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Volume 322, Issue 5898

COVER

Ordovician sedimentary rocks at Presqu'île de Crozon, Brittany, France. These rocks show high-frequency cycles of less than 500,000 years between bay and open marine conditions. This and similar records allow reconstruction of global sea level from 550 to 250 million years ago. The pink boulder at the bottom is about 15 centimeters across. See page 64.

Photo: Bilal U. Haq

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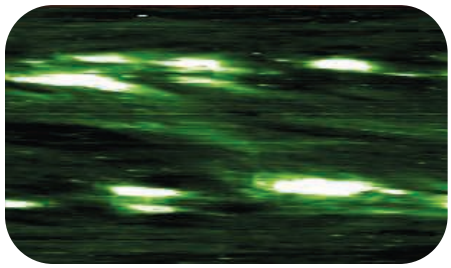

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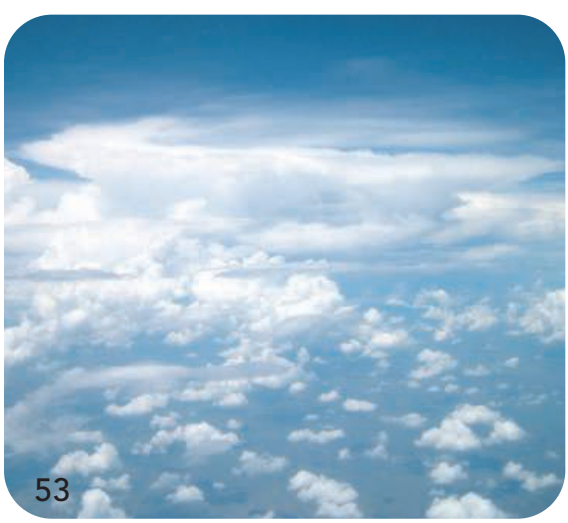

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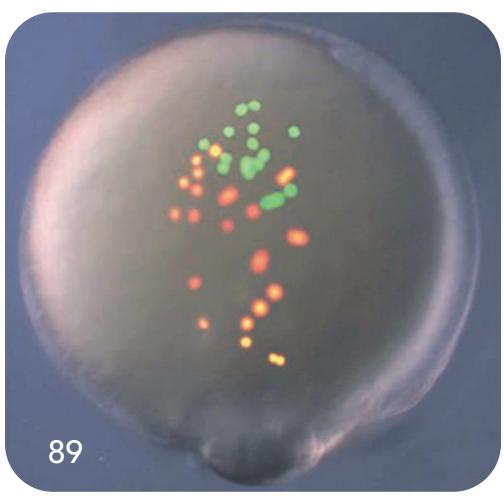

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Dangerous diet.

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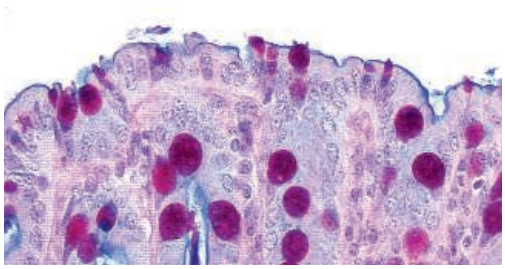
Something invisible is pulling on thousands of galaxies.



Purinergic receptor antagonists inhibit inflammation.

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RESEARCH ARTICLE: Purinergic Control of T Cell Activation by ATP Released Through Pannexin-1 Hemichannels
U. Schenk, A. M. Westendorf, E. Radaelli, A. Casati, M. Ferro, M. Fumagalli, C. Verderio, J. Buer, E. Scanziani, F. Grassi
Pannexin hemichannel-mediated release of ATP provides an autocrine, costimulatory signal for T cell activation.

RESEARCH ARTICLE: Kinome siRNA Screen Identifies Regulators of Ciliogenesis and Hedgehog Signal Transduction
M. Evangelista, T. Y. Lim, J. Lee, L. Parker, A. Ashique, A. S. Peterson, W. Ye, D. P. Davis, F. J. de Sauvage
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PERSPECTIVE: A Wnt-fall for Gene Regulation—Repression
N. P. Hoverter and M. L. Waterman
Recognition of a nonclassical Wnt-response element by the transcription factor TCF results in β-catenin acting as a transcriptional repressor of certain Wnt target genes.

PRESENTATION: Somatic Cell Genetics for the Study of NF-κB Signaling in Innate Immunity
R. Krumbach, S. Bloor, G. Ryzhakov, F. Randow
A forward genetic screen in immortalized cells identifies NF-κB signaling components required to transduce signals from Toll-like receptors.

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I. S. Levine
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B. L. Benderly
An unorthodox program helps young innovators turn inspiration into reality.

In Person: Ich bin Postdoctorin in Berlin
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The biggest challenges in moving abroad are not always scientific.

October 2008 Funding News
J. Fernández
Learn about the latest in research funding, scholarships, fellowships, and internships.

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EDITED BY STELLA HURTLEY

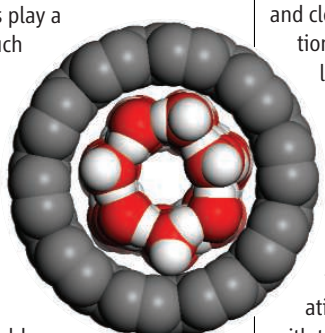
A Matter of Faith?

The intersection, if any, between science and religion is a hot-button issue guaranteed to inflame scientists and nonscientists alike. **Norenzayan and Shariff** (p. 58) review recent empirical approaches in social psychology, experimental economics, and evolutionary anthropology primarily aimed at studying prosocial behavior among humans past and present. A synthesis of these findings highlights issues that are being tackled in the current wave of experimental studies and the interdisciplinary interest in religion as a force for cooperative and altruistic human interactions.

Ups and Downs

Most of the geological history of the Paleozoic Era (542 to 251 million years ago) remains opaque, largely due to the difficulty of constructing records from such old and sparse remains. In particular, the history of sea level during the Paleozoic has remained piecemeal. **Haq and Schutter** (p. 64, cover) integrated published accounts of sea-level changes to reconstruct the history of sea-level fluctuations for the entire Paleozoic. One hundred seventy-two individual events were recorded, each lasting typically between half a million and three million years and varying in magnitude from a few tens to ~125 meters. Most events were not caused by glaciations, however, leaving unanswered the question of what caused more than half of these changes in Paleozoic sea level.

Temperature-Sensitive Water Layers



Water layers that interact with hydrophobic properties play a key role in processes such as protein folding and membrane transport, but their properties can be difficult to determine because they are themselves in contact with bulk water. The interior of single-walled carbon nanotubes (SWNTs) would be expected to be hydrophobic, and water will absorb in their interior. **Wang *et al.*** (p. 80) used a gentle method to open SWNTs with diameters of 1.4 nanometers and studied their absorption and nuclear magnetic resonance (NMR) properties over a range of different temperatures. The water actually underwent a transition from appearing to be in a hydrophobic environment at 22°C to appearing to be in a hydrophilic environment at 8°C.

Mighty Wheat >>

All over the world, wheat is one of the most important food crops, but due to its large and complex genome it has been deemed an impossible genome to sequence. Now Paux *et al.* (p. 101) have tackled the first task needed to get at the full genome by constructing a physical map of the largest wheat chromosome, chromosome 3B. At 1 gigabase, this chromosome alone is larger than all of the rice and human genomes. This feat demonstrates that, in the relatively near future, it should be possible to develop a physical map of large polyploid plant genomes (17 gigabases) using a chromosome-based strategy.

Back to the Future for Negative Refraction

Waves refract, changing their angle of propagation when going from one medium to another. The extent of refraction depends on the relative refractive indices of the media. In nature, all materials are run-of-the-mill positively refracting. However, recent work has demonstrated materials with a negative refractive index. The ability to manipulate electromagnetic radiation with such materials can lead to perfect lensing and cloaking. However, limitations on the fabrication of these metamaterials inevitably lead to losses, which can severely limit their implementation. Linking time-reversal processes with negative refraction, **Pendry** (p. 71, published online 28 August) discusses an alternate route that may overcome these limiting losses. Optically active materials, with the correct nonlinear optical properties, may be able to be made to mimic negative refraction without the losses associated with true negative refractive materials.

Lending an Electron

Catalysts for the preparation of chirally pure organic compounds tend to operate through paired electron mechanisms involving charged or highly polarized intermediates. Generation of an intermediate with an unpaired electron (a radical) can open other reaction pathways, favoring different products while avoiding undesirable competing reactions. In this vein, **Nicewicz and MacMillan** (p. 77, published online 4 September; see the Perspective by **Renaud and Leong**) demonstrate the utility of a photo-excitable ruthenium complex for shuttling single electrons to induce otherwise intractable reactions. The complex was combined with a chiral amine established for catalyzing a range of aldehyde transformations. Upon visible light irradiation, electron transfer to and from the Ru co-catalyst facilitates a radical mechanism for efficient asymmetric alkylation of the aldehydes, avoiding an aldehyde self-coupling reaction.

Gas from the Past

Carbon dioxide is the atmospheric trace gas with the largest influence on climate. Because the carbon cycle and climate are coupled so intimately, with CO_2 variations both causing and being caused by climate change, knowing how climate and atmospheric CO_2 have varied in the past is central to a better understanding of climate dynamics. **Ahn and Brook** (p. 83, published online 11 September) compare records of atmospheric CO_2 concentrations, Antarctic surface air temperatures, and Greenland climate during a relatively under-studied period: the last ice age, from 90,000 to 20,000 years ago.

CREDITS (TOP TO BOTTOM): CATHERINE FEUILLET; WANG *ET AL.*

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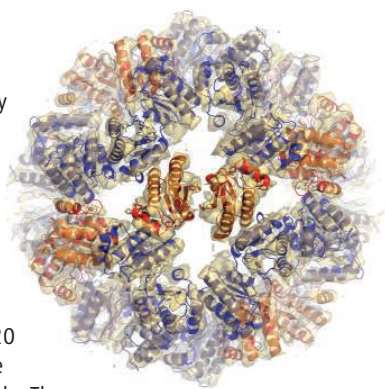
Life History Matters

In plants, changes in life history traits have been suggested to be correlated with their rate of evolution, but previous analyses have yielded conflicting results. In order to investigate whether the rate of molecular evolution correlates with life history traits, **Smith and Donoghue** (p. 86) tested the evolutionary rates across five groups of flowering plants. The rates of molecular evolution were generally low in trees and shrubs with long generation times in comparison to the relatively high rates of molecular evolution in related herbaceous plants, which have shorter generation times. Thus, evolutionary rates can indeed differ among closely related species, depending on their life history traits.

Getting to Grips with Gastrulation

Gastrulation involves the coordinated movements of germ layers to form the body axis. **Nair and Schilling** (p. 89, published online 21 August) studied chemokine regulation of endodermal morphogenesis and the positioning of the liver and pancreas in developing zebrafish. During development the endoderm normally migrates together with mesoderm, but the two germ layers could be physically separated by disrupting chemokine signaling, due to a loss of integrin-dependent adhesion to fibronectin. A chemokine-mediated adhesive interaction may thus normally tether endodermal cells to their mesodermal neighbors, providing a mechanism by which chemokines regulate embryonic cell movements distinct from their roles as classical chemoattractants.

Homing In on the Hub



Microorganisms respond to a variety of environmental stresses by up-regulating stress-response genes. In many cases the response is coordinated by a multiprotein signaling hub, the stressosome, which integrates multiple inputs to affect a single outcome. **Marles-Wright *et al.*** (p. 92) have fitted high-resolution structures of the stressosome components into an electron microscopy structure to determine a pseudo-atomic resolution structure of the stressosome from *Bacillus subtilis*. The complex has an icosohedral virus-capsid-like core with 20 protruding turrets. Sequences comprising the turrets are variable, perhaps allowing them to sense different signals. The conserved domains of the core may integrate these signals to give a single signaling outcome.

Homer-ing In on Memories

The neural correlates of remembering can only be studied with complete confidence in humans, because the subjects can verbally report their internal experience. Brain surgery in which therapeutic electrodes are implanted in the brain of patients with intractable epilepsy provides an opportunity for doing such studies. **Gelbard-Sagiv *et al.*** (p. 93, published online 4 September; see 5 September news story by **Miller**) report that neurons in and near the hippocampus of these patients showed specific patterns of activation for each episode of the television show *The Simpsons*. Later, when these same episodes were brought to mind by free recollection, the same pattern of neural activity was seen, demonstrating that, at least in the hippocampus, recall of a stimulus is accompanied by activation of the same neurons that were activated during the initial experience.

Controlling Conspiracy Theories

Believing oneself to be in control is a well-established and remarkably effective route to reduced anxiety and stress; conversely, being placed in an out-of-control situation activates behaviors aimed at regaining secure ground. **Whitson and Galinsky** (p. 115) show that the need for control is sufficiently strong as to influence perception to the extent of seeing patterns where they do not exist. In a series of studies, subjects were provided with feedback unrelated to their performance. Doing so increased their reported need for personal structure, increased the likelihood that they would see patterns in random visual static, and led them to see conspiracies where there were none. Allowing subjects to combat their anxiety through self-affirmation exercises brought their illusory perceptions under control.

CREDIT: MARLES-WRIGHT *ET AL.*

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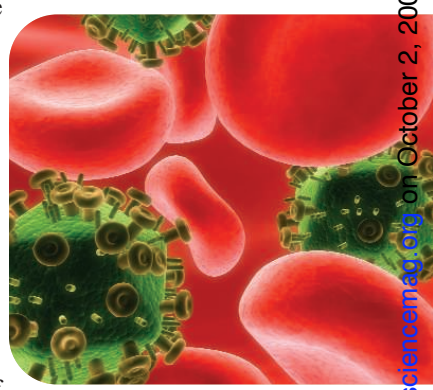
Jim Wells is a professor in the departments of Pharmaceutical Chemistry and Cellular and Molecular Pharmacology at the University of California at San Francisco.

Mary Woolley is president and chief executive officer of Research!America in Alexandria, VA.

A Populist Movement for Health?

ONE OF THE MOST EFFECTIVE SCIENCE-BASED MOVEMENTS TO RAISE PUBLIC AWARENESS OF a global problem has been Al Gore's efforts, complementing the science-based work of the Intergovernmental Panel on Climate Change, to expose the perils of global warming. Through decades of commitment, Gore and his team have laid out the science and consequences of unmitigated consumption of fossil fuels and the irredeemable impact this will have on the planet if unchecked. More than ever, this message is now resonating with the public.

Human health presents a similarly massive global problem. Globalization is accelerating the spread of AIDS, drug-resistant forms of tuberculosis, and other infectious agents. Industrialization, with its accompanying sedentary life-styles and extended life spans, is creating new epidemics of obesity, diabetes, cancer, and heart disease, among others. When a life-altering medical condition is diagnosed, too often even the best in the medical community have few clues as to the molecular mechanism at work, far less the ability to produce a cure or prevent others from experiencing a similar fate. Despite increased attention to health promotion, we focus on crisis and symptom management, as opposed to prevention and cure, reflecting a limited understanding of the molecular basis for disease.



Consider this: We now know that we are encoded by about 25,000 human genes and their products, many of which represent potential new drug targets. Yet we have drugs for fewer than 200 of these gene products. Moreover, of the approximately 20 to 30 new drug entities that the U.S. Food and Drug Administration has been approving each year, only 3 to 5 address a new molecular target or novel mechanism. At this rate, it will require hundreds of years to fully exploit our knowledge of human biology to develop robust medical treatments. Despite the tools and technologies of modern medical science, we are still in the Dark Ages of understanding our own biology and discovering agents that can provide cures.

How can we stimulate innovation and enlightened public policy? Is a Gore-like populist movement possible for global health? Although the science community has advocated more funding to support the basic science that is crucial to understand disease and develop cures, recent efforts have had little impact. In part, the science community is responsible because we have not effectively helped the public realize that without a higher national and international priority for basic research, a crisis in human health is not far off.

It is time for the scientific community to launch a bold combination strategy, the most important element of which is to identify the "Al Gore(s)" of basic science. This requires increased efforts and funding from scientific societies and advocacy organizations that are empowered to deliver compelling messages to media and elected officials and can identify and provide financial support for communicators for basic science. The research community needs champions who can articulate a compelling long-term vision for research that can accelerate the needed transition from a crisis/symptom mode to a prevention/cure mode of health care.

The second part of the strategy involves scientists' own time and, yes, money, to support such advocacy groups. Both are scarce resources, but if scientists want to spur basic science that underlies improving society, they must take personal responsibility to make it happen. Championing research in situations such as social gatherings does not come easily to many researchers, who may feel that their area of science is too complex for nonscientists to understand (or frankly don't feel a need to help them understand). Many community events and meetings now include discussions of carbon footprints and alternative energy. Scientists need to take or create more occasions to explain to the public how far we are from really understanding the basis of disease and our consequent vulnerability.

Now is the time to take bold actions both personally and through advocacy groups to accelerate public awareness in support of basic research. By failing to do so, we consign ourselves and future generations to a world with little hope for dramatically improving human health and well-being.

– Jim Wells and Mary Woolley

10.1126/science.1163960

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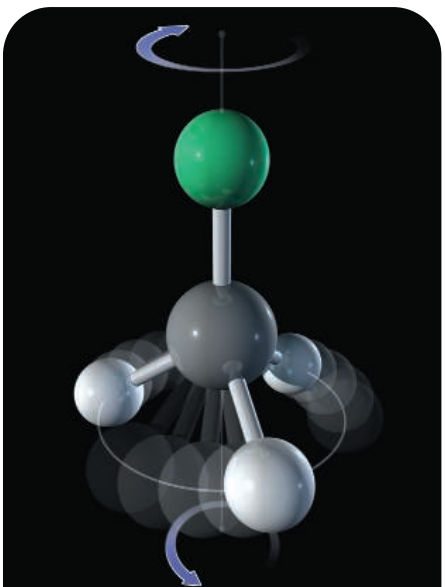
EDITED BY GILBERT CHIN AND JAKE YESTON



CHEMISTRY

Spinning in Place

Unlike macroscopic objects, molecules vibrate and rotate in discrete increments. To uncover the underlying quantum-mechanical restrictions governing such behavior, spectroscopists induce specific patterns of motion through light absorption. Thus, the molecules under study must be free to move about, but unless they are to some degree restricted, the flurry of different movements can be hard to disentangle. A promising compromise is the use of *para* hydrogen (p-H_2) matrices. When p-H_2 (H_2 with oppositely oriented nuclear spins) is cooled to low temperature, it forms an unusual medium, termed a quantum solid, in which the nuclei delocalize in space. Consequently, guest molecules embedded in a matrix of this solid retain a certain amount of flexibility. Lee *et al.* show through infrared absorption spectroscopy that CH_3F molecules can rotate about the C-F axis in such a matrix, but are restricted from tumbling in orthogonal directions. The study bolsters the utility of p-H_2 matrices for precise spectral characterization of small molecules. — JSY

J. Chem. Phys. **129**, 104502 (2008).

*Helen Pickersgill is a locum editor in *Science*'s editorial department.

MICROBIOLOGY

Adapting to Drug Resistance

Developing a new therapy for drug-resistant infections is an expensive and arduous process that may give relief for less time that it takes to develop the agent. Hence, delaying the onset of resistance by administering drugs in combination is a currently favored strategy, but two groups show this may not be quite so simple to implement wisely. By experimentation and modeling, Hegreness *et al.* made the counterintuitive discovery that synergistically acting drug pairs, such as doxycycline and erythromycin, may actually accelerate the evolution of resistance. In fact, antagonistic drug pairs are more effective at forestalling resistance emergence because as one drug becomes ineffective, its suppressive effect on the other diminishes and unmasks the potency of the second drug. Of course, the precise outcome depends on the drug ratios, doses, pharmacokinetics, and modes of action.

Developing policies for the implementation of drug combinations requires population modeling. Boni *et al.* compared the consequences of the standard wait-and-switch global deployment of drugs for malaria control with the simultaneous deployment of multiple drugs. Their model shows that if three different drugs are offered for use at the same time within a malarious population, the clinical burden is reduced, the emergence of resistance is delayed by two- to fourfold, and the number of failed treatments is almost halved. — CA

Proc. Natl. Acad. Sci. U.S.A. **105**, 13977, 14216 (2008).

DEVELOPMENT

Signal Stability

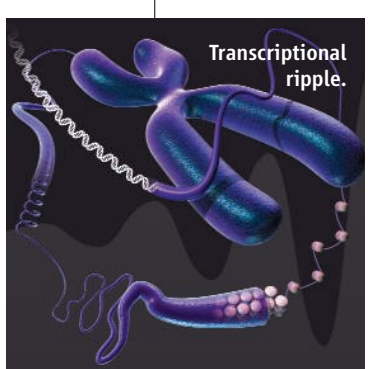
Chordin and BMP signaling develop opposing trends across the *Xenopus* embryo, defining between them the axis from dorsal to ventral and destinations in between. The interactions between these and other factors involve complex regulatory interactions, including both negative and positive feedback loops. Although predictions from some combinations of the known regulatory loops might suggest that axis establishment is rather tenuous, instead, observations of real embryos indicate that dorsal-ventral axis establishment in *Xenopus* is robust to perturbation. Inomata *et al.* identify the protein ONT1 as a stabilizing factor in the signaling networks defining the dorsal-ventral axis. The protein is expressed first in late blastula stages and is generally found in the more dorsal regions as the embryo develops; diminished ONT1 function results in dorsalization of the embryo. ONT1 binds to chordin and also to a protease known to degrade chordin, and seems to function as a scaffold enticing chordin to its demise. The biphasic outcome of this interaction ensures that enough, but not too much, chordin survives to define the developing dorsal axis. — PJH

Cell **134**, 854 (2008).

CELL BIOLOGY

Transcription Without Borders

In bacteria, genes encoding functionally related proteins are often grouped into coordinately regulated modules, one notable instance being the lactose operon. In mammals, the regulation of gene expression is thought to be controlled on an individual basis, such that specific proteins or RNAs bind to the regulatory elements of a single gene and activate or repress its transcription directly.



Using growth factors to induce transcription of immediate early genes (IEGs) in mammalian cells, Ebisuya *et al.* find that a gene that is being transcribed can incidentally activate the transcription of neighboring genes, enabling the coordinated expression of clusters of genes. Activation occurred via a ripple, which traveled both upstream and downstream from the IEG, and also passed through intergenic (non–protein coding) chromatin, resulting in the transcription of noncoding RNAs. Although protein-coding genes account for only 1.5% of the human genome, more than 70% of the DNA is

CREDITS (TOP TO BOTTOM): CHRIS BICKEL/*SCIENCE*

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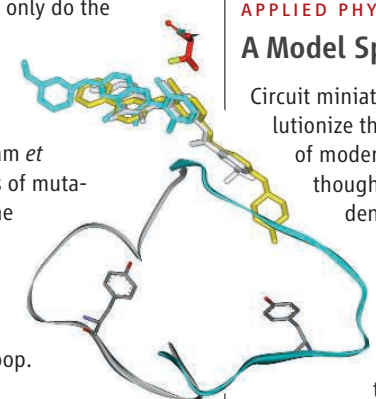
transcribed. These results provide a potential explanation for this pervasive transcription, which may serve to propagate transcriptional activation into neighboring genes. — HP*

Nat. Cell Biol. **10**, 1106 (2008).

BIOCHEMISTRY

Breaking the Back of BCR-ABL

One of the advances in the war on cancer has been the development of small molecules that target protein tyrosine kinases; one such drug, imatinib, is used to inhibit the BCR-ABL kinase in the treatment of chronic myelogenous leukemia. Nevertheless, elation has been tempered by the realization that resistance to imatinib can arise via mutation of a gatekeeper amino acid (threonine 315) to the bulkier and more hydrophobic isoleucine, which hinders access of the drug to its binding site. Similar resistance-mediating mutations have been observed for other drug–tyrosine kinase pairs in solid tumors. Not only do the mutations block drug binding, but they also tilt the kinase structure toward constitutively active conformations. Azam *et al.* have analyzed a series of mutations in a series of tyrosine kinases and find that the critical threonine sits atop a spine of hydrophobic residues linked to the activation loop. Replacing the threonine with isoleucine stabilizes and stiffens the spine and also enhances the coordination of ATP, thereby stimulating kinase activity. They used this insight to refine the inhibitor PD166326 into a candidate drug called compound 14, which packs neatly against the disrupted spine and inhibits the BCR-ABL variant T315I at 0.6 μM versus the lack of effect of PD166326 at 10 μM. — GJC



Interaction of PD166326 (blue), imatinib (yellow), and compound 14 (gray) with the activation loop (blue, gray) and the gatekeeper threonine (red).

CREDIT: AZAM *ET AL.*, *NAT. STRUCT. MOL. BIOL.* **15**, 10.1038/NSMB.1486 (2008)

Nat. Struct. Mol. Biol. **15**, 10.1038/nsmb.1486 (2008).

EVOLUTION

Neutral Plantings

The transcriptome of an organism encompasses all of its gene transcripts at a specific time and changes with the individual's environment and developmental stage. These changes either could be guided by adaptive selection or, like the neutral theory of gene evolution, may result from random events not under selection. Taking advantage of the genomic database of the plant *Arabidopsis*, Broadley *et al.* examined more than 18,000 gene transcripts in leaves of 14 taxa from the cabbage family. They found differences in the expression of a gene among taxa, suggesting that there was plasticity in expression in the most recent common ancestor or that the founder effect of a small population may have resulted in differential changes in gene expression among descendant taxa, but that the changes observed do not reflect functional adaptation. These findings show that appropriate null models are required when comparing transcriptomes in both time and space, and that modeling of transcriptome networks should take evolutionary effects into account. — LMZ

New Phytol. **180**, 10.1111/j.1469-8137.2008.02640.x (2008).

APPLIED PHYSICS

A Model Spin Amplifier

Circuit miniaturization has continued to revolutionize the speed and diverse capabilities of modern electronic systems. At present, though, the increase in device-packing density onto microelectronics chips and the associated problem of managing heat dissipation is becoming an issue in limiting performance. Using the spin of the electrons in place of traditional charge flow is therefore being explored as a possible route to circumvent that performance roadblock. The transistor is the present building block of microelectronics. However, the equivalent spin amplifier, or spin transistor, would require a room-temperature magnetic semiconductor. Because all the true magnetic semiconductors to date have been limited to cryogenic temperatures, the prospect of developing a practical spin transistor seems some way off. Breaking the process down into three stages—spin detection, signal amplification, and spin filtering of that amplified signal—Acremann *et al.* suggest an alternative method that may provide a spin amplifier using a sequence of electrical and magnetic field pulses to manipulate the magnetization of a patterned ferromagnetic layer. Such an engineered spin amplifier using presently available materials may bring forward the development of spintronics, and with it the additional functionality of having sensing, memory storage, and logical operation in a single device. — ISO

Appl. Phys. Lett. **93**, 102513 (2008).

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Inside Story

A dead boar in all its complexity is revealed in this photograph by Swedish physician Anders Persson, winner of this year's Lennart Nilsson Award for photography. Persson, director of the Center for Medical Image Science and Visualization at Linköping University, has combined magnetic resonance, ultrasound, and positron emission tomography to get 3D images from inside the body. Particularly useful for autopsies, his photos have been featured on the forensics TV show *CSI*.

Napoleon: Case Closed

Historians have long speculated about what killed Napoleon, who died in exile at 52 on the isle of St. Helena in 1821. His doctor said it was stomach cancer, but analysis of some hairs and accounts of his symptoms raised the notion that he was poisoned with arsenic.

Now the Italian National Institute of Nuclear Physics says it has ruled out homicide. Scientists analyzed several preserved samples of Napoleon's hairs, one from when he was only a year old and others cut a few days before his death, along with hairs from his son, his wife Josephine, and 10 other people living at the same time.

The hairs, placed in a nuclear reactor and bombarded with neutrons to determine their composition, were all found to be "extremely toxic," says institute director Ettore Fiorini and colleagues, with arsenic levels more than 100 times what would be found today. Napoleon's arsenic load registered 8.3 parts per million as an infant and 18.9 ppm when he died, the researchers report in the bulletin of the Italian Physical Society, *Il Nuovo Saggiatore.*

Fiorini notes that at the time, arsenic was everywhere–in paints, drugs, tapestries, and preserved food. Angela Santagostino, a toxicologist in the Department of Environmental Sciences at the University of Milan-Bicocca, says the scientists have finally come up with conclusive proof that there was "not an intentional poisoning."

THE BATTERED BRAIN

Last June, pro wrestler Chris Benoit strangled his family and hanged himself at age 37. Benoit had suffered various blows to his head in the course of his career. When neurosurgeon Julian Bailes of West Virginia University, Morgantown, examined the brain at the request of the Sports Legacy Institute, he found damage similar to that of advanced dementia.

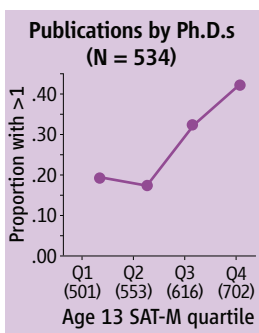
Now scientists at Boston University are hoping to get a better fix on what happens to banged-up brains with the establishment of a new Center for the Study of Traumatic Encephalopathy. Twelve athletes, including six retired NFL football players, have announced they will be donating their brains to aid studies of what happens after severe concussions. Big names include former New England Patriots linebacker Ted Johnson and former Olympic soccer champ Cindy Parlow.

Researchers have long suspected a link between athletes' head injuries and chronic traumatic encephalopathy (CTE). With donated brains, they'll be able to look for biomarkers of CTE, which can cause dementia-like symptoms and personality changes in patients, says neurologist Robert Stern, the center's co-director. Preliminary work suggests that CTE causes a buildup of tau protein, also implicated in Alzheimer's disease. Research also points to a genetic component. "We really need to understand this disease better—we're still in the infancy there," says co-director Ann McKee, a neuropathologist. McKee says she's most interested in learning how brain trauma in young adults can trigger brain damage that, as is possible in Benoit's case, surfaces many years later.

Little Gray Cells Add Up

To succeed in science, it helps to be very smart. But being very, *very* smart is even better.

That's what researchers at Vanderbilt University conclude from a longitudinal study begun at Johns Hopkins University in 1972. The Study of Mathematically Precocious Youth tracks the careers of students who were in the top 1% of scorers in the math portion of the SAT at the age of 13. Twenty-five years later, the crème de la crème within this elite group have produced the most publications and patents, psychologist David Lubinski and colleagues report. "Measures with high ceilings are needed" to reveal such distinctions, the authors say. For example, 28% of those with science doctorates had authored a peer-reviewed publication, but the probability rose with their SAT-M scores (see chart, above), according to a paper in the October issue of *Psychological Science*.



Psychologist Diane Halpern of Claremont McKenna College in California says the data are valid as far as they go. But "the flip side of this question" is how many top scientists "would score among the top 1% of the population on a math test. … I don't know what proportion of Nobel Prize–winners have IQs above 140 or 145, which would be predicted from the points made in this paper. "

CREDITS (LEFT TO RIGHT): SUSANA VERA/REUTERS; ANDERS PERSSON; SOURCE: PARK *ET AL.*, *PSYCHOLOGICAL SCIENCE*, VOL 19, NO 10, 2008

Three Q's >>

Fredy Peccerelli and his family fled Guatemala for New York City in 1980 after his father received death threats. He returned as a forensic anthropologist and since 1995 has helped identify some 5000 Guatemalan men, women, and children massacred during the country's 36-year armed conflict. In September, Peccerelli and imprisoned Cuban physician Oscar Elías Biscet received the New York Academy of Sciences' Heinz R. Pagels Human Rights of Scientists award.

Q: Why dig up a very painful past?
Our work provides evidence to back up the testimonies of individuals who lost their loved ones so that there can be an attempt to bring the killers to justice. It allows us to see the brutalities involved in the killings—for example, 25% of the bodies we have exhumed were children.

Q: How do you go about your work?
We meet up with family members of victims. We locate the graves and take the bodies to the lab to identify victims and determine the cause of death. We ultimately hand over our findings to the government prosecutor. We are launching our own DNA lab to strengthen the identification process.

Q: There have been only a handful of trials so far. What keeps you going?
I'm optimistic that there will be more attempts at justice—either in Guatemala or in international courts. I feel very lucky to have escaped the conflict. … [W]hile I was watching a Yankees game in New York, my fellow citizens were getting massacred. I want to repay the country by documenting the truth about these killings.

CREDITS (TOP TO BOTTOM): FAFG; IMAGE COURTESY OF ROYAL SOCIETY OF CHEMISTRY; INSET: SOURCE: R. LIU; SOURCE: COMMITTEE ON SCIENCE AND TECHNOLOGY/U.S. HOUSE OF REPRESENTATIVES

AWARDS

BRINGING HONOR. Anthropologist Stephen Houston, who has spent his career deciphering the Mayan glyph system, is one of 25 winners of this year's "genius grants" from the John D. and Catherine T. MacArthur Foundation. "There can be no rational sense of deserving" the 5-year, $500,000 prize, says Houston, a professor at Brown University, who combines linguistics, history, and ethnography to understand the classic Mesoamerican society. Houston compares the impact of deciphering Mayan writings on scholars to the effect decoding hieroglyphs had on Egyptologists. He plans to use the prize money to examine how Mayans viewed their bodies and which actions brought "honor or dishonor" to one's physical self.

A complete list of this year's winners is at www.macfound.org.

TWO CULTURES

SURF'S UP! So much for slogging through organic chemistry in some dank basement lab. University of Hawaii, Honolulu, chemist Robert Liu and colleagues have taken their synthetic chemistry to the beach. Liu, who specializes in photochemical reactions triggered by sunlight, developed a magazine-sized reactor that uses the sun's rays to produce variants of vitamin A. The reactions normally generate excess heat that must be dissipated using cold water. But in a report published online last month in *Green Chemistry*, Liu's team described how they built their reactor into a boogie board, which radiates unwanted heat into the Pacific Ocean as researchers ride the waves. Cowabunga, dude! The only problem: Good luck getting students back into the lab.

Got a tip for this page? E-mail people@aaas.org

<< Politics

LOCKED OUT. In a move that has sparked bipartisan outrage in Congress, officials at the U.S. Department of Veterans Affairs (VA) have barred a former VA microbiologist from entering one of its hospitals in Pittsburgh, Pennsylvania. The banishment came 2 days after microbiologist Janet Stout testified before the House Science Committee about a controversial VA decision to destroy her large collection of *Legionella* bacteria in 2006. At the hearing, committee members were harshly critical of that step, which Stout says followed a clash with VA officials over her lab's research priorities.

The move "appears to be punishment for Dr. Stout's appearance," representatives Brad Miller (D–NC) and Dana Rohrabacher (R–CA) wrote in a 19 September letter to VA officials. They want the agency to hand over all records relating to an 11 September e-mail from Terry Wolf, director of the VA Pittsburgh Health System, that orders the staff to block Stout's access "without prior approval of my office." Stout left the VA last year, but Wolf writes that she "has been seen on VA premises" and "still receives mail here. Both practices must be terminated immediately."

Stout, who now runs the private Special Pathogens Laboratory in Pittsburgh, says she is mystified by the effort to bar her from a public hospital "where people come and go freely." She periodically visits the building to consult with former colleagues on projects but hasn't yet tested the ban. "I don't know if they are trying to intimidate me or create fear among my former colleagues," she says. VA officials didn't return calls from *Science*.

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INFECTIOUS DISEASE

New Malaria Plan Called Ambitious By Some, Unrealistic by Others

It was standing room only last week at U.N. headquarters in New York City when a star-studded cast, including philanthropist Bill Gates, U2 rocker Bono, and British Prime Minister Gordon Brown, kicked off the latest in a string of grand plans to conquer malaria, the mosquito-transmitted scourge that kills some 1 million people a year, mostly African children.

Big guns. Celebrities and dignitaries, including U2 lead singer Bono, helped launch the Global Malaria Action Plan.

GOOD INTENTIONS

WHEN?	WHO?	GOAL?	WHAT HAPPENED?
1955	World Health Organization	Eradicate malaria	Campaign broke down in 1960s
1998	Roll Back Malaria partnership	Reduce cases and deaths by 50% by 2010	Little progress so far
2000	African heads of state (Abuja Declaration)	Reduce African malaria deaths by 50% by 2010	Little progress so far
2001	United Nations (Millennium Development Goals, MDG)	"Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases"	Appears feasible
2005	MDG Working Group on Malaria	Reduce cases and deaths by 75% by 2015	Too early to tell

The goals of the Global Malaria Action Plan (GMAP) are stunningly ambitious: Reduce malaria deaths to near zero by 2015, then progressively eliminate the disease from countries and regions until it is eradicated from the planet. That will take mosquito- and parasite-foiling technologies that have yet to be invented, along with billions of new dollars a year that the plan's architects hope generous donors will provide. GMAP, assembled over the past year with input from more than 250 experts, is the creation of the Roll Back Malaria (RBM) partnership, a coalition of international agencies, public and private donors, and malaria-affected countries.

Regina Rabinovich, head of infectious diseases at the Bill and Melinda Gates Foundation and one of the key forces behind the plan, calls the goals "ambitious but achievable." But many malaria experts say it's unlikely that GMAP will meet its targets—even with abundant funding—although they applaud the renewed commitment. Several also caution that donors and agencies should be careful in what they promise, given the humbling outcomes of previous grand plans (see table, above).

Scientists and the World Health Organization (WHO) also exuded confidence in the 1950s when they vowed to eradicate malaria, for instance. After that initiative's spectacular demise in the 1960s, malaria cases surged worldwide, and support for malaria control and research essentially dried up.

After a long hiatus, international health and development agencies reentered the fight against malaria in the late 1990s, setting a series of increasingly ambitious targets. They culminated in Bill and Melinda Gates' unexpected call last year to again attempt to eradicate the disease, a word that hadn't been uttered in the context of malaria for some 40 years (*Science*, 7 December 2007, p. 1544).

"We set year after year new goals and never meet any of them," says Christian Lengeler, a malaria researcher at the Swiss Tropical Institute. Lengeler, who has worked extensively in Tanzania, calls GMAP's 2015 target of zero deaths "totally unrealistic." "Silly," says another scientist. As for the eventual eradication of malaria, "maybe, but not in my lifetime," seems to be the general consensus.

This time it is different, insist Rabinovich and Awa Marie Coll-Seck, executive director of RBM. For one, coffers are flush. Thanks to contributions from the Gates Foundation, the Global Fund to Fight AIDS, Tuberculosis and Malaria, the World Bank, the President's Malaria Initiative, and others, international funding for malaria control jumped from $51 million in 2003 to an estimated $1.1 billion in 2008. Last week, the Global Fund announced that it will award $1.62 billion over the next 2 years to help poor countries fight malaria, and the World Bank pledged $1.1 billion to expand its Malaria Booster Program. These and other smaller contributions unveiled last week still fall significantly short of the $5 billion or $6 billion a year GMAP says is needed.

Also in the past few years, malaria interventions, such as long-lasting insecticide-treated bed nets and a new class of drugs known as artemisinin-based combination therapies (ACTs), have proved their mettle (*Science*, 26 October 2007, p. 556). A half-dozen African countries with committed leadership and a lot of outside support have scaled up these interventions rapidly—Ethiopia, for instance, distributed 20 million bed nets in just 18 months. A few of these countries or areas, those with small populations and high access to prevention and treatment, have seen roughly a 50% decline in malaria cases and deaths since 2000, WHO notes in its 2008 World Malaria Report. Ensuring universal access to these and other tools such as indoor insecticide spraying and preventive treatments in pregnant women can halve deaths by 2010, says GMAP, and then reduce them to near zero 5 years out. ▶

PHOTO CREDIT: KATHY WILLENS/AP PHOTO

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But none of the countries has reached the target of 80% coverage with existing interventions, set just a few years ago, much less the 90% called for by GMAP. Across the continent, just 23% of children slept under a bed net in 2006, and only 3% of patients were treated with ACTs, according to WHO estimates.

The challenges facing big countries like the Democratic Republic of the Congo (DRC) and Nigeria are especially daunting. They account for about 20% to 25% of malaria deaths, although hard data are scarce, and are plagued by civil unrest and weak health systems. "That it can be done in Zambia, with a population of 10 million and a dynamic minister of health, does not say a thing about what to do in DRC," agrees Rabinovich.

To develop the radical types of new vaccines, drugs, and insecticides needed for the toughest areas—as well as for eradication many decades from now—GMAP calls for pumping $750 million to $900 million a year into research. A working group is already hammering out a detailed research and development plan, which Rabinovich says should be ready in 15 months.

To prime the pump, Gates announced $168 million for research on the next generation of malaria vaccines. The award is going to the Bethesda, Maryland–based PATH Malaria Vaccine Initiative, which will try to build off the experience gained from vaccine candidates already in the pipeline, says MVI Director Christian Loucq. GlaxoSmithKline's RTS,S, which targets the malaria parasite form that infects the liver, for instance, is about to enter phase III trials—the first malaria vaccine candidate to get that far. MVI is investigating additional antigens that target different stages in the parasite's life cycle that could be used in combination, as well as novel adjuvants to boost vaccine power. Although expected to be significantly more efficacious, such second-generation vaccines won't be available until well after 2015 and, like RTS,S, will still be only partially protective.

Another intriguing possibility is a transmission-blocking vaccine that would be administered to humans but that would target the parasite after it is taken up by the mosquito in her blood meal. Loucq calls the approach "elegant," the equivalent of an "immunological bed net," but cautions that it is early days.

Whether the exact targets are met is beside the point, says RBM leader Coll-Seck. "I am a glass-half-full person," she says. If GMAP leads to a significant reduction in malaria cases and deaths—even if the plan promised much more—who would call that a failure, she asks.

–LESLIE ROBERTS

ANTHRAX INVESTIGATION

NAS Study May Fail to Settle Anthrax Case

The Federal Bureau of Investigation (FBI) has provided the U.S. National Academy of Sciences (NAS) with a list of 15 questions that it wants the academy to consider in its review of the scientific evidence in the FBI's case against Bruce Ivins, the Army microbiologist implicated in the anthrax letter attacks of 2001. Besides asking whether the genomic analysis carried out to trace the source of the anthrax was valid, the questions address aspects such as the source of silicon found in the spores and whether the attacker needed specialized equipment to grind the spores into an easily dispersible powder.

But even before the academy frames the scope of the study and seeks approval from its governing board, members of Congress and bioterrorism experts are voicing concerns that a purely scientific review won't counter skepticism that Ivins, working solo, was the perpetrator of the attacks. One expert calls the FBI's request "a nice little jujitsu move" to deflect attention from nonscientific questions about the investigation, such as how the FBI ruled out all the other individuals who had access to RMR-1029, the flask of anthrax under Ivins's control. Last week, those concerns prompted Representative Rush Holt (D–NJ) to introduce legislation proposing a commission—similar to the one that investigated the 11 September 2001 terrorist strikes—that would review all the evidence in the case.

Since Ivins committed suicide on 29 July, FBI officials have unsealed court documents that detail part of the scientific evidence linking the anthrax in the letters to the flask under Ivins's control at the U.S. Army Medical Research Institute of Infectious Diseases at Fort Detrick, Maryland. By requesting the NAS study, the FBI is essentially subjecting that evidence to peer review in lieu of a jury trial. The last question on the FBI's 15 September list is whether "testimony regarding the methods used to link the mailed anthrax to RMR 1029" would meet evidentiary standards in a court of law.

Closed. FBI boss Robert Mueller hopes the study will wrap up the case.

CREDIT: SUSAN WALSH/AP PHOTO

Gregory Koblentz, a biodefense researcher at George Mason University in Fairfax, Virginia, says even for a scientific review, the questions posed by the FBI don't go far enough. He and Alan Pearson of the Center for Arms Control and Non-Proliferation in Washington, D.C., want the academy to ask more probing questions about the science as well as undertake a broader investigation; they are submitting their suggestions to NAS. For example, says Pearson, referring to a question on the FBI's list, it isn't pertinent to ask whether "*Bacillus anthracis* samples dried with a rudimentary methodology can pose an inhalation hazard resulting in pulmonary anthrax. Of course they can. The question is whether [this method] can produce anthrax like that found in the letter."

"Our aim here is to lay out the facts gathered in this investigation and be as transparent as we can," says FBI spokesperson Paul Bresson. "That is all we can do and all we can control. As we have stated previously, we would have preferred to have brought this case to trial."

–YUDHIJIT BHATTACHARJEE

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ASTROPARTICLE PHYSICS

Europeans Think Big For Particle Detectors

Looking up. The MAGIC telescopes helped demonstrate gamma ray detection.

CREDIT: ASPERA/R. WAGNER, MPI FOR PHYSICS, MUNICH

European physicists who study particles from outer space made a pitch this week for the ambitious and costly experiments they want to build over the next decade. "We've worked hard to get the tools; now we need to move to large-scale detectors," says Christian Spiering of DESY, Germany's particle physics lab in Hamburg.

Astroparticle physicists aim to snare the likes of cosmic rays, neutrinos, gravitational waves, and dark matter particles as they pass by or through Earth. To better capture these elusive cosmic signals, ASPERA, a network of astroparticle physicists funded by the European Union, this week released a road map for future projects, along with a pitch to funding agencies to double the current €70 million annual spending on astroparticle physics over the next 8 to 10 years—a tall order in what's expected to be a tough funding climate.

Researchers have been detecting particles from space for decades, but so far the scientific breakthroughs from their sensors have been few. But this groundwork will soon pay off, says Spiering, who chairs ASPERA's road map committee. The road map, released on 29 September, divides the field into seven areas and identifies a key instrument in each.

Three of those instruments rely on tested technology, and construction could begin on them soon. First, the proposed Pierre Auger Observatory North, a vast array of detectors that would look for ultrahigh-energy cosmic rays, would likely be a bigger Northern Hemisphere version of the existing Auger array in Argentina. Second, the Cerenkov Telescope Array would look for incoming high-energy gamma rays, following the detection strategy of existing telescopes such as MAGIC in the Canary Islands. And the recently completed ANTARES, a neutrino observatory on the Mediterranean seabed, is the prototype for the third, KM3NeT, which would use a cubic kilometer of seawater as its detector. For these three proposals, "we have the technology; now we have to find the money," says ASPERA coordinator Stavros Katsanevas of France's CNRS research agency.

The road map doesn't detail the detector of choice for two other subfields, spotting dark matter and measuring neutrino mass from a phenomenon called double beta decay; the outcomes of ongoing experiments using a variety of techniques will inform those decisions. ASPERA's lineup finishes with two mammoth projects: an underground neutrino observatory called LAGUNA with a detector made from a million tons of either water or liquid argon, and a next-generation gravitational-wave antenna dubbed the Einstein Telescope. Both require more design work, and results from the Large Hadron Collider and current gravitational-wave detectors could change the specifications. "By mid next decade, we can launch these ambitious projects," says Katsanevas.

Metallurgist John Wood of Imperial College London, who headed a European Union–sponsored effort to identify research infrastructure projects, is skeptical of ASPERA's call for funding increases. "In the current climate, their chances are pretty slim," he says. "Politically, it's a very difficult time." But Katsanevas says, "I'm not afraid of that." The needed doubling of funding assumed that all of the road map's projects remained European-led, whereas he expects many will become collaborations with North America or Asia or both. In fact, French officials have asked the Organisation for Economic Co-operation and Development in Paris to act as a coordinating body, comparing regional road maps to find openings for collaboration. **–DANIEL CLERY**

Protection for Researchers

A California measure signed into law this week aims to protect researchers from harassment and attacks by animal-rights extremists. Publishing information about researchers that is likely to incite threats or acts of violence or trespassing on a researcher's property with the intent of interfering with his or her academic work is now a misdemeanor. Police hope arrests made for these infractions will yield evidence on shadowy extremist groups. Several university researchers have been targeted in recent attacks (*Science*, 8 August, p. 755). **–GREG MILLER**

Hubble Trouble … Again

The failure of a critical device that formats data aboard the orbiting Hubble Space Telescope has delayed this month's long-planned shuttle rescue mission until at least February. Agency officials say it will take several months to prepare the spare data system, which they want to send up because relying on a redundant component would leave the telescope without a backup. Changing out the component will add to the list of fixes, says John Shannon, shuttle program manager. But NASA science chief Edward Weiler says, "Hubble has a habit of coming back." **–ANDREW LAWLER**

Making Space Reservations

NASA will be allowed to buy seats through 2016 aboard the Russian Soyuz spacecraft, which ferries passengers to and from the space station, as part of a stopgap funding measure passed this week. The U.S. government slapped sanctions on Russia for alleged sales of nuclear material to Iran, which prohibited NASA from dealing with the Russian space industry. A waiver that allowed the space agency to carry out such spending was set to expire in 2011. Soyuz needs to be booked well in advance, however, and a failure to extend the waiver this year would leave Americans without a way to get into space if the shuttle, as planned, is taken out of service in 2010. **–ANDREW LAWLER**

Not Those Stock Analysts

The United States faces a shortfall of Ph.D.s to help analyze the status of its fisheries, according to a joint report by the departments of Commerce and Education. The report estimates that the National Oceanic and Atmospheric Administration (NOAA) alone will need to hire 150% more stock-assessment scientists (it now has 90) over the next decade, and universities are expected to confer about half the degrees needed each year. **–ERIK STOKSTAD**

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NATIONAL INSTITUTES OF HEALTH

Adding a Turn to the Roadmap, Zerhouni to Step Down

Without saying much about his next move, Elias Zerhouni announced last week that he is resigning from the U.S. National Institutes of Health (NIH). He will step down by the end of October after more than 6 years as director. During that time, he tried to break down institutional and scientific barriers at the $29 billion agency and push discoveries into medicine. Those efforts won praise from Congress and leaders in the research community. But he also had to deal with a string of ethics controversies, and it was a tough time for rank-and-file scientists, who were squeezed by 5 years of flat budgets.

Transition. Elias Zerhouni explains NIH's mission to lawmakers, seated with his deputy director, Raynard Kington (*left*).

Rumors have swirled since January that Zerhouni might replace Johns Hopkins University President William Brody, who is retiring at the end of this year. When reporters asked Zerhouni about this last week, he responded: "That's not been decided by me at all." Instead, he said he plans to "take some time out" and do some writing. He chose to depart before the 4 November presidential election, he said, so that the next Administration will "focus on NIH as early and as soon as possible."

As for why he's leaving at all, Zerhouni saw his departure as following "the natural cycle of tenures for this position," about 6 years. A look back at the previous eight directors shows that their terms varied in length; two stayed longer than 6 years: James Shannon (13 years) and James Wyngaarden (9 years).

Zerhouni, 57, an Algerian-born radiologist who invented several new imaging techniques, was an administrator at Johns Hopkins before he took the helm of NIH in May 2002. Zerhouni's background set him apart from his predecessor, the basic biologist Harold Varmus. Many observers say Zerhouni's management experience made him the right person for a time of belt-tightening. A 5-year doubling of NIH's budget from 1998 to 2003 was coming to an end, and Varmus and some other scientific leaders were concerned about NIH's unchecked administrative growth, including the creation in 2000 of an institute focused on imaging.

In response, Zerhouni created a formal plan called the NIH Roadmap, a set of initiatives aimed at moving basic discoveries to the bedside, funded at first by taxing each of NIH's institutes. But just as these new programs were taking off, NIH's budget stopped growing, sending success rates for research grants crashing from about 30% to 20% this year. Some members of the community blamed Zerhouni and his Roadmap. Defenders say, however, that the plan was useful as a selling point for biomedical research in Congress.

Although Congress has recently given NIH tiny budget boosts, some say it has significantly elevated the NIH director. It passed a 2006 law capping the number of institutes and centers at 27, giving the NIH director more control over NIH's portfolio, and creating a permanent fund for Roadmap-like projects. That pot of money had risen to $496 million, as large as many of smaller institutes. Varmus says the NIH director's new powers will make the position "a lot more interesting."

At the same time, some Roadmap components remain just experiments. A program to bring industry-style molecular screening to academia is beset by skeptics. And the new Clinical and Translational Science Awards, which are forcing medical schools to integrate clinical science programs, have been criticized as inadequate.

Zerhouni has been credited widely for trying to promote novel research and young investigators, including most recently for creating the "transformative" R01 award for risky projects. Although the total number of these awards so far is modest, "the important thing was that Zerhouni recognized" the need for them, says cell biologist Keith Yamamoto of the University of California, San Francisco, who also helped plan a major overhaul of peer review.

Zerhouni may have reaped more than the usual share of controversy. He defended sexual research grants to a Republican-led Congress and departed from the Bush Administration's tough line against human embryonic stem cell research. Addressing an uproar over industry consulting by NIH scientists, he banned such outside activities.

President George W. Bush has not yet named an acting NIH director, but Zerhouni has recommended current NIH Deputy Director Raynard Kington for the post. An M.D. and Ph.D. in health policy and economics who studied health disparities before coming to NIH, Kington is not well-known to the extramural biomedical research community. As deputy, much of his time has been taken up with dealing with the intramural ethics controversy.

The acting director will face a number of immediate challenges. One is deciding how to allocate the pain of a budget freeze through March, just approved by Congress in a continuing resolution (*Science*NOW, 29 September). Typically, NIH deals with such uncertainty by funding ongoing grants at the 80% level and funding fewer new awards until the next budget is approved. That will increase stress on investigators. In the short term, leading NIH "is going to be an even tougher job," says Howard Garrison, public affairs director of the Federation of American Societies for Experimental Biology in Bethesda, Maryland. Also requiring quick attention is a call from Senate investigators for a review of conflict-of-interest rules for extramural researchers. Given such pressures, many NIH watchers hope a new director will be in place before next spring.

–JOCELYN KAISER

CREDIT: UPI PHOTO/LANDOV

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NOAA

U.S. Oceans Chief Leaves a Mixed Legacy in His 7-Year Wake

For 7 years, former Navy Vice Adm. Conrad Lautenbacher has preached his mantra of "one NOAA" as a way to unify the hydra-headed National Oceanic and Atmospheric Administration (NOAA). Congress has rewarded his management prowess with larger budgets, allowing the agency to expand its efforts on everything from tracking wildfires to monitoring tsunamis. Last week, Lautenbacher announced he is leaving, and scientists say the spry technocrat leaves a reorganized and stronger NOAA research program—as well as some big headaches for the next U.S. oceans skipper.

Tucked into the Commerce Department, NOAA has responsibility for myriad activities in the air, at sea, and in space. "When I came to NOAA, I saw it as a holding company of six or seven multidisciplinary, very fine scientific enterprises," says Lautenbacher. "[But] it was too compartmentalized."

Lautenbacher sought to break down agency stovepipes with 44 programs that cut across issues such as aquaculture, environmental modeling, and geodesy. He also combined six agency labs in Boulder, Colorado, to create the Earth System Research Laboratory (ESRL). "He's done a good job of knitting the pieces of NOAA together," says marine geologist Rodey Batiza, a program manager at the U.S. National Science Foundation who has served as an outside reviewer for the agency. Congress apparently agreed: Legislators hiked the agency's budget from $3.1 billion to $4.2 billion during Lautenbacher's tenure, although they also pumped hundreds of millions of dollars into pet projects.

CREDIT: NOAA

Making waves. This spring, NOAA's Conrad Lautenbacher unveiled a management plan to preserve a fragile marine sanctuary in Hawaii.

The improved cooperation helped bolster tsunami monitoring efforts, says geophysicist Costas Synolakis of the University of Southern California in Los Angeles. Since the Sumatra tsunami of December 2004, NOAA's Pacific Marine Environmental Laboratory (PMEL) in Seattle, Washington, has collaborated with the National Weather Service on 33 new advanced undersea pressure gauges that have improved the service's predictive accuracy. The weather service is also installing new tsunami-modeling software developed by PMEL's scientists. By the same token, former NOAA advisory board chair Leonard Pietrafesa, a fluid physicist at North Carolina State University in Raleigh, says that ESRL has paved the way for better predictions of hurricane intensity.

While Lautenbacher was making it easier for NOAA's scientists to talk to one another, the agency itself was having trouble communicating with two other federal agencies on one of its most important programs, the National Polar-Orbiting Operational Environmental Satellite System. Delays and cost overruns in the $14 billion Earth-monitoring program, which NOAA manages with NASA and the Pentagon, triggered a 2006 Pentagon review that stripped from the system five climate sensors. A report that year by the Department of Commerce inspector general faulted NOAA leadership's "poor management oversight" of the program, and the three agencies are still trying to agree on a budget for it.

Lautenbacher says he did his best to manage the "poorly conceived" program, which was created in 1994. "I don't regret how NOAA managed it," he says. He reassures climate scientists that making precise climate data "operational" will be a priority for a "National Climate Service," a new entity that his deputies are proposing for the next Administration.

Lautenbacher, who will step down next month, plans to move to Atlanta, Georgia, to chart his future. Deputy NOAA Administrator William Brennan will serve as acting director.

–ELI KINTISCH

Italy Restricts Academic Hires

An attempt to address Italy's economic woes appears to place tough restrictions on academic hiring. An amendment to a newly enacted financial law restricts institutions to replacing at most 20% of the jobs lost through retirement and other reasons. "We cannot [hire] anyone until 2013, as there is nobody who is going to retire for the next few years," says physicist Stefano Fantoni, head of SISSA, the prestigious postgraduate science school in Trieste.

Italian scientists are also wary about a provision that authorizes public universities to look for sponsors and become private foundations. The new law comes on top of a proposed 10% cut in university funding by 2010. "In Italy, pure research is always the first sector in science to suffer," says Giancarlo Ruocco, head of the physics department at the University of Rome La Sapienza. **–LAURA MARGOTTINI**

Going Green Once, Twice …

North America's first carbon-emissions auction went smoothly last week. Organized by a consortium of 10 Northeast and Mid-Atlantic states aiming for a 10% reduction in carbon emissions from their power companies by 2018, the Regional Greenhouse Gas Initiative auction closed at a price of $3.07 per ton. Jim Rubens, an energy policy adviser with the Union of Concerned Scientists, called the price a "Goldilocks" figure: It's enough to impact carbon emissions from utilities in participating states without destabilizing the economy.

–RACHEL ZELKOWITZ

A Rewarmed Climate Report

In a surprising twist, White House officials plan to rework a draft report on climate change because of complaints that it hypes—not underplays—the threat of global warming. The Unified Synthesis Product, released in July, was meant to summarize the 21 previous federal Climate Change Science Program (CCSP) reports. But statements like "The future is in our hands" and "the choice is ours" have enraged critics such as Roger A. Pielke Sr. of the University of Colorado, Boulder. Pielke says the draft "promotes a particular narrow perspective."

CCSP staffer Chad McNutt says the report was released before it was ready because "we wanted to do this fast." Now editors are sifting through 500 pages of comments. One editor, Jerry Melillo of Woods Hole Oceanographic Institution in Massachusetts, doesn't think that the July version was overly politicized. But he says some points "could have been stated more clearly." **–ELI KINTISCH**

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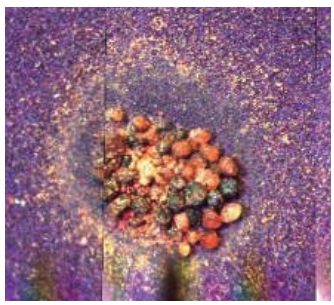
PLANETARY SCIENCE

Minerals Suggest Water Once Flowed on Mars—But Where?

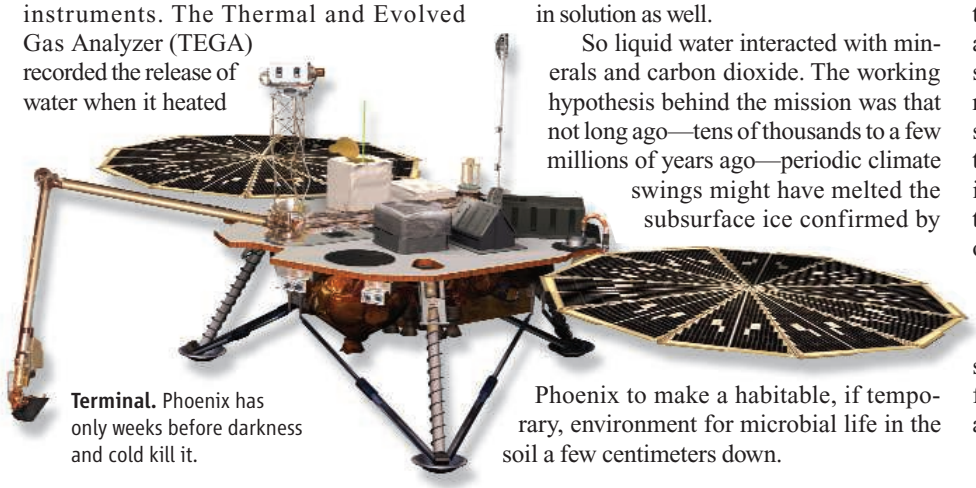
Scientists on the Phoenix mission to the high arctic of Mars announced this week that the rover had found some long-sought soil minerals. "These [minerals] are indicators of liquid water in the past," Phoenix principal investigator Peter Smith of the University of Arizona (UA), Tucson, said at a bicoastal press conference on 29 September. The minerals are exactly what Phoenix was sent to look for in the high-latitude soil just centimeters above the frozen water suspected from orbital data.

The catch is that from Phoenix observations so far, team members can't say for certain when or where the water was liquid: recently, where Phoenix found the minerals, or long ago, somewhere else on the planet. The minerals might have blown in from ancient deposits formed in the atmosphere. And time is running out for Phoenix to find answers. The gathering gloom of martian winter means it has only a couple of months to live.

The discoveries come from two Phoenix instruments. The Thermal and Evolved Gas Analyzer (TEGA) recorded the release of water when it heated a soil sample to high temperature, most likely when water was driven off from clay, said TEGA lead scientist William Boynton of UA. TEGA also detected carbon dioxide being driven off at high temperature—a clear sign that calcium carbonate was breaking down, Boynton said. The Microscopy, Electrochemistry, and Conductivity Analyzer confirmed the presence of calcium carbonate, said MECA lead scientist Michael Hecht of the Jet Propulsion Laboratory in Pasadena, California. It measured a stable pH of 8.3 in a soil slurry even after Phoenix added acid, evidence that calcium carbonate was buffering the pH. MECA detected calcium ions in solution as well.



Dirt. Martian soil harbors minerals formed from wet rock.



Terminal. Phoenix has only weeks before darkness and cold kill it.

So liquid water interacted with minerals and carbon dioxide. The working hypothesis behind the mission was that not long ago—tens of thousands to a few millions of years ago—periodic climate swings might have melted the subsurface ice confirmed by Phoenix to make a habitable, if temporary, environment for microbial life in the soil a few centimeters down.

That scenario could still hold, says geochemist Nicholas Tosca of Harvard University. "Liquid water is required to form these minerals," he says. "How much liquid water could be debated. A thin film could do it." That would be enough for microbes too. But scientists cannot yet show that the minerals formed where Phoenix found them. They may have formed billions of years ago where massive deposits of clay are found today. Also, carbonates reported in martian dust may have formed in the atmosphere and could have been blown to the Phoenix site, although Smith sees few signs of such transport. "I'm not sure what they could do to test that," says Tosca.

Now that Phoenix has completed its 90-day nominal mission and a 30-day extended mission, it's living on borrowed time. Martian winter is coming on, with the sun spending more and more time each day below the horizon, starving the spacecraft's solar panels. Mission managers are rushing to fill TEGA's last four sample cells before power levels fall too low for the sampling arm to operate. "We have not finished," declares Smith. Near the top of the team's remaining to-do list will be looking for organic matter possibly lingering from past life. "If there's any there, it's not very much," said Boynton, but "we are still looking."

By late November, the crushing cold should shut down the lander as carbon dioxide frost begins to encase it. Water-ice snow is already beginning to fall from passing clouds.

–RICHARD A. KERR

CRYPTOGRAPHY

Quantum Network Set to Send Uncrackable Secrets

Next week in Vienna, European scientists and engineers will put the bizarre and abstruse laws of quantum mechanics to a practical, everyday use. Researchers will demonstrate a network for transmitting uncrackable encoded messages in quantum-mechanical packets of light. Such quantum networks could soon link banks or government offices, some researchers say. "This is a moment when research turns into technology," says Chip Elliott, a network engineer at BBN Technologies in Cambridge, Massachusetts, who 5 years ago led efforts to build the more primitive DARPA network. Still, he cautions, "it's too early to say whether there are customers for this."

The product of a 4-year, €11.4 million collaboration funded by the European Union, the network will connect six sites across the city through eight existing fiber-optic links, all belonging to industrial giant Siemens. It will distribute the numerical "keys" for scrambling secret messages.

A message can be encrypted by converting it into a string of 0s and 1s and scrambling those bits by compounding them with a key, a random string of 0s and 1s. If only the sender, Alice, and the receiver, Bob, know the key, then only they can read the message. The trick is to transmit the key without its being seen by an eavesdropper, Eve. So-called quantum key distribution exploits the fact that it's impossible to measure a photon without also altering it.

For example, Alice can send Bob individual photons polarized horizontally to signify 0 or vertically to signify 1. Thanks to quantum weirdness, she can also send photons polarized both ways at the same time. If Eve tries to

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Too much. Ice coming off Jakobshavn Isbræ glacier surged after warm ocean water arrived.

GLACIOLOGY

Winds, Not Just Global Warming, Eating Away at the Ice Sheets

The surge of glaciers draining both the Greenland and West Antarctic ice sheets has alarmed scientists and the public alike. Global warming appeared to be taking an early toll on the planet's largest stores of ice while accelerating the rise of sea level. But two new studies point to random, wind-induced circulation changes in the ocean—not global warming—as the dominant cause of the recent ice losses through those glaciers. In Greenland, at least, "you're going to have trouble blaming this on global warming," says glaciologist Richard Alley of Pennsylvania State University in State College. But he says the results underscore the threat of global warming by showing how warmth can "hit ice sheets where it hurts," as glaciologist Robert Bindschadler of NASA's Goddard Space Flight Center in Greenbelt, Maryland, puts it.

The losses long puzzled glaciologists because the atmosphere over the glaciers didn't seem to have warmed enough to trigger them. Meltwater didn't lubricate glacial flow enough to explain the losses either (*Science*, 18 April, p. 301). Could the culprit be ocean waters? They can carry lots of heat to glaciers that float out onto coastal waters, but oceanographers had not been taking the ocean's temperature off the ice sheets.

So physical oceanographer David Holland of New York University and his colleagues turned to scientists of a different stripe: fisheries researchers. They had recorded bottom temperatures off southwest Greenland while surveying shrimp populations from 1991 to 2006. Holland and colleagues reported online this week in *Nature Geoscience* that an influx of warmer, saltier water in 1997 "coincided precisely" with the rapid thinning and subsequent acceleration of Jakobshavn Isbræ glacier, Greenland's most prolific outlet for ice. The warm water must have melted the glacier's exposed underside and weakened it, they say, leading to the breakup of the ice shelf that had been bracing the glacier against the shore and helping to hold it back. "I think it's fantastic," says Bindschadler. They've "got this nailed in Greenland."

Holland and colleagues traced the influx of ocean warmth back to the atmosphere over the North Atlantic. An abrupt weakening of winds due to a natural atmospheric phenomenon called the North Atlantic Oscillation drove more waters from the Irminger Sea near Iceland around the tip of Greenland, up onto the shelf, and under the ice.

A similar natural process may have been at work in recent heightened ice losses off West Antarctica, researchers reported in the 18 September *Geophysical Research Letters*. Glacier modelers Malte Thoma of the Alfred Wegener Institute for Polar and Marine Research in Bremerhaven, Germany, and colleagues, including Holland, had no water temperature data there, but they did have wind observations. When they plugged those numbers into an ocean-ice model, the shifting winds drew deeper, warmer offshore waters in the model up onto the continental shelf and under the ice at the same time in the mid-1990s that the real glaciers draining the West Antarctic Ice Sheet sped up. The wind shift may have been natural or caused by global warming, says co-author Adrian Jenkins of the British Antarctic Survey in Cambridge, U.K. Therefore, "whether we're going to see a continuation of [those losses] is not clear."

The vagaries of the atmosphere may be sending some confusing signals about global warming, researchers say, but that's no reason to stop worrying about the ice. "The really important thing is," says Alley, "when you look at [climate] projections, you have warming around Greenland." And that warmth now has an obvious way to get at the ice.

–RICHARD A. KERR

measure the light particles, that very act will "collapse" the two-way-at-once photons into either vertical or horizontal ones. Bob and Alice can detect that by comparing some randomly chosen bits.

A few companies make quantum systems to connect two users through a single link. The Vienna project weaves six disparate systems into an automated network. "You just make a connection to one node and can connect to any other user," says Andreas Poppe, a physicist at the Austrian Research Centers in Vienna.

In fact, the network will not be a fully quantum network, which would let Alice pass photons to Bob across any number of nodes. That would require devices called "quantum repeaters" that are at least a few years away. In the Vienna network, each user generates a key that is stored as classical (nonquantum) 0s and 1s in the node he or she links to. Those classical bits flow from node to node as needed, quantum mechanically encrypted as they cross each link. "What our network assumes is that you can trust each of the intermediate nodes," says Andrew Shields, a physicist with Toshiba Research Europe in Cambridge, U.K.

Nobody will be invited to try to hack the network, either. That's because hackers would likely ignore the quantum mechanics and attack the system's conventional parts, which wouldn't test the new concept, Poppe says.

Still, researchers hope the demonstration will signal the emergence of the new technology, especially for private networks. Some experts are skeptical. "I think the impact on the actual practice of cryptography is likely to be small," says Ronald Rivest, a computer scientist at the Massachusetts Institute of Technology in Cambridge. Current techniques, which rely not on shared secret keys but on mathematical manipulations that are practically impossible to work backward, already work well, says Rivest, who predicts that the niche for the quantum systems will be small.

Network developers hope for more. "I think, on our scale of things, it will be a historic day," says physicist Nicolas Gisin of the University of Geneva, Switzerland. The question is, will technologists and market analysts see it that way, too?

–ADRIAN CHO

CREDIT: BOB STRONG/REUTERS

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RESEARCH FOUNDATIONS

Biochemist Robert Tjian Named President of Hughes Institute

The Howard Hughes Medical Institute (HHMI), the largest private funder of biomedical research in the United States, has chosen a new president. He is University of California, Berkeley, biochemist Robert Tjian, a longtime Hughes investigator known as a driven researcher and devoted mentor. On 1 April, Tjian will replace Thomas Cech, who will return to research at the University of Colorado, Boulder.

The Chevy Chase, Maryland–based HHMI, which has an endowment of $17.5 billion and spent $685 million last year, supports more than 350 investigators at universities and funds education programs and scientists abroad. Tjian said "there are many reasons" why he accepted an offer from the Hughes board of trustees, which based its search on nominations. The main one, he says, is "to give back" to the institution that has funded him for 22 years. Moreover, Hughes "has a huge impact," and "I think it's a fantastic opportunity to try to help scientific research and science education in the United States and internationally," Tjian says.

Tjian, 59, studies the biochemistry of gene transcription. At Berkeley, he has been heavily involved in recruiting new faculty, reshaping its research and education programs, and directing its nearly decade-old health sciences initiative, which promotes interdisciplinary research. He also co-founded Tularik, a biotech company that was sold to Amgen in 2004 for $1.3 billion.

Multitasker. Biochemist Robert Tjian's broad experiences likely helped win him the job of HHMI president.

HHMI board of trustees member Joseph Goldstein says this range of experiences made Tjian "exactly right" for a job that has become "more complicated" in the past few years, as Cech began new programs and oversaw the creation of HHMI's first research campus, Janelia Farm, in Loudoun County, Virginia. Tjian is "an outstanding scientist, he's an excellent mentor to students and postdoctoral fellows, he's interested in education, he has a reputation for being very organized, and he has a broad view of biology and medicine," says Goldstein, a Nobel Prize–winning biochemist at the University of Texas Southwestern Medical Center in Dallas, who has known Tjian for more than 20 years.

As Cech did during his 8 years at HHMI, Tjian plans to keep his Berkeley lab—he says he wouldn't have taken the job otherwise—but will spend no more than 1 day a week there and at Janelia Farm. He has also agreed to give up his position on the boards of several biotech companies by April.

Tjian says that he has no specific new programs in mind coming in: "I need to go in there and take a look." For now, he plans to continue HHMI's aim of funding the "right people." He doesn't expect to tinker with Janelia Farm, which he considers an ongoing "experiment." He expects to visit Hughes in the coming months while Cech is still there to "learn the ropes." **–JOCELYN KAISER**

FELLOWSHIPS

An International Plan to Hatch Scientist-Entrepreneurs

TIANJIN, CHINA—Who said science and business don't mix? Last week, more than 100 young researchers from 60 countries were special guests at the summer meeting of the World Economic Forum (WEF), held near Tianjin, China's third biggest urban area. While corporate titans anguished over the U.S. bank bailout, young scientists and entrepreneurs explored how to forge new links.

To ease neophytes into the world of dealmaking, the InterAcademy Panel (IAP), a network that sponsors science-in-society programs on behalf of 100 national science academies, plans to award five $10,000 seed grants to the most compelling joint R&D proposals arising from interactions at the meeting between scientists and business leaders. "The idea is to nurture new linkages," says IAP co-chair Howard Alper, a chemist and chair of Canada's Science, Technology and Innovation Council. "Companies need not put in a cent at the beginning." Alper expects many academies to provide matching grants. The effort is timely, says Padmasree Warrior, chief technology officer at the California computer firm, Cisco Systems. "The lines are blurring between breakthrough, start-up, and scale-up," she says.

Top scientists are no strangers to WEF, famed for its winter meetings in Davos, Switzerland. Klaus Schwab, WEF's founder and executive chair, says he has long sought "to integrate technology even more into WEF activities." Last spring, Alper and fellow IAP co-chair Chen Zhu, China's health minister, persuaded Schwab to expand WEF's science program and invite young scientists. "We want to create a sustained integration of S&T [science and technology] in the forum," says Alper.

As a result, WEF's second annual "New Champions" meeting featured workshops on managing science and frontier science, and plenary sessions on nanotechnology and life sciences. "The academics seemed to embrace the idea that they needed to engage with the business community in language that the latter could understand," says Tom Ilube, chief executive officer of Garlik, a company based in Richmond, U.K., that specializes in protecting consumers against identify theft.

Guruprasad Madhavan cottoned on quickly. At the meeting, the S&T policy fellow at the National Academies in Washington, D.C., forged a partnership with entrepreneurs who will help him develop a low-cost medical device business model for poor villages in Tamil Nadu, his home state in southern India. With such tangible outcomes, Alper and others hope scientists have earned a permanent place at the WEF table.

–RICHARD STONE

CREDIT: BARBARA RIES/HHMI, 2008

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CREDIT: M. ENSERINK/SCIENCE

The Peanut Butter Debate

A new type of ready-to-use food is changing the way severe malnutrition is treated. But questions remain about how far to push its introduction—and science has a hard time providing the answer

SAE SABOUA, NIGER—On a scorching hot day in this dusty, dry corner of the Sahel, mothers carrying babies and small children line up outside a couple of big tents. Some of the infants look healthy but others are shockingly thin, their arms like broomsticks. They're waiting to enter a "therapeutic feeding center" operated by the French section of Médecins Sans Frontières (MSF). Once inside, the children are measured and weighed and receive a quick health checkup. If they're found to be severely malnourished, they immediately receive a silvery sachet containing a new type of food that might just save their lives.

Open and squeeze the sachet and out pour 92 grams of a brown paste that looks like dark peanut butter. It's called Plumpy'nut, and one serving has 500 calories and plenty of proteins, vitamins, and minerals. Aid organizations like MSF say the paste, a so-called ready-to-use therapeutic food (RUTF), has revolutionized care for malnourished children. Plumpy'nut has a long shelf life, it does not need to be mixed with water—a major risk with standard treatments based on milk powder—and it is simple for mothers to give to their children at home. Perhaps best of all, children love the sweet, sticky stuff.

Online
sciencemag.org
Podcast interview with the author of this article.

But the nutrition world is divided on just how far the introduction of these products should go. MSF wants to move beyond treating severe malnutrition and introduce peanut butter–like pastes to *prevent* that condition, which occurs in some 20 million children in Africa and South Asia every year. In one district in Niger, MSF has started giving the product to as many as 80,000 children between 6 and 36 months, in what's called "blanket distribution." MSF likens the move to the large-scale introduction of antiretroviral drugs in Africa, which it helped pioneer.

But others ask: Where's the science to support such a plan? Few dispute the power of RUTFs in treating severely wasted children. But there's little evidence that such products work equally well in preventing malnutrition. And besides, skeptics say, adding them to the regular diet of millions of children is too complicated and too costly—MSF's program cost more than $55 per child in 2007—to keep up in the long run. "For prevention, we need other products," says André Briend, a nutrition expert at the World Health Organization (WHO) in Geneva, Switzerland, who helped invent Plumpy'nut while working as a French government researcher.

The issue has pitted those who want to see solid evidence before embarking on a major aid program against those—impatient with talk about *P*-values, cost-effectiveness, and sustainability—who want to act now. "Thousands of kids are dying," says Milton Tectonidis, a former MSF nutrition expert and a vocal advocate of a massive introduction of RUTFs. "We have enough data now. Do something!"

A new approach

Part Sahara, part Sahel, Niger is one of the poorest countries in the world. More than 70% of the population is illiterate. Malnutrition is

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Sweet fix. Malnourished children receive sachets of Plumpy'nut at an MSF feeding center in Maradi province, Niger.

pervasive, especially during the so-called hunger gap—the 5 or 6 months before the annual harvest, when the previous year's supplies of sorghum and millet are running out. Protracted dry spells periodically lead to severe food crises, but even in good years, the essentially vegan diet doesn't always provide enough nutrition for fast-growing children younger than 3, says Susan Shepherd, a medical adviser at MSF in Geneva.

Until a few years ago, the standard treatment for severe malnutrition was F100, a milk powder fortified with dozens of vitamins and minerals. F100 was developed in the 1980s by veteran nutrition scientist Michael Golden, now a professor emeritus at the University of Aberdeen, U.K. It needs to be reconstituted with clean drinking water and consumed almost immediately. Left unrefrigerated for a few hours, it turns into a bacterial soup that can cause infectious diseases. That's why F100 is administered only in special nutrition "hospitals" where children often stay as long as 4 weeks with a caretaker, usually their mother.

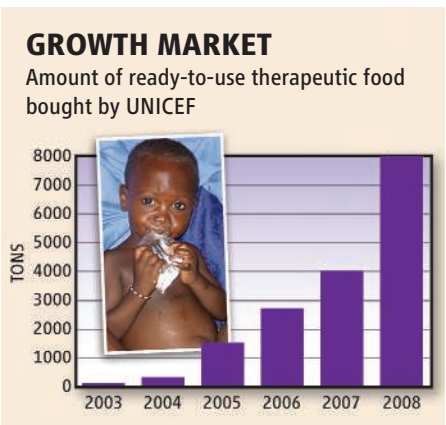
Those are serious drawbacks. A mother who leaves home and work may put other children or the harvest at risk. Hospital capacities are limited, forcing governments and aid organizations to turn away patients. During a 2002 famine in Angola, MSF treated 8000 children in in-patient centers, Shepherd says, far short of what was needed. Crowded hospitals also help spread infectious diseases. Studies have shown that only between 25% and 45% of patients make a full recovery—and as many as one in five dies.

Golden and others started looking for alternatives to F100 in the 1990s. In 1997, Briend, then at the Institute of Research for Development in Paris, teamed up with Michel Lescanne, the director of Nutriset, a food company in Normandy. Lescanne had experimented with Mars-like bars that had almost the same composition as F100; the problem was that they melted easily. Briend found his inspiration in a jar of Nutella, a hazelnut spread that his children loved; the duo developed a paste consisting of roasted, ground peanuts combined with vegetable oil, milk powder, sugar, and a mix of minerals and vitamins.

Plumpy'nut, as they called it, is less than 2% water, which makes it a hostile environment for microbes. Suspended in a fatty environment, the vitamins and minerals are very stable. Plumpy'nut can last for up to 2 years without refrigeration and does not spoil even after the package is opened.

Mark Manary, a nutrition scientist at Washington University in St. Louis, Missouri, was the first to test the product in clinical trials, in Malawi. Two studies published in 2004 showed that it was "really a breath of fresh air," Manary says: Almost 80% of severely malnourished children recovered. And the home-based treatment regimen proved easy to organize on a large scale.

Experiences elsewhere were similar. Steve Collins, who leads an Irish relief organization called Valid International, saw high recovery rates in Ethiopia, Malawi, and Sudan. MSF was sold on Plumpy'nut after it was able to treat as many as 60,000 children during a severe food crisis in Niger in 2005, says Shepherd—a vast improvement from the Angolan experience. In June of 2007, four United Nations agencies, including WHO and UNICEF, issued a joint statement advocating home treatment with RUTFs for severely malnourished children who don't have other illnesses.



As a result, demand and production have exploded. Nutriset is the biggest producer by far, making more than 15,000 tons in 2008. Although some are dismayed by Nutriset's patents on Plumpy'nut (see sidebar, p. 38), other companies are entering the market as well. In Malawi, Manary set up a Nutriset franchise that churns out 500 tons of Plumpy'nut a year. UNICEF, the biggest RUTF buyer in the world, may purchase as many as 8000 tons in 2008 and expects global production to grow to at least 50,000 tons by 2011.

Given that success, many were surprised when a series of major papers on malnutrition published in *The Lancet* earlier this year offered only lukewarm support for RUTFs. In a vociferous statement, MSF accused the authors of "undermining the support for this lifesaving intervention," which led to a rift with the journal (*Science*, 1 February, p. 555). WHO's Briend was dismayed as well. But the authors of the series have since said that they were misunderstood and that they do in fact support the use of RUTFs to treat severe malnutrition.

Daunting studies

Although there's consensus about treatment, prevention is a very different matter. MSF and some other nongovernmental organizations are now proposing giving peanut paste as a supplement to children who are moderately malnourished or just at risk of severe malnutrition. Every case of severe malnutrition starts as a milder one, says Shepherd—so why wait until a child is emaciated? "After 2005 we said, 'Hell, let's try to expand it.'"

Many alternatives haven't worked, experts agree. Severe malnutrition is the result of a downward spiral of poor-quality food, weak immunity, infections and diarrhea, loss of energy and appetite, and so on. Many approaches have been tried to stop that cycle: Children have been given an inexpensive, fortified blend of corn and soy flour, or tablets with specific micronutrients such as vitamin A or zinc. Mothers have been taught to breastfeed longer, cook better meals, or wash their hands to avoid infections. But nothing has really proven adequate.

Whether peanut pastes will do better is far from certain. When MSF's program started, only two studies had looked at their ability to prevent severe malnutrition, both by Manary's team in Malawi. They found that moderately malnourished children given RUTFs gained weight faster than those who received corn-soy flour, "but it wasn't a knockout," Manary says.

MSF was not deterred: The fact that it worked so well as a therapy was reason enough to believe it would work in prevention, too, says Shepherd. In 2006, MSF gave Plumpy'nut to all moderately malnourished children in its centers in one district, Guidan Roumdji. But simply identifying those children and supplying them with the peanut butter proved a huge logistical challenge; so in 2007, the agency decided to switch to mass distribution to all children between 6 and 36 months of age. Instead of Plumpy'nut, it used Plumpy'doz, a Nutriset product that comes in big jars. Mothers are supposed to give their children just three spoonfuls of Plumpy'doz per day; that way, children get only a quarter of the calories, but their intake of micronutrients stays about the same.

Nutrition science is difficult enough in Western countries; clinical trials to evaluate a food program in a country like Niger are an even bigger challenge, says Rebecca Freeman-Grais, a researcher at Epicentre, MSF's epidemiology division. The study population is hard to reach, and communication is difficult. Randomizing children to two different regimes within a village would have met with resistance, she says, so the

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Homemade. STA, in the Nigerien capital Niamey, is one of four Nutriset franchises that produce Plumpy'nut in the developing world.

PATENTS: A RECIPE FOR PROBLEMS?

NIAMEY, NIGER—A giant peanut roaster and grinder, a mixing and filling machine—it doesn't take all that much to produce the new ready-to-use therapeutic foods (RUTFs). A factory barely larger than a house in the quiet outskirts of Niger's capital produces some 500 tons of Plumpy'nut annually. But it can't do so on its own: The company, STA, is a franchise of Nutriset, a company in France that together with the French government owns the patent to Plumpy'nut and similar pastes.

As the market for RUTFs is booming, that situation has come under scrutiny. Aid organizations say there should be no patents on key humanitarian nutrition products, and some worry that Nutriset, a small family-run business, won't be able to meet the soaring demand. "That is absolutely becoming a problem," says Ellen 't Hoen of the Access to Medicine Campaign at Médecins Sans Frontières (MSF), one of Nutriset's main clients.

Most past inventions in humanitarian nutrition, such as a widely used fortified milk powder called F100, weren't patented; nor was oral rehydration therapy, a lifesaver for diarrhea patients. But Nutriset and the French Institute of Research for Development obtained patents for Plumpy'nut that last until 2018 and are valid in Europe, North America, and about 30 African countries. Nutriset has threatened lawsuits to keep others—including Compact in Norway and MSI in Germany—from selling similar pastes.

Nutriset's Adeline Lescanne says the company is rapidly boosting its own production capacity and at the same time taking the technology to the developing world, where it helps to stimulate the local economy. It has set up four franchises—in Niger, Malawi, Ethiopia, and the Dominican Republic—that have received equipment and training and now produce Plumpy'nut on a small scale. It has also signed a licensing deal that lets Valid International, an Irish charity, produce its own product under a different name.

MSF and UNICEF, another big buyer, acknowledge that so far there have been no shortages nor evidence of price gouging. Nor is the patent valid in many malnutrition hot spots, including India, where Compact is building a factory and several other companies are interested as well. Still, MSF and UNICEF don't like to be dependent on one major producer for delivering what is becoming an essential product to a large chunk of Africa. MSF says Nutriset and other companies entering the RUTF market should forgo patents—or at least be generous in cutting licensing deals.

It's unclear, meanwhile, whether the patent would withstand a challenge by a competitor. It covers not just Plumpy'nut but also, 't Hoen says, "pretty much any nut paste with milk powder, oil, and micronutrients." Other companies could market a similar product and see what happens in court if sued, she says—but neither Compact nor MSI have been willing to take that risk. Michael Golden, who formulated F100, believes the pressure should not be on Nutriset but on the French government; he hopes that France's foreign minister, Bernard Kouchner, a physician who helped found MSF in 1971, will intervene. **–M.E.**

researchers compared entire villages to which Plumpy'nut was given with others to which it was not—but of course, no two villages are exactly the same. MSF's decision to move to blanket distribution of Plumpy'doz interrupted the trial, which was supposed to last for 18 months, and forced the researchers to choose a different design that compared the two products. Other aid organizations distributed food in the area as well, introducing more possible confounders.

The data, which are now under review at *The Journal of the American Medical Association*, show that Plumpy'nut does lead to a substantial decrease in the incidence of severe malnutrition, says Philippe Guérin, Epicentre's medical director. But Plumpy'doz—although designed with prevention in mind—appears to be much less effective. That may be because children get fewer calories, but there may be other factors, says Guérin. A survey suggested that rather than giving a little bit every day, some mothers let their children eat it all early on. Plumpy'doz may also be more likely to be shared between the children in a household than the single-dose Plumpy'nut packages.

Epicentre's conclusion was not welcome news to MSF. MSF's Shepherd says it's important that the researchers analyze their data independently—but says she does not agree with Epicentre's analysis. Tectonidis, who believes Plumpy'doz works in prevention and has no faith in the Epicentre study, went further: In September 2007, while working at the MSF office in Rome, he visited the project in Niger and obtained a copy of the study's database. He then asked Golden, who was not previously involved in the study, to analyze it. Golden's unpublished manuscript says the Plumpy'doz intervention had a "dramatic effect." Guérin says he has not seen Golden's paper and declined to comment on it.

Is it practical?

Nutrition science aside, there are other questions. Even if Plumpy'nut or similar products work well for prevention, with their hefty price tag, are they the most cost-effective way? How long does the intervention go on, who pays for it, and doesn't it make a population dependent on foreign aid? "When you're going to tell the world what to do about hundreds of millions of children, it also has to work in practice," Manary says.

One solution may be to make peanut butters cheaper—for instance, by replacing all or part of the powdered milk, the most expensive ingredient, with soy. Perhaps that approach should be combined with very good infection control, says Manary. Many other ideas were on the agenda at a closed expert meeting at WHO headquarters this week, which participants said promised to be lively.

But for the moment, the debate is moot in the Guidan Roumdji district. In a spat unrelated to the scientific debate, the government of Niger accused MSF France of violating several rules and suspended all of its activities on 29 July. Negotiations are ongoing, but for now, both the treatment programs for severely malnourished children and the Plumpy'doz distribution to more than 80,000 children have come to an abrupt halt.

–MARTIN ENSERINK

CREDIT: M. ENSERINK/*SCIENCE*

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PLANETARY SCIENCE

Culture Wars Over How to Find an Ancient Niche for Life on Mars

Researchers seeking the next Mars rover landing site disagree about what makes for the most promising possibility: lots of water-altered minerals or familiar water-shaped terrain

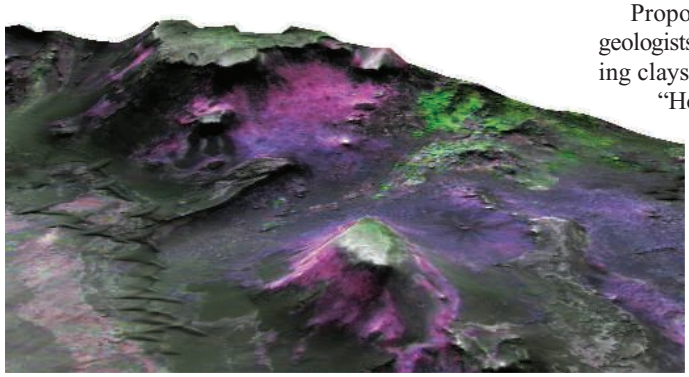
MONROVIA, CALIFORNIA—"This is not a contest," the workshop's organizers kept insisting, but it sure sounded like one. At the end of 3 days of sales pitches, cross examinations, and warm debate, more than 100 planetary scientists gathered* in a hotel ballroom here cast their ballots for the most scientifically inviting spot to send the $1.9 billion Mars Science Laboratory (MSL) in early 2010.

"Everyone wants to maximize the science," says planetary geologist James Rice of Arizona State University in Tempe. In deciding how to do that, most attendees aligned themselves with one of two parties. Spectroscopists, who find martian minerals from orbit by their distinctive spectral colors, tended to favor sites that beam strong spectral signatures of rock altered by water. Geologists, by contrast, preferred sites whose geological forms speak most eloquently of past water pooling on the surface.

Water is key because, as the official mission fact sheet puts it, NASA intends MSL to assess "whether the landing area ever had or still has environmental conditions favorable to microbial life." With that theme in mind, a lineup of paleontologists, geochemists, and geologists opened the workshop by explaining the most promising circumstances on ancient Earth for preserving evidence of habitability and traces of past life, such as river deltas that trap and preserve fossils and organic matter.

Then the wrangling began. Leading spectroscopists had proposed two of the seven landing sites still in the running (*Science*, 9 November 2007, p. 908) because the sites simply screamed "water!" to them. Jean-Pierre Bibring of the University of Paris, Orsay, is principal investigator of the OMEGA spectrometer onboard the Mars Express orbiter. To follow the water, he has argued, you should follow the clays. That's because clays form only after rock comes into prolonged contact with lots of water under mild conditions favorable for life. Microbes could draw energy and nutrients from the weathering rock, while the resulting clay would be ideal for preserving organic matter.

Bibring advocated landing on the highlands above Mawrth Vallis, a site blazing with the spectral colors of water-related minerals. Clays make up more than 50% of the surface there, Bibring reported—more abundant than anywhere else on Mars. The diversity of minerals—a half-dozen different clays plus a couple of other hydrated minerals—speaks of a changing environment as a layer cake of rock was altered. For similar reasons, John Mustard of Brown University and colleagues argued for landing in Nili Fossae, a great crack in the martian crust from which MSL could drive into a side canyon where many of the half-dozen aqueous minerals of the region outcrop.



Go for color. Near the proposed Nili Fossae landing site, erosion of 600-meter-high mesas reveals the spectral blue and magenta of much-sought clays.

CREDIT: NASA/JPL/JHU APL/UNIVERSITY OF ARIZONA/BROWN UNIVERSITY (B. EHLMANN, J. MUSTARD)

Geologists weren't sold on either Mawrth or Nili. The spectroscopists "argue that there's such [spectral] diversity, there must be something of interest there," says Horton Newsom of the University of New Mexico in Albuquerque, "but there's no geological evidence. It's essential to have both—a geological story with the spectra to back it up."

In the case of Mawrth, was the source of the clays sediment that washed into a lake? Was it volcanic ash that fell from the sky? Was it crustal rock altered by hot springs? "How is a story going to come out of this?" demanded geologist Linda Kah of the University of Tennessee, Knoxville. Figuring it out once the rover got there, as Bibring suggested, was too risky an option for geologists still smarting from having landed the Spirit rover on an apparent lakebed that turned out to be a barren lava plain.

To avoid disappointment next time, many geologists favored landing in 67-kilometer-wide Eberswalde Crater. "It's the natural place to go," says Rice, who led the pitch for the crater site. "It's the best delta on Mars," meaning a river must have flowed into a lake in Eberswalde, dropping its load of sediment on entering the still water. Several different clays appear in the beautifully layered delta deposits exposed by wind erosion. Eberswalde "would make it a lot of fun," said Kah. Other favorites of geologists were Holden Crater, another likely crater lake with layered, clay-bearing deposits but no true delta, and Gale Crater, whose 5-kilometer-high mound of layered deposits boasts a variety of water-related minerals, although the origin of the mound is uncertain.

Proponents of Nili and Mawrth took the geologists' point about the advantages of studying clays laid down in quiet standing water. "Holden is a very interesting site," says Mustard, but there are shortcomings. Gale Mound lacks a single strong geological story, he notes, and Eberswalde could prove to be a "one-trick pony" if organic matter doesn't turn up there.

After 2.5 days of consideration, more than 100 attendees voted on how mineralogically and geologically diverse each site is, how good a geologic story each is telling, how good the prospects for habitability are, and how good the chances for preservation are. Two sites that had neither a strong geological story nor good spectral diversity—Miyamoto Crater and southern Meridiani—came in dead last. Nili and Mawrth did considerably better but still trailed the three craters with layered deposits, Eberswalde leading them all.

The outcome didn't surprise Mustard. Nili, at least, "kind of scares people," he says. "It's hard to fit into a geological scenario." But it's not over for Nili or Mawrth. Mission managers together with a landing-site steering committee will decide within a month or so which three sites will receive further study. Engineering considerations—such as too much cold at far-southern Holden and Eberswalde—might clear the way for a brightly colored site. Then another open workshop next spring will recommend a single site.

–RICHARD A. KERR

*Third MSL Landing Site Workshop, 15–17 September, sponsored by the NASA-appointed Mars Landing Site Steering Committee and the MSL Project.

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PROFILE: EDWARD BUCKLER

Romping Through Maize Diversity

A computer whiz turned geneticist borrows tactics from Wal-Mart and cattle breeders to manage what may be the world's largest genetic analysis

ITHACA, NEW YORK—On a steamy July morning, Edward Buckler and a crew of technicians, graduate students, postdocs, and a visiting professor from Mexico have fanned out among the 2-meter stalks in a large field of corn here. Bar-code readers in hand, they snip, stretch, or poke individual plants in order to track dozens of traits important to the crop's growth and vitality. Each week, they record the height of every stalk; in early summer, they counted leaves, assessed surface "hairiness," and took small samples of tissue to freeze-dry and send to Germany.

Welcome to the Nested Association Mapping (NAM) project, arguably the world's largest controlled genetic study. It encompasses more than 1000 genetic markers in each of 5000 lines of maize in an effort to elucidate the relationship between genes and physical traits in plants. "It's basically the maize analog of the human HapMap Project, but it is much more powerful and cost-effective," says population geneticist Magnus Nordborg of the University of Southern California in Los Angeles.

Buckler, the 38-year-old plant geneticist running the show, doesn't believe in thinking small. If he gets his way, plane flights will one day monitor tens of thousands of plants daily. "I'd like to know what goes on every hour of every day," says Buckler, a U.S. Department of Agriculture (USDA) researcher based at Cornell University here.

Buckler has capitalized on his combination of computer and biology expertise to develop methods to find genes faster. He and his colleagues have also used existing maize variants to boost the vitamin A content of corn. "Ed seems equally at home in the field pollinating maize as in the lab or developing software or doing theory," says plant geneticist J. Antoni Rafalski of E. I. du Pont de Nemours & Co. (Inc.) in Wilmington, Delaware. Adds James Holland of USDA at North Carolina State University (NCSU) in Raleigh, "He has single-handedly influenced the plant genetics community to a remarkable extent."

The goal of the massive NAM study is two-pronged. Maize is the number-one crop produced around the world, and NAM will help breeders to exploit its natural variation to improve yields and nutritional value. In addition, Buckler expects to answer a fundamental question: Do a few genes underlie each complex trait, or is there a bewildering array, with each having a minor influence? The answer will not only help plant breeders, but it may also aid biomedical researchers trying to understand the genetics of diabetes, heart disease, and other disorders. "I expect we will learn a lot about quantitative genetics from the maize work, and this will, of course, help us to understand human variation as well," says Nordborg.

So far, its looks like more than a few genes control most traits. That realization will complicate attempts to pin down the genetic basis of disease. But with maize, even a 1% improvement in yield translates into millions more tons of food for people and animals, so genes of small effect can make a significant difference. Thanks in large part to Buckler's efforts, "people have changed their thinking, and companies are much more focused on natural diversity" as opposed to adding new genes to improve crops, says USDA plant geneticist Michael McMullen of the University of Missouri, Columbia.

Ed Buckler

CREDIT: E. PENNISI/*SCIENCE*

Genetics by second nature

Growing up in Arlington, Virginia, Buckler had unlimited access to a personal computer, on which he designed his own games. To him, genetics is basically life's equivalent of computer programming. "There are not many rules: You get to recombine and to mutate, but you can make incredibly complex things." Buckler laughs, giving his boyish smile: "And it's more rewarding to do genetics than programming."

After high school, he left for the University of Virginia, Charlottesville. He studied early American cultures and became both fascinated with the domestication of maize and appalled at how inefficient agriculture was. "I decided that if I wanted to do something worthwhile, plant genetics was the way to go," he says. With a Ph.D. from the University of Missouri, Columbia, and postdoc experience in statistical genetics at NCSU, Buckler joined USDA in 1998 to work on the Maize Diversity Project, part of the Plant Genome Initiative (*Science*, 23 October 1998, p. 652). Now poised for its second renewal, the project has morphed over time from an emphasis on genome evolution to a massive effort to conquer the genetics of complex traits, with NAM as a key component.

As the Maize Diversity Project matured, Buckler and his colleagues came up with a more efficient way to find genes that influence traits. Researchers typically take two approaches to this task. In one, linkage analysis, they use families—which in corn means plants that can be traced back to the same set of parents. The other approach, association studies, relies on unrelated individuals, be they corn seedlings or people. "What we've been doing is blending the lines between the two" approaches, Buckler explains.

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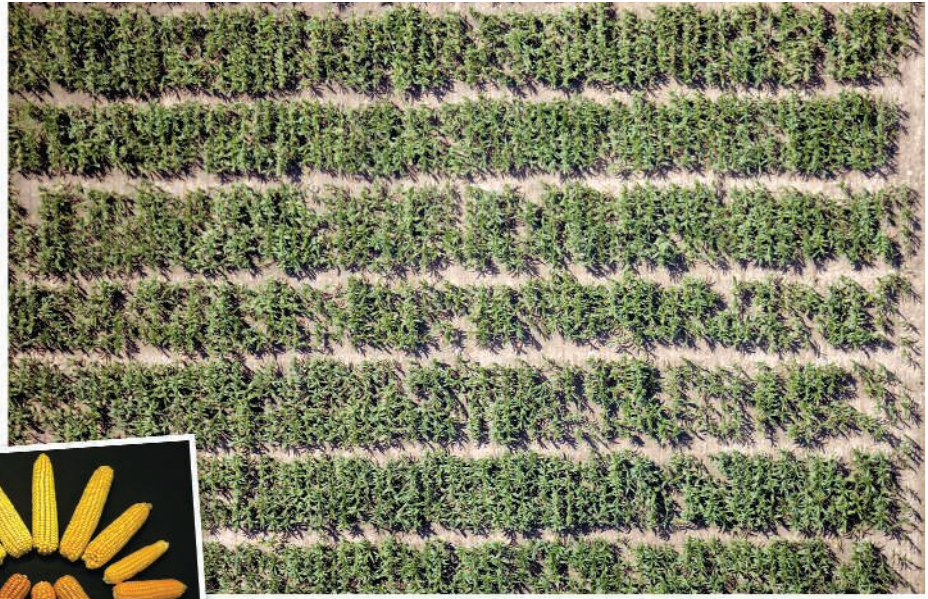

Maize maze. This experimental cornfield in upstate New York will help researchers pin down the genetic basis of traits such as kernel color (*inset*).

CREDIT: JON REIS; INSET: TORBERT ROCHEFORD AND CATHERINE BERMUDEZ KANDIANIS

In association studies, researchers often look for gene variants that co-occur with a trait, such as golden rather than yellow kernels. But many of the variants they find are false positives, for example, having no effect on kernel color at all. The number of such false positives can be influenced by kinship among individuals and by evolutionary history. For example, when two populations are isolated from each other, their genomes can diverge in such a way that a particular variant might seem to be associated with kernel color, even though it isn't. "That's really a complicated and difficult problem," says John Doebley, a plant geneticist at the University of Wisconsin, Madison. Likewise, when two individual plants are closely related, their kinship can skew any associations detected.

With Jianming Yu, now at Kansas State University in Manhattan, Buckler has found ways to incorporate both history and kinship into his analyses, eliminating many false associations. For example, to take account of how closely individual plants are related, Yu, Buckler, and their colleagues used genetic markers to assess kinship, then borrowed mathematical tricks used by cattle breeders to analyze giant pedigree matrices. The resulting "unified mixed model" method greatly reduced the number of false positives, they reported in the February 2006 issue of *Nature Genetics*. Buckler estimates, for example, that about 9 million DNA variants, or SNPS, would show up as linked to flowering time using the old approach. The new method narrows that to only a few thousand.

The method has also yielded natural gene variants that enrich maize in vitamin A. Buckler, Torbert Rocheford of the University of Illinois, Urbana-Champaign, and their colleagues measured the amount of the vitamin in hundreds of lines of corn that vary in kernel color—the more orange, the more vitamin A. Using association studies, they pinned down the gene variants responsible for producing more vitamin A precursors (*Science*, 18 January, p. 330). Without this method, "we would have had a lot more junk to deal with," says Buckler. Now researchers with HarvestPlus for Africa and elsewhere are using Buckler's genetic markers to breed those variants into maize varieties, thus boosting vitamin A without introducing foreign genes.

Bigger is better

Once Buckler started doing association studies, he hungered to make them more powerful. For NAM, he and his colleagues picked 25 unrelated "parent" lines of maize, including popcorn, sweet corn, tropical and temperate varieties, plus long-used commercial strains, representing the full range of diversity in this species. Buckler, Cornell colleague Stephen Kresovich, Holland, and, later, McMullen bred each line with the much-studied (and now draft-sequenced) B73 maize. From each "parent," they created a "family" of 200 new lines, for a total of 5000 lines. Thus this single study includes "families" available for linkage analysis, as well as a large, diverse population of 5000 lines for association studies. The next biggest genetic study involves mice, uses just eight strains, and has the ultimate goal of creating 1000 new strains (*Science*, 25 July 2003, p. 456).

NAM also presented an enormous data-crunching challenge. At the time, "it was not obvious to me how gene-phenotype association information could be jointly analyzed across the 25 cross-populations," Holland recalls. "Ed conceived of the analysis that would efficiently achieve that." Nor was Buckler daunted by the challenge of generating thousands of new maize lines and recording how individual plants grew. His response to his colleagues' concerns: Borrow methods from an operation that daily tracks tens of thousands of items—Wal-Mart. He outfitted his team with the same portable bar-code scanners that Wal-Mart uses for taking inventory and had them tag each plant.

Now that the hard work is done, anyone can grow out the seeds of the NAM lines or traipse through the project's fields to measure variation in their favorite trait, such as starch content. Then, using the project's analytical tools, they can home in on the genes affecting that trait.

Buckler calls the NAM project a "field of dreams," and, as in the movie of the same name, it's attracting attention and copycats. Dozens of private and academic researchers have ordered NAM seeds from USDA to start their own fields. Cornell's Rebecca Nelson and graduate student Jesse Poland are assessing the genetic basis of disease resistance in a NAM field next to Buckler's. Says Poland: "It's an incredible resource."

Yet even in the dream fields, pinning down genes will not be easy. "Association mapping is not without its problems," says Rafalski. Human geneticists have millions of markers to help navigate the human genome, and they still struggle to find gene variants connected to disease; maize researchers have only about 1100 markers. And picking out which associated variants are the most promising is always a challenge, he adds.

However, Buckler is still thinking big. He has $1 million from the U.S. National Science Foundation to partially sequence each parent NAM maize strain, which will yield many more markers. He has also set his sights beyond cornfields: He wants to apply genomics to USDA's vast archive of germ plasm—seeds and other tissues from all plants. Breeders can order any of some 600,000 crop varieties from USDA, but it's often hard to know which varieties will improve a crop the most. To begin to find out, Buckler is starting with the grape germ plasm on file, assessing 10,000 SNPs and, to a limited extent, their association to relevant traits. He's hopeful money will come through next year to assess the SNPs in the entire USDA collection. "That Ed is an idea person is as much of an understatement as you can say," says McMullen. "He's always proposing new ideas, and even before we can do the experiment, [the project] will be bigger."

–ELIZABETH PENNISI

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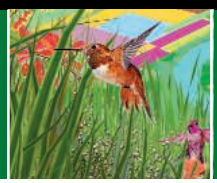

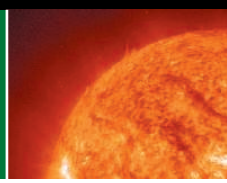

LETTERS

edited by Jennifer Sills

Keeping an Eye on the Prize

I WAS VERY DISAPPOINTED TO FIND OUT ("Fame inflation," Newsmakers, 1 February, p. 553) that I, like Steven Running, am not a Nobel laureate. According to the "Dear colleagues" letter I received from Ogunlade Davidson and Bert Metz on behalf of the IPCC, I am indeed a Nobel laureate, albeit perhaps along with many, many others. The letter says, "You no doubt have heard about the award of the Nobel Peace Prize to the IPCC, jointly with Al Gore of the USA. This makes all of you a Nobel laureate and we, as co-chairs, want to congratulate you wholeheartedly with this exceptional recognition." Additionally, a beautiful Nobel Peace Prize certificate with my name on it now adorns my wall. Although the financial remuneration has not yet arrived, I have enjoyed the celebrity status associated with the honor. **ROGER A. SEDJO**

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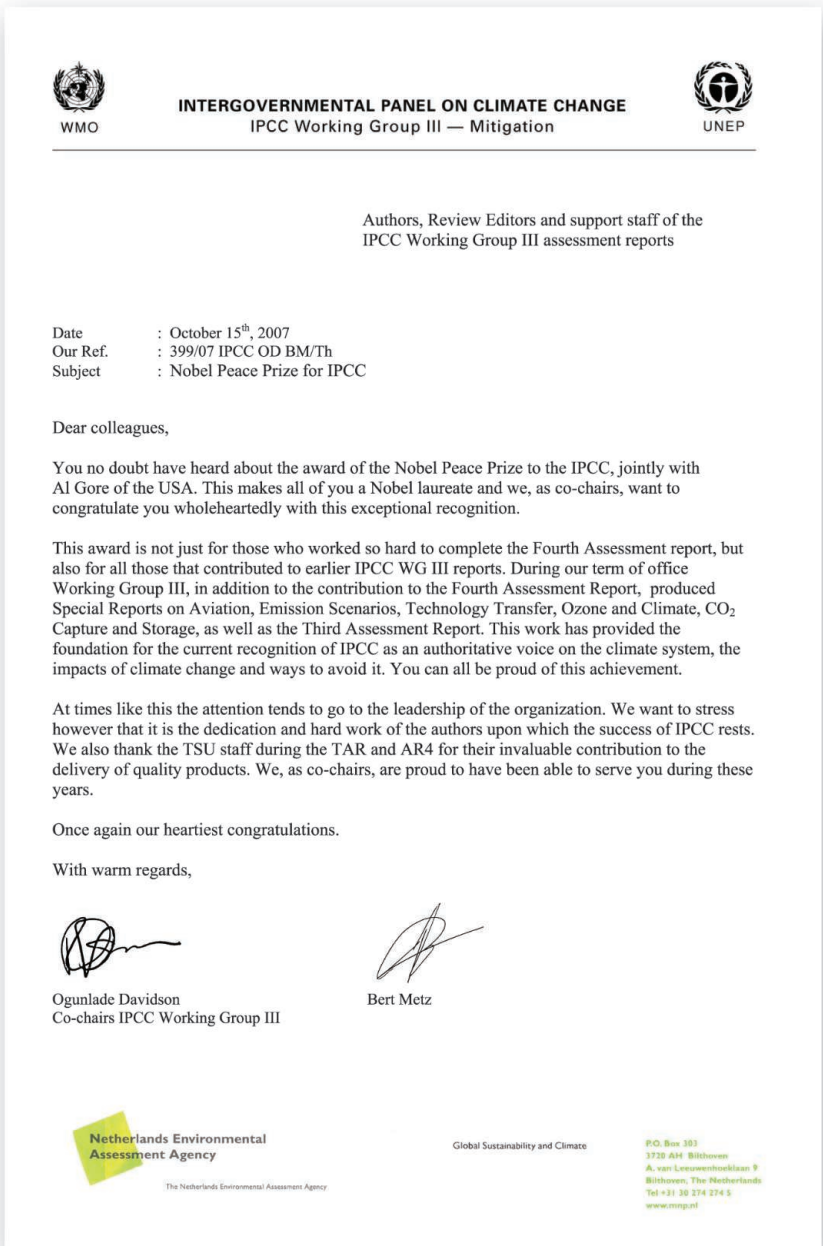

WMO

INTERGOVERNMENTAL PANEL ON CLIMATE CHANGE
IPCC Working Group III — Mitigation

UNEP

Authors, Review Editors and support staff of the
IPCC Working Group III assessment reports

Date : October 15th, 2007
Our Ref. : 399/07 IPCC OD BM/Th
Subject : Nobel Peace Prize for IPCC

Dear colleagues,

You no doubt have heard about the award of the Nobel Peace Prize to the IPCC, jointly with Al Gore of the USA. This makes all of you a Nobel laureate and we, as co-chairs, want to congratulate you wholeheartedly with this exceptional recognition.

This award is not just for those who worked so hard to complete the Fourth Assessment report, but also for all those that contributed to earlier IPCC WG III reports. During our term of office Working Group III, in addition to the contribution to the Fourth Assessment Report, produced Special Reports on Aviation, Emission Scenarios, Technology Transfer, Ozone and Climate, CO_2 Capture and Storage, as well as the Third Assessment Report. This work has provided the foundation for the current recognition of IPCC as an authoritative voice on the climate system, the impacts of climate change and ways to avoid it. You can all be proud of this achievement.

At times like this the attention tends to go to the leadership of the organization. We want to stress however that it is the dedication and hard work of the authors upon which the success of IPCC rests. We also thank the TSU staff during the TAR and AR4 for their invaluable contribution to the delivery of quality products. We, as co-chairs, are proud to have been able to serve you during these years.

Once again our heartiest congratulations.

With warm regards,

Ogunlade Davidson
Co-chairs IPCC Working Group III

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Epigenomics: A Roadmap, But to Where?

RECENTLY, THE DIRECTOR OF THE NATIONAL Institutes of Health (NIH) allocated $190 million for an "Epigenomics" Roadmap initiative (*1*). As investigators in this area, we endorse the idea that chromatin biology is an appropriate, if not essential, area for the NIH to support, not only for its fundamental biological significance but also its relevance to human disease. Nonetheless, we believe that this initiative, at least in its current form, will not yield significant benefits. If the use of the term "epigenome" is intended to equate the value of this Roadmap initiative with the Human Genome Project, it fails on several grounds.

First, it does not consider our current understanding of the roles of sequence-specific DNA recognition events and transcriptional networks in controlling epigenetic changes. A multifaceted effort that elucidates transcriptional circuits that tell us where and when signal-responsive, sequence-specific regulators function would be more useful for understanding cell type programming. Second, merely cataloging modification patterns offers comparatively little new or useful information. We already know that most genes are associated with one of a few patterns of chromatin modifications and that the patterns themselves do not tell us how that gene is regulated or how its expression state is inher-

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ited. Most histone modifications are highly dynamic and change rapidly in response to changes in signals that turn genes on or off.

This initiative will divert substantial resources, enough to fund 200 multiyear individual grants. There is a notion favored by some that individual scientists need to be corralled to work together under a more rigid, directed framework to solve important problems. We disagree. Real innovation comes from the bottom up, and good science policy requires promoting the free market of ideas rather than central planning (*2*).

HITEN D. MADHANI,[1]* NICOLE J. FRANCIS,[2] ROBERT E. KINGSTON,[3] ROGER D. KORNBERG,[4] DANESH MOAZED,[5] GEETA J. NARLIKAR,[1] BARBARA PANNING,[1] KEVIN STRUHL[6]

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References and Notes

1. NIH Roadmap for Medical Research (http://nihroadmap.nih.gov/epigenomics/).
2. Links to a full version of this letter and petition for readers to sign can be found at http://madhanilab.ucsf.edu/epigenomics/.

Protecting Aggregate Genomic Data

A PAPER PUBLISHED RECENTLY IN *PLOS Genetics* (*1*) describes a statistical method for resolving individual genotypes within a mix of DNA samples or data sets containing aggregate single-nucleotide polymorphism data. This scientific advance may have important implications for forensics and for genome-wide association studies (GWAS). It has also changed our understanding of the risks of making aggregate genomic data publicly available. While we assess the broader scientific, ethical, and policy implications of this development, NIH has moved swiftly to remove aggregate genomic data from our publicly available Web sites. Further information about changes in NIH open-access policies for GWAS is available on the NIH's GWAS Web site (*2*).

The paper by Homer *et al*. showed that a new statistical technique applied to aggregate data can determine whether a specific individual's genomic data are part of a given data set, including whether they are in the control group or the case (affected) group. It may also be possible to statistically infer whether a relative of the individual is a member of the case or control groups. The method requires having an individual's high-density genotype data in hand from another source. Though the specific identity of the individual who was the source of the data could only be determined if that source were known through other means or reference data, this discovery nonetheless has implications for how these summary data should be protected. As a result, NIH has removed from open-access databases the aggregate results (including *P* values and genotype counts) for all the GWAS that had been available on NIH sites (such as dbGaP and CGEMS). NIH intends to move the aggregate genotype data to the controlled-access database, where there is a firewall as well as protections and policies in place for appropriate data access, including review and approval of data access requests. The new finding does not have the same implications for data available through controlled access, and NIH access policies for individual-level genotype and phenotype data have not changed.

Sharing genomic data and, particularly, allele frequencies has become common practice, if not an imperative, in science. Yet, the protection of participant privacy and the confidentiality of their data are of paramount importance. These new statistical approaches have implications far beyond NIH data-sharing policies, as aggregate GWAS data have been provided in publicly available form in many other ways, including other research databases and Web sites, journal articles and other publications, and scientific presentations. NIH urges the scientific community to consider carefully how these data are shared and take appropriate precautions to secure aggregate GWAS data in order to protect participant privacy and data confidentiality.

In short order and over the coming months, NIH will work with our advisory groups and the wide range of stakeholders related to GWAS to further explore and address the policy implications of this finding. We call on our colleagues in the scientific community to join us in these important deliberations.

ELIAS A. ZERHOUNI[1] AND ELIZABETH G. NABEL[2]

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Closing a Loophole in the FDA Amendments Act

IN THEIR POLICY FORUM "MOVING TOWARD transparency of clinical trials" (7 March, p. 1340), D. A. Zarin and T. Tse caution that "FDAAA 801 still leaves areas of 'opacity.'" We would like to point out another loophole: FDAAA 801 will only cover future drugs. The thousands of drugs on the market today, including the controversial examples cited by Zarin and Tse, will be grandfathered in and not covered.

Whether this matters to public health depends on whether today's uncovered drugs will soon become obsolete. To address this

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 3 months or issues of general interest. They can be submitted through the Web (www.submit2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

CORRECTIONS AND CLARIFICATIONS

Reports: "Cell identity mediates the response of *Arabidopsis* roots to abiotic stress" by J. R. Dinneny *et al*. (16 May, p. 942). On page 945, the URL for the supporting online material was incorrect. The correct URL is www.sciencemag.org/cgi/content/full/1153795/DC1.

Books *et al*.: "The social origin of mind" by A. Jolly (7 September 2007, page 1326). The caption to the photograph should have read "Chacma baboons (*Papio hamadryas ursinus*) in the Okavango Delta, Botswana."

Reports: "The FERONIA receptor-like kinase mediates male-female interactions during pollen tube reception" by J.-M. Escobar-Restrepo *et al.* (3 August 2007, p. 656). On page 657, second column, second paragraph, the sentence "The *FER* open reading frame contains a single 175-bp intron in the 5′ untranslated region and produces a transcript of 2682 bp, which encodes a putative receptor-like serine-threonine kinase (RLK) (Fig. 1F)" contains two errors. It should read, "The FER primary transcript contains a single 175-bp intron in the 5′ untranslated region and produces an open reading frame of 2682 bp, which encodes a putative receptor-like serine-threonine kinase (RLK) (Fig. 1F)."

Reports: "Virus-enabled synthesis and assembly of nanowires for lithium ion battery electrodes" by K. T. Nam *et al*. (12 May 2006, p. 885). Reference 28 should be D. Guy, B. Lestriez, D. Guyomard, *Adv. Mater*. **16**, 553 (2004).

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question, we examined prescribing trends over the past 8 years for three drug classes cited by Zarin and Tse. From listings of the top 200 drugs (*1*) for the years 2000 through 2007, we extracted the numbers of prescriptions dispensed in U.S. retail pharmacies. Within these three drug classes, we totaled the annual number of prescriptions of brand and generic drugs that had been first marketed in the United States within the past 20 years.

We found that oral drugs for diabetes, including Avandia (*2*, *3*), are (as of 2007) being prescribed 265,000 times each day; their prescribing rate has been increasing 8% annually. Cholesterol-lowering drugs, including Zetia (*4*) and Baycol (*5*), are now being prescribed 528,000 times each day; this rate has been increasing 10% annually. Finally, antidepressants (*6*) are being prescribed 673,000 times each day; this rate has been increasing 22% annually.

These data indicate, in our opinion, that these drugs—none of which will be covered by FDAAA 801—are widely prescribed and unlikely to disappear soon from the U.S. market. It is unfortunate that FDAAA 801 grandfathers in currently marketed drugs. While this act provides for a registry and results database that is prospective, we need one that is also retrospective. Such a database has in fact existed for decades at the FDA (*7*). If we can make better use of it, a solution to this area of "opacity" lies readily within our grasp.

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Response

TURNER AND COLLEAGUES ARE CORRECT THAT the "basic results" provisions of Section 801 of the FDA Amendments Act (FDAAA 801) will not apply to trials that were completed prior to 27 September 2007. Thus, the body of data that was used to support approval for products currently on the market will not necessarily be made public under this provision. As all of the top 20 brand drugs by total U.S. prescriptions in 2007 (*1*) were approved prior to 2005, based on Initial Year of Original FDA Approval data listed in Drugs@FDA (*2*), it is readily apparent that much of the data underlying current medical decisions are unlikely to be submitted to ClinicalTrials.gov. The scope of the law is determined by the timing of the trial, however, not the date of approval of the drug; therefore, non–phase I trials of these approved products initiated after or ongoing as of late 2007 would meet the time criterion for applicability under FDAAA 801 and be required to report results.

Turner calls for public access to FDA reviews contained in all approved NDAs (*3*). In addition to this possibility, FDAAA 801

includes a provision whereby the Secretary of Health and Human Services may require registration and results reporting for certain clinical trials of FDA-approved drugs, biologics, and devices retrospectively to protect public health (trials completed up to 10 years prior to enactment of the act, i.e., September 27, 1997). Finally, FDAAA 801 explicitly provides for consideration, during the 3-year rule-making process, of mandatory results reporting from certain clinical trials of drugs, biologics, and devices not approved by the FDA. Such a policy would substantially broaden the evidence base available to the public.

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Big Payoffs Possible for Small-Molecule Screening

IN THE NEWS FOCUS "INDUSTRIAL-STYLE screening meets academic biology" (8 August, p. 764), J. Kaiser presents the discovery of several potential small-molecule therapeutics and probes for cellular function along with skeptical views from industrial scientists questioning "whether this massive effort is worth the time and money." The goals of the pharmaceutical industry and academia are very different. Industry scientists are focused on discovering a highly specific and potent compound that can benefit human health. Academic scientists focus on finding compounds that can reveal novel cellular mechanisms, a basic tenet in chemical biology (*1*). It is this pursuit that allows the academician to foster student learning and interdisciplinary collaborations with faculty that could lead to a novel biological probe or a potential therapeutic. The current $100 million-per-year funding from the NIH Molecular Libraries Initiative (MLI) is a wise investment in the training of future scientists and teachers. Students working with faculty mentors on these screening efforts learn how to solve problems across all areas of science and mathematics; indeed, the "challenge of merging two cultures—biologists and chemists" is an opportunity for a better education (*2*). Such an interdisciplinary approach to science education is timely, given the recently passed Public Law 110-69, "America Competes Act," which includes appropriation of $896 million for "education and human resources" (*3*) that will promote the training of future science and mathematics teachers. Regardless of the skepticism, I believe that the NIH MLI could "pay it forward" to our society in many ways.

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3. Public Law 110-69 (H.R. 2272), sec. 7002, fiscal year 2008.

EVOLUTION

A Challenge Standing on Shaky Clay

Michael Ruse

There were a number of ironies about the 2005 trial in Dover, Pennsylvania, in which a judge ruled that the local school board should not insist on the introduction of so-called intelligent design theory (IDT) into the curricula of state-supported biology classes. Most obvious was the fact that the judge who made the ruling was appointed by none other than President George W. Bush. Others included that both sides used philosophers as expert witnesses and that two scholars involved—against IDT, Robert Pennock of Michigan State University, and for IDT, Steve Fuller of the University of Warwick in England—were graduates of the same program at the University of Pittsburgh and their time there had even overlapped. Fuller has already written an account of the trial (*1*), and now in *Dissent over Descent* he gives his background thinking about the issues.

One certainly cannot critique Fuller for being less than forthright in his feelings and judgments. Early on we learn of the "deep and largely pernicious influence" of Thomas Kuhn's thinking on the general public and on some scientists. Then we are told how out of touch with the general scientific community are the London Royal Society and the American National Academy of Sciences, with the implication that their opposition to IDT should count for little. Charles Darwin, it appears, were he living today, would be in favor of IDT. The well-known geneticist (and former president of AAAS) Francisco Ayala is a Catholic, theistic evolutionist. Fuller holds that Richard Dawkins "arguably owes more to 18th-century secular theodicy than to Darwin's own 19th-century anti-theodicy." Thus it is not surprising to find him insisting a "literal reading of the Bible has done more to help than hurt science over the centuries."

I sense that these outrageous obiter dicta are intentional. The average reader, especially the average science reader, will be so incensed that he or she will fail to spot the underlying argument that Fuller wants to make. Fuller will get away with things by default. However, I too am a philosopher and, although not a Pittsburgh graduate, I know the tricks of the trade. More amused than cross, let me go to the heart of Fuller's case against Darwinian evolutionary theory and for IDT—for his is as much a negative critique of the opposition as a positive defense of his own beliefs. Fuller feels that Charles Darwin failed to make the case for his mechanism of natural selection. Darwin did not give a cause for evolution. He certainly did not unify the field. At most he gave lists of facts. Moreover, today if we feel that advance has been made, it is primarily in the molecular field, and this owes little or nothing to traditional evolutionary thought. At best Darwinism is a kind of tarted-up natural theology and, this being so, why not IDT?

Dissent over Descent
Intelligent Design's Challenge to Darwinism
by Steve Fuller
Icon Books, Cambridge, 2008. 278 pp. £12.99, C$26. ISBN 9781840468045.

CREDIT: JOE SUTLIFF

The important thing is that all of this is completely wrong and is backed by no sound scholarship whatsoever. In at least one case, Fuller makes his case by an egregious misreading—of something I wrote about the role of genetic drift in Sewall Wright's shifting balance theory (*2*). For the record, Charles Darwin set out to provide a cause, what he called—following his mentors like William Whewell (who in turn referred back to Newton)—a true cause or *vera causa*. Darwin felt, and historians and philosophers of science as well as practicing evolutionary biologists still feel, that he succeeded, for two reasons. First, he showed how organisms can be changed by human picking or selecting. Although Fuller repeatedly claims that Darwin intended no analogy here, that is simply not true. In the face of virtually everybody—including Alfred Russel Wallace, who (in the manuscript he sent to Darwin in 1858) explicitly denied a link between artificial and natural selection (*3*)—Darwin insisted that we can gain confidence about selection in nature from what happens when humans are active. Second, Darwin brought everything together in a "consilience of inductions." He argued that if you take selection as the causal mechanism, then you can explain instinct, the fossil record, geographical distributions of organisms, anatomy, systematics, and embryology. In turn, the success of these explanations feeds back to support the belief in selection. About as unifying a setup as it is possible to imagine.

One can go on to look at things today. It is ludicrous to claim that modern evolutionary biology is not integrated with molecular biology. Motoo Kimura's neutral theory (*4*) depends crucially on the claim that selection has little or no effect on processes down at the molecular level. Genetic fingerprinting has proved absolutely vital for observational and experimental studies of evolution. Someone like British ornithologist Nicholas Davies, working out the relationships among individual dunnocks (*Prunella modularis*) (*5*), would have been powerless without the technique. And in evolutionary developmental biology (evo-devo), currently the hottest area of evolutionary research (*6*), how does one speak of genetic homologies between fruitflies and humans without talking about molecules?

At Dover, the author supported the wrong side. Intelligent design theory is a form of Christianity made up to look like science. The judge correctly ruled that it has no place in science classrooms. Reading *Dissent over Descent* should not change anyone's verdict. As a historian and philosopher of science, I can only hope that the science community does not judge us all by Fuller's example.

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10.1126/science.1164798

PHYSICS

Some Science for Today's Electorate

Kenneth R. Foster

In *Physics for Future Presidents*, Richard Muller, a physics professor at the University of California, Berkeley, comments on the science that constrains potential solutions to a variety of issues: energy, terrorism, nuclear power, space exploration, global warming. The fine book is not a policy manual for candidates in the current U.S. election but rather a popularized version of Muller's science-and-society course for non–science majors (*1*).

Through his clear and entertaining text, Muller presents essentially quantitative arguments to nontechnical readers in simple and graphic ways. The level of writing roughly compares to that of the science coverage in major U.S. newspapers. Muller uses only elementary physics concepts, which he carefully explains to his readers.

Physics for Future Presidents
The Science Behind the Headlines
by Richard A. Muller
Norton, New York, 2008. 380 pp. $26.95, C$29.50, £15.99, €21. ISBN 9780393066272.

The author notes, for example, that the cost of energy varies tremendously depending on source, from less than one U.S. cent per kilowatt hour in generation costs from burning coal to $1000 per kilowatt hour for energy drawn from disposable AAA batteries. Owners of hybrid automobiles, he cautions, should not be too smug about the money they are saving in gasoline until they consider the costs of the inevitable replacement of the batteries in their car.

He explains that the low cost of generating electricity from coal and the plentiful supplies of this fuel are important factors in the issue of global climate change: "Coal produces more carbon dioxide per kilowatt-hour of energy than virtually any other source." But China builds an average of over 1 gigawatt of coal-fired generating capacity every week and has enough coal "to meet the worst scenarios of the global-warming models."

Muller offers readers "physics by total immersion" and stays "away from issues in politics, business, and diplomacy." But he often reaches beyond technical facts and sometimes expresses views that, undoubtedly, are widely shared by the scientific community even if he does not argue them out very carefully.

For example, Muller views alternative energy sources such as fusion and solar power, as well as recycling, hydrogen as fuel, and the Kyoto Protocol, as "nonsolutions" to the problem of global warming. He says that the low-hanging fruit lies in conservation.

Carrying a current. Muller performs an electrical demonstration for his students.

As another example, Muller is skeptical about the value of putting humans in space. He writes that the space shuttle "is the dream of man in space. … But it is not safe, it cannot be made safe, and it is not done for science." In his view, although space offers an excellent platform for some things—spying, gathering weather imagery, global positioning, satellite communications, and important scientific endeavors (such as the Hubble Space Telescope)—"these are best done with robotics." Muller recommends reducing the priority given to putting humans in space and making "science truly the primary [goal] of the government science program."

Many readers will be confused by Muller's chapters on climate change, in which he takes on former Vice President Al Gore and his 2006 film *An Inconvenient Truth* (*2*). Muller gives Gore credit for alerting the public to the dangers of carbon dioxide and global warming, a problem that Muller acknowledges is real and serious. But he complains that Gore accomplished this "through a combination of artistry, powerful writing, and exaggeration, mixed with some degree of distortion and a large amount of cherry picking" (i.e., selective quotation of data).

Muller discusses the famous comparison of plots of the variations in atmospheric carbon dioxide and in global temperatures over the past 600,000 years. Gore used the close tracking of the two graphs to bolster the claim that carbon dioxide drives global temperature. Muller claims that many climate scientists think the increases in atmospheric carbon dioxide are the result of increasing global temperatures, not the other way around. He cautions that when the public finds out "Gore has exaggerated the case, [it] may reject the truly scientific case for fossil fuel–induced global warming" and "throw out the baby with the dirty bathwater."

Muller himself may be guilty of a biased presentation here. Although for most of the past 600,000 years the global temperature increases preceded rises in atmospheric carbon dioxide, in modern times the order of the changes has reversed. Gore's presentation has been praised by climate change experts for its "striking clarity" (*3*). A more balanced discussion might have noted some of the other, worse distortions we have seen in the climate change debates. And if Gore has exaggerated or selectively represented data to further an agenda, that is a common problem in public life that cannot be remedied by a book such as Muller's.

Despite this mild caveat, *Physics for Future Presidents* is an outstanding example of public communication of science, and it would be a great holiday present even for people who might not end up in the White House.

The reviewer is in the Department of Bioengineering, University of Pennsylvania, Philadelphia, PA 19104–6392, USA. E-mail: kfoster@seas.upenn.edu

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10.1126/science.1165024

AGRICULTURE

Sustainable Biofuels Redux

Science-based policy is essential for guiding an environmentally sustainable approach to cellulosic biofuels.

G. Philip Robertson,[1*] Virginia H. Dale,[2] Otto C. Doering,[3] Steven P. Hamburg,[4] Jerry M. Melillo,[5] Michele M. Wander,[6] William J. Parton,[7] Paul R. Adler,[8] Jacob N. Barney,[9] Richard M. Cruse,[10] Clifford S. Duke,[11] Philip M. Fearnside,[12] Ronald F. Follett,[13] Holly K. Gibbs,[14] Jose Goldemberg,[15] David J. Mladenoff,[16] Dennis Ojima,[17] Michael W. Palmer,[18] Andrew Sharpley,[19] Linda Wallace,[20] Kathleen C. Weathers,[21] John A. Wiens,[22] Wallace W. Wilhelm[23]

CREDIT: ERIK SANDBERG/BERNSTEIN & ANDRIULLI

Last May's passage of the 2008 Farm Bill raises the stakes for biofuel sustainability: A substantial subsidy for the production of cellulosic ethanol starts the United States again down a path with uncertain environmental consequences. This time, however, the subsidy is for both the refiners ($1.01 per gallon) and the growers ($45 per ton of biomass), which will rapidly accelerate adoption and place hard-to-manage pressures on efforts to design and implement sustainable production practices—as will a 2007 legislative mandate for 16 billion gallons of cellulosic ethanol per year by 2022. Similar directives elsewhere, e.g., the European Union's mandate that 10% of all transport fuel in Europe be from renewable sources by 2020, make this a global issue. The European Union's current reconsideration of this target places even more emphasis on cellulosic feedstocks (*1*). The need for knowledge- and science-based policy is urgent.

Biofuel sustainability has environmental, economic, and social facets that all interconnect. Tradeoffs among them vary widely by types of fuels and where they are grown and, thus, need to be explicitly considered by using a framework that allows the outcomes of alternative systems to be consistently evaluated and compared. A cellulosic biofuels industry could have many positive social and environmental attributes, but it could also suffer from many of the sustainability issues that hobble grain-based biofuels, if not implemented the right way.

Although many questions about biofuel sustainability remain unanswered—indeed, some remain unasked—what we now know with reasonable certainty can be readily summarized. First, we know that grain-based biofuel cropping systems as currently managed cause environmental harm. In addition to questions of carbon debt created by land cleared elsewhere to replace displaced food production (*2*–*4*), farming our existing landscapes more intensively, with even greater quantities of biomass extracted, can easily exacerbate existing environmental problems. The effects of more intense agriculture are well documented: increased soil erosion, greater nitrate and phosphorus loss, and a decline in biodiversity, with concomitant impacts on ground and surface water quality, air quality, and biodiversity-based services such as pest suppression and wildlife amenities. Business as usual writ larger is not an environmentally welcome outcome.

Second, because grain-based ethanol will likely remain in the nation's energy portfolio, it is important to understand that appropriate practices can soften its environmental impact.

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Although the price of cellulosic feedstocks will likely remain lower than that of grain, the added costs of pretreatment and enzymes for cellulosic biomass refining will likely continue to make grain competitive with cellulosic feedstocks for the foreseeable future, even considering cheaper cellulosic biomass. There are many factors affecting the relative prices of ethanol derived from different feedstocks, but with the current infrastructure investment in grain ethanol refineries, it seems likely that grain ethanol will continue to consume a substantial proportion of U.S. corn production—25% in 2007, >30% in 2008—for at least the next decade. Thus, it makes sense to consider ways to minimize the environmental costs of additional intensive grain production.

We know, for example, that no-till farming can slow erosion and build soil organic matter where residue inputs are sufficient; that advanced fertilizer technologies can improve crop nitrogen capture and reduce nitrous oxide fluxes; that cover crops and riparian plantings can sequester soil carbon and intercept nitrate leakage and phosphorus runoff; that rotational diversity and inclusion of unmanaged habitat can better support pollinators and other beneficial insects, as well as wildlife; and that crop genetic improvements can reduce the need for pesticides and can increase stress tolerance and water- and nutrient-use efficiency. But improved practices require incentives to ensure their adoption, and current adoption rates are slow or stalled. Significant mitigation of the adverse environmental consequences of more intensive grain production requires incentives that work.

Third, we know that the development of cellulosic feedstocks has substantial promise for avoiding many of the environmental challenges that face grain-based biofuels. In the long term, most cellulosic feedstocks are expected to be generated from perennial crops grown specifically for that purpose. Perenniality eliminates the need for most chemical inputs and tillage after an establishment phase and lessens the need for nitrogen fertilizer. Further, cellulosic crops can be grown as more complex species mixes, including native polycultures (*5*) grown for additional conservation benefits. Moreover, the cultivation of cellulosic crops has the potential to promote soil carbon sequestration, reduce nitrous oxide emissions, provide to ecosystems in the surrounding landscape biodiversity-based services such as pollination and pest suppression, and afford much higher rates of energy return than grain-based systems.

But however promising, these environmental benefits are by no means given. Whether they are realized will depend on which, where, and how cellulosic biofuels are produced. And tradeoffs are unavoidable. Siting cellulosic biofuel crops on marginal lands, rather than on our most productive croplands, could mean preventing competition with food production and concomitant effects on commodity prices, as well as minimizing or even avoiding the carbon debt associated with land clearing. However, marginal lands can also be rich in biodiversity, may require sizable inputs of nutrients and water to make production economically viable, and may carry the opportunity cost (*6*) of forgone future carbon sequestration.

Management practices, including crop choice, intensity of inputs, and harvesting strategy, also will have a strong influence on the sustainability of cellulosic biofuels. For example, extensive monocultures may be economically favorable relative to polycultures but may reduce landscape diversity and the ecosystem services that more-diverse landscapes provide. Some proposed biofuels crops are exotic (*7*) and others are known to be invasive (*8*), which can have further negative influences on local-to-regional biodiversity. Other cellulosic crops may require substantial chemical inputs and irrigation, with the potential for water pollution, nitrous oxide emissions, and, in arid regions, further competition for water. In addition, excessive removal of "waste" residue from annual cropping systems will rob the soil of carbon (*9*), increase erosion (*10*), and reduce soil fertility. Also, excessive forest thinning will reduce long-term forest productivity and wildlife habitat. In sum, the potential benefits of cellulosic crops could too readily be negated by inattention to choices of location and management practices.

Globally, to produce an important amount of energy with biofuels will require a large amount of land—perhaps as much as is in row-crop agriculture today. This will change the landscape of Earth, not just the United States, in a significant way. To avoid perverse outcomes, such as U.S. policies that cause carbon debt elsewhere, we also need to keep a global perspective that recognizes effects of U.S. decisions on both the magnitude and direction of land-use change elsewhere.

The identification of unintended consequences early in the development of alternative fuel strategies will help to avoid costly mistakes and regrets about the effects on the environment. Policies that support long-term sustainability of both our landscapes and our atmosphere are essential if we are to chart a low-carbon economy that is substantially better than business as usual.

Getting to such an economy will also require a more comprehensive and collaborative research agenda than what has been undertaken to date. In particular, there is an urgent need for research that emphasizes:

(i) a systems approach to assess the energy yield, carbon implications, and the full impact of biofuel production on downstream and downwind ecosystems, however distant from the point of production;

(ii) a focus on ecosystem services—including those that are biodiversity-based—to provide the information necessary for the development and implementation of land-management approaches that meet multiple needs; and

(iii) an understanding of the implications of policy and management practices at different spatial scales—from farm and forest to landscapes, watersheds, food-sheds, and the globe—and an assessment of alternative cost-effective policies designed to meet sustainability goals.

Decision-makers at all levels need to understand that applying best available practices to biofuel crop production will have positive impacts both on the sustainability of our working lands and on providing a long-term place for biofuels in our renewable energy portfolio—and that the policies necessary to ensure this outcome are not currently in place. Legislated environmental performance standards for cellulosic ethanol production could, for example, go far toward promoting sustainable outcomes. Such standards could range from a prohibition of specific practices, such as growing invasive species for feedstock or removing excessive annual crop residue, to the provision of incentive payments based on avoided greenhouse gas emissions, both direct and indirect. We know enough today to begin formulating these standards, and both the industry and the environment will benefit from their early identification and refinement.

Sustainable biofuel production systems could play a highly positive role in mitigating climate change, enhancing environmental quality, and strengthening the global economy, but it will take sound, science-based policy and additional research effort to make this so.

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ASTRONOMY

The Shining Make-Up of Our Star

A revision to the chemical composition of the Sun based on models of its outer atmosphere is at odds with our understanding of its inner workings.

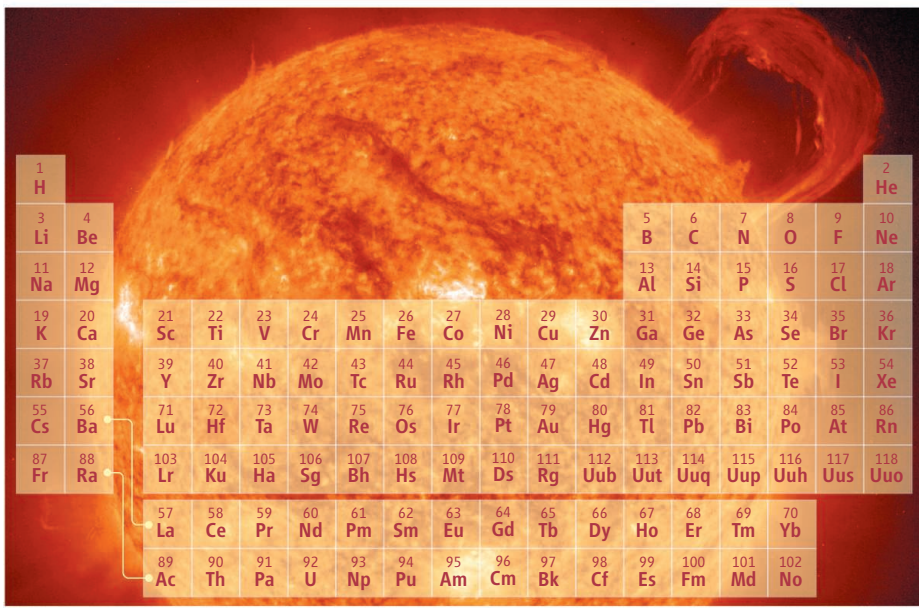
Martin Asplund

The content of chemical elements in the Sun functions as an astronomical yardstick against which the compositions of all other stars, gas clouds, and galaxies in the cosmos are referenced. Rather than being constant, as any good ruler should be, however, this elemental abundance scale has in the past few years undergone a substantial revision based on improved modeling of the solar surface layers and the emitted solar spectrum (*1*, *2*). Although this adjustment has been welcomed by most in the astronomy community, there is concern that it seems incompatible with our understanding of the solar interior.

The chemical composition of a star like the Sun is inferred from its spectrum, which provides the elemental fingerprint in the form of absorption lines. To convert the strength of a spectral line to an elemental abundance requires detailed modeling of the stellar atmosphere and the processes between atoms and radiation that shape the emergent solar spectrum. A major complication here comes from convection, which reaches up to the surface in the Sun and thereby modifies the atmospheric structure and spectrum formation. Instead of the traditional one-dimensional (1D) and hydrostatic modeling, the new analyses (*1*–*3*) use a 3D and hydrodynamical solar model in which the convective energy transport is realistically treated together with the interaction between the radiation field and the gas. Also, nonequilibrium atomic processes are considered when computing the emergent solar spectrum, and new input data for the spectral lines are used.

Together, these improved ingredients add up to almost half the derived solar abundances of carbon, nitrogen, oxygen, and neon compared with the canonical values from a decade ago (*2*, *4*). This revision is particularly noteworthy given that these are the four most abundant elements next to hydrogen and helium. The results seem highly robust as molecular lines and atomic transitions arising from excitation levels having vastly different sensitivities to the atmospheric conditions point to the same abundances.

One long-standing conundrum has been why the Sun that was born 4.5 billion years ago contained much more heavy elements



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than the present-day interstellar medium and young, massive stars in the Galactic neighborhood. The overall content of heavy elements in the Milky Way should steadily increase with time as stars die and spew out their nuclear-processed ashes from which subsequent stellar generations are formed (*5*). The revised lower solar content of C, N, and O has finally brought the Sun into line with its surroundings (*6*).

Modelers of the solar interior have been less enthusiastic (*7*). The lower content of heavy elements reduces the opacity, thus requiring changes to the computed temperature and density as a function of depth in the solar models. This would not have been such a serious problem had it not been for helioseismology, a technique that has been used to provide a window to peer into the solar interior. Sound waves generated by the convective motions in the outer ~30% of the Sun cause it to ring like a bell with a dominant period of about 5 min. Helioseismology maps the variation of sound speed with depth from measuring the exact frequencies of the different oscillation modes. Unfortunately, the inferred sound speed is inconsistent with the predicted values from interior models constructed with the new solar chemical composition. The irony is that solar-interior models based on the old abundances gave strikingly good agreement.

Ever since this "solar model problem" was first realized, much work has been devoted to identifying a solution. The most straightforward explanation would be that the opacity in the solar interior has been underestimated, requiring an increase by 10 to 20% throughout an extended region below the convection zone where the temperatures are 2 to 5×10^6 K (*7*). Subsequent studies have failed to identify such a shortcoming in existing atomic calculations, although a minor part of the missing opacity could well be forthcoming (*8*). Another way of compensating for the diminished opacity from the lower O abundance is to substantially increase the content of other elements such as Ne, which can only be indirectly inferred in the Sun. After receiving some initial support (*9*), this idea now appears inconsistent with the evidence from other nearby solar-like stars. Other hypotheses, such as a much higher metal content in the interior than in the solar atmosphere due to underestimated diffusion, have similarly been ruled out. Perhaps the only proposal still standing is internal gravity waves, which both induce mixing below the convection zone and enhance the effective opacity in the region with the largest helioseismology discrepancies (*10*, *11*). Although the expected effect goes in the right direction, unfortunately no detailed quantitative estimate of the impact on sound speed has appeared yet for this promising premise.

With the steady elimination of suggestions aimed at the solar interior modeling, the focus

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has partly shifted to confirming or refuting the new solar abundances of references *1–3*. Despite the more sophisticated modeling of the atmosphere and spectrum, could it be that the revised values are in fact underestimated and the real abundances closer to the old ones? Recently, independent analyses based on different 3D solar atmosphere models have appeared, which tend to find intermediate values (*12–15*). Unfortunately, these latest studies have been restricted to only oxygen and without considering the molecular transitions; hence, it remains to be shown that all available abundance indicators will yield consistent results. Reassuringly, the particular choice of 3D model turns out to be relatively unimportant. Instead, the main differences come from subtleties in the computations of the solar spectrum, especially how possible blending lines from other elements and collisional cross sections for the nonequilibrium spectral line calculations are treated, and how the strengths of the spectral lines are measured. However, the jury is still out on whether these alternative choices are preferable to those in the original 3D-based analyses that sparked the whole solar modeling problem. If true, these intermediate oxygen abundance results would alleviate but not remove the discrepancy with helioseismology. Another explanation working in concert would then still be required, presumably related to refinements in the solar interior modeling or opacity calculations.

Perhaps an amicable resolution to the solar modeling problem is possible after all through compromises by both the solar atmosphere and interior camps. Regardless of how the final blame is apportioned, studies of the Sun as well as other stars will then be on a much firmer footing. With stars as widely used cosmic probes, this will directly translate to a better understanding of the universe as a whole.

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ECOLOGY

Bugs' Bugs

Evaluation of the chemical relationship between a beetle and its microbial associates shows that microbial ecology can lead to potential drugs.

May R. Berenbaum[1] and Thomas Eisner[2]

Although scientific progress leads to constant reevaluation and revision of concepts and ideas, one observation that has remained robust in the face of accumulating evidence across the centuries is that there are a lot of insects in the world. In 1758, in his profoundly influential book *Systema Naturae*, Carolus Linnaeus (*1*) described all animal species known at the time; of the 4203 species of animals he named, 2102—more than half—were insects. Linnaeus also provided a flexible binomial framework for naming and classifying organisms; species descriptions of all kinds have accumulated apace, but since Linnaeus began this effort they have accumulated fastest for insects. Between 1758 and 1800, close to 60,000 insect species were described; from 1800 to 1850, about 360,000 additional species were identified. Today, about 950,000 species of insects have been described.

A robust corollary of the observation that there are a lot of insects in the world is that the greatest proportion of all insect species belongs to the order Coleoptera—more than one-third of all known species are beetles. Today, more than 300,000 species of beetles have been described. Erwin and Scott (*2*), in a 1-year study of only 19 individuals of a single tree species (*Luehea seemannii*) in Panama, found more than 950 species of beetles, many of them new discoveries (that count did not even include weevils, the largest family of beetles). How many beetles remain undescribed is anyone's guess, but some experts estimate that it is between 5 and 8 million species.

Focused on only a single (but well-known) species of beetle, *Dendroctonus frontalis*, Scott *et al*. on page 63 of this issue (*3*) dramatically illustrate that, as numerous as they may be, beetles may represent just the tip of the biodiversity iceberg. A single beetle species itself can house an entire community of associated species. *D. frontalis* infests pine trees but is dependent on two symbiotic fungi—*Entomocorticum* sp. A, and to a lesser extent, *Ceratocystiopsis ranaculosus*—which both grow in the vascular system of the tree and provide food for the beetle larvae. Another fungus, *Ophiostoma minus*, can be a symbiont that assists the beetle in overcoming the defenses of the host tree, but it can also inhibit growth of the principal

Medicinal sources? Microbes (by the thousands) associated with insects remain to be discovered and tested for chemicals. Shown is a *Camponotus* ant infested with a *Cordyceps* fungus, which is related to the beetle-killing fungus that produces cyclosporin, the well-known immunesuppressive drug. The pharmacological properties of the ant-infesting fungus have yet to be investigated.

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Entomocorticum fungal food source. The beetle deals with the aggressive fungus by harboring yet another species—an actinomycete bacterium—that secretes antibiotics to kill *O. minus*.

This coleopteran complexity eluded detection until now, even though *D. frontalis*, first described 140 years ago (*4*), is a widespread pest and arguably the most economically important pest of southern pine plantations in the United States. And it is by no means unique in harboring a complex microcosm of interacting species. *Acromyrmex* leaf-cutting ants associate with two very specialized symbiotic basidiomycete fungi that grow in underground gardens as food. At the same time, these ants maintain actinomycete *Pseudonocardia* bacteria on their cuticle to manufacture antibiotics that inhibit the growth of an unwelcome associate—*Escovopsis*, a parasitic fungus that attacks the food-source fungal garden (*5*). As Scott *et al*. suggest, in view of the enormous selection pressure that pathogens can exert, protective associations with antibiotic-producing bacteria may be a ubiquitous feature of insect-fungus partnerships. Given that more than 300,000 species of beetles are currently known, the number of partnerships, fungal associates, and bacterial symbionts yet to be elucidated is daunting.

According to May (*6*), the reasons for cataloging biodiversity are the "same reasons that compel us to reach out toward understanding the origins and eventual fate of the universe, or the structure of the elementary particles that it is built from." May also reminds us that Earth's biodiversity is declining at an unprecedented rate, due in large part to anthropogenic changes in land use, climate, soil, and water and air quality. How many beetles, with their communities of associates, will have ceased to exist before Scott *et al*. and other investigators can work out the details of their interrelationships is anyone's guess. According to the Red List of Threatened Species provided by the International Union for Conservation of Nature (*7*)—an authoritative accounting of rare, threatened, and endangered species—fewer than 800 of the 950,000 or so species of insects that have been described (~0.1%) have been evaluated as to their status. Moreover, of the insect species that have been evaluated, almost three-fourths are threatened. The powerful antibiotic chemistry exploited by the southern pine beetle that allows it to go about its business attacking trees is just one example of a more tangible benefit of examining terrestrial interactions than simply gaining insights into the cosmos.

There is no limit to what remains to be discovered in that interactive zone between macroorganism and microbe, where so many biological mutualisms and antagonisms play out. Microbes blanket the planet, and in their infinite variety they must be involved in infinite interactions. Deciphering these could lead to a vast increase in ecological knowledge, as well as to the isolation of natural products of unforeseen function. The latter possibility, clearly envisioned by Scott *et al*., is one that we take to be of particular importance. Chemical prospecting—the search for chemicals of use from nature, including medicinals—has been relegated to low priority by industry nowadays, in the belief that nature has already been exhaustively screened for such compounds. Scott *et al*. provide proof that such belief is unjustified, that the microbial world has been all but thoroughly explored (see the figure). Sure enough, microbes have been screened for some types of biotic and antibiotic action, but the bulk of their chemical capabilities remain to be uncovered. As demonstrated by Scott *et al*., even the least wanted among species can be the source of useful leads. A concerted effort to look into the more subtle aspects of microbial chemistry is therefore very much in order. The fact is that we don't even know the microbes themselves that inhabit our planet, let alone the molecules they need to secure their survival. Microbial ecology is still very much a part of the great frontier.

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ATMOSPHERIC SCIENCE

From Ocean to Stratosphere

Rising tropical sea surface temperatures alter atmospheric dynamics at heights of 16 kilometers or more.

Rudolf Deckert and Martin Dameris

The increasing burden of greenhouse gases from human activities, such as carbon dioxide, is warming the troposphere (the lowest part of Earth's atmosphere), whereas in the stratosphere (above the troposphere and extending from ~16 to 50 km), higher greenhouse gas concentrations cause a net radiative cooling that may delay ozone hole recovery in the Antarctic. But the picture is even more complex. Recent studies have shed light on how mass exchange between troposphere and stratosphere may be affected by tropical sea surface temperatures (SSTs) that are rising as a result of global warming.

The mass exchange between troposphere and stratosphere—the Brewer-Dobson circulation—is characterized by persistent upwelling of air in the tropics from the troposphere into the stratosphere. The air then downwells in the extratropics, mixing stratospheric air back into the troposphere, with a turnaround time of a few years (*1*). Some observational data indicate that the troposphere-stratosphere mass exchange is accelerating (*2*). Most numerical studies with coupled chemistry-climate models support this finding and relate it to the anthropogenic climate signal (*3*), but it is uncertain which mechanism communicates the anthropogenic climate signal to the mass exchange.

This mechanism needs to be pinpointed because the troposphere-stratosphere mass exchange affects the chemical composition and climate of Earth's atmosphere. The tropical upwelling branch of the Brewer-Dobson circulation lowers temperatures and ozone concentrations, especially in the lower stratosphere. The low temperatures in turn freeze-dry the upwelling tropospheric air. Furthermore, the upwelling controls the lifetime of anthropogenic ozone-depleting substances with sinks in the stratosphere. In the extratropical stratosphere, downwelling causes adiabatic warming and ozone accumulation until

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the air parcels return to the extratropical troposphere. This process contributes tropospheric ozone levels (*4*). Finally, changes in horizontal temperature gradients in the lower stratosphere cause remote shifts in surface weather and climate (*5*).

Evidence for a changing Brewer-Dobson circulation comes from satellite and radiosonde data, which indicate a reduction in temperatures and ozone and water vapor concentrations over the past four decades, particularly in the tropical lower stratosphere at all longitudes (*6*). This points to an accelerated tropical upwelling (*2*, *7*). Radiative changes as a result of anthropogenic ozone depletion might account for similar modifications (*8*), but cannot explain a sudden drop in tropical lower stratospheric temperatures in 2001 (*2*, *7*). Stratospheric mass transport trends derived from observations also tend to indicate accelerated upwelling but have large uncertainties (*7*, *9*).

Several independent studies with numerical global climate models confirm these observations (*3*, *10*–*13*). Consistently, the model studies find that lower temperatures and ozone concentrations occur in the tropical lower stratosphere as a result of a stronger tropical upwelling in a future warmer climate, although the high-latitude Brewer-Dobson response differs among the studies.

The model studies indicate that the upwelling intensification is mainly induced by a stronger driving from planetary waves; one to three troughs of these global-scale waves fit around a whole latitude circle. Planetary waves are produced in the troposphere by various processes, and can travel horizontally as well as vertically. Their life cycle usually ends when they disintegrate as a result of continuous damping or, more abruptly, due to wave breaking (like water waves approaching a beach). Some planetary waves can enter the stratosphere, where they usually vanish, conveying energy and momentum to the Brewer-Dobson circulation (*14*). During their life cycle, planetary waves are susceptible to SSTs, which affect location and intensity of their disintegration patterns.

Simulations show that there are various different latitudes where stratospheric wave disintegration responds to SST modifications (*10*, *12*). However, theoretical considerations imply that any year-round intensification in tropical upwelling requires enhanced stratospheric wave disintegration in the tropical/ subtropical region (*15*, *16*). The key question is how this low-latitude disintegration enhancement relates to higher tropical SSTs.

As an explanation, some model studies highlight the role of stronger zonal winds in the subtropical upper troposphere and lower stratosphere. These stronger winds are caused by the growing temperature contrast between the lower stratosphere, which cools, and the tropical upper troposphere, which warms, as a result of anthropogenic climate change. The altered zonal winds intensify planetary-wave disintegration in the stratosphere at low latitudes, thereby accelerating the tropical upwelling (*10*, *13*, *17*).

The warming of the tropical upper troposphere is mainly caused by higher tropical SSTs, which are part of global warming. The SST increase intensifies the activity of tropical thunderstorms (see the figure), which strengthens the associated latent-heat release, warms the tropical upper troposphere, and thus accelerates the zonal winds. However, it remains unclear whether altered wave generation or propagation dominate this SST-governed impact on the Brewer-Dobson circulation and whether waves generated in the tropics or extratropics are involved.

To address these open questions, an additional SST-related mechanism is being considered. The latent heat release from tropical thunderstorms causes pressure perturbations and hence generates tropical planetary waves, just like a stone hitting a water surface (*9*, *15*, *18*). The impact of this mechanism on the Brewer-Dobson circulation could strengthen as tropical SSTs rise and wave generation increases (*19*). In particular, observations show that SSTs in the western tropical Pacific Ocean—the highest SSTs on Earth—are anticorrelated with temperatures and ozone and water vapor concentrations in the tropical lower stratosphere (*2*). For example, high-SST anomalies coincide with low temperatures and ozone concentrations, and vice versa. The anticorrelation could be communicated via planetary-wave generation by tropical thunderstorms, as explained above (*6*).

Thus, heat and moisture at the sea surface affect not only tropospheric climate but also stratospheric dynamics. In particular, planetary waves appear to communicate modulations in tropical SSTs to the mass exchange between troposphere and stratosphere. This Brewer-Dobson circulation is likely to intensify in a future climate with higher tropical SSTs, with implications not only for the chemical composition and climate of the stratosphere but also at Earth's surface.

Tropical oceans and thunderstorms. Warmer tropical oceans intensify the activity of tropical thunderstorms, such as the "Hector" thunderstorm that develops nearly every year off the islands to the west of Darwin, Australia. As a result, the release of latent heat strengthens, affecting planetary waves and hence the mass exchange between troposphere and stratosphere.

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CHEMISTRY

A Light Touch Catalyzes Asymmetric Carbon-Carbon Bond Formation

The cooperation between a photoactivated catalyst and an organocatalyst enables a so far elusive stereoselective synthetic transformation.

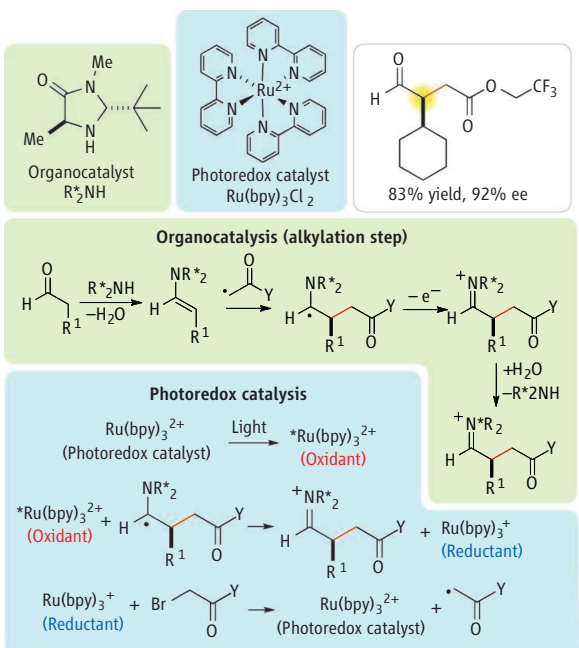
Philippe Renaud and Paul Leong

One of the most formidable tasks in organic synthesis is the formation of carbon-carbon bonds, in part because the activation of the carbon atoms requires the control of highly reactive species. Not only must these reactions form the correct bond connectivity, but they usually need to produce one enantiomer (the left- or right-handed arrangement of functional groups around each carbon atom that acts as a stereogenic center). The α-alkylation of carbonyl compounds (those containing a C=O group) with alkyl halides is a classical method, but it works much better for ketones (two alkyl groups on the C=O) than for aldehydes (one alkyl and one H on the C=O) and often requires stoichiometric amounts of additional reagents to direct the handedness at the stereocenter. On page 77 of this issue, Nicewicz and MacMillan report a remarkable approach for the enantioselective α-alkylation of aldehydes that not only is catalytic but uses a photoredox cycle to control the formation of highly reactive intermediates (*1*).

Prior to this work, asymmetric versions of these α-alkylation reactions that yield preferentially one enantiomer relied heavily on the use of chiral auxiliaries, which help direct the stereochemistry of the product (*2*). However, chiral auxiliaries, in contrast to catalysts, are used in stoichiometric amounts, and additional steps are required for their attachment and removal. These considerations alone render the chiral auxiliary approach unsuitable for large-scale applications. Consequently, the development of catalytic systems that generate enantiomerically pure compounds by using a minimal amount of an environmentally friendly catalyst is a field of intensive research (*3*).

Given that aldehydes are among the most widely used building blocks in organic synthesis, α-alkylation reactions of aldehydes that are both catalytic and enantioselective would be highly desirable. Despite extensive efforts, such reactions have remained elusive until recently (*4*). The problem is that alkyl halides are only modestly reactive toward nucleophiles (reagents that form a new chemical bond by donating both bonding electrons), which necessitates the use of highly reactive aldehyde enolates. Because aldehyde enolates are difficult to prepare and are expected to react faster with the starting aldehydes than with an alkyl halide, a truly catalytic cycle is nearly impossible to achieve.

Nicewicz and MacMillan have proposed a solution to this challenging problem in which the difficult and slow ionic alkylation step (a two-electron process) has been replaced by rapid steps based on less stable open-shell molecules involving one-electron pathways. MacMillan's and Sibi's groups had already introduced the concept of organo-SOMO catalysis (one-electron processes that make use of SOMOs, singly occupied molecular orbitals) for enantioselective α-allylation (*5*, *6*), α-vinylation (*7*), and α-oxygenation (*8*) of aldehydes. However, a stoichiometric amount of oxidant is required to generate the



Asymmetric catalysis via one-electron steps. The steps of the organocatalytic reaction (green shading) are carefully intertwined with the photoredox cycle of $Ru(bpy)_3^{2+}$ (blue shading). The photoexcited state of $Ru(bpy)_3^{2+}$ readily oxidizes the radical resulting from the coupling of the activated alkyl halide and the enamine, which is generated by condensation of the aldehyde with the organocatalyst. The bulky chiral organocatalyst directs the approach of these reactants so that alkyl group R^1 has a preferred stereochemistry; hydrolysis recovers the final product. The photocatalyst, now $Ru(bpy)_3^{+}$, reduces the alkyl halide by one electron to create the radical (the activated species with an odd electron) as well as the initial $Ru(bpy)_3^{2+}$. (**Upper right**) A typical product, its yield, and enantiomeric excess (ee).

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radicals. This requirement represents a major drawback in terms of atom economy and waste production.

To address this limitation, Nicewicz and MacMillan have investigated ruthenium bipyridine complexes, which are well-established photoredox catalysts. Under irradiation with blue light, tris(bipyridine)ruthenium(II), $Ru(bpy)_3^{2+}$, forms a more reactive species, $*Ru(bpy)_3^{2+}$, an excited state in which an electron on the metal transfers to the bpy ligand, where it has enhanced oxidative and reducing power relative to the ground state (*9*).

Nicewicz and MacMillan elegantly combined this photoredox process (see the figure, blue shading) with organo-SOMO catalysis so that the desired transformation can occur in the correct sequence to generate enolate radicals by a reductive process, and, after coupling with the chiral enamine, oxidize the reaction product. Here, the radical needed in the organo-SOMO catalysis is obtained by a one-electron transfer that reduces an α-bromocarbonyl compound with a Ru(I) species, $Ru(bpy)_3^{+}$. The enolate radical possesses an electrophilic character and adds efficiently to the electron-rich chiral enamine (the aldehyde-organocatalyst condensation product) to form an intermediate 1-aminoalkyl radical. This radical is readily oxidized by the excited $*Ru(bpy)_3^{2+}$ back to the corresponding iminium ion, which upon hydrolysis yields the final product; the oxidation step also regenerates the $Ru(bpy)_3^{+}$ ion so that the photoredox catalytic cycle can begin again.

A key feature is that the alkylation step proceeds stereoselectively because of the presence of the chiral secondary amine organocatalyst, which, after condensation with the aldehyde, gives an enamine that helps direct the approach of the incoming radical. Despite the delicately intertwined organo-photoredox catalytic cycles, this reaction is technically simple. It can be performed even with a household 15-W fluorescent light, with no external heating or cooling of the reaction mixture. For example, typical reaction conditions use a relatively high organocatalyst loading (20 mol %) with a minute amount of the photoredox catalyst (0.5 mol %). Indeed, alkylation of a series of aliphatic aldehydes with bromomalonates, α-bromoesters, and α-bromo-β-ketoesters occurs in excellent yield (63 to 93%) and with high stereochemical control (enantiomeric excess up to 99%) in all cases, even where two stereocenters are created (see the figure, upper right panel).

The selectivities for one enantiomer rival those observed for the classical ionic and concerted reactions, dispelling the previous notion that the high reactivity of radicals precludes their use in catalytic asymmetric synthesis. The cooperation of organo-SOMO catalysis and photoredox catalysis offers many possibilities for asymmetric transformations. A burgeoning field of research is likely to emerge from this seminal work.

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BIOCHEMISTRY

Not Comparable, But Complementary

New studies increase the number of protein-protein interactions but show little overlap. This is not a bad thing, though.

Lars Juhl Jensen[1,2] and Peer Bork[1,3]

It took many years between the introduction of DNA sequencing technologies in the mid-1970s and completion of the first genome sequences in the mid-1990s. Connecting the one-dimensional "parts lists" encoded within genomes—the proteins—into two-dimensional interaction maps is an even more daunting task, despite the introduction in the late 1980s of the yeast two-hybrid assay to identify protein–protein interactions (*1*) and high-throughput versions of this technology at the turn of the millennium (*2*, *3*). On page 104 in this issue, Yu *et al.* (*4*) identify 1809 interactions in the model organism budding yeast, of which more than 1500 are new relative to the early yeast two-hybrid studies (*2*, *3*). Together with the 2770 interactions recently determined by Tarassov *et al.* by a protein complementation assay (*5*), almost all of which are new, the number of binary interactions has more than tripled relative to earlier analyses (*2*, *3*). These studies bring us closer to a complete map of biophysical interactions in a single organism, and hence to the ultimate goal of functional understanding of the cellular machinery in space and time (*6*).

To document the quality of the identified interactions, the two groups performed extensive quality assessments, both on an absolute scale and relative to earlier large-scale studies. According to their estimates, only a few percent of the newly identified interactions are false-positives, which is more than an order of magnitude lower than suggested by previous quality assessments of large-scale yeast two-hybrid experiments (*7*, *8*). However, a direct comparison of those numbers is difficult and potentially confusing because each group used a different "gold standard" of known interacting and noninteracting protein pairs. Whereas Yu *et al.* take into account the genome-wide estimate for the number of interacting protein pairs relative to noninteracting ones, the standard used by Tarassov *et al.* is more than 40-fold enriched for interactions. This implicitly lowers the number of false-positives and hence inflates the estimated precision, which drops from 98.2% to around 50% if corrected for this bias. However, the latter value is overly pessimistic because the authors' reference set disfavors binary interaction assays.

A comparison of numbers becomes even more difficult when considering assays such as tandem affinity purification (*9*), which copurify proteins that are parts of the same complex. Four years after the first large-scale

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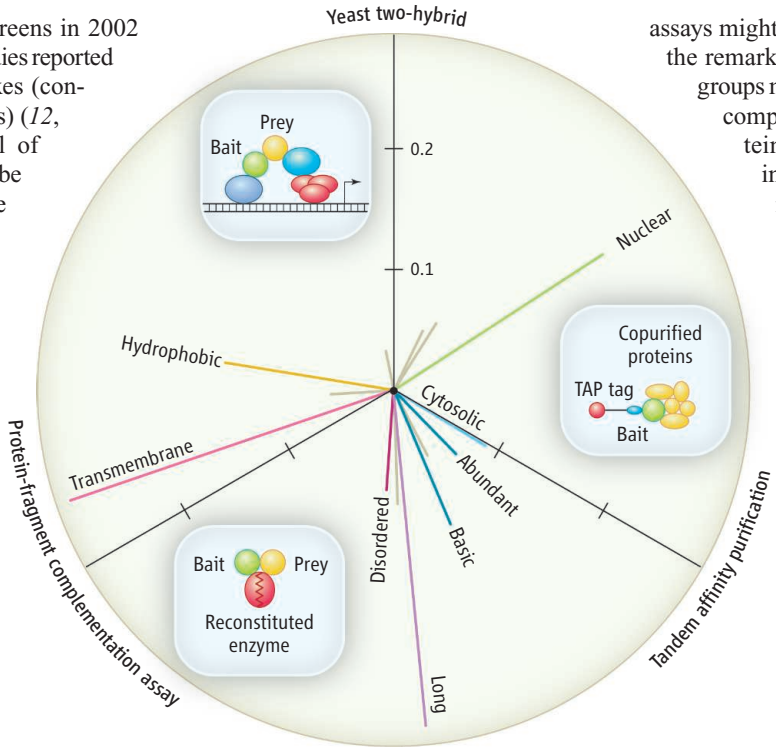
protein-protein interaction screens in 2002 (*10*, *11*), two genome-wide studies reported 491 and 547 protein complexes (containing more than two proteins) (*12*, *13*), respectively, and a total of 12,292 protein interactions can be inferred from the respective purifications. Yu *et al.* compared these inferred interactions and the nearly 3000 new and old interactions identified by the yeast two-hybrid assay (*2*–*4*) to their binary interaction gold standard and found the two-hybrid assay to be more precise than tandem affinity purification. Conversely, tandem affinity purification performs much better than the two-hybrid assay when using gold standards based on protein complexes (*4*, *5*, *7*, *8*). These results may seem contradictory, but as alluded to by Yu *et al.*, the approaches are in fact complementary: Binary interaction assays are better at identifying binary interactions, and complex purification assays are better at identifying co-complex interactions (all protein pairs that are part of the same complex) (*4*). The former provides evidence for direct interactions, whereas the latter allows the binary network to be subdivided into biologically relevant units (that is, complexes).



Protein preferences. The three methods shown for detecting protein interactions function in fundamentally different ways and hence have different physiochemical constraints. Of 15 protein features tested for biases between the sets of proteins for which interactions were identified by each assay, 8 differed significantly (false-positive rate of <0.001): presence of transmembrane helices, hydrophobicity, nuclear and cytosolic localization, abundance, predicted isoelectric point, length, and intrinsic disorder. The other seven protein features are shown in gray. The average normalized scores (*Z* scores) for each of these features are shown, projected onto a plane in which each axis corresponds to one of the three methods for detecting interactions. The length of each line thus represents the strength of the bias.

Although the conceptual difference might account for the poor agreement between the binary and the complex-purification methods, the only 63 interactions common between yeast two-hybrid (*2*–*4*) and protein complementation assay (*5*) screens likely reflect hidden physiochemical constraints inherent to each method. Thus, the different methods might simply capture interactions for different subsets of proteins. This complementation can be confirmed by biases in the types of proteins for which interactions were detected by each assay (see the figure). The most striking trend is that the protein complementation assay has been much better at detecting interactions for transmembrane (and thus hydrophobic) proteins than the other two assays, which Tarassov *et al.* highlight as one of its major strengths. Conversely, the yeast two-hybrid assay and tandem affinity purification both detect interactions for a higher proportion of nuclear proteins, which for the two-hybrid screen is to be expected, because the assay inherently functions inside the nucleus. Notably, interactions from low-throughput studies (*14*) are similarly biased toward nuclear proteins compared to all yeast proteins. Long proteins, unstructured proteins, and proteins with high isoelectric points are underrepresented among the interactions detected by the yeast two-hybrid assay, whereas tandem affinity purification shows a weak but statistically significant preference for abundant proteins and cytosolic proteins, as shown in the original studies (*12*, *13*), many of which form large stable complexes.

Because the tandem affinity purification approach is close to saturation in terms of protein coverage and, with the study by Yu *et al.*, most yeast proteins have now also been subjected to the two-hybrid assay, the apparent methodological complementation might suggest ways to improve the binary interaction map, because proteins amenable to a certain assay can be examined in greater depth. To improve coverage of interactions, numerous protein-specific optimizations of the existing assays might be necessary in the future, and the remarkable progress reported by both groups might be the last big step toward a complete catalog of all possible protein–protein interactions in budding yeast, which are estimated to number between 18,000 (*4*) and 30,000 (*7*, *8*).

Despite the challenging task of characterizing the complete binary "interactome," it is only a static, two-dimensional representation, because the interactions will never all happen at the same time in the same place. Spatial and temporal data will therefore be needed to decipher where and when an interaction takes place; for example, the interaction network changes considerably during the cell division cycle or other dynamic processes (*15*). Furthermore, interactions among proteins constitute only one part of the interactome, because associations to other biopolymers (including DNA and RNA), large lipids, and small molecules have to be considered. Finally, the directionality and functionality of the interactions need to be considered as observed, for example, in signaling networks. The growing high-quality interaction map of a model organism, highlighted by Yu *et al.* and Tarassov *et al.* provides the first layer of context to the "parts lists" and lays the foundation for integrating additional spatial, temporal, and functional dimensions necessary for a comprehensive understanding of the eukaryotic cell.

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The Origin and Evolution of Religious Prosociality
Ara Norenzayan, *et al.*
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The Origin and Evolution of Religious Prosociality

Ara Norenzayan* and Azim F. Shariff

We examine empirical evidence for religious prosociality, the hypothesis that religions facilitate costly behaviors that benefit other people. Although sociological surveys reveal an association between self-reports of religiosity and prosociality, experiments measuring religiosity and actual prosocial behavior suggest that this association emerges primarily in contexts where reputational concerns are heightened. Experimentally induced religious thoughts reduce rates of cheating and increase altruistic behavior among anonymous strangers. Experiments demonstrate an association between apparent profession of religious devotion and greater trust. Cross-cultural evidence suggests an association between the cultural presence of morally concerned deities and large group size in humans. We synthesize converging evidence from various fields for religious prosociality, address its specific boundary conditions, and point to unresolved questions and novel predictions.

Religious prosociality, or the idea that religions facilitate acts that benefit others at a personal cost, has many proponents. Indeed, religious texts of all major religions explicitly encourage prosociality in their adherents (*1*, *2*). Social science theories have long pointed to religion as a cultural facilitator of social cohesion and ingroup solidarity (*3*, *4*), often at the expense of rival groups. However, opinion, rather than careful observation, has dominated the debate on religion's role in prosocial behavior. Recent years have seen new developments in evolutionary explanations of religion, bolstered by a small but growing empirical base that unites several academic disciplines. Here, we critically examine and synthesize evidence from anthropology, sociology, experimental psychology, and experimental economics for religious prosociality. We also address empirical inconsistencies found in studies examining the association between religion and prosociality, offer possible resolutions, and point to remaining issues and future directions.

Various evolutionary theories of religion all predict that religious beliefs and behaviors have facilitated human prosocial tendencies, but there is no scientific consensus yet as to exactly how this might have occurred. Some argue that at least certain religious beliefs and behaviors are evolutionary adaptations for group-living in large communities that have maximized genetic fitness (*5*), perhaps even by multilevel selection (*4*). However, these accounts have difficulty explaining the differential cultural distribution and cultural change over time of religious beliefs and behaviors. Two additional evolutionary accounts, however, are compatible with such cultural variability. One proposes that religious content itself is a cultural by-product of a suite of psychological tendencies evolved in the Pleistocene for other purposes, such as detecting and inferring the content of other minds and sensitivity to one's prosocial reputation in the group (*6*, *7*). Religious beliefs, to the extent that they were compatible with these psychological tendencies, could then culturally spread through social learning mechanisms and could solve adaptive problems, particularly the problem of cooperation in large groups. A third evolutionary perspective, known as cultural group selection (*8*), maintains that competition among social groups may favor the spread of fitness-enhancing cultural beliefs and costly practices, such as religious prosociality (*4*, *9*, *10*). This last-mentioned view takes as its starting point that religious beliefs are cultural by-products of evolved psychology, but argues that reputation-sensitivity, although important, is not sufficient to explain the features of strong prosocial tendencies such as the ones found in religious behavior.

Despite these important differences, large agreement is emerging that selective pressures over the course of human evolution can explain the wide cross-cultural reoccurrence, historical persistence, and predictable cognitive structure of religious beliefs and behaviors. The tendency to detect agency in nature likely supplied the cognitive template that supports the pervasive belief in supernatural agents (*6*, *7*, *11*). These agents are widely believed to transcend physical, biological, and psychological limitations (*6*, *7*). However, other important details are subject to cultural variation. Although in many societies supernatural agents are not directly concerned with human morality, in many others, morally concerned agents use their supernatural powers to observe and, in some cases, to punish and reward human social interactions. Examples include the God of Abrahamic religions and Viracocha, the Incan supreme God, but also many morally concerned deities found in traditional societies, such as the *adalo*, ancestral spirits of the Kwaio Solomon islanders (*7*). These beliefs are likely to spread culturally to the extent that they facilitate ingroup cooperation. This could occur by conforming to individual psychology that favors reputation-sensitive prosocial tendencies, as the by-product account holds; by competition among social groups, as the cultural group selection account would suggest; or possibly by some combination of the two. Religious behaviors and rituals, if more costly to cooperating group members than to freeloaders, may have reliably signaled the presence of devotion and, therefore, cooperative intention toward ingroup members, in turn, buffering religious groups against defection from freeloaders and reinforcing cooperative norms. Religious prosociality, thus, may have softened the limitations that kinship-based and (direct or indirect) reciprocity-based altruism place on group size. In this way, the cultural spread of religious prosociality may have facilitated the rise of stable, large, cooperative communities of genetically unrelated individuals.

The acute human sensitivity to prosocial reputation (*12*) is a psychological mechanism, originally unrelated to religion, that evolved to facilitate strong reciprocal cooperative bonds within groups (*13*). In an intensely social, gossiping species, reputational concerns likely contributed to the evolutionary stability of strong cooperation between strangers. Individuals known to be selfish could be detected, subsequently excluded from future interaction, and even actively punished (*13*, *14*). The threat of being found out, therefore, became a potent motivator for good behavior. Accordingly, studies have repeatedly shown that experimentally reducing the degree of anonymity in economic games increases the rate of prosocial behavior (*15*). Exposure to photographic and even schematic representations of human eyes increases prosocial behavior in economic games (*16*) and decreases cheating in naturalistic settings (*17*). We argue that religion's effect on prosocial tendencies similarly depends on such reputational sensitivity. The cognitive awareness of gods is likely to heighten prosocial reputational concerns among believers, just as the cognitive awareness of human watchers does among believers and nonbelievers alike (*18*). However, supernatural monitoring, to the degree that it is genuinely believed and cognitively salient, offers the powerful advantage that cooperative interactions can be observed even in the absence of social monitoring.

This line of reasoning accounts for a wide range of empirical evidence linking religion to prosocial tendencies and predicts that this association ought to be context-sensitive, with clear boundary conditions. First, religious devotion, insofar as it involves habitual worship of morally vigilant deities, is expected to be associated with greater prosocial reputational concern. Second, religious situations, such as religious ritual performance or being in religious

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surroundings, would, in societies with morally concerned deities, activate thoughts of these deities and habitually facilitate prosocial behavior. Therefore, experimentally inducing religious thoughts would also increase prosociality even when the situation is objectively anonymous. But this should be the case only when thoughts of morally concerned supernatural agents are cognitively accessible in the moment when prosocial decisions are called for. Third, religious behavior that signals genuine devotion would be expected to mobilize greater cooperation and trust, and when internal and external threats to group survival are high, religious groups would be expected to outlast secular ones. Fourth, large societies that have successfully stabilized high levels of cooperative norms would be more likely than smaller ones to espouse belief in morally concerned gods who actively monitor human interactions. In the remainder of this paper, we critically examine the available empirical evidence in light of these four predictions.

Self-Reports: Religiosity and Charitability

If religions centered around moralizing gods promote prosociality, it would be expected that individuals who report stronger belief in such gods would have stronger altruistic tendencies. Sociological surveys suggest that this is the case. Those who frequently pray and attend religious services reliably report more prosocial behavior, such as charitable donations and volunteerism (*1*, *19*). This "charity gap" is consistent across surveys and remains after controlling for income disparities, political orientation, marital status, education level, age, and gender. These findings have been much publicized as evidence that religious people are more prosocial than the nonreligious (*19*). However, it remains unresolved whether this charity gap persists beyond the ingroup boundaries of the religious groups (*1*). More importantly, these surveys are entirely based on self-reports of prosocial behavior. Psychologists have long known that self-reports of socially desirable behaviors (such as charitability) may not be accurate, reflecting instead impression management or self-deception (*20*). If, as we hypothesize, religious individuals are more motivated to maintain a prosocial reputation than the nonreligious, then the former may be more likely to engage in prosocial reputation management. Supporting this hypothesis, psychological research summarizing many studies has found that measures of religiosity are positively associated with tests of socially desirable responding, a common human tendency to project an overly positive image of oneself in evaluative contexts (*21*). This association raises questions about the validity of self-report measures of prosocial behavior. To address these methodological limitations, experiments with behavioral outcomes must be consulted.

Behavioral Evidence: In Search of the Good Samaritans

In several behavioral studies, researchers failed to find any reliable association between religiosity and prosocial tendencies. In the classic "Good Samaritan" experiment (*22*), for example, researchers staged an anonymous situation modeled after the Biblical parable—a man was lying on a sidewalk appearing to be sick and in need of assistance (Fig. 1). Participants varying in religiousness were led to pass by this victim (actually a research confederate) on their way to complete their participation in a study. Unobtrusively recorded offers of help showed no relation with religiosity in this anonymous context (*22*). Only a situational variable—whether participants were told to rush or take their time—produced differences in helping rates.

Fig. 1. In the parable of *The Good Samaritan* [painting by Jacopo Bassano, d. 1592, copyright 2006, The National Gallery, London], Christ preaches universal compassion and prosocial behavior. A similar message is found in many religions. Modern research from social psychology, experimental economics, and anthropology suggests, however, that religious prosociality is extended discriminately and only under specific conditions.

Other behavioral studies, however, have found reliable associations between religiosity and prosociality, but under limited conditions. In one study (*23*), researchers compared levels of cooperation and coordination between secular and religious kibbutzim in Israel. In this economic game, two members of the same kibbutz who remained anonymous to each other were given access to an envelope with a certain amount of money. Each participant simultaneously decided how much money to withdraw from the envelope and keep. Players only kept the money they requested if the sum of the requests did not exceed the total amount in the envelope. If it did, the players received nothing. The results showed that, controlling for relevant predictors, systematically less money was withdrawn in the religious kibbutzim than in the secular ones (*23*).

Thus, unlike studies such as the Good Samaritan, there were greater levels of prosociality among the religious in this study. One key difference is that reminders of God are likely to be chronically present in religious kibbutz, where religious prayer and attendance are a daily part of life. Another, is that prosociality in the religious kibbutz was clearly confined to the ingroup. In the kibbutzim study, highly religious men, who engaged in daily and communal prayer, took the least money, thereby showing the greatest amount of coordination and/or cooperation with ingroup members. It is also possible that regular, communal prayer involves public ritual participation, which, independent of religious devotion, might also encourage more prosociality.

Another approach to clarifying the nature and boundary conditions of religious prosociality is to investigate the altruistic or egoistic motivation underlying the prosocial act. One possibility holds that the greater prosociality of the religious is driven by an empathic motive to ameliorate the condition of others. Alternatively, prosocial behavior could be driven by egoistic motives, such as projecting a prosocial image or avoiding guilt (failing to live up to one's prosocial self-image). The preponderance of the evidence supports the latter explanation. Studies repeatedly indicate that the association between conventional religiosity and prosociality occurs primarily when a reputation-related egoistic motivation has been activated (*2*). In one experiment, for example, participants were given the option of volunteering to raise money for a sick child who could not pay his medical bills (*24*). Participants in one condition were led to believe that they would certainly be called upon if they volunteered. In

another, participants could volunteer although told that they were unlikely to be called upon. In the latter condition, participants could reap the social benefits of feeling (or appearing) helpful without the cost of the actual altruistic act. Only in the latter situation was a link between religiosity and volunteering evident. Many studies have corroborated that religiosity predicts prosocial behavior primarily when the prosocial act could promote a positive image for the participant, either in his or her own eyes or in the eyes of observers (*2*).

As insightful as these behavioral studies are, however, causal inference has been limited by their reliance on correlational designs. If religiosity is related to prosocial behavior under some contexts, it is possible that having a prosocial disposition causes one to be religious or that a third variable (such as dispositional empathy or being prone to guilt) causes both prosocial and religious tendencies. Recent controlled experiments have addressed this limitation by experimentally inducing thoughts of supernatural agents and then measuring prosocial behavior.

Experimental Evidence: When Gods Are on Our Minds

In one such experiment (*25*), university students who were randomly assigned to a condition in which they were casually told that the ghost of a dead student had been spotted in the experimental room, cheated less on a rigged computer task. A different study conceptually replicated this effect—temporary, unconscious activation of God concepts lowered rates of cheating (*26*). Moreover, among those in the control condition, religiosity as an individual difference measure did not predict levels of cheating. In another experiment, children were explicitly instructed not to look inside a box, and then left alone in the room with it (*25*). Those who were previously told that a fictional supernatural agent—Princess Alice—was watching were significantly less likely to peek inside the forbidden box.

We have proposed that the cultural spread of religious prosociality may have promoted stable levels of cooperation in large groups, where reputational and reciprocity incentives are insufficient. If so, then reminders of God may not only reduce cheating, but may also increase generosity toward strangers as much as reminders of secular institutions promoting prosocial behavior. These hypotheses were supported in two anonymous economic game experiments, one with a sample of university students and another with nonstudent adults (*27*) (Fig. 2).

Thoughts of God, activated without conscious awareness (*28*), thus caused greater generosity between anonymous strangers. One explanation for this finding is that the imagined presence of a morally concerned supernatural watcher reduced the anonymity of the situation and heightened prosocial reputational concerns, thereby increasing prosocial behavior. Alternatively, it is possible that thoughts of God and thoughts of charity or benevolence are cognitively associated; thus, priming the former concept increased behavioral tendencies consistent with the latter (*27*). This explanation, however, begs the question as to why God concepts are mentally associated with charity in the first place. These alternative explanations await further experimental investigation. In either case, the effect occurred only to the extent that thoughts of a morally concerned divine agent were activated in the moment of decision-making. Self-reported belief in God or self-reported religious devotion was, as has been found before, not a reliable predictor of generous behavior in anonymous settings.

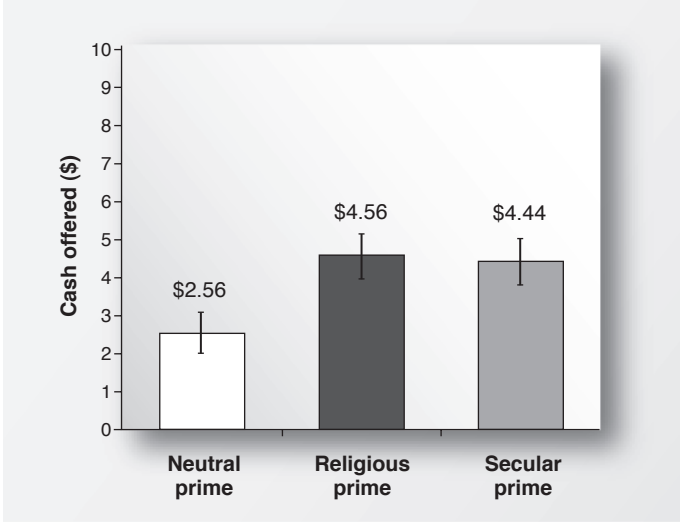

Fig. 2. Implicit activation of God concepts, relative to a neutral prime, increased offers in the one-shot, anonymous Dictator Game, $t(48) = 2.47$, $P = 0.02$, SE = 0.81, $d = 0.71$. (*27*). Priming secular concepts indicating moral authority had a similar effect, $t(48) = 2.29$, $P = 0.03$, SE = 0.82, $d = 0.67$. The results showed not only a quantitative increase in generosity, but also a qualitative shift in social norms. In the control group, the modal response was selfishness, a plurality of players pocketed all $10. In the God group, the mode shifted to fairness, a plurality of players split the money evenly ($N = 75$). It remains to be seen, however, whether these effects would occur if the recipient was clearly marked as an outgroup member.

Religious Prosociality, Costly Signaling, and Trust

In the absence of reputational information about a stranger's prosocial inclinations, outward evidence of sincere belief in the same or similar morally concerned gods may serve as a reliable cooperative signal. But a signal is only reliable to the extent that it is difficult to fake by potential freeloaders. Because professions of religious belief can be easily faked, theorists of religion have recognized that evolutionary pressures must have favored costly religious commitment, such as ritual participation and various restrictions on behavior, diet, and life-style, that validates the sincerity of otherwise unobservable religious belief (*5*, *29*). However, for costly signals to evolve as a stable strategy, religious behaviors ought to be more costly for cooperators than for freeloaders, and variation in costliness should predict degree of intragroup trust and cooperation. Mathematical models question the possibility that costly signaling as an individual fitness-maximizing strategy extends to nondyadic collective cooperation as in the case of religion (*9*, *10*), and models of costly signaling applied to religious behavior, with or without cultural group selection, are currently in their infancy (*30*). Nevertheless, qualitative and quantitative evidence is emerging, that, although not yet definitive, addresses parts of these predictions.

Attitudinal surveys show that religious individuals are perceived to be more trustworthy and more cooperative (*31*). From behavioral evidence, ethnographic examples such as the spread of Islam in Africa, which preceded the flourishing of wide-scale trade among Muslim converts (*32*), and the trade networks of Medieval Jewish Maghrebi merchants (*33*) are consistent with this idea. Costly commitment to the same supernatural deity may have lowered monitoring costs and fostered cooperation in communities spread across geographic and even ethnic boundaries. However, it is disputable whether membership in these religious groups was costlier than commitment to local deities or whether costliness was directly associated with greater intragroup trust; therefore, the ethnographic data are open to other interpretations, for example, that religious conversions led to greater access to preestablished trade networks along these religious lines.

To address these limitations, quantitative analyses are needed. Sociological analyses are consistent with the idea that religious groups imposing more costly requirements have members who are more committed. Controlling for relevant sociodemographic variables, "strict" Protestant (e.g., Mormon) and Jewish denominations (Orthodox) show higher levels of church and synagogue attendance and more monetary contributions to their religious communities (despite lower average income levels) than less strict ones (Methodist and Reform, respectively) (*30*). However, these findings do not demonstrate that strictness predicts community survival and growth. One systematic attempt to do so examined religious and secular communes in 19th-century America, whose survival de-

pended upon solving the collective action problem. Religious communes were found to outlast those motivated by secular ideologies, such as socialism (Fig. 3) (*29*). A further quantitative analysis of 83 of these religious and secular communes (*34*) for which more detailed records are available found that religious communes imposed more than twice as many costly requirements (including food taboos and fasts, constraints on material possessions, marriage, sex, and communication with the outside world) than secular ones. This difference emerged for each of the 22 categories of costly requirements examined. Importantly for costly religious signaling, the number of costly requirements predicted religious commune longevity (R^2 = 0.38) after the study controlled for population size and income and the year the commune was founded, although the number of costly requirements did not predict longevity for secular communes. Finally, religious ideology was no longer a predictor of commune longevity, once the number of costly requirements was statistically controlled, which suggests that the survival advantage of religious communes was due to the greater costly commitment of their members, rather than other aspects of religious ideology. However, these findings are correlational, making causal conclusions premature. They collectively imply, but do not definitively demonstrate, that the greater longevity of religious communes with costlier requirements was due to greater intragroup cooperation and trust levels, which have not been measured directly. These results also imply that greater costly commitment is at best a partial explanation as to why religious communes outlasted secular ones. Other aspects of religion that might promote greater community stability are open for investigation.

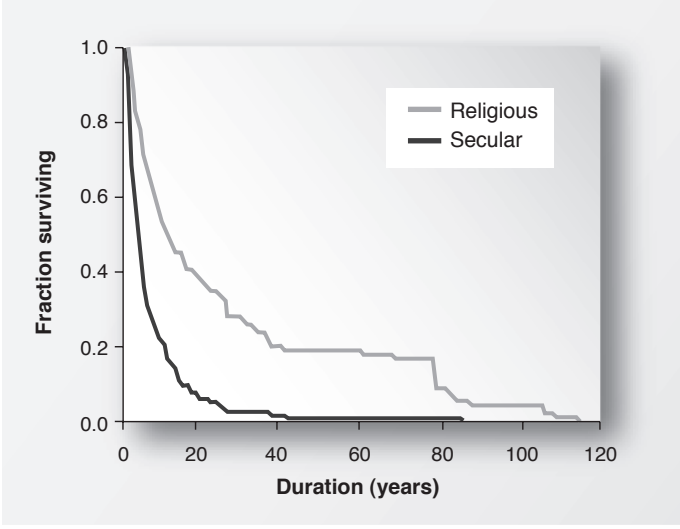

Fig. 3. Life expectancy of religious versus secular communes. An analysis of 200 religious and secular communes in 19th-century America (*29*), for every year of their life course, religious communes were about four times as likely to survive than their secular counterparts, log rank T statistic = 40.14, df = 1, $P <$ 0.00001. This difference remained after statistically controlling for type of commune movement, year founded, and year at risk of dissolution (the last control assesses major historical trends that may independently impact commune dissolution). [Copyright 2003, reprinted from (*29*) with permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.]

The few relevant laboratory studies corroborate that there is an empirical association between religion and trusting behavior. Trust can be operationalized as a costly investment in a person or entity, with the future expectation of return. In one well-researched laboratory game of trust (*35*), participants were randomly assigned to be a proposer (truster) or a responder (trustee). In the first step, the proposer decides how much money to forward to the responder, which gets multiplied. In the second step, the responder decides how much money to send back to the proposer. By transferring money to the responder, the proposer stands to gain, but only if the responder can be trusted to reciprocate. In a variation of this trust experiment (*36*), researchers measured individual differences in the religiosity of the proposer and the responder. In addition, in some trials, proposers knew about the level of religiosity of the responder in an anonymous context. Results indicated that more money was forwarded to responders perceived to be religious, and this was particularly true for religious proposers. Furthermore, religious responders were more likely to reciprocate the proposer's offer than less religious responders. These findings are consistent with the idea that outward evidence of religious devotion may engender more trust, although two issues remain unresolved: They do not show that costly religious behavior elicits more trust and cooperation than less costly behavior under controlled conditions, as required by costly signaling explanations of religion; or that members of religious groups that impose more costly requirements are more trusting and less likely to take advantage of others, particularly ingroup members, as would be expected from cultural group selection accounts.

The relation between religion and trust is, therefore, an area ripe for more research. Experimental studies and alternative mathematical models of costly religious behavior (either as a stable strategy characteristic of individuals or as a stable strategy that takes into account intergroup social competition) will place these theoretical predictions on firmer empirical ground. The existing evidence, however, suggests the possibility that religious belief, to the extent that it could be advertised with sincerity, may enhance within-group interpersonal trust, lower monitoring costs, and so further reinforce intragroup prosocial tendencies. Belief in morally concerned gods may stabilize prosocial norms even in the absence of social monitoring mechanisms. This, in turn, would be expected to expand the reach of such norms, facilitating the emergence of larger cooperative communities which otherwise would be vulnerable to collapse. We examine this hypothesized association between moralizing gods and large group size next.

Big Groups, Big Gods: Cross-Cultural Evidence

From large village settlements at the dawn of agriculture to modern metropolises today, human beings are capable of living in extraordinarily large cooperative groups. However, extrapolating from cross-species comparisons of neocortex size, it has been estimated that human group sizes cannot exceed 150 individuals before groups divide or collapse (*37*). Although this specific number has been disputed (*38*), and whereas some Pleistocene foragers possibly lived in large villages, it is apparent that the size of human settlements since the end of the Pleistocene far exceed the limitations that kin-based and reciprocity-based altruism place on group size.

Cultural evolution, driven by between-group competition for resources and habitats, has favored large groups. However, large groups, which until recently lacked institutionalized social-monitoring mechanisms, are vulnerable to collapse because of high rates of freeloading (*13*). If unwavering and pervasive belief in moralizing gods buffered against such freeloading, then belief in such gods should be more likely in larger human groups where the threat of freeloading is most acute. Because there is considerable variability in the cultural distribution of morally concerned deities, researchers could measure whether this variability correlates with group size across cultures. In a quantitative cross-cultural analysis of the 186 societies in the Standard Cross-Cultural Sample, this prediction was confirmed. The larger the group size, the more likely the group culturally sanctioned deities who are directly concerned about human morality (*39*). Although most cultures in the world do not promote morally concerned deities, those that do tend to have disproportionately larger populations. As a consequence, the majority of religious adherents in the world worship moralizing gods.

One alternative explanation is that Christian and Muslim missionary activity may have caused both more belief in the moralizing Abrahamic God and may have favored larger group size. Another, is that because large societies are more socially stratified, belief in moralizing gods serves to preserve political and economic inequality. However, although missionized societies and caste-stratified societies were indeed more likely to endorse a moralizing God, the association between large group size and the prevalence of

moralizing Gods remained strong even after statistically controlling for missionary activity and for two indicators of societal inequality, as well as for population density and geographic region. Similarly, controlling for the cultural diffusion of moralizing Gods via Christian and Muslim missionary activity, society size, population size, and societal inequality, moralizing gods are more likely in societies with high water scarcity—where the threat to group survival, and the need to minimize freeloading, is also pronounced (*40*). The cross-cultural evidence suggests that moralizing gods are culturally stabilized when freeloading is more prevalent or particularly detrimental to group stability. However, further empirical research is needed to clarify causal direction and to distinguish between alternative explanations for these associations.

Conclusions, Outstanding Questions, and Future Directions

Many religious traditions around the world explicitly encourage the faithful to be unconditionally prosocial (*1*, *2*); yet, theoretical considerations and empirical evidence indicate that religiously socialized individuals should be, and are, much more discriminating in their prosociality (*2*). Although empathy and compassion as social-bonding emotions do exist and may play a role in prosocial acts of religious and nonreligious individuals some of the time (*41*), there is little direct evidence to date that such emotions are systematically implicated in religious prosociality.

The preponderance of the evidence points to religious prosociality being a bounded phenomenon. Religion's association with prosociality is most evident when the situation calls for maintaining a favorable social reputation within the ingroup. When thoughts of morally concerned deities are cognitively salient, an objectively anonymous situation becomes nonanonymous and, therefore, reputationally relevant, or alternatively, such thoughts activate prosocial tendencies because of a prior mental association. This could occur when such thoughts are induced experimentally or in naturalistic religious situations, such as when people attend religious services or engage in ritual performance. This explains why the religious situation is more important than the religious disposition in predicting prosocial behavior.

Although religions continue to be powerful facilitators of prosociality in large groups, they are not the only ones. The cultural spread of reliable secular institutions, such as courts, policing authorities, and effective contract-enforcing mechanisms, although historically recent, has changed the course of human prosociality. Consequently, active members of modern secular organizations are at least as likely to report donating to charity as active members of religious ones (*42*). Supporting this conclusion, experimentally induced reminders of secular moral authority had as much effect on generous behavior in an economic game as reminders of God (*27*), and there are many examples of modern, large, cooperative, and not very religious societies (such as those in Western and Northern Europe), that, nonetheless, retain a great degree of intragroup trust and cooperation (*43*).

Any one study we have discussed can be subject to alternative accounts; therefore, specific evidence should be interpreted with caution. Nevertheless, convergent evidence is emerging from several disciplines using different methods and procedures that supply different pieces of the religious prosociality puzzle. Despite the recent scientific progress in explaining the effects of religion on prosociality, open and important questions remain. In particular, more research is needed to address the costliness of religious and nonreligious rituals, and few studies have attempted to quantify these costs in relation to prosocial behavior. The finding that religiosity evokes greater trust underscores the need for more experimental and theoretical research, including mathematical modeling, to establish the specific conditions under which costly religious commitment could evolve as a stable individual strategy and whether these models need to take into account intergroup competition. More broadly, the extent to which religion is implicated in human cooperation, and the precise sequence of evolutionary developments in religious prosociality, remain open to lively scientific debate. Further progress on these issues will require concerted collaboration among historians, archaeologists, social scientists, and evolutionary biologists.

In recent years, moral psychology has received a great deal of scientific attention (*44*), and although most of the studies reviewed here concern behavioral outcomes, the relation between religious prosociality and moral intuitions and reasoning is ripe for further investigation. More direct research on the possible role of prosocial motivations, such as empathy and compassion, in religious prosociality are needed. Finally, we have seen that religious prosociality is not extended indiscriminately; the "dark side" of within-group cooperation is between-group competition and conflict (*45*). The same mechanisms involved in ingroup altruism may also facilitate outgroup antagonism. This is an area of no small debate, but scientific attention is needed to examine precisely how individuals and groups determine who are the beneficiaries of religious prosociality, and who its victims.

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Bacterial Protection of Beetle-Fungus Mutualism

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The pervasiveness of beneficial associations between symbiotic microbes and plants and animals in every ecosystem illustrates how the acquisition of a microbe's physiological capacity confers substantial fitness benefits to hosts (*1*). However, dependence on mutualistic microbes becomes a liability if antagonistic microbes attack or outcompete beneficial ones (*2*). Therefore, mechanisms to preserve beneficial microbes must be a widespread, although poorly understood, component of host-microbe mutualisms. We show that a beetle uses a bacterium to protect its fungal food source from a competitor fungus.

Southern pine beetles, *Dendroctonus frontalis*, engage in a beneficial symbiosis with the fungus *Entomocorticium* sp. A, which provides nourishment for their developing larvae. Adult beetles carry *Entomocorticium* sp. A in a specialized storage compartment called a mycangium (Fig. 1A), excavate ovipositional galleries within the inner bark and phloem of host pine trees, and inoculate these galleries with *Entomocorticium* sp. A (*3*, *4*). The success of the *D. frontalis*–*Entomocorticium* sp. A mutualism is challenged by an antagonistic fungus, *Ophiostoma minus*, which can outcompete *Entomocorticium* sp. A and thereby disrupt beetle larval development (*3*, *4*). Our results indicate that successful maintenance of the *D. frontalis*–*Entomocorticium* sp. A mutualism is likely mediated by an actinomycetous bacterium that produces antibiotics that selectively inhibit *O. minus*.

The presence of previously unknown actinomycetes within the *D. frontalis*–*Entomocorticium* sp. A mutualism was established by scanning electron microscopy (SEM) and enrichment culture isolations (*5*). SEM revealed unexpected and profuse growth of actinomycetes within the galleries of *D. frontalis*, as well as inside the mycangia (Fig. 1B and fig. S1A). Isolations from 110 beetle individuals yielded 846 colony-forming units (CFUs) of actinomycetes, including at least one CFU from each of 92 individuals. Out of 164 actinomycete CFUs selected to be transferred to pure culture, 99 isolates had a red morphotype, whereas 65 isolates had a white morphotype. DNA sequence analyses confirmed the visual morphotype distinction, and within each of the two morphotypes there was complete 16S rDNA sequence identity. The two morphotypes form a monophyletic clade closely related to *Streptomyces thermosacchari*. Furthermore, we also isolated the same red morphotype from 5 of 10 mycangia sampled.

We explored the potential role of the actinomycetes in mediating the *D. frontalis* fungal community by using symbiont pairing bioassays and chemical analyses. The bioassays, which crossed all possible combinations of the two actinomycete morphotypes with *Entomocorticium* sp. A and *O. minus*, revealed that isolates of the red morphotype produced a diffusible activity that inhibits the beetle's antagonistic fungus, *O. minus*, but only slightly affects the beneficial fungus, *Entomocorticium* sp. A (Fig. 1C and fig. S1, B and C). Extensive chemical and spectral analyses on strains of the red morphotype revealed the antifungal molecule responsible for selective inhibition to be a polyene peroxide, which we named mycangimycin. Mycangimycin ($C_{20}H_{24}O_4$), which has not been previously reported, is a linear 20-carbon carboxylic acid with an endoperoxide linking C-3 and C-5 to form a 1,2-dioxolane and a conjugated *cis*, *cis*, *trans*, *trans*, *cis*, *trans*-heptaene spanning C-7 to C-20 (Fig. 1D). Liquid culture antifungal assays using purified mycangimycin showed *O. minus* to be almost 20 times more susceptible [minimal inhibitory concentration (MIC) = 1.0 μM] than *Entomocorticium* sp. A (MIC = 19.0 μM) (fig. S1D). The identification of an actinomycete that is localized in the mycangium and galleries, which produces an antibiotic that selectively suppresses the antagonistic fungus, *O. minus*, indicates that *D. frontalis* engages in an additional mutualism with bacteria to regulate the *Entomocorticium* sp. A–*O. minus* fungal community. Because other bark-beetle species also depend on successfully maintaining beneficial fungi, tripartite beetle-fungus-bacterium mutualisms may be widespread.

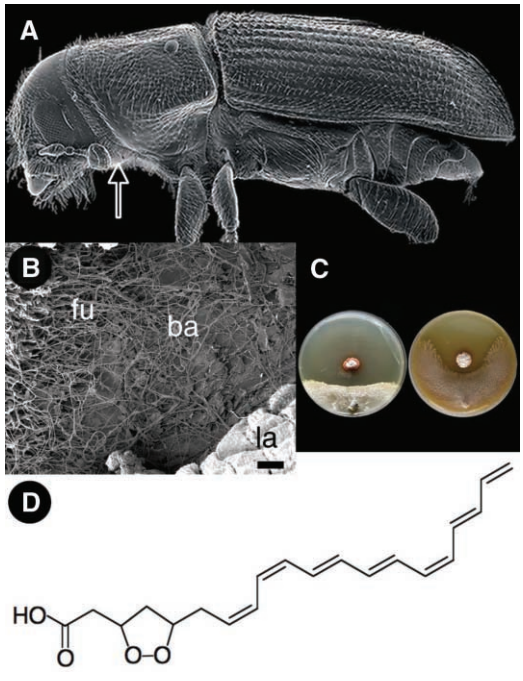

Fig. 1. (**A**) SEM micrograph of adult *D. frontalis* showing the location of a mycangium (arrow), which is used to transport *Entomocorticium* sp. A. (**B**) SEM micrograph from the *D. frontalis* gallery showing the actinomycetous bacterium (ba), fungus (fu), and beetle larva (la). (**C**) Representative examples of pairwise bioassay challenges illustrating inhibition of the fungal antagonist, *O. minus* (left), by a *D. frontalis* symbiotic actinomycete (strain SPB074). In contrast, the southern pine beetle's fungal mutualist, *Entomocorticium* sp. A, is relatively resistant (right) (see SOM for more details). (**D**) The structure of mycangimycin contains a seven-conjugated double bond chain and a five-membered endoperoxide ring.

Our study parallels earlier work on fungus-farming ants, which use actinomycetes to help protect their fungal gardens from pathogens (*6*). Taken together, these findings suggest that the use of antibiotic-producing actinomycetes may be a common method for maintaining beneficial microbes. Indeed, considering the importance of pathogens as a driving force in the evolution of all hosts, the benefit of such associations may extend to helping protect plants and animals from pathogens to which they themselves are susceptible (*7*, *8*). If, as seems likely, these associations are widespread, targeting them could be an effective strategy for locating novel biologically active natural products.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/322/5898/63/DC1
Materials and Methods
Fig. S1
References

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A Chronology of Paleozoic Sea-Level Changes

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A Chronology of Paleozoic Sea-Level Changes

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Sea levels have been determined for most of the Paleozoic Era (542 to 251 million years ago), but an integrated history of sea levels has remained unrealized. We reconstructed a history of sea-level fluctuations for the entire Paleozoic by using stratigraphic sections from pericratonic and cratonic basins. Evaluation of the timing and amplitude of individual sea-level events reveals that the magnitude of change is the most problematic to estimate accurately. The long-term sea level shows a gradual rise through the Cambrian, reaching a zenith in the Late Ordovician, then a short-lived but prominent withdrawal in response to Hirnantian glaciation. Subsequent but decreasingly substantial eustatic highs occurred in the mid-Silurian, near the Middle/Late Devonian boundary, and in the latest Carboniferous. Eustatic lows are recorded in the early Devonian, near the Mississippian/Pennsylvanian boundary, and in the Late Permian. One hundred and seventy-two eustatic events are documented for the Paleozoic, varying in magnitude from a few tens of meters to ~125 meters.

Although there has been substantial progress in recent years in integrating the record of Mesozoic and Cenozoic eustatic fluctuations (*1*, *2*), relatively little attention has been paid to reevaluating or synthesizing Paleozoic sea-level data, the coverage of which has been largely piecemeal. The Paleozoic Era encompasses more than half of the Phanerozoic Eon, featuring some of the most intriguing unanswered questions in Earth history. Unexplored Paleozoic strata also are believed to contain important unrecovered hydrocarbons. A reevaluation of the eustatic history of this Era therefore would not only serve as a tool for exploration geology but hopefully also revive interest in Paleozoic Earth science.

Sea-level curves provide utilitarian predictive models of sedimentation and thus are invaluable in geologic exploration. These curves offer a working representation of the long-term trends of the base level along continental margins and the individual inundations and drainings/desiccations of interior seaways, and thus the migration of hydrocarbon reservoirs and source facies. Where local tectonic influences are minimal and have not deformed the stratigraphic record (or where tectonics can be corrected for), these curves also can aid in first-order correlations. The relative magnitude and frequency of sea-level highs and lows, the extent and nature of the transgressive condensed intervals on the shelf (when organic-rich sediments accumulate), and the duration of subaerial exposure and incision of the shelf are also important exploration criteria (*3*). Here we present an integrated semiquantitative model of the Paleozoic sea-level history. It is based on widely distributed sequence-stratigraphic data within the biochronostratigraphic constraints of varying quality and reliability for various Paleozoic periods.

Although previous reconstructions of regional sea-level histories have been limited to discrete slices of time, they provide a wealth of information on the long- and short-term trends and have been an invaluable resource for this synthesis [see the supporting online material (SOM) text]. Particularly, the studies from relatively stable pericratonic and cratonic basins of North American and Australian cratons have been indispensable. As discussed later, we have designated reference districts (RDs) for various time segments (largely from North America and Australia, but also from northern and southern Africa, northwestern Europe, and China). We interpret the sedimentary record in these districts as representing the modal mean of change in sea level during intervals of relative tectonic quiescence. The RDs were also compared with sections elsewhere around the world to ascertain the broad transgressive/regressive trends and individual variations of sea levels and provide corroborative data. Because of spatial constraints, in this article we only report a brief account of our main findings (see also SOM text).

Timing and magnitude of sea-level events in the Paleozoic. Obstacles encountered in resolving the timing and magnitude of individual sea level events based on a synthesis of worldwide data of varying quality and utility are not specific to the Paleozoic; they are also applicable to the younger eras. The Paleozoic, however, has a special suite of constraints that sets it apart. For example, most Paleozoic oceanic crust has been subducted (with the exception of a few obducted ophiolite mélanges), making it unfeasible to directly estimate the mean age of the oceanic crust for deciphering long-term eustatic trends. Paleozoic stratigraphy is also strongly biased toward epi- and pericratonic basins, characterized by their plentiful unconformities and endemic faunas. Nevertheless, these attributes make these basins natural places for the study of "unconformity-bounded" units (depositional sequences). The unconformity-bounded subdivision also makes the existing Paleozoic literature, spanning over a century of research, relevant and useful.

An accurate time scale is of crucial first-order importance for any global synthesis. Geological time scales have been improving and becoming better integrated in recent years. The Paleozoic time scale in particular has been in a considerable state of flux, with major recent changes to the ages of period and stage boundaries. The most up-to-date published time scale is that compiled by Gradstein *et al*. (*4*). Some parts of this chronostratigraphy have been updated recently (*5*), which we have adopted here. Ongoing attempts at astronomical tuning and recalibration of $^{40}Ar/^{39}Ar$ ages will probably lead to further refinements of the boundary ages (*6*). However, with the exception of a few radiometrically determined boundaries, all of the Paleozoic correlations are actually based on fossil biozonations. Thus, the duration of a biozone in question provides a minimum measure of uncertainty in the correlations of sequence boundaries.

The degree of precision of correlations from one basin to another depends on the biostratigraphic fossil assemblage used for such purposes. For the Paleozoic, biochronostratigraphy is traditionally based on several groups of commonly occurring fossils, the majority of which tend to be endemic and/or facies-controlled (*7*). This underscores the need to use multiple overlapping criteria (biozonal assignments based on several groups) where possible, to enhance the chronostratigraphic signal-to-noise ratio.

The second issue of importance for a reconstruction such as this concerns the uncertainty in estimating the magnitude of rises and falls in sea level. In the Paleozoic, the general lack of data on ice-volume proxies, such as oxygen isotopes (because of severe diagenetic alterations), limits us to relying on physical measures of sea-level changes from stratigraphic data. A fundamental limitation for accurate physical estimates stems from the lack of a universal reference point against which sea level changes can be computed. For convenience, we often compare past eustatic fluctuations with present-day (PD) shorelines, but over the longer periods this comparative reference point becomes less meaningful because continents have changed both by horizontal accretion/destruction and vertical motions. It is often possible to determine when the sea withdrew below the extant shelf edge, but it is challenging to accurately gauge the amount of

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sea-level fall from stratigraphic data because of the unknown amount of erosion on the shelf. A rise in sea level is even more difficult to measure meaningfully because of the potentially less-than-complete filling of the accommodation space during the highstand or because of a subsequent fall in sea level that may erode part or much of the highstand systems tract. Thus, for practical purposes, all amplitude assessments from physical data must be considered relative rather than absolute.

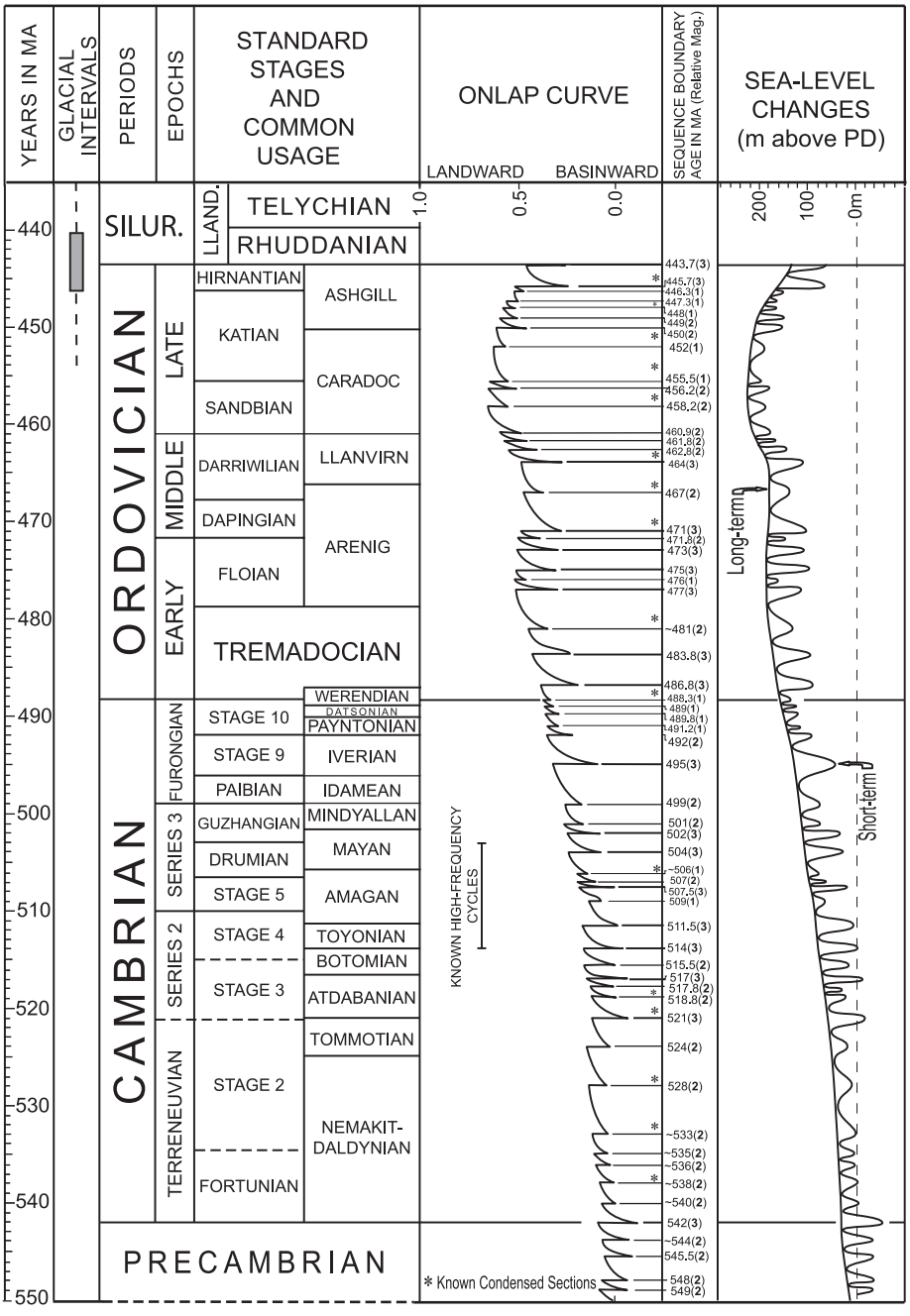

Fig. 1. Cambrian-Ordovician sea-level changes. The time scale and standard and regional stages are modeled after Gradstein *et al*. and Ogg *et al*. (*4*, *5*). The left half of Figs. 1 to 3 shows the stratigraphic subdivisions calibrated to the absolute time scale. Known intervals of continental glaciation (*26*–*28*) are indicated alongside the numerical time scale. The right half of each figure starts with an onlap curve, which is a measure of relative landward or basinward movement of the regional baseline as estimated in the RD sections. Sequences that are associated with known prominent condensed sections (indicated by asterisks) are also shown in this column. The biochronological ages of the sequence boundaries (estimated in the RDs and ancillary sections) are indicated in the next column. A semiquantitative measure of the relative magnitude of each short-term event is shown in parentheses [minor, **1** (<25 m); medium, **2** (25 to 75 m); and major, **3** (>75 m)]. Periods with known higher-frequency eustatic cycles and documented condensed sections are also indicated in this column, by vertical bars. This is followed to the right by the sea level curves, both the long-term envelope and the short-term curve of (third-order) fluctuations in the sea level (those suspected to be of fourth order are shown by dashed lines). The dashed vertical line in this column represents an approximation of the PD sea level. Long-term and short-term sea-level curves are calibrated to the PD sea level.

Backstripping can potentially refine such estimates through corrections for sediment loading and compaction and basin-floor subsidence (*8*, *9*). Nevertheless, considerable uncertainties remain in this approach because of long-ranging paleobathymetric indicators and the potential for differential subsidence. Corrections for the flexural response of a margin to the loading and unloading of water/ice and sediments are also not straightforward or precise and can bias the measurements in either direction. During this synthesis, the only meaningful approach we could adopt was to reproduce the magnitude estimates of rises and falls in sea level as gleaned from the RDs and ancillary sections (based variously on stratigraphic measures such as thickness of system tracts, bio- and lithofacies depth assessments, the depth of incision on shelves, and partial backstripping). We classified each event semiquantitatively (measured as a magnitude of fall from the previous highstand) as minor (<25 m), medium (25 to 75 m), or major (>75 m). From the worldwide data, it is apparent that although the overall long-term (cumulative) rise in sea level could be as much as 250 m, the individual third-order changes in sea level [that is, those occurring over ~0.5 to 6 million years (My)] rarely exceeded 150 m. Many of the higher-frequency (<0.5 My) variations are within the minor to medium range. These estimates will be subject to refinement in the future once various basins (in the RDs and elsewhere) have been effectively backstripped and when better paleobathymetric assessments are available.

Reconstruction of the Paleozoic sea-level history. Though Earth scientists have been interpreting changes in sea level based on stratigraphic data for over a century, the first attempt at an integrated history of the Paleozoic sea level was embedded in the broader presentation of seismic-stratigraphic methodology by Vail *et al*. (*10*). Hallam (*11*) also reviewed much of the Paleozoic sea level data accumulated up to the 1980s. More recently, Haq and Al-Qahtani (*12*) presented a regional history of the sea level in the Phanerozoic Arabian Platform and compared it with an updated eustatic sea level curve based on previous syntheses. However, the Paleozoic portions of those curves largely depicted second-order events, mostly cycles of >5 My duration.

The stratigraphic record is a composite of several orders of superimposed sedimentary cycles, depending on their causal mechanisms. They range from the high-frequency Milankovitch-scale climatic cycles (often 1 m to a few meters in thickness) to third-order (mostly 1 to 2 My in duration) and fourth-order (<0.5 My in duration)

eustatic cycles, and larger (several million years in duration) tectonic cycles. In practice, it is difficult to consistently separate third- and fourth-order cycles. Our ability to resolve the record chronostratigraphically in any given section depends on the thickness of the preserved section, the quality of the outcrop, the position of the section along the shelf-slope-basin profile, and the quality of biochronostratigraphic data. Here we have attempted to identify sequences at third-order resolution; however, a few fourth-order sedimentary cycles inevitably were also incorporated. Although the existence of higher-frequency cycles may be more widespread in the Paleozoic, some intervals more visibly preserve fourth-order (~400,000 years) cycles, such as the mid-Cambrian, mid-Devonian, mid- to late Carboniferous, and Permian (Figs. 1 to 3).

The Paleozoic sequence-stratigraphic data are derived entirely from public-domain outcrop sections (seismic data are generally lacking or spotty except for the late Paleozoic). The criteria for interpreting regional rises and falls in sea level from sequence-stratigraphic data and seismic data have been summarized elsewhere (*3*, *10*, *13*) and are not repeated here. In addition, several lithological features (condensed section deposits, transgressive coals, evaporites, carbonate megabreccias, and exposure-related and forced-regressive deposits) and paleontological attributes have also aided our interpretations in placing outcrop features within sequence-stratigraphic framework (see the description in the SOM text).

Reconstruction of the long-term envelope and the short-term history of changes in sea level requires differing approaches. The long-term changes are believed to be mostly driven by the slow tectonic processes that change the volumetric capacity of the ocean basins. Individually, each data set on which the long-term envelope can be based must be considered relative rather than absolute measures of eustatic trends. However, a long-term curve based on global continental flooding estimates (*14*–*17*), stacked regional sea-level data (evaluated by us), and modeling results for the mean age of the oceanic crust yields consistent results. Algeo and Seslavinsky (*17*) have presented an analysis of the flooding history and hypsometry of 13 Paleozoic landmasses and estimate that the long-term eustatic highs were 100 to 225 m above PD sea level. They also conclude that Paleozoic continents experienced an additional change of ±100 m in vertical movements because of epeirogeny. The upper limits of our estimates of long-term highs are influenced by this analysis.

More-recent modeling results of the Mesozoic-Cenozoic sea floor (*18*–*20*), although based on differing assumptions, consistently point to the mean age of the oceanic crust, rather than sea-floor spreading rates or ridge volume, as potential forcing for the long-term eustatic change. Cogné and Humler (*20*) have extrapolated their modeling results back to the Paleozoic, for which direct measurements of sea-floor isochrons are not possible because of subduction. Instead, they estimate land-ocean distributions from measurements of areas of continental landmasses based on paleomagnetic reconstructions. Their results show a credible agreement between periods of high fragmentation of the continents and high global sea levels through much of the Paleozoic. One recent aspect of the modeling efforts is the conclusion that continental margins could be subjected to a substantial degree of mantle flow–related vertical motions over relatively short geological intervals. This process causes changes in local dynamic topography, which may have led to an underestimation of changes in sea level from physical data in the past (*21*).

The shorter-term changes in sea level (third- and higher-order events) were more likely mostly driven by changes in the volume of water in the world ocean through glacial (and as yet unknown) processes. The short-term Paleozoic curve as portrayed here (Figs. 1 to 3) is based on the best of several sections in an area designated the RD, in which, according to our interpretations, tectonic influences were minimal and the eustatic signal is more likely to have been preserved. Sea level–change events identified in the RDs were then sought elsewhere worldwide (in the existing stratigraphic data) and documented in designated ancillary sections (SOM text).

The previous physically estimated magnitude of the shorter-term (third- and fourth-order) sea-

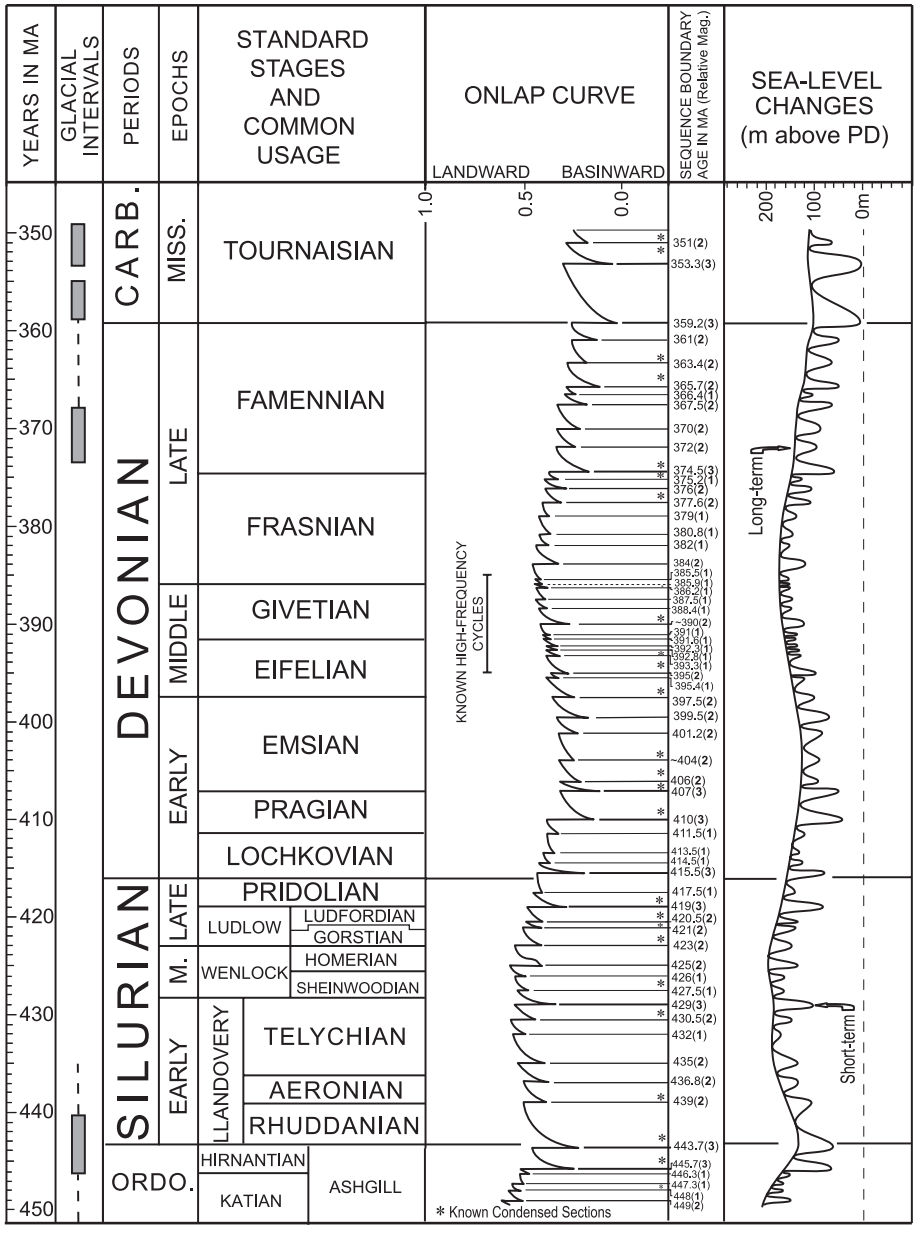

Fig. 2. Silurian-Devonian sea-level changes. See the caption of Fig. 1 for details.