24,247
Computer and information science	36,195
Mathematics	12,070
Psychology	74,060
Social sciences	127,101
Engineering	72,555

SOURCE: National Center for Education Statistics

FURTHER READING: Forecasting Demand and Supply of Doctoral Scientists and Engineers. *National Academy Press, Washington, D.C., 2000*

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news SCAN

DATA POINTS: WASTE FOR MONEY

Number of U.S. businesses and organizations supported by recycling: **56,000**

Number of people employed: **1.1 million**

Annual payroll: **$37 billion**

Annual government revenue through taxes on recycling industries:

Federal: **$6.9 billion**

State: **$3.4 billion**

Local: **$2.6 billion**

New York City's daily recycling haul of metal, glass and plastic: **1,100 tons**

Amount city will save by abandoning such recycling for 18 months: **$56 million**

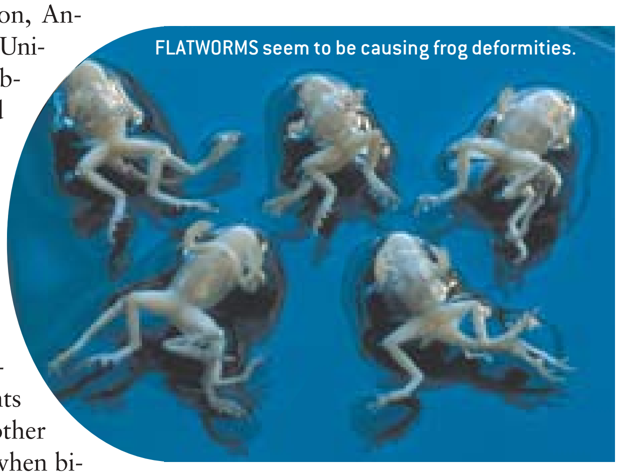
SOURCES: "U.S. Recycling Economic Information Study," National Recycling Council, July 2001 (commissioned by the U.S. Environmental Protection Agency); New York City Department of Sanitation

ECOLOGY

Kermit Had It Easy

Researchers may have pinpointed two factors contributing to the worldwide decline in frog populations. Pieter T. J. Johnson of the University of Wisconsin–Madison, Andrew R. Blaustein of Oregon State University and their colleagues observed that the frequency and severity of deformities common to frogs in some parts of the American West depended solely on the prevalence of the parasitic flatworm *Ribeiroia ondatrae*. *Ribeiroia* is carried by aquatic snails, whose numbers, the researchers say, may be climbing because of increased nutrients from fertilizer runoff, among other factors. If that weren't enough, when biologists at the University of California at Berkeley bathed male tadpoles in the popular herbicide atrazine, the croakers tended to grow female sex organs inside their testes and had smaller vocal organs. The reason may be that atrazine converts testosterone into estrogen, although the scientists note that atrazine's effect on reproduction itself still isn't clear. The parasite study is published in the May *Ecological Monographs*, and the atrazine research appears in the April 16 *Proceedings of the National Academy of Sciences*.

—JR Minkel



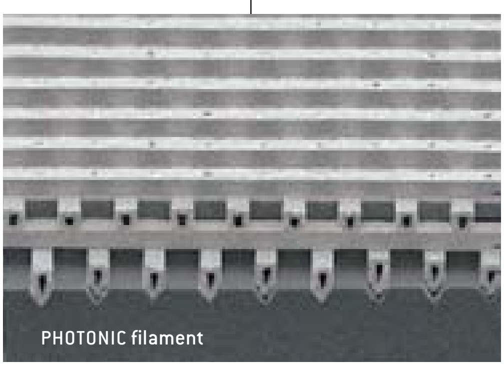
FLATWORMS seem to be causing frog deformities.

PHOTONICS

White Light, Less Heat

The average incandescent lightbulb sheds far more heat than light—90 percent of its energy is lost as heat. Even high-efficiency fluorescent bulbs essentially burn away roughly half their power. The future may prove brighter—and cooler—thanks to microscopic filaments being designed by researchers at Sandia National Laboratories. These filaments are photonic crystals, interwoven layered substances that control light waves the way semiconductors control electrons. The scientists have made 1.5-micron-wide tungsten photonic crystals that absorb infrared energy, which in turn might be transmuted efficiently into visible or ultraviolet light. The research can be found in the May 2 *Nature*.

—Charles Choi



PHOTONIC filament

GENETICS

Mutation Keeps Going and Going

It's no surprise that mice exposed to radiation can pass on genetic mutations. But researchers were puzzled two years ago to see that the offspring of irradiated male mice had higher-than-normal mutation rates in genes they received from their unexposed mothers. Confirming and extending their earlier result, Yuri E. Dubrova and his colleagues at the University of Leicester in England now report that this effect extends down to all the grandchildren of three strains of male mice exposed to mutation-causing neutrons or x-rays. They infer that the radiation introduces a signal independent of any particular gene that causes the whole genome to accumulate errors, but beyond that, Dubrova says, he's stumped. The study appears in the May 14 *Proceedings of the National Academy of Sciences*.

—JR Minkel

FRANS LANTING *Minden Pictures* (*top*); SANDIA NATIONAL LABORATORIES (*bottom*); ILLUSTRATION BY MATT COLLINS

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MEDICINE

Stem Cell Alternative?

A finding could fuel the debate over embryonic stem cells and cloning. Investigators from the University of Oslo and the biotechnology company Nucleotech in Westport, Conn., have reprogrammed skin cells to become more like other cells. To effect the partial transformation, the team immersed skin cells in extracts that contained components from the nucleus and cytoplasm from either immune cells or nerve cells. The skin cells then took on some of the characteristics of those other cell types. One type of reprogrammed cell, for example, developed the immune system's T cell receptors. For these changes to have occurred, the nucleus of the skin cells may have taken up transcription factors and other signaling molecules from the extract. The researchers hope the technique will lead to a viable alternative to embryonic stem cells and cloning. But even if it doesn't, it might illuminate the processes that a cell employs to reprogram itself. The work appears in the May *Nature Biotechnology*. *—Benjamin Stix*

MATERIALS SCIENCE

Stretching Out the Nanotube

Science-fiction buffs dream of the potential offered by the extraordinary strength and lightness of carbon nanotubes, imagining that these tubes can form cables that stretch from Earth to orbit. Unfortunately, in real life these hollow strands—only nanometers in diameter—are rarely much longer than they are wide, thereby limiting their utility. Now scientists at Rensselaer Polytechnic Institute have built single-walled carbon nanotubes 20 centimeters long. To do so, they modified the standard chemical vapor deposition process, using hexane as the source of the carbon and adding ferrocene, thiopene and hydrogen under optimum conditions. The technique, reported in the May 3 *Science,* yielded more and better nanotubes than were made by previous methods that generated long nanotubes. *—Charles Choi*

CARBON NANOTUBE can now be inches long.

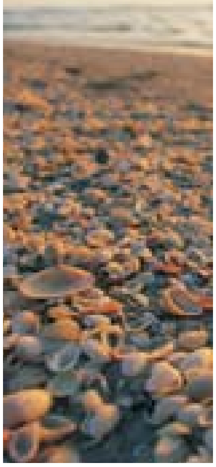
HUMAN EVOLUTION

Food for Thought

Our fat babies make us unique among land-dwelling mammals. There's a good reason for the chubbiness: at birth, the human brain—which attains a size far larger than that of our closest relative, the chimpanzee—demands over 60 percent of the body's energy intake, making fat reserves vital in times of scarcity. Curiously, as 50-day-old fetuses, chimps and other nonhuman primates have brains just as large as humans and thus seem to have comparable embryonic potential for extensive brain growth. So how did humans alone exploit this potential? Genetic mutations promoting the fetal fatness necessary for brain expansion must have occurred at some point in human evolution, Stephen Cunnane of the University of Toronto told researchers at a meeting of the American Association of Physical Anthropologists in April. But to take advantage of these mutations, our ancestors needed a high-quality diet and a lifestyle sufficiently sedentary to permit fat deposition, he asserted.

Conventional wisdom holds that early human evolution took place on the savanna and in woodland areas. Yet only shore environments would have offered reliably abundant resources to hungry hominids not yet capable of hunting, Cunnane argues. Such settings would have provided easy access to aquatic creatures rich not just in calories but in iodine, omega fatty acids and other nutrients essential for brain growth. Archaeological support for this scenario is, for the moment, inconclusive, so whether the shore-based subsistence hypothesis will hold water remains to be seen. *—Kate Wong*

CALORIES GALORE wash up onshore.



RENSSELAER POLYTECHNIC INSTITUTE (*top*); L. CLARKE *Corbis* (*bottom*)

WWW.SCIAM.COM/NEWS

BRIEF BITS

- A study of 1,900 heart attack survivors found that **caffeinated tea has a protective cardiovascular effect**—those who drank 19 cups or more a week had a 44 percent lower death rate than those who didn't drink any. /050702/2.html
- Physicists have devised **a single polymer molecule that converts light into work**: the polymer would stretch according to the wavelength of light shining on it and be able to push an object. /051002/2.html
- As the most luminous objects in the universe, **gamma-ray bursts** may provide the means to illuminate dust-shrouded galaxies, which might be obscuring 80 percent of all stars. /043002/2.html
- Researchers have discovered that **implanted electrodes permitted rats' movements to be guided** from afar. Like the cockroaches wired for remote control by Japanese scientists in 1997, the robo-rodents might be useful for search and rescue or for covert surveillance. /050202/2.html

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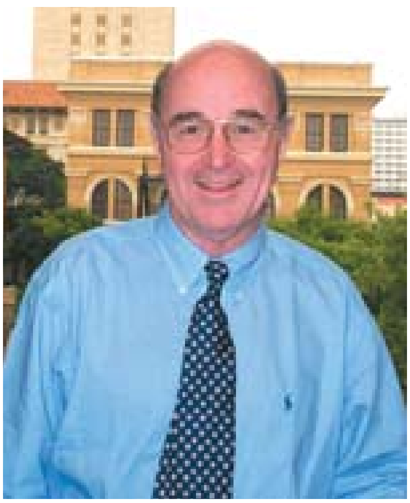
Breaking the Mold

Big-name researchers are moving to commercialize nanomanufacturing By GARY STIX

During the early 1990s IBM investigators decided to explore the capabilities of an atomic-scale imaging device called an atomic-force microscope. They looked for defects in the small holes that represent digital bits on the surface of a CD-ROM. The testing process revealed that the nickel mold that was used to make a CD-ROM had a defect, a tiny bump less than a few hundred nanometers in height. Everyone in the laboratory nicknamed it a zit. C. Grant Willson, a fellow at IBM, marveled at how the mold produced an exact replica of the defect in disk after disk. The metal pimple served as an inspiration of sorts. As he looked at the atomic-force image, Willson mused that this ability to create perfectly formed nanostructures might portend an entirely novel method of making small things.



DEFECT in a mold for making a CD-ROM inspired C. Grant Willson to develop a novel method for nanofabrication.

That insight led him to become one of several pioneers who may turn nanotechnology from hyperbole into technological reality. Willson and other leading researchers at Princeton University, Harvard University and the California Institute of Technology have begun to commercialize molding, stamping, printing and embossing methods reminiscent of children's toys or industrial processes used by automakers. Eventually these endeavors may transform the manufacturing of devices used by the semiconductor, telecommunications and biomedical industries.

For Willson, the path to nanomanufacturing began when he left IBM in 1993 because he disliked the prospect of having to lay off, during a period of corporate upheaval, many of the investigators in a materials research group that he managed. Taking a job at the University of Texas, he ended up collaborating with a mechanical engineering professor, S. V. Sreenivasan, on research directly influenced by his original work on the nanozit.

The researchers developed a manufacturing method that begins by making a bas-relief mold in a quartz plate that contains an indented image of transistors, wires or other components of electronic circuits. The mold is then set down atop a layer of a liquid monomer on the surface of a chip. The liquid fills the recesses of the mold before an ultraviolet light shines through the quartz to harden the liquid into a polymer. The chip is then subjected to further finishing steps. Features in the circuits produced by what is called step-and-flash imprint lithography can be as small as five nanometers, the size of some molecules. "It's like the first printing press, like Gutenberg," Willson notes. "I would never have thought you could mold something that small."

Last year Willson and Sreenivasan convinced veteran entrepreneur Norman E. Schumaker, who had previously founded a successful semiconductor equipment manufacturer, Emcore, to head a start-up, Molecular Imprints, to commercialize the technique. By year's end Molecular Imprints expects to deliver the first step-and-flash machines for testing and research to customers in the semiconductor industry—potentially including Motorola and KLA-Tencor, which have also invested in the start-up.

Semiconductor companies have put money into Molecular Imprints to hedge their bets. The industry would dearly like to dismiss step-and-flash as an interesting academic exercise, opting instead for the status quo. Advanced forms of conventional lithography will make circuits by exposing a photosensitive chemical, termed a resist, to very short wavelengths of ultraviolet light. But the growing cost of this latter approach may still favor step-and-flash. A world-renowned materials researcher, Willson plays both sides of the fence. Work in his laboratory also targets polymer resists for

H. V. TRAN

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advanced optical lithography. So he knows intimately the "frightening" challenges that remain: optical resists require a whole new set of untested materials. But it doesn't really matter to Willson which approach prevails. "My job is to produce students," he says. "Both projects are wonderful for producing students."

Stephen Y. Chou has spent his career extending miniaturization to its limits. Before the word "nanotechnology" came into widespread usage, he was building "submicron structures." Beginning in the 1980s he established records for crafting the smallest transistors, for creating transistors that switch on and off using a single electron, for building magnetic storage devices from "nanopillars" and for fashioning optical networking elements smaller than the wavelength of light. "For me, the most important thing was to break the length-scale limit," says Chou, who got his undergraduate degree from the University of Science and Technology in Beijing and a doctorate from the Massachusetts Institute of Technology before going on to an academic career at Stanford University, the University of Minnesota and now Princeton.

In the early 1990s he would present his work at conferences and have to field questions constantly about commercializing the technology. Making a device feature smaller than the wavelength of light using the optical lithography employed in chipmaking is exceedingly difficult—it resembles trying to draw a very thin line with the point of a very blunt crayon. Like Willson, Chou set about exploring methods for fabricating devices that do not depend on optical radiation. Throughout the decade Chou, with backing from federal agencies, developed a manufacturing process for subwavelength nanostructures, elements smaller than about 200 nanometers. In the past three years Chou has pioneered early commercial uses for nanomanufacturing with a molding technique similar to Willson's to make subwavelength optical devices. Rather than using ultraviolet light to cure a polymer, as Willson does, Chou heats the material until it flows into the mold; it hardens on cooling. That mold can then pattern structures on the surface of a chip.

Chou's company, NanoOpto, aims to integrate optical components on a chip, as if it were a memory chip or microprocessor. Instead of creating transistors and resistors, the firm will produce devices such as filters, waveguides and the cavities for a laser. The manufacturing process, nanoimprint lithography, holds the promise of automating the making of optical components that, until recent years, often required costly hand assembly. Fabricating these components in large batches could bring down the prices of the amplifiers, switches, lasers and the larger systems in which they are incorporated.

Moreover, subwavelength components can improve network performance. "You can bend light in ways that are impossible using classical optical elements," Chou says. NanoOpto, which has built a manufacturing plant in Somerset, N.J., has delivered to major telecommunications customers test samples of discrete devices that polarize, combine or split light beams. Because of the unique properties of the nanostructures—the smallest features that process light boast 20-nanometer dimensions—a combiner can merge light beams that enter the device at widely varying angles. The relaxed tolerance means that the combiner does not have to be carefully aligned with an adjoining optical fiber by hand, thereby enabling cost-saving automated assembly by robots.

Chou's company put together a management team consisting of former executives from Lucent Technologies, Sun Microsystems and Agere Systems. It has also served as an employment agency for Chou's graduate students: five now labor at the company. For the moment, NanoOpto must contend with a serious depression in the market for optical-networking equipment, although it has continued to receive modest venture financing. Another company set up by Chou, Nanonex, will focus on supplying customers with commercial tools for performing nanoimprint lithography.

MR. SMALL, Stephen Y. Chou, was spurred by basic research to create a process for nanomanufacturing.

DENISE APPLEWHITE

Nanomanufacturing is a technological platform that can fabricate a vast array of miniaturized components. "The challenge is to make a lot of the right decisions about what products represent the right opportunity," says Barry J. Weinbaum, NanoOpto's president and chief executive. "What companies should we partner with, and which companies are going to make it in the marketplace?" A nano misstep could turn into a large and potentially fatal error. SA

Next month Innovations will focus on researchers involved in soft lithography, a process capable of building microstructures or nanostructures.

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Legal Circumvention

Molecular switches provide a route around existing gene patents   By GARY STIX

Since 1980 the U.S. Patent and Trademark Office has granted patents on more than 20,000 genes or gene-related molecules. This thicket of intellectual property can make it difficult to develop biotechnologies without bumping up against patents held by others. In response, a number of companies have devised ingenious technological means of getting around such IP hurdles.

To obtain a patent, one of the things an inventor must prove is that a creation is truly novel. Genes, proteins, kidneys and all endogenous living tissue in its natural form do not meet that criterion. "A basic tenet of patent law is that you can't patent something as it is found in nature," says Kathleen Madden Williams, an attorney with the Boston law firm of Palmer and Dodge. "It has to encompass something new." The genomics gold rush revolves around genes that have been isolated and purified outside an animal, plant or microorganism. But turning on a gene to make a protein while the DNA is still lodged inside the body—or in the nucleus of a cell in a laboratory dish—would allow someone to avoid infringing a patent.

A few biotechnology companies, each using a different method, have helped partners doing research on drug candidates to switch patented genes on while in the body or a cell. Of its 25 deals with pharmaceutical and biotechnology companies, Sangamo BioSciences in Richmond, Calif., has made about a fourth of them to bypass patent restrictions by using its "zinc finger protein" transcription factors, proteins that turn genes on and off. "These collaborations were driven largely by intellectual property," says Edward O. Lanphier II, Sangamo's president and chief executive. Similarly, Athersys in Cleveland has crafted about a third of its 12 collaborations to assist partners in working around existing patents with a technique that inserts pieces of DNA into cells to turn on genes randomly and then screen for the protein of interest.

Endogenous gene activation is most lucrative if it does more than just let companies do research on drug candidates and actually serves to create close knockoffs of protein-based drugs without violating a competitor's patent. The pitfalls of this approach were highlighted in January of last year, when a federal district court in Boston ruled that Transkaryotic Therapies (TKT) in neighboring Cambridge had infringed patents of Amgen in Thousand Oaks, Calif., on an anti-anemia drug based on the protein erythropoietin (EPO). TKT had used a type of DNA gene switch to make EPO. But to administer the protein therapeutically, TKT would have had to purify the protein from the cell line in which it was produced, one of the actions that were judged to infringe Amgen patents.

Increasingly, as with Amgen's intellectual property, companies patent not only a gene but the protein made by the gene. Again, technological fixes may help. Sangamo's zinc finger protein switches, for instance, can be given directly to a patient: the zinc finger can turn on a gene that expresses a protein inside the body to alleviate a disease state—no purification step to remove the protein from a cell is required.

As for the TKT technology, not all patent estates are as extensive as Amgen's on EPO. Last year TKT defended itself successfully against a lawsuit that charged it with violating a patent licensed exclusively to Genzyme, also in Cambridge, for a method of making a drug to treat Fabry's disease, a rare fat storage disorder. Both the Amgen and the Genzyme cases have been appealed. But no matter what the outcome, the gene-switch companies are proving that however dense the intellectual-property thicket becomes, someone will find a way to crawl through it if the incentives are sufficient. SA

JOHN McFAUL

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Vox Populi

The voice of the people reveals why evolution remains controversial By MICHAEL SHERMER

There is no more contentious subject in science today than evolution. This fact was brought to light for me in the overwhelming response to my February column on evolution and "intelligent design" creationism. I typically receive about a dozen letters a month, but for this one no less than 134 were submitted (117 men, four women and 13 whose identity was not revealed). I found reading the critical letters mildly disconcerting until I hit on the idea that these are a form of data to be mined for additional information on what people believe and why. Conducting a content analysis of all 134 letters, I discovered patterns within the cacophonous chaos. First I read them quickly and then separated them into about two dozen one-line categories that summed up the reader's main point. I next condensed these into six taxonomic classes and reread all the letters carefully, placing each into one or more of the six (for a total of 163).

Excerpts from the letters illustrate each taxon. Not surprisingly, only 7 percent agreed on the veracity of evolution (and the emptiness of creationism). Nearly double that number, 12 percent, argued that evolution is God's method of creating life. For instance, one correspondent concurred "that evolution is right—but still I see God in the will and cunning intention in the genetic system of all living organisms and in the system and order present in the laws of nature. Seeing all the diversity in the methods of camouflage in animals and plants for an example, I know that there is a will behind it."

The 16 percent that fell into the third taxon—critics of evolution—hauled out an old canard that every evolutionary biologist has heard: "I want to point out that evolution is only a theory." And: "To my knowledge, evolution is just a theory that has never been put to the test successfully and is far from being conclusive."

That evolution requires faith to believe (the fourth class, an opinion held by 17 percent of the writers) found many adherents, such as this one: "In his zeal to defend his faith in evolutionary theory, Shermer violates those standards." Another echoed a refrain we hear often at *Skeptic* magazine about misplaced skepticism: "I applaud your skepticism when it comes to creationism and astrology and psychic phenomena, but how can you be so thickheaded when it comes to the glaring weaknesses of Darwinian evolution? Honestly, you come across as both a brainwashed apologist and a high school cheerleader for Darwinian evolution."

The penultimate taxon (at 23 percent) held that intelligent-design creationism must be true because life is simply too complex to be explained by evolution. For example: "ID theorists also see a variety of factors, constants and relationships in the construction of the universe that are so keenly well adjusted to the existence of matter and life that they find it impossible to deny the implication of intelligent purpose in those factors."

With evolution, we face the ultimate question of genesis and exodus.

Intriguingly, the greatest number of responses, 25 percent, fell into a noncommittal position in which the readers presented their own theories of evolution and creation: "Evolution is not a theory. It is an analytic approach. There are three elements of science: operation, observation and model. An observation is the result of applying an operation, and a model is chosen for its utility in explaining, predicting and controlling observations, balanced against the cost of using it." And: "There is nothing that scientists have ever discovered, or could ever discover, that can prove or disprove the existence of God. Thus, there is no conflict between the Bible and science when each is kept in its proper place."

In my experience, correspondents in this final classification are more intent on launching their own ideas into the cultural ether than responding to the column in question itself. With no subject is this as apparent as it is with evolution; it is here we confront the ultimate question of genesis and exodus: Where did we come from and where are we going? No matter how you answer that question, facing it with courage and intellectual honesty will bring you closer to the creation itself. SA

Michael Shermer is publisher of Skeptic *magazine (www.skeptic.com) and author of* In Darwin's Shadow: The Life and Science of Alfred Russel Wallace.

BRAD HINES

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Keeping the Mad Cows at Bay

Veterinarian Linda A. Detwiler helps to ensure that a fatal brain disease that can afflict humans doesn't appear in U.S. cattle. It can be a thankless task By PHILIP YAM

Plastic cup in hand, Linda A. Detwiler is ready to begin. "Hold its nose, and usually it urinates," she explains of sheep. The flock's burly owner, Dick Sisco, tucks the head of a recalcitrant 200-pound lamb under one arm and clasps its muzzle with both hands. Almost immediately, the translucent sample container fills about a quarter of the way. "I didn't think it was going to be that easy," Detwiler remarks. As senior staff veterinarian for the U.S. Department of Agriculture's Animal and Plant Health Inspection Service (APHIS), the 44-year-old Detwiler is collecting urine from certified healthy sheep on a New Jersey farm. The request comes from researchers hoping to create a urine test that can detect the presence of an invariably fatal neurodegenerative disease. In sheep it's called scrapie, because some afflicted ovine scrape themselves raw. In cows it's bovine spongiform encephalopathy (BSE)—mad cow disease.

LINDA A. DETWILER: BSE WATCHER

- Grew up in Middlesex County, N.J., where her family raised hogs on plate waste—leftovers from restaurants and other establishments.
- First USDA job after vet school at Ohio State University: coordinating Ohio's scrapie program in 1985; in charge of BSE surveillance since 1996.
- On her career: "I wouldn't change a thing. Even with the death threats."

Besides roiling economies, BSE threatens human health (unlike foot-and-mouth disease, with which BSE is often confused). It has already doomed about 120 people, in the guise of the brain-wasting variant Creutzfeldt-Jakob disease. The cause seems to be a misfolded prion protein that triggers normal prions in the body to adopt the pathogenic conformation. The U.S. announced its first case in April, a 22-year-old Florida woman who had probably contracted the illness during her U.K. childhood.

BSE emerged in the mid-1980s. Turning docile ruminants into staggering, aggressive beasts, the disease has stricken nearly 200,000 cattle so far, and millions of apparently healthy animals have been slaughtered as a precaution. Modern industrial agriculture unleashed the epidemic: most likely, scrapie-infected sheep meat entered into cattle feed by way of rendering, a process that turns carcasses into feed. The unintended export of contaminated feed spread BSE to the indigenous herds of Japan and most of Europe.

With the U.S. Food and Drug Administration, the USDA moved to protect domestic herds even before BSE was known to pose a hazard to humans. In 1989 the U.S. banned the importation of British cattle. More stringent import rules soon materialized, in addition to regulations governing feed—for instance, protein from ruminants may not be fed back to ruminants (although it may given to pigs, chickens and domestic pets).

The U.S. began BSE surveillance in 1990. In 1996 Detwiler became coordinator of the program, which also keeps tabs on scrapie and the chronic wasting disease spreading among deer and elk out West. (The gen-

PHOTOGRAPHS BY FLYNN LARSEN

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eral term for these conditions is transmissible spongiform encephalopathy, or TSE.) She also provides technical advice to national and international advisory committees. "She's first-rate," states Paul Brown of the National Institutes of Health, who has been studying TSEs since the 1960s. "Whatever she says, you can put it in the bank." Stanley B. Prusiner of the University of California at San Francisco, who won the Nobel prize for developing the prion concept, concurs: "She's A-plus. The American people are lucky to have her."

The federal responses to keep the U.S. BSE-free seem to have paid off. A Harvard University risk assessment concluded last November that the odds are extremely low, even though industry adherence to all the rules has lapsed on occasion. But it also found that at then existing surveillance levels a mad cow could have slipped by unnoticed. So the APHIS has upped annual BSE testing of cattle from 5,000 to 12,500 this year.

"That's still inadequate," asserts Michael K. Hansen of the Consumers Union in Yonkers, N.Y., and a longtime critic of American TSE policy. He and others point to the power of the \$56-billion cattle industry and the economic hit BSE would cause, suggesting that it is neither economically nor politically expedient to discover the disease. (Japan's first three BSE cases have reportedly cost the country \$2.76 billion.) "It's almost a 'don't look, don't find'" attitude, he remarks. Hansen cites the European approach of mass screenings of hundreds of thousands to millions of cattle annually as an example of a sounder way. (In a few European countries, BSE occurs at an annual rate of one or two per million cattle over two years of age.)

Surveillance is more than a numbers game, Detwiler says: "It depends on the population you're testing and how good your rate of return is." The U.S. focuses on the highest-risk animals: neurologically ill and nonambulatory ("downer") cows, in which most BSE cases occur. The U.S. has about 200,000 downer cows every year, "and if you test 12,500 out of that population, you should be able to detect it at that rate of one per million," Detwiler states. Moreover, Europe has a different reason for testing. Whereas the U.S. simply wants to see if BSE has arrived, European nations know they have it and test "to pull more animals out of the food chain," she explains.

Testing animals at slaughter might be pointless anyway. BSE typically incubates for four to five years, and most infections are not detectable until cattle are older than 32 months—far longer than the usual age of slaughter (88 percent are killed before 18 months). Other countries have fallen into the trap of testing very young animals that almost certainly will come up negative in order to bolster their overall numbers, Detwiler notes. "It would be a disservice to the public for us to test millions of animals where we'd be unlikely to find it, to do it just as a feel-good," she adds. "Testing doesn't buy you protection." None of the thousands of brains examined since testing began have revealed any evidence of a TSE-like disease in cattle.

Despite the current low risk, the U.S. is considering additional measures. One rule would ban a slaughterhouse stunning method that injects air into a cow's brain—the air pressure can send bits of brain (the organ, along with the spinal cord, with the most infectivity) into kidneys, lungs and other parts not classified as risky. The USDA is mulling whether to prohibit as food the distal ileum, a part of the intestine that can be sold as a "variety meat." The distal ileum is the only organ that shows infectivity in young, presymptomatic cattle. The U.K. itself destroys it.

ON THE FARM: Detwiler collects sheep urine for a possible new scrapie test.

Detwiler and her colleagues are also deciding on various "rapid tests" that might be practical for the U.S. A big advance would be a test that works without the need for brain tissue—which is why researchers are excited about the reported detection of prion protein in urine. The samples from the scrapie-free Sisco sheep farm will serve as the negative controls.

If a mad cow shows up on American soil, Detwiler will most likely be the lightning rod for angry charges, as she was last year when the APHIS "depopulated" two sheep flocks in Vermont. The forebears of those sheep were imported from Belgium and the Netherlands and may have consumed tainted feed. The sheep were euthanized and their carcasses dissolved in boiling lye. Barn surfaces and implements were disinfected with sodium hypochlorite or incinerated, and the pastures have been put off limits for five years to allow residual infectivity to diminish.

The USDA actions led to complaints of government strong-arming. Still, even with placards denouncing "Dr. Deathwiler" and threatening phone messages, Detwiler describes the controversy calmly. She says she patiently took the time to explain the reasons to concerned citizens who called her. She was surprised, however, by the criticism in the press. "I said to reporters, 'You're critical of the government about not doing enough for BSE, and here we are trying to take a preventive measure,'" Detwiler remarks. "Scientifically, to me, it's a big risk to let these sheep go," where they might introduce new scrapie strains. (Two of the sheep did test positive.)

Despite the heat her job can bring, Detwiler has no regrets. She had doubts about a USDA career at first "because I heard from the outside that only slackers work for the government." But her tenure has proved worthwhile, she believes: "To look at the committees that I served on and the people I worked with, we did enact certain things at certain times that, I think, have been important to keep the risk low." SA

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SUGAR BIOTECH SUCCESS: Aranesp, an improved version of an existing anemia-fighting drug, has been on the market for almost a year. Two sugar chains added to the original drug molecule give Aranesp longer staying power in the body.

Sweet medicines

Sugars play critical roles in many cellular functions and in disease. Study of those activities lags behind research into genes and proteins but is beginning to heat up. The discoveries promise to yield a new generation of drug therapies

By Thomas Maeder

RANDI BEREZ

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Now that the human genome has been deciphered, much of the fanfare surrounding it has transferred to the proteome, the full complement of proteins made from the genetic "blueprints" stored in our cells. Proteins, after all, carry out most of the work in the body, and an understanding of how they behave, the press releases say, should translate into a font of ideas for curing all manner of ills. Yet living cells are more than genes and proteins. Two other major classes of molecules—carbohydrates (simple and complex sugars) and lipids (fats)—play profound roles in the body as well. These substances, too, need to be considered if scientists are to truly understand how the human machine operates and how to correct its maladies.

Sugars in particular perform an astonishing range of jobs. Once regarded mainly as energy-yielding molecules (glucose and glycogen) and as structural elements, they are now known to combine with proteins and fats on cell surfaces and, so situated, to influence cell-to-cell communication, the functioning of the immune system, the ability of various infectious agents to make us sick, and the progression of cancer. They also help to distinguish one cell from another and to direct the trafficking of mobile cells throughout the body, among other tasks. So ubiquitous are these molecules that cells appear to other cells and to the immune system as sugarcoated.

Recognizing the importance of sugars in health and disease, increasing numbers of researchers in academia and the biotechnology industry have recently stepped up efforts to learn the details of their structures and activities and to translate those findings into new therapeutic agents. These pioneers have also gained support from the federal government. In October 2001 the National Institutes of Health awarded a five-year, $34-million "glue" grant to the Consortium for Functional Glycomics, a group of 54 investigators around the world who aim to coordinate and facilitate research in the area, such as by developing a library of synthetic sugar chains and a structural database available to all. The grant, says James C. Paulson of the Scripps Research Institute in La Jolla, Calif., the consortium's principal investigator, is "a vote of confidence" in the field.

Overview/*Sugars*

- Sugars modify many proteins and fats on cell surfaces and participate in such biological processes as immunity and cell-to-cell communication. They also play a part in a range of diseases, from viral infections to cancer.
- Scientists are finally overcoming the obstacles impeding efforts to decipher the structures of complex sugars and to synthesize sugars for use in research and as drugs.
- The advances are leading to new medicines for a variety of ills.

Clearing Roadblocks

THE WORDS "functional glycomics" in the consortium's title announce that the research complements more ballyhooed efforts to catalogue human genes and proteins (genomics and proteomics), decipher their functions and open broad new fields of applied biology. The term "glycomics" derives from "glycobiology," which Raymond A. Dwek of the University of Oxford coined in 1988. Until then, carbohydrate research was spoken of as the science of oligosaccharides (chains of sugars), vocabulary that lay interviewers and even some scientists had trouble pronouncing. In chemistry, the prefix "glyco" refers to sweetness or sugar.

It is easy to see why observers might feel daunted by all the terms that carbohydrate researchers throw around. Simple sugars—such as glucose and sucrose (table sugar), which consist of some carbon atoms, oxygen and hydrogen—are often referred to as monosaccharides, disaccharides and so on, depending on how many sugar units they contain. The term "oligosaccharide" typically refers to larger chains, whereas *really* big molecules are called polysaccharides. And molecules formed by the pairing of carbohydrates with proteins or fats are known as glycoconjugates or, more specifically, as glycoproteins and glycolipids. And that's just Sugar 101.

Scientists of the past did not neglect sugars from lack of interest. They were stymied by a dearth of tools for deciphering the structure of complex versions and for synthesizing such molecules readily, reproducibly and in the amounts needed for study or for formulation as drugs.

The problems stemmed, in large part, from the extraordinary structural variability of sugars. The four nucleotides that make up DNA, and the 20 common amino acids that form proteins, link together in linear fashion like beads on a string, always joined by the same chemical connection. In contrast, the roughly 10

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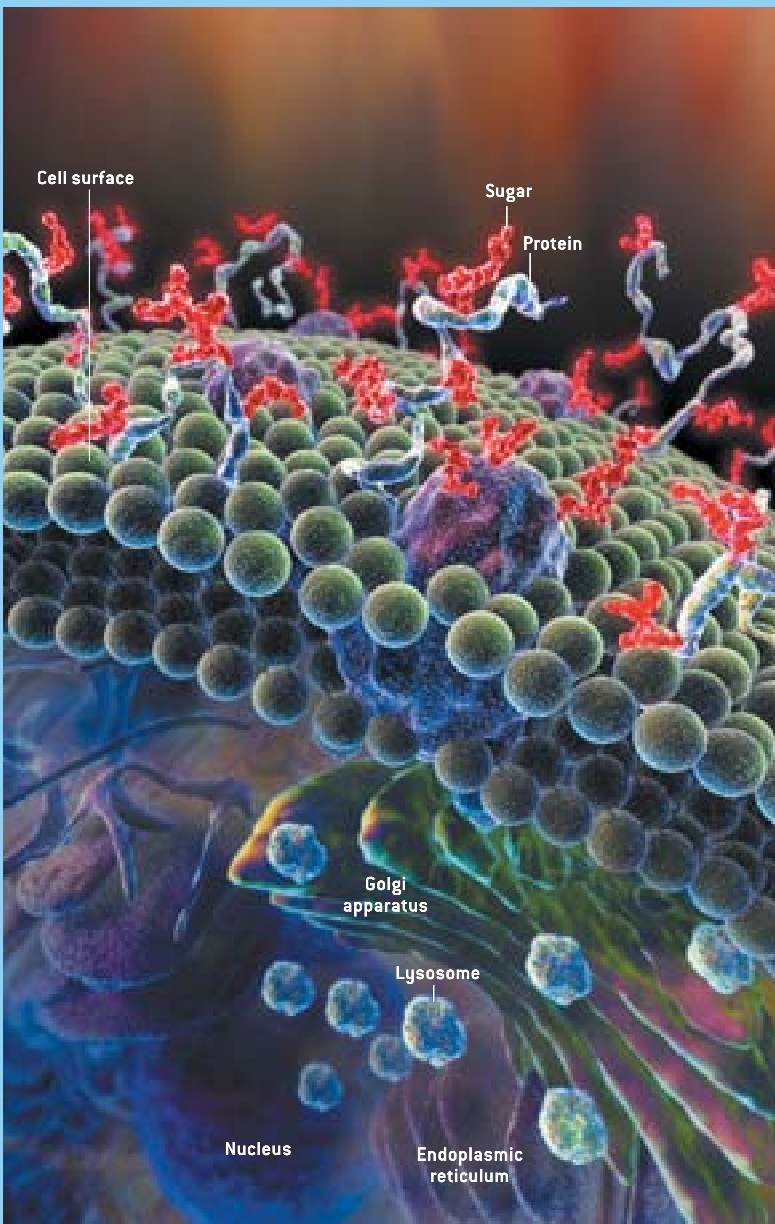
Glyco Drugs at Work

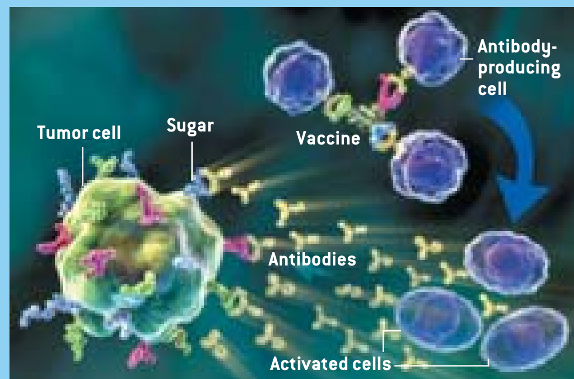
SUGARS DECORATE many proteins and lipids (fats) on the surfaces of cells (*below*). Cells add the sugars through enzymatic reactions carried out in compartments called the endoplasmic reticulum and the Golgi apparatus, and they break down sugared molecules (glycoconjugates) in structures known as lysosomes. The figures at right and bottom depict some of the therapeutic ideas that have emerged from insights into the structure, function and processing of carbohydrates in the body.



TREATMENT APPROACHES

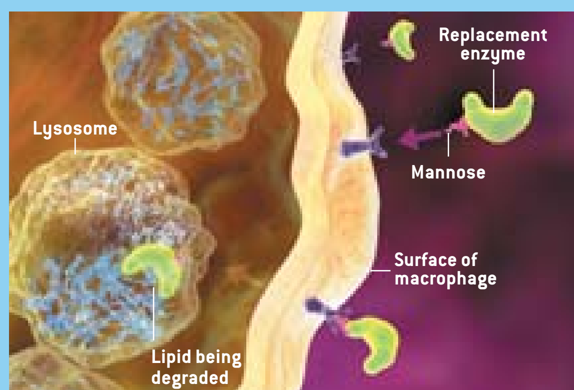
Combating Cancer

Tumor cells often display unusual versions of sugars. One proposed treatment (*below*) would incorporate those sugars in a vaccine. This vaccine would induce the immune system to produce antibodies able to recognize the selected sugars on cancer cells and would thus facilitate the cells' destruction.



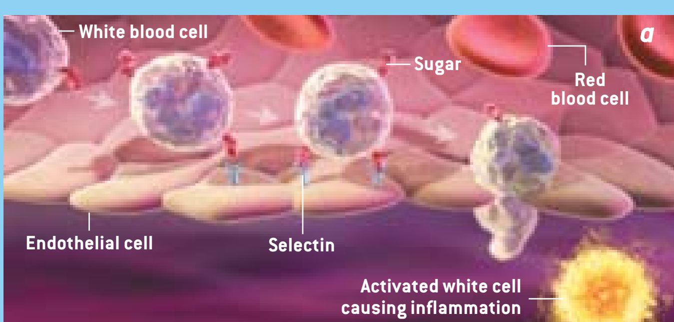
Easing Lysosomal Storage Diseases

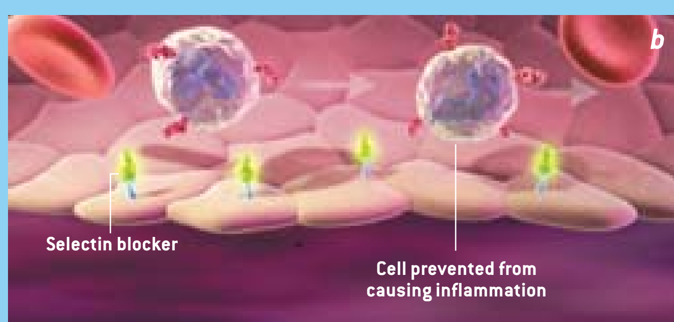
Many inherited disorders arise because some enzyme needed to break down sugar-bearing lipids in lysosomes is defective. A drug for Gaucher's disease (*below*) consists of a replacement enzyme that has been modified to display the sugar mannose, which guides the enzyme to macrophages, cells sorely affected by the lack of a functional enzyme.



Interfering with Inflammation

Inflammation occurs when white blood cells invade tissues (*below, a*). To leave the blood, the cells first bind through a sugar to molecules called selectins on the endothelial cells that line blood vessel walls. Anti-inflammatory drugs under study aim to prevent the white cells from binding to selectins (*b*).





JEFF JOHNSON *Hybrid Medical Animation*

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Sugar-Taming Technologies

Technical breakthroughs are laying the groundwork for the development of new drugs that consist of or act on sugars

ADVANCES IN SEQUENCING and data processing have driven some of the most significant breakthroughs in recent biomedical science. Such advances could be especially energizing to the emerging field of glycomics. As drug developers learn more about the structure and function of complex sugars and about how to control their synthesis, they are also uncovering fresh ideas for treating disorders that involve sugars.

Straightforward sequencing of the type common with linear gene or protein sequences, in which subunits are enzymatically lopped off and identified one at a time, is impossible with huge, complex branching sugars, which require every trunk, branch and twig to be tracked. Instead Ram Sasisekharan of the Massachusetts Institute of Technology and his colleagues work simultaneously from the global toward the specific and from the particular to the more general, bracketing an answer in the middle. First they determine a target molecule's size and use a computer algorithm to generate a master list of the vast number of theoretically possible sequences, including those of each fork and branch in nonlinear structures. They then rule out many of these possibilities, for example, by running tests that reveal which monosaccharides (one-unit sugars) are present in what relative proportions or by examining the molecule's susceptibility to enzymes that cleave linkages between specific units or at particular branch points.

"Once you have the exhaustive tool kit, it's not that complicated," says Ganesh Venkataraman of M.I.T. Each successive constraint shrinks and refines the originally unwieldy universe of possibilities into something a little more manageable. "You go back to the database, put in the answers and eliminate everything that doesn't satisfy [the constraints]. It's like those puzzles where seven people are at a table, and you have clues about who does or does not sit next to whom and have to figure out the seating arrangement."

The reciprocal problem of constructing sugars has similarly enjoyed significant progress only recently. Proteins are read from a genetic "blueprint" that can be used to generate limitless copies. No blueprint exists for sugars. Different enzymes must operate in series to build complex sugar chains (oligosaccharides). When the needed enzymes are available in nature, they can be used to link specific building blocks efficiently and in the desired orientation. But if scientists do not have such enzymes, they have to find alternative, more laborious ways to construct the structures.

M.I.T.'s Peter H. Seeberger and his co-workers have developed a method of oligosaccharide assembly analogous to an approach devised by R. Bruce Merrifield of the Rockefeller University for protein synthesis. Sugars join at sites where they have an OH (hydroxyl) group. So the scientists begin by anchoring one monosaccharide to a polymer bead and masking all the hydroxyl groups except the one meant to form a link. Then they expose the first sugar to a second, partly masked one and allow the two to interact. Next they unmask a new OH site and repeat the process, adding one new sugar at a time. Most linkages and branches can now be made very reliably, although the process is not yet as simple as the routine automated synthesis of peptides and DNA molecules. The largest sugars produced in Seeberger's laboratory to date are 12 units long and take 16 hours to make. Fortunately, a good number of important sugars, including those that help to distinguish one cell surface from another, fall within this range. Longer molecules can be cobbled together from smaller modular units.

RAM SASISEKHARAN sits by a sophisticated sugar-sequencing unit. After enzymes chop up a complex sugar, advanced high-pressure liquid-chromatography equipment (*on cart*) sorts the resulting fragments, and a mass spectrometer (*right*) characterizes the building blocks in the separated pieces. Computers analyze the results from both procedures to arrive at the full sequence of simple sugars in the complex molecule.

An alternative, "one-pot" synthetic method requires more careful advance planning but has simpler execution. A single reaction chamber is filled with all the needed ingredients at once, and a preprogrammed reaction sequence is determined by the degree of reactivity of differently protected sugars. The most reactive form bonds first and the least reactive last, and thus the order of reaction strengths determines the sequence of the final molecule.

Glycomics researchers are also perfecting methods for learning about the various functions of a sugar. Often this effort involves producing animals that have a defective or missing sugar—say, by genetically altering the biological pathways involved in sugar synthesis or by delivering abnormal monosaccharides that inhibit sugar-processing enzymes or disrupt interactions between normal sugars and other kinds of molecules. By observing what goes wrong when a sugar is faulty or missing, researchers obtain clues to the molecule's usual activities.

"Sugars used to be a nuisance, because the technology to understand them wasn't there," Sasisekharan says. Now they are considered an opportunity. *—T.M.*

RANDI BEREZ

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(depending on who's counting) simple sugars common in mammalian carbohydrates can join with one another at many different points and can form intricate branching structures. Moreover, two linked units do not always orient in the same way: sometimes a building block will point up relative to the other unit, and sometimes it will point down. The four nucleotides in the DNA "alphabet" can combine to produce 256 different four-unit structures, and the 20 amino acids in proteins can yield about 16,000 four-unit configurations. But the simplest sugars in the body can theoretically assemble into more than 15 million four-component arrangements. Although not all these combinations occur in nature, the possibilities remain overwhelming.

Determining the sequences of the building blocks in complex sugars and producing such sugars remain challenging, but scientists have devised ingenious methods that make these tasks more feasible [*see box on opposite page*]. Progress in glycomics, even more than in genomics, will be driven by advances in molecular sequencing technology and bioinformatics (the cyber-methods that bring order to massive amounts of sequence data).

A number of investigators are taking aim at infectious diseases, an arena in which sugar-related drugs have already had some dramatic success.

Better Already

AT THE SIMPLEST LEVEL, better understanding and control of sugars can improve existing therapies. Heparin, an anticoagulant sugar chain administered to prevent blood clots from forming during surgery, is the most conspicuous example. It is among the top-selling drugs in the world and has been used since the mid-1930s. Yet most commercial preparations, extracted from pig intestinal lining, are a heterogeneous and poorly characterized mix of compounds between 200 and 250 monosaccharide units long. Heparin's potency and potential for unwanted side effects vary not only from manufacturer to manufacturer but from one lot to the next, so that it must be empirically checked on a batch-by-batch basis.

Pharmaceutical makers today sell smaller, low-molecular-weight versions of the heparin molecule that, trimmed of many parts not needed for the drug's activity, produce fewer side effects. But as with the larger molecule, the manufacturers have difficulty making homogeneous batches. In 2000 Ram Sasisekharan and his colleagues at the Massachusetts Institute of Technology applied tools they developed to decipher the sequence of heparin's entire active site, the region responsible for the compound's biological activity. This information is now guiding efforts to synthesize potent low-molecular-weight heparins more reliably and to tailor their pharmacological properties for specific applications.

Enhanced control of sugars should likewise improve the effectiveness of proteins made by recombinant DNA technology. To work effectively, certain therapeutic proteins must have particular sugars attached to them at precise spots. Current technology is not always up to the task. Take the recombinant drug erythropoietin, delivered to stimulate red blood cell production in patients who have anemia or who are undergoing kidney dialysis. For years one company, Amgen, discarded 80 percent of the drug it generated because of inadequate glycosylation, which results in too rapid clearing from the blood. Then the company found a way to add two extra sugars to those normally found on erythropoietin. This newer version, sold as Aranesp, stays in the blood much longer than the original drug and thus requires less frequent dosing.

Beyond improving existing drugs, pharmaceutical developers are studying sugars to develop innovative therapies for a variety of disorders. Sometimes these treatments might consist of sugars or glycoconjugates themselves; other times they might consist of molecules that influence interactions between sugars and other molecules, including interactions with enzymes (biological catalysts) that control the synthesis or breakdown of sugar-bearing molecules.

Scotching Infections

A NUMBER OF investigators are taking aim at infectious diseases, an arena in which sugar-related drugs have already had some dramatic success. A sterling representative is the vaccine that targets *Hemophilus influenzae* type b (Hib). This vaccine has freed much of the world from the sometimes deadly meningitis caused by Hib. By presenting a sugar from the bacterium to the immune system, the vaccine primes the system to destroy the microbe swiftly once it enters the body. An early version consisting of just a sugar chain from Hib proved disappointing. But highly effective glycoconjugate preparations, in which the sugar is joined to a protein that boosts immune responsiveness, have been available since the late 1980s. Other glycoconjugate vaccines for infectious diseases—including one meant to ward off hard-to-treat *Staphylococcus aureus* infections in certain hospitalized patients—are under study.

Various disease-causing organisms, or pathogens, use carbohydrates to recognize and interact with their preferred host cells, and both existing and proposed drugs enlist sugars or sugar mimics to block such contact. The influenza virus, for example, enters the cells it infects by first docking with a sugar (sialic acid) that protrudes from glycoproteins on the cell surface. Attachment to the sugar essentially turns a key that opens cell "doors," freeing the virus to penetrate cells and to replicate within them. When newly formed viruses then bud from the cell, they can be trapped by the same sugar and must de-

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ploy an enzyme called neuraminidase to snip the sugar and free themselves. Two marketed drugs, Tamiflu and Relenza, shorten the duration of the flu by binding tightly to the enzyme's active site, thereby preventing it from acting on sialic acid. With the neuraminidase enzyme shackled, the virus has difficulty spreading to and infecting other cells.

In the case of the influenza virus, the drug essentially outcompetes the true sugar, winning access to the enzyme and inhibiting its activity—a phenomenon known as competitive inhibition. Competitive inhibition by synthetic analogues of problem sugars might fight other infectious diseases as well. Notably, the bacterium *Helicobacter pylori,* which causes stomach ulcers and inflammation, gains a foothold in the body by attaching to a sugar on the surface of the cells that line the stomach. And the bacterium *Shigella dysenteriae,* which causes deadly diarrheal epidemics, produces a toxin that binds to a sugar on intestinal cells. Sugar mimics that act as decoys, binding to *H. pylori* or to the *S. dysenteriae* toxin in ways that prevent docking with cells, are showing promise in laboratory tests.

Drug researchers are pursuing a similar strategy against septic shock (an often fatal shutdown of the circulation) caused by gram-negative bacteria. (Bacteria are termed "gram-positive" or "gram-negative" based on their reaction to a particular stain.) Shock sets in when the bacteria die—frequently in response to antibiotic treatment—and release a glycolipid, lipid A, into the bloodstream, eliciting a disastrous inflammatory response. Delivery of a lipid A analogue that cannot incite a strong immune response might reduce or eliminate shock by acting as a decoy to keep immune system cells away from the real lipid A in the body. Investigators have reason to believe that such analogues could also limit bacterial replication and production of lipid A.

Almost all infectious diseases are caused by bacteria, viruses, fungi or parasites. But in some brain disorders, such as Creutzfeldt-Jakob disease (a relative of mad cow disease), misfolded proteins known as prions are thought to be the infectious agents. Research by John Collinge of St. Mary's Hospital in London suggests that the troublesome hardiness of prions has to do with improper glycosylation of the proteins, which are unusually resistant to enzymatic degradation. Deciphering the precise role of the sugars may lead to ideas for counteracting these mysterious infections.

Restoring Balance

SUGAR-BASED DRUGS could have a role in fighting an array of noninfectious disorders as well, among them conditions marked by excess inflammation. After wounding or infection, endothelial cells that line blood vessels begin to display large numbers of carbohydrate-binding proteins called selectins. Selectins on endothelial cells bind loosely to a specific carbohydrate called sialyl Lewis x on the surface of circulating white blood cells of the immune system. Like a tennis ball rolling across a strip of Velcro, the white blood cells tumble along the vessel wall and slow down enough to migrate across the wall into injured tissue, where they set about containing the threat. That response is important for preserving health but can cause illness if it becomes chronic or excessive. Substances that interfere with contact between sialyl Lewis x and selectins are now under develop-

Once and Future Therapies

A SAMPLING of the sugar-related drugs on the market or in development is listed below. Some are glycoconjugates, consisting of sugars paired with peptides (short chains of amino acids), proteins (longer sequences of amino acids) or lipids (fats).

DRUG	DESCRIPTION	MAKER	STAGE OF CLINICAL TESTING
CEREZYME (imiglucerase)	Glycolipid-degrading enzyme; compensates for the enzyme deficiency responsible for Gaucher's disease	GENZYME *Cambridge, Mass.*	On the market
VANCOCIN (vancomycin)	Glycopeptide antibiotic often used against antibiotic-resistant infections; inhibits the production of a sugary component (peptidoglycan) of the bacterial wall	ELI LILLY *Indianapolis*	On the market
VEVESCA (OGT 918)	Sugar mimic; aims to reduce the synthesis of the glycolipid that accumulates in Gaucher's disease	OXFORD GLYCOSCIENCES *Abingdon, England*	U.S. regulators are reviewing data from phase III trials (large studies of efficacy)
GMK VACCINE	Vaccine containing the sugar ganglioside GM2; designed to trigger an immune response against cancer cells bearing GM2	PROGENICS PHARMACEUTICALS *Tarrytown, N.Y.*	In phase III trials for melanoma
STAPHVAX	Vaccine containing a bacterial sugar coupled to a protein; meant to prevent hospital-acquired *Staphylococcus* infections	NABI BIOPHARMACEUTICALS *Boca Raton, Fla.*	In phase III trials for patients with kidney disease
BIMOSIAMOSE (TBC1269)	Sugar mimic; aims to stop selectins (sugar-binding molecules) on blood vessel walls from promoting inflammation	TEXAS BIOTECHNOLOGY *Houston*	In phase II (relatively small) trials for asthma and psoriasis
GCS-100	Sugar that interferes with the action of a sugar-binding protein on tumors	GLYCOGENESYS *Boston*	In phase II trials for pancreatic and colorectal cancers
GD0039 (swainsonine)	Sugar mimic that blocks production of carbohydrates important to cancer's spread in the body (metastasis)	GLYCODESIGN *Toronto*	In phase II trials for kidney cancer
PI-88	Sugar that inhibits growth factors responsible for angiogenesis (new blood vessel formation) and interferes with an enzyme involved in metastasis	PROGEN *Darra, Australia*	In phase II trials for multiple myeloma (a blood cancer); in phase I/II (safety and efficacy) trials for melanoma
UT231B	Sugar mimic that hampers the hepatitis C virus from infecting cells	UNITED THERAPEUTICS *Silver Spring, Md.*	Phase I (safety) trials have been completed

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ment as potential anti-inflammatory drugs.

Researchers are also exploring several sugar-related strategies for fighting cancer. For example, malignant cells often display incomplete or abnormal sugars on their surface. Workers are therefore attempting to incorporate such sugars into therapeutic vaccines that would induce the immune system to recognize and destroy cancer cells bearing those sugars.

Sasisekharan's group at M.I.T. recently showed in mice that heparan sulfates, sugars found on normal and malignant cells, can enhance or limit cancer growth depending on how those sugars are cleaved by cellular enzymes. This discovery has led to suggestions of treating cancer by delivering the growth-slowing fragment of the sugar or by delivering some substance that would cause cancer cells themselves to produce a healthier amount of the desirable fragment.

er, enzymes in membrane-bound compartments called lysosomes break up glycolipids and glycoproteins that are no longer useful. In a heartbreaking family of ailments that includes Gaucher's and Tay-Sachs diseases, one lysosomal enzyme or another is defective, leading to a destructive buildup of glycolipids in the body. Certain of these disorders, such as Gaucher's, can be eased these days by delivery of the normal enzyme after the enzyme has been modified to display a sugar that targets it to a specific cell type. In the case of Gaucher's therapy, the sugar mannose directs the glycolipid-degrading enzyme to macrophages, which are especially sensitive to the enzyme's loss.

Enzyme therapy is expensive, however, and must be delivered intravenously, because enzymes are proteins and would be broken down by the digestive tract if taken orally. Moreover, enzymes do not

is currently reviewing the clinical data.

Glycomics research might even lead to advances in the ability to transplant pig organs into people when human versions are in short supply. One obstacle to such cross-species, or xeno-, transplantation is that pig tissue displays a sugar not found on human tissues. That sugar would elicit a swift graft-destroying reaction by the recipient's immune system. This impediment could, in theory, be surmounted in several ways—among them, delivering sugar mimics as decoys and genetically altering pigs so that their enzymes do not give rise to the offending sugar.

Serious problems confront the development of carbohydrate-based drugs, especially ones composed of true sugars. The digestive system generally regards sugars as food, so they would have to be packaged to avoid degradation or injected. In the bloodstream, too, sugars may

Glycomics research might even lead to advances in the ability to transplant pig organs into people when human versions of needed tissues are in short supply.

Cancers usually kill by metastasizing: malignant cells break away from a tumor and plow through connective tissue into the bloodstream. Then they travel through the blood (or lymph) to distant tissues, where they leave the circulation and establish new tumors. One of the molecules that seem to abet such travel is a sugar-binding protein known as galectin-3, which additionally appears to facilitate metastasis by participating in angiogenesis (the formation of new blood vessels) and by helping tumor cells resist signals instructing them to kill themselves. GlycoGenesys, a Boston biotechnology company, is conducting clinical trials with a carbohydrate derived from citrus pectin that attaches to galectin-3 and basically tells tumor cells, "Do not adhere to sugar targets along your metastatic route, do not form new blood vessels, and do allow your self-destruct program to operate."

Cells produce glycoconjugates in a series of steps, during which various enzymes add or remove sugar groups. Later, …

cross from the blood to the brain and so cannot combat damage to nerve cells in the brain. Researchers are therefore trying to limit the glycolipid buildup in these afflictions in another way: by reducing the amount made in the first place—mainly by delivering small compounds, such as sugar mimics, able to inhibit enzymes involved in glycolipid synthesis. One such drug, developed by Oxford GlycoSciences in Abingdon, England, would be taken by mouth and has been shown in human trials to work against Gaucher's disease; the U.S. Food and Drug Administration

be broken down by enzymes, and because carbohydrates often act by binding loosely to many sites rather than by binding tightly to a few, they may need to be given in large quantities. None of these hurdles is insurmountable, however. Meanwhile a growing awareness of the roles that sugars play in the body and improved techniques for sequencing and manipulating them promise to open an entirely new dimension in therapeutics. SA

Thomas Maeder is a science writer based in Pennsylvania.

MORE TO EXPLORE

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Consortium for Functional Genomics: **http://glycomics.scripps.edu**

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AS BUSINESSES adopt free-space optics technology, nearby residents could get affordable access to broadband multimedia services.

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Last Mile by Laser

Short-range infrared lasers could beam advanced broadband multimedia services directly into homes and offices

By Anthony Acampora

Imagine a city water distribution system that doesn't deliver water to buildings and residences because its pipes don't reach far enough. Much the same situation exists for America's high-speed data-transfer network. The multibillion-dollar optical-fiber backbone that was built to bring truly high-performance multimedia services to office and home computers across the nation has come up a bit short—for nine out of 10 U.S. businesses with more than 100 workers, less than a mile short. Despite swelling user demand, the prospect of delay-free Web browsing and data library access, electronic commerce, streaming audio and video, video-on-demand, video teleconferencing, real-time medical imaging transfer, enterprise networking and work-sharing capabilities, as well as numerous business-to-business transactions, still lies just over the horizon—actually, buried under local streets and sidewalks.

Traditional copper wires and coaxial cables connecting buildings to telephone and cable television systems simply do not possess the gigabit-per-second capacity necessary to carry advanced bandwidth-intensive services and applications, whereas optical-fiber bridges needed to connect millions of users to the optical-fiber backbone would cost too much to install (between $100,000 and $500,000 a mile). As a result, only 2 to 5 percent of that nationwide network is being used today.

Although various fiber-free data-transmission technologies, including microwave radio, digital subscriber lines and cable modems, are attempting to span the broadband connectivity gap, free-space optics (FSO)—basically, fiber-optic communications without the fiber—is thought by many experts to have the best chance of succeeding. Newly revived over the past few years after having been invented in the 1970s, FSO relies on low-power infrared laser transceivers that can beam two-way data at gigabit-per-second rates. Small-scale FSO systems have already been installed around the world by several vendors [*see box on page 53*].

The low-power infrared lasers, which operate in an unlicensed electromagnetic-frequency band, either are or can be made to operate in an eye-safe manner. Unfortunately, however, the lasers' limited power restricts their range. Depending on weather conditions, FSO links can extend from a few city blocks to one kilometer—far enough, though, to get broadband traffic from the backbone to many end users and back. Because bad weather—thick fog, mainly—can severely curtail the reach of these

CHIP SIMONS

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line-of-sight devices, each optical transceiver node, or link head, can be set up to communicate with several nearby nodes in a network arrangement. This "mesh topology" would ensure that vast amounts of data can be relayed reliably from central dissemination centers out to entire cities, towns or regions.

Commercially available FSO equipment provides data rates much greater than those of digital subscriber lines or coaxial cables—from 10 megabits to 1.25 gigabits a second, more than enough for most high-end broadband services and applications. Furthermore, state-of-the-art laser diodes already on the market can be turned on and off at speeds that could transmit information at even higher rates—as much as 9.6 gigabits a second. Although this equipment has not yet been adapted for FSO use, such a system would feature optical pulses lasting a mere 100 picoseconds (100 trillionths of a second) each.

Free-space optics systems can cost one third to one tenth the price of conventional underground fiber-optic installations. Moreover, burying cabling can take anywhere from six to 12 months, whereas an FSO link can be up and running in a few days. It is little wonder, therefore, that nearly a dozen companies are developing FSO technology. If things go as proponents predict, the industry could grow from approximately $120 million in 2000 to more than $2 billion annually by 2006, according to a study conducted by the Strategis Group, a Washington, D.C.–based telecommunications research firm.

Bridging the Last Mile

FREE-SPACE OPTICS uses apparatus and techniques originally created for optical-fiber cable systems, the very technology it is meant to supplement. Digital information in the form of electronic signals (the 1's and 0's that make up binary computer codes) is sent through a roof- or window-mounted infrared laser diode transmitter that converts each logical 1 into a narrow pulse of optical energy. When the system is operational, the absence of such an invisible pulse represents a logical 0. The process of modulating data into a digital optical signal is known as on/off signaling, or keying. Transmission efficiency is enhanced by packetizing data—splitting traffic into independent packets that can be individually addressed and sent. In addition, FSO can support wavelength division multiplexing (WDM), a technique that allows a single optical path to carry tens of separate signal channels, as long as each is encoded in a slightly different wavelength.

After being emitted by the 850- or 1,550-nanometer laser diode, the optical pulses are focused by a lens and sent out as a collimated beam of light, like that generated by a flashlight. Despite focusing by the lens, the power of the beam disperses with distance. When some of the transmitted light strikes the aperture lens of a receiver (located on a roof or in a window), the collected optical power is focused onto a photodetector, which converts the pulses into a weak electrical signal. A sensitive electronic receiver next amplifies and regenerates the weak signal, completing the data-transfer link [*see top illustration on opposite page*].

Although the transmitted infrared beam is narrow, it does diverge, forming a cone with a fairly large breadth by the time it arrives at the receiving link head. The degree of beam spreading is determined by the size of the transmitting lens, varying inversely with lens diameter. As a result, the amount of energy actually striking the collecting lens falls off rapidly with distance (received energy varies inversely with the square of the distance). For any given data rate, transmitted optical power, optical receiver sensitivity and size of the receiving lens, this beam divergence imposes a maximum range over which the optical link can operate.

To increase this link distance, larger-diameter transmitting lenses must be used, thereby reducing beam spread and causing more optical power to strike the receiving lens. As the beam is narrowed, however, minute targeting variations produced by building sway and the thermal expansion and contraction of construction materials make it necessary to introduce auto-tracking capabilities at both ends. This requirement adds complexity and cost. Active tracking systems use movable mechanical platforms or articulated mirrors to point the pencil beam at the receiving lenses and to keep the receiving aperture pointed at the transmitter. Feedback controls provide regular adjustments to keep the transmitter and receiver on target.

Free-space optics systems can cost one third to one tenth the price of conventional underground fiber-optic installations.

Applications for Free-Space Optics

- **Last-mile access:** High-speed data links that connect business and consumer end users with Internet service providers and other metropolitan-area and wide-area fiber networks.
- **Cellular backhaul:** The means to carry cell-phone traffic from local antenna towers back to facilities wired into the public switched-telephone network.
- **Enterprise connectivity:** Easy interconnection of local-area-network segments housed in separate buildings of businesses.
- **Fiber backup:** Low-cost redundant links to back up optical fiber, replacing a second buried fiber cable link.
- **Service acceleration:** Temporary high-speed service for customers waiting for an optical-fiber infrastructure to be laid. Emergency communications network installation.

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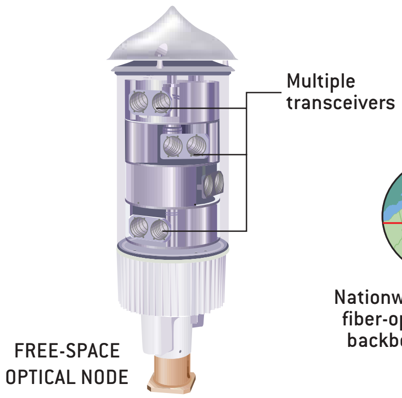
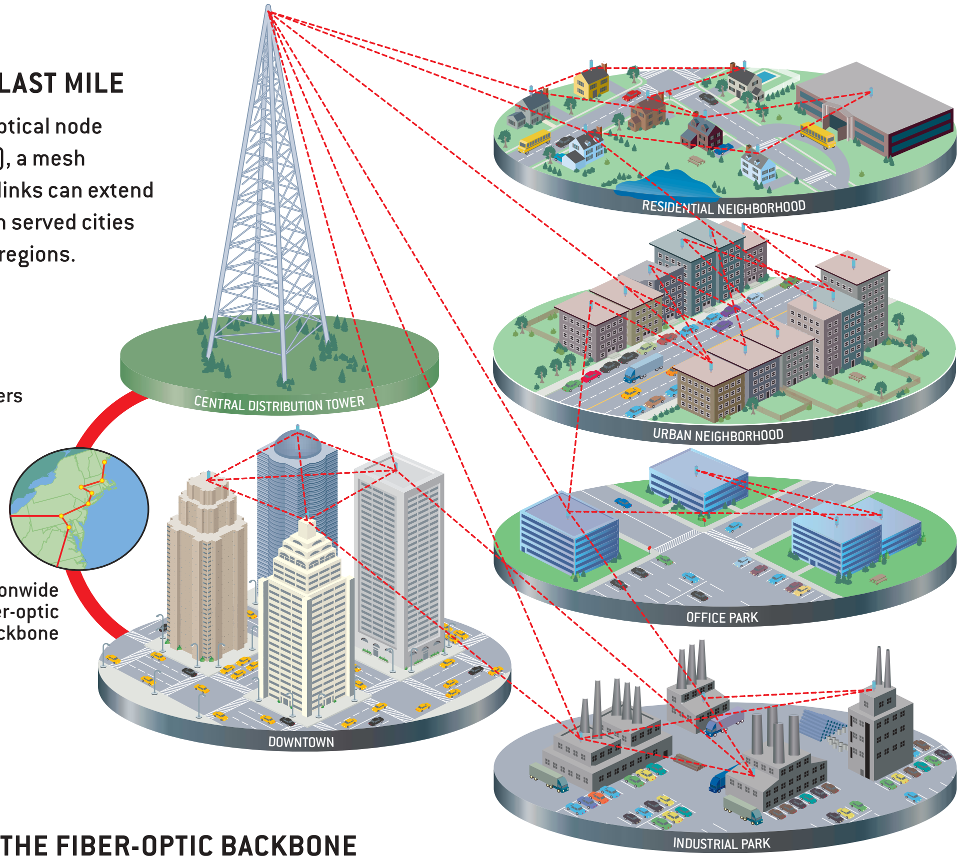
Spanning the Connectivity Gap

EXTENDING BROADBAND THE LAST MILE

With the multitransceiver free-space optical node (*below*) installed on buildings (*at right*), a mesh network of short-range, two-way laser links can extend the distribution of broadband data from served cities out to towns, neighborhoods and even regions.



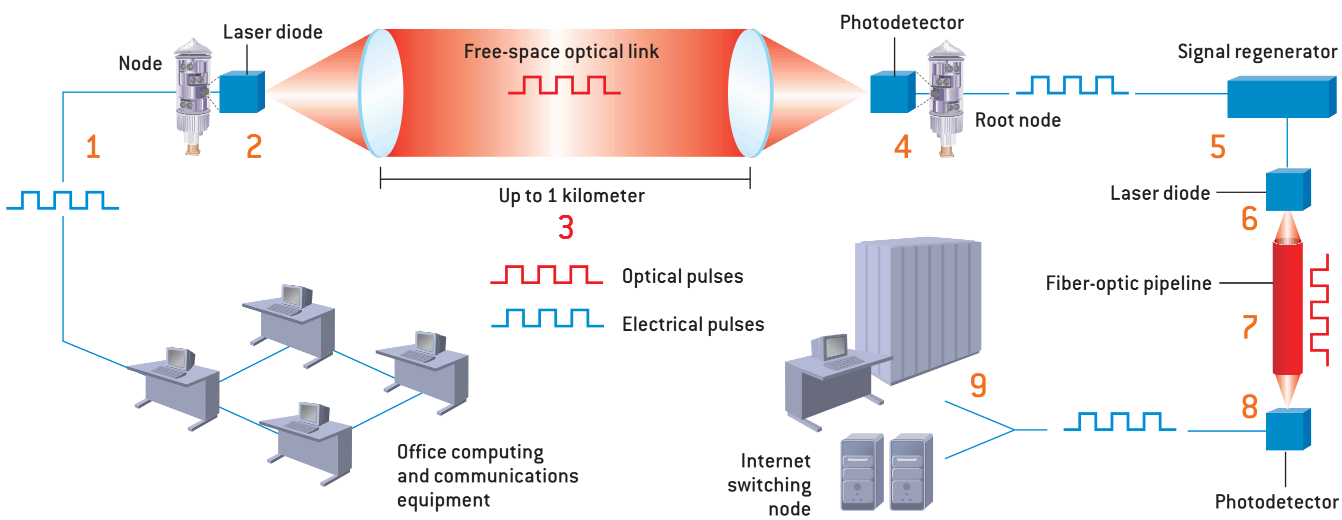


FREE-SPACE OPTICAL LINK TO THE FIBER-OPTIC BACKBONE

BEAMING BROADBAND data across the neighborhood at high speed is the principal function of a free-space optical (FSO) link. FSO links can provide the "last-mile" connection to the high-capacity fiber-optic backbone that wends its way across the U.S. Coded data for broadband applications and services that run on digital office equipment (and, in the future, their residential counterparts) are sent to a roof- or window-mounted FSO transceiver node (*1*).

The laser diode in the transceiver converts the data into infrared optical pulses that are collimated by a lens (*2*) and beamed (*3*) to another FSO node (in this case, a "root" node connected to the optical-fiber pipeline) attached to a nearby building. The receiving lens of that transceiver focuses the optical pulses into a photodetector that converts them back into electrical pulses (*4*). The pulses are then amplified and cleaned up by a signal regenerator (*5*).

Next, the electrical signals are sent down a wire to another laser diode, which optically codes them (*6*) for transmission by a fiber-optic cable that is part of the nationwide backbone (*7*). A photodetector at the end of the fiber-optic cable (*8*) reconverts the signals into electrical pulses for use by mainframe computers and servers at a major Internet switching node (*9*), which links to broadband application and service providers.



LAURIE GRACE

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Lost in a Fog

SUSCEPTIBILITY TO FOG has slowed the commercial deployment of free-space optical systems. It turns out that fog (and, to a much lesser degree, rain and snow) considerably limits the maximum range of an FSO link. Fog causes significant loss of received optical power. This optical attenuation factor scales exponentially with distance. In moderately dense fog, for example, the optical signal might lose 90 percent of its strength every 50 meters. This means that 99 percent of the energy is expended over a span of 100 meters and that 99.9 percent is dissipated after traveling 150 meters. Thus, to be practical, a free-space optical link must be designed with some specified "link margin," an excess of optical power that can be engaged to overcome foggy conditions when required.

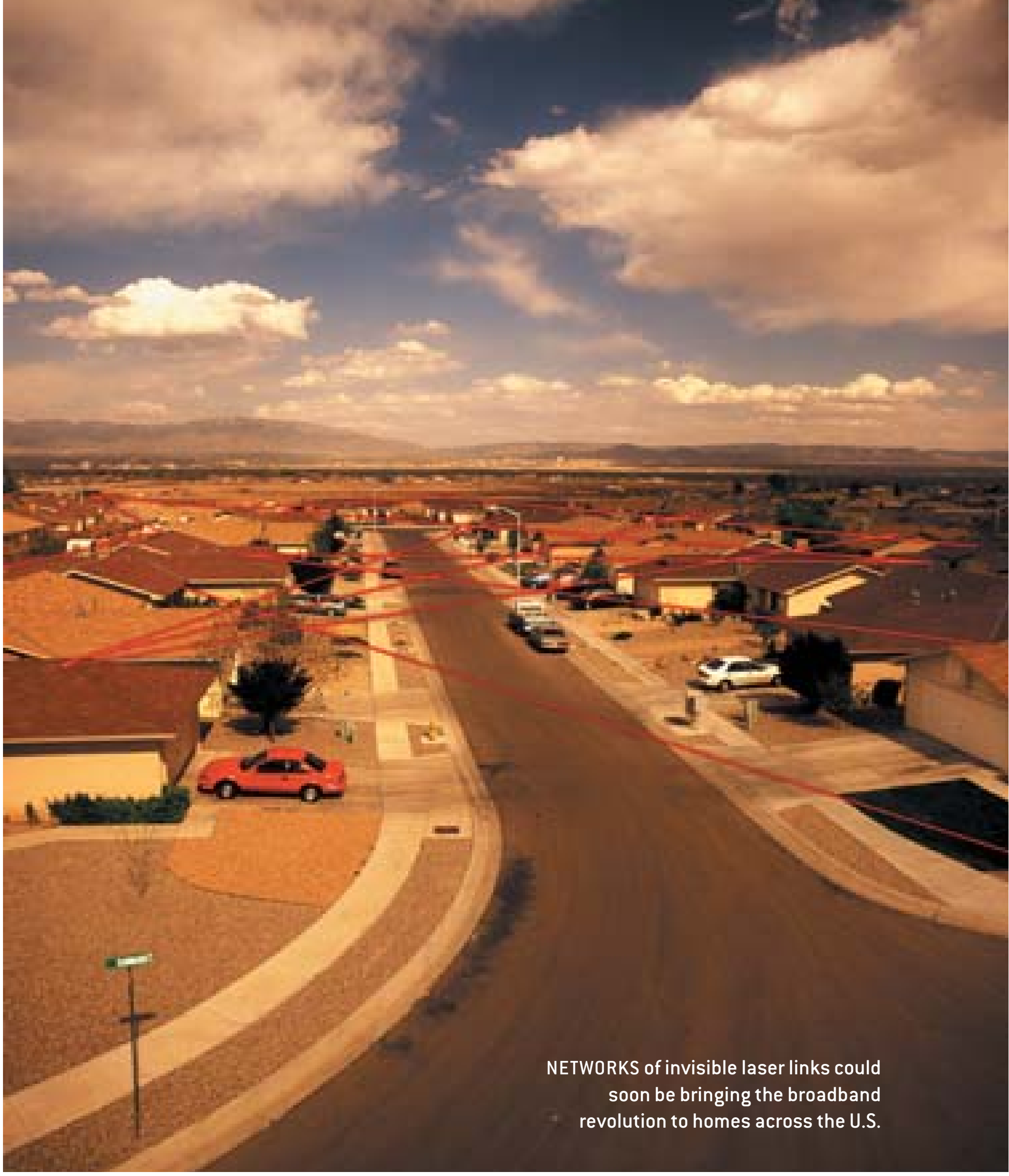
For a given link margin, it becomes meaningful to speak of another metric—the link availability, which is the fraction of the total operating time that the link fails as a result of fog or other physical interruption. Link-availability objectives vary with the application. When FSO technology is used for private-enterprise networking (for instance, to connect two offices of the same company situated in separate buildings), 99.9 percent uptime may be acceptable. This value corresponds to a downtime of about nine hours a year.

In contrast, public carrier-class service, which is provided to a carrier's prime business customers, demands a link availability of 99.999 percent (in the telecommunications business, the so-called five-nines benchmark), which translates into only five minutes of allowable downtime a year. Fiber-optic systems regularly operate at the five-nines service level. It is noteworthy that a key potential application for FSO, cellular backhaul—transmission systems that connect cellular-radio base stations with mobile switches connected to the public switched-telephone network—requires an operational availability somewhere in between, around 99.99 percent.

Achieving this high level of performance is a challenge for free-space optics. The greater the density of the fog, the greater the attenuation, the poorer the availability and the shorter the allowable range. In regions where dense fog occurs rarely, excellent link availability may be achieved at a range approaching the maximum allowable, approximately one kilometer. In less favorable climates, however, this distance would be far less.

To solve the range/reliability problem, FSO systems can be designed with limited link lengths as part of an interconnected optical mesh topology, a spiderweb-like arrangement that extends broadband service to many buildings that would otherwise be too distant from the fiber-optic backbone to be reached by a single FSO link. In a mesh network, the building located closest to the optical-fiber terminus is equipped with an FSO "root" node that attaches to the fiber and contains several optical transceivers. Other served buildings are also equipped with FSO nodes with multiple transceivers. These transceivers allow the nodes to communicate with nearby neighbors in an interconnected mesh arrangement.

Signals intended for a particular building are sent from the root node down a particular set of mesh links, with intermediate nodes serving as regenerative repeaters along the way. Similarly, signals are sent from a given building to the root node along another route. Thus, the



NETWORKS of invisible laser links could soon be bringing the broadband revolution to homes across the U.S.

CHIP SIMONS

THE AUTHOR

ANTHONY ACAMPORA is professor of electrical and computer engineering at the University of California, San Diego, where he works on leading-edge telecommunications networking technology. He is also chief scientist and co-founder of AirFiber, a San Diego–based company that is developing free-space optical technology. Holder of 30 patents, Acampora has performed research at Columbia University and AT&T Bell Laboratories. He received his doctorate in electrical engineering from the Polytechnic Institute of Brooklyn.

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length of each optical link is kept sufficiently short to achieve high immunity to fog. Should a link fail, signals would be redirected along an alternative pathway, making use of redundant routes, thereby facilitating rapid recovery from equipment failures. Finally, a mesh can be connected to several root nodes, thereby providing greater overall capacity to the collection of served buildings.

In addition to requiring a few optical transceivers, each regenerator/repeater station in a mesh system must contain an electronic switch to combine the signal traffic (multiplexing) from the local building with that beamed from other nearby buildings and to route signals between the root node and each served building. Furthermore, the necessary multiplexing, demultiplexing and switching functions mean that all the signals from all the users' diverse computing and communications equipment must be converted into a common format. This signal format conversion is accomplished by a device called a network termination unit. Although data can be passed through many nodes along various paths, it appears to users as if each signal has been delivered to the fiber backbone by means of its own dedicated transmission line. Fiberlike bandwidth can therefore be provided over wide areas, and new nodes can be installed relatively quickly and easily to bring buildings "on-net."

For each signal from each building, the network management software chooses a pathway through the mesh that passes through one of the system's root nodes. Because node failure can be sensed by the software, affected signals can be instantly directed around the problem. By reserving some unallocated capacity on each optical link, the network designer can ensure that there is sufficient capacity to reroute and recover from single- or multiple-link failures that might occur.

Free-Space Optics Developers

AirFiber (San Diego) *www.airfiber.com*

Cablefree Solutions (Middlesex, England) *www.cablefreesolutions.com/index.htm*

Canon USA (Lake Success, N.Y.) *www.usa.canon.com/html/industrial_canobeam/canobeam.html*

fSONA Communications (Richmond, B.C.) *www.fsona.com*

LightPointe (San Diego) *www.lightpointe.com*

Optical Access (San Diego) *www.opticalaccess.com*

Optical Crossing (Pasadena, Calif.) *www.opticalcrossing.com*

PAV Data (Warrington, England) *www.pavdata.com*

Plaintree Systems (Ottawa, Ontario) *www.plaintree.com*

Terabeam (Kirkland, Wash.) *www.terabeam.com*

Competing with free-space optics to unclog the last-mile bottleneck is point-to-point microwave radio, a technology that is immune to fog attenuation. On the negative side, licenses are needed to operate in most microwave radio bands, and the spectrum available in most bands is limited, which means that capacity is restricted. Microwave radio is also more costly than FSO systems and may be susceptible to transmission interference. Further, microwave radio is subject to significant signal attenuation in heavy rain, especially at higher frequencies where more spectrum might be available.

If microwave radio were operated at a frequency of 60 gigahertz, however, it could complement free-space optics. The U.S. Federal Communications Commission has allocated some unlicensed spectrum at 60 GHz for high-speed applications. The greater spectrum allocation at 60 GHz implies that more capacity can be provided and a less spectrally efficient (hence, lower-cost) modulation scheme might be used, such as simple on/off signaling. Because severe rain (which might cause a radio link failure) and dense fog (which might cause an FSO link failure) do not exist simultaneously, the opportunity exists to boost network reliability by combining 60-GHz radio with FSO. Linking the two technologies would mean that the resulting system could be highly reliable over significantly greater distances.

Although free-space optics has some distance to go in addressing its remaining concerns, it's still the best bet to reach across the last mile and bring about the long-awaited broadband revolution. SA

The optical mesh extends broadband service to many buildings that would otherwise be too distant to be reached by a single free-space optical link.

MORE TO EXPLORE

UniNet: A Hybrid Approach for Universal Broadband Access Using Small Radio Cells Interconnected by Free-Space Optical Links. A. Acampora, S. Krishnamurthy and S. H. Bloom in *IEEE Journal on Selected Areas in Communications,* Vol. 16, No. 6, pages 973–988; August 1998.

A Broadband Wireless Access Network Based on Mesh-Connected Free-Space Optical Links. Anthony Acampora and Srikanth V. Krishnamurthy in *IEEE Personal Communications* (now called *IEEE Wireless Communications*), Vol. 6, No. 5; October 1999.

Free-Space Laser Communication Technologies. Special issue of *Proceedings of SPIE* (published annually).

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The NOSE Takes a STARRING Role

THE STAR-NOSED MOLE HAS WHAT IS VERY LIKELY THE WORLD'S FASTEST

By Kenneth C. Catania

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AND MOST FANTASTIC NOSE

The renowned physicist John Archibald Wheeler once suggested, "In any field, find the strangest thing and then explore it." Certainly it is hard to imagine an animal much stranger than the star-nosed mole, a creature you might picture emerging from a flying saucer to greet a delegation of curious earthlings. Its nose is ringed by 22 fleshy appendages that are usually a blur of motion as the mole explores its environment. Add large clawed forelimbs, and you've got an irresistible biological mystery. How did this creature evolve? What is the star? How does it function, and what is it used for? These are some of the questions that I set out to answer about this unusual mammal. It turns out that the star-nosed mole has more than an interesting face; it also has a remarkably specialized brain that may help answer long-standing questions about the organization and evolution of the mammalian nervous system.

It may comfort you to know that star-nosed moles (*Condylura cristata*) are small animals, tipping the scales at a mere 50 grams, about twice the weight of a mouse. They live in shallow tunnels in wetlands across much of the northeastern U.S. and eastern Canada and hunt both underground and underwater. Like the other roughly 30 members of the mole family (Talpidae), the star-nosed mole is part of the mammalian order Insectivora, a group known for its high metabolism and voracious appetite. So the tiny star-nosed mole with its big appetite must locate enough prey to survive cold northern winters. It finds earthworms in soil, as other moles do, but in addition it has access to a host of small invertebrates and insect larvae found in the rich mud and leaves of its wetland habitat and in the ponds and streams where it swims along the murky bottom to root out prey. And seeking prey is where the star comes into play. The star is not part of the olfactory system—which governs smell—nor is it an extra hand used to gather food. Instead the star is a touch organ of unsurpassed sensitivity.

PINK STAR makes this mole's nose unmistakable. It also makes it one of the most sensitive touch organs observed in the animal kingdom—one that works uncannily like an eye.

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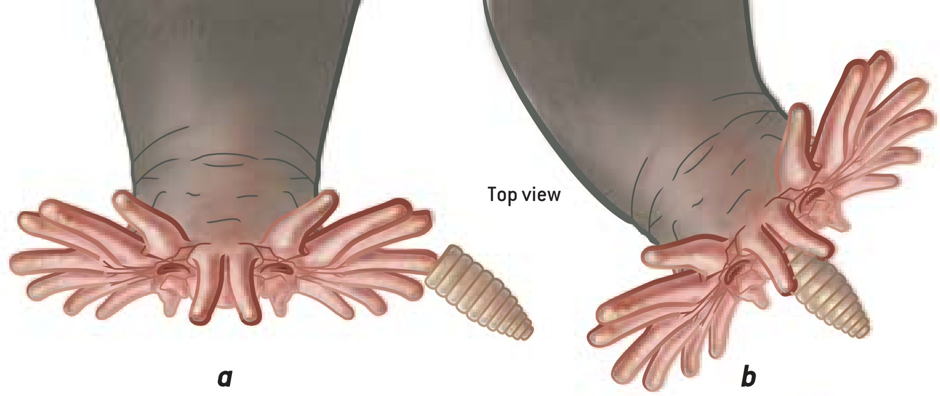

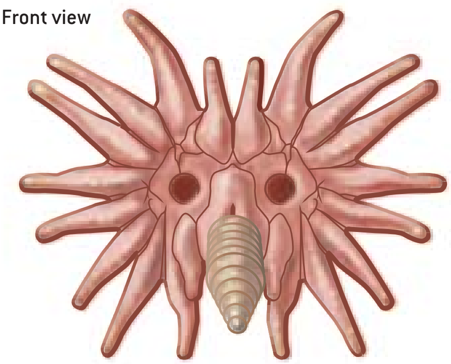

PREY IDENTIFICATION by the star-nosed mole takes place in less than half a second. When the longer appendages touch an interesting object (*a*), the nose moves so that the shortest and most sensitive appendage can rapidly touch and identify the item (*b*), which is immediately consumed.

Getting Close to the Star

WHEN I BEGAN to explore the anatomy of the star with a scanning electron microscope—an instrument that reveals the microscopic structure of the skin surface—I thought I would see touch receptors here and there in various places across the skin. Instead I was surprised to find that the star, like the retina in the human eye, is made up *entirely* of sensory organs. The surface of each of the 22 appendages that ring the nostrils is composed of an aggregation of microscopic protuberances, or papillae, called Eimer's organs. Each Eimer's organ, in turn, is made up of an array of neural structures that signal different aspects of touch.

Three distinct sensory receptors accompany each Eimer's organ. At the very bottom of the organ is a single nerve ending that is encircled by many concentric rings, or lamellae, of tissue formed by a Schawann cell, a specialized support cell. This lamellated receptor transmits relatively simple information about vibrations or about when an individual organ first contacts an object. Above this receptor is another nerve fiber that makes contact with a specialized cell called a Merkel cell. Unlike the lamellated variety, the Merkel cell-neurite complex signals only the sustained depression of the skin. Both of these receptors are commonly found in mammalian skin.

At the top of each Eimer's organ, however, lies a receptor unique to moles. A series of nerve endings forms a circular pattern of neural swellings in a hub-and-spoke arrangement just below the outer skin surface. Our recordings from the brains of star-nosed moles suggest that this latter sensory component provides the most significant aspect of touch perception: an index of the microscopic texture of various surfaces.

More than 25,000 Eimer's organs form the star, although it has a surface area of less than one square centimeter. Together these sensory organs are supplied by more than 100,000 nerve fibers that carry information to the central nervous system and eventually to the highest mammalian processing center, the neocortex. With this formidable array of receptors, the mole can make incredibly fast sensory discriminations as it prowls its haunts looking for prey.

The star moves so quickly that you can't see it with your naked eye. A high-speed camera revealed that the star touches 12 or more areas every second. Scanning its environment with a rapid series of touches, a star-nosed mole can find and eat five separate prey items, such as the pieces of earthworm we feed them in the laboratory, in a single second.

Acting Like an Eye

EVEN MORE SURPRISING than this astonishing speed is the manner in which the mole uses the star. The star functions like an eye. Try reading this sentence without moving your eyes, and you will soon appreciate that your visual system is divided into two distinct functional systems. At any given time only a small portion of a visual scene (about one degree) is analyzed with the high-resolution central area of your retina, the fovea. The much larger low-resolution area of your retina locates potentially important areas to analyze next. The characteristic rapid movements of the eyes that reposition the high-resolution fovea are called saccades.

Just as we scan a visual scene with our eyes, star-nosed moles constantly shift the star to scan tactile scenes as they travel through their tunnels, quickly exploring large areas with the Eimer's organs of all 22 appendages. But when they come across an area of interest—such as potential food—they always shift the star so that a single pair of appendages can carry out more detailed investigations. Humans have a fovea for sight, and star-nosed moles have a fovea for touch. The mole's fovea consists of the bottom pair of short appendages, located above the mouth, each designated as the 11th appendage. Like the retinal fovea, this part of the star has the highest density of sensory nerve endings. Moreover, the rapid movements of the star that reposition this tactile fovea onto objects of interest are analogous to saccades in the visual system.

The analogy goes even further. In our visual system it is not only the movements of the eyes and the anatomy of the retina that revolve around the high-resolution fovea; human brains are specialized to process information predominantly from this part of the visual scene.

A characteristic feature of information processing in mammalian sensory

THE AUTHOR

KENNETH C. CATANIA first encountered star-nosed moles when he worked at the National Zoo in Washington, D.C., many years ago. Catania, who is assistant professor of biological sciences at Vanderbilt University, studies the sensory system of mammals and the organization of the neocortex. He received his undergraduate degree in zoology from the University of Maryland and his Ph.D. in neuroscience from the University of California, San Diego. Catania has received the Capranica Foundation Award in Neuroethology and the International Society of Neuroethologists/ Young Investigator Award and is a Searle Scholar.

KENNETH C. CATANIA (*preceding pages*); PORTIA SLOAN (*above*)

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systems is the topographic organization of information from sensory receptors. Visual areas contain maps of the retina, auditory areas provide maps of the cochlea (the receptors in the ear, which are maps of tones), and touch areas contain maps of the body's surface. Such mapping is perhaps nowhere better illustrated than in the somatosensory system of the star-nosed mole.

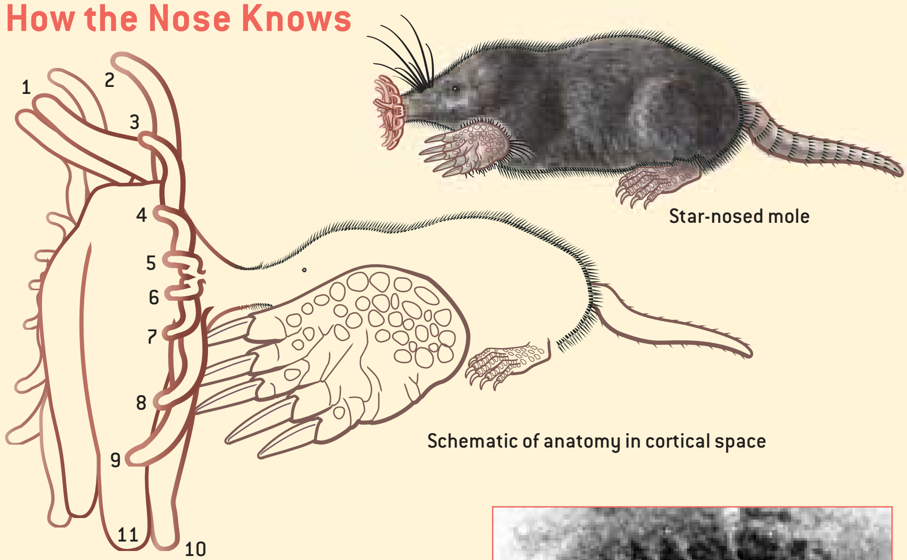
Charting Touch

WORKING WITH my Vanderbilt University colleague Jon H. Kaas, I was able to explore the organization of the star-nosed mole's neocortex. By recording the activity from neurons that compose different cortical areas, we charted the neural representation of the star, showing where and how neurons in the cortex respond to tactile stimulation of the Eimer's organs. We identified three separate maps of the star where the responses of neurons reflect the anatomy of the nose on the opposite side of the face. (In all mammals, the left half of the body is represented predominantly in the right side of the cortex, and vice versa.) To our amazement, we also found that these maps are visible in sections of the brain that were stained for various cell markers—we could literally see a star pattern in the cortex.

When we compared the sizes of cortical brain maps with the appendages of the star, we noticed an obvious discrepancy. The 11th appendage, which is one of the smallest parts of the star, had by far the largest representation in the cortex. The discrepancy is a classic example of what has been termed cortical magnification: the most important part of the sensory surface has the largest representation in the brain, regardless of the actual size of the sensory area on the animal.

The same phenomenon occurs in the visual system, in which the small retinal fovea has by far the largest portion in visual cortex maps. We also discovered that neurons representing the 11th appendage responded to tactile stimulation of very small areas, or receptive fields, on the 11th appendage, whereas neurons representing the other appendages responded solely to stimulation of larger areas. The smaller receptive fields for the 11th appendage re-

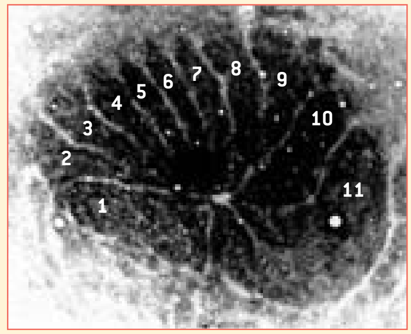
How the Nose Knows



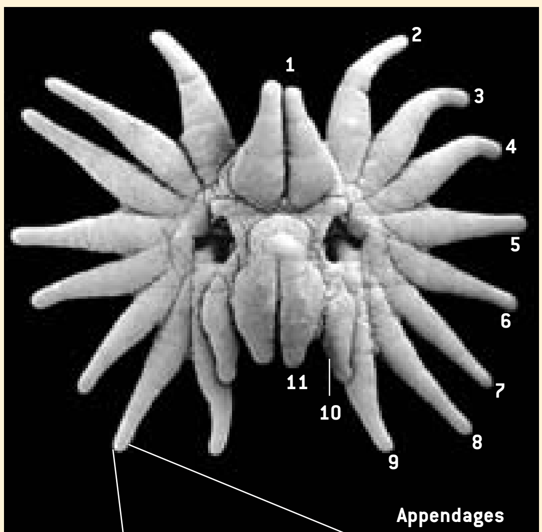
Star-nosed mole

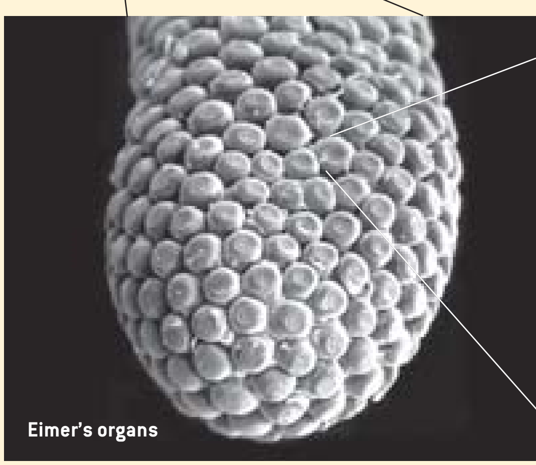
Schematic of anatomy in cortical space

CORTICAL MAPS of the star-nosed mole reveal the importance of the 11th appendage. As this schematic shows, the most sensitive appendage gets the most space in the cortex (*above*). The same is true for the most sensitive part of the human eye. The organization of the cortex also beautifully mirrors the position of the appendages (*right*) and their relative importance.

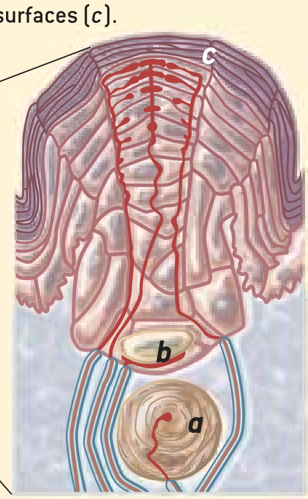


Right cortex





APPENDAGES of the star are made up entirely of sensory organs. These Eimer's organs have elements that are common to many animals' skin receptors: a single nerve ending at the very base (*a*), which relays information about vibrations and initial contact with an object, and another nerve fiber that records sustained pressure (*b*). But the very tip of the Eimer's organ is found only in moles: neural swellings arrayed just below the outer skin, which are amazingly sensitive to the details of surfaces (*c*).



MICROGRAPHS BY KENNETH C. CATANIA; ILLUSTRATIONS BY PORTIA SLOAN

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flect a greater acuity for this region and mirror the organization of visual systems.

The discovery of a somatosensory fovea in the star-nosed mole suggests that this organizational scheme is a general evolutionary solution to constructing a high-resolution sensory system. Visual systems with a fovea are the most familiar, but auditory systems can have an acoustic fovea as well, as has been elegantly demonstrated by Nobuo Suga of Washington University in mustached bats. Many bats emit an echolocation call that contains a narrow frequency range and then analyze returning echoes to navigate and to detect prey. A large proportion of the bat's auditory receptors (hair cells in the cochlea) and large areas in the bat's brain are devoted to analyzing a narrow frequency range corresponding to a single harmonic of the returning echo. This is an example of an acoustic fovea.

Although it is hard to imagine, bats have an auditory version of a saccade as well. This is necessary because returning echoes are Doppler-shifted to different frequencies—depending on the speed of the bat and its target, usually an unfortunate insect—and often fall outside the frequency range of the acoustic fovea. Because the hunting bat cannot change its acoustic fovea, it constantly changes the frequency of its outgoing pulses so that the Doppler-shifted returning echo will be at the frequency of its acoustic fovea. The behavior is called Doppler-shift compensation and is the acoustic equivalent of moving the eyes, or the star, to analyze a stimulus with the high-resolution area of the sensory surface and the corresponding computational areas of the brain.

The presence of a sensory fovea in the mammalian visual system, auditory system and somatosensory system is a dramatic case of convergent evolution and points to common constraints in the way evolution can construct a complex brain. After all, why not just wire the entire sensory system for high-resolution input and eliminate the need to constantly shift the eyes, star, or echolocation frequency? One reason, of course, is that it would take a massive enlargement of the brain—and the nerves carrying sensory inputs to it—to accomplish this task.

It is staggering to consider just how much larger the human brain would have to be if the entire retina were to have the same resolution as the fovea. To accomplish this, the human brain would have to be at least 50 times bigger. Your head would no longer fit through a doorway. Clearly, it is more efficient to devote a large part of the computational resources of the brain to a small part of the sensory system and then to move that area around like a spotlight to analyze important aspects of the world.

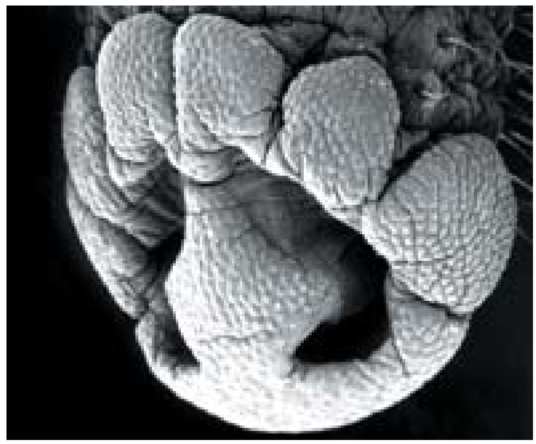
Space Race in the Brain

AS OFTEN OCCURS, our observations about the star-nosed mole's sensory system raised as many questions as they answered. How does part of a sensory surface acquire such a large section of the brain's map in the first place? The traditional understanding has been that each sensory input acquires the same average amount of area in a cortical map during development, and thus the enlarged representation of a sensory fovea simply reflects the greater number of neurons collecting information from the foveal region. This theoretical framework, suggesting that each input has equal squatter's rights in the brain, is appealing in its simplicity. But a number of studies have recently challenged this democratic assessment of cortical parcellation in the primate visual system by showing that inputs from the fovea are allocated more cortical territory than those containing peripheral information.

To see what was happening in the star-nosed mole, we decided to measure the cortical representations of the 22 appendages and to compare those areas with the number of nerve fibers collecting information from each appendage. It was obvious (after counting more than 200,000 nerve fibers!) that sensory neurons collecting information from the 11th appendage are granted far more cortical territory in the brain maps than inputs from the other appendages. This is another parallel between the mole's somatosensory system and primate visual systems, and it shows not only that important areas of a sensory surface can have the highest number of sensory neurons collecting information per unit area but also that each of these inputs can be allocated extra computational space in the brain.

This observation, however, does not explain how these sensory inputs manage to take the most territory in cortical maps. The question belongs to one of the most fascinating areas of current research in neuroscience, because changes to cortical maps could be a critical component of learning complex skills and recovering from brain injuries or strokes. Several studies indicate that a combination of intrinsic developmental mechanisms and experience-dependent plasticity affects the shape and maintenance of brain maps.

These findings are especially intriguing in the case of the star-nosed mole, because the pattern of use of the nose—as measured by how the mole touches prey with the different appendages—very closely matches the pattern of magnification for the appendage representations in the cortex. The correspondence suggests that behaviors may shape the way the cortex is organized. Alternatively, intrinsic developmental mechanisms may match the size of cortical maps to their behavioral significance. It is the classic question of nature versus nurture.



The Developing Star

LOOKING AT HOW the star develops in mole embryos can help clarify this matter. Because the star develops before its representation in the cortex, sensory inputs from the star have an opportunity to influence the way that the cortical maps form during potentially critical periods of development.

MICROGRAPHS BY KENNETH C. CATANIA

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STAR-NOSED EMBRYO provides clues to the animal's evolutionary history. The appendages start as tubes embedded in the mole's face. They break free of the skin before birth. Two weeks after birth, they begin to bend forward. Perhaps these unusual noses began as organs that lay flat against the snout, just as they do in the adult coast mole (*left*).

Star-nosed mole embryos come in about the strangest-looking varieties imaginable. Although most embryos look odd, star-nosed moles appear especially weird because the embryonic hands are gigantic—all the better to dig with later—and the nose is obviously unique.

Studies of the embryos revealed that appendage 11 was the largest appendage during early development, despite its relatively small size in adults. It also became clear that Eimer's organs on the star, and the neural structures within each Eimer's organ, matured first on the 11th appendage. It is as if this appendage gets a head start compared with all the other ones, which later overtake it in size and number of Eimer's organs. As it turns out, the retinal fovea in the visual system also matures early.

When we examined the corresponding patterns in the somatosensory cortex, we found that markers for metabolic activity appear first in the representation of the 11th appendage. This suggests that the early development of the fovea results in greater activity in the developing cortical representation of this area, which could allow these inputs to capture the largest area in the cortical map. Strong evidence from the developing visual system of primates indicates that sensory inputs with the greatest level of activity are able to capture the largest areas in the cortex during development. But it is also possible that early behavioral patterns in star-nosed moles—which use the 11th appendage to suckle—contribute to activity-dependent expansion of the fovea in the cortical maps. Sorting out the relative contributions of these different influences is one of our goals.

How the Mole Got Its Star

ONE CAN'T HELP but wonder how the star-nosed mole evolved. Examining the embryos provided a road map to star-nosed mole evolution, or at least to that of its enigmatic nose. The appendages that form the star develop unlike any other known animal appendage. Rather than growing directly out of the body wall, the star appendages form as cylinders, facing backward and embedded in the side of the mole's face. In the course of development, these slowly emerge from the face, break free from the skin and then, about two weeks after birth, bend forward to form the adult star. The backward developmental sequence suggests that ancestral star-nosed moles might have had strips of sensory organs lying flat against the sides of the snout. These might have been slowly raised up over many generations until the star was formed.

Of course, without further evidence, this might remain a "Just So" story. But there exist two mole species—the coast mole (*Scapanus orarius*) and Townsend's mole (*S. townsendii*)—that have short strips of sensory organs lying flat against the upper side of their noses, and these adult noses bear an uncanny resemblance to the embryonic star. These intermediate forms strongly suggest that such an ancestor gave rise to the full-fledged star we see today. However they came to be, these unlikely noses may help reveal much about the influence of innate developmental mechanisms and behavioral patterns on the organization of the cortex. SA

MORE TO EXPLORE

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Sensory Exotica: A World beyond Human Experience. Howard C. Hughes. MIT Press, 1999.

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JAMES WORRELL

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A YEAR AFTER DOCTORS BEGAN IMPLANTING THE ABIOCOR IN DYING PATIENTS, THE PROSPECTS OF THE DEVICE ARE UNCERTAIN

The Trials of an Artificial HEART

By Steve Ditlea

The permanent replacement of a failing human heart with an implanted mechanical device has long been one of medicine's most elusive goals. Last year this quest entered a crucial new phase as doctors at several U.S. hospitals began the initial clinical trials of a grapefruit-size plastic-and-titanium machine called the AbioCor. Developed by Abiomed, a company based in Danvers, Mass., the AbioCor is the first replacement heart to be completely enclosed within a patient's body. Earlier devices such as the Jarvik-7, which gained worldwide notoriety in the 1980s, awkwardly tethered patients to an air compressor. In contrast, the AbioCor does not require tubes or wires piercing the skin. In July 2001 Robert L. Tools, a 59-year-old former Marine whose heart had become too weak to pump effectively, became the first recipient of this artificial heart.

Over the next nine months, surgeons replaced the failing hearts of six more patients with the AbioCor. But the initial trials have had mixed results. As of press time, five of the seven patients had died: two within a day of the implantation procedure, one within two months, and two within five months. (Tools died last November.) One of the two survivors has lived for more than eight months with the device, the other for more than six months. Because all the patients were seriously ill to begin with—only people deemed likely to die within a month were eligible for implantation—Abiomed officials argue that the artificial heart is proving its worth. The company has acknowledged, however, that a flaw in the device's attachments to the body might have led to the formation of the blood clots that caused strokes in three of the patients.

ABIOCOR, an artificial heart made of plastic and titanium, has been in clinical trials for the past year.

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With the clinical trials only a year old, it is obviously too early to say whether the AbioCor will be a breakthrough or a disappointment. If the U.S. Food and Drug Administration decides that the device shows promise, it may allow Abiomed to implant its artificial heart in patients who are not as severely ill as those in the initial group. Company officials hope that eventually the rate of survival after implantation will surpass the rate after heart transplants (about 75 percent of the recipients of donor hearts are still alive five years after the transplant). Fewer than 2,500 donor hearts become available every year in the U.S., whereas more than 4,000 Americans are on waiting lists for transplants; for many of those patients, AbioCor could be a lifesaver.

But the artificial heart is competing against less radical treatments, one of which has already proved quite successful. Doctors have been able to restore adequate cardiac function in thousands of patients by attaching a pump to the left ventricle, the chamber most likely to fail. These ventricular-assist devices were originally intended as a short-term therapy for people awaiting transplants, but recent studies show that the pumps can keep patients alive for two years or more [*see box on pages 66 and 67*]. Meanwhile other studies have overturned generations of medical wisdom by suggesting that the human heart can repair itself by generating new muscle tissue. Researchers are now racing to develop therapies using stem cells that could help the heart heal [*see box on page 68*].

Heart History

THE ORIGINS of the artificial heart go back half a century. In 1957 Willem J. Kolff (inventor of the dialysis machine) and Tetsuzo Akutsu of the Cleveland Clinic replaced the heart of a dog with a polyvinyl chloride device driven by an air pump. The animal survived for 90 minutes. Seven years later President Lyndon B. Johnson established an artificial-heart program at the National Institutes of Health. In 1969 Denton A. Cooley of the

Overview/*AbioCor Heart*

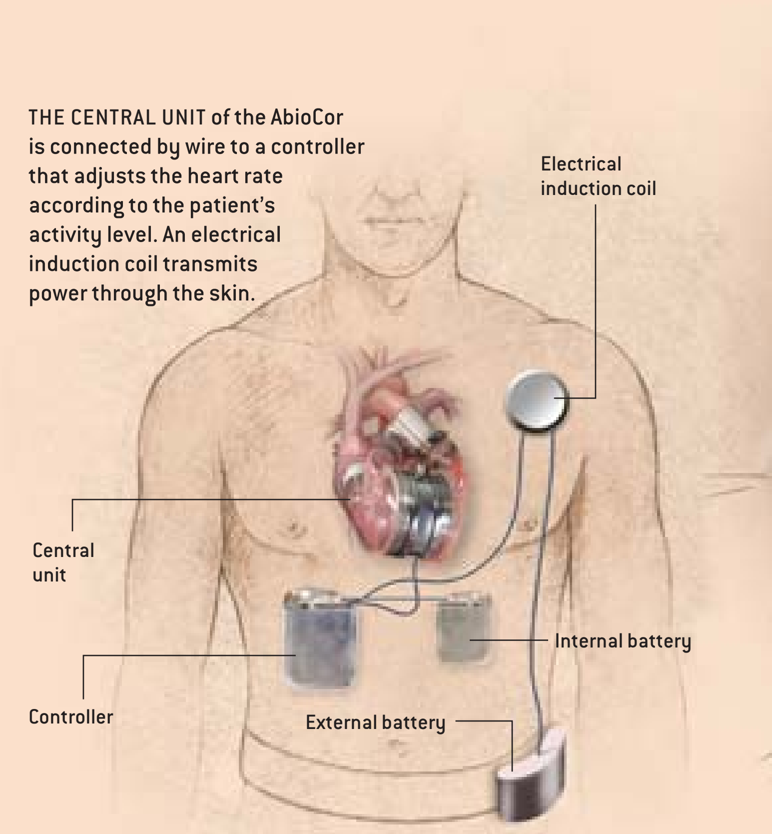
- The goal of implanting a permanent mechanical substitute for a failing human heart was all but abandoned after controversial attempts in the 1980s. The clinical trials of the AbioCor, a new artificial heart designed to be completely enclosed in a patient's body, began in July 2001.
- The trials have had mixed results so far. Of the seven severely ill patients who received the AbioCor, two died within a day of the implantation, one within two months, and two within five months. Although the artificial heart did not cause infections, three patients suffered strokes.
- If the survival rate of the AbioCor improves, it could eventually become an alternative for people on the long waiting lists for heart transplants. But the device may have to compete with less radical treatments such as ventricular-assist devices and therapies using stem cells.

LIKE A HUMAN HEART, the AbioCor has chambers for pumping blood on its left and right sides. Oxygenated blood from the lungs flows into and out of the left chamber, and oxygen-depleted blood from the body flows into and out of the right chamber. Between the chambers is the mechanical equivalent of the heart's walls: a hermetically sealed mechanism that generates the pumping motions.

At the center of this mechanism, an electric motor turns a miniaturized centrifugal pump at 5,000 to 9,000 rotations a minute. The pump propels a viscous hydraulic fluid; a second electric motor turns a gating valve that allows the fluid to alternately fill and empty from the two outer sections of the pumping mechanism. As fluid fills the left section, its plastic membrane bulges outward, pushing blood out of the AbioCor's left chamber. At the same time, hydraulic fluid empties from the right section and its membrane deflates, allowing blood to flow into the device's right chamber.

The AbioCor's four valves are made of plastic and configured like natural heart valves. The inflow conduits are connected to the left and right atria of the excised heart, and the outflow conduits are fitted to the arteries. The device weighs about one kilogram and consumes about 20 watts of power. The internal battery, electrical induction coil and controller module add another kilogram to the implanted system. Lithium-ion batteries worn on the patient's belt continuously recharge the internal battery using the induction coil. A bedside console can also be used as a power source and monitoring system. *—S.D.*

THE CENTRAL UNIT of the AbioCor is connected by wire to a controller that adjusts the heart rate according to the patient's activity level. An electrical induction coil transmits power through the skin.



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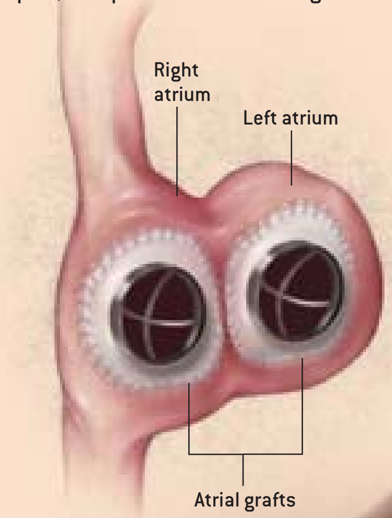
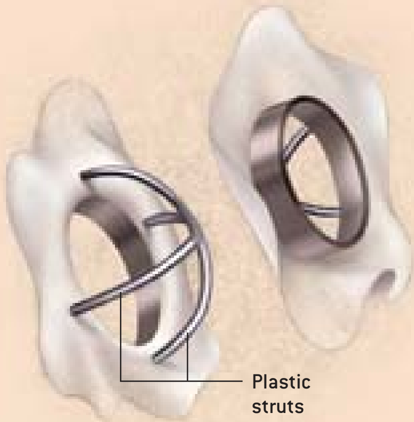
HOW THE ABIOCOR WORKS

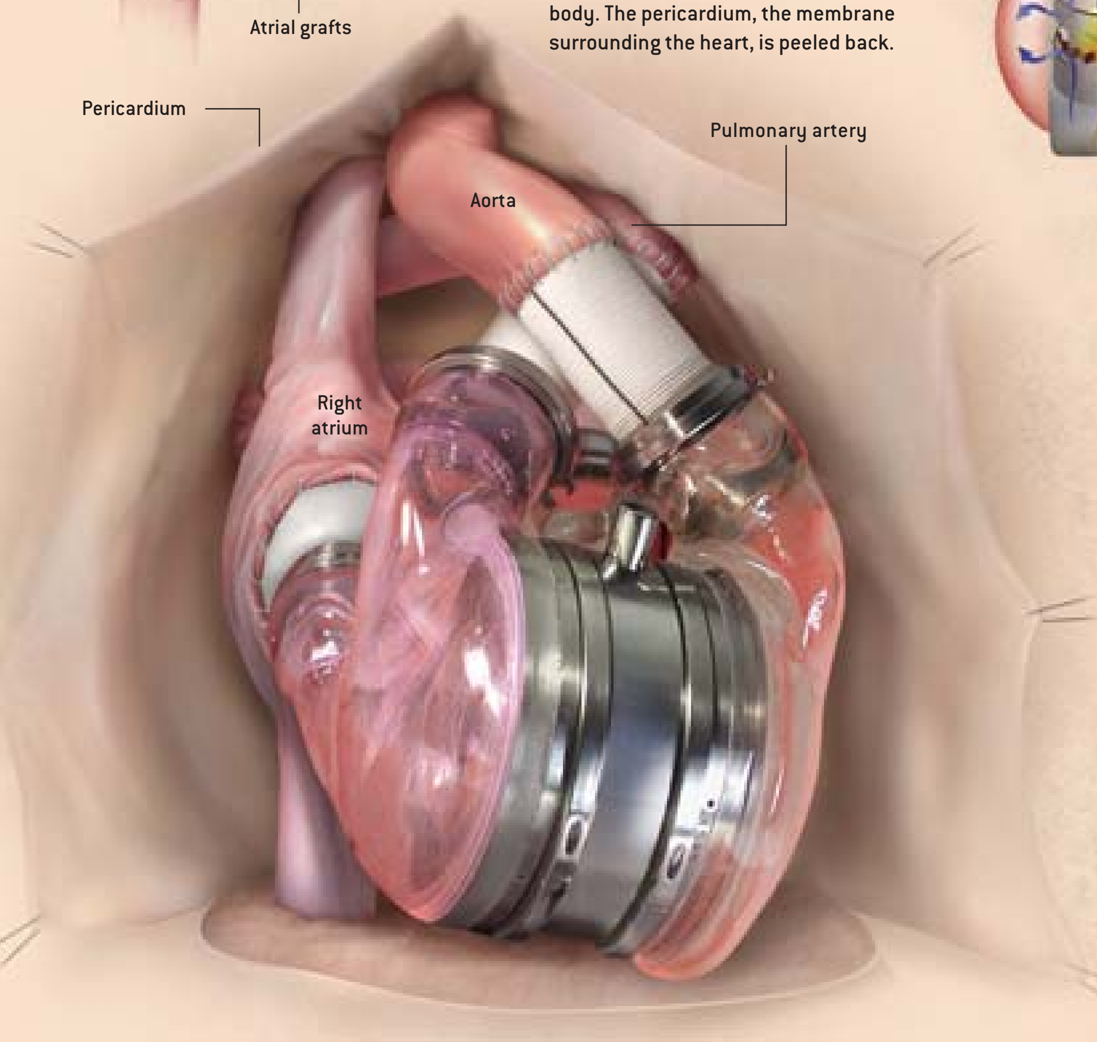
THE ABIOCOR is attached to the remnants of the right and left atria of the patient's excised heart. The grafts used in the first six patients had plastic struts designed to keep the atrial walls apart; autopsies showed clotting on these struts.



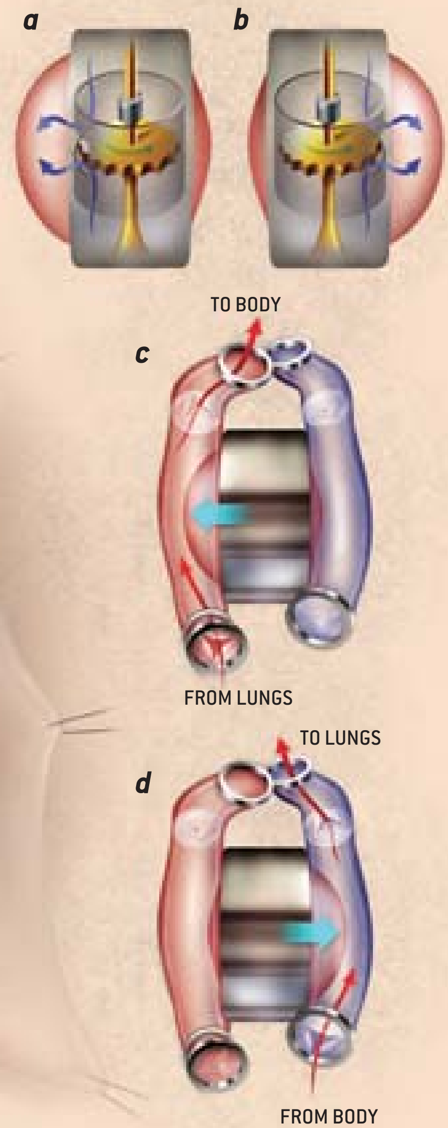
DETAIL OF ATRIAL GRAFT



IN THIS ARTIST'S rendering, the AbioCor is shown after implantation in the patient's body. The pericardium, the membrane surrounding the heart, is peeled back.



THE ABIOCOR'S pumping mechanism mimics the beating of a human heart by propelling hydraulic fluid back and forth. (The diagrams below show the device from the rear perspective.) A centrifugal pump turns continuously in one direction while a gating valve alternately shunts the hydraulic fluid to the left and right (*a* and *b*). When the fluid flows to the left, it pushes a plastic membrane into the AbioCor's left chamber, pumping oxygenated blood to the body (*c*). When the fluid flows to the right, it pushes a membrane into the right chamber, pumping oxygen-depleted blood toward the lungs (*d*).



KEITH KASNOT

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ETHICS OF THE HEART

The AbioCor trials revive some troubling questions

DURING THE CLINICAL TRIALS of the Jarvik-7 artificial heart, medical ethicists voiced concern about the suffering of the patients and the intense media coverage that descended on them. Now those issues have surfaced anew with the human testing of the AbioCor. So far ethicists give mixed grades to Abiomed (the maker of the device), the doctors and the press.

"The core ethical issues for the patient remain the same," says Arthur Caplan, director of the Center for Bioethics at the University of Pennsylvania School of Medicine. "First, can you get truly informed consent from a desperate, dying person? Dying is extremely coercive. There's very little you can't get a dying person to consent to." In Abiomed's favor, he rates the firm's 13-page consent form as "very strong" in terms of disclosing risks, and he commends the company's funding of independent patient advocates to inform patients and their families. But Caplan wonders whether the right patients are enrolled in the trials: "I've argued that for some treatments it doesn't make sense to test first in the most severely ill, because you have an impossible time sorting out what's caused by the illness and what's caused by the device."

George J. Annas, a professor at the Boston University School of Public Health, contends that the consent procedure for the AbioCor "should be much more detailed about how you're going to die. No one's going to live for a long time on one of these. You have to plan for death. How is it going happen? Who's going to make the decision and under what circumstances?" In two cases during the clinical trials, family members agreed to shut off the AbioCor's power, overriding its alarms, so a terminally failing patient could die.

Another source of controversy has been Abiomed's policy of limiting the release of information from the trials. For example, company officials will not announce a patient's identity until 30 days after an implantation (leaks at the hospital, however, have sometimes forced them to do so sooner). Although the policy has prevented a repeat of the media frenzy surrounding the Jarvik-7 trials, some ethicists have emphasized the need for full disclosure of the medical problems encountered during the human testing. Renee Fox, a social sciences professor at the University of Pennsylvania, notes that Abiomed's reporting of negative developments has been timely, for the most part. But, she adds, "there has been a tendency by the company and the physicians to interpret adverse events as not due to the implanted heart. In each case there has been an attempt to say that this is due to the underlying disease state of the patient rather than any harm that the device may have done."

Ethicists point out that journalists have erred, too, by writing overoptimistic stories about the AbioCor. It was a hopeful cover story in *Newsweek* that convinced Robert L. Tools to volunteer for the first implant. Says Ronald Munson, a professor of philosophy of science and medicine at the University of Missouri at St. Louis, "The press shouldn't evangelize a medical procedure." *—S.D.*

Texas Heart Institute in Houston implanted an artificial heart into a person for the first time, but only as an emergency measure. The device was intended as a bridge to transplant—it kept the patient alive for 64 hours until a human heart could be found for him. (The patient received the transplant but died two and a half days later.) The next artificial-heart implant was not attempted until 1981. The patient lived for 55 hours with the bridge-to-transplant device before receiving a human heart.

Then came the most publicized clinical trials in modern medicine: cardiac surgeon William DeVries's four permanent implants of the Jarvik-7 artificial heart. When DeVries performed the first cardiac replacement in 1982 at the University of Utah Medical Center, patient Barney B. Clark became an instant celebrity. His medical status was reported almost daily. Reporters tried to sneak into the intensive care unit in laundry baskets or disguised as physicians. By the time Clark died 112 days later—from multiple organ failure after suffering numerous infections—the media had provided a detailed chronicle of the medical problems and discomfort he had experienced.

Nearly two years later DeVries performed his next Jarvik-7 implant, this time at Norton Audubon Hospital in Louisville, Ky., on patient William Schroeder. Schroeder survived on the artificial heart for 620 days, the longest of anyone to date, but it took a tremendous toll on him: strokes, infections, fever and a year of being fed through a tube. The third Jarvik-7 recipient lived for 488 days, and the fourth died after just 10 days. Although several hospitals successfully used a slightly smaller version of the Jarvik-7 as a bridge-to-transplant device for hundreds of patients, most medical professionals abandoned the idea of a permanent artificial heart.

But an engineer named David Lederman believed that the concept still held promise. Lederman had worked on developing an artificial heart at the medical research subsidiary of Avco, an aerospace company, and in 1981 he founded Abiomed. He and his colleagues closely followed the clinical trials of the Jarvik-7 and considered ways to improve it. The external air compressor that powered the device was bulky and noisy. Infectious bacteria could easily lodge where the tubing pierced the patient's skin. And inside the heart itself were surface discontinuities where platelets and white blood cells could coagulate into a thrombus, a solid clot that could circulate in the blood and lodge in the brain, causing a stroke.

In 1988 the National Heart, Lung and Blood Institute at the NIH decided to cut off support for replacement-heart research and instead channel funds to ventricular-assist pumps. Lederman went to Washington along with representatives from oth-

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er research teams to lobby against the change. They convinced a group of senators from their home states to help restore NIH support, resuscitating research programs at two universities (Utah and Pennsylvania State) and two companies (Nimbus in Rancho Cordova, Calif., and Abiomed). Today Abiomed is the last artificial-heart developer left from that group. The company has received nearly $20 million in federal research grants. Its government funding ended in 2000, but that same year Abiomed raised $96 million in a stock offering.

Lederman and his colleagues are doggedly pursuing a medical technology whose time others believe may have already come and gone. In the conference room at Abiomed's headquarters in an office park north of Boston, Lederman attributes his firm's tenacity to its team of researchers: "No one else had the commitment to say there is no alternative to success. This is important stuff. I take pride in the fact that we took it so seriously." It is also evident that for Lederman this is a personal matter: in 1980 his father died suddenly of a heart attack.

Designing AbioCor

THE ABIOCOR is not powered by an air compressor as the Jarvik-7 was. Hidden behind the device's central band of metal is the heart of this heart: a pair of electric motors driving a pump-and-valve system. This pumping mechanism propels hydraulic fluid back and forth, causing a pair of plastic membranes to beat like the inner walls of a human heart [*see box on pages 62 and 63*].

But this innovation was only the start. To be truly self-contained, the device needed a small, implantable controller that could vary the heart rate to match the patient's activity level. The controller developed by Abiomed is the size of a small paperback; implanted in the patient's abdomen, it is connected to the artificial heart by wire. Sensors inside the heart measure the pressure of the blood filling the right chamber—the blood returning to the heart from the body—and the controller adjusts the heart rate accordingly. The rate can range from 80 to 150 beats a minute. If the clinical trials show that this control system is adequate, it could be shrunk down to a single microchip that would fit on the AbioCor's central unit.

Abiomed also developed a way to power the artificial heart's motors without the use of skin-penetrating wires, which can leave the patient prone to infections. An internal battery implanted in the patient's abdomen can hold enough charge to sustain the heart for 20 minutes. This battery is continuously recharged through electromagnetic induction—the same process used in electric toothbrushes. The internal battery is wired to a passive electrical transfer coil under the patient's skin. Another coil outside the patient's skin, wired to an external battery, transmits power through the skin tissue with minimal radiation and heat. The patient can wear the external battery on a belt, along with a separate monitor that alerts the patient if the battery's charge runs low.

A major concern was to design the AbioCor so that it could pump blood without creating clots. When Lederman had worked for Avco, he had conducted four years of research on the interaction between blood and synthetic materials, studying

ABIOCOR RECIPIENTS: Robert L. Tools (*above*), shown holding an artificial heart like the one in his chest, became the first AbioCor patient in July 2001. He died in November after suffering a severe stroke. The second recipient, Tom Christerson (*below*), has lived the longest with the AbioCor—more than eight months as of press time. Shown here with a physical therapist at Jewish Hospital in Louisville, Ky., Christerson returned home in April.

JOHN LAIR *AFP/Corbis* (*top*); BRIAN BOHANNON (*bottom*)

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the reaction rates of various coagulation processes. Essentially the AbioCor minimizes clotting by making sure that the blood cells do not have time to stick together. Blood flows swiftly through the device, and there are no areas where pooling can occur. All the surfaces of the device that are in contact with blood are made of Angioflex, a biologically inert polyurethane plastic. The contact surfaces are also extremely smooth because clots can form on irregular surfaces. Says Lederman, "We had to make a system that was totally seamless."

Trial and Error

AFTER TESTING its artificial heart in calves and pigs, Abiomed received permission from the FDA in January 2001 to begin clinical trials in humans. The FDA would determine the success of the trials by reviewing the patients' survival rates and quality of life, as measured by standard assessment tests. Only patients who were ineligible for a heart transplant could volunteer for the implantation. The size of the AbioCor also ruled out certain patients: the device can fit inside the chests of only half of adult men and 18 percent of adult women. (Abiomed is developing a smaller, second-generation heart that would fit most men and women.) For each procedure, Abiomed agreed to pay for the device and its support. Hospitals and doctors participating in the trials would donate facilities and care. The total cost of each implantation and subsequent treatment: more than $1 million.

On July 2, 2001, the first AbioCor was implanted in Robert L. Tools at Jewish Hospital in Louisville, Ky., by surgeons Laman A. Gray, Jr., and Robert D. Dowling in a seven-hour operation. Tools had been suffering from diabetes and kidney failure as well as congestive heart failure. Before the heart replacement, he could barely raise his head. After the procedure, Tools experienced internal bleeding and lung problems, but within two months his kidney function had returned to normal and he had enough strength to be taken on occasional outings from the hospital. His doctors hoped he would be able to go home by Christmas. Tools's bleeding problems persisted, however, making it difficult for doctors to administer the anticoagulant drugs intended to prevent clot formation. On November 11 he suffered a severe stroke that paralyzed the right side of his body. He died 19 days later from complications following gastrointestinal bleeding.

The second recipient of the AbioCor, a 71-year-old retired businessman named Tom Christerson, has fared much better so far. Surgeons at Jewish Hospital implanted the device in Christerson on September 13, 2001. After a steady recovery, he left the hospital in March to take up residence in a nearby hotel, where he and his family could learn how to tend to the artificial heart on their own. The next month he returned to his home in Central City, Ky. In the following weeks, Christerson continued his physical therapy and visited Jewish Hospital for weekly checkups. His car was wired so that he could use it as a power source for his artificial heart.

At the Texas Heart Institute, O. H. "Bud" Frazier—the surgeon who has the record for performing the most heart transplants—implanted the AbioCor into two patients. One lived with the device for more than four months before dying of complications from a stroke; the other died within a day of the implantation, succumbing to uncontrolled bleeding after spending 20 hours on the operating table. Implantations have also been performed at the University of California at Los Angeles Medical Center and Hahnemann University Hospital in Philadelphia. The Los Angeles patient lived for a little less than two months before heart support was withdrawn following multiple organ

HEARTMATE PUMP, the most widely used ventricular-assist device, is implanted in a patient's abdomen, as shown in this artist's rendering. Attached to a failing left ventricle, the device pumps oxygenated blood to the body.

COURTESY OF THORATEC

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HEART HELPERS

Ventricular-assist devices emerge as an alternative to heart replacement

IN NOVEMBER 2001, soon after human testing of the AbioCor began, researchers reported that another clinical trial had demonstrated the benefits of a less drastic treatment for heart failure. The left ventricular assist device (LVAD)—a pump implanted in the chest or abdomen and attached to the heart's left ventricle, the chamber that pumps oxygenated blood to the body—had been developed as a short-term therapy for patients awaiting heart transplants. But the trial showed that LVADs can keep patients alive for two years or more, and the Food and Drug Administration is expected to approve the devices for long-term use.

The study evaluated 68 patients with implants of the HeartMate, the most widely used LVAD, and 61 patients who received medical therapy, including potent cardiac drugs. After a year, more than half of those with LVADs were still alive, compared with only one quarter of those on medical therapy. At two years, the survival rates were 23 percent for the LVAD group and 8 percent for the medical group. The longest stint on the HeartMate is now more than three years; the longest survivor of the medical group died after 798 days. "There are still 21 patients ongoing with the devices," notes Eric Rose, surgeon in chief at Columbia Presbyterian Medical Center in New York City and principal investigator for the trial. "This sets a new benchmark for treating the disease."

The HeartMate, made by Thoratec in Pleasanton, Calif., is far from perfect. Many of the implanted test subjects suffered serious infections because the device is connected to an external battery by a skin-piercing tube. Other HeartMate patients died from mechanical malfunctions such as motor failure. But Thoratec has already improved on the current version of the device and is developing second- and third-generation systems designed to last eight and 15 years, respectively.

JARVIK 2000 is the only assist device small enough to fit within the left ventricle. Robert K. Jarvik, inventor of the Jarvik-7 artificial heart, now develops assist devices rather than replacement hearts.

Another LVAD, called the LionHeart, made by Arrow International in Reading, Pa., is a fully implantable system with no skin-piercing tubes or wires. Now in clinical trials, the LionHeart uses an electrical induction coil like the AbioCor's to transmit power through the skin. The MicroMed DeBakey VAD is also fully implantable, but it propels blood in a steady flow rather than pumping it like a natural heart. Proponents of this technology tout its efficiency and reliability; critics argue that a pulsating heartbeat is needed to keep blood vessels clear. Cardiac pioneer Michael E. DeBakey, who performed the first successful coronary bypass in 1964, developed the device in collaboration with one of his patients, David Saucier, a NASA engineer who had had heart transplant surgery.

Robert K. Jarvik, inventor of the Jarvik-7 artificial heart and now CEO of New York City–based Jarvik Heart, has introduced the Jarvik 2000, the only assist device small enough to be lodged inside the left ventricle. Like the DeBakey VAD, the Jarvik 2000 pumps blood in a steady flow. The device is currently in trials for bridge-to-transplant use and has been implanted in some patients for long-term use as well. Jarvik believes the device could help a less severely damaged heart to repair itself, perhaps in combination with stem cell treatments [*see box on next page*]. Another potential combination therapy might be the use of LVADs with the steroid clenbuterol to strengthen the heart. In a test reported last year, Magdi Yacoub of Harefield Hospital in London administered clenbuterol to 17 patients with implanted LVADs. In five of the patients, the hearts recovered enough to allow the removal of the LVADs. *—S.D.*

COURTESY OF TEXAS HEART INSTITUTE

failure. The Philadelphia patient, 51-year-old James Quinn, received the AbioCor on November 5, 2001. Although he suffered a mild stroke in December, the next month he was discharged from the hospital to a nearby hotel. This past February, however, he was readmitted to the hospital with breathing difficulties. Doctors treated him for pneumonia, which became life-threatening because his lungs were already weakened by chronic emphysema and pulmonary hypertension. Quinn was placed on a ventilator to help him breathe, but his recovery was slow. By mid-May, though, his condition was improving, and doctors began to wean him from the ventilator.

In January, Abiomed reported preliminary findings from the clinical trials at a press conference. Lederman noted that the artificial heart had continued to function under conditions that

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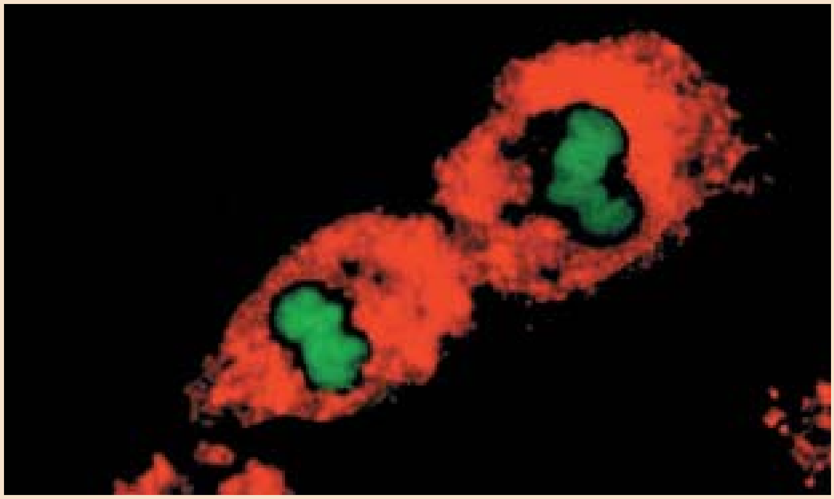
MENDING BROKEN HEARTS

Stem cells may prove to be the best medicine for injured hearts

EVERY SO OFTEN, unexpected findings turn scientific wisdom upside down. Two studies recently published in the *New England Journal of Medicine* have refuted the long-held notion that the human heart cannot repair itself after a heart attack or other injury. The research indicates that new muscle cells can indeed grow in adult hearts and that they may arise from stem cells, the undifferentiated building blocks of the body. The discovery may pave the way for therapies that encourage natural healing.

Research teams at the New York Medical College (NYMC) in Valhalla, N.Y., and the University of Udine in Italy conducted the iconoclastic experiments. The first study found chemical markers indicating new growth of muscle cells in heart samples taken from patients who had died four to 12 days after a myocardial infarction (the medical term for a heart attack). The second study, which involved the postmortem examination of female hearts transplanted into men, showed the presence of stem cells with Y chromosomes in the donated hearts. Although these stem cells could have migrated from the male recipient's bone marrow, they could have also come from the cardiac remnant to which the female heart was attached.

"Our paper suggests the possibility that cardiac stem cells may exist," says Piero Anversa, director of the Cardiovascular Research Institute at the NYMC. "We need to determine all the characteristics that prove that we are dealing with a primitive cell in the heart. And then we need to see whether we can mobilize these cells in areas of heart damage to promote repair."



HEART MUSCLE CELL, or myocyte, is shown dividing in this microscope image of tissue taken from a patient who died shortly after a heart attack. The evidence suggests that, contrary to prevailing medical opinion, new myocytes can grow to replace damaged ones.

Other medical researchers are pursuing regenerative cardiac therapies with stem cells taken from other parts of the body. Philippe Menasché, professor of cardiovascular surgery at the Bichat-Claude Bernard Hospital in Paris, has injected primitive muscle cells from patients' legs into damaged areas of their hearts during cardiac bypass surgery. Initial results from the clinical trials have been encouraging, showing thickening of heart muscle walls with functional tissue. But Menasché is cautious about therapeutic outcomes. "At best, these cells may help enhance other treatments," he says. "Imagining that you'll be able to completely regenerate an infarcted heart is probably unrealistic."

But some biotechnology firms are entertaining even wilder hopes. Advanced Cell Technology, the Worcester, Mass.–based company that gained notoriety last year with its human cloning experiments, has already turned stem cells into beating heart cells and is trying to create transplantable patches for repairing larger areas of damage. "Eventually we want to engineer a full heart," says Robert Lanza, the company's vice president for medical and scientific development. The task would require generating cardiac muscle and blood vessel tissue as well as fabricating a dissolvable biological scaffolding material for building the heart. How far off is a biological artificial heart? According to Lanza, "We could produce a functioning heart in 10 years, with clinical trials in maybe 15 years." *—S.D.*

could have damaged or destroyed a natural heart, such as a severe lack of oxygen in the blood and a fever of 107 degrees Fahrenheit. Also, no patient had suffered an infection related to the device. But Abiomed acknowledged a design flaw in the artificial heart's connections to the body. The AbioCor is attached to remnants of the atria of the patient's excised heart; autopsies on two patients had shown clotting on the plastic struts of thimble-size "cages" that were intended to maintain the separation of the remaining atrial walls [*see illustration on page 63*]. Because these clots could cause strokes, Abiomed declared that it would no longer use the plastic cages when implanting the AbioCor. The cages were needed to test the device in calves but are unnecessary in humans.

In early April, Abiomed announced that it would not be able to meet its original schedule of implanting the AbioCor in 15 volunteers by the end of June. The company said that it wanted to devote further study to its first six cases. But a week later doctors at Louisville's Jewish Hospital performed another implantation, the first using an AbioCor without the plastic cages. The artificial heart functioned properly, but the 61-year-

"EVIDENCE THAT HUMAN CARDIAC MYOCYTES DIVIDE AFTER MYOCARDIAL INFARCTION," BY A. P. BELTRAMI ET AL. IN THE *NEW ENGLAND JOURNAL OF MEDICINE*, VOL. 344, NO. 23; JUNE 7, 2001. COPYRIGHT © 2001 MASSACHUSETTS MEDICAL SOCIETY. ALL RIGHTS RESERVED

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old patient died within hours of the procedure after a clot lodged in his lungs. According to Laman Gray, who performed the operation with colleague Robert Dowling, the clot did not originate in the AbioCor.

The surgeons who have worked with the AbioCor remain convinced of the device's potential, despite the recent setbacks. Frazier of the Texas Heart Institute believes the formation of clots in the AbioCor's plastic cages was a complication that could not have been anticipated. "Fortunately, this one can be corrected," he says. "It's not something inherently wrong in the device." Gray concurs: "In my opinion, it's very well designed and is not thrombogenic at all. The problem has been on the inflow cage. I'm truly amazed at how well it has done in initial clinical trials." (Both surgeons consulted on the AbioCor's design and were responsible for much of its testing in animals.)

But not everyone is as sanguine as Frazier and Gray. "Total heart replacement by mechanical devices raises a number of questions that have not been addressed in this small group of patients," says Claude Lenfant, director of the National Heart, Lung and Blood Institute. "What quality of life can a total-heart-replacement patient expect? Will there be meaningful clinical benefits to the patient? Is the cost of this therapy acceptable to society?" And Robert K. Jarvik, the developer of the Jarvik-7 device that made headlines 20 years ago, now argues that permanent artificial hearts are too risky. "Cutting out the heart is practically never a good idea," he says. "It was not known in 1982 that a heart can improve a lot if you support it in certain very common disease states. That's why you should cut out the heart only in the most extreme situations."

JUST BEFORE IMPLANTING the AbioCor into patient Tom Christerson, surgeons Laman A. Gray, Jr. (*left*), and Robert D. Dowling (*right*) evacuate the air from the artificial heart to prevent blood clotting. The procedure was performed on September 13, 2001, at Louisville's Jewish Hospital.

AFB/CORBIS

Heart of the Matter

AS THE ABIOCOR TRIALS continue, the most crucial objective will be reducing the incidence of strokes. Doctors had originally hoped to guard against this risk by prescribing low levels of anticoagulant drugs, but some of the test subjects were so severely ill that they could not tolerate even these dosages. Because these patients had medical conditions that made them susceptible to internal bleeding, determining the best dosage of anticoagulants became a delicate balancing act: giving too much might cause the patient to bleed to death, and giving too little might cause a stroke.

Despite the need for more refinement, Lederman is satisfied with the clinical results to date. The initial goal of the trials was to show that AbioCor could keep the patients alive for at least 60 days, and four of them surpassed that mark. Says Lederman, "If most of the next patients go the way the first ones have gone but without unacceptable complications such as strokes, we plan to ask the FDA to authorize clinical use of the system for patients who are on their last breath. We think we have a convincing argument that we can give patients with less than 30 days to live many months of quality life." But some medical ethicists have questioned this approach, saying that people at death's door might consent to any procedure, no matter what the consequences [*see box on page 64*].

And then there is the issue of how to define an acceptable quality of life. In 1981 Jarvik wrote that for the artificial heart to achieve its goal "it must be forgettable"—that is, the device should be so unobtrusive and reliable that patients would be able to ignore it [see "The Total Artificial Heart," by Robert K. Jarvik; Scientific American, January 1981]. Does the AbioCor meet that standard? Tools's wife, Carol, says that her husband was aware that his old heartbeat had been replaced by the AbioCor's low, steady whir. "Sometimes he'd lie there, and he would listen to it," she says. "But other times he would forget it.... [He] always knew it was there, because he still had to power it. It's not like replacing a hip." Still, she believes that the quality of life during his last months was good: "He had a chance to live quite well, although unfortunately, it was shorter than we would have liked." She adds, "He never had any regrets about it." SA

MORE TO EXPLORE

More information about Abiomed, the manufacturer of the AbioCor, is available at **www.abiomed.com**

The Web site of the Implantable Artificial Heart Project at Jewish Hospital in Louisville, Ky., is **www.heartpioneers.com**

The Texas Heart Institute in Houston: **www.tmc.edu/thi**

The National Heart, Lung and Blood Institute at the National Institutes of Health: **www.nhlbi.nih.gov/index.htm**

Steve Ditlea is a freelance journalist based in Spuyten Duyvil, N.Y. He has been covering technology since 1978.

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A strange, elusive phenomenon called supersymmetry was conceived for elementary

Uncovering Supersymmetry

PROVERBIAL APPLES AND ORANGES are as different as the types of quantum particles called fermions and bosons. Just as an ordinary mirror cannot make an apple look like an orange, no ordinary symmetry in physics can transform a fermion into a boson, or vice versa. To do that trick requires supersymmetry, an extraordinary class of symmetries that may hold the key to a deep understanding of the universe.

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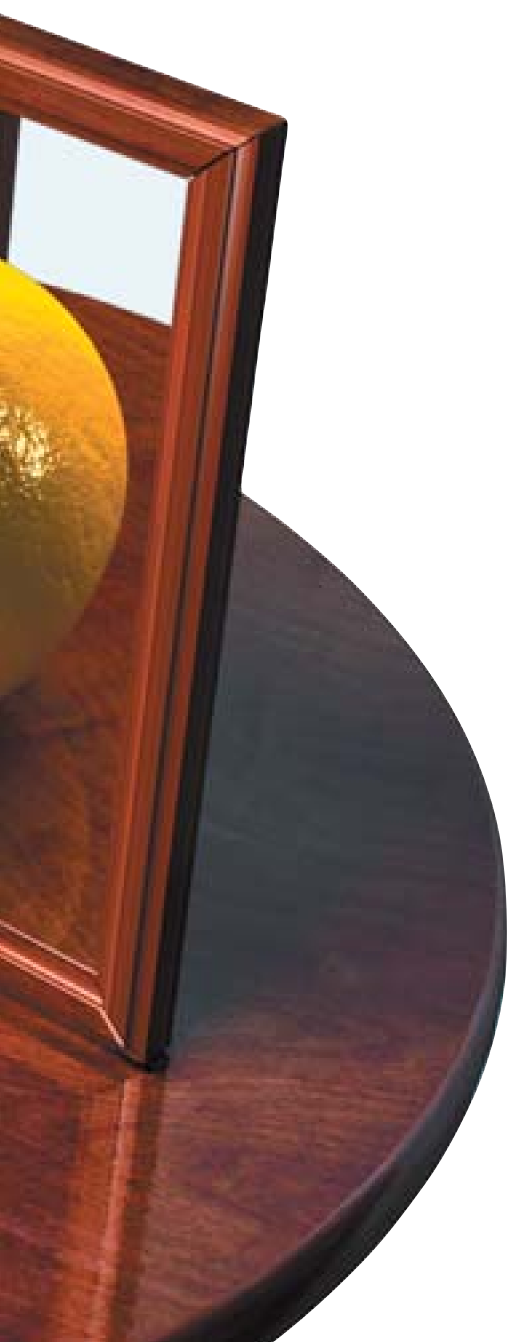
particle physics—but has come to light in nuclei of platinum and gold

Uncovering Supersymmetry

By Jan Jolie

Illustrations by Bryan Christie Design



Supersymmetry is a remarkable symmetry. In elementary particle physics, it interchanges particles of completely dissimilar types—the kind called fermions (such as electrons, protons and neutrons), which make up the material world, and those called bosons (such as photons), which generate the forces of nature. Fermions are inherently the individualists and loners of the quantum particle world: no two fermions ever occupy the same quantum state. Their aversion to close company is strong enough to hold up a neutron star against collapse even when the crushing weight of gravity has overcome every other force of nature. Bosons, in contrast, are convivial copycats and readily gather in identical states. Every boson in a particular state encourages more of its species to emulate it. Under the right conditions, bosons form regimented armies of clones, such as the photons in a laser beam or the atoms in superfluid helium 4.

Yet somehow in the mirror of supersymmetry, standoffish fermions look magically like sociable bosons, and vice versa. Figuratively, you might say it is a symmetry that lets you compare apples and oranges. Hold up an apple to the supersymmetry mirror, and its reflection looks and tastes like an orange. All the ordinary symmetries of physics lack that sorcery. Those symmetries may act like the distorting mirrors of a funhouse, making familiar electrons look like ghostly neutrinos, for instance, but they can never change a fermion into a boson. Only supersymmetry does that.

At least that's the theory. Elementary particle theorists have studied supersymmetry intensively since its invention in the 1970s, and many believe it holds the key to the next major advance in our understanding of the fundamental particles and forces. Experimenters, however, have searched at their highest-energy colliders for particles predicted by supersymmetry, so far to no avail.

In the 1980s nuclear theorists proposed that superviolent collisions were not necessarily the only way to see supersymmetry; they predicted that a different form of supersymmetry could exist in certain atomic nuclei. Here, too, the symmetry relates what in physics are quite dissimilar objects: nuclei with even numbers of protons and neutrons and those with odd numbers. (This again involves fermions and bosons, because a composite particle made of an odd number of fermions is itself a fermion, whereas an even number produces a boson.)

To better understand the nuclear supersymmetry, picture a roomful of ballroom dancers in place of the nucleons that make up a nucleus. When there are an even number of dancers, everyone has a partner and the room is neatly described as couples dancing. The odd case is marred by one additional person stumbling around the floor without a partner. In the supersymmetric mirror, that person magically looks like another couple, dancing in step with all the others. Similarly, the nucleus with an odd number of protons and neutrons, collectively called nucleons, is related to one in which all the nucleons are paired.

Experimenters recently observed a version of this extraordinary symmetry in isotopes

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of gold and platinum, with protons and neutrons acting as two separate groups of dancers—students from two high schools holding their proms in the same ballroom, perhaps. In this nuclear supersymmetry, four cases instead of two are tied together: the one in which both schools have an odd man out (odd numbers of protons and neutrons), the two in which one school does (an even number of protons but an odd number of neutrons, or vice versa), and the one in which everyone is partnered (even numbers of protons and neutrons).

The atomic nucleus is a fascinating quantum system holding many secrets. Its study over the decades has been a continuous source of unexpected observations. Theorists must use many tools to understand all the facets of the very complicated physics of nuclei. The new result adds supersymmetry to the toolkit—and it shows that supersymmetry is not just a mathematical curiosity but exists in the world.

Nuclear physics research also provides tools needed to understand other quantum systems that have general features similar to nuclei—the so-called finite many-body systems, containing anything from a few particles to hundreds of them. Experimental methods now allow the study of such objects built from small numbers of atoms or molecules. Supersymmetry might also be important to those fields of physics.

Mysterious Nuclei

EVERYTHING OF SUBSTANCE in the world around us is made of atoms, clouds of electrons surrounding tiny massive atomic nuclei. Physicists and chemists understand very well how the electrons arrange themselves and how the properties that govern our material world arise from those structures. Some of the most precise predictions in science relate to fine details of energy levels of electrons in atoms. Atomic nuclei, in contrast, have remained far more inscrutable.

The fundamental reason for this disparity is the nature of the forces involved. Electrons are held in their orbitals around atoms by the electromagnetic force, which is relatively weak. The dominant force inside nuclei is about 100 times stronger (hence the name: the strong nuclear force). Theoretical techniques that successfully describe weak forces such as electromagnetism break down for one as strong as the nuclear force. In addition, electrons are structureless elementary particles, whereas protons and neutrons are themselves complex bundles of particles called quarks and gluons. The force between these nucleons is not directly a fundamental force like electromagnetism, whose equations we know exactly. Instead the nuclear force acting between nucleons is a complicated by-product of the interactions of their constituent quarks and gluons.

The nuclear force is strongly attractive for a few femtometers (10^{-15} meter) and then falls to zero. This force packs the nucleons closely together, and each nucleon interacts strongly with all the other nucleons that are within range. (In contrast, electron orbitals lie some 10,000 times farther away.) The resulting structure is one of the most challenging quantum systems known, and over the decades physicists have developed many theoretical models to try to describe it [*see box on opposite page*]. Some models treat the nucleus as a droplet of quantum fluid that can vibrate and oscillate in specific ways. Others mimic the structure that works so well for the orbiting electrons: shells of discrete orbitals that the nucleons steadily fill up, starting from the lowest energy level.

The different models tend to work best for specific classes of nuclei, depending on how many nucleons are involved overall and how full the outermost shells of protons and neutrons are. Because the protons and neutrons like to form pairs, the behavior of a nucleus depends critically on whether it has even or odd numbers of protons and neutrons [*see illustration on page 74*]. So-called even-even nuclei tend to be simplest, followed by even-odd, with odd-odd the most difficult of all.

Symmetry is an important and powerful tool for developing and using such models. Symmetry principles occur throughout physics, often in ways that one wouldn't expect. For example, the law of conservation of energy can be derived from a symmetry principle involving the flow of time. The shells of orbitals, both for electrons and nucleons, are distinguished by properties related to symmetries, such as the angular momentum of particles in the orbital and whether the orbital is unchanged if it is reflected (a property called parity). The equations governing elementary particle physics are fundamentally based on symmetries.

A key aspect of symmetry in quantum physics is the division of particles into bosons and fermions, which have fundamentally dissimilar quantum states and completely different behaviors. Fermions obey the Pauli exclusion principle, meaning that two fermions of the same species cannot be in the same quantum state at

Overview/*Dances with Nucleons*

- In quantum physics, all particles and fields are divided into two extremely dissimilar types: fermions and bosons. Fermions include the electrons, protons and neutrons that make up matter. Bosons include photons (responsible for electromagnetism) and gluons (which bind quarks together).
- Symmetries play major roles throughout physics. All ordinary symmetries respect the distinction between bosons and fermions. Supersymmetry theories incorporate powerful mathematical properties that interchange bosons and fermions. Such theories may be crucial for deeply understanding particle physics, but experimenters have not yet detected supersymmetry of elementary particles.
- In atomic nuclei, protons and neutrons each form pairs that behave like composite bosons. Nuclei thereby form four distinct classes (even-even, even-odd, odd-even and odd-odd) depending on whether the protons and neutrons can each completely pair off. Physicists predicted that a variant of supersymmetry should relate a "magic square" of four nuclei of these types. Experimenters have now confirmed that prediction.

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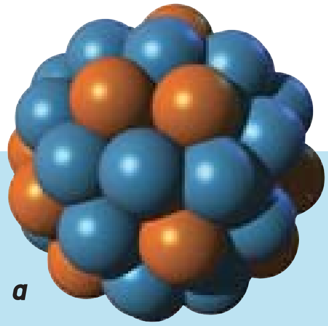
Nuclear Models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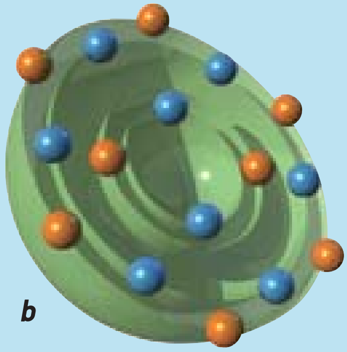
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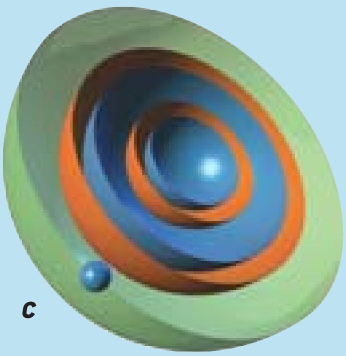
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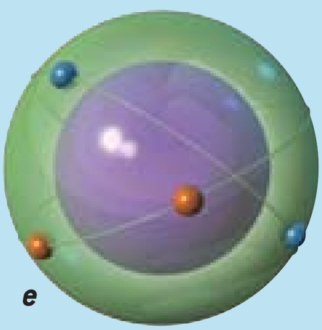
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ONE HUNDRED TRILLION (10^{14}) times denser than water, nuclei (*a*) are very tightly packed bundles of protons (*orange*) and neutrons (*blue*). Because of the strength and complexity of the strong nuclear force that holds nuclei together, physicists have long resorted to approximate models to describe the quantum states of nuclei.

The shell model (*b*) is very similar to the description of electrons in atoms. It considers the atomic nucleus to be an ensemble of weakly interacting neutrons and protons (nucleons) held in a potential energy well. The nucleons can occupy various orbits, analogous to the orbits of electrons around an atom, but now with two sets of them—one for protons, one for neutrons. Like electrons, nucleons are fermionic particles and the exclusion principle applies, so two cannot occupy the same orbit. The orbits form shells, or groups of orbits having similar energies with large energy gaps between them. Nuclei with a closed (full) shell of protons or a closed shell of neutrons (and especially those with both) show great stability, similar to noble-gas atoms with full shells of electrons.

For nuclei with a few additional nucleons beyond a closed shell (*c*), one can neglect to an extent the individual nucleons in the closed shell and concentrate on the few that are outside the shell. Interactions among these outer nucleons, however, must also be taken into account. In heavy nuclei with many nucleons outside the last closed shell, the calculations become prohibitively complex even with modern computers.

The collective, or liquid-drop, model (*d*) applies to heavy nuclei, which are formed by about 100 or more nucleons. The model does not track individual nucleons but instead views the nucleus as a droplet of a quantum liquid that can undergo various vibrations and rotations. The properties of the nucleus are encapsulated in features such as the density and surface tension of the liquid and the electric charge distributed throughout it. This model has been extremely successful in describing certain classes of nuclei far from closed shells—that is, those that have a large number of nucleons in the outermost shell.

In quantum physics, excitations such as the vibrations of a droplet take on many properties of particles and can behave like fermions or bosons. When the collective model is applied to the simplest systems—even-even nuclei, which have even numbers of both protons and neutrons—the basic constituents of the model, the surface vibrations, behave as bosons. For an odd number of nucleons, the last nucleon occupies an orbit that depends on the state of the droplet, and excitations are fermions.

The interacting boson model (*e*) connects the shell model and the liquid-drop model by making use of the pairing property of the nuclear force [*see box on next page*]. The model analyzes heavy even-even nuclei as collections of pairs of nucleons outside a closed shell, like describing people on a dance floor as couples (rather than individuals) moving about. When two nucleons pair up, they resemble a boson, but different types of pairs are possible. In the dance analogy, some couples are doing a slow waltz while others are rushing around in a polka. *—J.J.*

once. Bosons, in contrast, prefer to collect in identical states, as demonstrated by helium 4 atoms in a superfluid.

Helium 4 is an example of a composite particle that is a boson. It is made up of six fermions (two protons, two neutrons and two electrons). Nucleons themselves are actually composite fermions, containing three fundamental fermions (quarks). The general rule is that an even number of fermions make up a composite boson, whereas an odd number make up a composite fermion. Ordinary symmetries necessarily map bosons onto bosons and fermions onto fermions. By mapping bosons onto fermions, and vice versa, supersymmetry opens up a new class of possible relations among particles. Also, the novel mathematics of these relations results in far greater computational power for analyzing or predicting a system's behavior.

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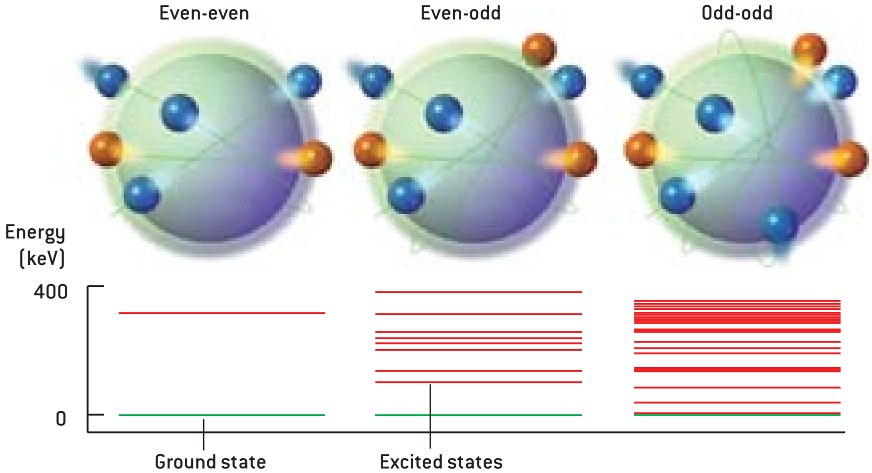
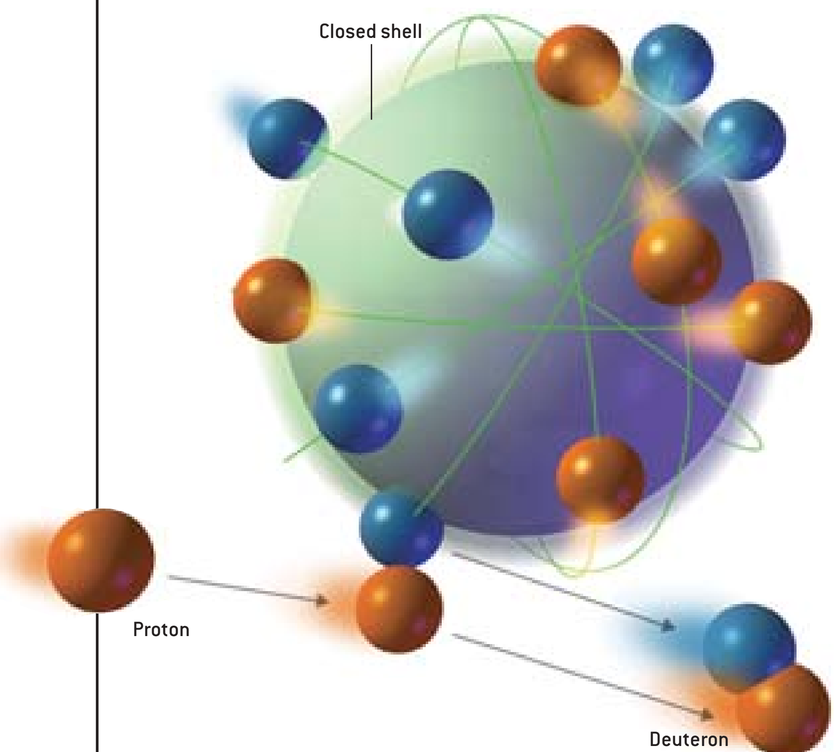
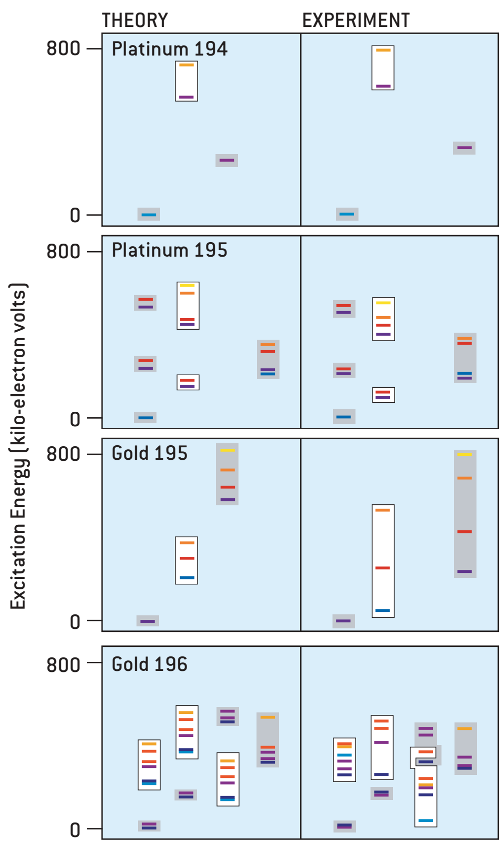
MEASURING AND IDENTIFYING NUCLEAR STATES

NUCLEI DIFFER GREATLY depending on whether they have even or odd numbers of protons and neutrons (*right*). These differences occur because the protons (and, separately, the neutrons) in a nucleus tend to form pairs that move in stable, coordinated states. Maria Goeppert Mayer introduced this concept in the 1950s while at the University of Chicago. In the simplest type of nuclei, even-even, all the protons and all the neutrons are paired up. These nuclei have very few low-energy excited states. In even-odd nuclei, which have an even number of one nucleon type and an odd number of the other, the one unpaired nucleon introduces more excitations. Odd-odd nuclei have an unpaired proton and an unpaired neutron and are correspondingly more complicated.



TRANSFER REACTIONS provided crucial data for observing nuclear supersymmetry by determining the excited states of gold 196. In a typical transfer reaction (*below*), an accelerated proton strikes a nucleus and carries off one of its neutrons, forming a deuteron. The daughter nucleus will be in an excited state whose energy can be determined directly from the energy of the deuteron.





NUCLEAR SUPERSYMMETRY is revealed in the lowest energy states of four nuclei, as modeled by the supersymmetry theory (*above, left*) and as measured (*above, right*). Colors signify angular momenta of the states, which are grouped in accord with the supersymmetry. The agreement between theory and experiment, though not exact, is impressive for such a complicated nuclear system.

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Nuclear Symmetries

SYMMETRY PLAYS a key role in the so-called interacting boson model of nuclei, which was introduced in the mid-1970s by Akito Arima of the University of Tokyo and Francesco Iachello, then at the University of Groningen in the Netherlands [*see box on page 73*]. This model analyzes nuclei as being made of paired protons and neutrons—the pairs are the bosons of the model. Arima and Iachello found three special types of even-even nuclei in their model, each one associated with a particular symmetry. Two of the classes and their symmetries were already known from the older liquid-drop model and had been studied in experiments, but the third involved a symmetry that had never been seen in nuclei. In the late 1970s Richard F. Casten and Jolie A. Cizewski, both then at Brookhaven National Laboratory, discovered that platinum nuclei displayed the new symmetry, greatly boosting the interacting boson model. Soon it became evident that the interacting boson model was a good approximation for many nuclei.

The symmetries predicted by the interacting boson model are of a special type known as dynamical symmetries. Ordinary (nondynamical) symmetries can be pictured as being much like the everyday symmetries that we see around us. An object has mirror symmetry, for example, if it looks the same when viewed in a mirror. Your left hand is approximately the mirror image of your right hand. Dynamical symmetries, in contrast, relate not to the objects themselves but to the equations that govern the dynamics of the objects. Unfortunately for experimenters, only a limited class of nuclei can exhibit dynamical symmetries.

The interacting boson model naturally works best for even-even nuclei. Odd-even nuclei always have an unpaired nucleon left over, like one extra person wandering among a room of dancers. Such a nucleus is described in the model by n bosons and one fermion, the unpaired nucleon. In some cases, dynamical symmetries can be used for analyzing odd-even nuclei, but the procedure is much more complicated than in the even-even case. In 1980 Iachello, by then at Yale University,

Supersymmetry in Particle Physics

IN THE STANDARD MODEL of particle physics, all the particles that make up matter—quarks and electrons—are fermions, as are the related particles the muon, the tau and the neutrinos. All the particles that generate forces—photons, gluons, and *W* and *Z* particles—are bosons. So, too, are the postulated graviton and Higgs particle.

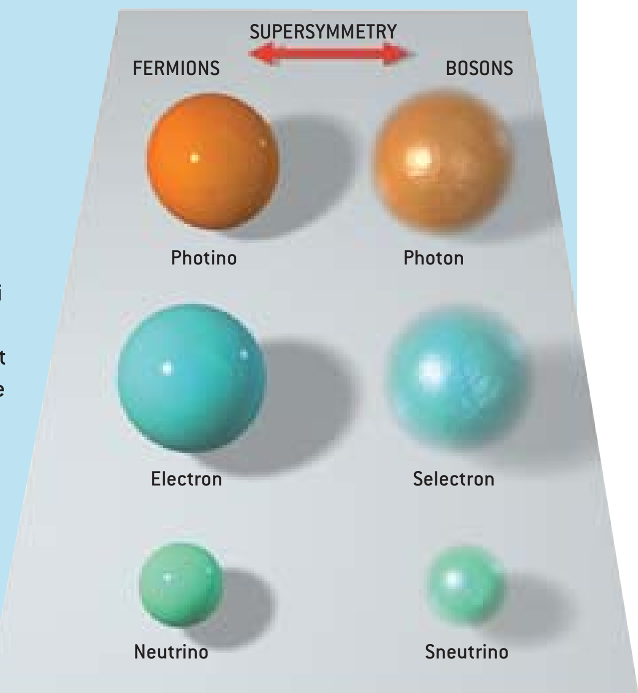
Symmetries form the foundation of the Standard Model. Electrons and electron neutrinos, for example, are related by one symmetry, which also relates "up" quarks to "down" quarks. A different manifestation of the same symmetry associates *Z* and *W* particles. Gluons are all related by a "color" symmetry, which also relates different "colors" of quarks. All these symmetries relate fermions to fermions and bosons to bosons; the quantum states of bosons and fermions are too dissimilar for an ordinary symmetry to connect them.

The underlying difference between bosons and fermions is this: in a collection of particles, if two identical fermions are swapped (for instance, switch two electrons), the total quantum state of the collection is inverted (imagine crests and troughs of a wave being interchanged). Swapping two identical bosons, in contrast, leaves the total state unaltered. Those characteristics lead to the Pauli exclusion principle, which prevents two fermions from occupying the same state, and to bosons' propensity to collect together in a common state, as in laser beams and Bose-Einstein condensates.

Ordinary symmetries are described by mathematics called groups and Lie algebras (named after Norwegian mathematician Sophus Lie). Lie algebras and groups cannot introduce or cancel the strange inversion that occurs when fermions are swapped, so they cannot transform fermions to bosons, or vice versa. Supersymmetry, devised in the 1970s, uses "graded Lie algebras," or superalgebras. In essence, the supersymmetry transformations add another fermionic component to each particle, which suffices to interchange fermions and bosons.

For the known particles to obey supersymmetry, they must each have a "superpartner"—every boson must have a fermionic counterpart, and vice versa. The known particles do not have the right properties to be one another's partners, so new particles are predicted. The Standard Model is extended to the supersymmetric standard model. The postulated fermionic partners go by the names photino, gluino, Wino, Zino, gravitino and higgsino. The bosonic partners have an "s" added to their names: selectron, smuon, sneutrino, squark and so on. None of these particles have yet been detected.

This elementary particle supersymmetry is also intimately related to the symmetries of spacetime that underlie Einstein's theory of special relativity. That is, the supersymmetry extends those symmetries. The supersymmetry of nuclei is fundamentally different because it does not have that connection to spacetime. The common ground between these two applications of supersymmetry in physics is that they both rely on superalgebras. *—J.J.*



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The Symmetric Universe

THE NATURAL WORLD AROUND US abounds with symmetries and approximate symmetries—the bilateral symmetry of most animals, the rotational symmetry of the sun, the fivefold symmetry of many starfish, and the manifold symmetries of fruit and flowers. Symmetry becomes so commonplace it takes something as extraordinary as a snowflake to awaken our awe.

Much of fundamental physics, it turns out, amounts to uncovering other kinds of symmetries that characterize the universe. Einstein's theory of special relativity, for example, is a theory of the symmetries of empty space and time, which are governed by the Poincaré group. (Groups are the mathematical structures that describe symmetries.) Effects such as length contraction and time dilation, which flatten fast-moving clocks and make them run slow, are operations of the symmetry group, similar to rotating your point of view in space, but with time as part of the "rotation."

Particle physics is replete with symmetries: in particular, the fundamental forces are dictated by symmetries called gauge symmetries. Specify the gauge group and the interaction strength, and essentially all the behavior of the force is determined. For instance, electromagnetism involves a gauge symmetry group called U(1), which is the symmetry of rotations of a circle in a plane.

Conservation of electric charge is a consequence of the U(1) symmetry. As proved by mathematician Emmy Noether in 1915, whenever a symmetry appears in mechanics, there is also a conservation law. Her theorem works for both classical and quantum mechanics and tells us, for instance, that the law of conservation of energy follows from symmetry with respect to translations in time. That is, energy is conserved because the equations of motion yesterday are the same as those today. Conservation of momentum (symmetry under translation in space) and angular momentum (symmetry under rotations) are similar.

Finally, take the very definition of a "particle" in quantum field theory that originated with physicist Eugene Wigner: a particle is an "irreducible representation of the Poincaré group." This direct linkage of symmetry to the most basic structure of matter and forces is what requires electrons and other particles to have an intrinsic quantity of angular momentum known as spin. The spin acts as a label specifying which "irreducible representation" the particle is and happens to associate with rotations and hence with angular momentum. A particle's mass is also a symmetry-related label.

Compared to the symmetries that govern the universe, snowflakes start to seem quite mundane. *—Graham P. Collins, staff writer and editor*

THE AUTHOR

JAN JOLIE began his career as a theorist, receiving his Ph.D. in theoretical physics from the University of Ghent in Belgium in 1986. After five years at the Laue-Langevin Institute in Grenoble, France, Jolie turned his focus to experimental work when, in 1992, he accepted a position at the University of Fribourg in Switzerland. In addition to the experiments reported in this article, he has worked on more down-to-earth applications, such as gamma-ray and neutron tomography and the construction of tunable gamma-ray sources. He now leads the Institute for Nuclear Physics at the University of Cologne in Germany. In 2000 Jolie was awarded Yale University's Leigh Page Prize for his work on dynamical symmetries and supersymmetries in atomic nuclei.

suggested a daring extension of the interacting boson model to describe odd-even nuclei in a neater fashion.

Iachello proposed using supersymmetry to relate the nucleus with n bosons and one fermion to that with $n + 1$ bosons. If this dynamical supersymmetry occurred in nature, it would reveal itself in the pattern of excited states of an odd-even nucleus and the adjacent even-even one—for example, in the states of arsenic 75 (33 protons and 42 neutrons) and selenium 76 (34 protons and 42 neutrons). Quantum states are classified by their quantum numbers, which organize the states into groups according to properties such as their angular momentum. With dynamical supersymmetry, a single set of quantum numbers would serve to classify the states of two nuclei into related groups. One could start with the simpler states of the even-even selenium 76 and predict the states of arsenic 75 (that is, predict which states would exist and properties such as their angular momentum and approximate energy).

During the 1980s experimenters gathered data from nuclei capable of exhibiting dynamical symmetries and found hints of supersymmetry, but they could not confirm Iachello's idea unambiguously. The structure of an odd-even nucleus could not be determined completely starting from the associated even-even nucleus.

Magic Squares

IN 1984 Pieter Van Isacker, Kristiaan L. G. Heyde and I (all then at the University of Ghent in Belgium), together with Alejandro Frank of the University of Mexico, proposed an extension of Iachello's supersymmetry. The idea was to keep track of the neutron and proton pairs separately. This extended supersymmetry allows one to describe a quartet of nuclei in a common framework. This quartet, called a magic square, consists of nuclei having the same total number of bosons (paired nucleons) and fermions (unpaired nucleons). It consists of an even-even nucleus, two odd-even nuclei and an odd-odd nucleus. Heavy odd-odd nuclei, those having more than 100 or so nucleons, are the most complex objects found in the study of low-energy nuclear structure, but if this

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new dynamical supersymmetry worked in nature, one could predict the energy spectrum of the odd-odd nucleus from the simpler spectra of its three partners. Observing such a symmetry experimentally was of importance not only for nuclear physics but for all other applications of supersymmetry in physics: though widely used by theorists, supersymmetry lacked experimental verification.

To confirm these ideas required detailed knowledge of heavy odd-odd nuclei, and many experimental and theoretical groups around the world began such studies. Some limited evidence of the supersymmetry was found, but the holy grail of such investigations, a detailed map of the states of gold 196, remained out of reach. This nucleus, with 79 protons and 117 neutrons, is considered to be the ultimate test of supersymmetry in nuclear physics for three reasons. First, its region of nuclei (those that have about 80 protons and about 120 neutrons) is known to exhibit dynamical symmetries and to fulfill other technical conditions needed for the supersymmetry to be present. Second, its region is the most difficult in which to describe odd-odd nuclei. Finally, in 1989, when we used supersymmetry to predict a major group of its states, none of those states was experimentally known; experiments could confirm or kill the theory.

The Experimental Quest

TO STUDY ATOMIC NUCLEI, physicists bombard them with neutrons, photons or accelerated particles to excite them and observe how they react. The excited states are unstable, and the nucleus quickly returns to its lowest energy state by cascading down through a series of states, emitting energetic gamma- or x-ray photons, which can be measured precisely.

The radiation observed from odd-odd nuclei is extremely complex, however, because very many states are populated, and the photons' energies are the differences in energies between states. Even-even and even-odd nuclei are simpler, having fewer such states at low energies. The gold 196 isotope presents an additional challenge because it is radioactive and decays in about a week, most often by capturing an electron and turning into platinum 196. Experimenters have to create it continuously by bombarding a stable isotope with accelerated particles such as protons.

The structure of gold 196 turned out to be so difficult to deduce from such measurements that some teams abandoned the effort. One team proposed that the experimental data must mean that the dynamical supersymmetry was broken. At that moment of despair in the mid-1990s, a new collaboration was established, joining my group at the University of Fribourg in Switzerland and the groups of Christian Günther at the University of Bonn and Gerhard Graw at the University of Munich. Later Casten's group at Yale also contributed. We planned to make one last attempt to study gold 196 using in-beam spectroscopy, which measures radiation emitted by gold 196 ions created in a beam of particles. We used three facilities: the Philips cyclotron of the Paul Scherrer Institute in Switzerland, the Bonn cyclotron, and the WSNL Tandem accelerator at Yale.

Graw's group performed a "transfer" experiment that complemented the in-beam results and solved a fundamental puzzle—the reason for the difficulties that had stymied earlier efforts. In a transfer experiment the projectile hits the target nucleus and carries away one of its nucleons, leaving behind a daughter nucleus in an excited state [*see illustration on page 74*]. We identify the outgoing particle and measure its energy. When we balance the books, the excitation energy of the daughter nucleus will be "missing." In this way, transfer experiments produce different data than the in-beam spectroscopy does: they directly determine the energy of excited states of a nucleus instead of the much larger number of energy differences between states. Moreover, by using beams of polarized projectiles and studying how the collision products fly away, we can learn about the angular momenta of the excited states.

To study the very closely spaced energy levels of gold 196, we used the state-of-the-art instrumentation provided by the magnetic Q3D spectrometer of the accelerator laboratory in Munich. When Alexander Metz and his collaborators at the University of Munich analyzed the transfer experiments, they found that the ground state of gold 196 is a doublet—two very closely spaced energy levels. This discovery was crucial for solving the problems encountered before in analyzing the nucleus's states. These experiments also revealed directly the energies of most of the excited states. With this framework in place, the in-beam data could then be used to establish the spin and parity of each excitation.

The results agreed well with the theoretical predictions based on dynamical supersymmetry [*see illustration on page 74*]. The states of all four nuclei could be classified by a common set of supersymmetric quantum numbers, and a single mathematical expression with only a few parameters matches the energy levels reasonably well. That this is possible for one of the most complex atomic nuclei is a strong confirmation of dynamical supersymmetry, but it also presents a new challenge to theoreticians. One can study gold 196 as an individual case of many quantum objects interacting. The theorists should explain, from that perspective of quantum many-body theory, why the excitations of gold 196 are governed by dynamical supersymmetry. Several groups are working intensively on this question.

Paired fermions behaving as bosons occur in various fields of physics, including superconductivity. Dynamical supersymmetry like that seen in atomic nuclei might be useful in those fields as well. One thing is certain: symmetries, whether "super" or ordinary, will continue to lead the dance in quantum physics. SA

MORE TO EXPLORE

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15 Answers to Creationist Nonsense

By John Rennie

Opponents of evolution want to make a place for creationism by tearing down real science, but their arguments don't hold up

When Charles Darwin introduced the theory of evolution through natural selection 143 years ago, the scientists of the day argued over it fiercely, but the massing evidence from paleontology, genetics, zoology, molecular biology and other fields gradually established evolution's truth beyond reasonable doubt. Today that battle has been won everywhere—except in the public imagination.

Embarrassingly, in the 21st century, in the most scientifically advanced nation the world has ever known, creationists can still persuade politicians, judges and ordinary citizens that evolution is a flawed, poorly supported fantasy. They lobby for creationist ideas such as "intelligent design" to be taught as alternatives to evolution in science classrooms. As this article goes to press, the Ohio Board of Education is debating whether to mandate such a change. Some antievolutionists, such as Philip E. Johnson, a law professor at the University of California at Berkeley and author of *Darwin on Trial,* admit that they intend for intelligent-design theory to serve as a "wedge" for reopening science classrooms to discussions of God.

Besieged teachers and others may increasingly find themselves on the spot to defend evolution and refute creationism. The arguments that creationists use are typically specious and based on misunderstandings of (or outright lies about) evolution, but the number and diversity of the objections can put even well-informed people at a disadvantage.

To help with answering them, the following list rebuts some of the most common "scientific" arguments raised against evolution. It also directs readers to further sources for information and explains why creation science has no place in the classroom.

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1. Evolution is only a theory. It is not a fact or a scientific law.

Many people learned in elementary school that a theory falls in the middle of a hierarchy of certainty—above a mere hypothesis but below a law. Scientists do not use the terms that way, however. According to the National Academy of Sciences (NAS), a scientific theory is "a well-substantiated explanation of some aspect of the natural world that can incorporate facts, laws, inferences, and tested hypotheses." No amount of validation changes a theory into a law, which is a descriptive generalization about nature. So when scientists talk about the theory of evolution—or the atomic theory or the theory of relativity, for that matter—they are not expressing reservations about its truth.

In addition to the *theory* of evolution, meaning the idea of descent with modification, one may also speak of the *fact* of evolution. The NAS defines a fact as "an observation that has been repeatedly confirmed and for all practical purposes is accepted as 'true.'" The fossil record and abundant other evidence testify that organisms have evolved through time. Although no one observed those transformations, the indirect evidence is clear, unambiguous and compelling.

All sciences frequently rely on indirect evidence. Physicists cannot see subatomic particles directly, for instance, so they verify their existence by watching for telltale tracks that the particles leave in cloud chambers. The absence of direct observation does not make physicists' conclusions less certain.

NAUTILUS SHELL: Designed or evolved?

2. Natural selection is based on circular reasoning: the fittest are those who survive, and those who survive are deemed fittest.

"Survival of the fittest" is a conversational way to describe natural selection, but a more technical description speaks of differential rates of survival and reproduction. That is, rather than labeling species as more or less fit, one can describe how many offspring they are likely to leave under given circumstances. Drop a fast-breeding pair of small-beaked finches and a slower-breeding pair of large-beaked finches onto an island full of food seeds. Within a few generations the fast breeders may control more of the food resources. Yet if large beaks more easily crush seeds, the advantage may tip to the slow breeders. In a pioneering study of finches on the Galápagos Islands, Peter R. Grant of Princeton University observed these kinds of population shifts in the wild [see his article "Natural Selection and Darwin's Finches"; SCIENTIFIC AMERICAN, October 1991].

The key is that adaptive fitness can be defined without reference to survival: large beaks are better adapted for crushing seeds, irrespective of whether that trait has survival value under the circumstances.

GALÁPAGOS FINCHES show adaptive beak shapes.

LAYNE KENNEDY *Corbis* (*top*); PATRICIA J. WYNNE (*bottom*)

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3. Evolution is unscientific, because it is not testable or falsifiable. It makes claims about events that were not observed and can never be re-created.

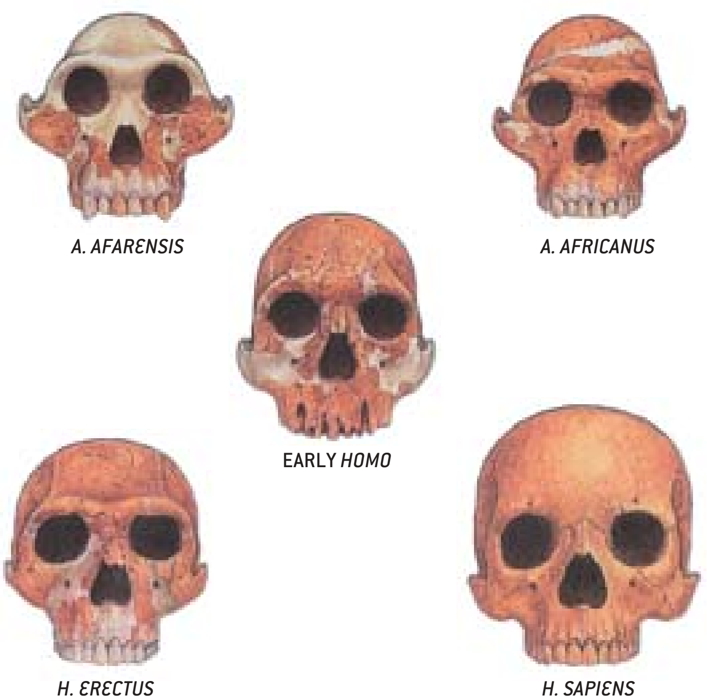
This blanket dismissal of evolution ignores important distinctions that divide the field into at least two broad areas: microevolution and macroevolution. Microevolution looks at changes within species over time—changes that may be preludes to speciation, the origin of new species. Macroevolution studies how taxonomic groups above the level of species change. Its evidence draws frequently from the fossil record and DNA comparisons to reconstruct how various organisms may be related.

These days even most creationists acknowledge that microevolution has been upheld by tests in the laboratory (as in studies of cells, plants and fruit flies) and in the field (as in Grant's studies of evolving beak shapes among Galápagos finches). Natural selection and other mechanisms—such as chromosomal changes, symbiosis and hybridization—can drive profound changes in populations over time.

The historical nature of macroevolutionary study involves inference from fossils and DNA rather than direct observation. Yet in the historical sciences (which include astronomy, geology and archaeology, as well as evolutionary biology), hypotheses can still be tested by checking whether they accord with physical evidence and whether they lead to verifiable predictions about future discoveries. For instance, evolution implies that between the earliest-known ancestors of humans (roughly five million years old) and the appearance of anatomically modern humans (about 100,000 years ago), one should find a succession of hominid creatures with features progressively less apelike and more modern, which is indeed what the fossil record shows. But one should not—and does not—find modern human fossils embedded in strata from the Jurassic period (65 million years ago). Evolutionary biology routinely makes predictions far more refined and precise than this, and researchers test them constantly.

Evolution could be disproved in other ways, too. If we could document the spontaneous generation of just one complex life-form from inanimate matter, then at least a few creatures seen in the fossil record might have originated this way. If superintelligent aliens appeared and claimed credit for creating life on earth (or even particular species), the purely evolutionary explanation would be cast in doubt. But no one has yet produced such evidence.

It should be noted that the idea of falsifiability as the defining characteristic of science originated with philosopher Karl Popper in the 1930s. More recent elaborations on his thinking have expanded the narrowest interpretation of his principle precisely because it would eliminate too many branches of clearly scientific endeavor.



SKULLS of some hominids predating modern humans (*Homo sapiens*).

REPRINTED BY PERMISSION OF WADSWORTH/THOMSON LEARNING FROM *BIOLOGY: CONCEPTS AND APPLICATIONS*, BY CECIE STARR, © 1991

4. Increasingly, scientists doubt the truth of evolution.

No evidence suggests that evolution is losing adherents. Pick up any issue of a peer-reviewed biological journal, and you will find articles that support and extend evolutionary studies or that embrace evolution as a fundamental concept.

Conversely, serious scientific publications disputing evolution are all but nonexistent. In the mid-1990s George W. Gilchrist of the University of Washington surveyed thousands of journals in the primary literature, seeking articles on intelligent design or creation science. Among those hundreds of thousands of scientific reports, he found none. In the past two years, surveys done independently by Barbara Forrest of Southeastern Louisiana University and Lawrence M. Krauss of Case Western Reserve University have been similarly fruitless.

Creationists retort that a closed-minded scientific community rejects their evidence. Yet according to the editors of *Nature, Science* and other leading journals, few antievolution manuscripts are even submitted. Some antievolution authors have published papers in serious journals. Those papers, however, rarely attack evolution directly or advance creationist arguments; at best, they identify certain evolutionary problems as unsolved and difficult (which no one disputes). In short, creationists are not giving the scientific world good reason to take them seriously.

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5. The disagreements among even evolutionary biologists show how little solid science supports evolution.

Evolutionary biologists passionately debate diverse topics: how speciation happens, the rates of evolutionary change, the ancestral relationships of birds and dinosaurs, whether Neandertals were a species apart from modern humans, and much more. These disputes are like those found in all other branches of science. Acceptance of evolution as a factual occurrence and a guiding principle is nonetheless universal in biology.

Unfortunately, dishonest creationists have shown a willingness to take scientists' comments out of context to exaggerate and distort the disagreements. Anyone acquainted with the works of paleontologist Stephen Jay Gould of Harvard University knows that in addition to co-authoring the punctuated-equilibrium model, Gould was one of the most eloquent defenders and articulators of evolution. (Punctuated equilibrium explains patterns in the fossil record by suggesting that most evolutionary changes occur within geologically brief intervals—which may nonetheless amount to hundreds of generations.) Yet creationists delight in dissecting out phrases from Gould's voluminous prose to make him sound as though he had doubted evolution, and they present punctuated equilibrium as though it allows new species to materialize overnight or birds to be born from reptile eggs.

When confronted with a quotation from a scientific authority that seems to question evolution, insist on seeing the statement in context. Almost invariably, the attack on evolution will prove illusory.

6. If humans descended from monkeys, why are there still monkeys?

This surprisingly common argument reflects several levels of ignorance about evolution. The first mistake is that evolution does not teach that humans descended from monkeys; it states that both have a common ancestor.

The deeper error is that this objection is tantamount to asking, "If children descended from adults, why are there still adults?" New species evolve by splintering off from established ones, when populations of organisms become isolated from the main branch of their family and acquire sufficient differences to remain forever distinct. The parent species may survive indefinitely thereafter, or it may become extinct.

7. Evolution cannot explain how life first appeared on earth.

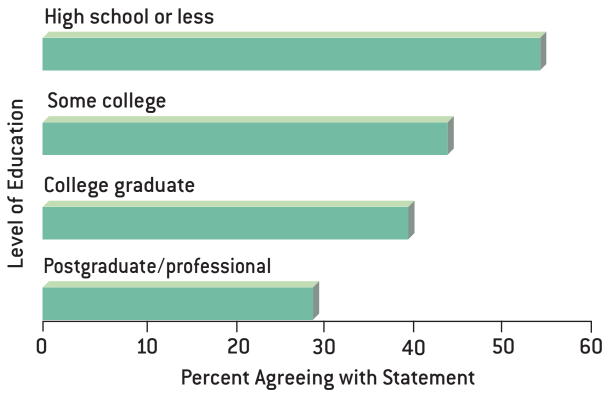
The origin of life remains very much a mystery, but biochemists have learned about how primitive nucleic acids, amino acids and other building blocks of life could have formed and organized themselves into self-replicating, self-sustaining units, laying the foundation for cellular biochemistry. Astrochemical analyses hint that quantities of these compounds might have originated in space and fallen to earth in comets, a scenario that may solve the problem of how those constituents arose under the conditions that prevailed when our planet was young.

Creationists sometimes try to invalidate all of evolution by pointing to science's current inability to explain the origin of life. But even if life on earth turned out to have a nonevolutionary origin (for instance, if aliens introduced the first cells billions of years ago), evolution since then would be robustly confirmed by countless microevolutionary and macroevolutionary studies.

8. Mathematically, it is inconceivable that anything as complex as a protein, let alone a living cell or a human, could spring up by chance.

Chance plays a part in evolution (for example, in the random mutations that can give rise to new traits), but evolution does not depend on chance to create organisms, proteins or other entities. Quite the opposite: natural selection, the principal known mechanism of evolution, harnesses nonrandom change by preserving "desirable" (adaptive) features and eliminating "undesirable" (nonadaptive) ones. As long as the forces of selection stay constant, natural selection can push evolution in one direction and produce sophisticated structures in surprisingly short times.

"GOD CREATED HUMANS IN THEIR PRESENT FORM WITHIN THE PAST 10,000 YEARS OR SO."



SOURCE: The Gallup Organization, 1999

As an analogy, consider the 13-letter sequence "TOBEORNOTTOBE." Those hypothetical million monkeys, each pecking out one phrase a second, could take as long as 78,800 years to find it among the 26^{13} sequences of that length. But in the 1980s Richard Hardison of Glendale College wrote a computer program that generated phrases randomly while preserving the positions of individual letters that happened to be correctly placed (in effect, selecting for phrases more like Ham-

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let's). On average, the program re-created the phrase in just 336 iterations, less than 90 seconds. Even more amazing, it could reconstruct Shakespeare's entire play in just four and a half days.

9. The Second Law of Thermodynamics says that systems must become more disordered over time. Living cells therefore could not have evolved from inanimate chemicals, and multicellular life could not have evolved from protozoa.

This argument derives from a misunderstanding of the Second Law. If it were valid, mineral crystals and snowflakes would also be impossible, because they, too, are complex structures that form spontaneously from disordered parts.

The Second Law actually states that the total entropy of a closed system (one that no energy or matter leaves or enters) cannot decrease. Entropy is a physical concept often casually described as disorder, but it differs significantly from the conversational use of the word.

More important, however, the Second Law permits parts of a system to decrease in entropy as long as other parts experience an offsetting increase. Thus, our planet as a whole can grow more complex because the sun pours heat and light onto it, and the greater entropy associated with the sun's nuclear fusion more than rebalances the scales. Simple organisms can fuel their rise toward complexity by consuming other forms of life and nonliving materials.

10. Mutations are essential to evolution theory, but mutations can only eliminate traits. They cannot produce new features.

On the contrary, biology has catalogued many traits produced by point mutations (changes at precise positions in an organism's DNA)—bacterial resistance to antibiotics, for example.

Mutations that arise in the homeobox (*Hox*) family of development-regulating genes in animals can also have complex effects. *Hox* genes direct where legs, wings, antennae and body segments should grow. In fruit flies, for instance, the mutation called *Antennapedia* causes legs to sprout where antennae should grow. These abnormal limbs are not functional, but their existence demonstrates that genetic mistakes can produce complex structures, which natural selection can then test for possible uses.

Moreover, molecular biology has discovered mechanisms for genetic change that go beyond point mutations, and these expand the ways in which new traits can appear. Functional modules within genes can be spliced together in novel ways. Whole genes can be accidentally duplicated in an organism's DNA, and the duplicates are free to mutate into genes for new, complex features. Comparisons of the DNA from a wide variety of organisms indicate that this is how the globin family of blood proteins evolved over millions of years.

11. Natural selection might explain microevolution, but it cannot explain the origin of new species and higher orders of life.

Evolutionary biologists have written extensively about how natural selection could produce new species. For instance, in the model called allopatry, developed by Ernst Mayr of Harvard University, if a population of organisms were isolated from the rest of its species by geographical boundaries, it might be subjected to different selective pressures. Changes would accumulate in the isolated population. If those changes became so significant that the splinter group could not or routinely would not breed with the original stock, then the splinter group would be *reproductively isolated* and on its way toward becoming a new species.

Natural selection is the best studied of the evolutionary mechanisms, but biologists are open to other possibilities as well. Biologists are constantly assessing the potential of unusual genetic mechanisms for causing speciation or for producing complex features in organisms. Lynn Margulis of the University of Massachusetts at Amherst and others have persuasively argued that some cellular organelles, such as the energy-generating mitochondria, evolved through the symbiotic merger of ancient organisms. Thus, science welcomes the possibility of evolution resulting from forces beyond natural selection. Yet those forces must be natural; they cannot be attributed to the actions of mysterious creative intelligences whose existence, in scientific terms, is unproved.

12. Nobody has ever seen a new species evolve.

Speciation is probably fairly rare and in many cases might take centuries. Furthermore, recognizing a new species during a formative stage can be difficult, because biologists sometimes disagree about how best to define a species. The most widely used definition, Mayr's Biological Species Concept, recognizes a species as a distinct community of reproductively isolated populations—sets of organisms that normally do not or cannot breed outside their community. In practice, this standard can be difficult to apply to organisms isolated by distance or terrain or to plants (and, of course, fossils do not breed). Biologists therefore usually use organisms' physical and behavioral traits as clues to their species membership.

Nevertheless, the scientific literature does contain reports of apparent speciation events in plants, insects and worms. In most of these experiments, researchers subjected organisms to various types of selection—for anatomical differences, mating behaviors, habitat preferences and other traits—and found that they had created populations of organisms that did not breed with

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outsiders. For example, William R. Rice of the University of New Mexico and George W. Salt of the University of California at Davis demonstrated that if they sorted a group of fruit flies by their preference for certain environments and bred those flies separately over 35 generations, the resulting flies would refuse to breed with those from a very different environment.

13. Evolutionists cannot point to any transitional fossils—creatures that are half reptile and half bird, for instance.

Actually, paleontologists know of many detailed examples of fossils intermediate in form between various taxonomic groups. One of the most famous fossils of all time is *Archaeopteryx,* which combines feathers and skeletal structures peculiar to birds with features of dinosaurs. A flock's worth of other feathered fossil species, some more avian and some less, has also been found. A sequence of fossils spans the evolution of modern horses from the tiny *Eohippus.* Whales had four-legged ancestors that walked on land, and creatures known as *Ambulocetus* and *Rodhocetus* helped to make that transition [see "The Mammals That Conquered the Seas," by Kate Wong; Scientific American, May]. Fossil seashells trace the evolution of various mollusks through millions of years. Perhaps 20 or more hominids (not all of them our ancestors) fill the gap between Lucy the australopithecine and modern humans.

Creationists, though, dismiss these fossil studies. They argue that *Archaeopteryx* is not a missing link between reptiles and birds—it is just an extinct bird with reptilian features. They want evolutionists to produce a weird, chimeric monster that cannot be classified as belonging to any known group. Even if a creationist does accept a fossil as transitional between two species, he or she may then insist on seeing other fossils intermediate between it and the first two. These frustrating requests can proceed ad infinitum and place an unreasonable burden on the always incomplete fossil record.

Nevertheless, evolutionists can cite further supportive evidence from molecular biology. All organisms share most of the same genes, but as evolution predicts, the structures of these genes and their products diverge among species, in keeping with their evolutionary relationships. Geneticists speak of the "molecular clock" that records the passage of time. These molecular data also show how various organisms are transitional within evolution.

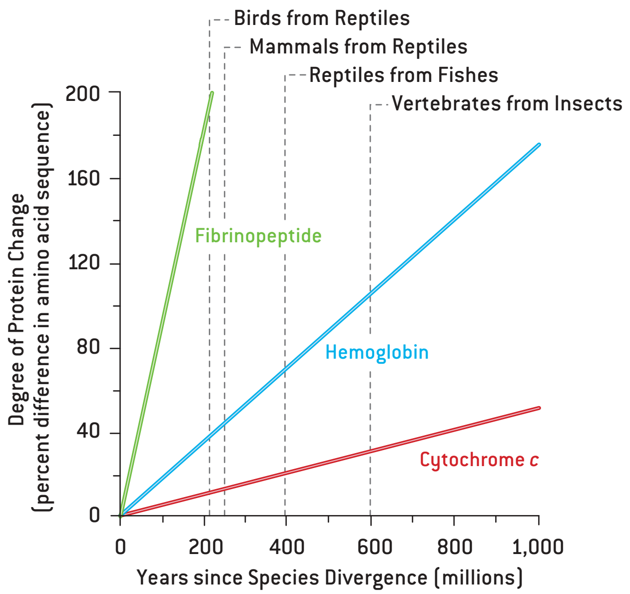
14. Living things have fantastically intricate features—at the anatomical, cellular and molecular levels—that could not function if they were any less complex or sophisticated. The only prudent conclusion is that they are the products of intelligent design, not evolution.

This "argument from design" is the backbone of most recent attacks on evolution, but it is also one of the oldest. In 1802 theologian William Paley wrote that if one finds a pocket watch in a field, the most reasonable conclusion is that someone dropped it, not that natural forces created it there. By analogy, Paley argued, the complex structures of living things must be the handiwork of direct, divine invention. Darwin wrote *On the Origin of Species* as an answer to Paley: he explained how natural forces of selection, acting on inherited features, could gradually shape the evolution of ornate organic structures.

Generations of creationists have tried to counter Darwin by citing the example of the eye as a structure that could not have evolved. The eye's ability to provide vision depends on the perfect arrangement of its parts, these critics say. Natural selection could thus never favor the transitional forms needed during the eye's evolution—what good is half an eye? Anticipating this criticism, Darwin suggested that even "incomplete" eyes might confer benefits (such as helping creatures orient toward light) and thereby survive for further evolutionary refinement. Biology has vindicated Darwin: researchers have identified primitive eyes and light-sensing organs throughout the animal kingdom and have even tracked the evolutionary history of eyes through comparative genetics. (It now appears that in various families of organisms, eyes have evolved independently.)

Today's intelligent-design advocates are more sophisticated than their predecessors, but their arguments and goals are not fundamentally different. They criticize evolution by trying to demonstrate that it could not ac-

PROTEIN EVOLUTION REFLECTS SPECIES DIVERGENCE



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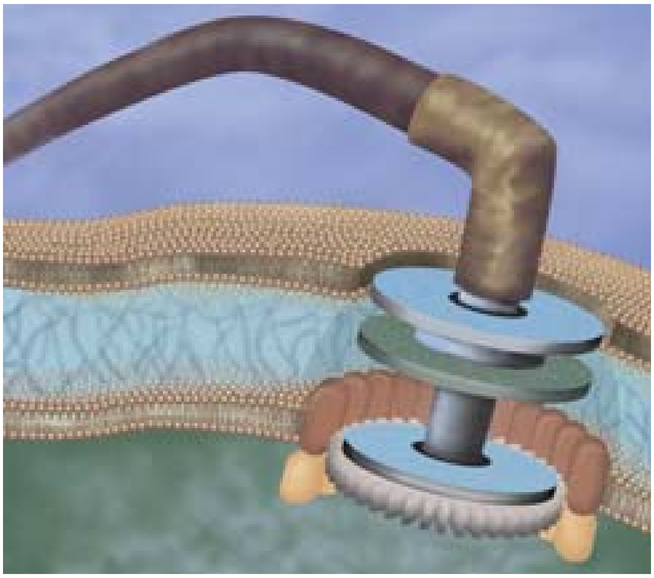
count for life as we know it and then insist that the only tenable alternative is that life was designed by an unidentified intelligence.

15. Recent discoveries prove that even at the microscopic level, life has a quality of complexity that could not have come about through evolution.

"Irreducible complexity" is the battle cry of Michael J. Behe of Lehigh University, author of *Darwin's Black Box: The Biochemical Challenge to Evolution*. As a household example of irreducible complexity, Behe chooses the mousetrap—a machine that could not function if any of its pieces were missing and whose pieces have no value except as parts of the whole. What is true



CLOSE-UP of a bacterial flagellum.

of the mousetrap, he says, is even truer of the bacterial flagellum, a whiplike cellular organelle used for propulsion that operates like an outboard motor. The proteins that make up a flagellum are uncannily arranged into motor components, a universal joint and other structures like those that a human engineer might specify. The possibility that this intricate array could have arisen through evolutionary modification is virtually nil, Behe argues, and that bespeaks intelligent design. He makes similar points about the blood's clotting mechanism and other molecular systems.

Yet evolutionary biologists have answers to these objections. First, there exist flagellae with forms simpler than the one that Behe cites, so it is not necessary for all those components to be present for a flagellum to work. The sophisticated components of this flagellum all have precedents elsewhere in nature, as described by Kenneth R. Miller of Brown University and others. In fact, the entire flagellum assembly is extremely similar to an organelle that *Yersinia pestis,* the bubonic plague bacterium, uses to inject toxins into cells.

The key is that the flagellum's component structures, which Behe suggests have no value apart from their role in propulsion, can serve multiple functions that would have helped favor their evolution. The final evolution of the flagellum might then have involved only the novel recombination of sophisticated parts that initially evolved for other purposes. Similarly, the blood-clotting system seems to involve the modification and elaboration of proteins that were originally used in digestion, according to studies by Russell F. Doolittle of the University of California at San Diego. So some of the complexity that Behe calls proof of intelligent design is not irreducible at all.

Complexity of a different kind—"specified complexity"—is the cornerstone of the intelligent-design arguments of William A. Dembski of Baylor University in his books *The Design Inference* and *No Free Lunch*. Essentially his argument is that living things are complex in a way that undirected, random processes could never produce. The only logical conclusion, Dembski asserts, in an echo of Paley 200 years ago, is that some superhuman intelligence created and shaped life.

Dembski's argument contains several holes. It is wrong to insinuate that the field of explanations consists only of random processes or designing intelligences. Researchers into nonlinear systems and cellular automata at the Santa Fe Institute and elsewhere have demonstrated that simple, undirected processes can yield extraordinarily complex patterns. Some of the complexity seen in organisms may therefore emerge through natural phenomena that we as yet barely understand. But that is far different from saying that the complexity could not have arisen naturally.

"Creation science" is a contradiction in terms. A central tenet of modern science is methodological naturalism—it seeks to explain the universe purely in terms of observed or testable natural mechanisms. Thus, physics describes the atomic nucleus with specific concepts governing matter and energy, and it tests those descriptions experimentally. Physicists introduce new particles, such as quarks, to flesh out their theories only when data show that the previous descriptions cannot adequately explain observed phenomena. The new particles do not have arbitrary properties, moreover—their definitions are tightly constrained, because

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the new particles must fit within the existing framework of physics.

In contrast, intelligent-design theorists invoke shadowy entities that conveniently have whatever unconstrained abilities are needed to solve the mystery at hand. Rather than expanding scientific inquiry, such answers shut it down. (How does one disprove the existence of omnipotent intelligences?)

Intelligent design offers few answers. For instance, when and how did a designing intelligence intervene in life's history? By creating the first DNA? The first cell? The first human? Was every species designed, or just a few early ones? Proponents of intelligent-design theory frequently decline to be pinned down on these points. They do not even make real attempts to reconcile their disparate ideas about intelligent design. Instead they pursue argument by exclusion—that is, they belittle evolutionary explanations as far-fetched or incomplete and then imply that only design-based alternatives remain.

Logically, this is misleading: even if one naturalistic explanation is flawed, it does not mean that all are. Moreover, it does not make one intelligent-design theory more reasonable than another. Listeners are essentially left to fill in the blanks for themselves, and some will undoubtedly do so by substituting their religious beliefs for scientific ideas.

Time and again, science has shown that methodological naturalism can push back ignorance, finding increasingly detailed and informative answers to mysteries that once seemed impenetrable: the nature of light, the causes of disease, how the brain works. Evolution is doing the same with the riddle of how the living world took shape. Creationism, by any name, adds nothing of intellectual value to the effort. SA

John Rennie is editor in chief of Scientific American.

A broadcast version of this article will air June 26 on *National Geographic Today,* a program on the National Geographic Channel. Please check your local listings.

OTHER RESOURCES FOR DEFENDING EVOLUTION

How to Debate a Creationist: 25 Creationists' Arguments and 25 Evolutionists' Answers. Michael Shermer. Skeptics Society, 1997. This well-researched refutation of creationist claims deals in more depth with many of the same scientific arguments raised here, as well as other philosophical problems. *Skeptic* magazine routinely covers creation/evolution debates and is a solid, thoughtful source on the subject: **www.skeptic.com**

Defending Evolution in the Classroom: A Guide to the Creation/Evolution Controversy. Brian J. Alters and Sandra M. Alters. Jones and Bartlett Publishers, 2001. This up-to-date overview of the creation/evolution controversy explores the issues clearly and readably, with a full appreciation of the cultural and religious influences that create resistance to teaching evolution. It, too, uses a question-and-answer format that should be particularly valuable for teachers.

Science and Creationism: A View from the National Academy of Sciences. Second edition. National Academy Press, 1999. This concise booklet has the backing of the country's top scientific authorities. Although its goal of making a clear, brief statement necessarily limits the detail with which it can pursue its arguments, the publication serves as handy proof that the scientific establishment unwaveringly supports evolution. It is also available at **www7.nationalacademies.org/evolution/**

The Triumph of Evolution and the Failure of Creationism. Niles Eldredge. W. H. Freeman and Company, 2000. The author, a leading contributor to evolution theory and a curator at the American Museum of Natural History in New York City, offers a scathing critique of evolution's opponents.

Intelligent Design Creationism and Its Critics. Edited by Robert T. Pennock. Bradford Books/MIT Press, 2001. For anyone who wishes to understand the "intelligent design" controversy in detail, this book is a terrific one-volume summary of the scientific, philosophical and theological issues. Philip E. Johnson, Michael J. Behe and William A. Dembski make the case for intelligent design in their chapters and are rebutted by evolutionists, including Pennock, Stephen Jay Gould and Richard Dawkins.

Talk.Origins archive (www.talkorigins.org). This wonderfully thorough online resource compiles useful essays and commentaries that have appeared in Usenet discussions about creationism and evolution. It offers detailed discussions (some of which may be too sophisticated for casual readers) and bibliographies relating to virtually any objection to evolution that creationists might raise.

National Center for Science Education Web site (www.ncseweb.org). The center is the only national organization that specializes in defending the teaching of evolution against creationist attacks. Offering resources for combating misinformation and monitoring antievolution legislation, it is ideal for staying current with the ongoing public debate.

PBS Web site for evolution (www.pbs.org/wgbh/evolution/). Produced as a companion to the seven-part television series *Evolution,* this site is an enjoyable guide to evolutionary science. It features multimedia tools for teaching evolution. The accompanying book, *Evolution,* by Carl Zimmer (HarperCollins, 2001), is also useful for explaining evolution to doubters.

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WORKINGKNOWLEDGE

WINDMILLS

Turn Turn Turn

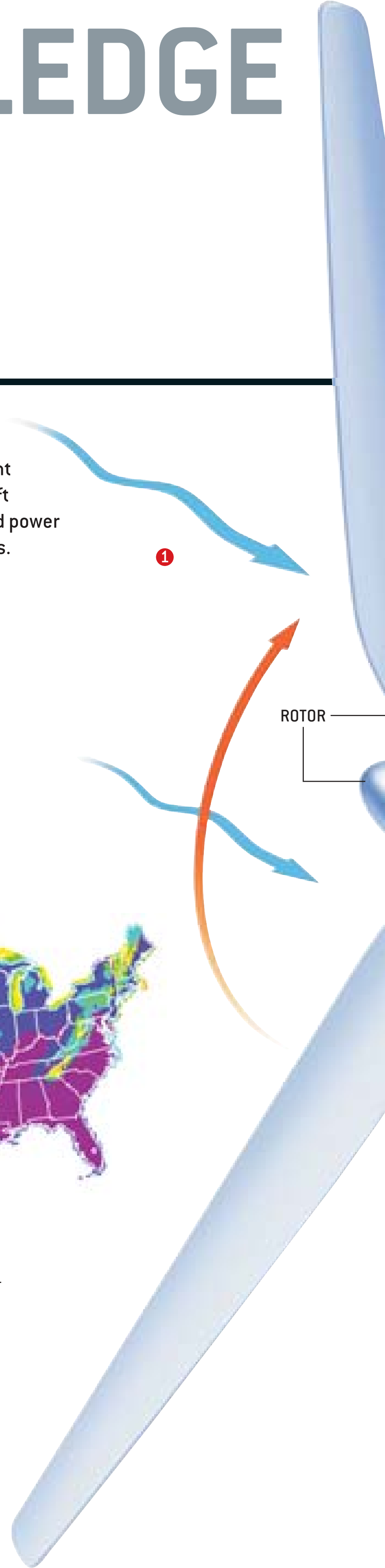
Humans have harnessed wind power for centuries. But advances in rotor design and high-voltage integrated-circuit controllers have enabled the latest wind turbines to generate 30 percent more power than pinwheels the same size did just a decade ago.

So why aren't the machines everywhere? Modern windmills aren't terribly noisy. They don't interfere with TV reception, because they're made of composite materials, not metals. In areas with strong, steady winds they generate electricity for four to six cents per kilowatt-hour—competitive with coal, natural gas, and nuclear power plants, all of which provide power at three to 10 cents per kilowatt-hour. "The real issue," says Alan Laxson, senior project manager at the Department of Energy's National Wind Technology Center in Golden, Colo., "is that because the wind is intermittent, a turbine operator can't tell the local utility how much power he can reliably provide." Windmills also can't be readily ramped up like a power plant to meet varying demand. Better ways to store wind energy, such as fuel cells, are key to substantial long-term growth, and they are improving.

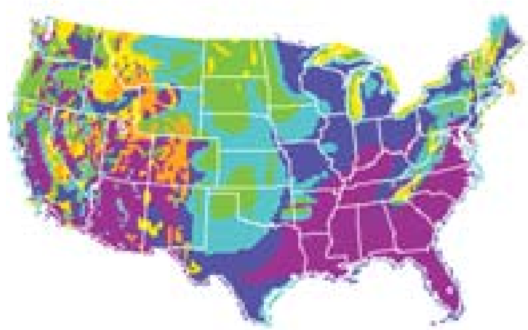
Critical, too, is sustained funding, which has twisted in the economic wind. Rural electrification following the Great Depression made farm windmills obsolete. Federal R&D money blew in after the 1973 and 1979 oil crises, only to wane when oil prices dropped again and cheap Canadian natural gas became abundant. Private investors who later built wind farms and sold power to utilities faced major nonpayments during the California power shortages of 2001.

The breeze has picked up again. Today the U.S. has about 4,300 megawatts of wind-power capacity installed, feeding about 1 percent of the country's demand. The amount almost doubled in only 18 months, Laxson says, as tax credits were put in place, as citizens pressured utilities to diversify their power sources in the wake of the shortages and Middle East conflicts, and as consumers agreed to pay a bit more for electricity generated by nonpolluting technologies. Europe—notably Denmark and Germany—leads the world, with more than 14,000 megawatts of capacity. The incentive? Energy prices there have risen relentlessly. —*Mark Fischetti*

MODERN WIND TURBINE
Twisted airfoils, made from light composite materials, exploit lift almost entirely, capturing wind power more efficiently than drag does.



WHERE THE WIND BLOWS



POWER CLASS	AVERAGE WIND POWER AT 50 METERS (watts per meter squared)	AVERAGE SPEED (meters per second)
1	<200	<5.6
2	200–300	5.6–6.4
3	300–400	6.4–7.0
4	400–500	7.0–7.5
5	500–600	7.5–8.0
6	600–800	8.0–8.8
7	>800	>8.8

ILLUSTRATIONS BY GEORGE RETSECK; SOURCE: U.S. NATIONAL WIND TECHNOLOGY CENTER

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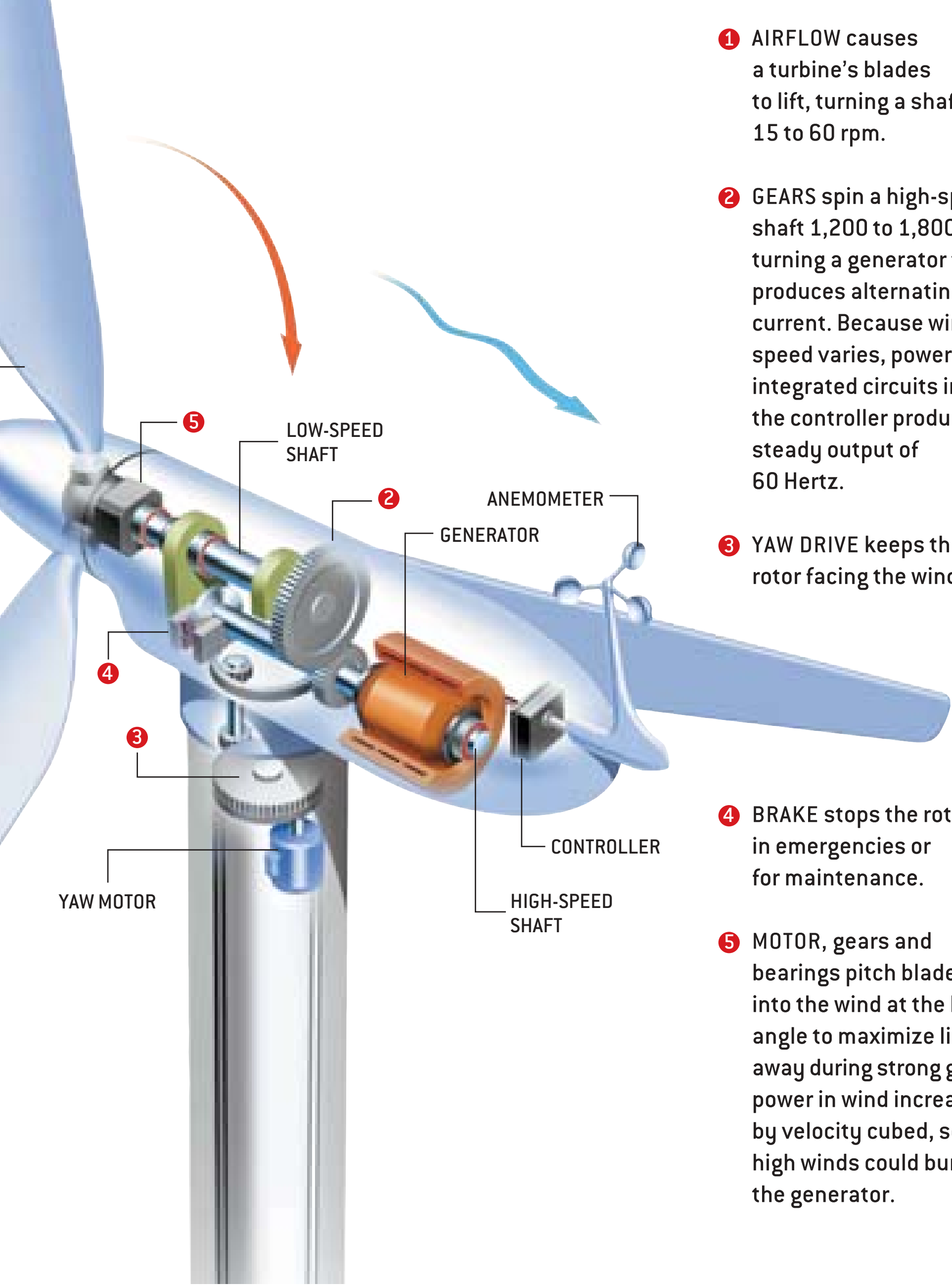
DID YOU KNOW . . .

➤ DAILY GRIND Technology historians estimate that windmills were first built in Persia and China from 200 B.C. to A.D. 500. Sails made of reeds spun around a vertical shaft. During the Renaissance, the Dutch affixed wooden blades to a horizontal shaft atop a multistory tower, which enclosed floors devoted to milling grain and removing chaff. A windsmith who lived at the bottom manually oriented the rotor into the wind. In Crete today hundreds of sail windmills still pump water for crops.

➤ GEARED UP Old Dutch windmills with wide blades, and American farm windmills with numerous blades, rotated slowly but provided the high torque needed. Modern turbines, with better gearboxes, require only a few narrow, long blades to capture lift efficiently and rotate quickly enough to drive an electrical generator.

➤ COAST NOT CLEAR Cape Wind Associates in Boston has submitted draft environmental plans to build a $600-million wind farm in the shallows south of Cape Cod to catch the stiff sea breezes between the islands of Martha's Vineyard and Nantucket. The company would erect 170 turbines, each rising 410 feet from the water, to deliver half the demand from the cape and the islands [News Scan, March]. Opponents say the giant props would succumb to salty sea air and inexorable waves and would harm fisheries, disenchant tourists and kill numerous seabirds, which would wash onto beaches.



1 AIRFLOW causes a turbine's blades to lift, turning a shaft 15 to 60 rpm.

2 GEARS spin a high-speed shaft 1,200 to 1,800 rpm, turning a generator that produces alternating current. Because wind speed varies, power-integrated circuits in the controller produce a steady output of 60 Hertz.

3 YAW DRIVE keeps the rotor facing the wind.

4 BRAKE stops the rotor in emergencies or for maintenance.

5 MOTOR, gears and bearings pitch blades into the wind at the best angle to maximize lift, or away during strong gusts; power in wind increases by velocity cubed, so high winds could burn out the generator.

SAILS or wooden paddles of ancient windmills harnessed wind drag (push) and lift to do work, mostly to grind (mill) grain or pump water.

ANGLED BLADES of a farm windmill better tapped aerodynamic lift and drag to grind grain, pump water or generate electricity.

This month's topic was suggested by reader Gerald Rees.
Have an idea for a future column? Send it to workingknowledge@sciam.com

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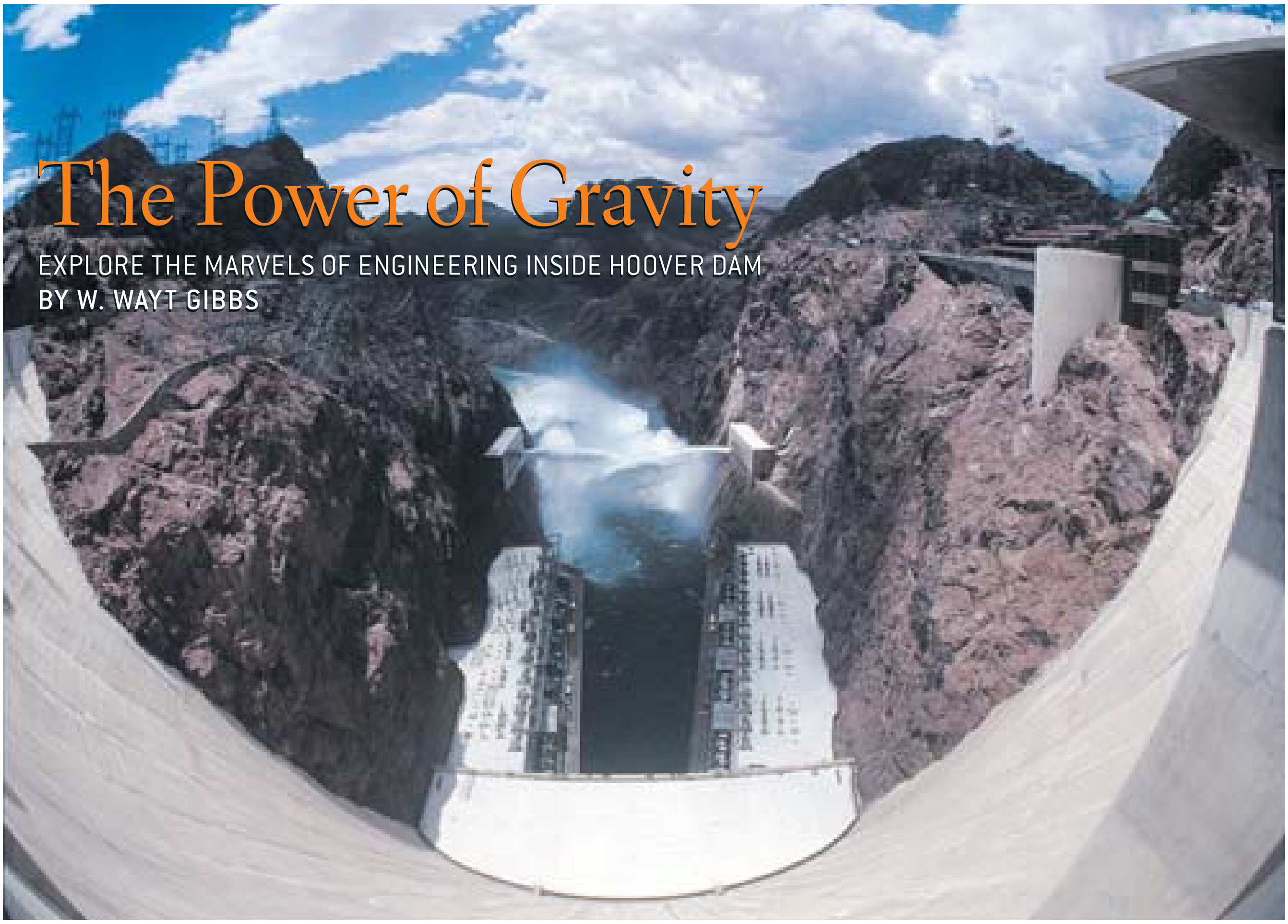
The Power of Gravity

EXPLORE THE MARVELS OF ENGINEERING INSIDE HOOVER DAM
BY W. WAYT GIBBS



IMPRESSIVE ARC of concrete at Hoover Dam is just 45 feet thick at the top of the span. But it swells to 660 feet at its bottom to restrain more than 300 pounds per square inch of water pressure.

PHOTOGRAPHS COURTESY OF THE BUREAU OF RECLAMATION

"Shh!" Gregory Burkhart hushed his tour group into silence as an alarm buzzer sounded. All 20 gazes fixed on him as he raised a hand and looked around. The floor shuddered and started to quiver as a roar filled the cavernous hall. It was the groan of the Colorado River, surging through giant pipes beneath our feet, as it was tortured for its potential energy.

Seventy years ago the green waters of the Colorado ran wild down the 275 miles from the Grand Canyon in Arizona to Black Canyon, here on the border of Nevada. The river flowed unhindered through a sheer 700-foot gorge it had carved out of the sharp-crested Black Mountains. It was warmed by summer sun that at times would bake the canyon to well over 120 degrees Fahrenheit. And it was protected from humans by an utter lack of roads, water and electricity.

Yet in 1931 this seemed to the U.S. Bureau of Reclamation the perfect spot to construct the tallest dam yet built. Today Hoover Dam is just one of 52 that restrain the waters feeding the Colorado River. Every year generators tap about 10 billion kilowatt-hours of energy from the flow. Although Hoover is no longer the largest dam in the world, it is a National Historic Landmark and one of the few giant dams that encourage visitors and that allow the public a glimpse of their innards.

A security clampdown last winter placed off-limits many of the interior passageways that were once open to tourists. But visitors can now walk at their own pace among the seven stations of the "Discovery Tour" that explain how this engineering wonder was built and how it holds back the water that makes Las Vegas and other southwestern cities habitable.

To begin the tour (which I took last August, before the country lurched into war), Burkhart crammed all 21 of us into an elevator sized for 10. The 506-foot descent from the crown of the dam into the bowels of the canyon wall was mercifully brief, but any claustrophobes in the group must have been dismayed to see the doors open into a dark tunnel of volcanic rock. As we made our way through the 250-foot tunnel to the power plant, some of us looked with concern at the rivulets of water seeping down the walls. "Don't

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worry," Burkhart said. "The water comes from natural springs, not from leaks in the dam. So don't try to plug the cracks with your bubble gum."

The dam does leak a little, however, as Burkhart elaborated later in the tour. "Concrete releases heat as it cures, and that can cause cracks," he said. "This dam won't be fully cured for about 1,500 years. So water finds its way through and is collected by a drainage system." I asked how much water leaks in. "It varies," he answered. "About 100 to 150 gallons—a minute."

Especially after our confining journey through the canyon wall, the generator room was an awesome sight. Through the floor rose the top 30 feet of nine red generators, each 70 feet tall, weighing 2,000 tons and capable of producing 130 million watts of power. We were standing by one of these monsters when the alarm sounded and the building shook.

"That noise was the wicket gates opening up on the N7 generator," Burkhart explained after the sound subsided. The water now spinning N7 up to 180 revolutions per minute, he said, was just seconds ago at the bottom of Lake Mead. From another station on the tour, you can walk out a gangplank over the water to one of the intake towers that rise from the lake bed north of the dam. The water that enters there gushes through a steel penstock pipe 30 feet in diameter, then swerves into a 13-foot-wide tube leading to the powerhouse. It sweeps by a massive butterfly valve at 22,000 gallons per second and spirals around the turbine case, its speed regulated by 24 wicket gates to

LAKE MEAD is a 9.2-trillion-gallon reservoir. Cities as far south as Tucson and San Diego depend on water released by Hoover Dam and use power from its generators (*right*).

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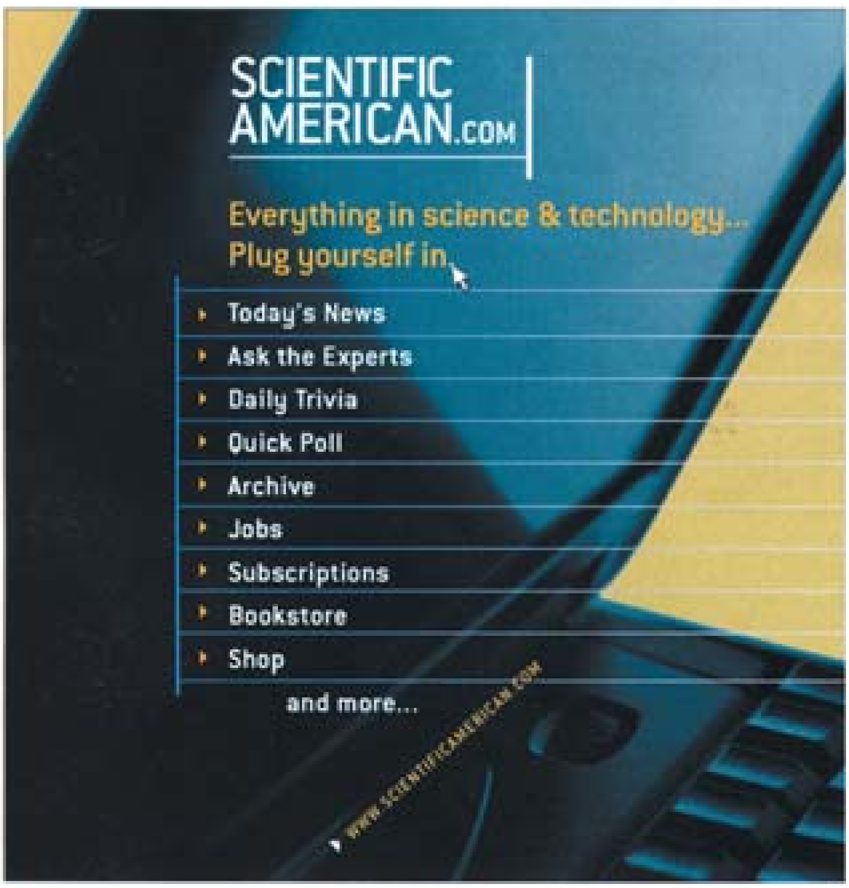

produce precisely 60 cycles per second on the power lines.

"There is a building just like this one on the Arizona side of the river," Burkhart said, as he flung open a door and pointed across the river. I squinted against the desert sun. The temperature at the visitor center was 104 degrees F in the shade. The railings on the overlook were too hot to touch. Even the backs of my hands were sweating.

But discomfort again yielded to amazement when I peered down over the graceful arc of the dam's face to the river 726 feet below. Released from confinement, the jets of cold water roiled the surface with what energy they still possessed. I made an about-face to look across the roadway spanning the crest of the dam. Lake Mead, penned to a height of 548 feet over its natural level and stretching almost as far as the horizon, seemed like an illusion, implausible and vaguely alarming. Not for the first time, I wished I had never seen *Superman: The Movie*.

In the old exhibit building, recently reopened, you can get a Superman-like view of the Colorado River basin. An enormous topographic model traces the river's 1,400-mile run from its headwaters in the Rockies down to the Gulf of California, to which it now contributes a mere trickle of heavily polluted runoff. Perhaps more than any other major river in the world, the Colorado has been harnessed to serve human society. Hoover Dam serves as a monument to the ingenuity and determination of humanity—and to our grasping self-centeredness.

The dam is a mere 30 miles southeast of Las Vegas, but allow no less than 90 minutes for the drive if you visit during the busy summer months, because traffic can back up for miles. Tickets for the Discovery Tour can be purchased in advance by calling 800-634-6787. Parking costs $5, and admission is $10 for adults, $8 for seniors and $4 for youths. Kids six and under get in free. For more information, see www.hooverdam.usbr.gov/service/newtour.htm on the Web. SA

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Climatic and Evolutionary Whiplash

HOW SUDDEN SHIFTS IN CLIMATE MAY HAVE BOOSTED HUMAN INGENUITY BY JEFFREY H. SCHWARTZ

A BRAIN FOR ALL SEASONS: HUMAN EVOLUTION AND ABRUPT CLIMATE CHANGE
by William H. Calvin
University of Chicago Press, 2002 ($25)

Imagine going to the first meeting of a course you'd long waited to enroll in. You sit down at your computer, open an e-mail message from your professor, in this case the author William H. Calvin, and get your first lesson. Your professor is thousands of miles away. In fact, he's at 51.4ºN, 0.1ºE. Where? Why, Charles Darwin's home in Kent, England, of course, the famous Down House.

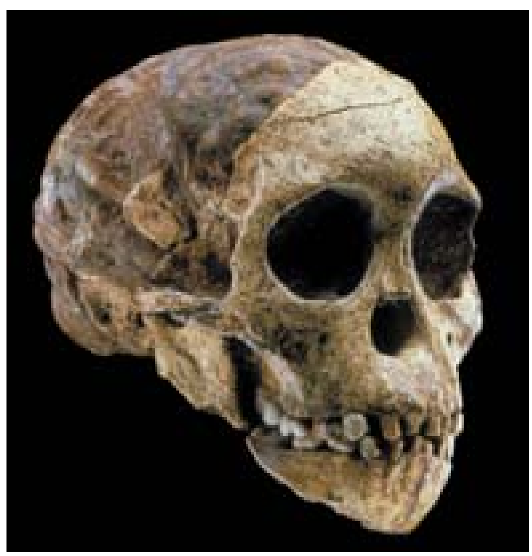
So begins Calvin's journey through evolution, particularly human evolution, as he leads his "class" from the home of the man many would call the father of evolution to various locales that provide fodder for his ultimate message: human evolution, like that of other organisms, is not a gradual transformation of form and behavior over time. Rather, like the shifts in the environments in which organisms find themselves, evolutionary change is abrupt, even catastrophic. A neurobiologist by training (he is at the University of Washington School of Medicine), Calvin leads us along a trail that links sudden worldwide coolings to the origin of our large brains and modern human behavior. By modern behavior, he is thinking not just of sophisticated toolmaking; he includes such social behavior as pair bonding and, ultimately, language, a sense of the aesthetic, and "abstract thinking, planning depth, innovation, and symbolic behavior."

The sudden coolings, Calvin tells us, reduced rainfall, induced dust storms and fires, and produced bottlenecks in the populations of our forebears. The few survivors had to adapt within one generation to, for example, a climate in which only grass grew well, spurring them to develop innovative techniques for hunting the large grazing animals that converted the grass into edible energy. Thus, he concludes, the cycles of "cool, crash, and burn" drove increased brain size and complexity. I think it unlikely that the climatic shifts were behind changes in the physical size and complexity of the brain, but these sudden jolts could certainly have spurred early humans to exploit the existing potential of the brain.

To make his points, Calvin takes us, his class, on a peripatetic journey as he visits museums, attends conferences, pays homage to a variety of African human fossil sites, and flies over huge African expanses and the vast Nordic seas. As one might expect, this approach is not always successful, but if you forget the formatting at the beginning of each brief chapter (a nod toward an e-mail message, but one without typos, code abbreviations and non sequiturs), the read flows a bit better.

Calvin's premise—that human evolution is correlated with climatic swings—is, of course, not new. Indeed, the traditional Darwinian view holds that evolution proceeds through organisms tracking their environments. And well over a decade ago paleontologist Elisabeth Vrba proposed that changes in species representation over time, as evidenced especially in the South African fossil record of antelopes and early hominids (such as *Australopithecus* and *Paranthropus*), were rapid and correlated with shifts between wetter and drier conditions.

But Calvin's presentation differs from the others in that it really is an attempt to think globally about past and present climatic change and its possible effects on creatures and their evolution. As one of the authors whose work on human evo-



FOSSILIZED CAST of early hominid brain (*Australopithecus africanus*), about 2.5 million years old.

DAVID BRILL

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lution he cites as recommended reading, I found his discussion of the fossils less engaging than the climate-related information. The book definitely picks up steam when he moves away from trying to discuss human fossils and digs into issues of global warming, shrinking polar ice caps, and oceanic currents. (This may be because much of this section had already been published as "The Great Climate Flip-Flop" in the *Atlantic Monthly*.) Here he seems to have more fun, getting across an image, for example, of subsurface oceanic water behavior by describing what happens when you pour very cold heavy cream over a spoon into a cup of hot coffee (it sinks as a column) and explaining North Atlantic Ocean current movements by way of a story about incorrectly hooking up a hot-water tank with a toilet that then acted as a radiator.

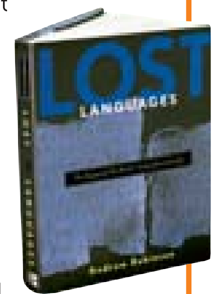
Heading back home to Seattle on the long, great-circle-route flight from Nairobi, over the Gulf Stream and Greenland, Calvin muses on the present global warming brought about by human activities. It could, he says, paradoxically trigger another episode of sudden cooling. The accumulation of greenhouse gases in the atmosphere could induce an abrupt shutting down of the oceanic "conveyor belt" that sends warmer waters into the North Atlantic, plunging much of the earth into a deep chill. But he doubts that another boom-then-bust cycle will jack up our brain power. We're now smart, he concludes, "in ways that owe little to our present brain power, but rather to the accumulated experience of the people that have lived since the last ice age ended. Education. Writing. Technology. Science." And he suggests that if we're *really* smart, our accumulated experience may just help us find a way to avoid this looming threat. SA

Jeffrey H. Schwartz teaches physical anthropology at the University of Pittsburgh and is author of Sudden Origins: Fossils, Genes and the Origin of Species *(Wiley, 1999).*

THE EDITORS **RECOMMEND**

LOST LANGUAGES: THE ENIGMA OF THE WORLD'S UNDECIPHERED SCRIPTS

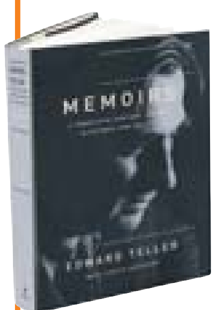
by Andrew Robinson. McGraw-Hill, New York, 2002 ($34.95)



It is baffling and humbling to confront an incomprehensible form of writing, such as Chinese for most Westerners. People who try to decipher the scripts of lost languages face an even sterner challenge, because there are no contemporary speakers or writers to help. That is the challenge depicted learnedly and fascinatingly by Robinson, literary editor of the *Times Higher Education Supplement* in London. He sets the stage by describing the hard work that went into the "three great decipherments": Egyptian hieroglyphs, Linear B of Crete, and Mayan glyphs. Then he poses the problems presented by nine undeciphered scripts, among them the languages of the Etruscans and the people of Easter Island. Success at deciphering, Robinson writes, requires "fanatical perseverance and devotion to detail and wide linguistic and cultural knowledge." The book's many illustrations of the enigmatic scripts make vivid the difficulty of the decipherer's task.

MEMOIRS: A TWENTIETH-CENTURY JOURNEY IN SCIENCE AND POLITICS

by Edward Teller, with Judith L. Shoolery. Perseus Publishing, Cambridge, Mass., 2001 ($35)



Whatever one thinks of physicist Teller's reputation as a hawk in military matters and a controversial figure in science politics, he and his collaborator, Shoolery (a writer, editor and former science teacher), have produced a page-turner. Teller, now 94 years old, participated in many of the developments in 20th-century physics, so the book—which presents the science clearly—stands as a history of the period as well as an account of his work and his relations with other prominent physicists. And he leavens the book with a profusion of entertaining anecdotes. Examples: his ride through two islands of Denmark on the back of a motorcycle piloted by George Gamow and his "only experience as a thespian, when I played the part of a corpse in a production of *Arsenic and Old Lace*."

CHARLES LINDBERGH AND THE SPIRIT OF ST. LOUIS

by Dominick A. Pisano and F. Robert van der Linden. Harry N. Abrams, New York, 2002 ($22.95)

May 21, 1927. Le Bourget Airport, Paris. Thirty-three hours, 30 minutes and 3,610 miles since takeoff from Roosevelt Field on Long Island. "After circling the field one last time, Lindbergh throttles back. His reflexes are now quite dull from fatigue, and he finds himself struggling to control his aircraft." But he lands safely to a tumultuous reception and enduring fame as the first person to fly nonstop alone from New York to Paris. Pisano and van der Linden—respectively, chair of the aeronautics division and curator of air transportation and special-purpose aircraft at the National Air and Space Museum of the Smithsonian Institution—almost put the reader in the cockpit of that single-engine airplane to share the challenge and ordeal of the flight. Many pictures of the pilot, the plane and scenes related to the flight enliven the story.

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Blind Justice

BY DENNIS E. SHASHA

A mathematically inclined judge uses a unique form of arbitration to settle monetary disputes. As in most arbitrations, the plaintiff and defendant present their evidence to the judge. But before the plaintiff begins, he writes down on a piece of paper how much money he thinks he should get—let's call the amount P—and puts the paper in a sealed envelope. Then the defendant writes down how much she is willing to pay—call it D—and puts that number in a separate envelope.

The judge does not know P or D. Once the plaintiff and defendant have presented their evidence, the judge determines an equitable monetary award, called J. But in this form of arbitration, the amount actually paid to the plaintiff is determined by comparing J with P and D. If J is closer to P, the defendant pays P; if J is closer to D, the defendant pays D. For example, say the plaintiff thinks he deserves $18 million, the defendant thinks she should pay nothing, and the judge decides the complaint is worth $8 million. Because $8 million is closer to zero than to $18 million, the plaintiff gets nothing.

Your challenge is to find the best strategy for the plaintiff. Suppose the judge hints that his award will be between $3 million and $10 million, with all numbers in that range having the same probability of being chosen. How much money should the plaintiff request to maximize his expected compensation? And should he change his request if he suspects that the defendant will be able read the number P through the sealed envelope? SA

Dennis E. Shasha is professor of computer science at the Courant Institute of New York University. His latest book is Dr. Ecco's Cyberpuzzles: 36 Puzzles for Hackers and Other Mathematical Detectives *(W. W. Norton, 2002).*

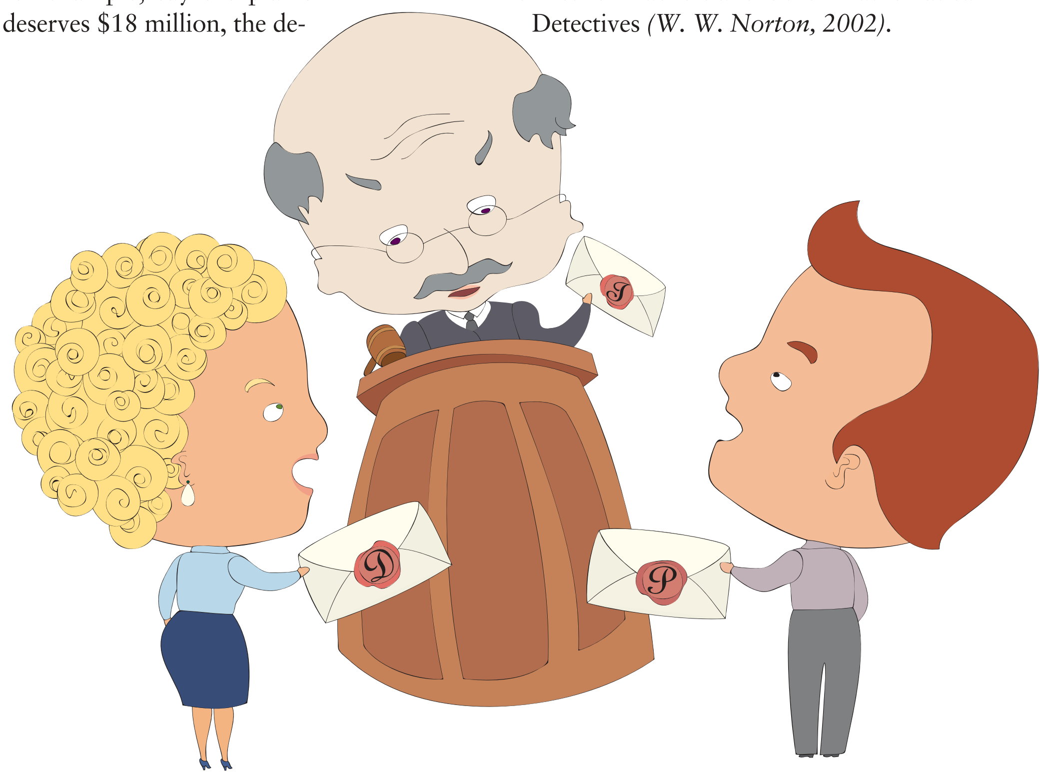
Answer to Last Month's Puzzle

C entered A's hut.
D entered F's hut.
C told F that D entered F's hut.
B told E that A entered E's hut.
A told F that D entered F's hut.
F told A that C entered A's hut.
E told B that A entered B's hut.
A told B that C entered B's hut.

A full explanation of the solution can be found at www.sciam.com

Web Solution

For a peek at the answer to this month's problem, visit www.sciam.com



SARA CHEN

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ANTIGRAVITY

Heads Up

EXTRAORDINARY CLAIMS REQUIRE EXTRAORDINARY EVIDENCE, OR AT LEAST A SECOND LOOK BY STEVE MIRSKY

The official Linnean designation for our species is *Homo sapiens,* which translates to "wise man." It's kind of an inside joke, as a quick scan of the front page of the newspaper whatever day that you read this will probably show. And if scientists have a tough time coming up with an accurate name for ourselves, it's no surprise that classification of organisms in general can be a dicey proposition.

Take, for instance, the strange creature found by a four-year-old girl in Hopkinton, Mass., in a swimming pool in the middle of April. As the local paper, the *MetroWest Daily News,* described the situation in a headline, "Girl finds two-headed toad in Hopkinton." The accompanying article offered a detailed description of the marvelous sideshow attraction: "The two toads are stacked on top of each other.... The toad on top is smaller and a lighter color. Its front legs have grown into the back of the larger frog, and it appears the bottom jaw may be connected to the larger toad's head."

Now, a brief rumination about the logistics summarized in this account may bring to mind fairly normal animal activity often found on the Discovery Channel, the Learning Channel and, for that matter, the Playboy Channel. On the other hand, the author of the short newspaper piece was none other than the renowned novelist and trustworthy journalist Norman Mailer. Or so it seemed, because it's easy to make mistakes when a first glance appears to uncover something really special.

Indeed, a second glance revealed that the byline actually read "Norman Miller," presumably a staff reporter at the paper, not Norman Mailer. And, as the *MetroWest Daily News* reported three days later, a second glance at the beast with two heads revealed it to be the more common beast with two backs, a pair of one-headed *Bufo*s boffing. Or, as the follow-up story succinctly put it, "It was just a couple of horny toads." The mistake presumably was listed in the paper's Errata *and* Erotica sections. (Please do not read the above as a knock on Mr. Miller, as merely getting things wrong is one of the great traditions of American journalism, still practiced everywhere. For example, many people consider this entire page of *Scientific American* to be an error every month.)

The tale of two toads shows that amateur mistakes may be amusing. But if you're looking for something done really wrong, turn to professionals, who also have problems classifying some of the oddball organisms cobbled together by evolution. One of the most spectacular and well-known examples was a creature considered so weird that it received the genus name *Hallucigenia*. In the original interpretation of the fossil remains, *Hallucigenia*'s tube of a body rested on multiple pairs of stiff quills, while a row of seven tentacles, replete with what seemed to be mouths at the ends, waved from its back. Later fossil finds, however, revealed a second set of the tentacles alongside the first. The creature suddenly made a lot more sense if you turned it upside down: the twin sets of flexible appendages were probably its legs, and the daggers originally thought to be legs most likely stuck up from its back, protecting it and keeping paleontologists from ever finding a fossil of two of these things clamped together in an experts-only exercise from the Cambrian Kama Sutra.

It's no surprise that classification of organisms can be a dicey proposition.

Yes, misclassification can be fun. Unfortunately, a bad identification can also be fatal: it's far safer to make a mistake with a *Hallucigenia* fossil than with a hallucinogenic mushroom. The journal *Internal Medicine* recently reported on a mushroom-related death and noted that "it may be that those who seek hallucinogenic mushrooms are less discerning and more prone to species misidentification than other foragers." Such fungi foragers, therefore, are advised to consult a knowledgeable companion before biting any buttons. For, as has been demonstrated innumerably, two heads are better than one. SA

ILLUSTRATION BY MATT COLLINS; PHOTOGRAPH BY FRANK VERONSKY

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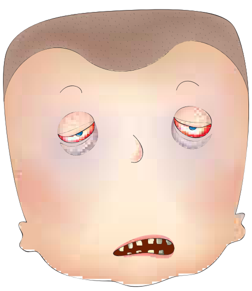
How long can humans stay awake?

J. Christian Gillin is at the San Diego Veterans Affairs Medical Center and is professor of psychiatry at the University of California at San Diego, where he conducts research on sleep, chronobiology and mood disorders. Gillin supplies the following response:

The quick answer is 264 hours, or 11 days. In 1965 Randy Gardner, a 17-year-old high school student, set this apparent world record as a science-fair project. Several other research subjects have remained awake for eight to 10 days in carefully monitored experiments. None experienced serious medical or psychiatric problems, but all showed progressive and significant deficits in concentration, motivation, perception and other higher mental processes. Nevertheless, all returned to relative normalcy after one or two nights of sleep. Other, anecdotal reports describe soldiers staying awake for four days in battle and unmedicated patients with mania going without sleep for three to four days.



SARA CHEN

The more complete answer revolves around the definition of the word "awake." Prolonged sleep deprivation in normal subjects induces numerous brief episodes of light sleep (lasting a few seconds), often described as "microsleep," alternating with drowsy wakefulness, as well as loss of cognitive and motor functions. Many people know about the dangerous drowsy driver on the highway and sleep-deprived British pilots during World War II who crashed their planes, having fallen asleep while flying home from the war zone. Gardner was "awake" but basically cognitively dysfunctional at the end of his ordeal. Excluding accidents, however, I am unaware of any deaths in humans from sleeplessness.

In certain rare medical disorders, the question of how long people can remain awake receives surprising answers—and raises more questions. Morvan's syndrome, for example, is characterized by muscle twitching, pain, excessive sweating, weight loss, periodic hallucinations and sleeplessness. Michel Jouvet and his colleagues in Lyons, France, studied a 27-year-old man with this condition and found that he had virtually no sleep over a period of several months. During that time, the man did not feel sleepy or tired and did not show any disorders of mood, memory or anxiety. Nevertheless, nearly every night between approximately nine and 11 he experienced 20 to 60 minutes of auditory, visual, olfactory and somesthetic (sense of touch) hallucinations, as well as pain and vasoconstriction in his fingers and toes.

The ultimate answer to this question remains unclear. Indeed, the U.S. Department of Defense has offered research funding for the goal of sustaining a fully awake, fully functional "24/7" soldier, sailor or airman. Will bioengineering eventually produce soldiers and citizens with a variant of Morvan's syndrome, who need no sleep but stay effective and happy? I hope not. A good night's sleep is one of life's blessings. As Coleridge wrote in *The Rime of the Ancient Mariner*, "Oh sleep! it is a gentle thing, / Beloved from pole to pole!"

When *Tyrannosaurus rex* fell, how did it get up, given its tiny arms?

—B. Lawrence, Montreal

Paleontologist Gregory M. Erickson of Florida State University provides this explanation:

I think we can look to birds (avian dinosaurs) for the answer, because they can stand up without the aid of arms. It's simply a matter of getting the legs below the center of gravity—where the front and back halves of the body will balance. Furthermore, tyrannosaurs would have had the aid of their tails. From skeletal evidence and tracks from tyrannosaur cousins known as albertosaurs, in which the tails did not drag, it is clear that tyrannosaur tails acted as counterbalances. The tail would have helped a 10,000-pound *T. rex* keep its center of gravity near its hips as its legs moved into position. Clearly, tyrannosaurs got up at least once during their lives (at birth), and there is no reason to believe that they could not do so throughout life—pathetic arms or not. SA

For a complete text of these and other answers from scientists in diverse fields, visit www.sciam.com/askexpert

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FUZZY LOGIC

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