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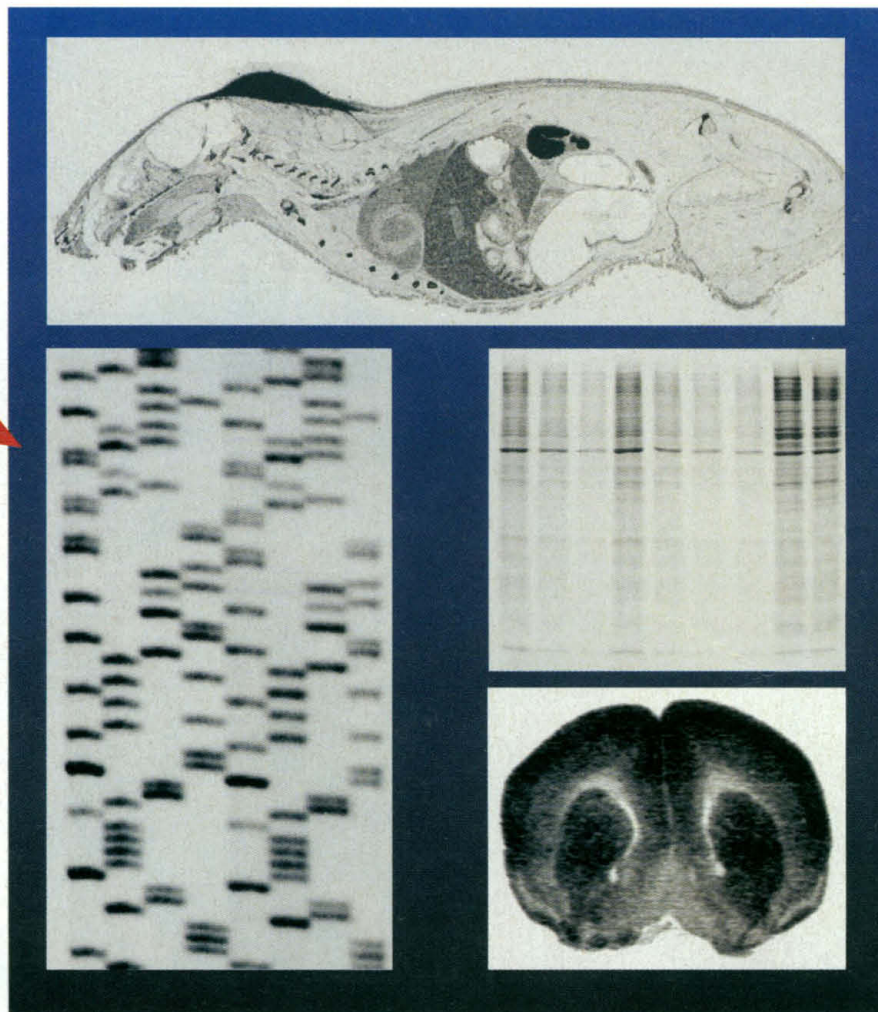
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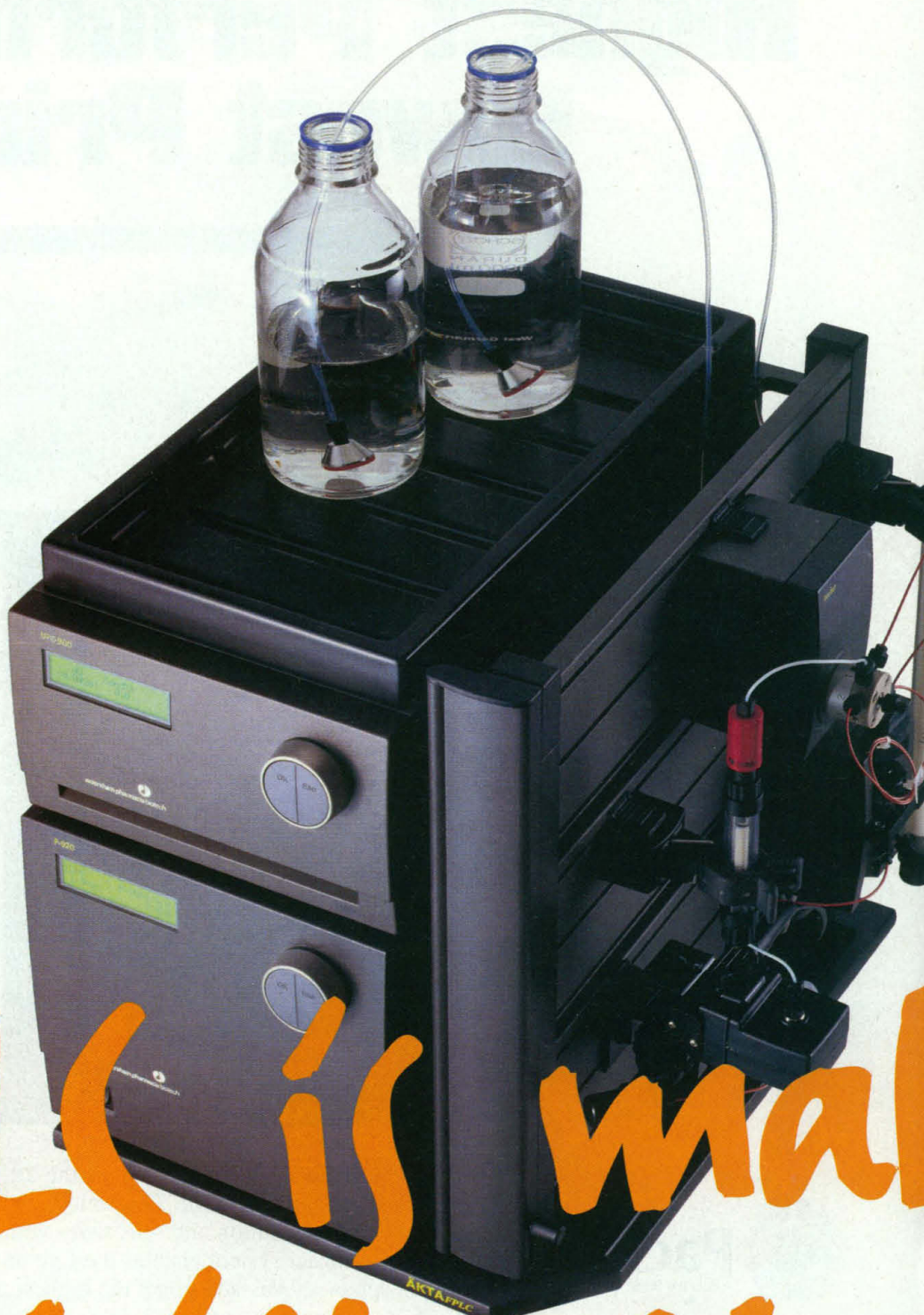
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A photograph of a laboratory FPLC (Fast Protein Liquid Chromatography) system. The system consists of two stacked modules, a pump (P-920) and a detector (SPD-920), both from Pharmacia LKB. Two clear plastic bottles containing liquid are placed on top of the modules, connected by thin tubing. The system is black and has a digital display and a control knob on each module. The text "FPLC is making history." is overlaid in a large, orange, handwritten font.

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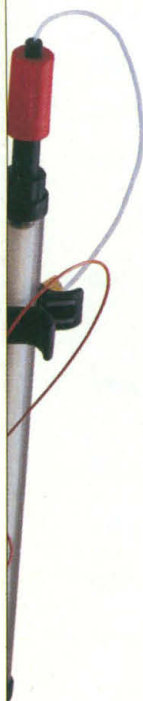
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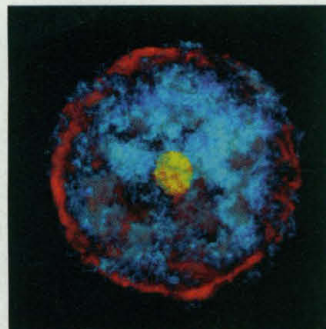


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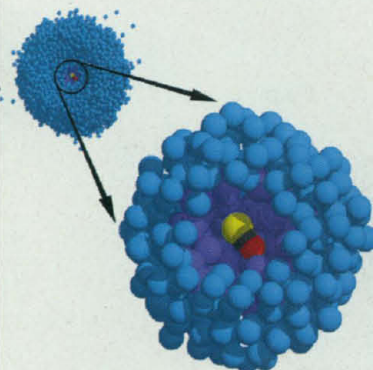


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2030

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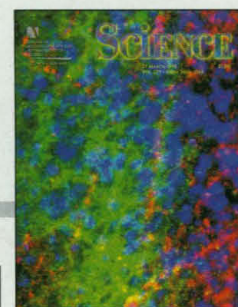
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COVER

High-magnification confocal image of the border between the eye-specific layers in the lateral geniculate nucleus (LGN) of an 11-day-old ferret (image width ~225 micrometers). Retinal ganglion cell axons are labeled with the lipophilic tracers Dil (green; right eye)

and DiI (red; left eye); LGN neuron nuclei are stained with Hoechst (blue). The formation of these eye-specific layers depends on interocular competition driven by spontaneous activity present in the retina before vision. See page 2108. [Image: A. Penn and T. Brotz]



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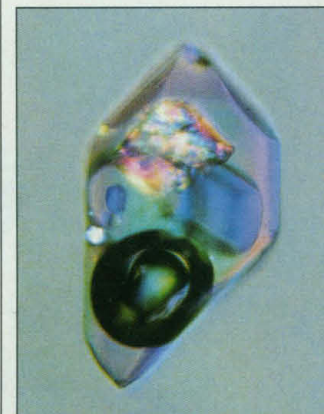
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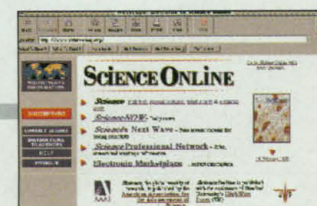
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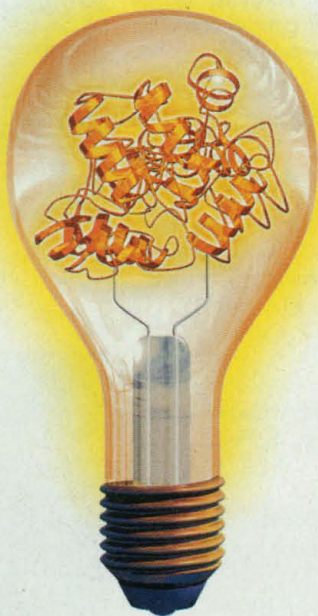
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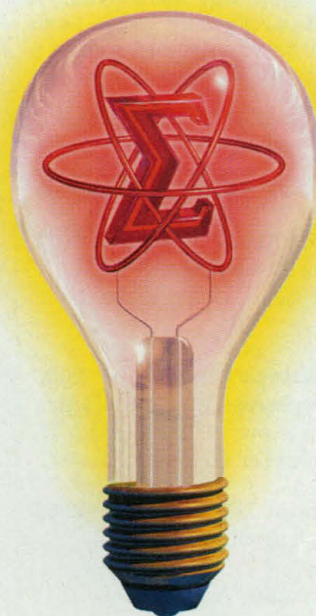
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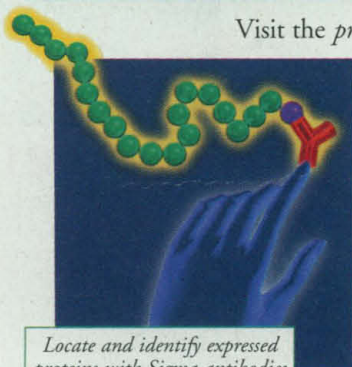


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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Intrinsically incoherent

Landau's theory of normal metals, which describes the conduction electrons as a Fermi liquid state, predicts that electron transport properties are coherent in all directions even in the limit of low energies and low temperatures. Layered metals, especially the normal states of layered cuprate and organic superconductors, exhibit anomalous transport in the direction normal to the layers. Clarke *et al.* (p. 2071) review experimental evidence of such incoherent transport in the normal state of an organic superconductor, including the absence of certain interference effects expected of coherent electrons. They present a theoretical description for these "quantum-classical" metals, which are coherent (quantum) in some directions and incoherent (classical) in others.

Binding assay

Many medical and biological studies rely on quick and simple assays to monitor ligand-receptor binding, and there are many competing approaches for developing improved assays. Gupta *et al.* (p. 2077) have developed a technique based on reorientation of liquid crystal films upon ligand binding. The optical signal from the liquid crystals can be read by eye, and there is no need for electrical power for performing the assay. The method is best suited for diagnostic assays requiring a yes or no answer, rather than for quantitative measurements. The technique requires nanogram quantities of material and can be localized to regions with micrometer resolution, suggesting its use in screening of patterned arrays of chemical species.

An unusual benzene valence isomer

Within the numerous chemical structures known to chemists, one might assume that most benzene

Dragging satellites around a spinning Earth

General relativity predicts that the orbit of an object rotating around a spinning central mass will be perturbed by the spinning body and alter its space-time reference frame. Such "frame dragging," as Einstein called it, has been named the Lense-Thirring effect, but proof of its existence has been difficult to obtain because the time perturbations should be small. Ciufolini *et al.* (p. 2100) used two laser-ranged satellites, LAGEOS and LAGEOS II, both of which orbit about 6000 kilometers above Earth, to try to detect the Lense-Thirring effect. The authors measured the total travel time of laser beams reflected off of these satellites with an accuracy of a few millimeters and looked for perturbations in these travel times during a 4-year period. Earth's oscillations related to tides and mass fluxes on the surface and in the interior are a significant source of error in these measurements and could make these small perturbations indistinguishable from noise. By using the latest Earth gravitational model (EGM-96), these noisy artifacts were reduced, and small perturbations of the laser beam travel times attributed to frame dragging were detected.

and benzene valence isomers are known. However, many of them have been postulated yet not observed. Canac *et al.* (p. 2080) synthesized a benzene valence isomer with four phosphorus atoms and show that this isomer is a tricyclic biradical. The compound contains a six-electron, four-center bonding system, formally resulting in one-electron bond between two phosphorus atoms.

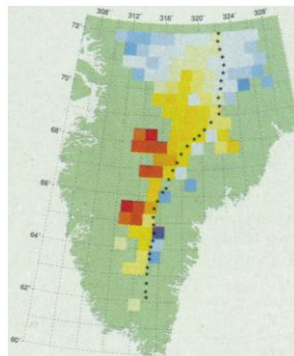
Microscopic superfluidity

Superfluidity is observed for helium isotopes ^3He and ^4He at very low temperatures and is characterized by extremely low viscosity and high heat conductivity. Most observations to date are of macroscopic manifestations of superfluidity. Grebenev *et al.* (p. 2083; see the commentary by Lehmann and Scoles, p. 2065) studied the behavior of mixed $^3\text{He}/^4\text{He}$ droplets containing an OCS molecule. Because the temperature for the onset of superfluidity is lower for ^3He than for ^4He , choosing an appropriate temperature ensures that only ^4He is superfluid. The ^4He concentrates in the center of the droplet around the OCS molecule. If sufficient ^4He is present, the molecule rotates nearly without friction, indicating that

it exists in a superfluid environment. Only about two layers of ^4He surrounding the molecule are necessary for this effect.

Slower Greenland growth

An assessment of whether the Greenland ice sheet as a whole is growing or shrinking is important for resolving its response to climate change and for understanding changes in sea level. An early satellite study implied that it was



growing at perhaps up to 20 centimeters per year. Davis *et al.* (p. 2086) have now recalibrated the satellite data and extended the analysis and find that the rate of growth is much more modest, perhaps at most about 2 centimeters per year.

Ringing the Earth

Oscillations (or the ringing) of Earth are assumed to be caused by large earthquakes or mass fluctuations within the interior. Suda *et al.* (p. 2089; see the commentary by Kanamori, p. 2063) used a global network of sensitive gravimeters to record minute changes in gravitational accelerations during a 10-year period. They found low frequency oscillations that are not associated with earthquakes or interior fluctuations. This background ringing may be caused by some unknown coupling between the solid Earth and the atmosphere.

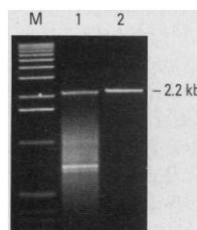
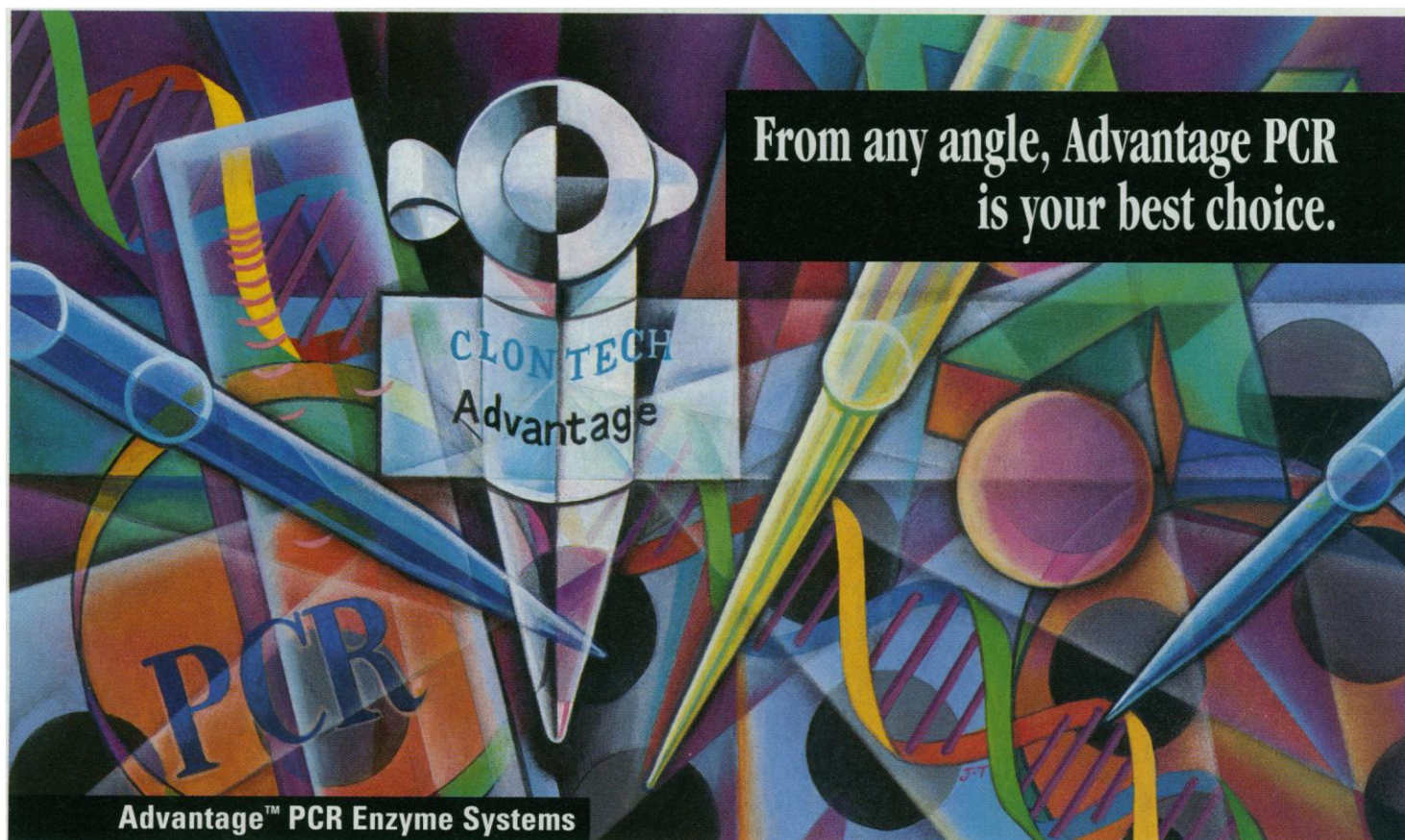
Ore origins

Many important ore deposits are formed from magmatic fluids carrying metals in solution. Cooling or depressurization of these fluids, or mixing with waters of other origins or reactive rocks, can lead to rapid mineralization and concentration of the metals. As minerals form, they typically trap the parent fluids in tiny, micrometer-sized inclusions. Audétat *et al.* (p. 2091; see the commentary by Barnes and Rose, p. 2064) obtained a detailed chemical analysis of these trapped fluids using a laser-ablation inductively coupled plasma mass spectrometer. By examining an extended sequence of fluids trapped as quartz crystals grew in a vein in a world-class tin deposit in Australia, the Yankee Lode, they show how the composition, pressure, and temperature of the fluid varied with time and formed the deposit. Tin precipitation began when the magmatic fluid mixed with cooler meteoric fluids.

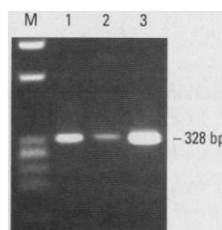
Strain at Yucca Mountain?

Yucca Mountain is the proposed site for high-level nuclear waste disposal; it is also situated in the

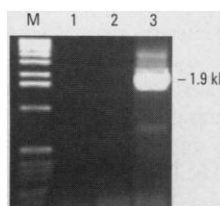
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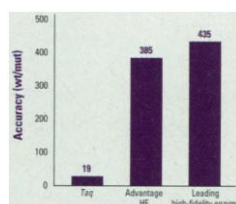
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(Continued from page 2013)

Basin and Range province of the western United States, a region undergoing crustal extension since about 40 million years ago. The extension, and typically associated volcanic activity, appears now to be primarily focused on the margins of the province, but understanding the stability of the Yucca Mountain region is important for assessing the stability of the disposal site and also for evaluating the pattern of extension through the region. Wernicke *et al.* (p. 2096; see the news story by Kerr, p. 2040) conducted a Global Positioning System survey from 1991 to 1997 across the Yucca Mountain region, extending an earlier survey started in 1983. The data show that the region extended in a west-northwest direction by about 1.7 millimeters per year. This rate is anomalously high in view of the geologic evidence in the region and may imply that strain accumulates episodically rather than continuously in the region and perhaps throughout the Basin and Range.

Assessing our reserves

Conservation planning can be more of an art than a science. Two reports discuss the issues of maximizing species preservation in the purchase of land reserves and the use of biodiversity markers (see the commentary by Pimm and Lawton, p. 2068). Ando *et al.* (p. 2126) introduce the often avoided question of land price. Taking into account the substantial differences in land value from county to county across the United States, they show that minimizing land area for a given conservation goal is not always the most cost-effective approach. Van Jaarsveld *et al.* (p. 2106) assess the agreement among different surrogate indicators of biodiversity using data from the Transvaal, South Africa. They find discouragingly little congruence

among the different approaches, which calls the current principles of planning into question.

Before you look

Visual input from both eyes is balanced and combined in the lateral geniculate nucleus (LGN) of the mammalian brain. The allocation of territory in the LGN to input from each eye can be shifted by altering the visual experience. Penn *et al.* (p. 2108; see the cover) now show that the brain's balancing act begins much earlier: Before the eyes open, spontaneous electrophysiological activity in the retinas signals to the LGN to begin to build a balanced input from both active retinas.

Chance and evolution

Much debate has centered on the effect of chance and history in the outcome of evolutionary events. Losos *et al.* (p. 2115; see the news story by Vogel, p. 2043) analyze the evolution of lizards on Caribbean islands and find that the answer depends on the frame of reference. On any single island, who gets where first appears to determine what latecomers can do with the available ecological niches. However, when the islands are viewed as a group, the fate of any particular lizard lineage was not constrained by its previous evolutionary history. On the four islands studied, independent evolutionary events resulted in similar outcomes.

Monoallele for IL-2

T cells secrete proteins, called cytokines, that initiate, regulate, and modulate the immune response. Interleukin-2 (IL-2) is a cytokine that is important for T cell proliferation after exposure to antigen. Hollländer *et al.* (p. 2118; see the commentary by Chess, p. 2067) examined individual T cells and determined that IL-2 is tran-

scribed exclusively from a single allele in any given cell. This phenomenon implies that transcription of autosomal genes that are not odorant receptors or antigen receptors also can be regulated by some form of allelic exclusion, to ensure monoallelic expression.

Arginine to NO

Three structures of the oxygenase domain of nitric oxide synthase with the pterin cofactor, with the substrate arginine, and with the product analog thiocitrulline complete the picture of how this amino acid is converted into a gaseous messenger. Crane *et al.* (p. 2121) find that the pterin cofactor is not directly involved in either the hydroxylation or the

subsequent oxidation, but instead serves to trigger the dimerization and closure of the oxygenase domains, which yields a sequestered channel connecting the substrate and the heme-bound dioxygen.



Within this environment, the initial availability of a substrate proton favors hydroxylation of arginine; the lack of another proton steers the second reaction toward oxidation and the synthesis of citrulline and NO.

Technical Comment Summaries

Constitutive Expression of FasL and Thyrocytes

C. Giordano *et al.* studied (Reports, 14 Feb. 1997, p. 960) cells from the thyroid glands of patients with Hashimoto's thyroiditis (HT). These thyrocytes constitutively expressed the ligand for the Fas antigen (Fas-L). Giordano *et al.* also found that "interleukin-1 β , abundantly produced in HT glands, induced Fas expression in normal thyrocytes," resulting in apoptosis. They concluded that "Fas-FasL interactions among HT thyrocytes may contribute to clinical hypothyroidism."

T. A. Stokes *et al.* studied the expression of Fas and FasL on the surface of thyrocytes with the use of reverse transcriptase-polymerase chain reaction, ribonuclease protection techniques, immunohistochemical staining, and protein immunoassays. They did not observe "the expression of mRNA for FasL in primary cultured thyrocytes from more than 20 normal and thyroiditis tissue samples." They conclude that it is "difficult to predict the relative importance of Fas-mediated apoptosis in thyroiditis."

P. Fiedler *et al.* also performed various assays with the use of "a panel of human tumor cell lines" to study the antibodies used in the report. They found that two of the antibodies "might not be specific for FasL" and conclude that results from several published studies "should be reinterpreted...or repeated."

In response, Giordano and her colleagues (G. Papoff *et al.*) state that, although one antibody "may give a relatively high background signal in a stain," further experiments show that "normal thyrocytes express substantial amounts of FasL in vivo." They also retested antibodies, which "gave a specific staining only in transfected cells." They state that "it is not clear why" other investigators are obtaining contradictory results, but "recommend the simultaneous use of several FasL antibody reagents" when studying FasL expression.

The full text and figures of these comments can be seen at www.sciencemag.org/cgi/content/full/279/5359/2015a

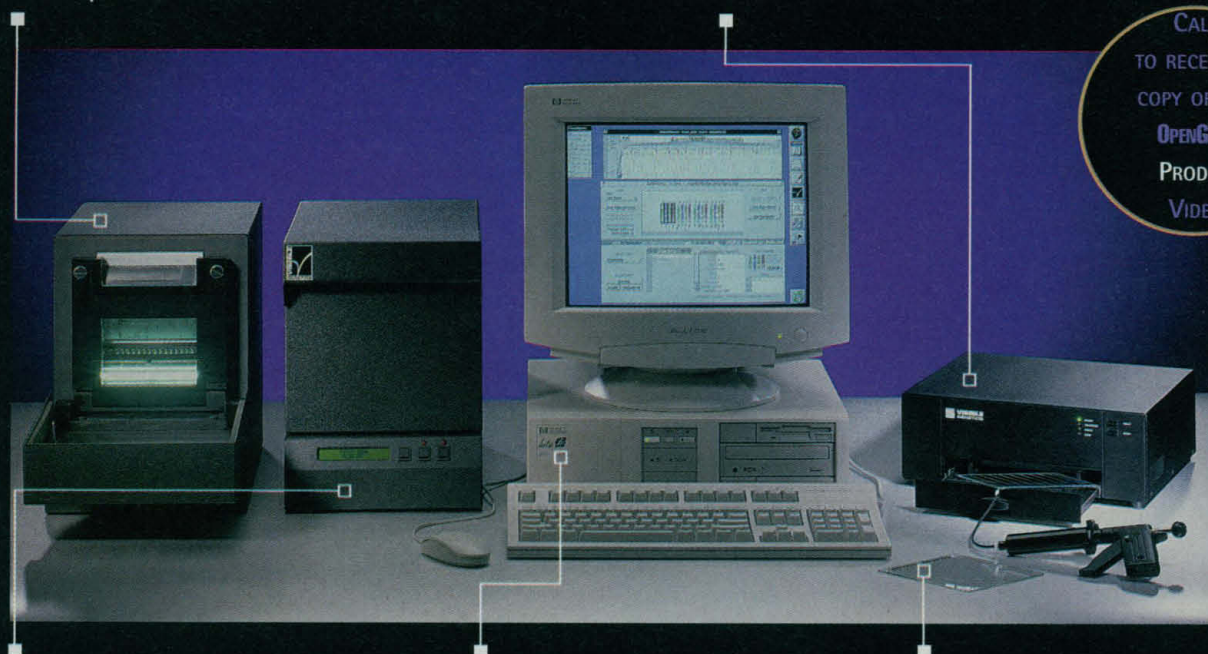
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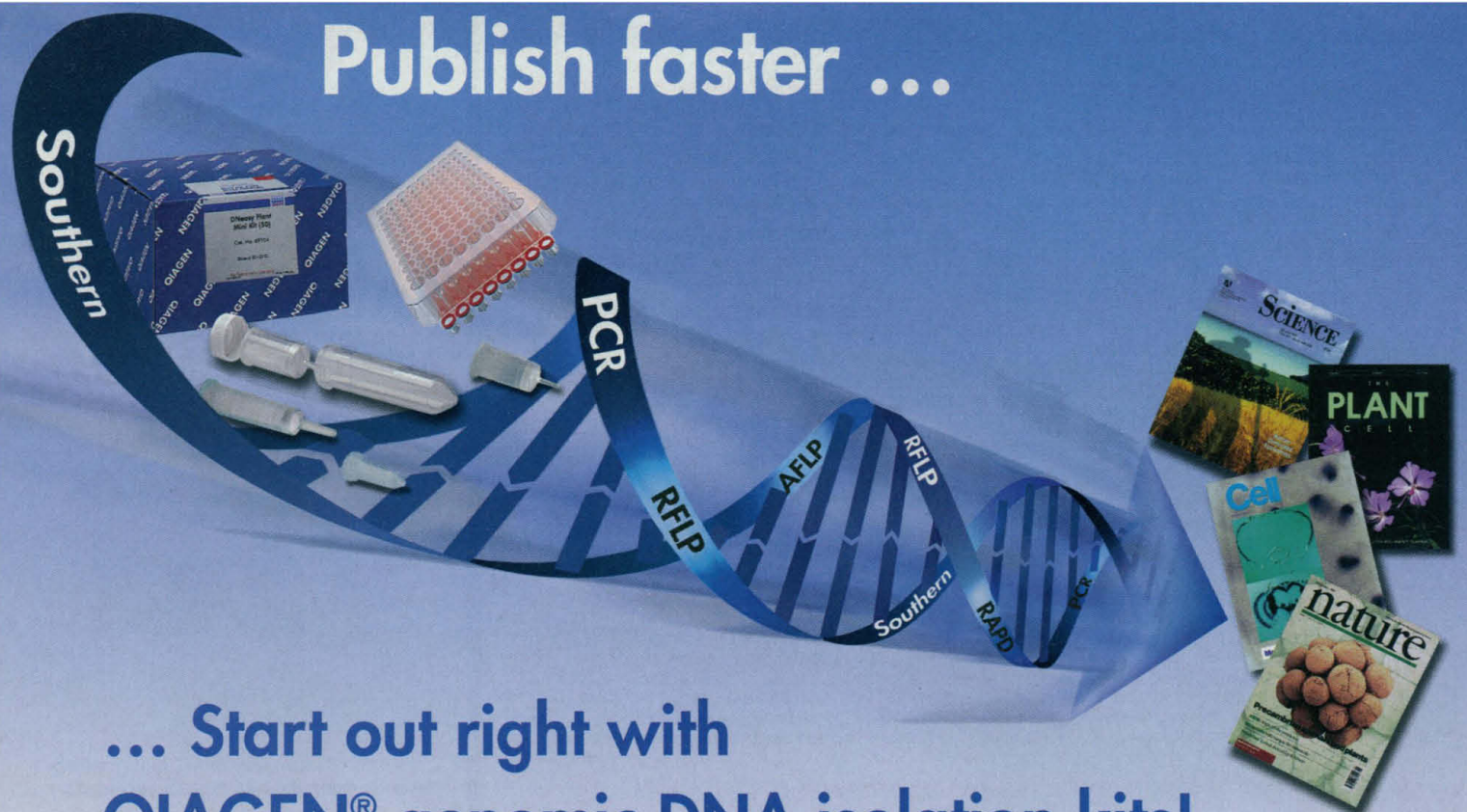
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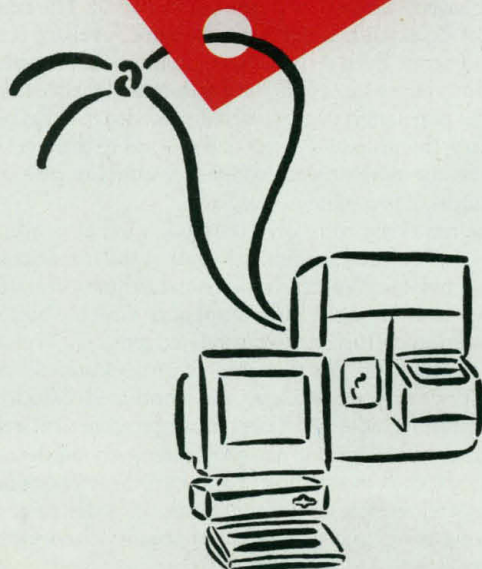
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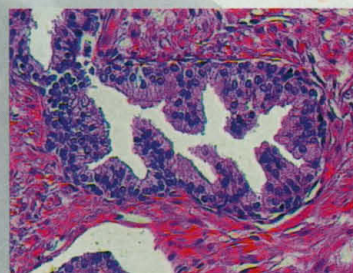
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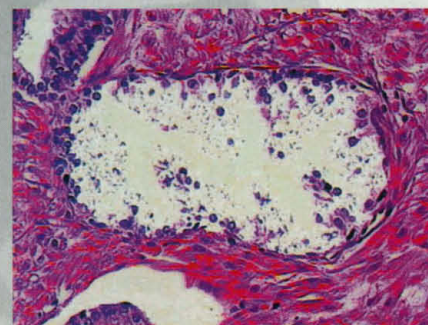


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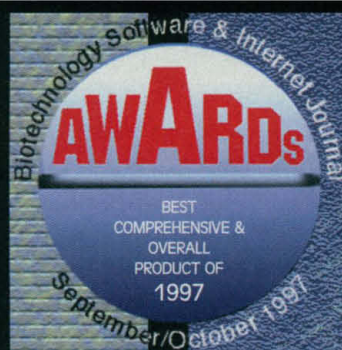
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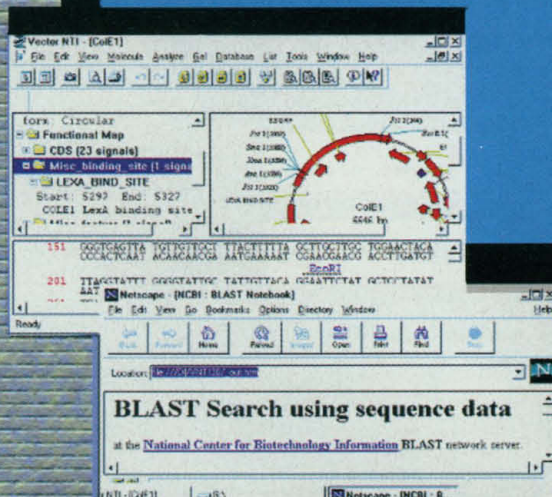
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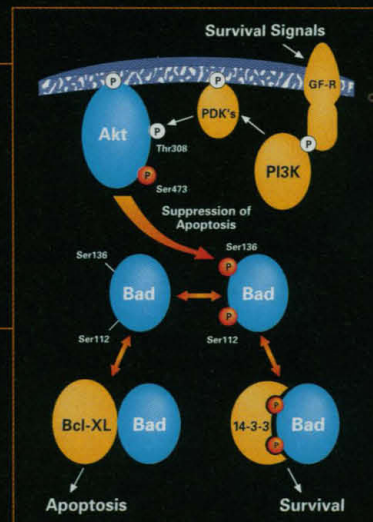
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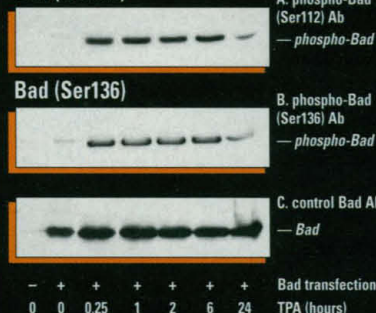


Akt (Ser473)



Western blots of cell extracts from PDGF (50 ng/ml) treated NIH 3T3 cells using (A) phospho-Akt or (B) control Akt Antibodies.

Bad (Ser112)



Western analysis of cell extracts from 293 cells transfected with GST-Bad and treated with TPA using (A) Phospho-Bad (Ser112) Antibody (B) Phospho-Bad (Ser136) Antibody and (C) Bad Antibody.

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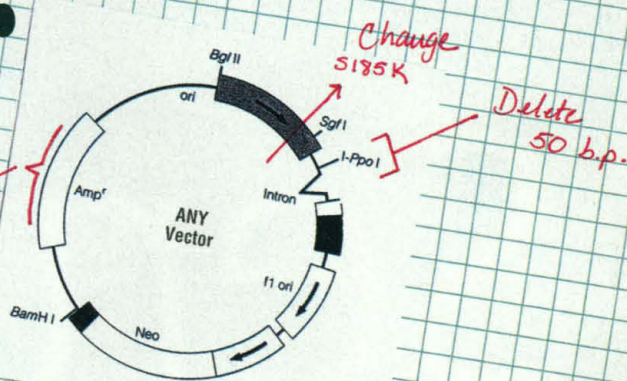
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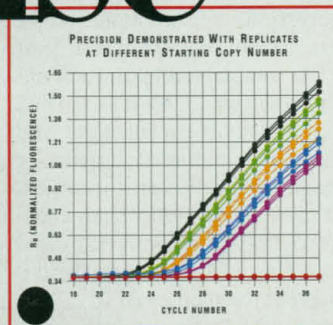
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Among all living things, the human body is blessed with particularly sophisticated—but virtually mysterious—mechanisms. Unlocking these enigmas is an extraordinary task but an imperative one, for it could lead to the discovery of revolutionary new drugs. At Takeda, our team of dedicated research experts is progressing ever closer toward such discoveries.



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