Illustration

FIRST PLACE

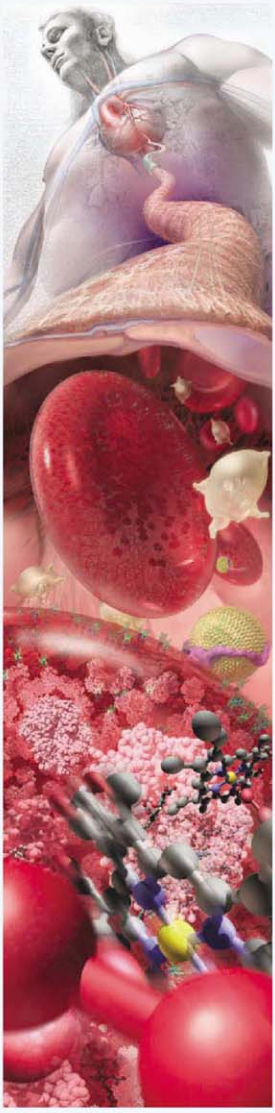
ZOOM INTO THE HUMAN BLOODSTREAM

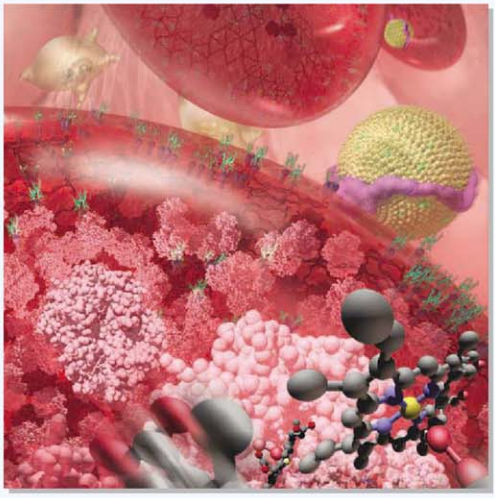
Linda Nye and the Exploratorium Visualization Laboratory,
The Exploratorium

A DISCUSSION OF THE HUMAN CIRCULATORY SYSTEM TYPICALLY BEGINS AND ENDS with the heart. But in this illustration, the team manipulates perspective to show the relationship between the tiniest oxygen atom and the comparatively giant organ. Jennifer Frazier, who directed the project by San Francisco's Exploratorium, says her team used a common technique in landscape paintings to fit multiple scales into a single image. "Something very large can appear small because it's on the horizon, and something very small can appear large because it's in the foreground."

In the image, illustrated by artist Linda Nye, a human heart is in the background and a viewer's eye follows the artery downward to an interior view of the bloodstream in the foreground. The magnification at each level of the image increases 10-fold to show red blood cells and even the oxygen atom within a heme group with colorful clarity.

The goal is to show the interactions between the macro and micro, Frazier says: "The system requires multiple scales to make things happen." The image is meant for display within museums, and its appropriateness for that audience impressed judges, says panel of finalist judges member Alisa Machalek: "It really accomplished the goals of using art to explain science." Fellow judge Michael Keegan adds, "It's just a good way of presenting that macro-micro situation where tiny parts of the circulatory system contribute to the life of the whole body."

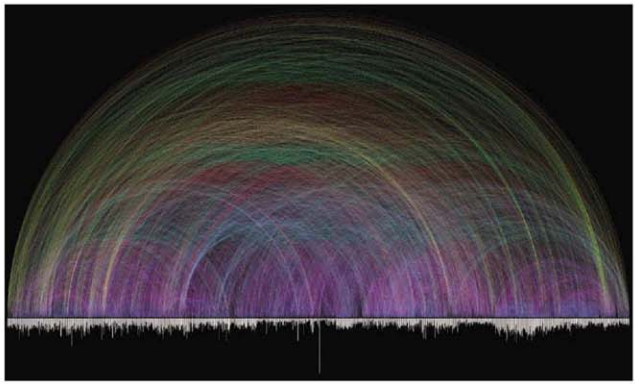




HONORABLE MENTION

VISUALIZING THE BIBLE

Chris Harrison, Carnegie Mellon University, and Christoph Römhild, North Elbian Evangelical Lutheran Church



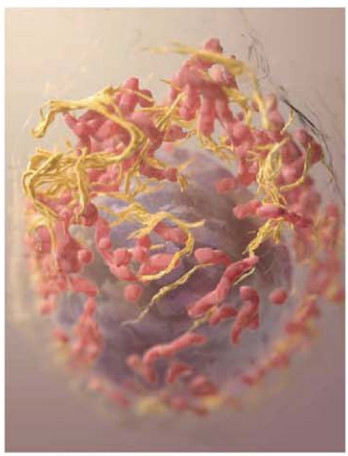
THE FIRST ILLUMINATED BIBLES were produced in the early Middle Ages by monks who painstakingly detailed illustrations for their sacred verse. Chris Harrison, a doctoral student at Carnegie Mellon University in Pittsburgh, Pennsylvania, and Christoph Römhild of the North Elbian Evangelical Lutheran Church in Hamburg, Germany, present an illustrated Bible with a modern twist. Römhild started with a list of verses in different versions of both the Old and New Testaments that referred to figures or ideas from earlier passages, then combed through both books for additional examples. Using a custom-built computer program, Harrison translated the trove of data into "Visualizing the Bible." Each bar on the graph along the bottom represents a chapter of the Bible; the bar length corresponds to the number of verses in the passage. The rainbowlike arcs represent references from a chapter in one book to a chapter in another. "It almost looks like one monolithic volume," Harrison says.

HONORABLE MENTION

3D IMAGING OF MAMMALIAN CELLS WITH ION-ABRASION SCANNING ELECTRON MICROSCOPY

Donald Bliss and Sriram Subramaniam, National Library of Medicine, NIH

THE DELICATE SWIRLS OF PINK AND GOLD IN THIS IMAGE COULD HAVE COME FROM BOTTICELLI'S brush, but there's nothing angelic about the subject, a melanoma cell. It is seen here by an ion-abrasion scanning electron microscope that uses a method of 3D imaging being developed at the U.S. National Cancer Institute. The microscope sends beams of gallium ions across an object, blasting away layers of the surface 20 nanometers at a time. By scanning each newly created surface, the microscope can compile three-dimensional images with unprecedented detail and resolution, says image creator Donald Bliss, a medical illustrator at the National Library of Medicine in Bethesda, Maryland. The images show almost too much detail—"It's like looking at a bowl of spaghetti suspended in clear Jell-O," he says—so Bliss chose to highlight some of the data. Here, he shows the nucleus as the dark sphere, engulfed by mitochondria (in pink) and endoplasmic reticulum (in gold).



Informational Graphics

FIRST PLACE

"MAD HATTER'S TEA" FROM ALICE'S ADVENTURES IN A MICROSCOPIC WONDERLAND

Colleen Champ and Dennis Kunkel, Concise Image Studios

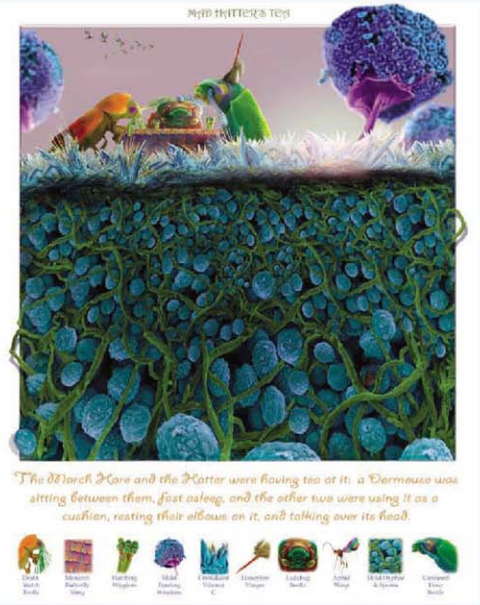
WHILE WANDERING THROUGH THE FOREST OF WONDERland, Alice stumbles upon three beetles having tea. That's not exactly how Lewis Carroll's classic tale goes, but this recreation of the Mad Hatter's tea could certainly belong in the story.

Freelance illustrator Colleen Champ produced her own version of the scene using micrographs by photomicrographer Dennis Kunkel. The goal was to demonstrate the fantastic nature of reality by arranging the actual images in fanciful ways, Champ says: "You cannot create anything yourself that hasn't already been created in nature."

She used Photoshop to transform three beetles into the Mad Hatter, March Hare, and the sleepy Dormouse. They sip tea at a table made of butterfly wings, set in a field of crystallized vitamin C while aphids fly overhead. A key beneath the main illustration identifies the source of each image, including the mold spores that make up the vast underground.

Kunkel plans to develop a series of children's books based on Champ's images.

The interplay between fact and fancy impressed the judges, who used the words "innovative" and "delightful" to describe the piece. Panel of finalist judges member Michael Keegan called it a "palatable introduction" to science, saying it provides an excellent way to attract children to the subject matter.



HONORABLE MENTION

STREAM MICRO-ECOLOGY: LIFE IN A BIOFILM

Andrew Dopheide and Gillian Lewis, University of Auckland

ONE MAN'S SLIME IS ANOTHER MAN'S BIOFILM. RESEARCH TECHNICIAN Andrew Dopheide of the University of Auckland in New Zealand spends his days studying biofilm in streams under the direction of Gillian Lewis. Hoping to foster wider appreciation for his subject, Dopheide put together an informational graphic on the science of slime. He shows different magnifications of the primary biofilm dwellers: algae, bacteria, protozoa, cyanobacteria, fungi, and viruses. Factoids containing a brief description of the organism and its role in the system accompany the images. "There are all these quite fascinating things going on in this layer of slime. It's an important aquatic ecosystem," Dopheide says. The poster has already been distributed to schools and at scientific conferences in the country.

Interactive Media

FIRST PLACE

GENOMICS DIGITAL LAB: PLANT CELLS

Jeremy Friedberg and Tommy Sors, Spongelab Interactive

"PLANTS ARE BORING." WHICH BIOLOGY teacher hasn't heard that complaint? Jeremy Friedberg and his colleagues at Spongelab Interactive in Toronto, Canada, along with Tommy Sors, a student at Purdue University in West Lafayette, Indiana, set out to give teachers an effective response with a computer program and educational game dedicated to plant biology. The Genomics Digital Lab uses flash animation and 3D graphics to present plant life in a dynamic light. As the name implies, the program focuses on the genomics approach to exploring biology. A few clicks of the mouse take users deep inside a plant cell, where they can choose among the chloroplast, mitochondria, and nucleus for further exploration. Each organelle lab contains a brief explanation of its function and a game in which students must pick the best light, water, and soil conditions for the plant to ensure the organelle's optimal performance. The goal is to help students understand the connection between the tiny organelles and the entire plant, Friedberg says: "We have to look at the whole and how something fits in that whole."

The Genomics Digital Lab enjoyed a surge of popularity when Apple Inc. posted the program on its Web site in January. To date, teachers in 22 different countries have downloaded the program, Friedberg says.

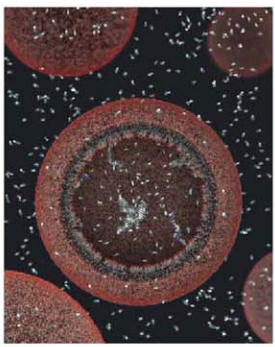
The interactive nature of the program earned high marks from the judges. "I remember studying very basic cell biology and being bored to death, but the fact that it was an interactive computer game you could get your hands on and see direct results of too much sun and not enough sun was very pertinent in this day and age when folks are so far removed from the plant and the planet," says panel of finalist judges member Malvina Martin.

HONORABLE MENTION

EXPLORING LIFE'S ORIGINS

Janet Iwasa, Massachusetts General Hospital

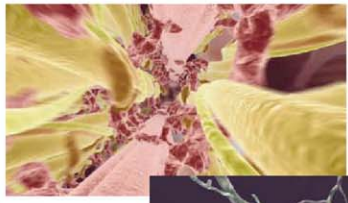
THE QUESTION OF HOW LIFE FIRST EMERGED lies at the heart of one of today's most contentious science debates. Biochemist Janet Iwasa wanted to fill an apparent gap in most documentaries on the origins of life. There were few visual explanations of how the first cells may have formed and operated on a molecular level, she says. So, while serving a fellowship at Massachusetts General Hospital, she produced this Web site using animation to illustrate topics such as how the original RNA polymers were assembled from nucleotides. See the Web site at www.exploringorigins.org.

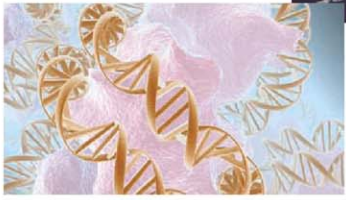


HONORABLE MENTION

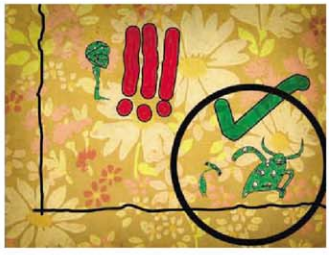
A WINDOW INTO LIFE

Travis Vermilye and Kenneth Eward





EVEN WHILE AT REST, OUR BODIES PULSE WITH furious activity. Neurons fire, cells divide, and proteins form, only to be dismantled in short order. This movie shows vignettes of the microscopic plane of life on which our everyday lives depend. Designed for display within the Cincinnati Children's Hospital Medical Center, the movie explores some of the basic science behind the hospital's research projects. Freelance illustrator Kenneth Eward and freelance animator Travis Vermilye, who collaborated to produce the film, give a whirlwind tour of the assembly-line process by which RNA builds proteins. They also sneak up close to a neural synapse as it fires a message to a nearby muscle fiber and show how the eye develops from the embryonic stage to the mature form. The goal is to present the dynamic complexity of life on the smallest scale: "I'd like people to be inspired by the beauty that goes on inside of us," Eward says.

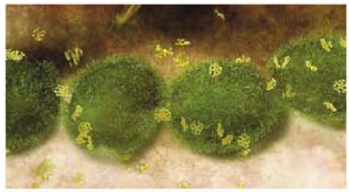


HONORABLE MENTION

SMARTER THAN THE WORM

Mirjam Kaplow and Katharina Strohmeier, Fraunhofer FIRST

WHEN THE DREADED ERROR MESSAGE FLASHES on the screen, it's easy to envision an army of malevolent gremlins wreaking havoc on your computer. The real mechanism of a computer worm or virus isn't quite that dramatic, but producer Mirjam Kaplow and Katharina Strohmeier of Fraunhofer FIRST in Berlin, Germany, play on that tension to explain how those pests operate and how computer software protects against them. "We came up with the idea of making a movie with the symbol on a metaphorical level," Kaplow says. The story takes place at the gates of a fortress city, where a guard examines each visitor before granting them access. But simple disguises—a new bow tie or a pair of sunglasses—confuse the guard, and he lets a worm slip through. While the city burns, the narrator explains how a new type of software can keep a computer smarter than the worm, whatever that worm looks like.



HONORABLE MENTION

FIGHTING INFECTION BY CLONAL SELECTION

Etsuko Uno and Drew Berry, The Walter and Eliza Hall Institute of Medical Research

IN 1960, AUSTRALIAN IMMUNOLOGIST FRANK BURNET won a Nobel Prize for his contributions to immunology. Etsuko Uno and colleagues at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia, explain Burnet's clonal selection theory in an animation of the body's response to *Streptococcus pyogenes*, the bacterium that causes strep throat. Proteins from the invader enter the lymph node and grab the attention of one of billions of B cells. That B cell then clones itself thousands of times and sends antibodies via the bloodstream to the infection site. There, the antibodies bind to the strep bacteria, acting as a red flag that alerts other immune system cells to destroy the infectious agent. "We hope that the animation will pique people's interest in how the immune system works and that they will appreciate the impact of Burnet's clonal selection theory on our understanding of the immune system," Uno says.

LETTERS

edited by Jennifer Sills

Fixing the Leaky Faucet

A. I. LESHNER'S EDITORIAL "JUST GIVE THEM GRANTS" (16 May, p. 849) is an urgent call for dedicated funding for new investigators in science. However, without a means to sustain new investigators once their laboratories have been established, another crisis will quickly follow: the inability to retain the talent brought to the bench. This leaky-faucet phenomenon is already well known to women in medicine and science, with much good will to slow down these departures but little resolution in sight. The academic and funding community must be committed to the full length of the science career, not just the early part of it. Why recruit if we cannot retain? To do so will only create disillusionment and distrust among those in whose hands the future of science lies.

JUDY ILLES

Department of Neurology, National Core for Neuroethics, The University of British Columbia, Vancouver, BC V6T 2B5, Canada. E-mail: jilles@interchange.ubc.ca

Redefining Academic Success

A. I. LESHNER MAKES SUCH A COMPELLINGLY simple recommendation in his 16 May Editorial ("Just give them grants," p. 849) that one cannot but wonder why it need be made at all. If junior academic scientists need a government-funded grant to launch their independent research career, why not just give them grants? Problem solved. However, if the academic research community is really going to tackle what is, despite the Editorial's straightforward prose, a very complicated issue, then it should also consider another seemingly simple question extracted from the Editorial's first sentence. Why is it that securing external funding for independent research is a "gold standard" for academic success, particularly in the first few years of a career spanning decades? Shouldn't the early investment in a junior faculty member's scholarly research be the responsibility of the institution hiring him or her? Might not considerations of success also include the originality of the individual's research, the contributions the research could make to the intellectual content of his or her chosen field of research, and the value of the individual as a colleague? Surely there are ways for institutions to develop internal metrics of success. So, here is another simple recommendation: It is time for academic institutions to stop ceding their promotion and tenure decisions to the NIH and other external funding bodies.

SUSAN M. FITZPATRICK* AND JOHN T. BRUER

James S. McDonnell Foundation, St. Louis, MO 63117, USA.

*To whom correspondence should be addressed. E-mail: susan@jsmf.org

Caught in the Middle?

AS A POSTDOCTORAL FELLOW ENTERING THE market for biology faculty positions, I was happy to hear that 25% of NIH Research grants are going to new investigators who have never received an RO1 (Editorial, "Just give them grants," A. I. Leshner, 16 May, p. 849). My sense of schadenfreude was fulfilled to hear that these funds will come off the backs of senior investigators who, despite clearly being deadwood, are hogging multiple grants. But then I wondered what will happen to me in the phase between being a new investigator and a senior investigator. Surely there must be some intermediate step. The transformation from plucky young innovator to conservative graybeard cannot be instantaneous. After that first RO1, I will have some publications and some data, but not as many as my more senior competitors. And the funding situation for me will be even tighter than before, because a significant fraction of funds will be going to those undeserving, knee-biting, new investigators. Additionally, I will have reached a stage where I have significant responsibilities—graduate students and postdocs will be depending on me for their career advancement and livelihood. So I am left asking, what will happen to new investigators once their honeymoon is over?

SANJAY S. P. MAGAVI

Picower Institute for Learning and Memory, Massachusetts Institute of Technology, Cambridge, MA 02139, USA. E-mail: smagavi@mit.edu

Just Give Them Fellowships

IN THE RECENT EDITORIAL HIGHLIGHTING THE issues faced by young academics in securing funding for their own research ("Just give them grants," 16 May, p. 849), A. I. Leshner touches on an important point: the subversion of personal research interests during postdoctoral training periods. As an example, UK government-funded research

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.

How cancer spreads

1785

Bidding high!

1788

councils typically expect grant recipients to be appointed at a higher education institute, with a minimum position of Lecturer, before applying for a research grant. As a result, the pressure on freshly minted Ph.D.'s in academia is, as stated, to follow the path of postdoctoral research on established projects, rather than trying to secure their own funding.

Clearly, the UK research councils place strong emphasis on the training of postgraduates, but there appears to be little incentive for those students to remain within academia in the hope of pursuing their own lines of research by obtaining individual postdoctoral fellowships (*1*). Such fellowships provide opportunities for young scientists to "make their mark" in their respective fields without being tied to lines of research that they do not wish to pursue. By awarding more fellowships, funding organizations may retain more individuals to contribute to the continuity of scientific enterprise and, in turn, fellows may find getting that first grant or tenure position a little bit easier.

ANGELO P. PERNETTA

CEH Wallingford, Centre for Ecology and Hydrology, Benson Lane, Crowmarsh Gifford, Wallingford, Oxfordshire OX10 8BB, UK. E-mail: anpp@ceh.ac.uk

Reference

1. Research Councils UK (www.rcuk.ac.uk).

Destabilizing the Pyramid Scheme

A. I. LESHNER'S EDITORIAL "JUST GIVE THEM grants" (16 May, p. 849) suggests yet another well-meaning "fix" for the poor funding support for advancing research careers of postdocs and young investigators in the United States, especially in the biomedical fields. Setting "funding quotas" by earmarking a percentage of new grants, those from the NIH in particular, to investigators younger than a certain age probably will not aid a situation that is, largely, a pyramid scheme.

Pyramid schemes provide considerable incentives for those at the top [funded principal investigators (PIs), tenured faculty, and most medical school faculty] and virtually no tangible incentive to those at the bottom, who support the scheme at the laboratory bench (graduate students, postdocs, and research associates). Perhaps it is time for some disincentives for those at the top. Some suggestions follow.

(i) Any grant proposal that gives salary support for postdocs must also include funds for postdoc-only projects (mini-grants within a grant). (ii) Any PI who proposes to put postdocs on the grant payroll should have documentation that he or she has also done a stint as a postdoc. Who better knows the value of mentoring than those who have been mentored? (iii) Postdoc

training is a disheveled cottage industry. Establish a central clearinghouse of "post-doc specialists" akin to "Matching Day" for medical school graduates seeking advanced training in limited residency training positions. (iv) If postdocs are to be a necessary part of the research enterprise, then PIs, or their departments or institutions, should provide some guarantee of financial support beyond the tenure of a particular grant to those postdocs who provide credible service to that grant but who cannot find their own support elsewhere.

DUAINE R. JACKOLA

8436 Second Avenue South, Bloomington, MN 55420, USA. E-mail: drjackola@q.com

Biotechnology Innovation in Africa

AFRICA IS PRESENTLY AT THE PRECIPICE OF A socioeconomic renaissance. However, diseases such as malaria, AIDS, and hypertension remain common and important health problems facing the continent. The recent Policy Forum by T. J. Tucker and M. W. Makgoba ("Public-private partnerships and scientific imperialism," 23 May, p. 1016) should invoke further discussions on new approaches for increasing the effectiveness of global efforts against neglected African diseases.

In the 1970s, 70% of resource flows from the United States to the developing world were from official development assistance and 30% were private. Today, 85% of resource flows from the United States to the developing world are private and 15% are public. These changes in resource flows reflect the emergence of the private for-profit sector and the nongovernmental sector as crucial participants in the development process (*1*). They have formed many new alliances and programs in addition to government aid. Unfortunately, when funds for these programs run out, the progress often stagnates or even reverses. Few public and private donor programs exist to support more sustainable programs, such as small indigenous African bioscience businesses that are evolving biotechnological innovations specifically relevant to the region.

Developing local biotechnology capacity is essential for ensuring availability and access of health care products in a sustainable manner. Several governments in sub-Saharan Africa (such as Nigeria and South Africa) recognize this and have increasing public sector support for biotechnology innovation and entrepreneurship to encourage small indigenous biotechnology companies that are working to translate relevant research discoveries to usable products. National and regional public policies and priorities are encouraging the local development and manufacture of essential rapid diagnostics and genuine medicines that are critical to health care needs of the people, as a way of making these products and services more readily accessible to more people. In response, an increasing number of entrepreneurial scientists of African descent (led by Africans in The Diaspora) are establishing local, small, socially responsible biotechnology enterprises. These efforts are inspired primarily by necessity and a focus on translating relevant discoveries to products and services that address regionally prevalent diseases.

A model that has not gained broad acceptability among private donors is direct support in the form of pass-through grants to small indigenous for-profit bioscience businesses. Robert Grant had proposed a similar context in his "Research in situ" model (*2*, *3*). By working with indigenous for-profit bioscience companies, multilateral funding organizations and agencies can potentially deliver more sustainable change. This is especially crucial because many developed nations have modeled small businesses as the core of their biotechnology development strategy, strengthened through government and investor-backed small business grants and loan programs. Streamlined donor support to indigenous small bioscience businesses can enable the development of specific new products and services consistent with the socioeconomic needs of the continent. Additionally, through expanding collaborations with universities and institutes, the indigenous biotechnology firms are evolving to create open avenues of knowledge sharing to create these products in a sustainable manner. This can potentially drive the development of biotechnology on the continent.

EDDY C. AGBO,[1]* SIMON AGWALE,[2] CAMELLUS O. EZEUGWU,[3] BOITUMELO SEMETE,[4] HULDA SWAI,[4] ANTHONY IKEME,[5] RICHARD I. SOMIARI[6]

[1]Fyodor Biotechnologies, 26 Ogui Road, Enugu, Nigeria, and 3607 Frankford Avenue, Baltimore, MD 21214, USA. [2]Innovative Biotech Ltd., 1 Abdu Abubakar Street, GRA, Post Office Box 30, Keffi, Nasarawa State, Nigeria. [3]The Johns Hopkins University School of Medicine, Department of Medicine (JH Cardiovascular Group Inc.), Baltimore, MD 21201, USA. [4]Council for Industrial Scientific Research (CSIR)—Polymer and Bioceramics, Post Office Box 395, Pretoria, South Africa. [5]Clintriad Pharma Services, Exton, PA 19341, USA. [6]ITSI-Biosciences, Johnstown, PA 15904, USA.

*To whom correspondence should be addressed. E-mail: eddy.agbo@fyodorbio.com

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CORRECTIONS AND CLARIFICATIONS

Reports: "Alignment uncertainty and genomic analysis" by K. M. Wong *et al.* (25 January, p. 473). C. Dewey, A. Schwartz, N. Bray, and L. Pachter kindly directed our attention to an inconsistency in Fig. 1, which shows six different estimated trees for seven different alignments of the open reading frame (ORF) YPL077C, and the Supporting Online Material containing the maximum likelihood estimates for the 1502 ORFs that we examined. When equally likely trees are accounted for, maximum likelihood yields only four different trees for YPL077C. We intended to illustrate an extreme example in which alignment uncertainty produces different estimates of phylogeny, and not to select among equally likely trees to make the differences as great as possible. Indeed, there was no reason to do so, because we could have illustrated the point with five other ORFs, all with one estimated tree for each alignment and resulting in six different trees for the seven alignment treatments (see the Supporting Online Material). Of potentially more importance, however, our results did not account for equally likely trees, something that occurs in 1.5% of the phylogenetic analyses. Figure 1 repeats the analyses performed in the original Report and accounts for equally likely trees. As before (Fig. 2A), we see a significant positive correlation between alignment distances among alignment treatments and the distances between trees estimated from the alignments. Accounting for equally likely trees does not change the relation between alignment variability and phylogeny estimation we originally discussed.

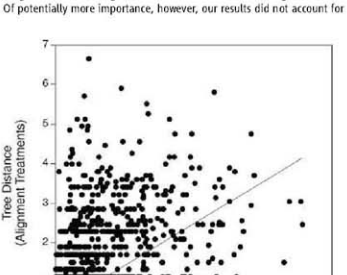

Fig. 1. Positive correlation between the Robinson and Foulds [D. Robinson, L. Foulds, *Math. Biosci.* **53**, 131 (1981)] measure of topological distance among trees estimated from different alignment methods and alignment variability among alignment treatments (Spearman's rank correlation: $r_s = 0.52$, $P < 0.0001$; note that the correlation coefficient changes from $r_s = 0.53$ to $r_s = 0.52$ when equally likely trees are accounted for).

ECONOMICS

For Equality, Education Matters

Thomas Lemieux

CREDIT: CURTIS PARKER/GETTY IMAGES

Throughout most of the 20th century, the economic performance of the United States was simply remarkable. Fueled by technological advances and an ever-more-educated workforce, productivity grew steadily and standards of living of each generation far exceeded those of the preceding one. Defying the old adage that there is a tradeoff between equality and efficiency, all this growth was achieved while the gap between rich and poor was declining. Furthermore, America's education system delivered on the promise of equal opportunity by making a good education, the best gateway to well-paying jobs, accessible to most irrespective of their background and circumstances. By the 1970s, the United States was not only the richest country in the world, it also boasted the most educated population while inequality was no higher than in most other rich countries.

But then something happened. Beginning in the 1970s, productivity stalled and inequality started growing rapidly. The combination led to declining incomes and standards of living for a substantial fraction of the U.S. population. To make things worse, the great progress in higher education that had run through most of the 20th century came to an abrupt halt. A college degree would have guaranteed to most young people standards of living as good as or better than those of their parents, but the fraction of young Americans completing college hardly changed in the last quarter of the 20th century.

The Race Between Education and Technology

by Claudia Goldin and Lawrence F. Katz

Belknap Press (Harvard University Press), Cambridge, MA, 2008. 496 pp. $39.95, £25.95, €28. ISBN 9780674028678.

Not surprisingly, these developments have had many economists scratching their heads and wondering what went wrong in the last few decades. With inequality now reaching highs not seen since the Great Depression, considerable effort has gone into understanding why inequality increased so much. Many have pointed their finger at technological change. For sure, technological progress has always been a leading source of the growth of nations. But the benefits of technological change are not evenly shared among the whole workforce (*1*). Globalization and offshoring, institutional factors like the minimum wage and unionization, and broader social norms about how much inequality is acceptable in a society have also been suggested for explaining the growing gap between rich and poor.

The key contribution of Claudia Goldin and Lawrence Katz's masterful *The Race Between Education and Technology* to the inequality debate is to take another look at the recent changes through the lenses of history. Doing so yields a number of important insights. In particular, history tells us that though technological change may be a source of growing inequality, this cannot be the whole story. Indeed, there have been other historical episodes of fast technological change, such as electrification in the 1910s and 1920s, that did not result in higher inequality. Why is that? The book's main conclusion is that in those days rapid technological change was accompanied by stunning gains in educational achievement that provided enough qualified workers to meet the demands of an increasingly technologically sophisticated economy.

As is often the case in economics, this story boils down to supply and demand. Technological change increases the demand for highly educated workers who can most effectively use the new technologies in the workplace. If the supply of highly educated workers does not increase fast enough, however, firms start bidding up the wages of these workers to attract them, while others who lack proper qualifications lose ground. So, as the book's title suggests, whether inequality increases or not is best thought of as an ongoing race between education and technology.

Combining this simple but appealing idea with a deep knowledge of the histories of the U.S. labor market and educational institutions, Goldin and Katz (economics professors at Harvard) conclude that whereas education was winning the race for most of the 20th century, technology caught up in the 1970s and has since prevailed. The authors' most insightful point is that the root cause of the recent growth in inequality is not faster technological progress during the past three decades but rather the surprising stagnation in the level of education of young Americans.

Besides addressing the increasing inequality, the book provides a fascinating history of the American education system over the last century that is a must for anybody interested in this important topic. Although the United States may be best known for its top private universities that are the envy of the world, Goldin and Katz convincingly show that the source of the country's long educational supremacy had much more modest origins. By 1940, most young Americans attended publicly funded high schools, a situation simply unthinkable in the rest of the world at the time. Post–World War II, the G.I. Bill continued from where the high school movement of 1910 to 1940 had left off, opening college to the masses.

But things have very much changed since then, and many other countries have now caught up. Young Americans no longer have the educational advantage that their parents or grandparents enjoyed over the rest of the world. For the United States to regain its leadership role and win the race against technology, more resources must go to making sure high school students are college-ready and that those who are college-ready have financial access to higher education. The difficulty is that doing so will cost money. As the analysis presented by Goldin and Katz indicates, the well-being of the new generations will critically depend on whether America is up to this challenge.

The reviewer is at the Department of Economics, University of British Columbia, Vancouver, BC V6T 1Z1, Canada. E-mail: tlemieux@interchange.ubc.ca

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HISTORY OF SCIENCE

Regime Change in Scientific Depiction

Alan Richardson

It is nearly universally accepted that science aims for an objective view of the world—and that this is a virtue of science. Indeed, it can seem axiomatic that if you are seeking the truth about nature, then you ought to approach nature objectively. What other option is there? A knowledge-seeker, surely, ought not approach nature with a socially inculcated or individual bias, with emotional attachment to a theoretical view already in hand, or with an aesthetic or moral or financial interest in the subject. Therefore, when scientists hear that Lorraine Daston and Peter Galison, two of the world's most distinguished historians of science, claim in *Objectivity* that, in a crucial sense, science only began to strive for objectivity in the 19th century and is now moving away from it, they might worry that once again social historians of science are attempting to debunk the practices and goals of science.

This would be an unfortunate reaction, for although Daston (Max Planck Institute for the History of Science, Berlin) and Galison (Harvard University) are indeed historicizing the notion of objectivity and making important claims about its place in the history of science, theirs is not a project of unmasking or debunking. The point of their enterprise is neither to look at how claims to objectivity disguised powerful social or gender bias nor to dismantle the concept of objectivity. They take for granted the complexity in the notion of objectivity, as they take for granted both the social character of scientific practice and the complicated and varied social places of science across times and cultures. What they are interested in are the 19th-century rise of an account of science that stressed science's objectivity and how the science framed by that account differed from science earlier and later.

Objectivity is, for Daston and Galison, a specific epistemic ideal of science, entailing certain epistemic virtues the scientist ought to have. These virtues are motivated by specific anxieties about obstacles to knowledge—and they are secured not only by exhortations in their favor but also by practices that structured scientific work in accordance with them. Those practices were forms of "collective empiricism" employed to implement the regulative ideal of objectivity. None of this means that other respectable and equally empirical regimes of science are not possible, and the authors argue that such regimes have been and are now being pursued.

Objectivity
by Lorraine Daston and Peter Galison
Zone, New York, 2007. 504 pp. $38.95, £25.95. ISBN 9781890951788.

The authors provide their argument not in abstracto but through examination of distinct practices of one widespread type of scientific activity: the making of scientific atlases. They contrast regimes of objectivity (mechanical and structural) with truth-to-nature and expert judgment. At the end, they suggest that recent image galleries in science are again moving in new directions: away from representation of already existing objects and toward presentation of objects made in the very process of depicting them—as in the famous nanotechnological depiction of xenon atoms formed into an advertisement for IBM, an image produced by the very probe that arranged the atoms.

The authors' argument here is complicated but fascinating (and, because the argument is about images, the book is beautiful). Daston and Galison hold that notions of objectivity and subjectivity as they have been deployed since the 19th century were forged in the crucible of German philosophy and expressed new anxieties about the self as the chief obstacle to accurate knowledge of the world. The 19th-century atlas makers, therefore, carefully attempted to remove their own judgment from their images, often deploying new photographic technologies to keep the images free from their own interventions. Thus, Daston and Galison call the scientific project of the day "mechanical objectivity," with the machine as the mindless, will-less helper (the camera renders depiction objective precisely because it neither sees nor interprets). The authors contrast this "blind sight" with an 18th-century practice of explicit intervention into atlas images, images meant to depict not individual specimens but rather the ideal type of the object. These earlier images required the theoretical knowledge of the atlas makers, who carefully policed their illustrators' drawings not to erase idealizations but to guide them. Similarly, Daston and Galison argue that by the mid-20th century a more self-confident and widely dispersed community of scientific experts again changed the practices of making and reading atlases, substituting a regime of expert judgment for the practices of mechanical objectivity. These later scientists again often substituted drawings for photographs and again self-consciously altered images, but now not to depict ideal types but rather to help train the reader into having an expert eye.

Observer as machine. In his figures, such as these blood crystals, Otto Funke "attempted to reproduce the natural object in its minutest details ... above all things prohibiting the slightest idealization."

CREDIT: OTTO FUNKE, PLATE 10, FIGURE 2, IN (1)

Are not all these regimes, because they are all concerned with accurate representation of nature, in some sense, regimes of objectivity? Certainly. But to rest content with this "in some sense" would be to limit, within historical inquiry, the motive to treat objects of inquiry with the specificity and precision that guide Daston and Galison's "mechanical objectivity." It would also leave us fewer conceptual tools for thinking about both the newly aesthetisized, newly commercialized, newly interactive, and newly object-creating images of 21st-century science and the new type of scientist who makes such images.

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The reviewer is at the Department of Philosophy, University of British Columbia, Vancouver, BC V6T 1Z1, Canada. E-mail: alanr@interchange.ubc.ca

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ASSESSMENT

School Performance Will Fail to Meet Legislated Benchmarks

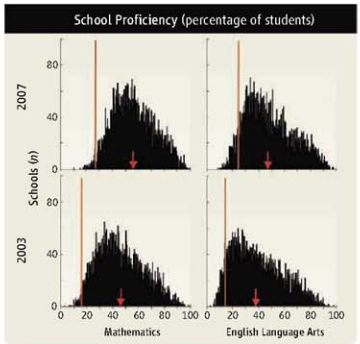
Federally mandated progress goals may translate into widespread failure of California elementary schools.

M. J. Bryant,[1,4] K. A. Hammond,[1] K. M. Bocian,[2] M. F. Rettig,[3] C. A. Miller,[1] R. A. Cardullo[1]*

There is widespread concern that U.S. students entering college do not have the educational foundation to succeed in introductory science courses. Mathematics is of particular interest because proficiency in mathematics may predict performance in introductory college science courses (*1*). In the United States, numerous educational reforms (*2*) focus on the accountability of schools for proficiency (mainly in mathematics and English Language Arts). However, agreement on proficiency goals that accurately reflect the needs of a diverse student population has been problematic.

Downward trends in U.S. student test performance from 1963 to 1980 led to recommendations for increased accountability for schools and school districts (*3*). The Improving America's Schools Act (IASA), Title I, legislation in 1994 (*4*) mandated that states should set standards by 1999 and have in place assessments to measure achievement by 2000. The "No Child Left Behind Act of 2001" (NCLB), which mandates that 100% of students will be proficient in English Language Arts (ELA) and mathematics by 2014, is the strongest current implementation of this accountability (*5*).

Under NCLB, a school's progress toward having 100% of students proficient is monitored by Adequate Yearly Progress (AYP), a series of calculated academic performance factors for each state, local education agency, school, and numerically significant student subgroup within a school [English language learner (ELL), socioeconomic status, etc. (table S1)]. All states must use as AYP criteria: (i) the percentage of students scoring proficient or advanced on state standards tests in ELA and mathematics, (ii) standardized testing participation rate, and (iii) increases in the high school graduation rate. However, each state determines its own specific assessments and cutoff scores for proficiency, and these vary widely from state to state (*6*). All states are required to report proficiency in mathematics and ELA.



Divergent proficiencies of California schools. The proficiency of California elementary schools in 2003 (n =4850) and 2007 (n = 4917) is defined by the percentage of total students in that school who achieved a score of proficient or advanced. Red line, AYP benchmarks; arrow, statewide mean school proficiency.

California also includes additional subjects such as science as part of its Academic Performance Index (table S1).

Although NCLB mandates an evidence-based, research-driven approach to educational reform, each state determines how the 2014 benchmark of 100% proficiency will be achieved. This presumably allows each state to look at local conditions and to tailor programs, assessments, and sanctions to reach the 2014 target. In reality, lack of consensus about proficiency benchmarks makes it difficult to assess the value of NCLB as a research-driven, national-scale force for education reform (*7*–*13*). Nonetheless, it is possible to analyze the data from individual states to determine whether NCLB targets will be met in that state (*13*).

California, with over one-eighth of the U.S. population, has comprehensive data for AYP analyses. The state has (i) a large number of schools and accessible test results, (ii) a sufficient number of population subgroups identified by NCLB legislation, and (iii) a consistent standardized assessment tool for monitoring gains in student learning across schools. We used data from California elementary schools to ask if achievement gains will reach 100% proficiency by 2014. Although this question has been addressed elsewhere (*14*, *15*), the analyses reported here raise questions about the distribution of school-level achievement in terms of the specific test subject and vulnerable subgroups of students.

Evaluating School Performance

We collected data available through the California Department of Education's accountability progress reporting system and extracted the following data for all students and numerically significant subgroups within elementary schools: the number of students tested and the percentage of students scoring proficient or advanced for both the mathematics and ELA test. We employed linear, polynomial, and logistic models to make comparisons with state and federal growth targets for students scoring proficient or advanced within schools (*16*).

A school is held accountable to a specified percentage of students scoring proficient or advanced and, if it fails to meet this, the school may be sanctioned. This holds true if either the targeted percentage of all students in a school or the percentage of any numerically significant subgroup fails to reach the annual benchmark for either mathematics or ELA tests. We define the AYP criterion that matters from a legislative and school perspective as the lowest percentage of students scoring proficient or advanced on either test and from any group or subgroup (SOM), because it is the lowest percentage that may initiate sanctions.

Insufficient Achievement Gains

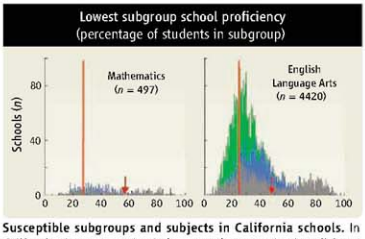
Students in California elementary schools show a wide range of proficiencies in mathematics and ELA (see chart, above). From 2003 to 2007, three evident trends are that (i)

[1]Department of Biology, University of California, Riverside, Riverside, CA 92521, USA. [2]The ALPHA Center, University of California, Riverside, Riverside, CA 92521, USA. [3]Department of Chemistry, University of California, Riverside, Riverside, CA 92521, USA. [4]School of Critical Studies, California Institute of the Arts, Valencia, CA 91355, USA.

*Author for correspondence. E-mail: cardullo@ucr.edu

overall performance is higher for mathematics than for ELA; (ii) in both subjects, the mean school proficiency increased; and (iii) there has been negligible reduction in interschool variation as would be implicit in a target of 100% proficiency.

For ELA, the logistic model best reflected the observed achievement gains. For mathematics, it was the polynomial model (table S2). All models estimated average annual growth rates under 4% from 2003 to 2007. However, to meet the goal of 100% proficiency mandated for 2014, the AYP targets designated by Californian and federal legislation will increase annually by 10.8% (ELA) and 10.5% (mathematics) from 2008 onward. We predict that ~50% of all California elementary schools will fail to meet AYP by 2011 (fig. S1). Our candidate models permitted optimistically rapid acceleration in student achievement. However, both logistic and polynomial models indicate a deceleration in achievement gains. The data currently available suggest that a large number of schools (and thus students) will not make the 2014 target of 100% proficiency.



Susceptible subgroups and subjects in California schools. In California elementary schools (n = 4917), more school proficiency failures are due to ELA within the ELL student subgroups (year 2007). The subgroup school proficiency is defined by the lowest percentage of students within a subgroup achieving a score of proficient or advanced. ELL students, green; Socioeconomic Disadvantaged students, blue; all other students, gray. Red line, AYP benchmarks; arrow, statewide mean school proficiency based on all students.

We asked which group or subgroup reflected the lowest level of proficiency for each school and if that level of proficiency was based on the mathematics or the ELA test (see chart, above). For most schools, the greatest risk of failing AYP lies with ELA proficiency. Additionally, it is the Socioeconomic Disadvantaged and ELL subgroups that are most likely to fail to meet AYP in California. These data suggest that very little change in this pattern can be anticipated over the next 5 years (fig. S2).

Modest Gains Will Not Meet Goals

We demonstrate that nearly all elementary schools in California will fail to meet the AYP requirements for proficiency by 2014. Recent gains in the statewide percentage of students scoring proficient or advanced in California have been used to suggest that accountability initiatives such as NCLB are effective in causing increased student learning. However, these documented gains for state-level performance conceal the fact that it is individual schools that are sanctioned under NCLB (*17*). Ignoring the variation around statewide averages obscures important patterns and information that may guide future professional development, the creation of new assessment tools, or legislation.

California's large, diverse public school population allows data on trends in various subgroups to be examined for significant differences with regard to AYP. Within a school, the performance of just one subgroup on one test subject can determine whether that school will meet AYP and escape sanctions. Redirecting the focus to the lowest performing subgroups at each school results in a different distribution in school performance that reveals a profound acceleration in the date at which schools will fail to meet AYP.

The weakness of ELA progress suggests that more emphasis should be placed on ELA, although that would be a shortsighted solution. Schools are also in need of support in mathematics, for which we predict nearly 100% failure, with current approaches, to meet AYP by 2014. A student's success in further education depends on the ability of that student's schools from kindergarten through completion of high school to deliver an effective curriculum that includes both ELA and mathematics, as well as the social and natural sciences. The data examined here suggest that the elementary schools in California are not meeting these teaching challenges and that resources to improve the situation are not available or have not been applied to date.

Accountability of schools is useful only to the degree that the assessments are valid and reliable. The assessment data must also be analyzed in a meaningful way that can positively affect instruction. By focusing the attention on the central tendencies of the highest performing students (proficient and advanced), we risk ignorance of the progress of the lower-performing students—ignorance that potentially leaves behind those who were to be served by NCLB. The richness in the current California data set is compromised because the categories below proficient are not routinely examined for gains. (California has three lower-performance levels: basic, below basic, and far below basic). Because the lower proficiency groups are not usually analyzed, we cannot adjust and apply interventions for these troubled students.

Future educational reform legislation would benefit from a comprehensive research focus. Reforms should tie educational experiences to instructional challenges experienced by a particular school, focusing each school's own resources to serve its own unique student population. As called for in "A Nation at Risk" (*3*), we must not lose sight of the importance of educating our children well. From providing a well-educated voting public to improving the numbers, preparation, and diversity of our college-bound students, this mission deserves our greatest effort.

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Supporting Online Material
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PHYSICS

For Quantum Information, Two Wrongs Can Make a Right

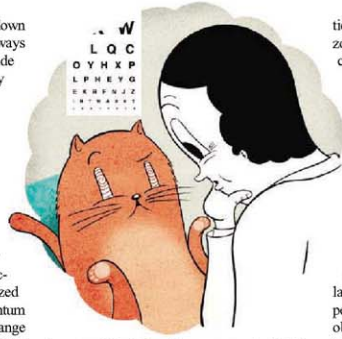
A channel too noisy to send quantum information can send secret messages, and, when combined with a similarly noisy channel, can reliably send quantum states.

Jonathan Oppenheim

Can you reliably send information down a telegraph wire that doesn't always transmit signals correctly? Claude Shannon put classical information theory on a firm footing when he showed that you can correct for transmission errors as long as there is some tiny correlation between what gets sent and what is received. What's more, Shannon quantified how much information could be reliably communicated. From its onset, classical information theory was intimately entwined with communication. The birth of quantum information theory began from an apparently different direction—cryptography—when it was realized that if you can reliably send someone quantum states, then you can use those states to exchange private messages that cannot be cracked by even the most powerful computer (*1*). This cannot be done classically without exchanging a physical key beforehand that is as long as the message you want to send. However, we are still wrestling with the corresponding question that was so central to classical information theory: How much quantum information can we reliably send down a noisy channel? On page 1812 of this issue, Smith and Yard (*2*) have discovered that we may be further from answering this question than we think, but that intriguing clues might come from the very place that initially sparked our interest in quantum information: cryptography.

Classically, a telegraph wire that is so noisy that no information can be reliably sent through it is useless. These are called zero-capacity channels. But what about the quantum case, such as trying to send information (which might be conveyed by the polarization of a single photon) through a fiber-optic cable that is so noisy it cannot be used to send any quantum state reliably?

Because our intuition tends to be classical, it was generally believed that a channel that cannot convey quantum information would also be useless. Yet a few years ago, the Horodecki brothers and I found that although these channels cannot be used to send quantum states, they can be used to send classical private messages. Indeed, one can classify all states that, if shared over some channel, are private (*3*). What's more, this privacy is verifiable, which means that practical cryptography can be performed over these zero-capacity fibers (*4*). The belief that quantum cryptography required being able to reliably send quantum states turned out to be wrong.



Quantum blindsight. "You appear to be blind in your left eye and blind in your right eye. Why you can see with both eyes is beyond me..."

Now, Smith and Yard, using results from (*5*), have shown a remarkable property of these zero-capacity quantum channels that can send private messages: They can be combined with another channel that also has zero capacity and can be used to convey quantum information. To find that two zero-capacity channels have finite capacity is a bit like finding out that 0 + 0 = 1 (see the illustration). Each channel individually is useless for sending quantum information, but when used together, they can be used to reliably send a quantum system in any state.

Despite how perplexing this result appears from a classical perspective, there is a fairly simple way to illustrate it. Let us start with the main idea behind cryptography. Consider two parties, Alice (A) and Bob (B), who can talk on the telephone and exchange quantum states—for example, polarized photons or qubits. These are represented by vectors in a linear superposition of two states, $|0\rangle$ and $|1\rangle$, so that the horizontal polarization of a photon is $|0\rangle$, the vertical polarization is $|1\rangle$, and linear superposition can give rotations to any angle. Imagine that Alice and Bob can succeed in sharing a maximally entangled quantum state whose wave function ψ_0 can be represented as $|\psi_0\rangle = (|00\rangle_{AB} + |11\rangle_{AB})/\sqrt{2}$. In this case, Alice and Bob have their qubits in a superposition of the $|00\rangle$ quantum state and $|11\rangle$ state, with Alice (A) possessing one of the qubits and Bob (B) in possession of the other.

This $|\psi_0\rangle$ state is pure, meaning that nothing in the external world can be correlated with it. As a result, Alice and Bob can perform measurements in this $|0\rangle$, $|1\rangle$ basis and obtain a string of correlated and secret bits (their measurement outcomes will be that they each obtain 0 or each obtain 1). This string can then be used to share a private message (*6*). Any channel that can be used to share $|\psi_0\rangle$ can be used to share any other state of their choosing and is said to have positive channel capacity. Likewise, if they can share the state $|\psi_1\rangle = (|00\rangle_{AB} - |11\rangle_{AB})/\sqrt{2}$, which is also maximally entangled but has negative phase, then they can also share a private message and send quantum states.

Now, consider a channel that half of the time results in $|\psi_0\rangle$ being shared and the other half of the time results in $|\psi_1\rangle$ being shared. One can show that this channel can only send classical messages—it cannot create entanglement unless $|\psi_0\rangle$ is shared more often than $|\psi_1\rangle$ (or vice versa). To make it more interesting, the channel also sends a flag—an additional state that labels which of the two maximally entangled states has been sent. If Alice and Bob can distinguish the two flags by performing measurements on them, then they will know which entangled state they share, and they can then send private messages or quantum states as before. They can even perform a correction to the state to convert $|\psi_1\rangle$ into $|\psi_0\rangle$.

As it turns out, there exist flags that can be completely distinguished when Bob holds the entire flag, yet are arbitrarily difficult to distinguish when Alice and Bob hold different parts of the flag and must perform measurements on them in separated labs (*7*) (even if they could communicate classically with a

Department of Applied Mathematics and Theoretical Physics, University of Cambridge, Cambridge CB3 0WA, UK. E-mail: jono@damtp.cam.ac.uk

CREDIT: RYAN SNOOK

telephone). In such cases, they will hardly ever know whether they share $|\psi_0\rangle$ or $|\psi_1\rangle$, and their ability to send quantum states to each other is arbitrarily close to zero (one can make it exactly zero by adding small errors). However, this state is still useful for sending private messages, because Alice and Bob can still just measure as they did before in the $|0\rangle$, $|1\rangle$ basis to obtain a secret key. An eavesdropper may know whether they share $|\psi_0\rangle$ or $|\psi_1\rangle$ but not whether they obtained $|00\rangle$ or $|11\rangle$ after measurement. Thus, channels that produce these flagged states can be used to share private messages, but they cannot be used to send quantum information—they have zero quantum capacity.

Now consider another zero-capacity channel, an erasure channel, that, with probability ½, lets the quantum state through perfectly, and the rest of the time it erases the state; the receiver Bob knows an error occurred because he will measure the error state $|e\rangle$. Such a channel turns out to be useless by itself for sending quantum information, but if Alice first uses the previous zero-capacity private channel and then puts her half of the flag down the erasure channel, then half of the time Bob can combine Alice's part of the flag that he receives from this channel with the other half that he received from the zero-capacity private channel. He can then distinguish the flag. So, half of the time, he will know whether they share $|\psi_0\rangle$ or $|\psi_1\rangle$, and he can perform a correction so that they both share the $|\psi_0\rangle$ state. This means that ¼ of the time, Alice and Bob share $|\psi_0\rangle$ instead of $|\psi_1\rangle$. This is significantly greater than half the time, and enough to create entanglement and get a positive channel capacity.

By using both the zero-capacity private channel and the zero-capacity erasure channel together, Alice and Bob can send any quantum state reliably. In the case above, the inputs that Alice sends through the two channels are not even entangled, but only classically correlated. What's more, this procedure can be easily generalized. All cryptographic protocols must distill the private states of (*3*), and the above protocol can be adapted to work for all of them.

This result raises many questions, not the least of which is what this work may say about the yet unknown formula for quantum capacity. We do not know the optimal procedure for activating a private channel, whether every channel that has zero capacity (but is not classical) can have positive capacity when combined with another zero-capacity channel, or even whether every such zero-capacity channel is also a private channel. Whatever the answers, it is clear that the structure of quantum information theory is much richer than most of us ever anticipated.

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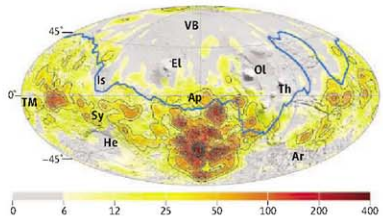
PLANETARY SCIENCE

The Past Martian Dynamo

Numerical dynamo modeling studies may explain the observation that strong magnetic fields are only found in Mars' southern hemisphere.

Benoit Langlais[1] and Hagay Amit[2]

Measurements by Mars Global Surveyor (MGS) have revealed intense magnetic anomalies mostly located south of the crustal dichotomy, the topographic boundary separating the southern cratered highlands and the northern smooth lowlands. Assuming the dynamo of Mars was similar to that of Earth—dipolar, axial, and centered, the magnetic dichotomy implies that the magnetization of the northern hemisphere was erased at some time, and thus that the dynamo stopped operating very early in its history (*1*). On page 1822 of this issue, Stanley *et al.* propose an alternative model in which the dynamo is driven by a hemisphere-scale heat flux pattern at the core-mantle boundary (CMB) (*2*). The proposed thermal constraint is compatible with martian mantle convection models (*3*) and can also explain the crustal dichotomy (*4*). In this new scenario, the much weaker crustal magnetization in the northern hemisphere is not a result of a post-dynamo process such as a giant impact (*5*), but rather, it was never magnetized in the first place.



A magnetic dichotomy. Predicted magnetic field intensity (nT) at 300 km altitude (from (*17*), iso-contours are 25 nT), on top of a shaded relief of the martian surface. Northern hemisphere magnetic field anomalies are of the same order of magnitude as terrestrial magnetic field anomalies at similar altitude, and approximately one-tenth of what is measured in the southern hemisphere. The large impact craters, as well as the large volcanic provinces, show no appreciable magnetic fields at high altitude. Blue line represents the crustal dichotomy. VB, Vastitas Borealis; El, Elysium; Ol, Olympus; Is, Isidis; Th, Tharsis; Ap, Apollinaris Patera; TM, Terra Meridiani; Sy, Syrtis Major; He, Hellas; Ar, Argyre.

Thermal core-mantle coupling can explain some features related to Earth's dynamo. Evidence suggests that the heterogeneous lower mantle affects convection and dynamo action in Earth's outer core. Paleomagnetic field models time-averaged over the past 5 million years show deviations from axial symmetry (*6*). Core flow models time-averaged over the past 150 years show persistent non-axisymmetric features (*7*), and the seismic properties of the upper part of Earth's inner core also exhibit an east-west hemispheric dichotomy (*8*).

Dynamo simulations with heterogeneous heat flux boundary conditions have been used to study the possible impact of the mantle on Earth's dynamo (*9*). The models successfully

[1]Laboratoire de Planétologie et Géodynamique, CNRS UMR 6112, Université de Nantes, 44322 Nantes cedex 3, France. E-mail: benoit.langlais@univ-nantes.fr [2]Équipe de Géomagnétisme, Institut de Physique du Globe de Paris, CNRS UMR 7154, 75252 Paris cedex 5, France. E-mail: hagay@ipgp.jussieu.fr

explain some of the observed non-axisymmetric features, such as the locations of the high-latitude intense geomagnetic flux patches in the modern era (*10*). A recent study recovered large parts of the time-averaged patterns of the paleomagnetic field, historical core flow, and inner-core buoyancy flux hemispheric dichotomy (*11*). In these models, core convection is primarily driven from below, whereas the variable boundary heat flux controls its long-term pattern. An upper bound for dynamo action was reported for this type of moderate heat flux anomaly amplitude (*9*).

Stanley *et al.* assume much stronger heat flux heterogeneities at the martian CMB, with convection driven from above maintaining the dynamo. Other aspects that differ from most geodynamo models (*9*–*11*) include stress-free boundary conditions and hyperdiffusivities. Two additional modeling issues concern the state of the martian core and the heat flux pattern. First, it is thought that the martian core was completely liquid during the first 500 million years (the Noachian era) (*12*). The effect of absence of an inner core therefore has to be evaluated. Second, the proposed dynamo model concentrates its field lines where the heat flux is the largest, i.e., below a cold downwelling mantle, whereas others (*4*) suggest that the thickened crust of the southern hemisphere is related to upwelling. The hemisphere-scale convection pattern in the mantle and its relationship with surface features clearly need to be better understood. Recovery of the single-hemisphere dynamo using different dynamo modeling methods and assumptions may strengthen the robustness of the proposed scenario.

Very little is known about the weak magnetic field signature of the northern lowlands. At 400 km altitude, where MGS spent most of its time, it is indeed very low, with a maximum of 20 nT above Vastitas Borealis. The absence of magnetization in the northern hemisphere (see the figure) may well be due to the single-hemisphere dynamo proposed by Stanley *et al.*, but one can invoke other hypotheses. For example, serpentinization of the southern hemisphere lithosphere, associated with magnetite crystallization and crustal material density decrease (*13*), could also explain the magnetic and topographic patterns on Mars, as could rapidly varying magnetization directions resulting in null to weak fields at spacecraft altitudes.

The proposed model of Stanley *et al.* resolves a number of apparent discrepancies on Mars. The existence of such thermal wind dynamos may open a new avenue for dynamo modeling, for Earth but also for other planets, such as Mercury (*14*). As with Uranus and Neptune, and as opposed to Earth, Jupiter, and Saturn (*15*), the current model shows that the past martian magnetic field was possibly non-dipolar and non-axisymmetric. Additional computations and observations are required to validate or dismiss their model. The next breakthrough will come from new observations, first when low-altitude measurements of the magnetic field are made (*16*) and when surface geophysical (seismic, magnetic, and heat flow) measurements are taken as planned by the European Space Agency's forthcoming Exomars rover and associated lander mission. These measurements will give some hints on the current lithosphere thickness, its origin, its relationship with possible hemisphere-scale convection, and the existence of a solid inner core. Combined with thermal evolution models, it will be possible to estimate the thermodynamic conditions on Mars during its early days. These inferences will introduce new geodynamic constraints on models of the past martian dynamo and may shed light on the reasons for its demise. The martian magnetic history is not yet over.

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CANCER

The Metastasis Cascade

Christoph A. Klein

The view of evolution of tumor cells toward metastasis takes a new twist.

The 20th-century philosopher of science, Thomas Kuhn, proposed that when sufficient observational data accumulate that conflict with "received wisdom," the prevailing model gives way to a new paradigm (*1*). With the findings of Podsypanina *et al.* on page 1841 in this issue (*2*), and those of three papers published earlier this year (*3*–*5*), the field of cancer metastasis seems to be undergoing such a paradigm shift.

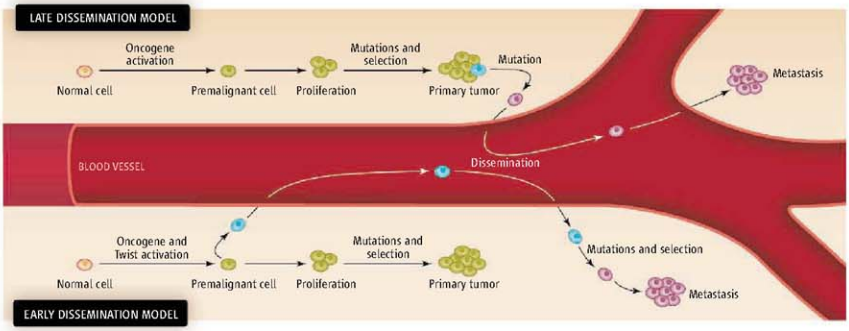
For decades, the metastatic dissemination of cancer has been considered the final stage in a deteriorating process. Genetic and (more recently) epigenetic changes have been thought to accumulate in the primary tumor over years before cancer cells are sufficiently mature to spread, having become "fully malignant" (see the figure). Now, Podsypanina *et al.* show that phenotypically normal mouse mammary epithelial cells injected into a recipient animal's bloodstream can survive at ectopic sites such as the lung, until expression of the oncogenes (altered versions of normal genes) they harbor is activated, driving cell proliferation and colonization of a new site. Their findings complement work by Hüsemann *et al.* (*4*) who show that oncogene activation in mouse mammary cells triggers a genetic program, possibly governed by the transcription factor Twist, which enables dissemination of such premalignant cells from mammary tissue to lungs and bone marrow before the appearance of mammary tumors.

How do these results change our understanding of cancer metastasis? The late metastasis model faces the problem that events predisposing a cancer to metastasis are initially unselected, in that they do not provide a growth advantage over neighboring cells (*6*). Thus, the changes promoting metastatic dissemination are mostly associated with tumors large enough to make the change—such as a mutation—a likely event. Proponents of this model hold that by the time of migration, tumor cells harbor compound aberrations that enable their survival by inactivating programmed cell death, which would otherwise be induced by an ectopic environment. Yet Podsypanina *et al.* observed that apparently

Division of Oncogenomics, Department of Pathology, University of Regensburg, Franz-Josef-Strauss-Allee 11, 93053 Regensburg, Germany. E-mail: christoph.klein@klinik.uni-regensburg.de

normal mammary epithelial cells injected into the mouse bloodstream survived for prolonged periods in the lungs, proliferated there, and could form mammary glands when reimplanted into mammary fat tissue. Equally surprising is the number of mammary cells that survived in the lungs—as many as 1.2 per 10,000 intravenously injected cells. This is in contrast to the few metastases that arise from millions of injected tumor cells from established cell lines (*7*), and the observation that billions of cancer cells shunted from the peritoneal cavity of patients into their venous systems do not result in more metastases (*8*). Podsypanina *et al.* found that most of the single disseminated tumor cells in bone marrow (*10*) and has been applied to both individuals suffering from various epithelial cancers and those without cancer (controls). Whereas 20 to 60% of cancer patients without manifest metastasis harbor disseminated epithelial tumor cells in bone marrow, only 2% of more than 800 controls had disseminated tumor cells, which is similar to the background noise of the assay (*11*). This suggests that even if resistance to programmed cell death is an inherent trait of (some) healthy epithelial cells, it is insufficient to account for cell migration. An alternative explanation, such as lack of access to premalignant lesions (*4*). Twist activity also confers the ability of a cell to self-renew (*5*), a prerequisite for metastatic growth.

What are the consequences of this new view of the metastatic cascade for research and clinical practice? The central aspect here is not "early" versus "late" tumor cell dissemination, but the evolution of malignant cells inside versus outside the primary lesion. Collectively, the recent findings suggest a note of caution about conclusions and hypotheses based on the late metastasis model. These include the use of advanced-stage cancer cell lines for metastasis research, which might reveal nonphysiological mecha-



Evolution of malignancy. (Top) The late metastasis model places selection of genetic and epigenetic alterations mostly inside the primary tumor. If so, late-disseminating cells are genetically similar to the primary tumor, which can be used as a surrogate marker to choose a drug against disseminated tumor cells. **(Bottom)** By contrast, early-disseminated tumor cells accumulate such alterations at distant sites and diverge genetically from the primary tumors. Consequently, they may respond differently to drugs that are administered systemically.

surviving cells started to proliferate once the oncogenes (*Kras*^{D12} and *MYC*, or *PyMT*) they carried were activated in animals.

In the context of the high frequency of some nonmalignant disorders, these results are less surprising. Endometriosis, a condition affecting 6 to 10% of women, originates from epithelial cells of the uterus that have been displaced. These untransformed epithelial cells have been found in the pelvic cavity, pericardium, pleura, aorta, and brain (*9*), arguably as "metastases."

The discrepancy between metastatic efficiencies of cancer cells versus healthy cells raises questions of whether advanced-stage cancer cells might be more sensitive to programmed cell death, and why dissemination of normal epithelial cells from healthy tissues to ectopic sites is not more frequent or continual. A sensitive immunoassay detects blood vessels, must contribute a more substantial barrier to the spread. If so, actively invasive behavior is likely a critical determinant of metastasis.

If dissemination is not selected as a mutational event, it must be the consequence of a change that generates fitter cells. Activation of oncogenes increases cell proliferation, but as an initiating event, it is counteracted by senescence, a genetic program inducing irreversible growth arrest. One pathway that might be selected after oncogene activation is regulated by *Twist* genes, recently shown by Ansieau *et al.* to override senescence in murine and human cells (*3*). In addition, Twist regulates two genetic programs important for metastasis. It activates a cell migration-invasion program that is involved in embryonic development (called epithelial mesenchymal transition) and also in dissemination of cells from nisms, and the assumption that therapeutic targets that are genetically activated in primary tumors will be activated in early disseminated cancer cells, small colonies of cancer cells, and metastases. The early dissemination model forces us to identify the epigenetic and genetic alterations that induce malignant development and metastatic spread. We need to distinguish changes that do initiate cell transformation from those that are merely able to. Given that cancer spread is early and selection for growth occurs at sites distant from the primary tumor, we need to establish the critical determinants of this process. If they differ from those at the primary site and lead to selection of different genotypes and phenotypes, then primary tumors present insufficient molecular markers to select "catch-all" targeting therapies. A shift of paradigm toward a model of ectopic

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malignant evolution will hopefully accelerate the diagnosis, prevention, and treatment of metastatic disease.

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SOCIAL SCIENCE

Unlocking the Potential of the Spoken Word

Douglas W. Oard

Advances in speech processing may soon place speech and writing on a more equal footing, with broad implications for many aspects of society.

The best available evidence suggests that the human brain, and the human facility for language, were already well developed at least by 50,000 years ago (*1*). For most of the time since then, the spoken word provided the only practical way of using language to share our understanding of the world with others. To this day, people find spoken expression and its visual correlates (such as gesture and facial expression) to be a fluid and compelling way of communicating. It was the invention of writing, however, that ignited the continuing cycle of innovation that we associate with modern society. We now stand at the threshold of a new era, one in which the spoken word can again rise to prominence.

About 5000 years ago, we see the first indications of the emergence of written language (*2*). Writing has important features that the spoken word lacks, including a degree of permanence that can help to overcome some limitations of human memory. It rapidly proliferated well beyond mere commercial records to play a multifaceted role in complex forms of social organization. This proliferation inspired other innovations: ways of finding documents again, and ways of writing that conveyed the needed context to a reader. The written word also has other attractive qualities (for example, you can read at your own pace), but permanence, findability, and contextualization are responsible for its foundational role in human civilization.

College of Information Studies and Institute for Advanced Computer Studies, University of Maryland, College Park, MD 20742, USA. E-mail: oard@umd.edu

For the past century and a half, inventors have chipped away at those advantages. The earliest known recording of a human voice was made in 1860 by Edward Lyon Scott's phonautograph, although it was not until Edison's 1877 better-known phonograph that the human voice could also be reproduced using technology from the same era (*3*). Later technologies, from wire recorders through reel-to-reel tape recording, were widely adopted for commercial purposes. It was, however, introduction of the compact cassette in 1962 that ultimately made sound recording technology robust and affordable. By the end of that decade, ordinary people could record hundreds of hours of speech, for media costs of about a dollar an hour. Today, digitized speech is easily acquired (for example, using any of the world's 2.5 billion mobile phones), easily transferred over digital networks, and easily stored, all for just a few cents per hour. It would take just $100 or so of networked disk storage to record everything that you will speak or hear this year.

Digital storage is a great equalizer with regard to permanence: The same infrastructure that can reliably store digital text can equally well store digital speech. Why, then, do we not record our lives in this way? Actually, some people do. For example, researchers at Carnegie Mellon University crafted a memory aid by recording their side of conversations and then using face recognition to cue up audio from an earlier meeting—no more forgetting people's names (*4*)! Gordon Bell at Microsoft has gone further, assembling digital materials from his entire life (*5*). This works well for some things (such as e-mail), but speech is not one of them—searching through large collections of spontaneously produced speech has remained a challenge.

This situation is about to change. Commercial "media management" systems can now reliably find specific content in the well-articulated speech of news announcers, and laboratory systems can handle much of the substantial variation in speaking styles that have made automatic transcription of interviews, meetings, and telephone conversations difficult. Hardware costs are higher for speech than for born-digital text (around a factor of 100 for storage, and perhaps a factor of 1000 for processing), but it is possible today to acquire, store, and process digitized speech at lower cost than was possible for born-digital text at the dawn of the Web. Robust accommodation to noisy environments and unfamiliar words remain important challenges, however, limiting the tasks to which present speech technology can be applied.

As increasingly capable systems emerge from the laboratory, we will soon find ourselves in a world in which speech need no longer be ephemeral. How will that change our society? No one can know for sure, but it is not difficult to envision some questions that might arise. The Carnegie Mellon system recorded only one side of the conversation because it is illegal in Pennsylvania (and 11 other U.S. states) to record full conversations without the explicit consent of all parties. Will a new balance between social costs and benefits lead us to think in more nuanced ways about when recording conversations should be permissible, just as many of us have learned to think differently about e-mail privacy at home and at the office? The wide diffusion of writing required standardization to facilitate mutual intelligibility. Will increasingly broad

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dissemination of spoken language accelerate the demise of regional dialects and less widely spoken languages? Written contracts today have greater legal standing than verbal ones. Will that distinction persist in a world in which spoken and written words have equal permanence? How can we harness this new technology to accelerate access to new knowledge, and what would be the implications of the resulting compression of innovation cycles?

Our parents complained that our generation relied on calculators rather than learning arithmetic. Will we complain when our grandchildren rely on speech-enabled systems rather than learning to read and write? Near-universal literacy has been one of humankind's greatest accomplishments, with 82% of the world's adult population now able to read and write. But it was the ephemeral nature of speech that gave rise to the imperative for literacy, and it is intriguing to imagine what will happen as that imperative abates. In Plato's *Phaedrus*, the Pharaoh Thamus says of writing, "If men learn this, it will implant forgetfulness in their souls: They will cease to exercise memory because they rely on that which is written" (*6*). Plato could not anticipate all the ways in which writing would be used for so much more than merely to augment memory—from an Internet that transports ideas through time and space, to great works of literature that transport our imagination to places that do not exist. What would a modern-day Plato have to say about the rise of speech to stand alongside writing as a cornerstone for our society? Our generation will unlock the full potential of the spoken word, but it may fall to our children, and to their children, to learn how best to use that gift.

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ECONOMICS

Can Neural Data Improve Economics?

Researchers are exploring how neurobiology can guide economic experiments and refine economic models.

Eric Maskin

Modern neuroimaging techniques—functional magnetic resonance imaging (fMRI), positron emission tomography scans, and so on—allow us to peer inside the brain and see what is going on when experimental subjects make economic decisions such as how to bid in auctions. The data on, say, dopamine release in the nucleus accumbens, or—as Delgado *et al.* (*1*) report on page 1849 of this issue—blood oxygen in the striatum, are certainly fascinating in their own right. But can they improve our understanding of economic behavior?

Opinions diverge on this question. Neuroeconomists Camerer *et al.* recently predicted that "We will eventually be able to replace the simple mathematical ideas that have been used in economics with more neurally-detailed descriptions" (*2*). By contrast, economic theorists Gul and Pesendorfer maintain that neuroscience evidence is irrelevant to economics because "the latter makes no assumptions and draws no conclusions about the physiology of the brain" (*3*). Limited to current practice in economics, the Gul-Pesendorfer assertion is correct. In a standard economic model, a decision-maker is confronted with several options, and the purpose of the exercise is to predict which one the subject will select. The model assumes and asserts nothing about the subject's brain states, nor is there any call for it to do so as long as the prediction is accurate. But predictions based on standard choice models are sometimes far from satisfactory, and so in principle, we might improve matters by allowing predicted behavior in the model to depend not only on the economic options but also on neurophysiological information.

Buying behavior. Why do people overbid for items at auction?

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So far, the field of neuroeconomics has not developed such an expanded model. Moreover, even when it does so, there are knotty problems of obtrusiveness and privacy to be resolved before one could perform brain scans outside the laboratory. The field has been moving quickly enough so that there is cause for optimism that all this will ultimately transpire, but integrating neural information into everyday economics is probably a good many years off.

What can be done with brain scans before that happy time? One possibility advocated by Delgado *et al.* is to use them for discriminating among standard economic models, in which neurophysiological variables (such as changes in blood oxygen levels) do not appear. Most puzzling economic phenomena admit quite a few conceivable alternative explanations, and neural data can streamline the process of finding the best one—suggesting follow-up experiments or new hypotheses. The authors use this approach to try to illuminate subjects' behavior in high-bid auction experiments. While they are probably right about how neural data can be useful, their application of this principle to auctions does not seem entirely successful.

In a high-bid auction, each potential buyer for the item being sold makes a sealed bid (i.e., quotes an amount of money without disclosing that amount to the other buyers). The buyer making the highest bid wins the item

School of Social Science, Institute for Advanced Study, Einstein Drive, Princeton, NJ 08540, USA. E-mail: maskin@ias.edu

and pays the seller that bid. High-bid auctions call for strategic behavior by buyers. If the item is worth v to a buyer, she will bid strictly less than v, because bidding her actual valuation would gain her nothing: She would get something worth v but also pay v. How much she "shades" her bid—that is, bidding below what the item is worth to her—will depend on what she expects others will do. Game theory predicts that each buyer will bid so as to maximize her expected payoff, given that all other buyers do the same. The result is what is called an equilibrium.

In one of the Delgado *et al.* experiments, there are two buyers, whose assigned valuations for the item being sold are drawn independently from a uniform distribution on the numbers between 0 and 100. If the buyers are risk-neutral—that is, if a buyer's expected payoff is her net gain from winning (valuation minus bid) times the probability of winning—then in equilibrium, the buyer will bid half her valuation. However, Delgado *et al.* found—as have many other similar experiments—that subjects generally bid more than this: They "overbid."

Delgado *et al.* discuss two standard explanations for overbidding. One is that subjects are risk-averse rather than risk-neutral—they strictly prefer the expectation of a monetary gamble to the gamble itself. The other is that they get an extra psychic benefit from beating out another buyer. What the authors do not mention, however, is that both hypotheses are now considered somewhat dubious: Recent experimental evidence seems in conflict with each of them (*4*). Thus, it is welcome that Delgado *et al.* propose their own explanation, based on fMRI studies they performed.

Unfortunately, it is not completely clear what this new hypothesis is. The fMRI data show that subjects experience a lower blood oxygen level in the striatum in response to losing an auction, but no significant change in reaction to winning one. The authors interpret this result as suggesting that subjects experience "fear of losing" and that this fear accounts for their overbidding. But actually modeling fear explicitly—making it precise—does not seem straightforward.

A natural modeling device would be simply to subtract something from the subject's payoff when she loses. However, such a modification would not accord with the authors' findings in their subsequent experiment. In the follow-up, there were two treatments: one in which a subject is initially given a bonus sum of money S but told that she has to return it if she loses the auction; the other in which the subject is promised that if she wins she will get S. The two treatments are, *ex post*, identical: In both cases, the subject ends up with the bonus if and only if she wins. However, in practice, subjects bid more in the former treatment than the latter. Such behavior sharply contradicts the "payment subtraction" hypothesis, under which behavior in the two treatments would be the same. Moreover, it seems difficult to find a natural alternative formulation of the "fear of losing" idea that explains the results simultaneously from both Delgado *et al.* experiments. Even so, there is a well-known principle that could account for the behavioral discrepancy between the two treatments in the follow-up experiment: the "endowment" effect (*5*). When a subject is given a bonus S at the outset, she may become possessive and so move more aggressively to retain it than she would act to obtain a contingent bonus at the end of the experiment.

As for why subjects overbid, perhaps the answer is that high-bid auctions are just too complex for a typical buyer to analyze completely systematically. The buyer will easily see that she has to shade her bid (bid strictly below v) to get a positive payoff. Still, she won't want to shade too much because shading reduces her probability of winning. A simple rule of thumb would be to shade just a little. But this leads immediately to overbidding, because risk-neutral equilibrium bidding entails a great deal of shading: A buyer will bid only one-half her valuation.

In short, Delgado *et al.*'s discovery of a dip in striatal blood oxygen levels when buyers lose in an auction is an intriguing neurophysiological finding, although it is not so clear that it has yet led to a better economic model of buyers' behavior. Still, the philosophy of Delgado *et al.*—that neural findings show great potential for improving economic analysis—is one that should be endorsed, well before the time when neuroscience and economics become one.

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CHEMISTRY

Nonlinear Thinking About Molecular Energy Transfer

Richard M. Stratt

Although solvent molecules move about randomly in a liquid, an experiment showed that changing their initial arrangement affected the rate of a chemical process.

In the movies, nobody cares what the extras are doing or saying, but you would notice if they were missing. Chemical reactions in solution are similar. The solvent molecules need to be there to ferry energy into and out of the reacting molecules, but when chemists study how molecules change into one another in chemical reactions, solvent molecules barely show up in the credits. In fact, the working hypothesis of most studies of chemical reactions run in solution is that the details of how the reaction funnels energy into the solvent tend to average out: The ability to transfer energy depends on the solution's friction (its intrinsic ability to absorb energy), not on precisely how the energy is donated. This notion, which sanctions not having to remeasure or recalculate results with every tiny shift in reaction conditions, receives its justification from linear response theory, an idea that is used in many fields to understand complex systems. Thus, the observation that linear response does not always work as expected, as Bragg *et al.* (*1*) demonstrate on page 1817 of this issue for the simplest chemical reaction—shifting an electron—is striking.

A basic tenet of linear response theory is that the energy flow in macroscopic systems is proportional to whatever causes it, with the proportionality constant a measure of the relevant friction. Linear response theory accounts for current being proportional to voltage in Ohm's law, for example (with the resistance a constant, reflecting the constancy of the friction) (*2*). However, in more recent

Department of Chemistry, Brown University, Providence, RI 02912, USA. E-mail: Richard_Stratt@brown.edu

applications to ultrafast laser studies of chemical events in solution, these same ideas are being applied, with remarkable success, at a molecular level (*3*).

This molecular connection occurs because chemical reactions are energy converters. A typical reaction rearranges the internal energy stored in chemical bonds, along with the external energy available from molecular translational kinetic energy, into the energy needed to create other bonding patterns. However, there is often energy left over, and this residual energy relaxes into molecular vibrational and translational energy.

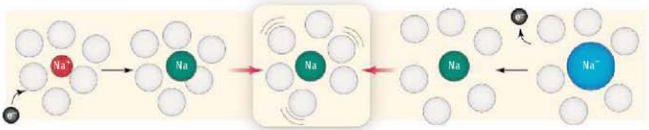
In even the best studies of this energy relaxation in chemical reactions, experiments keep track of relatively few of the actors (*4*). The precise molecular energies that come into play after a chemical reaction in solution are not easy to mimic in the laboratory, but some recent experiments have deposited as much as 40 kJ/mol of energy into a single, well-defined quantum transition of a C-H or an O-H stretching vibration and obtained spectroscopic signatures of energy flowing from place to place within (*5*) and between (*6*) molecules during the subsequent relaxation. Nonetheless, these energies are not close to the 200 to 300 kJ/mol that is often rearranged in chemical reactions. Worse, different ways of inserting the same amounts of energy into a molecule could, in principle, lead to different dynamics (*7*).

Given the many uncertainties, it would be convenient to have linear response theory to rely on to say that many of these details do not matter. Indeed, some of the first computer simulations of energy relaxation confirmed the accuracy of linear response predictions at the molecular level in solvation processes (*3*, *8*, *9*), the essence of which is the energy lowering induced by rearranging solvent molecules around a newly created solute (or, more frequently, around a newly altered state of a solute, such as its charge). These studies showed that the linear response theory could account for transfers of large quantities of energy, even though one might have thought that linearity would rely on getting small effects out of small perturbations (*2*). More modern perspectives tend to attribute linearity to the consistency of the random Gaussian fluctuations that a solute usually sees when surrounded by a macroscopic number of other molecules (*10*, *11*). Although nonlinear responses were seen in a few simulations of solvation (*12*), they could all be attributed to specific variations in these Gaussian fluctuations triggered by gross changes in the surrounding solvent structure (*13*).

What Bragg *et al.* developed was an elegant experiment to look for nonlinearities in solvation. The usual experimental protocol has been to electronically excite a dissolved dye molecule and interpret the evolution of its fluorescence with time (*3*). Instead, Bragg *et al.* generated a ground-state neutral sodium atom (Na) in tetrahydrofuran (THF) by two different electron-transfer routes—ejecting an electron from a sodium anion (Na^-) and shifting an electron from a nearby iodide ion to a sodium cation (Na^+) (see the figure). Had the subsequent rearrangements of THF molecules exhibited a linear response, the electronic absorption spectra of the neutral Na products would have had identical patterns of time evolution, despite their different starting points. The observation of appreciable differences seems to show that nonlinearity can appear even with the solvation changes encountered when a single electron is transferred (*14*).

Still, removing an electron from a single, reasonably small, atomic anion does create a hole in the liquid that is fairly substantial on the scale of the anion. We know, both from previous work from Schwartz's group (*15*) and from more recent experimental and theoretical studies of high-energy rotational energy relaxation (*13*, *16*) (yet another example of nonlinearity), that such a void is likely to be a much more significant perturbation to the solvent's fluctuations than a minor local excess solvent density (such as that induced by adding an electron). The failure of linear response theory here may not be all that different from that expected theoretically.

What these special instances of nonlinear energy transfer do promise, however, are some long-sought experimental entries into the microscopic origins of friction. The slowing down of mechanical motion by friction is nothing but the effectively irreversible transfer of molecular kinetic energy into a sea of countless other molecular degrees of freedom. The second law of thermodynamics guarantees that such transfers occur, but it cannot explain how or when they happen, or reveal the specific molecular motions involved. Linear response theory in this case is the villain, as it hides all of this detail in quantities set by the materials involved (the Ohm's law resistance, for example) and not by the specifics of the motion. These new experiments offer welcome instances when the obscuring fog of microscopic linear response lifts, revealing those missing molecular details.



Do the details matter? Whether an electron is added to Na^+ (**Left**) or removed from Na^- (**Right**), the immediate outcome is a neutral Na atom surrounded by solvent molecules (open circles) in unfavorable locations. Although the resulting solvent arrangements differ appreciably, both situations relax to a more favorable arrangement (**Middle**) within tens of picoseconds. Linear response theory predicts that this relaxation is determined solely by the solvent fluctuations shown in the middle panel, meaning that the two solvation pathways in red should exhibit identical dynamics, hiding the differing details of their starting points. Bragg *et al.* showed that the right-hand side pathway is noticeably slower.

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17. The author's work is supported by the NSF (CHE-0809385).

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EDUCATION

Innovations Liven Up Undergraduate Science Classes

A comic book may seem like an odd choice for assigned reading in a college class, but biology professor Jay Hosler has transformed the medium into a resource for his undergraduate students. Where comics are best known for telling the stories of superheroes and goofy teenagers, *Clan Apis* and other Hosler comics instead explore the evolution of the eye, the stages of cell division, and the life cycle of the honey bee.

Clan Apis follows the life cycle of a bee named Nyuki.

"Comic books are an example of a great innovative education model to reach students who are nervous or not confident in the science classroom," said Hosler, explaining his second life as comic author and illustrator at Juniata College in Huntington, Pennsylvania.

Hosler's color-splashed pages were among the intriguing resources discussed at the 2008 Course, Curriculum, and Laboratory Improvement (CCLI) conference held 13 to 15 August in Washington, D.C. The event, cosponsored by AAAS, brought together more than 500 stakeholders in an effort to transform science, technology, engineering, and mathematics (STEM) teaching on college campuses across the country.

Since 1999, the National Science Foundation (NSF) has distributed grants to colleges and universities through the CCLI program, encouraging them to adopt a more innovative approach to STEM teaching. Last year, NSF provided around $67.5 million supporting 262 new initiatives on 203 campuses around the country.

AAAS's Education and Human Resources (EHR) division has been a partner in the initiative since organizing the first CCLI conference in 2004. This year's event is in keeping with AAAS's mission to improve STEM curricula and help science faculty collaborate with their colleagues across disciplines, said EHR Deputy Director Yolanda George.

"Undergraduate courses are usually the last chance we get to help citizens and future leaders understand the nature of science and the importance of STEM to our lives—as individuals and as members of the larger society," said EHR Director Shirley Malcom. "We can't emphasize enough how important it is to improve education at this level."

The meeting's participants shared their own innovative lesson plans, which included a wall-climbing robot with gecko feet, the materials engineering of a snow ski, and geometry concepts illustrated by the students' own drawings and sculptures.

Another way that the CCLI program has encouraged science teaching for nonscience majors is to "focus more on public and civic issues such as sustainability and the ethics of genetic engineering and the use of nanotechnology in consumer products," said Myles Boylan, one of the directors of the CCLI program. "Science has so much to say about this, and students find it very motivating."

Many of Hosler's students are interested in becoming primary or elementary school teachers, but they "are scared out of their minds about science," he said. "And if they are afraid of science, there is no way they could teach it well. We need to show them that they can not only learn about it but, eventually, teach it to the next generation."

Jeanne Narum, director of Project Kaleidoscope, an informal alliance to improve undergraduate STEM education, said colleges and universities are sometimes hesitant to try new educational approaches because the ability of the new models to increase student comprehension is untested or not widely understood.

Evaluating new STEM methods is a critical part of the CCLI program, according to Boylan. "We've heard it loud and clear from our grantees: 'Help us do a better job of assessing our projects,'" he said.

Robert Grossman, a professor of chemistry at the University of Kentucky, said faculty members might be able to convince their university's administrators to implement innovative programs by showing that they are in the institution's best interest.

Several years ago, Grossman said, his institution discovered that students receiving low or failing grades in chemistry were more likely to withdraw from the course or college as a whole, at great expense to the university.

In an effort to increase student success, a colleague of Grossman used a CCLI grant to develop ChemExcel, a peer-led tutoring program for undergraduates in chemistry. Grossman said the University of Kentucky eagerly supported the program after it was shown to reduce student failure rates.

—*Benjamin Somers*

INTERNATIONAL

An Emerging Engagement on Rwandan Education

A high-level AAAS delegation pledged to work with top Rwandan science and education leaders on development of science-related curricula during 2 days of meetings in the central African nation.

The talks on 27 and 28 August focused on Rwanda's plan to use science and technology to drive economic growth and build human capital as it continues to recover from the 1994 genocide that left nearly 1 million people dead.

Throughout the meetings, Rwandan Education Minister Daphrosa Gahakwa, Science Minister Romain Murenzi, and other key S&T officials stressed that education will be critical to the plan's success. Representing AAAS were Shirley Malcom, head of Education and Human Resources; Vaughan Turekian, chief international officer; and Sarah Banas, program associate in the International Office.

"During our visit we were again reminded of the central role that Rwanda's leadership is placing on science and technology in their development strategy," said Turekian. "This provides a very good opportunity for AAAS and other science-based organizations to share experiences and work together to help build capacity."

Malcom said AAAS will provide Rwandan officials with science education resources developed by Project 2061, the association's pioneering science literacy initiative.

Over the past year, AAAS and Rwandan leaders have built a promising relationship. Last October, AAAS Board Chair David Baltimore visited Rwandan President Paul Kagame and other officials. Kagame traveled to Boston in February to deliver a plenary address at the AAAS Annual Meeting.

CREDIT: JAY HOSLER

AAAS Annual Election: Preliminary Announcement

The 2008 AAAS election of general and section officers will be held in November. All members will receive a ballot for election of the president-elect, members of the Board of Directors, and members of the Committee on Nominations. Members registered in more than one section will receive ballots for elections for each section they are enrolled in.

Candidates for all offices are listed below. Additional names may be placed in nomination for any office by petition submitted to the Chief Executive Officer no later than October 26. Petitions nominating candidates for president-elect, members of the Board, or members of the Committee on Nominations must bear the signatures of at least 100 members of the Association. Petitions nominating candidates for any section office must bear the signatures of at least 50 members of the section. A petition to place an additional name in nomination for any office must be accompanied by the nominee's curriculum vitae and statement of acceptance of nomination.

Biographical information for the following candidates will be enclosed with the ballots mailed to members in October.

Slate of Candidates

GENERAL ELECTION

President: Alice Huang, California Institute of Technology; Harold Mooney, Stanford Univ.

Board of Directors: Jerry Melillo, Marine Biological Laboratory; Julia Phillips, Sandia National Laboratories; David Sabatini, NYU Medical Ctr.; Maria Elena Zavala, California State Univ., Northridge.

Committee on Nominations: Steven Chu, Lawrence Berkeley National Laboratory; Jack Dixon, Howard Hughes Medical Institute; Jonathan Dordick, Rensselaer Polytechnic Institute; Steven Fienberg, Carnegie Mellon Univ.; Paul Friedman, UCSD Medical Center; M.R.C. Greenwood, UC-Davis; Susan Hackwood, California Council on Science & Technology; Sallie Keller-McNulty, Rice Univ.

SECTION ELECTIONS

Agriculture, Food, and Renewable Resources

Chair Elect: Harry Klee, Univ. of Florida; Brian Larkins, Univ. of Arizona

Member-at-Large of the Section Committee: Barbara Valent, Kansas State Univ.; Jeff Volenec, Purdue Univ.

Electorate Nominating Committee: Charles Brummer, Univ. of Georgia; Candace Haigler, North Carolina State Univ.; Ann Hirsch, UCLA; Mark Sorrells, Cornell Univ.

Council Delegate: Daniel Cosgrove, Pennsylvania State Univ.; Stanley Roux, Univ. of Texas, Austin

Anthropology

Chair Elect: Clark Larsen, Ohio State Univ.; Christopher Ruff, Johns Hopkins Univ.

Member-at-Large of the Section Committee: Carol Ward, Univ. of Missouri; Sarah Williams-Blangero, Southwest Foundation for Biomedical Research

Electorate Nominating Committee: Daniel Brown, Univ. of Hawaii; Dolores Piperno, Smithsonian Institute; Dawnie Wolfe Steadman, Binghamton Univ.; Anne C. Stone, Arizona State Univ.

Astronomy

Chair Elect: Alan P. Boss, Carnegie Institution of Washington; Mario Livio, Space Telescope Science Institute

Member-at-Large of the Section Committee: Jack O. Burns, Univ. of Colorado; Donald Campbell, National Astronomy and Ionosphere Ctr.

Electorate Nominating Committee: Giovanni G. Fazio, Harvard Smithsonian Ctr. for Astrophysics; Arlo U. Landolt, Louisiana Univ.; James E. Neff, College of Charleston; Michael Werner, Jet Propulsion Laboratory

Atmospheric and Hydrospheric Sciences

Chair Elect: Alan Robock, Rutgers Univ.; Donald Wuebbles, Univ. of Illinois

Member-at-Large of the Section Committee: Leo Donner, Geophysical Fluid Dynamics Laboratory; Kevin E. Trenberth, National Center for Atmospheric Research

Electorate Nominating Committee: Jim Coakley, Oregon State Univ.; Qiang Fu, Univ. of Washington; Margaret (Peggy) Lemone, National Center for Atmospheric Research; Mark H. Thiemens, UCSD

Biological Sciences

Chair Elect: Trudy Mackay, North Carolina State Univ.; James R. Spotila, Univ. of Arkansas

Member-at-Large of the Section Committee: Nipam H. Patel, UC-Berkeley; Margaret Werner-Washburne, Univ. of New Mexico

Electorate Nominating Committee: Chris T. Amemiya, BRI, Virginia Mason Medical Ctr.; Joan W. Bennett, Rutgers Univ.; Judith Berman, Univ. of Minnesota; Eric Ursell Selker, Univ. of Oregon

Chemistry

Chair Elect: Charles Casey, Univ. of Wisconsin-Madison; Dale Poulter, Univ. of Utah

Member-at-Large of the Section Committee: Peter Wipf, Univ. of Pittsburgh; Ronald Woodard, Univ. of Michigan College of Pharmacy

Electorate Nominating Committee: Jonathan Ellman, UC-Berkeley; Charles Craik, UC-San Francisco; Brian Stoltz, California Institute of Technology; Amos B. Smith, III, Univ. of Pennsylvania

Dentistry and Oral Health Sciences

Chair Elect: Francis Macrina, Virginia Commonwealth Univ.; Margarita Zeichner-David, Univ. of Southern California

Member-at-Large of the Section Committee: Richard Lamont, Univ. of Florida; Ira B. Lamster, Columbia Univ. College of Dental Medicine

Electorate Nominating Committee: Peter Ma, Univ. of Michigan School of Dentistry; Laurie McCauley, Univ. of Michigan School of Dentistry; Frank Scannapieco, School of Dental Medicine Univ. at Buffalo; Robert G. Quivey Jr., Univ. of Rochester

Education

Chair Elect: Joe Krajcik, Univ. of Michigan; Mary Nakkhleh, Perdue Univ.

Member-at-Large of the Section Committee: Angelo Collins, Knowles Science Teaching Foundation; Jay B. Labov, National Academy of Science

Electorate Nominating Committee: Mary Atwater, Univ. of Georgia; Linda Froschauer, Weston Public Schools; Jon D. Miller, Michigan State Univ.; Suzanne O'Connell, Wesleyan Univ.

Engineering

Chair Elect: H. Vincent Poor, Princeton Univ.; Duncan T. Moore, The Institute of Optics

Member-at-Large of the Section Committee: Christine Maziar, Univ. of Notre Dame; Jerome Schultz, UC-Riverside

Electorate Nominating Committee: Rena Bizios, Univ. of Texas, San Antonio; Kathy Ferrara, UC-Davis; Kristen Fichthorn, Univ. of Pennsylvania; Pradeep Khosla, Carnegie Mellon Univ.

Council Delegate: Jose Cruz, Ohio State Univ.; Gail H. Marcus, Consultant; James L. Merz, Univ. of Notre Dame; C.D. (Dan) Mote Jr., Univ. of Maryland

General Interest in Science and Engineering

Chair Elect: Charles Lytle, North Carolina State Univ.; Kathryn D. Sullivan, Ohio State Univ.

Member-at-Large of the Section Committee: Sharon M. Friedman, Lehigh Univ.; Alexander Polonsky, Marine Hydrophysical Institute

Electorate Nominating Committee: Suzanne Gage Brainard, Univ. of Washington; Robert Griffin, Marquette Univ.; Marilee Long,

Colorado State Univ.; Gloria J. Takahashi, La Habra High School

Geology and Geography
Chair Elect: Malcolm Hughes, Univ. of Arizona; Stephen Jackson, Univ. of Wyoming
Member-at-Large of the Section Committee: Sally P. Horn, Univ. of Tennessee; Jean Lynch-Stieglitz, Georgia Institute of Technology
Electorate Nominating Committee: Elizabeth Canuel, College of William & Mary; Eugene Domack, Hamilton College; Timothy Fisher, Univ. of Toledo; David Stahle, Univ. of Arkansas

History and Philosophy of Science
Chair Elect: Richard Creath, Arizona State Univ.; Jeffery L. Sturchio, The Merck Company Foundation *Member-at-Large of the Section Committee*: Robert Brandon, Duke Univ.; Heather Douglas, Univ. of Tennessee
Electorate Nominating Committee: Mark Largent, James Madison College; Nancy Nersessian, Georgia Institute of Technology; Peter Railton, Univ. of Michigan; Alain Touwaide, Smithsonian Institution
Council Delegate: Jane Maienschein, Arizona State Univ.; Virginia Trimble, UC-Irvine

Industrial Science and Technology
Chair Elect: Jennie C. Hunter-Cevera, Univ. of Maryland Biotechnology Institute; Vijayan Nair, Univ. of Michigan
Member-at-Large of the Section Committee: Manuel Gomez, Univ. of Puerto Rico; Harry S. Hertz, NIST
Electorate Nominating Committee: Robert Boily, Inforex Inc.; Quinghuang Lin, IBM; John Pizzonia, Fujifilm Life Science's Applications Laboratory; Harold Schonhorn, retired
Council Delegate: Orlando Auciello, Argonne National Laboratory; Steven Popper, The Rand Corporation

Information, Computing, and Communication
Chair Elect: Bart Selman, Cornell Univ.; Manuela Veloso, Carnegie Mellon Univ.
Member-at-Large of the Section Committee: Julia Gelfand, UC-Irvine; John (Jack) Hill, USGS
Electorate Nominating Committee: Christine Borgman, UCLA; Bonnie Carol, Information International Associates; Casimir Kulikowski, Rutgers Univ.; William Woods, ITA Software

Linguistics and Language Science
Chair Elect: David W. Lightfoot, Georgetown Univ.; Thomas Wasow, Stanford Univ.
Member-at-Large of the Section Committee: Suzanne Flynn, MIT; Mark Liberman, Univ. of Pennsylvania
Electorate Nominating Committee: William J. Poser, Yinka Dene Language Institute; Edward Stabler, UCLA; Elizabeth Traugott, Stanford Univ.; Douglas H. Whalen, Haskin Laboratories Mathematics
Chair Elect: Kenneth Millett, UC-Santa Barbara; Williams Velez, Univ. of Arizona
Member-at-Large of the Section Committee: Tony F. Chan, National Science Foundation; Carl C. Cowen, Indiana University-Purdue Univ.
Electorate Nominating Committee: Douglas Arnold, Univ. of Minnesota; Jonathan Borwein, Dalhousie Univ.; Wade Ellis, West Valley Community College; Robert M. Fossum, Univ. of Illinois, Urbana-Champaign

Medical Sciences
Chair Elect: Gary A. Koretsky, Univ.of Pittsburgh School of Medicine; Judy Lieberman, Harvard Medical School
Member-at-Large of the Section Committee: Robert Doms, Univ. of Pennsylvania; Rino Rappuoli, Chiron Corporation
Electorate Nominating Committee: Wendy Brown, Washington State Univ.; Beverly Davidson, Univ. of Iowa; Phil Greenberg, Univ. of Washington; Thomas B. Nutman, National Institutes of Health
Council Delegate: Etty (Tika) Benveniste, Univ. of Alabama, Birmingham; Terence Dermody, Vanderbilt Univ.; James M. Hughes, Emory Univ.; Marcelo Jacobs-Lorena, John Hopkins School of Public Health; Jennifer M. Puck, UC-San Francisco; Reed Pyeritz, Univ. of Pennsylvania; Gwendalyn J. Randolph, Mount Sinai School of Medicine; Douglas Richman, UC-San Diego; Paul Rothman, Univ. of Iowa; Thomas Wellems, National Institutes of Health

Neuroscience
Chair Elect: Nominees to be announced
Member-at-Large of the Section Committee: Richard Huganir, John Hopkins Univ.; Gail Mandel, Oregon Health & Science Univ.
Electorate Nominating Committee: Erik D. Herzog, Washington Univ.; Frank LaFerla, UC-Irvine; Michael S. Wolfe, Harvard Medical School/Brigham and Women's Hospital; Tony Wyss-Coray, VA Palo Alto Health Care System

Pharmaceutical Science
Chair Elect: Kenneth Thummel, Univ. of Washington; Gary Pollack, Univ. of North Carolina
Member-at-Large of the Section Committee: William Beck, Univ. of Illinois; David Ross, Univ. of Colorado
Electorate Nominating Committee: Per Artursson, Uppsala Univ.; Kenneth Brouwer, Qualst; Donald E. Mager, Univ. at Buffalo; Craig K. Svensson, Purdue Univ.

Physics
Chair Elect: S. James Allen, UC-Santa Barbara; Charles W. Clark, NIST
Member-at-Large of the Section Committee: Richard F. Casten, Yale Univ.; Alexander L. Fetter, Stanford Univ.
Electorate Nominating Committee: Patrick D. Gallagher, NIST; Elizabeth H. Simmons, Michigan State Univ.; Michael Witherell, UC-Santa Barbara; Ali Yazdani, Princeton Univ.

Psychology
Chair Elect: Judy Deloache, Univ. of Virginia; Stephen Suomi, National Institutes of Health
Member-at-Large of the Section Committee: Randolph Blake, Vanderbilt Univ.; Jenny Saffran, Univ. of Wisconsin
Electorate Nominating Committee: Randall Engle, Georgia Tech; Denise Park, Univ. of Texas, Dallas; Barbara Rolls, Pennsylvania State Univ.; David Shapiro, UCLA
Council Delegate: Bennett I. Bertenthal, Indiana Univ.; John Gabrieli, MIT

Social, Economic, and Political Sciences
Chair Elect: Eugene Rosa, Washington State University; Cora B. Marrett, National Science Foundation
Member-at-Large of the Section Committee: Ronald J. Angel, Univ. of Texas, Austin; Wendy Baldwin, Population Council
Electorate Nominating Committee: Anil Deolalikar, UC-Riverside; Don C. Des Jarlais, Albert Einstein College of Medicine; Howard Leventhal, Rutgers Univ.; Robert F. Rich, Univ. of Illinois
Council Delegate: Nicholas Christakis, Harvard Medical School; Guillermina Jasso, New York University

Societal Impacts of Science and Engineering
Chair Elect: Bruce Lewenstein, Cornell Univ.; Stephen D. Nelson, Virginia Tech. Univ.
Member-at-Large of the Section Committee: Kevin Finneran, Issues in Science and Technology; Melanie Leitner, Prize4Life
Electorate Nominating Committee: Lida Anestidou, The National Academies; Ezra Heitowit, Universities Research Association, Inc.; Robert M. Simon, US Senate Committee on Energy & Natural Resources; Michael L. Telson, Univ. of California System

Statistics
Chair Elect: Joel B. Greenhouse, Univ. of Pittsburgh; Jessica Utts, UC-Irvine
Member-at-Large of the Section Committee: Charmaine Dean, BC Cancer Agency; Kenneth W. Wachter, UC-Berkeley
Electorate Nominating Committee: Paul P. Biemer, Univ. of North Carolina; May A. Foulkes, George Washington Univ.; Subir Ghosh, UC-Riverside; Nancy Reid, Univ. of Toronto

Assembling Materials with DNA as the Guide

Faisal A. Aldaye,[1] Alison L. Palmer,[2] Hanadi F. Sleiman[1]*

DNA's remarkable molecular recognition properties and structural features make it one of the most promising templates to pattern materials with nanoscale precision. The emerging field of DNA nanotechnology strips this molecule from any preconceived biological role and exploits its simple code to generate addressable nanostructures in one, two, and three dimensions. These structures have been used to precisely position proteins, nanoparticles, transition metals, and other functional components into deliberately designed patterns. They can also act as templates for the growth of nanowires, aid in the structural determination of proteins, and provide new platforms for genomics applications. The field of DNA nanotechnology is growing in a number of directions, carrying with it the promise to substantially affect materials science and biology.

Today, we can chemically synthesize complex molecules such as palytoxin, vitamin B12, or Taxol with remarkable angstrom-scale precision and fabricate intricately designed micron-scale electronic components at the rate of billions per second. These advances may suggest that we have conquered most major frontiers of chemical construction. Yet, nature illustrates that we are nowhere near the limit of exquisite control over organization; it possesses an extraordinary capacity to assemble complex nanostructures with active and specialized functions. Our ability to precisely position components on the nanometer scale the way nature does, and to do so in a parallel rather than a serial manner, is still limited and is a key goal in nanotechnology and materials science.

Self-assembly, the spontaneous association of components into organized structures using noncovalent interactions, is the chief method that nature uses to achieve complexity. Of the natural self-assembling molecules, DNA is arguably the most remarkable. A cooperative interplay of hydrogen-bonding, π-stacking, electrostatic, and hydrophobic interactions drives one DNA strand to assemble with its complement into a double helix according to extremely precise base-pairing rules. Additional attributes, such as rigidity on the nanoscale, a diameter of ~2 nm, and a near-infinite number of potential sequences, extend DNA's reach beyond a genetic blueprint for life. DNA is emerging as an attractive tool for nanoscience as well; it is a highly promising template for organizing nanomaterials in a programmable way. Research in this area promises to allow us to use DNA to dictate the precise positioning of materials and molecules into any deliberately designed structure, thus approaching the effortless manner in which nature generates complexity and function.

Structural DNA Nanotechnology

By exploiting DNA's structural features and powerful base-pairing rules, the field of structural DNA nanotechnology aims to generate nanopatterned materials and to control motion at the nanoscale. Its initial challenge was to convert the one-dimensional (1D) DNA molecule into 2D and 3D structures. Seeman and his research group looked to nature's branched DNA structures (for example, the Holliday junction) to meet this challenge. By assembling four DNA strands into a stable four-way junction and incorporating single-stranded "sticky ends" at the periphery for hybridization, Seeman developed an artificial branched DNA "tile" (Fig. 1A, top) (*1*). The second major challenge of DNA nanotechnology was to generate more rigid junctions, which are essential to achieve well-defined 2D DNA assemblies. By joining two DNA double helices with a single strand that begins on one helix and switches onto an adjacent helix, Seeman generated tiles that have "crossovers" and addressable sticky ends at their edges and are of greater rigidity (Fig. 1B, left). The group used these tiles to construct well-defined 2D lattices with predesigned periodicity (*2*).

These principles of construction have since been used, adapted, and developed to generate systems with very fine control over design and function (*2*). A number of basic structural motifs have been designed that can be classified as planar tiles, branched junctions, or helix bundles. Planar tiles are formed from several parallel helices joined by crossover junctions (Fig. 1B, left) and were used to synthesize linear arrays, 2D lattices, and DNA nanotubes. Branched junctions are constructed with multiple DNA arms that radiate from a focal point and are held together with crossover junctions to minimize flexibility (Fig. 1B, middle). They have been used to generate 2D arrays with square, hexagonal, and compound cavities. Helix bundles are tiles constructed by joining parallel DNA helices that are not coplanar (that is, they cooperatively produce a curvature) by using multiple crossover junctions (Fig. 1B, right). They have been assembled into extended 2D arrays and well-defined DNA nanotubes. These structural motifs (*2*) collectively provide a toolbox to rationally access a rich number of 2D DNA architectures and refine DNA materials assembly. It is of note that in structural DNA nanotechnology, DNA is used to provide all the parameters for self-assembly: connectivity, structural features, and programmability.

In this approach, DNA tiles are typically made using strands with different sequences to prevent the formation of undesired structures. In practice, however, this requires synthesizing a large number of components and mixing these in exact stoichiometric ratios for successful assembly. By incorporating identical sequences (sequence symmetry) in DNA strands, Mao found that a stable four-way junction can be constructed from three strands instead of nine and that it assembles into the desired square grid array with an increased long-range order (*2*). Yan used sequence symmetry to tackle the problem of constructing finite arrays, rather than extended 2D assemblies, from a small number of DNA tiles (*2*). Thus, judicious incorporation of sequence symmetry in DNA strands merely used as architectural elements, such as struts and junctions, can simplify tile-based assembly. Winfree proposed the concept of "algorithmic DNA self-assembly" to increase complexity in DNA assembly. This was achieved by designing a set of DNA building blocks that represent "Wang tiles." Conceptually, Wang tiles contain a single color on each of their four sides and assemble so that the adjacent sides of each square are of the same color. This requirement necessarily means that each tile can fit in a specific manner within the assembly. Winfree adapted this methodology to construct rectangular-shaped DNA tiles, with four addressable sticky ends at each side as Wang tiles, and demonstrated the feasibility of assembling these according to a set of algorithmic rules initiated by a nucleating strand. Impressively complex fractal patterns can be generated using this approach, from a minimal set of DNA tiles (*3*).

In addition to tiles created by simple Watson-Crick base-pairing of DNA, many other nucleic acid motifs have been developed. For example, Jaeger showed that folded RNA molecules could be assembled together like a jigsaw puzzle (Fig. 1C) (*4*); Willner synthesized a polycatenated DNA ladder as a mechanically interlocked system onto which proteins, nanoparticles, and dyes were fixed with precise control (Fig. 1D) (*5*); and Sen demonstrated the "synapsing" together of two DNA duplexes into a ladderlike structure through guanine-quadruplex formation (Fig. 1E) (*6*).

[1]Department of Chemistry, McGill University, 801 Sherbrooke Street West, Montreal, QC H3A 2K6, Canada. [2]Canadian Institute for Advanced Research, 180 Dundas Street West, Suite 1400, Toronto, ON M5G 1Z8, Canada.

*To whom correspondence should be sent. E-mail: hanadi.sleiman@mcgill.ca

Two-dimensional DNA templates provide the opportunity to template the positioning of materials with nanoscale precision. For example, nanoparticle assemblies are promising components for functional devices. Their collective properties, such as electron transport, optical coupling, and magnetic interactions, depend on their relative arrangement; thus, the DNA-mediated control of nanoparticle organization promises to greatly affect the fields of nanoelectronics and nanooptics, among others. Sequence-specific DNA-templated 1D organization of gold nanoparticles was demonstrated by Alivisatos by labeling gold nanoparticles with DNA strands that determined their exact position onto complementary single-stranded DNA templates (*7*). Kiehl (*8*), Seeman (*9*), and Yan (*10*) showed the sequence-encoded organization of gold nanoparticles into well-defined rows on a number of 2D DNA lattices, demonstrating remarkable control over periodicity and arrangement. In addition to nanoparticles, the organization of proteins on DNA templates can possibly lead to "enzyme factories" and substrates for proteomics and can also shed light on the nature of protein-protein interactions. The biotin-avidin interaction was used by LaBean and Yan to generate an alternating assembly of streptavidin molecules onto a 2D square DNA array (Fig. 1F) (*11*). Antigen-antibody interactions enabled Mao (*12*) and Yan and Chaput (*13*) to organize antibodies to fluorescein and c-*myc*, respectively, on antigen-modified DNA arrays. Aptamer-protein interactions are particularly interesting because it is possible to discover aptamers for any protein by using the systematic evolution of ligands by exponential enrichment (SELEX), which means that these interactions can potentially be adapted to organize any protein. For example, Yan used a 2D DNA array, modified with two different aptamers, to assemble two proteins into alternating lines with no unwanted cross-talk (Fig. 1G) (*14*). Although the previous examples require labeling the DNA array with molecules that recognize the materials to be patterned (for example, DNA strands, biotin, antigens, and aptamers), unmodified DNA arrays can also be used to template materials assembly. The Dervan lab developed a class of polyamides that sequence-selectively bind the minor groove of DNA. These molecules can selectively bind to 2D DNA arrays and, when modified with biotin, they mediate the organization of streptavidin into lines with control over sequence and periodicity (*15*).

A number of applications of materials assembled by structural DNA nanotechnology are already starting to emerge in both biotechnology and materials science. Precisely positioned 2D DNA and protein nanoarrays (rather than conventional microarrays) can be useful in many areas of genomics, proteomics, diagnostics, and tissue engineering. By assembling different DNA tile arrays, each with a specific recognition molecule and "bar-coded" with a specific dye, Yan developed a platform that allows the simultaneous detection of multiple biological analytes. This method may be simpler than DNA or protein microarrays for small-scale profiling of bioanalytes (*16*). Mao employed a 2D DNA array as a reusable "mask" to create 2D gold nanopatterns via vapor deposition into the array's cavities (*17*). This method is promising for controlling topography in the nanoscale regime at a much higher resolution than conventional photolithography. Turberfield showed the binding of the protein RuvA to the four-way junctions of a DNA 2D lattice. This resulted in a 2D crystalline array of this protein, which allowed for its structural elucidation by using cryogenic transmission electron microscopy with a resolution of 30 Å. Interestingly, this DNA-binding protein was found to dramatically modify the geometry of the DNA motif by changing the structural features of these junctions when bound to them (*18*).

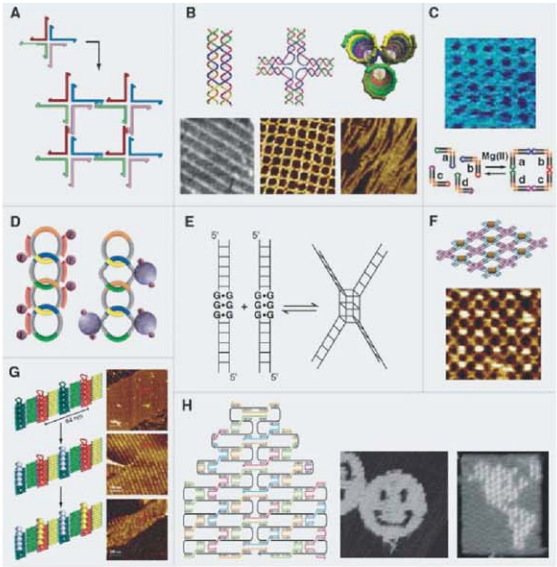

Fig. 1. **(A)** Four DNA strands assemble into a four-way junction with sticky ends, which can further assemble into 2D structures. **(B)** Motifs in structural DNA nanotechnology. Tiles (left) can assemble into periodic 2D arrays; junctions (middle), such as this four-way junction, can result in a 2D square lattice; and helix bundles (right), such as this triple bundle, can generate a 1D DNA nanotube. **(C)** Folded RNA molecules are used to selectively construct extended RNA arrays with different cavity sizes and shapes. **(D)** Interlocked DNA circles form catenated ladder-assemblies, containing single-stranded sides for molecule organization (left) or for protein binding when folded into aptamers (right). F, fluorophore. **(E)** Guanine tracks incorporated into duplexes can be used to snap four strands into a four-way junction composed of a guanine quadruplex. **(F)** A four-arm junction modified with biotin is used to organize streptavidin onto a periodic square array. **(G)** Four tiles are assembled into a 2D array with alternating rows of two different aptamers to organize two different proteins into alternating lines. **(H)** In DNA origami, a long DNA strand is folded into the desired structure and is held into shape using many stapling strands (left). This approach is used to access different 2D architectures (middle) and to draw 2D shapes, such as the map of the Western Hemisphere (right).

DNA Origami

In "DNA origami," a single continuous strand of DNA is systematically folded using a large number of smaller DNA strands. This approach was first reported by the group of Joyce, who synthesized a single continuous DNA strand that is 1.6 kb long and, in a single step, annealed it in the presence of five smaller strands to generate a DNA octahedron (*19*). Ingeniously, Rothemund

generalized this approach to fold naturally occurring genomic DNA into any 2D shape (*20*). In his DNA origami approach, the long strand is folded into the desired shape by a number of smaller strands ("stapling strands") (Fig. 1H, left). The sequences of these strands are computationally designed. Rothemund was able to assemble the same initial long strand of DNA into squares, rectangles, stars, smiley faces (Fig. 1H, middle), and many other 2D shapes. The power of this approach lies in its addressability: Because each stapling strand is a unique sequence, each strand is also a spatially addressable bit. Hairpins were incorporated into stapling strands to write words, such as "DNA," and to draw complex objects, such as the outline of the Western Hemisphere (Fig. 1H, right). DNA origami will be useful for accessing larger DNA shapes with highly addressable surfaces. In a recent application, Yan constructed origami-based DNA nanoarrays for label-free RNA detection of the three genes *Rag*-1, *c-myc*, and *β-actin* (*21*). Shih, Chou, and Douglas synthesized DNA nanotubes by "rolling" a DNA origami array and used the alignment made by these liquid crystalline materials to measure nuclear magnetic resonance parameters in transmembrane proteins (*22*), a powerful way to use DNA organization in protein structure determination.

Supramolecular DNA Assembly

Supramolecular chemistry exploits intermolecular forces to control the organization of organic and inorganic assemblies. After 40 years of research, it has generated a toolbox of molecular components that assemble with a high degree of control (*23*). These components are structurally rigid, geometrically diverse, and intrinsically functional (for example, are photoactive or redox active or possess magnetic properties), in contrast to the more passive DNA branch points. Now a new research area is evolving that brings the tools of supramolecular chemistry and DNA nanotechnology together. "Supramolecular DNA assembly" blends rationally designed DNA building blocks with synthetic organic and inorganic molecules, which give structural and functional advantages both to the initial self-assembly process and to the final construct.

One exciting potential of incorporating synthetic molecules into DNA is that they can dramatically influence the structure of assemblies and introduce different motifs in DNA nanotechnology. Bergstrom (*24*), Shchepinov (*25*), and von Kiedrowski (*26*) presented branched DNA structures with organic corner units that self-assemble into well-defined nanostructures. Because these structures contained identical DNA strands, however, mixtures of DNA assemblies were obtained. Sleiman developed DNA building blocks, containing two arms of different sequences, and a rigid organic corner unit, which selectively assembled into a discrete DNA hexagon (*27*). This approach was used to organize six gold nanoparticles into a hexagon (Fig. 2A), thus providing model systems to study single-electron transport and optical coupling in gold nanoparticle assemblies.

Synthetic molecules can bring a number of additional interactions into DNA nanotechnology. For example, replacing the DNA bases with supramolecular building blocks can expand the genetic alphabet: self-complementary isoguanines, with two hydrogen-bonding faces that are oriented at an angle that forms a pentameric assembly, result in a higher-order DNA pentaplex rather than the classical duplex (*28*). Incorporating extended aromatic molecules as connectors of DNA strands allows folding of these strands through π-π stacking (DNA "foldamers") (Fig. 2B) (*29*), and replacing the termini of DNA strands with ligands allows metal coordination to override base-pairing and loop DNA into a cycle (*30*). Attaching a polymer to the end of DNA can cause microphase separation, resulting in DNA micellar aggregates (Fig. 2C) (*31*). Synthetic molecules can also covalently link DNA structures. They have been used to create, for example, parallel DNA helix bundles with porphyrins at their cores (*32*) and to "snap" together DNA-modified organic conjugated modules into tailor-made conjugated assemblies (*33*).

Another important impact of incorporating synthetic molecules (for example, transition metals) is that they can give much needed function to the passive DNA scaffolds. Metal complexes can be photoactive and electroactive and can possess magnetic and catalytic properties. In contrast to growing materials on the exterior of a DNA strand, incorporating transition-metal complexes into DNA can create pure and monodisperse DNA structures with preserved self-assembly capabilities. Two approaches have been investigated. The first designs nucleobases for complexing transition metals. Shionoya incorporated five consecutive copper-DNA base pairs into a DNA duplex to create a copper stack likened to a self-assembling DNA nanomagnet (Fig. 2D) (*34*) and later, with Carell, created DNA multimetallic stacks with two selectively incorporated transition metals (*35*).

The second approach, which uses metal complexes as vertices, has allowed for coordination geometries, bond angles, and functionalities unavailable to carbon compounds. Sleiman reported the synthesis of metal-linked branched-DNA building blocks, and assembled a cyclic metal-DNA nanostructure with luminescent metal vertices and DNA arms (*36*). Han constructed a DNA triangle with three iron-corner units and three DNA arms (*37*), and McLaughlin showed the synthesis of a ruthenium complex with six DNA arms (*38*). However, because these approaches require using a small subset of completely unreactive metal complexes, very few additional metals have been incorporated as vertices. Sleiman recently incorporated a range of reactive transition metals into DNA junctions, using a method that allows the DNA duplexes and transition metal complexes to synergistically stabilize each other (Fig. 2E) (*39*). Many applications can be expected for metal DNA nanostructures in such areas as multimetallic catalysis, sensing, artifi-

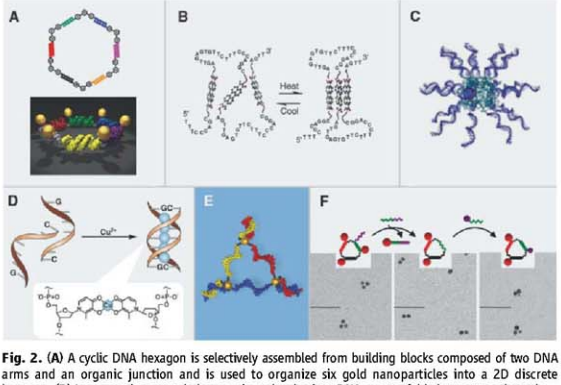

Fig. 2. (A) A cyclic DNA hexagon is selectively assembled from building blocks composed of two DNA arms and an organic junction and is used to organize six gold nanoparticles into a 2D discrete hexagon. **(B)** Incorporating extended aromatic molecules into DNA creates folded structures through π-stacking. **(C)** DNA strands attached to polymers result in block copolymers that assemble into micelles via microphase separation of the incompatible blocks. **(D)** Replacing DNA bases with coordinating hydroxypyridone ligands generates copper stacks within DNA strands. **(E)** A metal-DNA nanostructure: a DNA triangle with iron bis(terpyridine) vertices. **(F)** A write/erase experiment using discrete gold nanoparticle assemblies from single-stranded and cyclic DNA templates with organic vertices. A single particle is selectively removed using a fully complementary strand and is replaced with a differently sized particle.

cial photosynthesis, data storage, nanooptics, and nanoelectronics.

In supramolecular DNA assembly, synthetic molecules can contribute to the connectivity and the structure of the final molecule, and DNA is used as the programmable component. One direct consequence of this is that the structures no longer need to be double-stranded and interwoven with crossover units but can now be single-stranded and dynamic. Sleiman reported the synthesis of single-stranded and cyclic DNA structures with rigid organic corners and used them as dynamic scaffolds to organize gold nanoparticles (*40*) with the ability to write/erase and structurally switch these assemblies upon addition of added specific DNA strands (Fig. 2F). The group then constructed 3D DNA cages capable of switching and changing their size between three predefined states (*41*). There have been many elegant designs for DNA nanomachines that respond to specifically added DNA strands or other molecules (*42*). All these examples have led to the development of molecule-responsive DNA materials. In contrast to other environmentally responsive materials (for example, materials that change with pH, light, or oxidation), these allow for the selective control of different parts within the same device and for the incorporation of many molecular triggers to cause individual changes, thus increasing our ability to communicate and externally manipulate structures.

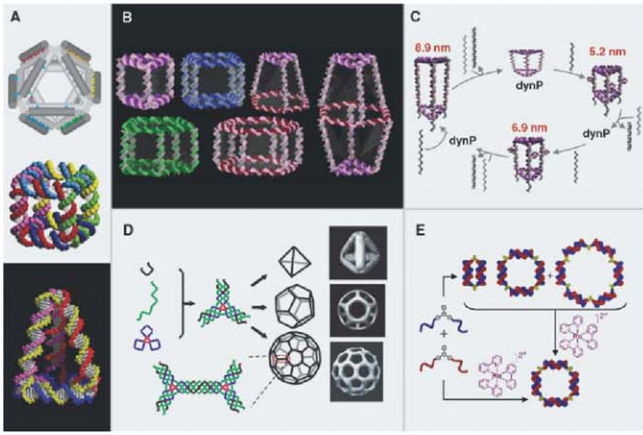

Fig. 3. (A) A DNA octahedron (top), cube (middle), and tetrahedron (bottom). **(B)** Single-stranded and cyclic DNA triangles, squares, pentagons, and hexagons with organic vertices as their corner units are assembled into 3D triangular prisms, cubes, pentameric and hexameric prisms, a heteroprism, and a biprism. **(C)** 3D DNA assemblies generated using this approach can also be dynamic. A triangular prism is switched between three predefined lengths using a series of strands capable of rigidifying and erasing. dynP, dynamic prism. **(D)** A symmetric three-arm junction assembles into a 3D tetrahedron, octahedron, or buckyball. Access to the desired structure is determined by the flexibility and concentration of the symmetric junction. **(E)** The molecule $Ru(bpy)^{2+}$ affects the self-assembly outcome of two symmetric DNA building blocks and selectively mediates the assembly of a single product, a DNA square.

Three-Dimensional Assembly

Three-dimensional structures made of DNA have tremendous potential to encapsulate and release drugs, regulate the folding and activity of encapsulated proteins, selectively encage nanomaterials, and assemble 3D networks for catalysis and biomolecule crystallization. Seeman reported early examples of 3D DNA objects with the topology of a cube (*43*) (Fig. 3A, middle) and a truncated octahedron. Joyce reported the synthesis of an octahedron (*19*) (Fig. 3A, top), and Turberfield generated a rigid and chiral DNA tetrahedron (Fig. 3A, bottom), in which the group encapsulated the protein cytochrome c (*44*). More recently, new methods that increase the range of 3D structures and their ease of synthesis have been reported. Sleiman developed a face-centered approach to 3D DNA construction (Fig. 3B). By breaking down 3D objects into discrete 2D DNA shapes, such as triangles, squares, pentagons, and hexagons with organic vertices, a large number of 3D DNA cages were quantitatively accessed. These include a triangular prism, a cube, a pentameric and hexameric prism, a heteroprism, and a biprism (*41*). The approach also allowed for the construction of the first dynamic 3D DNA capsule, whose size was switched reversibly between three different lengths (Fig. 3C) (*41*). Mao adopted the rules of symmetry to access 3D assemblies from building blocks with identical arms. By controlling the flexibility within a symmetric three-arm junction, the group synthesized a tetrahedron, a dodecahedron, and a buckyball from a minimal set of building blocks (Fig. 3D) (*45*). Turberfield also showed dynamic switching of a DNA tetrahedron (*44*), and von Kiedrowski reported the synthesis of a DNA dodecahedron with organic vertices (*46*).

In a different approach, Mirkin (*47*) and Gang (*48*) created 3D gold nanoparticle crystals with long-range order without using a preassembled DNA template. Instead, they modified gold nanoparticles with single-stranded DNA, which allowed them to control the interparticle distances and packing dynamics, and induced crystallization.

Current Challenges

These examples illustrate the power and promise of DNA as a template to precisely position materials on the nanoscale. In order to move this research forward, two challenges need to be addressed: the correction of errors that arise in DNA assembly, and the replication and scale-up of DNA nanostructures.

As the complexity of DNA assemblies increases, so will the number of the DNA sequences required to form them. This will necessitate using overlapping, degenerate strands that may assemble into undesirable products. Biological systems have developed a number of elegant strategies to proofread and remove errors during and after assembly. Inspired by these systems, Lu used an approach in which deoxyribozymes (DNAzymes) specifically locate and cleave misassembled structures in gold nanoparticle assemblies (*49*). In the presence of the "correct" DNA strands, the DNAzyme is not properly folded and is inactive; however, in the presence of the "incorrect" DNA strands, the DNAzyme is properly folded and proceeds to cleave and remove the errors. Using the rules of dynamic combinatorial chemistry, Sleiman used an external molecule to proofread and correct for errors (*50*). DNA building blocks with identical arms initially generated a library of many assemblies, but adding the small molecule $Ru(bpy)_3^{2+}$, an electrostatic binder of DNA, forced the library to converge to only one member, a DNA square (Fig. 3E). Pierce generated a number of metastable folded intermediates that systematically

interact with each other in a cascading approach to generate the final product (*51*). By programming the biomolecular pathway leading to the final assembly, and not just the final product, Pierce's approach prevents error formation.

To enable practical applications, it is necessary to develop techniques that copy, amplify, and scale up the synthesis of these structures. Assemblies generated using DNA origami are constructed from a single long DNA strand and, in principle, could readily be amplified using the already existing biological machinery. Seeman and Yan recently reported the successful enzymatic amplification of a building block found in classical DNA nanotechnology: a branched DNA tile containing several double cross-over motifs (*52*).

Assemblies generated using supramolecular chemistry can also be amplified. Von Kiedrowski showed the chemical copying of a molecule composed of three single-stranded DNA arms that branch out from a single organic vertex (*53*). Ultimately, today's materials are synthesized in large amounts using chemical approaches. It is therefore worthwhile to further investigate chemical methods to economically amplify these molecules. In principle, as long as the base-pair information within DNA is preserved, different backbones could also be used. Lynn copied the information from DNA into a daughter molecule, with preserved base sequence and a synthetic oligomeric backbone (*54*). The development of economically feasible amplification methods will allow for the structures developed by DNA nanotechnology to be widely used in materials science.

Conclusions and Outlook

DNA's simple code forms our genetic blueprint for life. But the field of DNA nanotechnology has invited us to look at the code in a whole new way: as a means to precisely position materials. This code can now help dictate the specific location of materials and the structure of assemblies, creating linear, 2D and 3D assemblies. It can also control motion, creating capsules that expand and contract, molecular "walkers" that move directionally along a track, and tweezers that grab desired targets (*55*). The DNA code can even dictate specific mechanistic pathways, enabling DNA origami to fold and DNA hairpins to open each other sequentially.

Nature builds complexity in a hierarchical way. It progressively increases length scales and relies on a number of noncovalent interactions, including DNA base-pairing, to drive assembly. Supramolecular DNA assembly is a means to weave in principles of hierarchical complexity and new interactions into DNA nanostructures, and opens the door to assembling more diverse functional structures with greater ease.

The next step will be to investigate the possibilities for making practical materials with DNA nanotechnology. DNA's ability to guide patterning of transition metals, nanoparticles, and proteins into deliberate designs gives it tremendous potential for answering many important challenges in science. For instance, is it now conceivable to assemble an artificial photosynthesis system, create a multienzyme catalytic "factory," or access complex nanoelectronic circuitry, using DNA? Can DNA be employed to generate combinatorial patterns of precisely positioned small-molecule ligands that probe cooperative binding and allosteric interactions in proteins and aid in the discovery of new multivalent drugs? Can DNA cages be used as biodegradable and molecule-responsive materials for the specific on-demand delivery of drugs to diseased cells? Can 3D DNA crystalline arrays be created and used as designer molecular hosts to template protein crystallization, as initially anticipated by Seeman, or to induce catalysis and new chemistry within their cavities?

These are only a handful of the opportunities created by our remarkable control over the organization of materials using DNA. It is by identifying the important challenges of biology, chemistry, physics, engineering, and medicine that we can put these patterned nanomaterials to the test and evolve this exciting field into an applied, central area of research.

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Magnetic Source Separation in Earth's Outer Core

Kenneth A. Hoffman[1,2]* and Brad S. Singer[2]

The dipole component of the geomagnetic field is anomalously strong at both Earth's surface and the core-mantle boundary (CMB). Because dipole terms are of the lowest degree, they are the most capable of reaching the CMB from sources deep within the outer core (*1*). Nondipole (higher-degree) terms need originate from sources residing closer to the CMB if they are to emerge. Yet, the power associated with the equatorial dipole terms is compatible with the nondipole power spectrum [e.g., (*2*)], leaving the axial dipole to stand alone given its unique strength. The question then is whether the source of the axial dipole is physically distinct from sources responsible for the rest of the field, the so-called nonaxial dipole (NAD) field.

Analyses of the NAD field at Earth's surface indicate that its present structure is similar to that when time-averaged over the past 400 years (*3*); the most intense patches of vertical flux (Fig. 1, right) appear almost motionless, indicative of long-term control over shallow core fluid by the lowermost mantle. Hence, the time-averaged NAD field may be used as a proxy for the modern-day NAD field and vice versa.

Twentieth-century observatory data suggest further that these standing features strengthen at independent rates (*4*). The effect about the globe of this NAD field secular variation is displayed in Fig. 1 (left): Localities close to (and hence dominated by) a single flux feature, versus those more equally proximate to multiple features, experienced lesser and greater vector field changes, respectively.

We focus on two widely separated sites—West Eifel, Germany, and Tahiti, French Polynesia—from which we have available paleomagnetic transitional field data obtained from lavas that erupted since the Matuyama-Brunhes polarity reversal. The $^{40}Ar/^{39}Ar$ age determinations of West Eifel lavas indicate the recording of five excursions spanning some 200,000 years, including the Big Lost Event (table S1). The transitional lavas from Tahiti also record the Big Lost Event (*3*) and the Matuyama-Brunhes reversal (*5*). Virtual poles recorded in transitionally magnetized lavas from West Eifel are spread across Eurasia, whereas the two events recorded on Tahiti are associated with the same tightly clustered virtual geomagnetic pole (VGP) location west of Australia, where the most intense NAD field flux feature exists at Earth's surface (Fig. 1, right).

Modern-day NAD field structure and behavior tend to explain the paleomagnetic findings: The site of West Eifel lies within the sphere of influence of three concentrations of NAD field flux within the area of greatest directional secular change. In contrast, Tahiti is considerably closer to one, the Australasian feature, and is within the area of least secular change. Thus, both the wide east-west spread in West Eifel Brunhes–aged transitional VGPs and the nearly identical Tahitian VGP clusters are compatible with recent and historic geomagnetic findings.

Also plotted in Fig. 1 (right) are south VGPs associated with the NAD field at both sites throughout the 20th century (*6*). These recent-field virtual poles, associated with complete removal of the axial dipole term, show behavior similar to the paleomagnetic data, both in angular change and location, for both sites. From these correlations, we conclude that polarity transitions first involve the demise of the source generating the axial dipole, which leaves the field generated only in the shallow core with a pattern strongly controlled by the physical variability of the lower mantle. Hence, we suggest that there are two significantly independent field sources: one generated deep within the outer core; the other generated in the shallow core, which we designate the SCOR field.

The SCOR field is essentially the NAD field; however, its complex pattern most assuredly contains a small contribution to the axial dipole. The deeper-core field then provides nearly all of the observed axial dipole, yet it must also contain a (small) contribution to lower-degree harmonics in the observed NAD field (*7*). Such a field source dichotomy may be the key to solving the problem of the reversing geodynamo.

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1. Having the longest spatial wavelengths, dipole components are least likely to be screened out by overlying electrically conductive fluid.
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6. The dynamo is blind to the field sign, so either case is equally valid.
7. Some field asymmetry is required by Cowling's theorem to maintain dynamo action.
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[1]Physics Department, California Polytechnic State University, San Luis Obispo, CA 93407, USA. [2]Department of Geology and Geophysics, University of Wisconsin-Madison, Madison, WI 53706, USA.

*To whom correspondence should be addressed. E-mail: khoffman@calpoly.edu

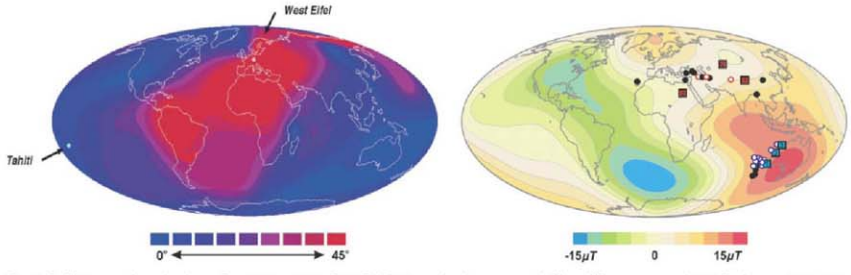

Fig. 1. (**Left**) Contoured angular change from 1900 to 2000 of NAD field VGPs about the globe. (**Right**) (**i**) Transitional north VGPs recorded in lavas on Tahiti (clustered near west Australia) and West Eifel (spanning much of Eurasia), each case spanning ~200,000 years (Big Lost Event VGPs, which were recorded at both sites, have open symbols), and (**ii**) concurrent south VGPs for the years 1900, 1950, and 2000 (indicated on the map by 1, 2, and 3, respectively) NAD field at Tahiti (blue squares) and West Eifel (red squares) plotted on the 1590–1990 time-averaged surface NAD field.