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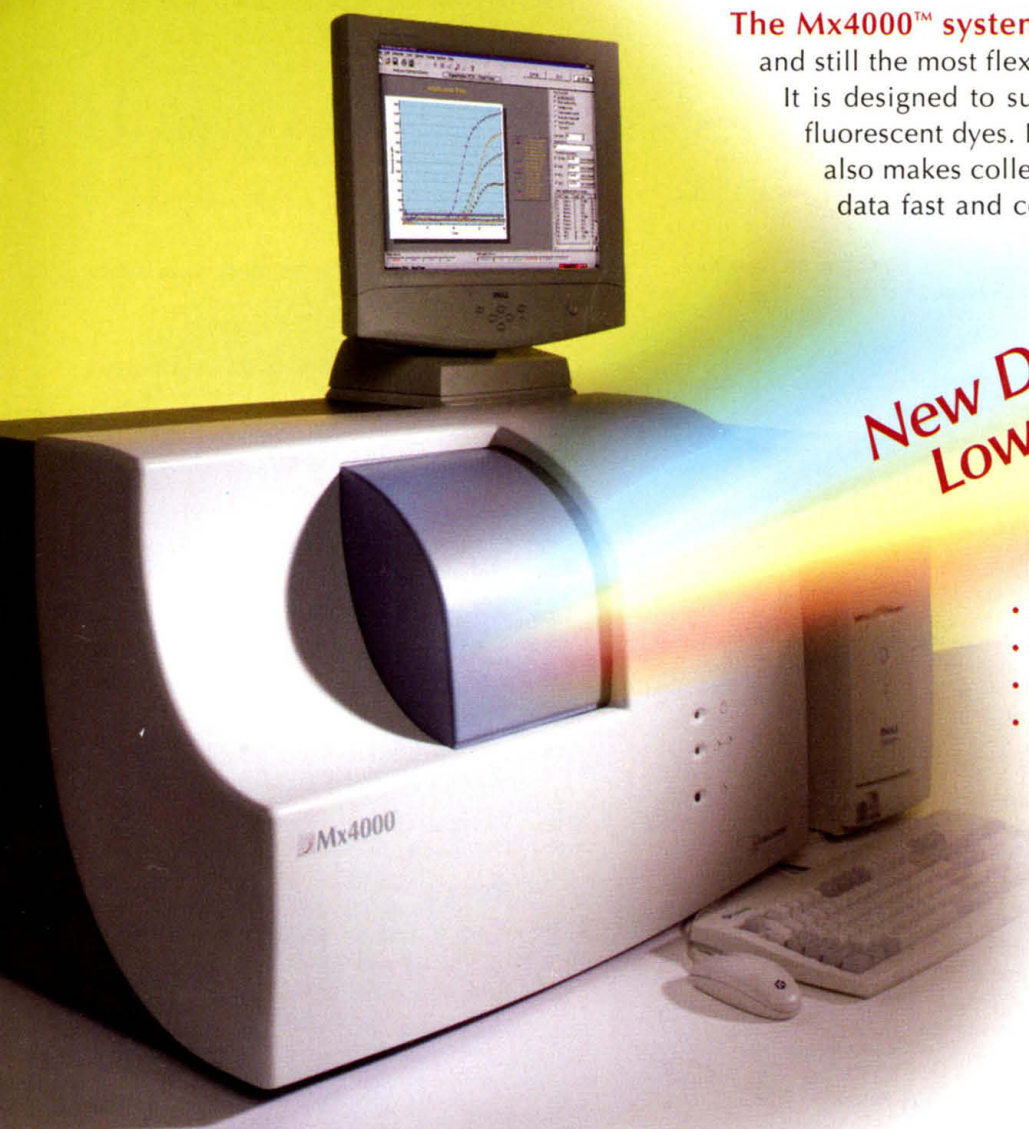
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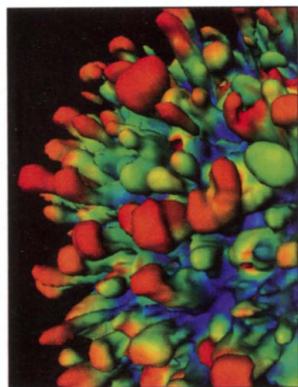
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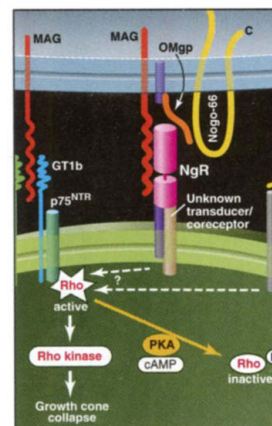
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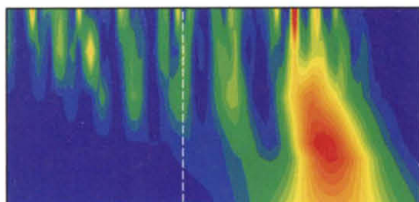
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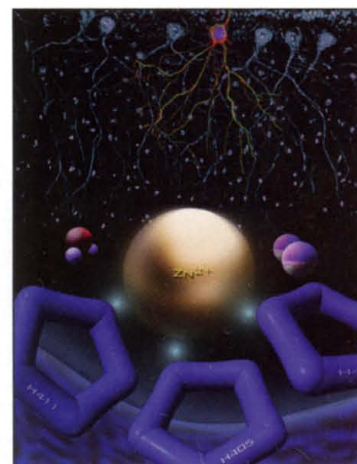
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COVER 1183

Bacterial cells simultaneously expressing two different fluorescent proteins (red and green) from identical promoters. Because of stochasticity ("noise") in the process of gene expression, even two nearly identical genes often produce unequal amounts of protein. The resulting color variation shows how noise fundamentally limits the accuracy of gene regulation. [Image: M. B. Elowitz]



1186

Regulating MMP's Zn-cysteine switch

New on Science Express

Salting out aerosol pollution



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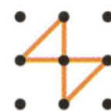
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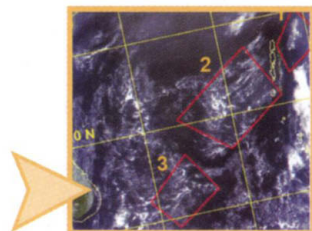
SCIENCE EXPRESS

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The Role of Sea Spray in Cleansing Air Pollution over Ocean via Cloud Processes

D. Rosenfeld, R. Lahav, A. Khain, M. Pinsky

Sea salt nuclei initiate the formation of raindrops over the oceans, which help cleanse the atmosphere of air pollution.



Role of Predicted Metalloprotease Motif of Jab1/Csn5 in Cleavage of NEDD8 from CUL1

G. A. Cope *et al.*

Role of Rpn11 Metalloprotease in Deubiquitination and Degradation by the 26S Proteasome R. Verma *et al.*

Similar motifs control cleavage of ubiquitin and ubiquitin-like moieties.

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career resources for scientists

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A Ph.D. aiming to improve science teaching in schools.

CANADA: Choosing an Advisor J. Andraos
Finding the right graduate advisor is critically important—throughout your career.

US: Negotiating Your First Real Salary D. Jensen
Just how much are your ideas and expertise worth to a prospective employer?

UK: Want to Learn How to Start a Business?
J. Maldonado-Saldivia
Check out the new entrepreneurship Masters program at the Cambridge-MIT Institute.

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NOTEWORTHY THIS WEEK: No Supermodel M. Leslie
Cancer pathways might differ in mice and humans.

NOTEWORTHY THIS WEEK: Nerve Verve M. Beckman
Nerve growth factor invigorates mice with Lou Gehrig's disease.

NOTEWORTHY THIS WEEK: Menopause Mouse M. Beckman
Hormone-hampered rodents mimic menopause.

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signal transduction knowledge environment

REVIEW: Responding to Hypoxia—Lessons from a Model Cell Line K. A. Seta, Z. Spicer, Y. Yuan, G. Lu, D. E. Millhorn

Lessons from PC12 cells provide clues to how signaling pathways lead to gene expression in response to reduced O₂.

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THIS WEEK IN Science

edited by Phil Szuromi

Getting a Kick Out of Light

In the usual photoionization process, the absorption and emission of photons between the light field and the photoexcited electron packet is an arbitrary process that broadens the energy distribution of the electrons. However, there is no net exchange of energy between the two, and the drift velocity of the electron packet is unchanged. Kienberger *et al.* (p. 1144; see the Perspective by Lewenstein) used ultrafast x-ray pulses only several hundred attoseconds (1 attosecond is 10^{-18} second) in duration to generate a packet of electrons. They could then control where the packet interacted relative to the phase of much more intense (but slower and longer wavelength) laser light field. The confinement of the packet to a particular region of the light field not only allows the acceleration and deceleration of the electron packets, but also provides a powerful probe for use in attosecond metrology. ✕

Marine Light Alkyl Nitrates

The light alkyl nitrates in the atmosphere play an important role in controlling tropospheric ozone levels, and their sources have been assumed to be exclusively anthropogenic. Chuck *et al.* (p. 1151; see the Perspective by Ballschmiter) show that assumption to be erroneous. They report measurements of methyl and ethyl nitrate in seawater which indicate that large areas of the Atlantic Ocean are supersaturated for both compounds, thereby providing direct evidence for an oceanic source. Upper-ocean depth profiles suggest that biological processes are involved in their production.

Electrons Swimming on Surfaces

Electron solvation in layers of organic molecules adsorbed on the Ag(111) surface has been studied by Miller *et al.* (p. 1163). A probe laser pulse was used to excite electrons from the metal into discrete energy levels (image potential states) in overlayers of acetonitrile or butyronitrile, and a later pulse then probed the state of the electron. They observed a constant ener-



1148

Pictures of Quasiparticle Interference

Interference patterns of electron waves, such as those surrounding defects, have often been observed with scanning tunneling microscopy (STM). Hoffman *et al.* (p. 1148; see the 26 July news story by Cho) have used STM to look more closely at the "checkerboard" pattern formed in the high-temperature superconducting cuprate, $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_{8+\delta}$. By Fourier transforming the energy and spatial data, they can capture the dispersion relations of the superconducting quasiparticles in real space. The results, which suggest that the patterns arise from the interference of quasiparticle states located at different parts of the Fermi surface, may provide an explanation for the various incommensurate phenomena observed in these materials. ✕

And in Brevia ...

A method developed by Yan *et al.* (p. 1143) for determining the variation in expression levels of genes in normal humans shows that inherited variations are fairly common.

gy difference between the first and second levels which suggests that the primary effect of solvation is to lower the local work function. They also observed the localization of the image electron, to a region about the size of a single absorbate, on a time scale of a few hundred femtoseconds.

Nitrogen Balance

The nitrogen isotopic ratios of the mantle and the crust are significantly different, but some volcanic rocks derived from the mantle show a crustal nitrogen signature. Subduction has been suggested as a vehicle for recycling nitrogen. Fischer *et al.* (p. 1154) measured the nitrogen and helium isotopic concentrations of gaseous emis-

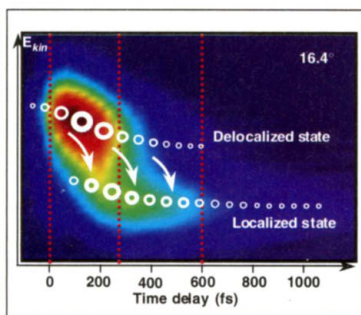
sions from arc volcanoes in Guatemala and Costa Rica, where the arc volcanism is caused by the subduction of the Cocos plate beneath the Caribbean plate. Heavy nitrogen (^{15}N) from the crust is carried down into the mantle wedge and then recycled back to the surface in the arc magmas, rather than into the mantle. If similar recycling occurs at other subduction zones, then methods of balancing nitrogen recycling and volatile fluxes need to be reconsidered.

Survey Says...

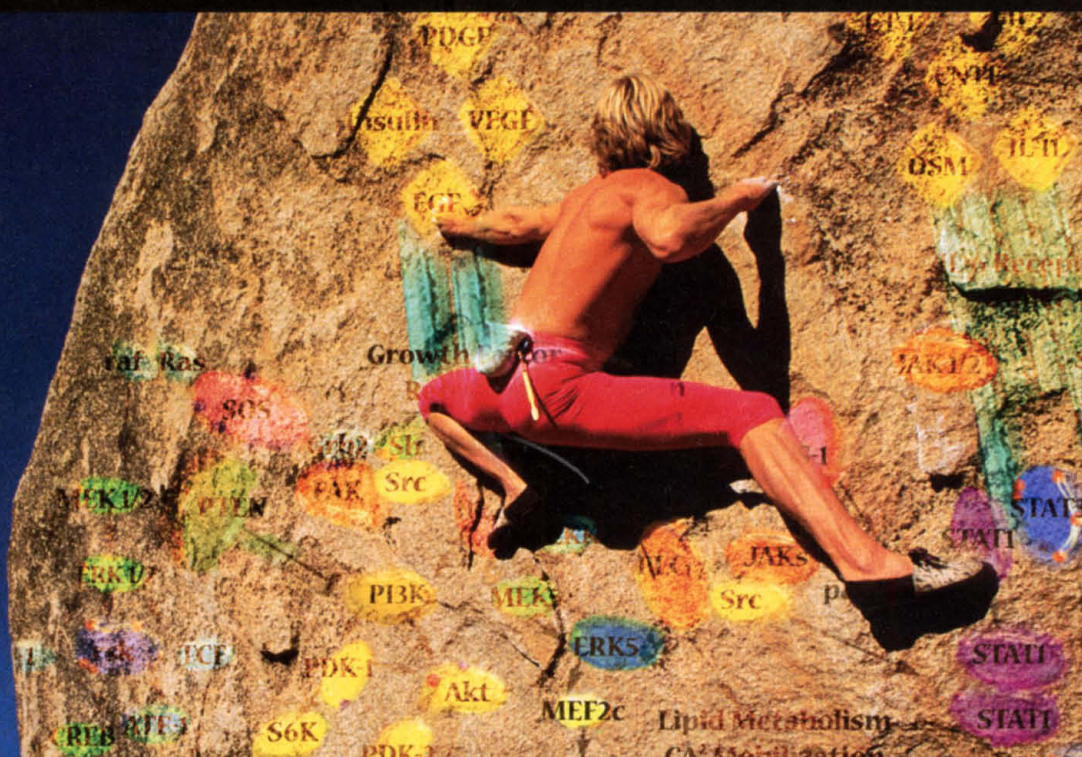
The "public information hypothesis" (or "habitat copying hypothesis") proposes that individual animals cue on the local reproductive success of other members of their species to assess and choose their breeding site. Doligez *et al.* (p. 1168; see the news story by Withgott) performed a long-term manipulation of reproductive success of the collared flycatcher in Sweden at the scale of numerous entire patches of breeding habitat. From studies of more than 1000 nesting attempts, they found that birds used public information to decide whether to emigrate from, and settle in, a patch of breeding habitat.

Keep Those Platelets Rolling

At sites of vascular damage, von Willebrand factor (VWF) that is bound to the cell matrix interacts transiently with platelet receptor glycoprotein $\text{Ib}\alpha$ ($\text{GpIb}\alpha$) and slows down the platelets so that they can respond to the injury. Huizinga *et al.* (p. 1176; see the Perspective by Sadler) have determined structures of the $\text{GpIb}\alpha$ amino-terminal domain and its complex with the VWF A1 domain at 1.9 and 3.1 angstrom resolution, respectively. In the complex, an area of weak electrostatic interaction



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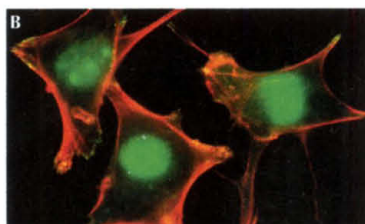
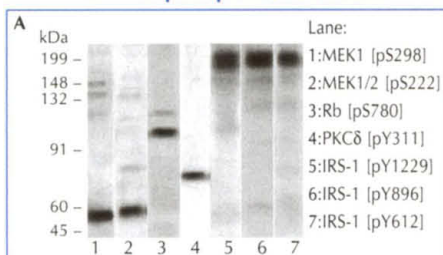
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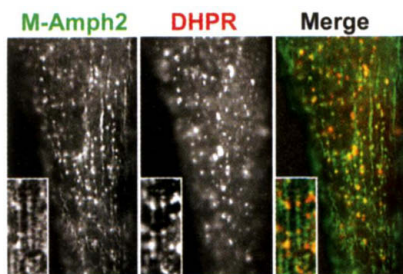
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bridges two contact areas that are potential targets for antithrombotic drugs. Conformational changes in GpIb α and the A1 domain are required for interaction at the two contact sites, and mutations that cause gain-of-function diseases favor the bound conformation at both sites. The authors propose a model based on these structures for shear-induced activation.

Transverse Tubule Biogenesis



Amphiphysins are part of the cellular machinery that facilitates invagination of the plasma membrane during endocytosis. Lee *et al.* (p. 1193) report that a muscle-specific form of amphiphysin 2 (also called Bin1) directs invagination of the membrane into tubules and is critical for transverse (T) tubule biogenesis during mammalian muscle development. This amphiphysin localizes to the plasma membrane through a domain that recognizes specific phosphoinositides that are highly concentrated in the T-tubule system. Thus, the amphiphysins appear to have a conserved role in membrane deformation and morphogenesis.

concentrated in the T-tubule system. Thus, the amphiphysins appear to have a conserved role in membrane deformation and morphogenesis.

Controlling Population Expansion

Several genes that function in eye development display a surprising level of conservation in gene function between mammals and invertebrates. One of these genes, mammalian *Six6*, is expressed early in development of the retina and also in the pituitary gland. Li *et al.* (p. 1180; see the 19 July news story by Vogel) investigated whether this factor is involved in cell-type determination or cell proliferation of precursor cells. In *Six6*^{-/-} mice, all neuronal cell types in the retina and all pituitary cell types were found, but the cell types were decreased in number, and defects were observed in both organs. *Six6* associates with the corepressor Dach to block cyclin-dependent inhibitors and allow for early progenitor cell proliferation. Hence, a tissue-specific repressor and corepressor regulate the cell cycle in an organ-specific manner. Σ

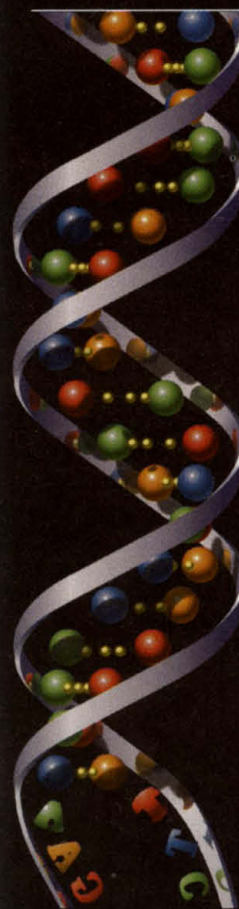
The Ups and Downs of Expression

Gene expression varies substantially from one cell to another, and depending on the history of the cell, its interactions, the state of its regulatory machinery, and so on. Elowitz *et al.* (p. 1183; see the cover and the Perspective by Fedoroff and Fontana) have focused on the noise in gene expression that is left when all other regulatory influences are equal. To measure this "intrinsic noise," they used strains of *Escherichia coli* in which two alleles encoding distinguishable green fluorescent proteins were controlled by identical promoters. In these single bacterial cells, genes have essentially the same intracellular environment, so the variation in their expression is a measure of intrinsic noise. Intrinsic noise accounted for a substantial amount of the total variation in gene expression and amount of noise varied with changes in other factors like transcription rate.

Redundant Pathways Against Neuronal Regeneration

In vertebrates, severed nerves in the limbs can regrow and re-innervate their targets, restoring movement and sensory input. Similar injuries to the brain or spinal cord are not repaired, however, because of two inhibitory molecules in the myelin sheaths of central nerves that prevent neural regeneration—Nogo and myelin-associated glycoprotein (MAG). The glycosyl-phosphatidylinositol-linked receptor for Nogo has no intracellular domain, but the receptor for MAG is not definitively known, although it does bind sialic acid. In a screen designed to find other membrane proteins that might mediate the transmembrane signal of the Nogo receptor, Liu *et al.* (p. 1190; see the Perspective by Woolff and Bloechlinger) identified MAG as a primary ligand. This binding is of an appropriately high affinity to control the growth-cone-collapsing effects of MAG and to ensure that expression of the Nogo receptor confers MAG sensitivity to embryonic neurons. Thus, both MAG and Nogo activate the Nogo receptor and act as redundant signals to inhibit neural regeneration. Σ

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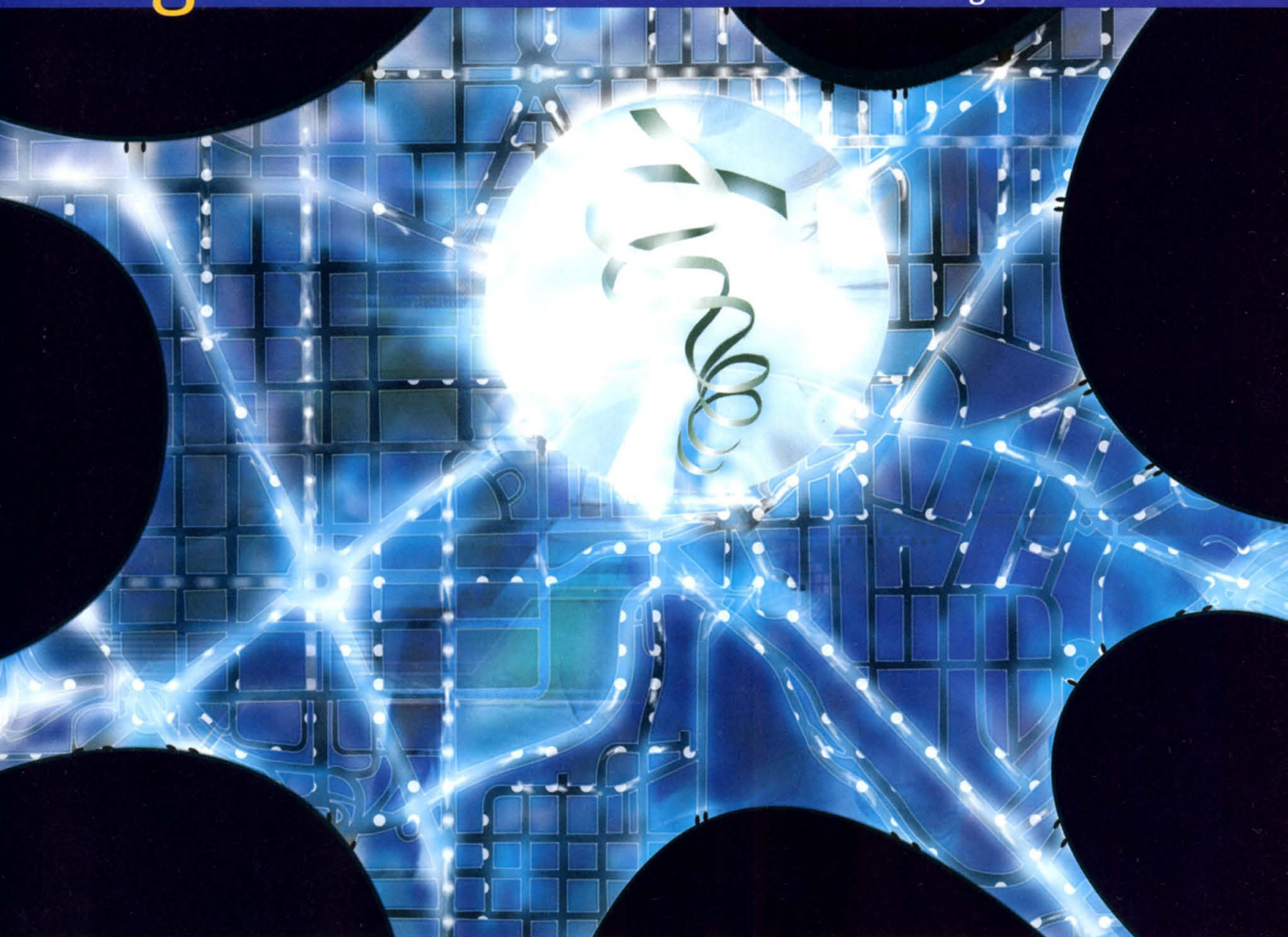
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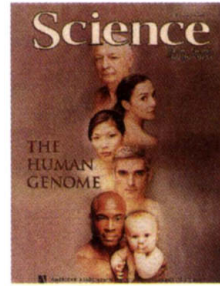
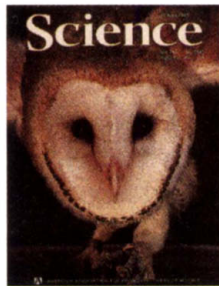
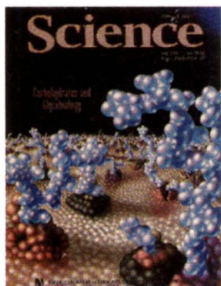


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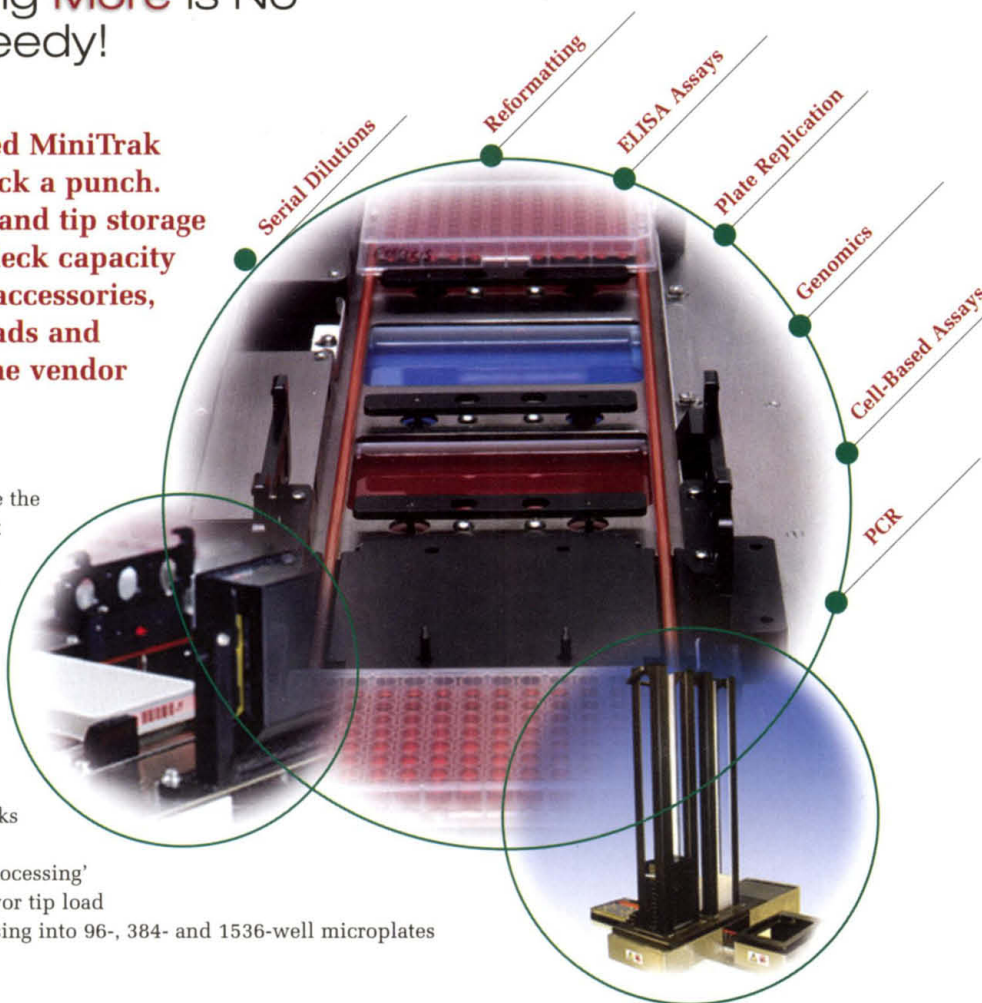
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