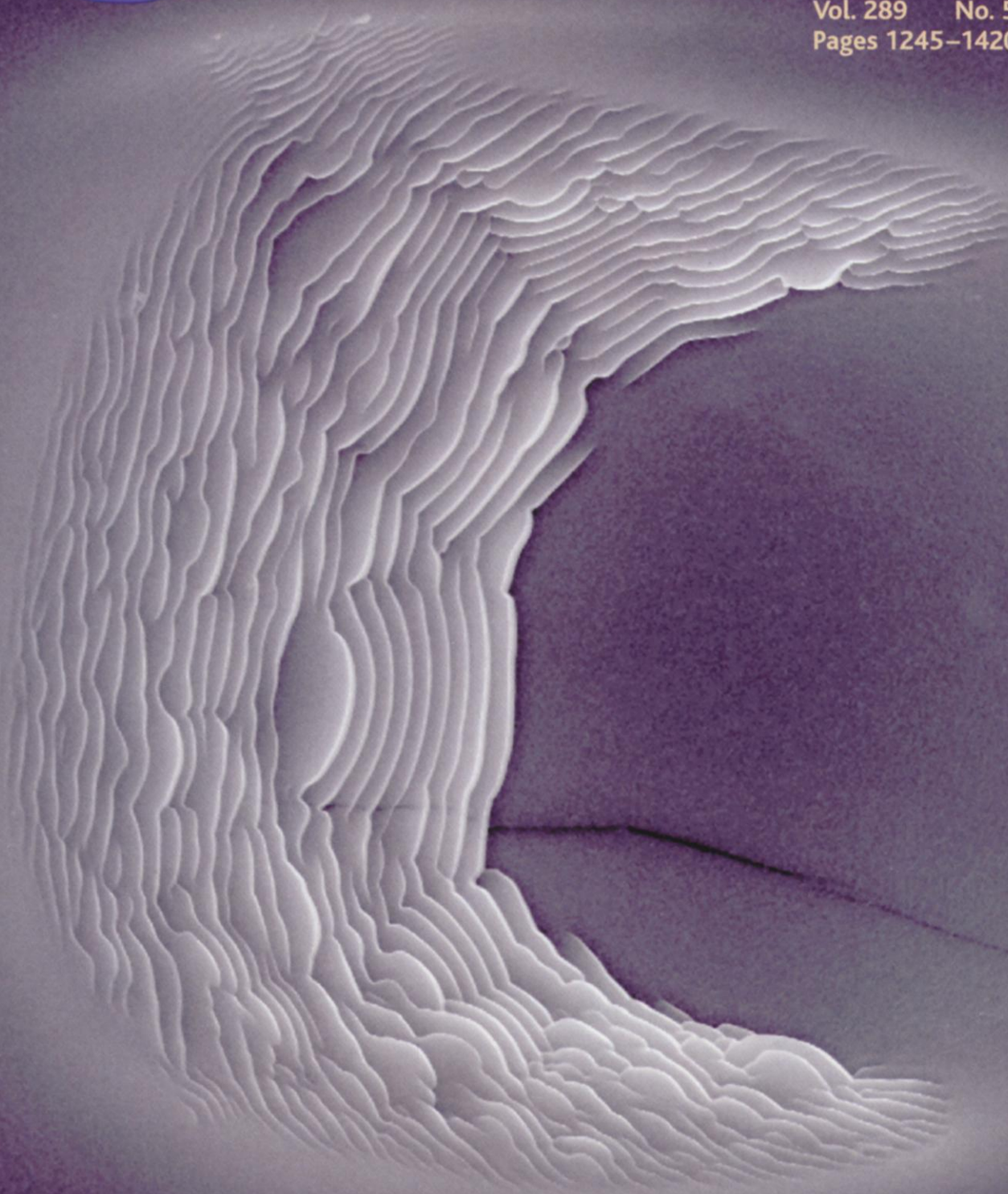


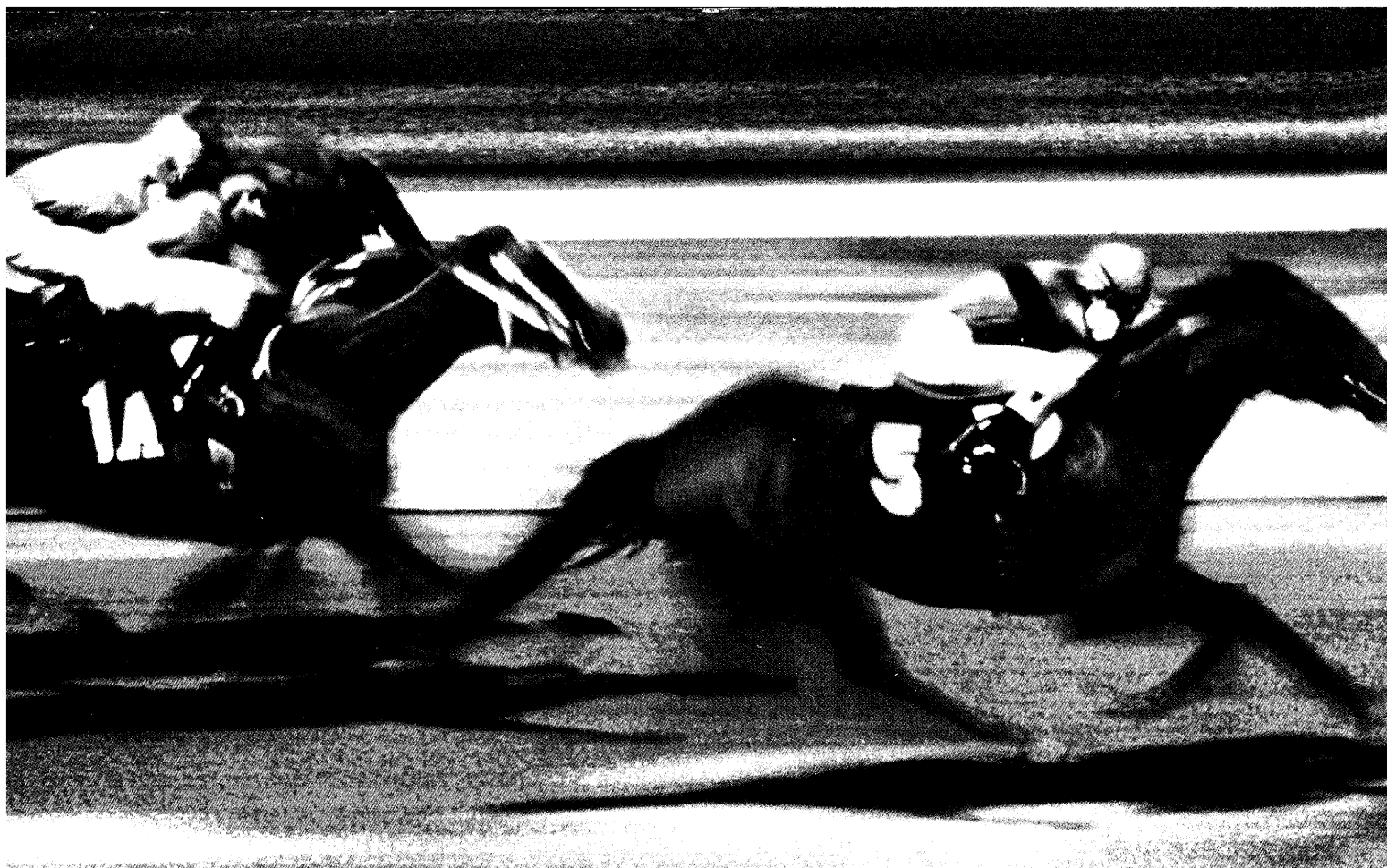
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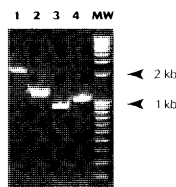


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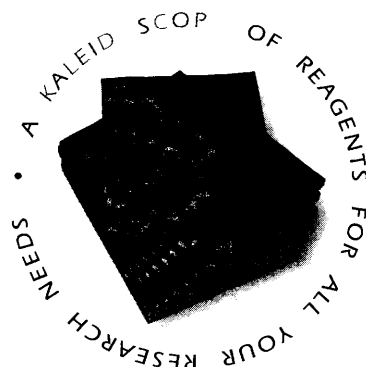
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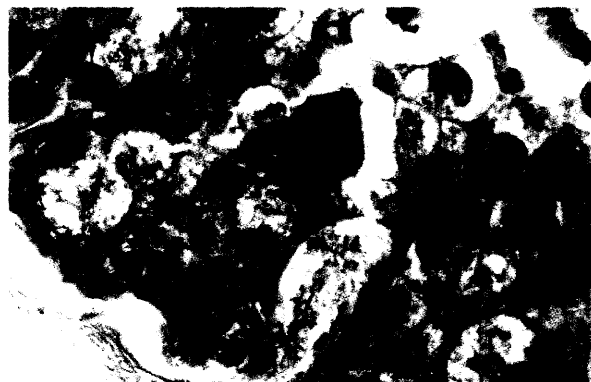


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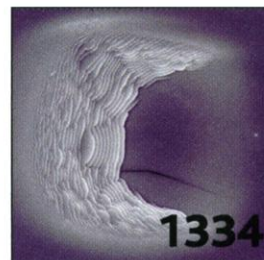
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COVER Scanning electron micrograph of a crater that was created during analysis of a melilite crystal from a calcium-aluminum-rich inclusion in the Allende meteorite. This ~40-micrometer-diameter crater was produced by oxygen ion bombardment during secondary ion mass spectrometry. The results indicate that the sample may have contained short-lived radioactive beryllium-10 at the time of its crystallization in the early solar nebula. [Photo: K. D. McKeegan and G. Jarzebinski]



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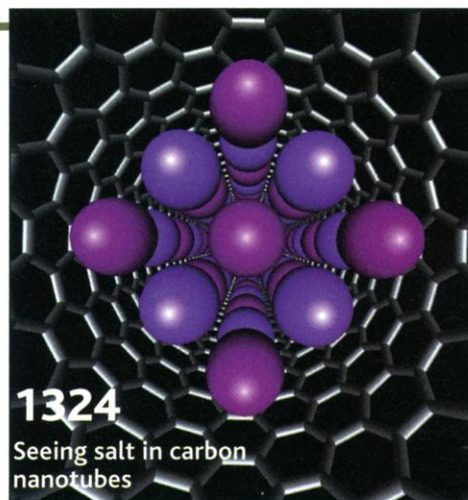
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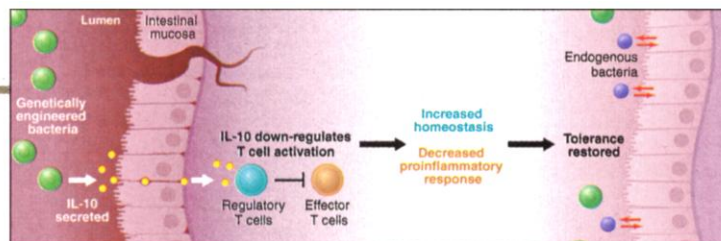
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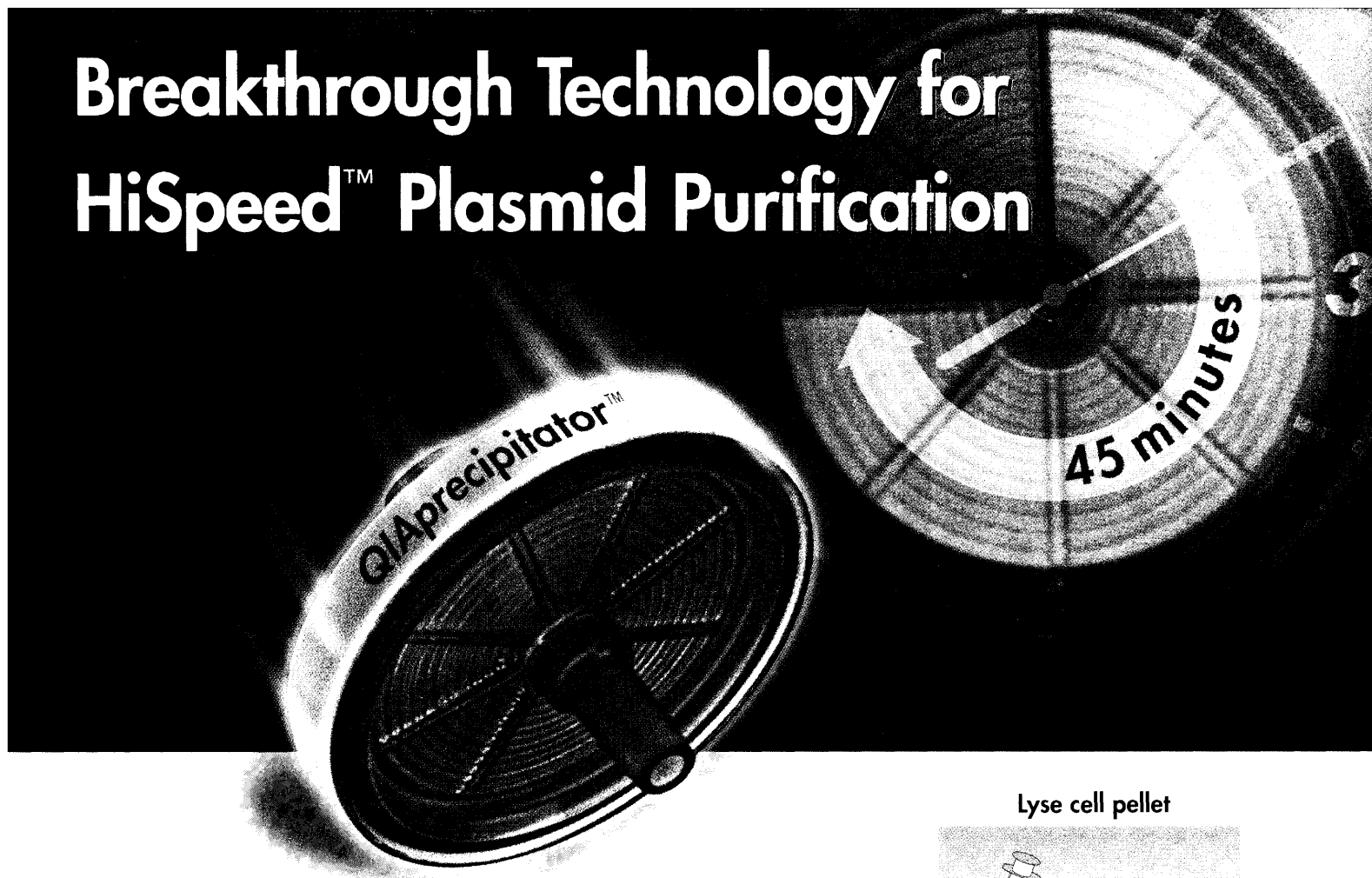
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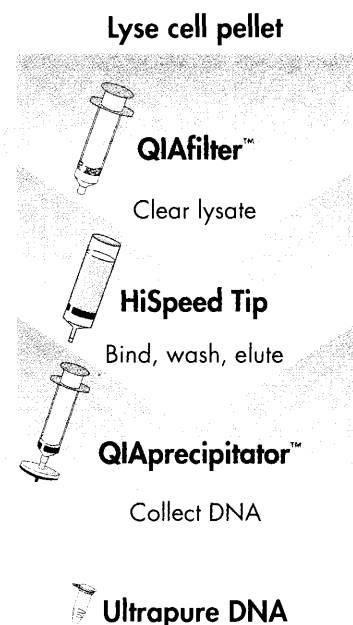
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A HOT BEGINNING

Calcium-aluminum-rich inclusions (CAIs) are found in the most primitive meteorites and are thought to represent some of the first solid particles that formed in the early solar system. McKeegan *et al.* (p. 1334) measured boron isotopes in CAIs to demonstrate that ^{10}B (which decays to ^{10}B and forms only from nuclear spallation reactions) was present in the early solar system (see the cover). Its presence is consistent with one model for formation of CAIs and other early solar system materials in which the early solar system was bombarded by intense radiation. Possible support for this model also comes from Guan *et al.* (p. 1330), who studied aluminum isotopes (which indicate the presence in the early solar system of ^{26}Mg) and other aspects of the geochemistry of CAIs in enstatite chondrites. These CAIs formed under more oxidizing conditions than their host chondrites, and thus the CAIs likely formed earlier in a different location of the solar system.

IBERIAN ICE

Heinrich events, periodic massive discharges of icebergs from Arctic ice sheets, have showered the sea floor with continental debris many times during the past glacial cycle. Although their impact on the North Atlantic is well documented, it is less clear for areas outside the main ice-rafting belt. E. Bard *et al.* (p. 1321) have combined a variety of geochemical proxies, in a well-dated marine sediment core from the subtropical northeast Atlantic, to demonstrate that cooling and advection of low-salinity water from the Arctic affected the midlatitudes during the three Heinrich events of the past 32,000 years. Their results illuminate the internal com-

plexity of these events and illustrate the utility of combining data from organic and inorganic sediment fractions.

FUNNELING ENERGY

The dynamics of the charge-separated excited states (excitons) in the conjugated polymers that find use in light-emitting diodes is complicated by their rapid quenching and by their movement along and between polymer chains. Yu *et al.* (p. 1327) found that by rigorously excluding O_2 , which rapidly quenches excitons, the effects of polymer conformation on exciton dynamics in the solid state could be studied. They dissolved the conjugated polymer MEH-PPV in nonphotoactive polymers, such as polystyrene, in order to avoid interchain effects and then took spectra of single molecules. They found an unexpected sharp, red-shifted emission feature that they attributed to a particular chain conformation, a defect cylinder, which forms through tetrahedral defects. These defects effectively trap and localize the exciton on a chain, and thus act as an "energy funnel" for excitons formed many chain units away.

SQUEEZING OUT PYRUVATE

One model for the origin of life is that the necessary building blocks originated at hydrothermal vents in a series of reaction steps where metal sulfides at elevated pressures and temperatures catalyzed carbon fixation and the formation of more complex organic molecules. Cody *et al.* (p. 1337; see the Perspective by Wächtershäuser) performed experiments that simulate some of the possible conditions of marine hydrothermal systems and show more complex organometallic species forms in this environment that catalyze the formation of

pyruvate, a critical biochemical molecule. High pressures appear to compensate for the high temperatures that would normally cause pyruvate to decompose.

EUROPA'S OCEAN STILL AFLOAT

Interpretations of previous data from the Galileo spacecraft have suggested that Europa, the smallest of the Galilean satellites orbiting Jupiter, may have a layer of fluid beneath its icy surface. Kivelson *et al.* (p. 1340; see the Perspective by Stevenson) used magnetometer data collected by Galileo during the 3 January 2000 close flyby of Europa to confirm that changes in Europa's induced magnetic field are driven by a shallow conductive layer. A model of a spherical shell conductor located about 7.5 kilometers below the surface with a conductivity similar to Earth's ocean water fits their new data well.

PRION CONVERSION MECHANISM

The role of protein conformation in the expression and propagation of prion states in yeast is now well established. Serio *et al.* (p. 1317) examined in vitro the mechanism of conformational conversion of one of the yeast prion proteins, Sup35. The soluble protein goes through a series of conformation states in a process, termed nucleated conformational conversion, that leads to assembly into fibrils.

ARCTIC HIDEOUTS

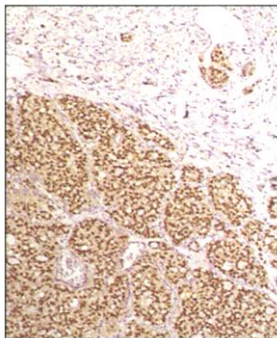
What happened to the flora and fauna of high latitudes during the Pleistocene glaciations? Did they persist in isolated pockets—refugia—where conditions were more benign, and if so, where were these refugia? Abbott *et al.* (p. 1343) present molecular evidence to indicate where one circumpolar arctic plant—the purple saxifrage—initially occurred in the Arctic, the migration routes it followed to achieve a wide distribution, and the refugia it occupied during Pleistocene glaciations. These results provide strong support for the existence of refugia for arctic-alpine plants in the Arctic itself at the time of the last glacial maximum.

MAKING ALL A'S

One of the signatures of messenger RNAs (mRNAs) is a tail of repeated adenylate bases. Unlike most nucleic acid polymerizations, this reaction does not utilize a template; instead, incoming molecules of adenosine triphosphate are

FATEFUL FUSION

Chromosomal translocations that produce oncogenic fusion proteins are common in leukemias and soft-tissue tumors but have rarely been observed in solid tumors (carcinomas), which account for 90% of all cancers. In a study of human thyroid follicular carcinomas, Kroll *et al.* (p. 1357) identified a common translocation that fuses the DNA binding region of the PAX8 transcription factor to peroxisome proliferator-activated receptor (PPAR) $\gamma 1$, a member of the nuclear hormone receptor superfamily. The fusion protein inhibited transcriptional transactivation by PPAR $\gamma 1$ in a dominant-negative manner. Discovery of this fusion event opens up new possibilities for diagnosis and treatment of thyroid cancer.



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THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 1253

added directly to the 3' end of the mRNA. J. Bard *et al.* (p. 1346) present the crystal structure of poly(A) polymerase from yeast in complex with two adenine nucleotides, one of which appears to represent the last base attached with the other being the next to be added. In addition to details about the active site mechanism, they describe the structural comparison to other nucleic acid polymerases and the factors contributing to processivity of this enzyme.

WHEN THE ATTRACTION IS GONE

Environmental cues that are attractive or repulsive tell a migrating axon where to go by sending signals through the appropriate cell surface receptors. How is it then that for retraction to occur, a cell surface receptor must first engage with the repulsion factor and then overcome the adhesive force? Hattori *et al.* (p. 1360) and Galko and Tessier-Lavigne (p. 1365) report that these interactions can be broken by metalloprotease enzymes that result in the release of the axon from its captor. In a Perspective, Pasquale discusses how the involvement of cell surface metalloproteases in regulating axon guidance is a compelling solution to this puzzling paradox.

VITAL DRUG DELIVERY

The cytokine interleukin-10 (IL-10) has shown promise in clinical trials for treatment of inflammatory bowel disease (IBD). Because the cytokine is administered systemically, high doses are re-

quired that often lead to adverse side effects. Steidler *et al.* (p. 1352; see the Perspective by Shanahan) describe a new method of localized IL-10 delivery that allows the therapeutic dose to be reduced substantially. They engineered *Lactococcus lactis*, a bacterium used to produce fermented foods, to secrete high levels of IL-10. Delivery of the live recombinant bacteria by intragastric inoculation prevented the onset of IBD in one mouse model and reversed symptoms of pre-existing IBD in another. In principle, this technology could be used for efficient delivery of any protein therapeutic that is unstable or difficult to produce in large quantities.

WHISTLING IN THE SEA

Dolphins have long been known to communicate by means of a rich repertoire of vocalizations. However, studies have been based mostly on captive individuals, and little has been known about communication in the wild. Janik (p. 1355; see the Perspective by Tyack) has developed a technique that allows the measurement of vocalizations between bottlenose dolphin individuals in the sea without the presence of human observers. Individuals respond to each other using learned, matching whistles over distances of up to half a kilometer. The development of vocal imitation is an important step in the evolution of communication and has implications for the evolution of human language.

TECHNICAL COMMENT SUMMARIES

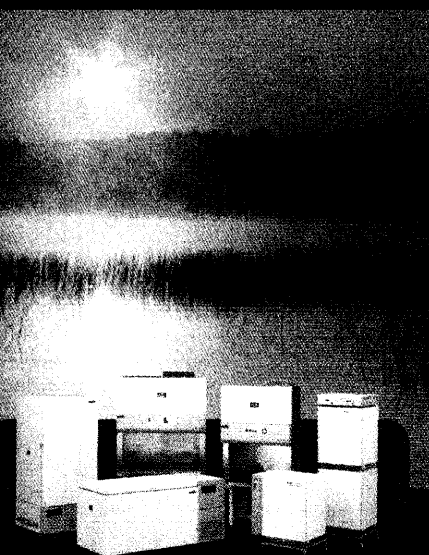
Plant Diversity and Productivity

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/289/5483/1255a

Reporting on a major experiment on plant diversity and productivity in European grasslands, Hector *et al.* (Research Articles, 5 November 1999, p. 1123) found "an overall log-linear reduction of average aboveground biomass with loss of species." Huston *et al.* object to that conclusion, arguing, among other things, that the eight sites studied did not show a consistent positive relationship between diversity and productivity, that the experiments did not properly test for overyielding (i.e., that the productivity of a given polyculture exceeds that of any species from the mixture grown in monoculture), and that some of the observed effects may have stemmed from the "fertilization effect" of the nitrogen-fixing legume *Trifolium pratense*. Huston *et al.* conclude "that species richness per se has no statistically or biologically significant effect on plant productivity across the eight sites."

Hector *et al.* defend their main result, and note that while a small fraction of polycultures were dominated by species that had not been tested in monocultures, excluding those plots from the analysis "does not alter conclusions . . . across all sites." And, although the effects of *T. pratense* on productivity were larger than those of other species, that does not invalidate the broad result, according to Hector *et al.*: "In principle, all effects [of species richness on productivity] can be attributed to the traits of individual species and their interactions." (See the news story by Kaiser.)

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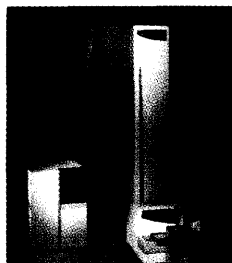
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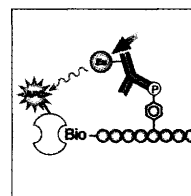
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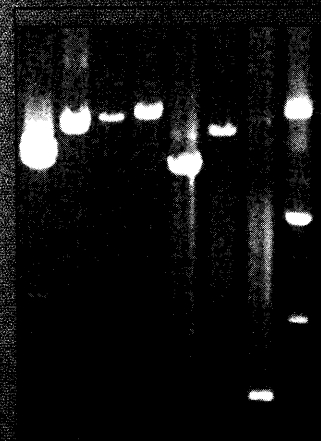
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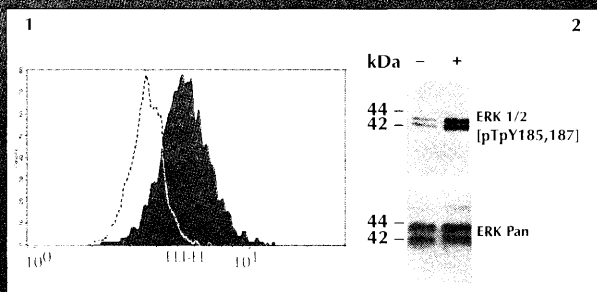
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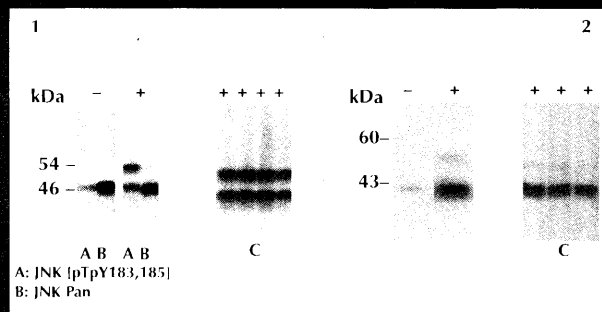
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Show Me! (1) Flow Cytometry data show treated (red) and un-treated (green) Jurkat cells stained with (anti-ERK 1/2 [pTpY185/187] FITC conjugate (cat.#44-6808). The blue dotted line shows treated cells stained with FITC conjugate pre-incubated with blocking peptide. (2) Activation of MAP Kinase in PC12 cells treated with NGF is demonstrated by comparison to unstimulated control (anti-ERK 1/2 [pTpY185/187] (cat.#44-680).

MAP Kinase Superfamily



Show Me! Activation of MAP Kinase Superfamily proteins in HEK 293 cells treated with UV is demonstrated by comparison to unstimulated controls (anti-JNK 1/2 [pTpY183/185] (cat.#44-682), p38 [pTpY180/182] (cat.#44-684). Evaluation of consecutive lots each of anti-JNK [pTpY183/185] and p38 [pTpY180/182] phosphorylation site-specific antibodies is shown in panel C. The data demonstrate the reproducibility of the antibody production process.

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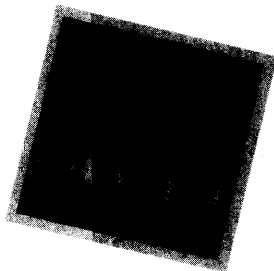
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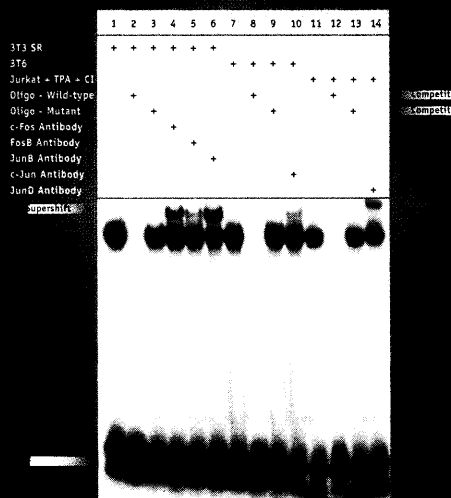
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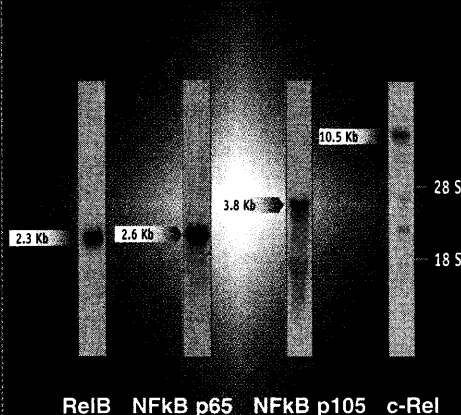
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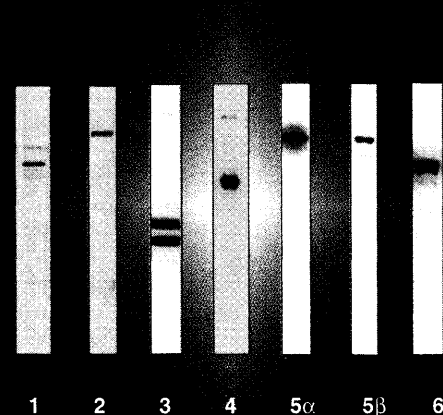
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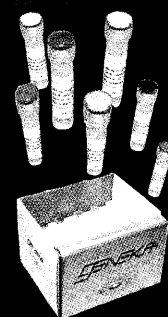
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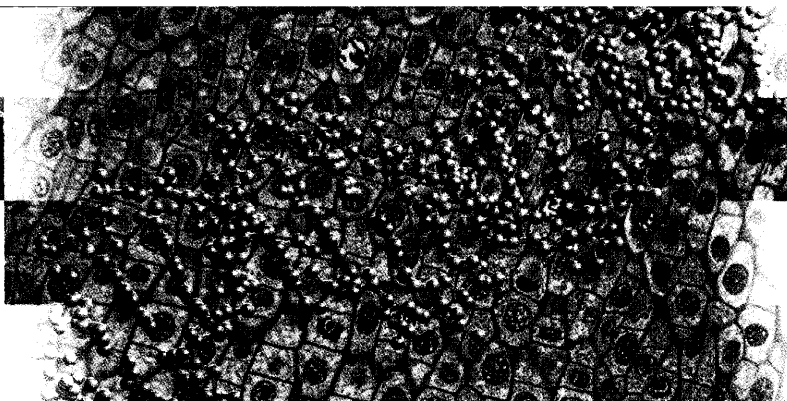
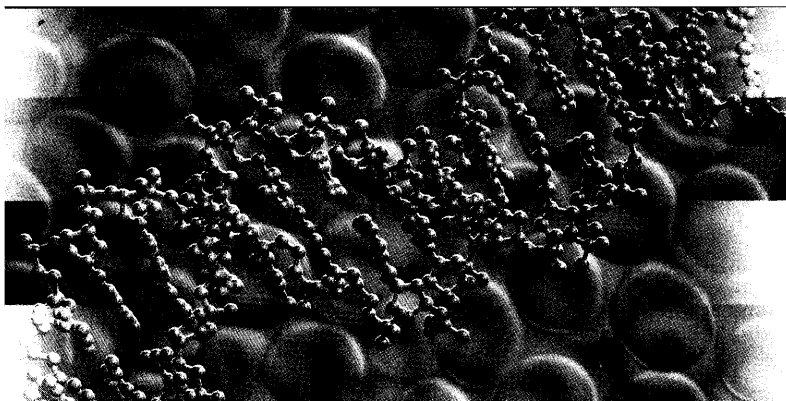
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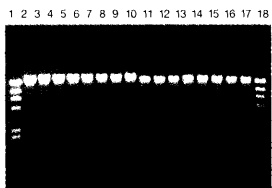
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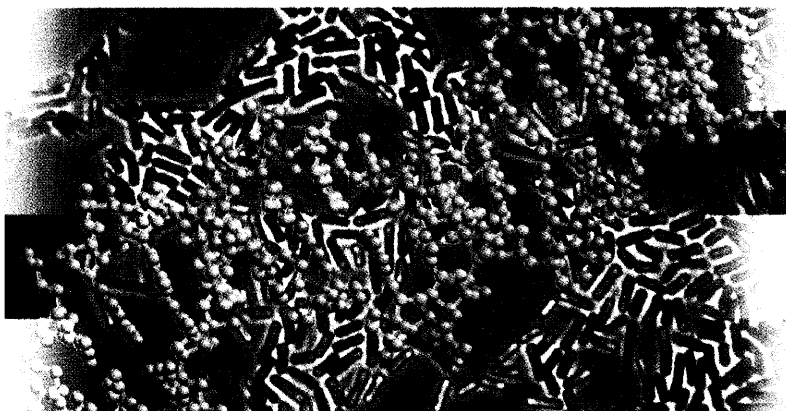


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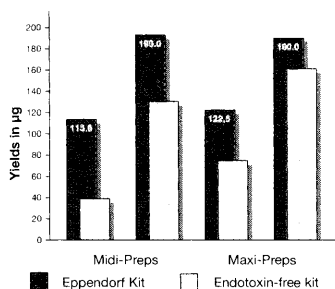


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Lanes 1 and 18: λ Hind III Marker
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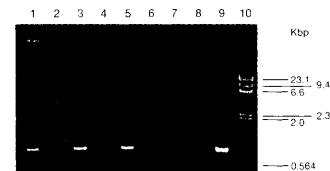
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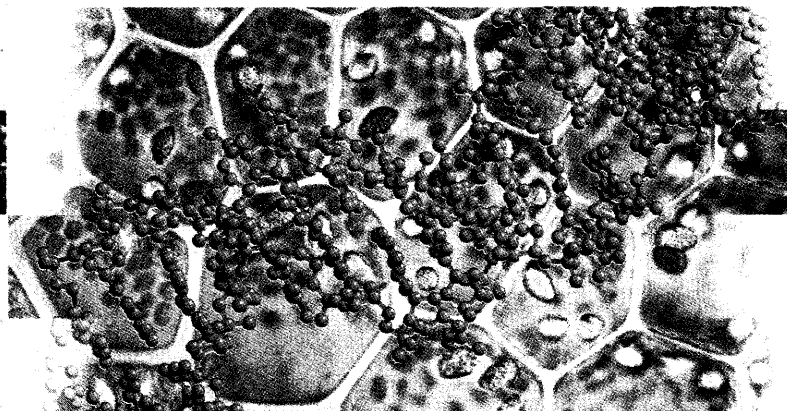
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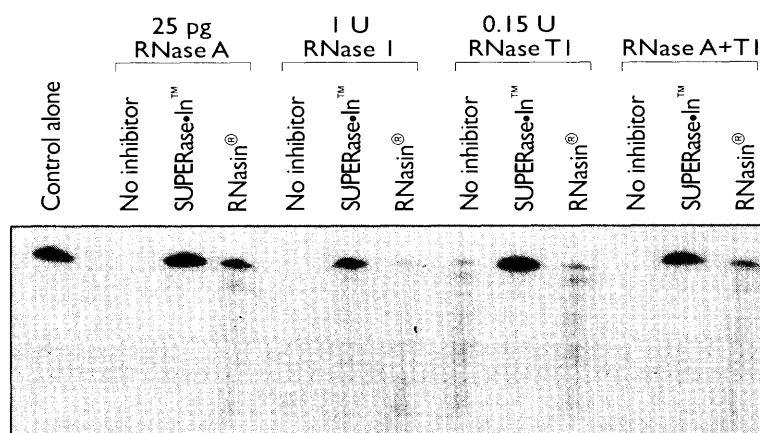
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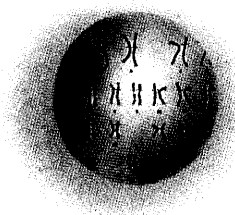
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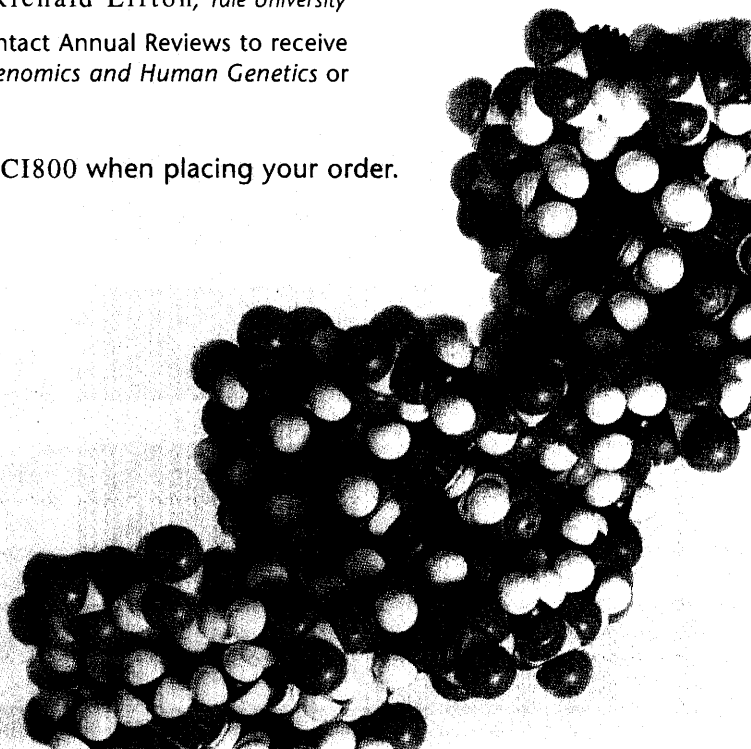
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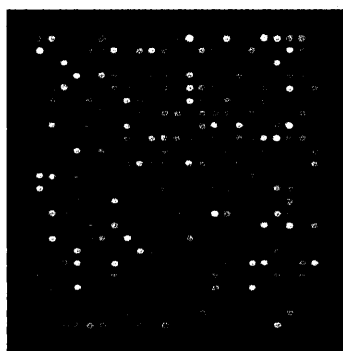
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ready -'red'i: ME [if READY d.] 1 m. Make ready; prepare; put in order. Now chiefly N. edging, foil by up. ME. b spec. Make ready; make (N. & fol. pag. 12)

1) *adj.* Genuine; authentic; actually present; not simulated or pretended. "The genuineness of his intentions was beyond question." "He has a genuine sense of humor."

honest, loyal, true
(in full *honest, loyal, true*; pronounced *on-est, loy-ol, true*)
a) A small short coat and breeches formerly used in Spain and Spanish-speaking countries.

front of MP 117 (4th quad. road) see
ROYAL, Cf. 1181 & 1800 road, Knott

real (real, *adj.*, *no.* & *adv.* CME Tōhō 1. AN (no. 04) really; later 1 vs source, late L *really*, *tr. L* (no. 04) thing are *adj.* Cf. *real* *n.* / *A* *adj.* 11 Law *n.* 04 *no.* action for the recovery of a specific thing. CME *b* Consisting of or performing an immovable property such as lands and buildings. (CME, 12 Attached or pertaining to the person. 126 M. 3. Raining *no.* on the mountain. 16. 1b *adj.*, written

1. *Real*, *realist*. A philosophical realist. 116-117. 2. A real thing; a thing having (or conceived as having) a real existence. 117. 3. *The real*, that which actually exists, as opposed to a counterfeit or ideal. 117. 4. *Realism*, the doctrine that the real is as it is, not as it appears. 119. 5. *Realist*, a real philosopher. 119.

sent, not merely

fact. 3. Sincere,

realia, *reālīa*, *reālīe*, *spl.* *reā* (Late L. use as n. of *reus*, pl. of *reus* REAL; cf. see -*reā*). 1 Objects which may be used as teaching aids but were not made for the purpose. *N. Amer.*, *reā*. 2 Real things, actual facts, esp. as distinct from theories about them. *reā*.

realisation n., realise v. v.arts. of REALIZATION,

realism, idealism = *vsq.* [C. 384. *ad* + *lat*] *Plato* & The doctrine of universals have an objective or absolute existence. Opp. NOMINALISM. Etymology: *from* *lat.* *re-* + *lat.* *realis* 'pertaining to reality'.

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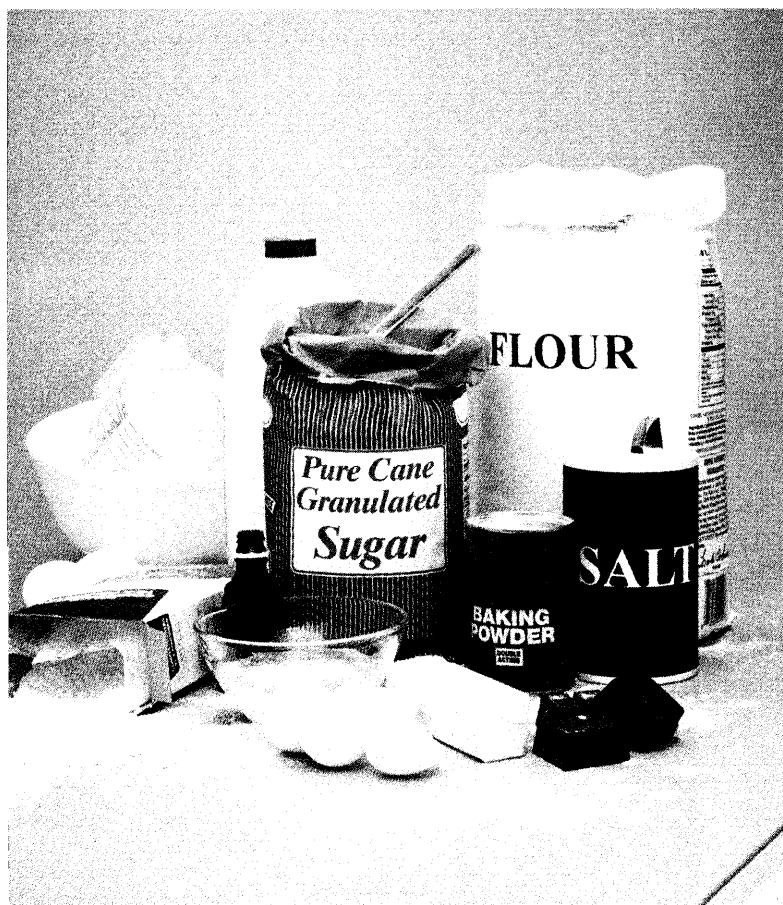
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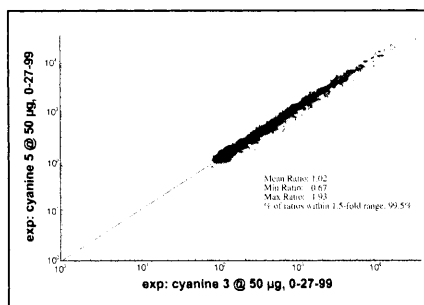
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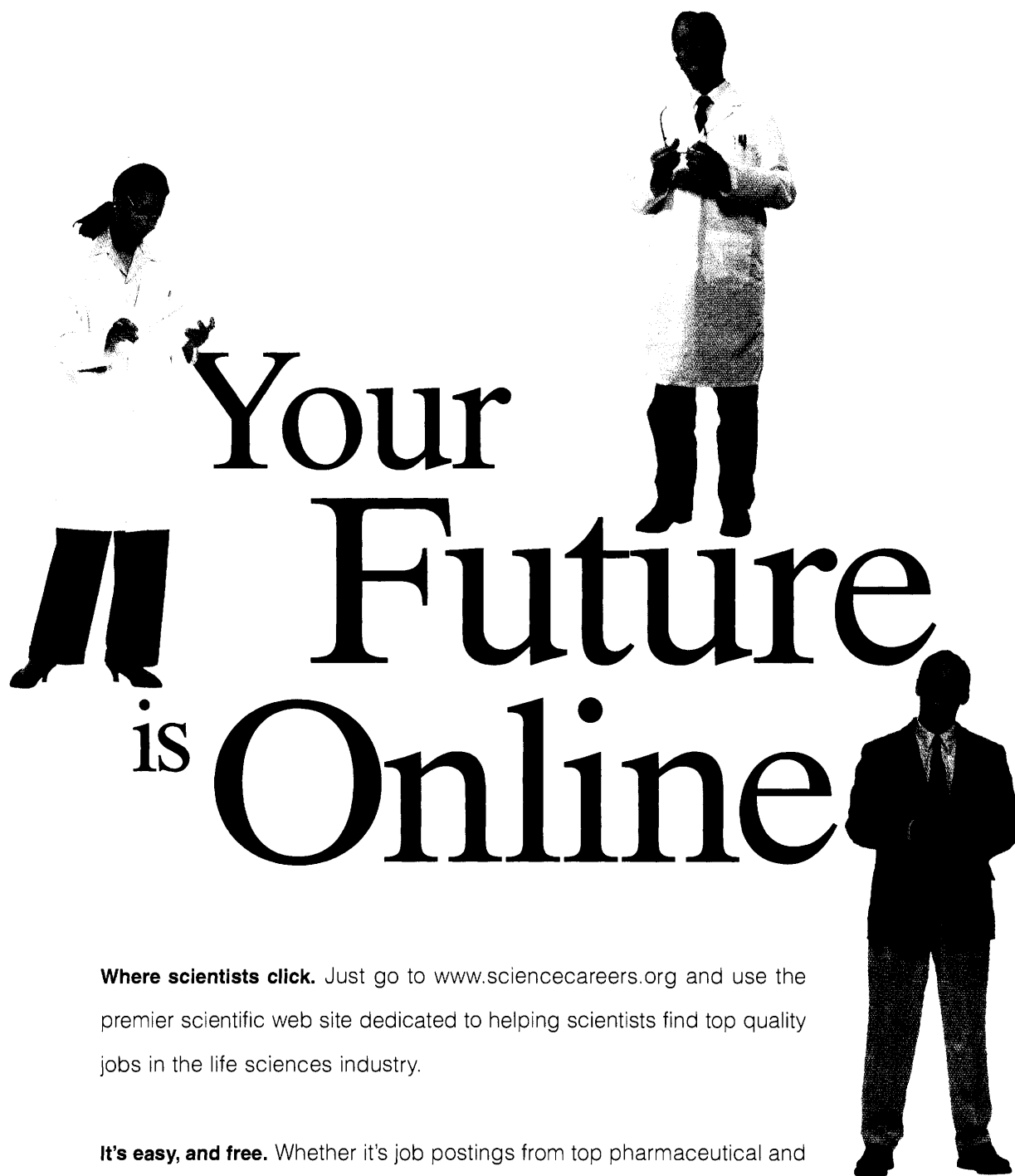
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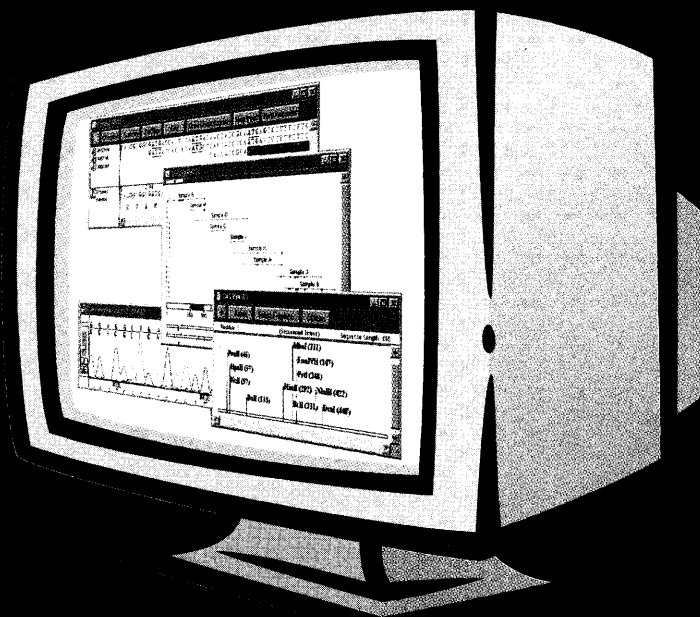
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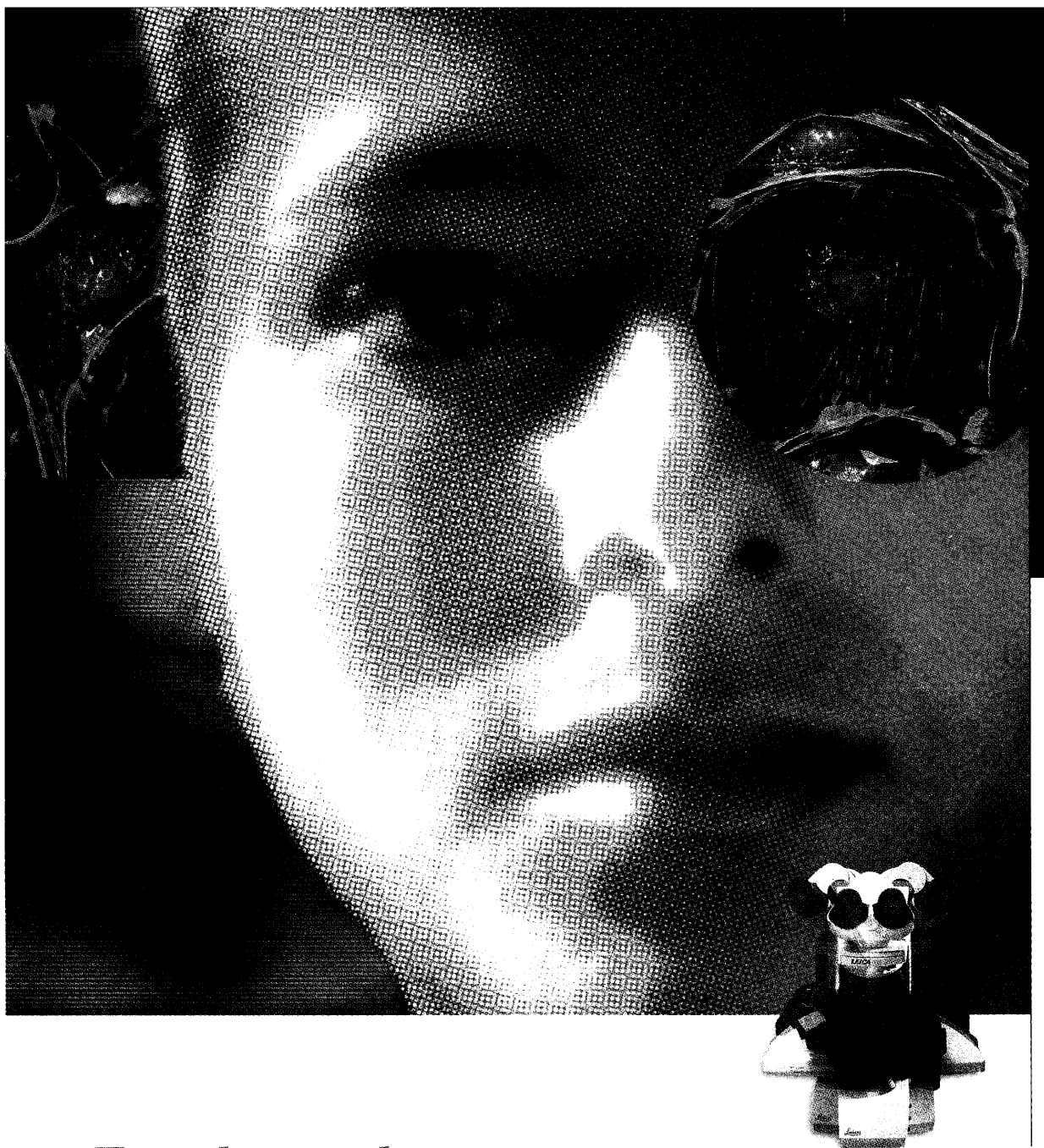
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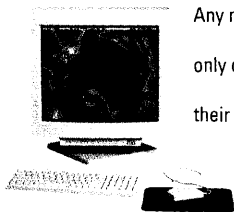
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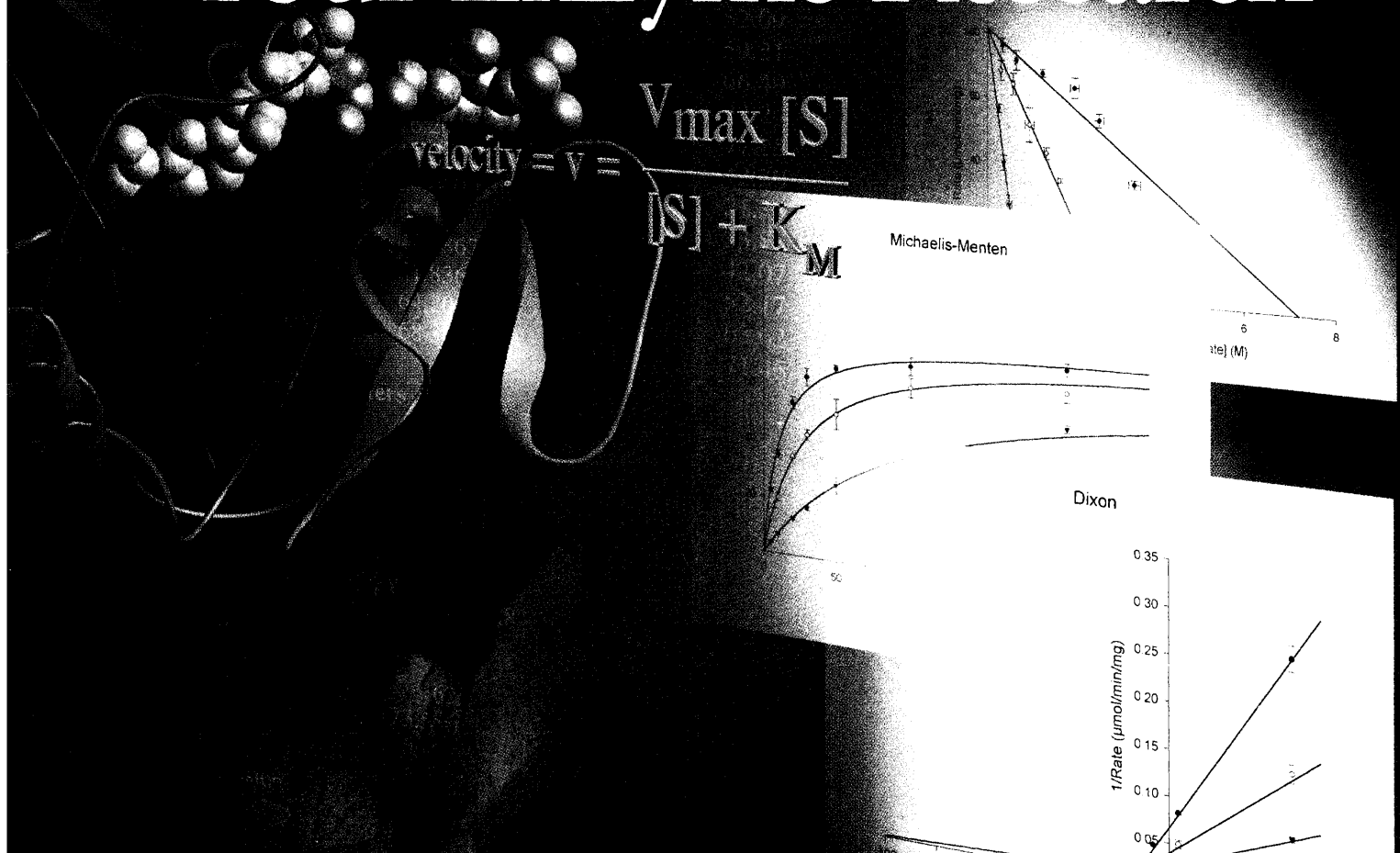
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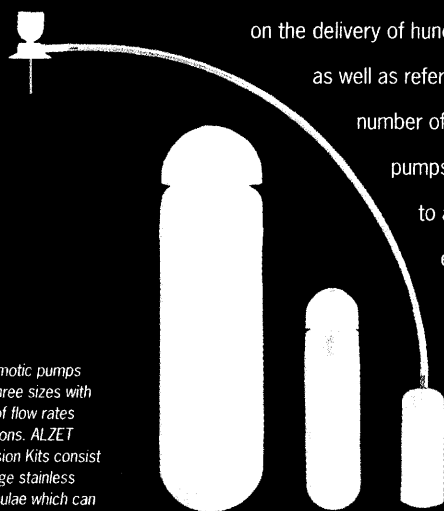
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on the delivery of hundreds of compounds, as well as references on delivery via a number of different routes. ALZET pumps give you the power to achieve and maintain an effective drug concentration for a sustained period of time, resulting in more accurate data.

Fig. 2

ALZET osmotic pumps come in three sizes with a variety of flow rates and durations. ALZET Brain Infusion Kits consist of 28 gauge stainless steel cannulae which can penetrate 3-5 mm below the skull surface.



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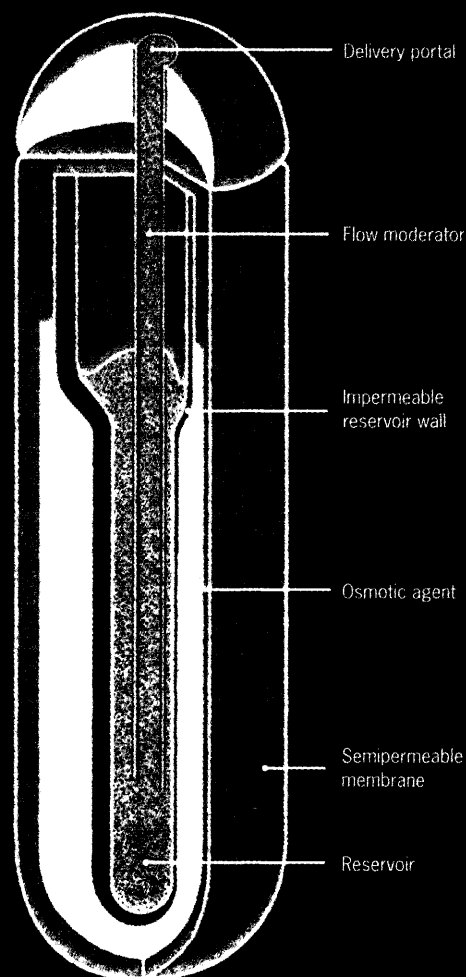
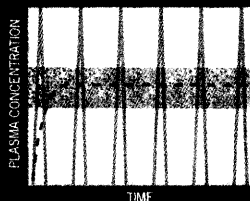


Fig. 1

The ALZET pump operates as interstitial fluid is attracted into the pump by the osmotic layer at a rate limited by the outer, semi-permeable membrane. As the osmotic layer hydrates, it compresses the flexible reservoir, which expels drug from the delivery portal of the pump.



Eliminate Fluctuations in Plasma Drug Concentration

Fig. 3

Prolonging exposure to recombinant proteins by multiple daily injections results in repeated fluctuations in the level of protein in plasma and tissues, and corresponding variations in protein effects over time. Because the protein concentration is constantly changing during the course of the experiment, the resulting data can be misleading as to the nature of the protein's effects and the dose required to elicit them. ALZET pumps provide continuous drug infusion to maintain a constant plasma level (dashed line) within the effective concentration range (shaded bar).

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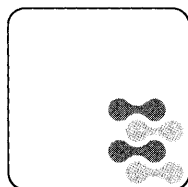
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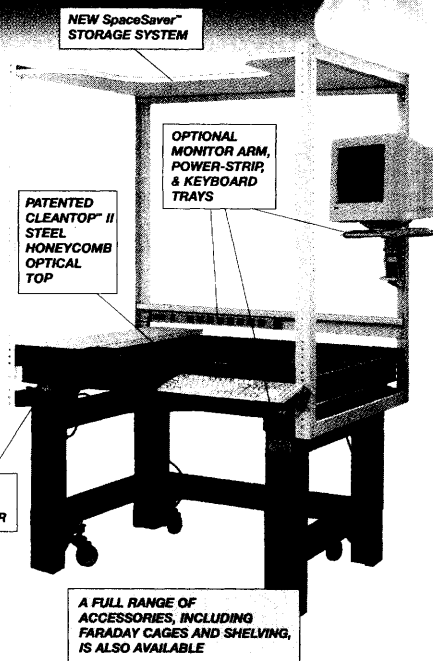
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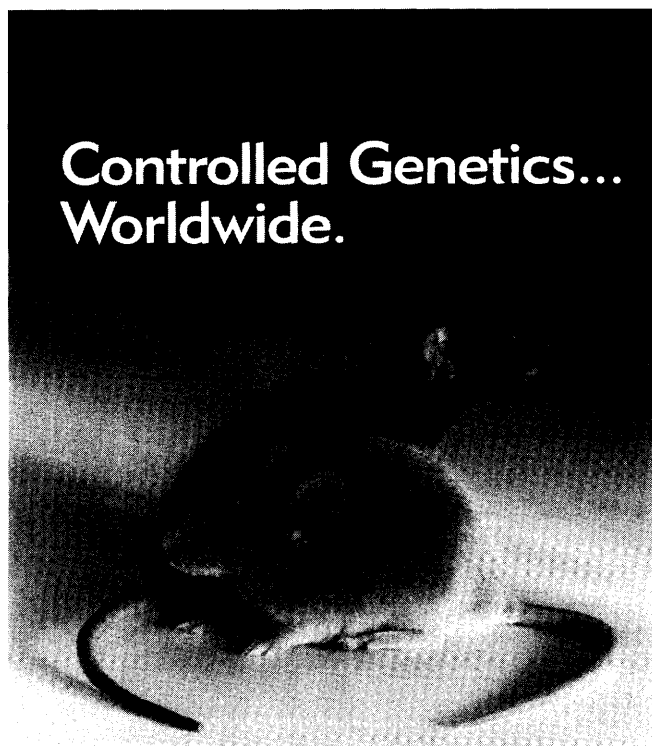
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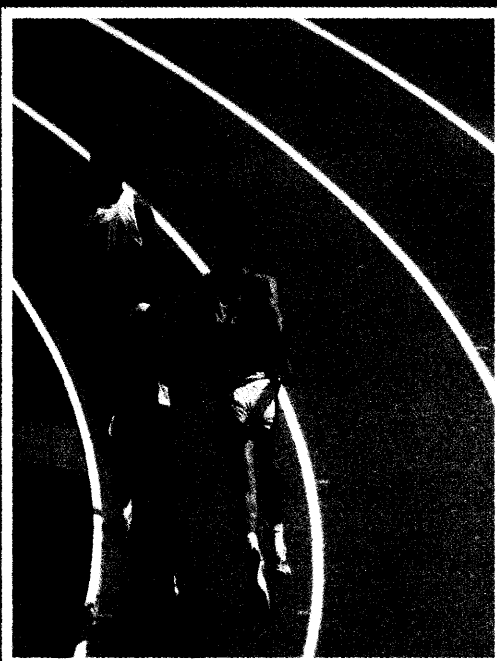
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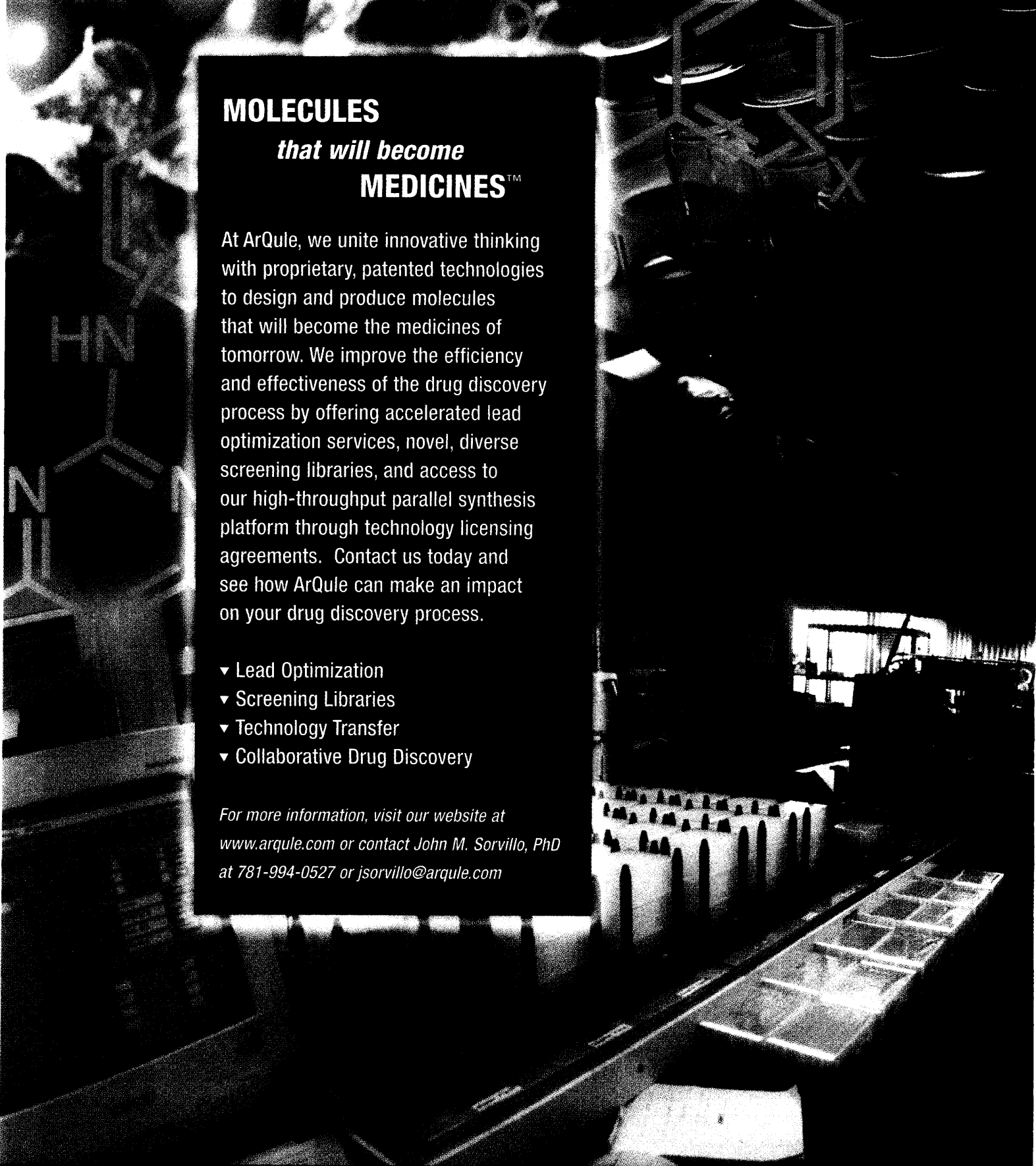
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