30 July 1999

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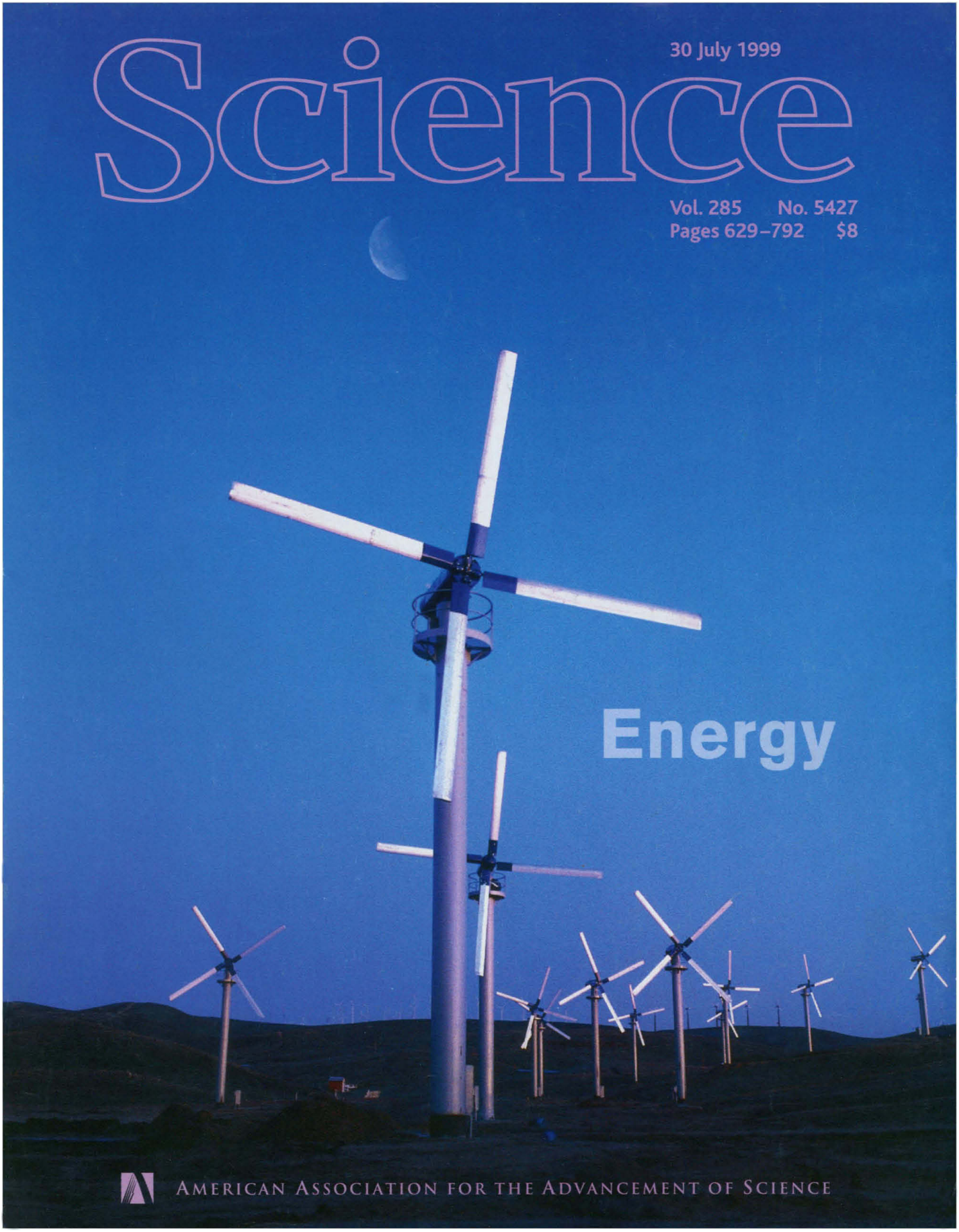

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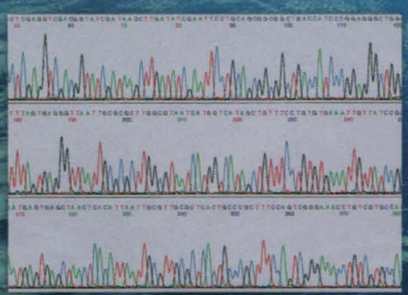

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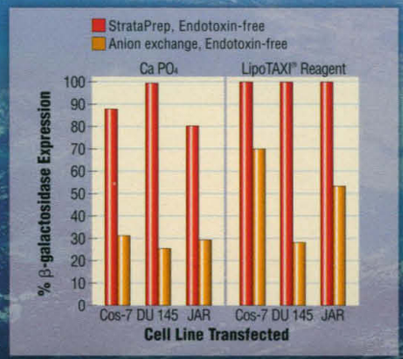

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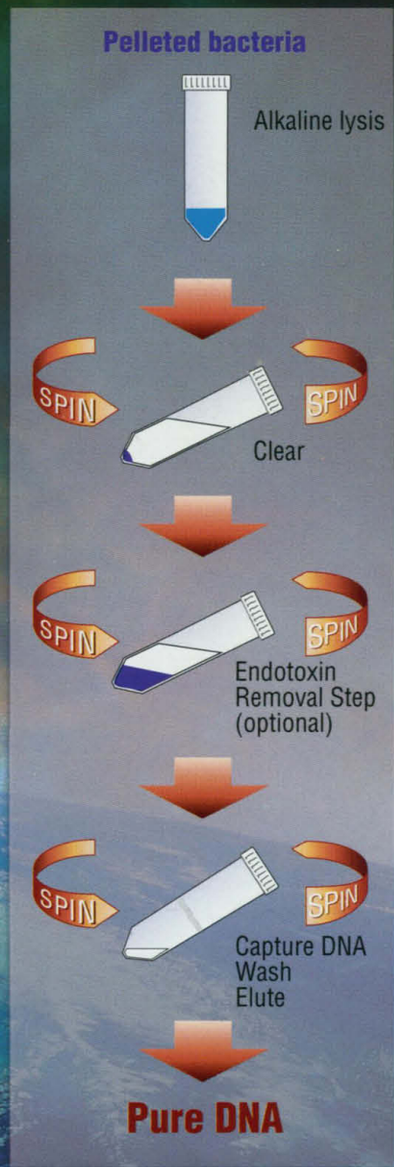

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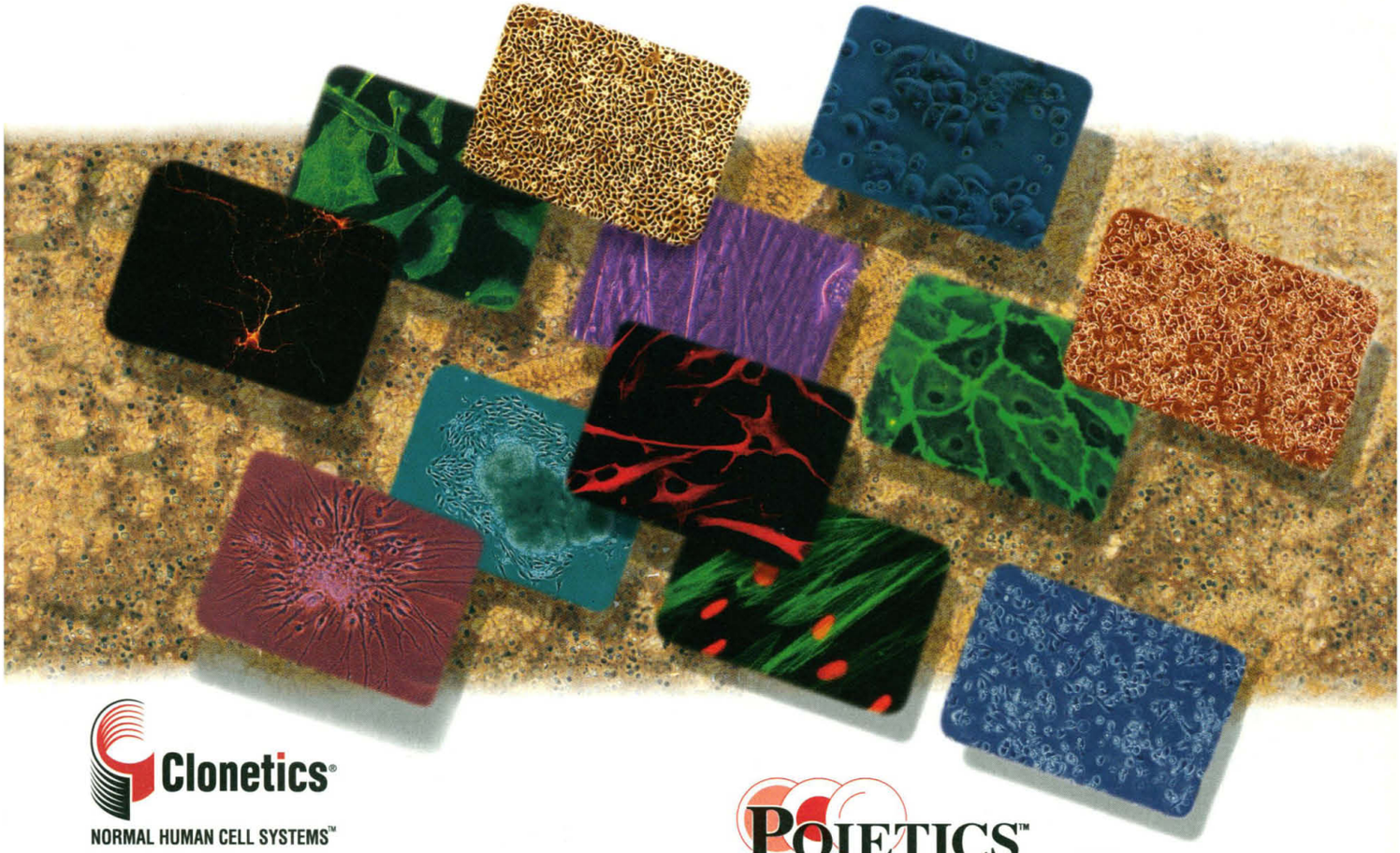

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Science

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COVER Low global energy prices for fossil fuels have slowed investment in renewable energy technologies such as wind turbines. Increases in energy demand, as well as supply limitations or disruptions, may bring about higher prices, and concerns about pollution and global warming may lead to restricted fossil fuel use. The Energy special section, beginning on page 677, focuses on alternative approaches for generating, distributing, and conserving energy. [Image: Peter Menzel]

652
New heyday for x-ray astronomy

718
Slipping and skipping at depth

See related NetWatch on p. 635 and Editorial on p. 662.

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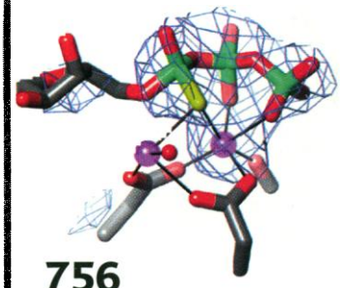

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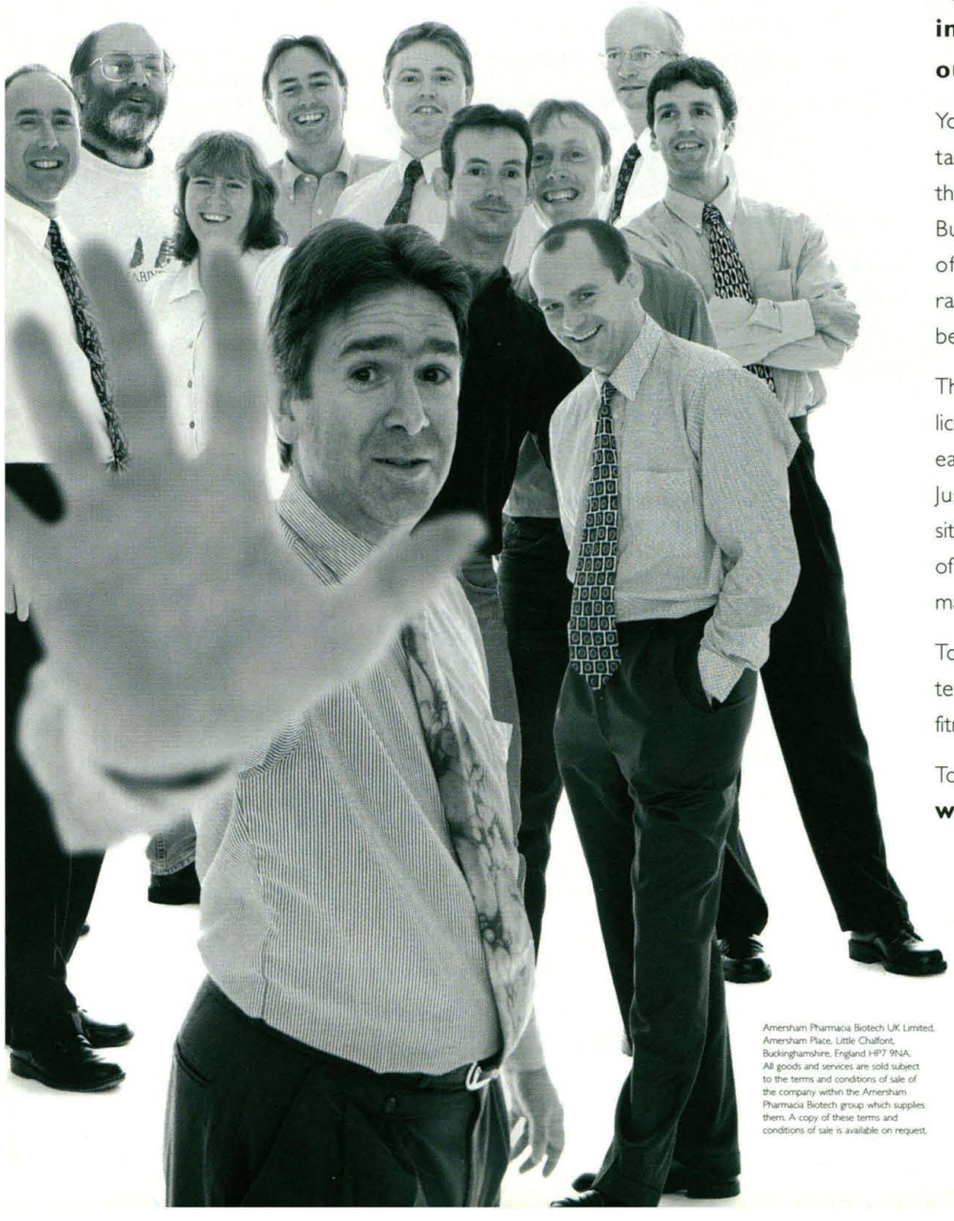

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A GREENER ROUTE TO ETHYLENE?

Numerous chemicals and materials are produced from ethylene, which is made by steam cracking of alkanes. The scale of ethylene production is enormous (25 billion kilograms per year in the United States), but heat needed for the process requires the burning of at least 10% of the starting materials and formation of large amounts of CO_2, a greenhouse gas. Bodke *et al.* (p. 712; see the Perspective by Pereira) describe an oxidative route to ethylene from ethane and oxygen. Greater than 85% selectivity at 70% conversion was achieved over a platinum-tin catalyst at 950 degrees Celsius when excess hydrogen was added to the reactants. Hydrogen reduced overall CO_2 and CO formation to less than 5%, and subsequent reactions actually generated more hydrogen than was introduced. Several aspects of the chemistry are still unexplained—ethane somehow suppresses the explosive nature of the hydrogen-oxygen mixture, and the reaction delivers a product mixture far from equilibrium despite the high temperatures.

FILLING QUANTUM DOTS TO THE BRIM

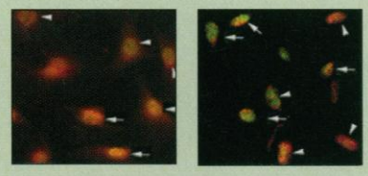
Recent measurements on adding electrons to quantum dots reveal that it is not just a matter of inserting them one by one into a ladder of discrete states but that the process is rather more complicated. Zhitenev *et al.* (p. 715) report on the electronic structure of quantum dots from capacitance spectroscopy. At low electron density, the electrons occupy localized states. As more electrons are added, the dot splits into two distinct regions—an inner core of delocalized (metallic-like) states and an outer periphery of localized states. At the highest electron densities, the states in the periphery are the last to make the transition to being delocalized.

DEEP FAULT MOVEMENTS

Although the rate at which the surface of a fault slips can be measured directly, determining the rate beneath the surface is difficult. Nadeau and McEvilly (p. 718; see the Perspective by Tullis) estimate this rate along the San Andreas Fault at Parkfield, California, from the recurrence intervals of small magnitude earthquakes. These microearthquakes occurred within the same area and with the same seismic waveform over periods of months to years, and these events are thought to represent creeping of the fault due to the tectonic load without any significant change in the rheology. The recurrence intervals varied as a consequence of a series of four large magnitude earthquakes, and these variations were used to estimate the slip rate to a depth of about 10 kilometers.

DNA REPAIR IN BREAST CANCER

The *BRCA1* gene is mutated in about half of the cases of hereditary breast cancers. To investigate the function of the *BRCA1* gene product, Zhong *et al.* (p. 747) searched for BRCA1 binding proteins. Among the binding partners



identified was Rad50, a protein that forms a multifunctional complex with Mre11 and p95 and participates in repair of DNA double-strand breaks and homologous recombination. Wild-type BRCA1 colocalizes with the Rad50-Mre11-p95 complex in nuclear foci that form after cell irradiation, and transfection of wild-type *BRCA1* rescued cells that normally are hypersensitive to a DNA damaging agent. These data suggest that BRCA1 is important in the Rad50-mediated cellular response to DNA damage.

UNDERWATER DESALINATION

It has been difficult to model the steady-state salt content of the ocean, which reflects input from rivers and losses through several processes. de Villiers and Nelson (p. 721; see the news story by Kerr) now show that the magnesium ion concentration of the ocean is not constant, as had been thought previously. It is markedly decreased above ocean ridges, where it is scrubbed out of the oceans by the reaction of seawater with basalt in hydrothermal systems. The extent of the decrease implies that the low-temperature circulation of water through mid-ocean ridges is much greater than had been assumed; adding this factor to the calculation of sources and sinks of Mg^{2+} and of other major ions in the ocean will help to balance the accounts.

ANCIENT GREENHOUSE WARMING

An abrupt warming event about 55 million years ago may be one of the closest analogs in Earth's history to current anthropogenic climate change because of its rapidity. It is thought to have been caused by an abrupt release of greenhouse gases into the atmosphere or ocean. Bains *et al.* (p. 724) now provide a close look at the course of this event using two widely separated ocean core sites. The records from these cores show many common features, which implies that the climate response was global. Earth's climate seemed to warm in steps coincident with apparent pulses of greenhouse gas emissions, perhaps from episodic breakdown of methane hydrates on and in the sea floor.

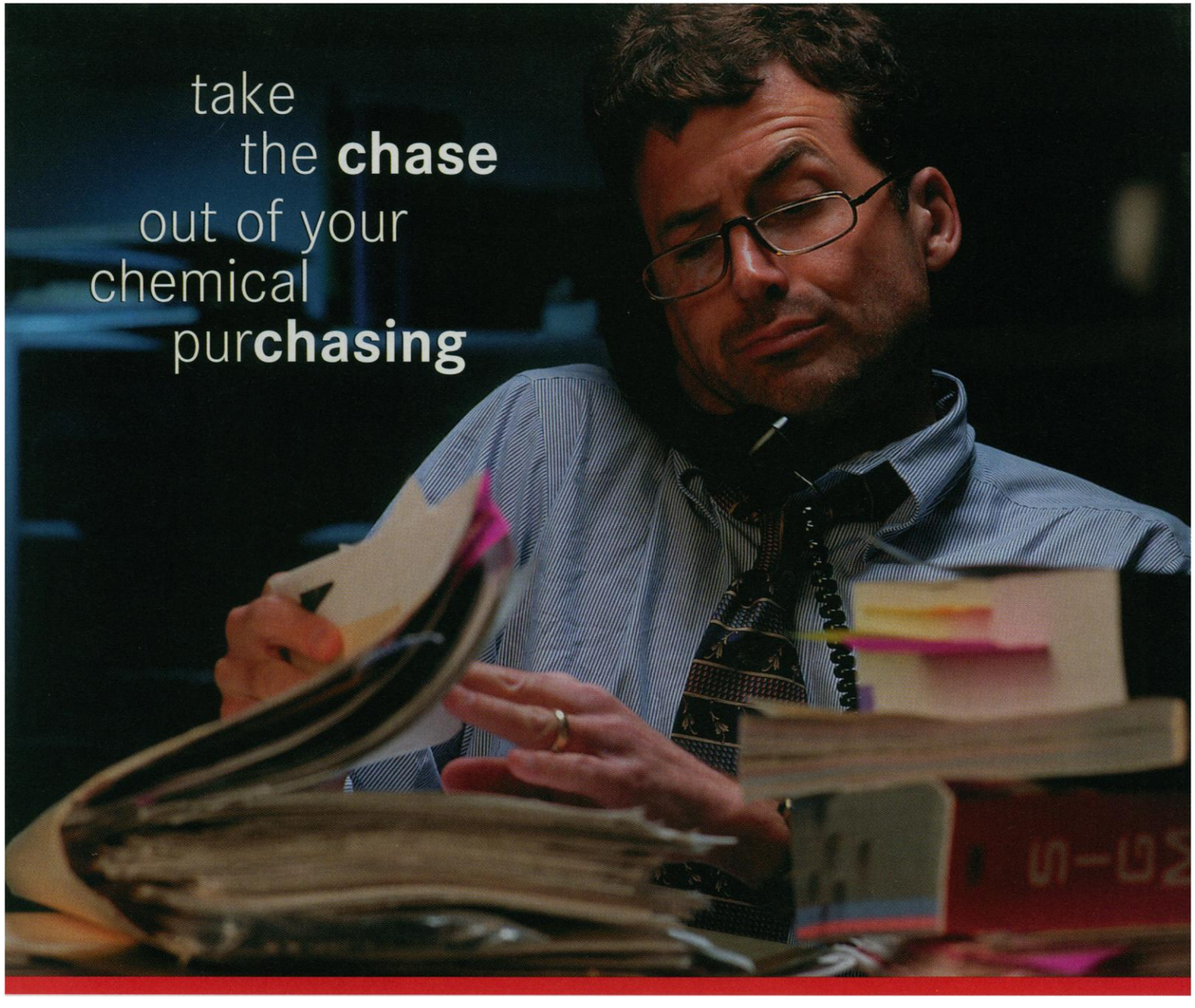
CONTROLLING STRESS

The nonclassical class I–like proteins MICA and MICB are induced by stress on intestinal epithelium and are present on many epithelial tumors. Such molecules mark cells for immune system responses, but their particular receptors on natural killer (NK) cells were unknown. Bauer *et al.* (p. 727; see the news story by Hagmann) have identified the MICA receptor as NKG2D, an orphan member of a family of C-type lectin-like receptors found on NK cells, most $\gamma\delta$ T cells, and $CD8^+$ $\alpha\beta$ T cells. Ligation of NKG2D induced killing activity of these cells toward MICA-transfected cells or epithelial tumors. Wu *et al.* (p. 730) identified and cloned a transmembrane protein called DAP10, which associates tightly with NKG2D. A phosphorylated motif in DAP10 becomes associated with the p85 subunit of PI-3 kinase, which may activate a signaling pathway toward effective killing. The identification of a stress-induced mechanism for killing cells may offer a new therapeutic approach for treating tumors.

BLOCKING ESTROGEN

The estrogen receptor is a nuclear hormone receptor that has been implicated in many breast cancers, and antiestrogens are widely prescribed to block binding of the natural ligands to the receptor. To better understand how estrogen and its agonists and antagonists interact with the estrogen receptor, Norris *et al.* (p. 744) used a phage display assay to identify peptides that bind differentially to various ligand-bound estrogen receptors. These binding complexes show that es-

CONTINUED ON PAGE 639



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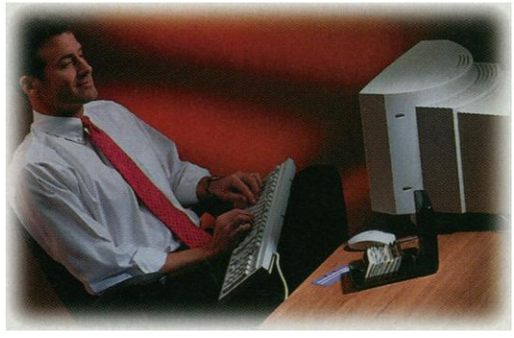

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trogen and the partial agonist tamoxifen interact with estrogen receptor through different mechanisms.

PARTNER PROTEIN PREDICTIONS

Proteins often interact with other proteins to accomplish their tasks within metabolic or signaling pathways. Marcotte *et al.* (p. 751) have devised a method of predicting, from sequence information on multiple organisms, whether two proteins are likely to interact. The premise is that if two proteins are distinct in one organism—that is, they are encoded by two separate genes—but are discovered to form domains of a single protein in a second organism (encoded in one gene), then they are likely to undergo a functional interaction in the first organism. They have found 6809 possible protein-protein interactions in *E. coli* and 45,502 interactions in yeast.

HARNESSING STEM CELLS FOR NEURAL TRANSPLANTS

Embryonic stem cells can differentiate into a wide variety of cell types, but manipulating the differentiation process has been challenging. Using a defined series of growth factors and culture media, Brüstle *et al.* (p. 754; see the news story by Steghaus-Kovac) have channeled the multipotentiality of embryonic stem cells to produce specific neuronal cell types, including cells responsible for myelination in the central nervous system. Transplantation of these cells into a rat with genetic deficiencies in myelination demonstrates the potential for the incorporation of functional graft cells in the central nervous system.

STRIPPING AWAY THE CAMOUFLAGE

Bacterial surface proteins not only promote interaction between the invading pathogen and host cells but also provide a means of evading detection by the host immune response. These proteins are tethered covalently to the bacterial cell wall by a mechanism that resembles transpeptidation and is known as cell wall sorting. Mazmanian *et al.* (p. 760) used a genetic approach to identify the enzyme in *Staphylococcus aureus* that catalyzes the formation of this tether and show that the corresponding gene is conserved in other pathogenic Gram-positive bacteria. This enzyme, called sortase, may be a useful target for the development of new antimicrobial drugs.

REPLICATION AND SIGNAL TRANSDUCTION

The concept of second messengers originated with the discovery of cyclic AMP, a compound synthesized from the nucleotide adenosine triphosphate by adenylyl cyclase. Cyclic AMP is an activator of protein kinases and thus of signal transduction pathways, but how did this unusual cyclic structure arise? Tesmer *et al.* (p. 756) present a structural analysis of the active site of this enzyme based on the essential involvement of two aspartic acid side chains and two divalent metal ions, manganese and zinc. They infer from the structural and mechanistic homology of adenylyl cyclase to DNA polymerases, the enzymes responsible for the replication of the genome, that these present-day cellular mainstays evolved from a common enzymatic ancestor.

TECHNICAL COMMENT SUMMARIES

Energy for Neurotransmission

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/285/5427/639a

P. J. Magistretti *et al.* (Perspectives, 22 Jan., p. 496) discussed how "the metabolic signals detected by functional brain imaging techniques bring us part way to understanding how neuronal processes such as action potentials and neurotransmitter release lead to a given brain activity and its resulting behavioral state." They described findings that begin to "identify and quantitate the specific cellular and molecular mechanisms of neuronal activity that are coupled to energy metabolism," and they gave central role to activities involving glutamate release.

L. Hertz and S. A. Robinson comment that "the association [between glucose utilization and glutamine formation] could not be as simple" as suggested in the Perspective. J. L. Griffin states that Magistretti *et al.* "offer an intriguing explanation of the complex link between activation and metabolism in the brain. There are a number of perplexing issues, however, that they did not address."

In response, Magistretti *et al.* state, "our results provide room for the energy roles in vivo for several of the neurotransmitter systems." Nevertheless, alternative metabolic pathways "cannot be taken to disagree with our explanation," they say, until relative rates "are quantified in vivo."

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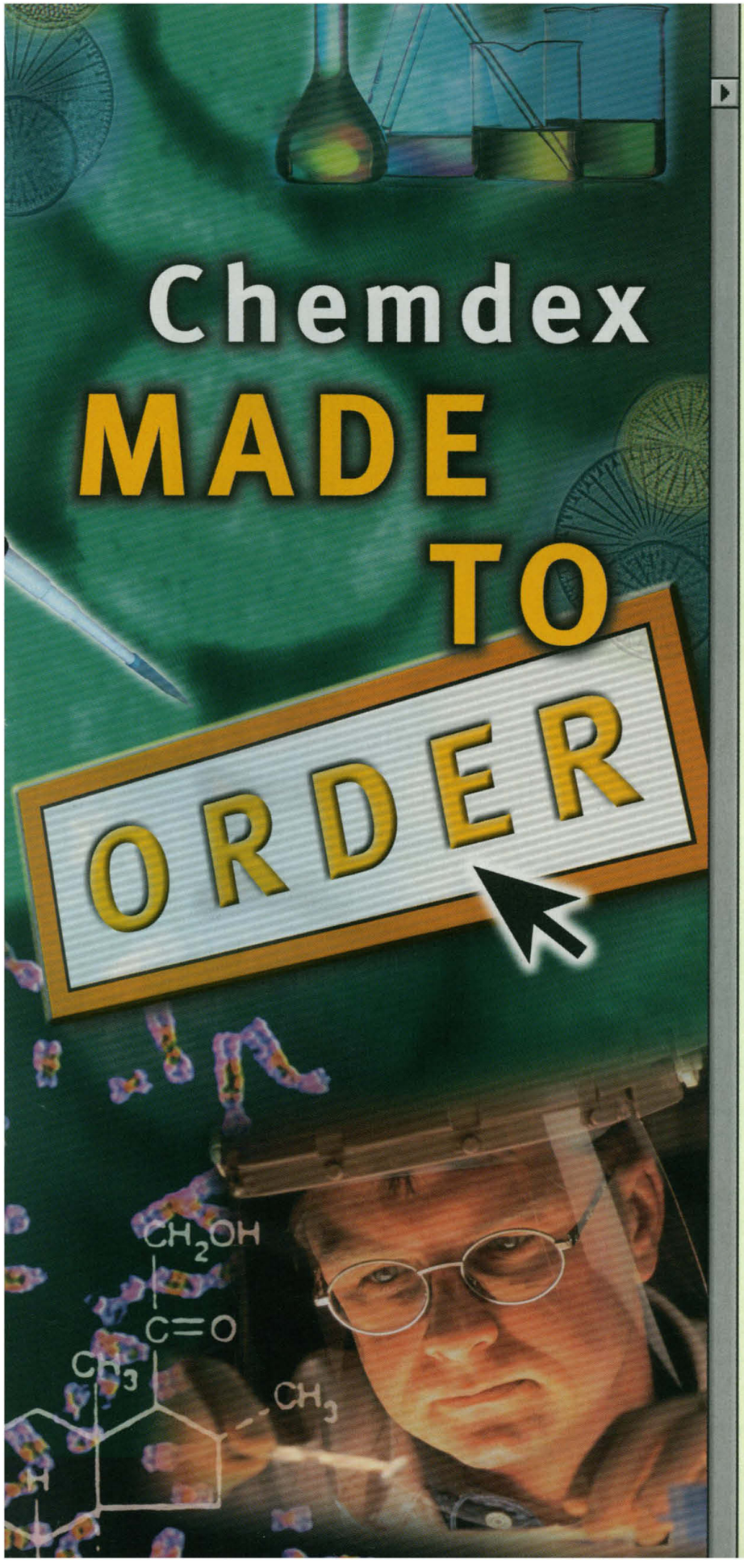

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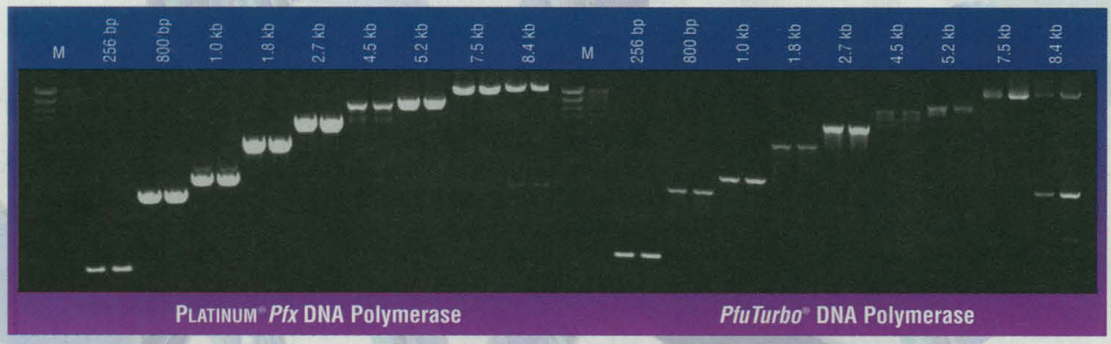

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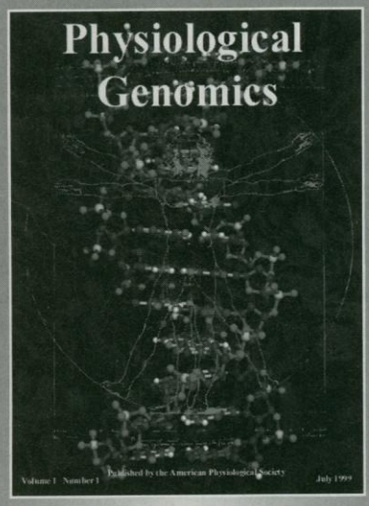

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