21 June 2002

Science

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Pages 2089–2284 $9

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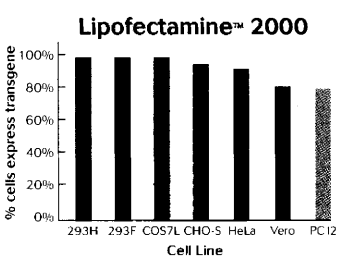

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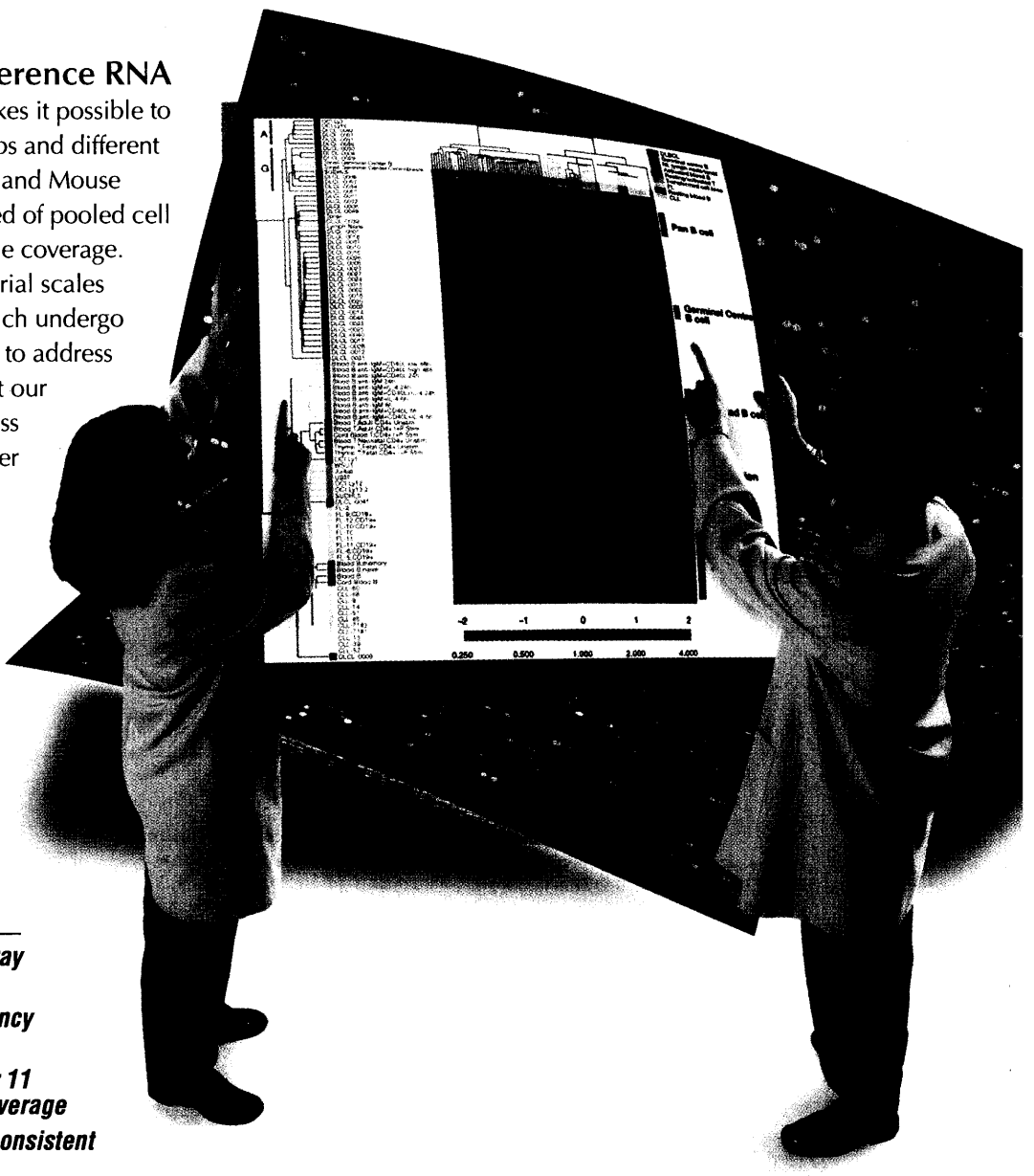

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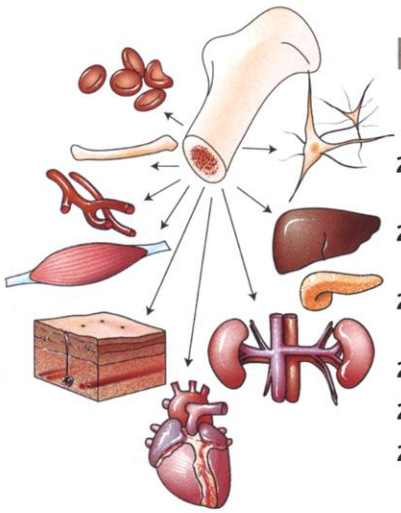

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Stem cells: A question of commitment

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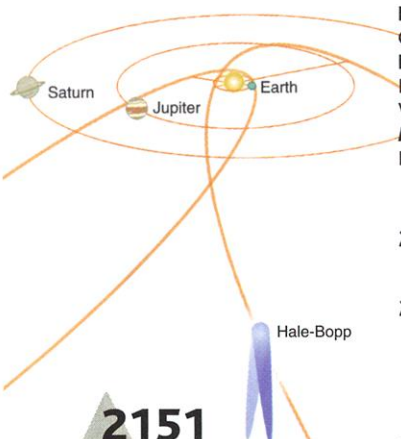
SCIENCE'S COMPASS



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Why comets remain a puzzle

2158
Climate change and wildlife disease

RESEARCH

BREVIA

RESEARCH ARTICLE

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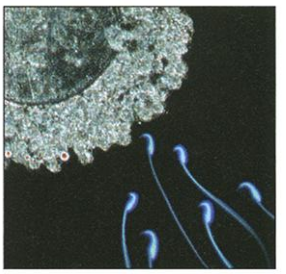
REPRODUCTIVE BIOLOGY

NEWS

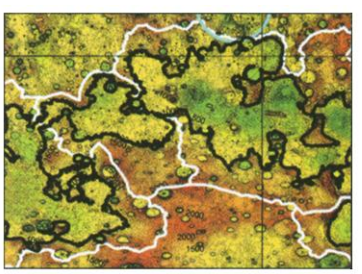
REVIEWS

See also* Science's STKE *on p. 2095*, Science *Express Report by Feng* et al. *on p. 2095, and Editorial on p. 2101.



COVER 2163

Male germline stem cells carrying modified genes (blue), transplanted to recipient seminiferous tubules (bottom), produce rat spermatozoa (middle). These sperm can fertilize newly ovulated oocytes (top) to generate transgenic animals. How species achieve their most fundamental goal—procreation—is the focus of the special section in this issue. [Image: J. Hayden, RBP (Bio-Graphics) and R. L. Brinster]



2209

Remnants of an overflowing martian lake

New on *Science* Express Spermatogenesis in vitro

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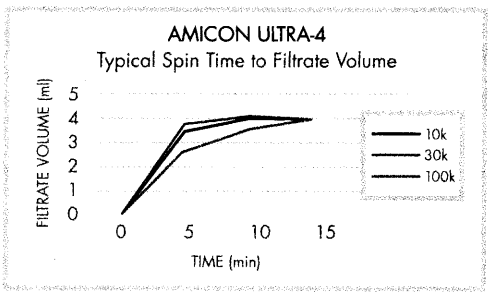

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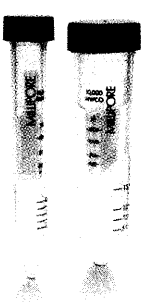

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THIS WEEK IN Science

edited by Phil Szuromi

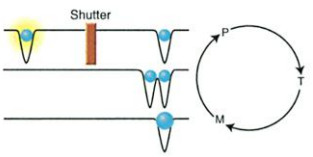
Weather Caught Underground

The dramatic cooling that occurred approximately 8200 years ago has been associated with increased melting of the Laurentide ice sheet of North America that then perturbed North Atlantic thermohaline circulation. Baldini *et al.* (p. 2203) present a high-resolution trace element record of the "8200-year" event from a stalagmite in southwest Ireland which shows that the event was characterized by rapid initiation, a brief intra-event relaxation, enhanced seasonality, and an abrupt termination.

One-Way Trips

The Oort cloud is a somewhat spherical region at the edge of the solar system that contains about a trillion comets but feeds them into the inner solar system at a rate of only about 12 per year. Dynamical models have predicted more returning comets than are actually observed. Levison *et al.* (p. 2212; see the Perspective by Bailey) combined observations with new simulations to show that most of these missing returning comets are destroyed, not darkened by space weathering (so that they are considered dormant and unobservable). Thus, returning Oort cloud comets are more prone to destruction than their returning Kuiper belt cousins, which have been observed in relatively greater numbers.

Loading Condensates Continuously



One of the long-standing goals in the field of Bose-Einstein condensates has been to realize a continuous-beam atom laser. Atom lasers have either been operated in a pulsed mode or run until the initial reservoir of atoms is depleted. The problem has been to overcome the technical barriers of topping off the reservoir without destroying the delicate condensate itself. Chikkatur *et al.* (p. 2193; see the Perspective by Pfau) can now maintain more than 1 million atoms in a reservoir by using an optically trapped condensate as the reservoir and optical tweezers to transfer a "scoop" of condensed atoms from another condensate into the reservoir.

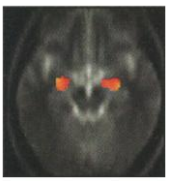
Antibodies Give Membranes a Handedness

For pharmaceuticals, often only one of several possible chiral forms (enantiomers) is actually active, and thus there is an increasing demand for separating enantiomers. One approach that allows continuous separation is to use membranes. Lee *et al.* (p. 2198) now show that derivatizing alumina nanopore membranes with antibodies allows the separation of the RR from the SS forms of a drug molecule. The binding strength of the antibody and, hence, the flux through the membrane was tuned by adding an organic molecule, dimethyl sulfoxide, to the buffer solution.

2195 Disordered but Coherent

Diluting a ferromagnetic with non-magnetic ions usually results in the loss of the ferromagnetic ordering, and at low temperatures the system would be expected to freeze into a glasslike state with little long-range coherence. Ghosh *et al.* (p. 2195) instead find that a disordered magnet does exhibit coherence at low temperature with properties quite different from that of a normal glass. The relaxation rates actually sharpen up, which suggests that the system behaves as a distribution of coupled oscillators.

And in Brevia ...



Canli *et al.* (p. 2191) show that the activation of the amygdala, a part of the brain involved in processing facial expressions, varied with the degree of extroversion in subjects viewing happy

Martian Lake Runneth Over

Using data from the Mars Global Surveyor Laser Altimeter, Irwin *et al.* (p. 2209) have determined that the 900-kilometer long and 8- to 15-kilometer wide Ma'adim Vallis was probably formed by overfilling of a large lake. A breach in the lake's boundary rapidly incised the valley and flooded several prominent impact craters down slope. The valley is older than 3 billion years, and the identification of a large lake, where surface water played a prominent role in the development of Ma'adim Vallis, indicates the possible intensity and complexity of the early martian hydrologic cycle.

Shaking Molecules by Their Tails

When vibrational energy is deposited in one part of a molecule, it will eventually redistribute, but the actual progress is difficult to observe. Wang *et al.* (p. 2201) have achieved sufficient resolution in ultrafast spectroscopy to observe the transfer of vibrational energy through various liquid-phase alcohols. They excite the O-H stretching vibrations and then can see energy transfer, both up and down, to CH_2 or CH groups before reaching the CH_3 group.

Cutting Peptides Inside Membranes

Signal peptides can have multiple functions. They are inserted into membranes and are required for the biosynthesis of membrane and secreted proteins. Some are enzymatically cleaved and release peptides that are functionally important. Weihofen *et al.* (p. 2215) have identified this elusive signal peptide protease (SPP). It joins a growing family of multipass intramembrane cleaving proteases, whose founding member is presenilin. In a Perspective, Wolfe and Selkoe discuss how characterization of SPP may quell the controversy over presenilin's proteolytic activity.

RNAs Made Mainly in the Plane

RNA replication of positive-strand RNA viruses such as poliovirus and hepatitis C virus occurs on the surface of cytoplasmic membranes of the host cell. Poliovirus RNA synthesis is catalyzed by a vi-

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CONTINUED ON PAGE 2099

CREDITS: (TOP) CANLI *ET AL.*; (BOTTOM) PFAU

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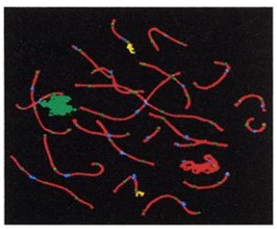
rally encoded RNA-dependent RNA polymerase. Lyle *et al.* (p. 2218) show that purified polymerase oligomerizes to form planar or tubular arrays that correlate with optimal RNA binding and elongation. Poliovirus infection of cells produced vesicles with structures consistent with sheets of polymerase coating the vesicle membranes. The two-dimensional enzyme arrays may confer the advantages of surface catalysis to viral RNA replication.



CREDIT: LYNN ET AL.

Mixing It Up

During male germ-cell meiosis, homologous chromosomes pair and exchange genomic content and allow for genetic variability in offspring. Lynn *et al.* (p. 2222) studied human spermatocytes with immunofluorescence microscopy and found substantial variations in the rates of recombination within and among males. In addition, they identified a relation between this variation and the differences in the length of the synaptonemal complex. This finding is consistent in both humans and mice and may allow for a better understanding of the mechanisms involved in aneuploidy.

The Substructure of Human Variation

With approximately 4 million of the estimated 10 million common single nucleotide polymorphisms of the human genome already in databases, it is increasingly practical to study common genetic variation. Combinations of such variants seen on individual chromosomes in populations are called haplotypes. Gabriel *et al.* (p. 2225) conducted a genome-wide survey in samples from Africans, Asians, Caucasians, and African Americans. They conclude that most of the human genome consists of blocks over which there was little historical recombination and within which an average of three to five common haplotypes accounted for 90% of all chromosomes in each population sample.

Bacterium Versus Fungus

Many of the bacteria that cause many animal diseases likely evolved in a broad ecological system, and by looking elsewhere we may find alternative tractable experimental models for investigating disease mechanisms. Hogan and Kolter (p. 2229) have observed a range of antagonistic interactions among a selection of mutants of two commonly coexisting opportunistic pathogens, the bacterium *Pseudomonas aeruginosa* and the fungus *Candida albicans*. The bacterium attaches by its poles to the filamentous form of the fungus, developing a biofilm over the filaments and finally killing the fungus. Bacterial attachment requires the adherent virulence factor known as type IV pili. When under assault, the fungus reverts into a yeastlike form that appears to be impervious to the bacteria.

Building Up and Tearing Down

Hormone induction can stop very rapidly once the hormone is removed, but it has not been clear why. Freeman and Yamamoto (p. 2232; see the news story by Marx) show that molecular chaperones can disassemble the large multisubunit complexes that form on promoters and that induce gene expression. The authors used chimeric constructs to increase the local concentration of the chaperones in vivo and showed that when the chaperone p23 is localized to a promoter region, transcription is down-regulated. Hence, chaperones may play dual roles in the assembly and disassembly of transcription complexes.

Transcriptional Dysfunction in Huntington's Disease

The neurodegeneration characteristic of Huntington's disease (HD) is caused by mutations that induce expansion of a polyglutamine tract in the huntingtin protein. Mutant huntingtin is believed to interfere with transcription of genes that may be important for neuronal survival. Dunah *et al.* (p. 2238; see the Perspective by Frieman and Tjian) report that mutant huntingtin interferes with transcription mediated by the transcriptional activator Sp1 and its coactivator TAFII130. Coexpression of Sp1 and TAFII130 in cultured striatal cells from HD transgenic mice reversed the transcriptional block caused by mutant huntingtin. Soluble mutant huntingtin prevented binding of Sp1 to DNA in postmortem brain tissue from patients with presymptomatic and symptomatic HD, which suggests that transcriptional dysfunction caused by mutant huntingtin is an early event in HD pathogenesis.

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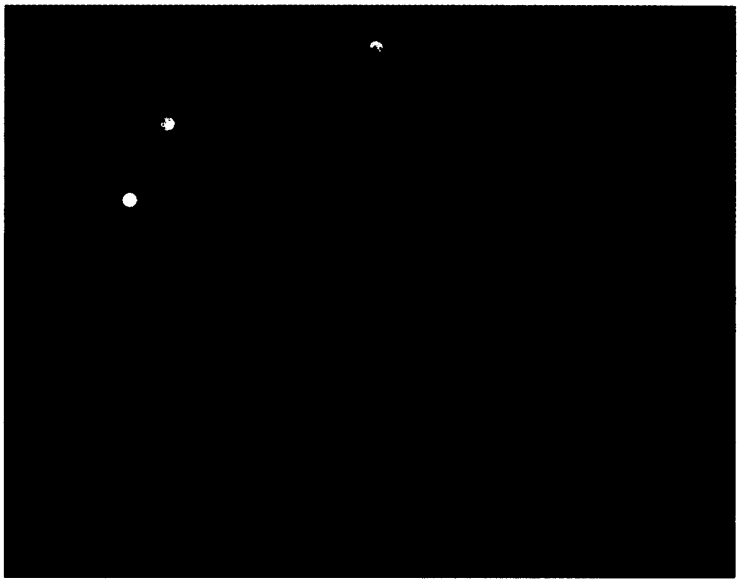

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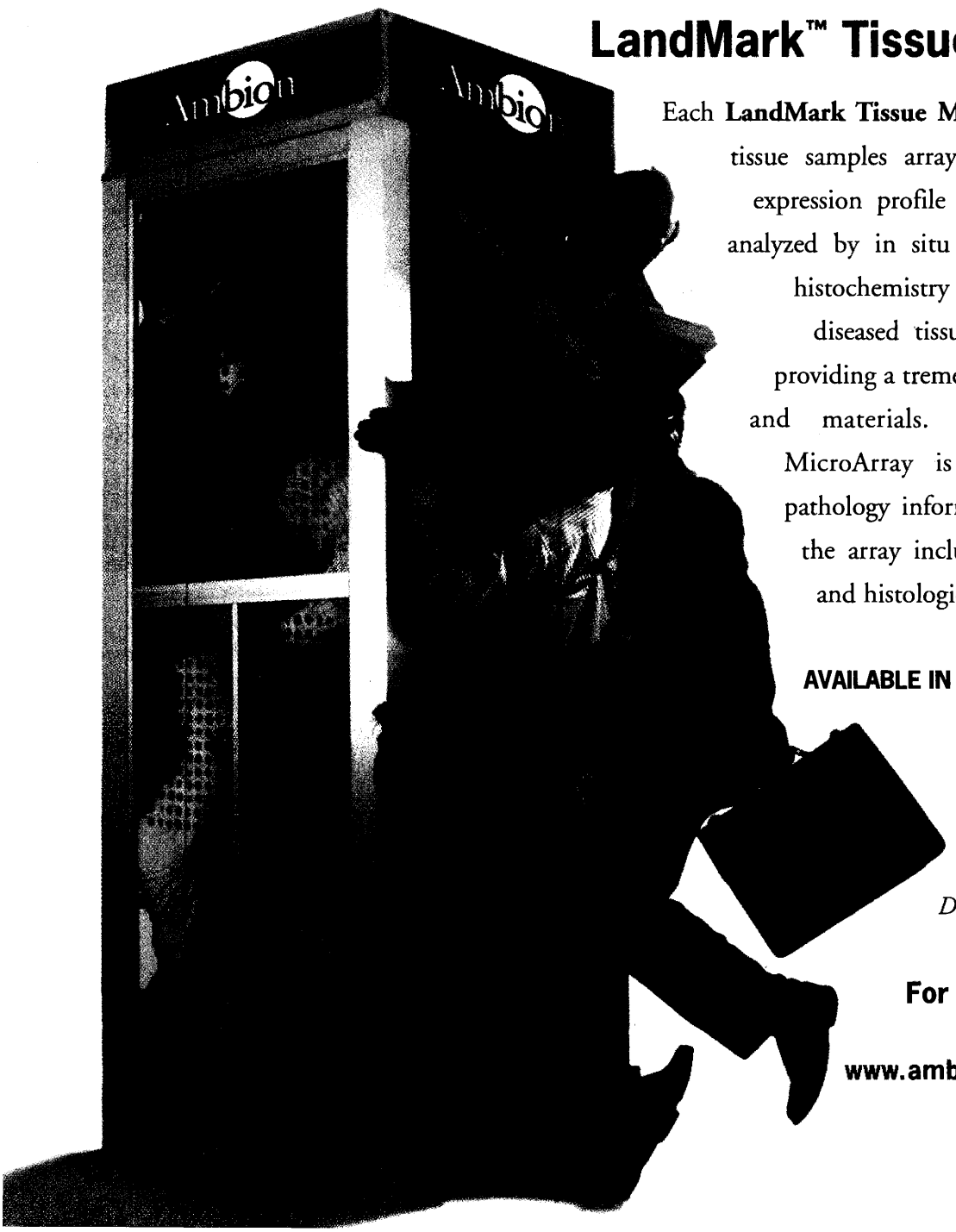

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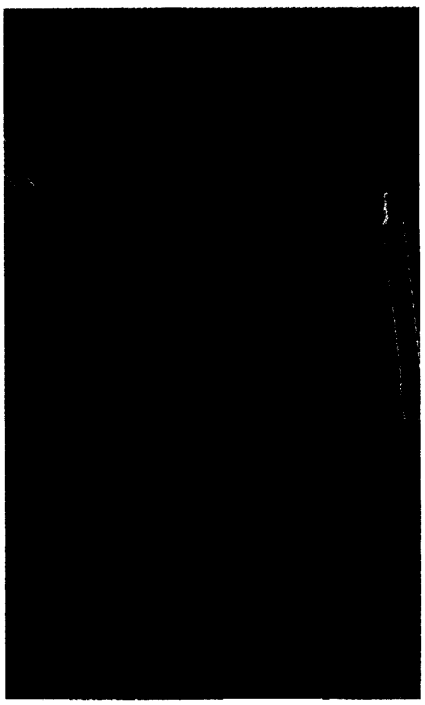

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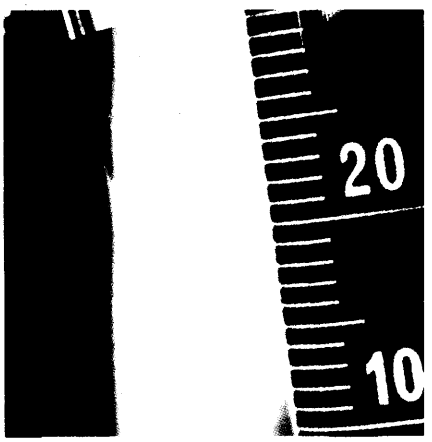

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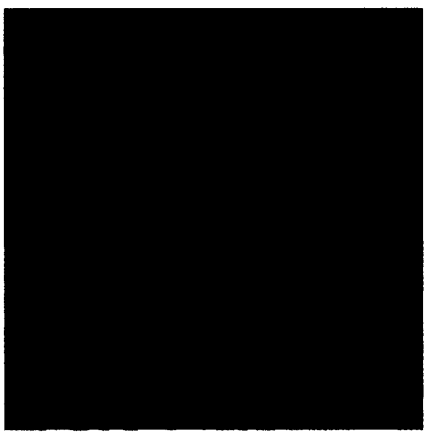

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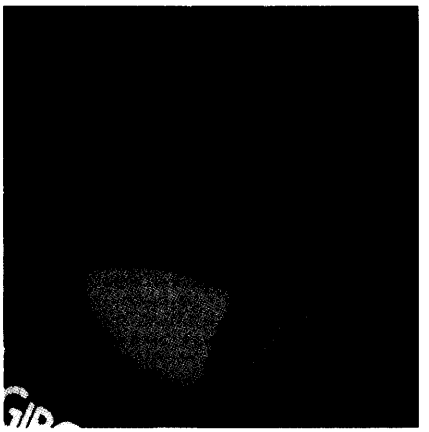

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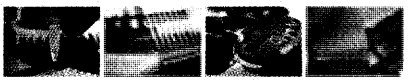

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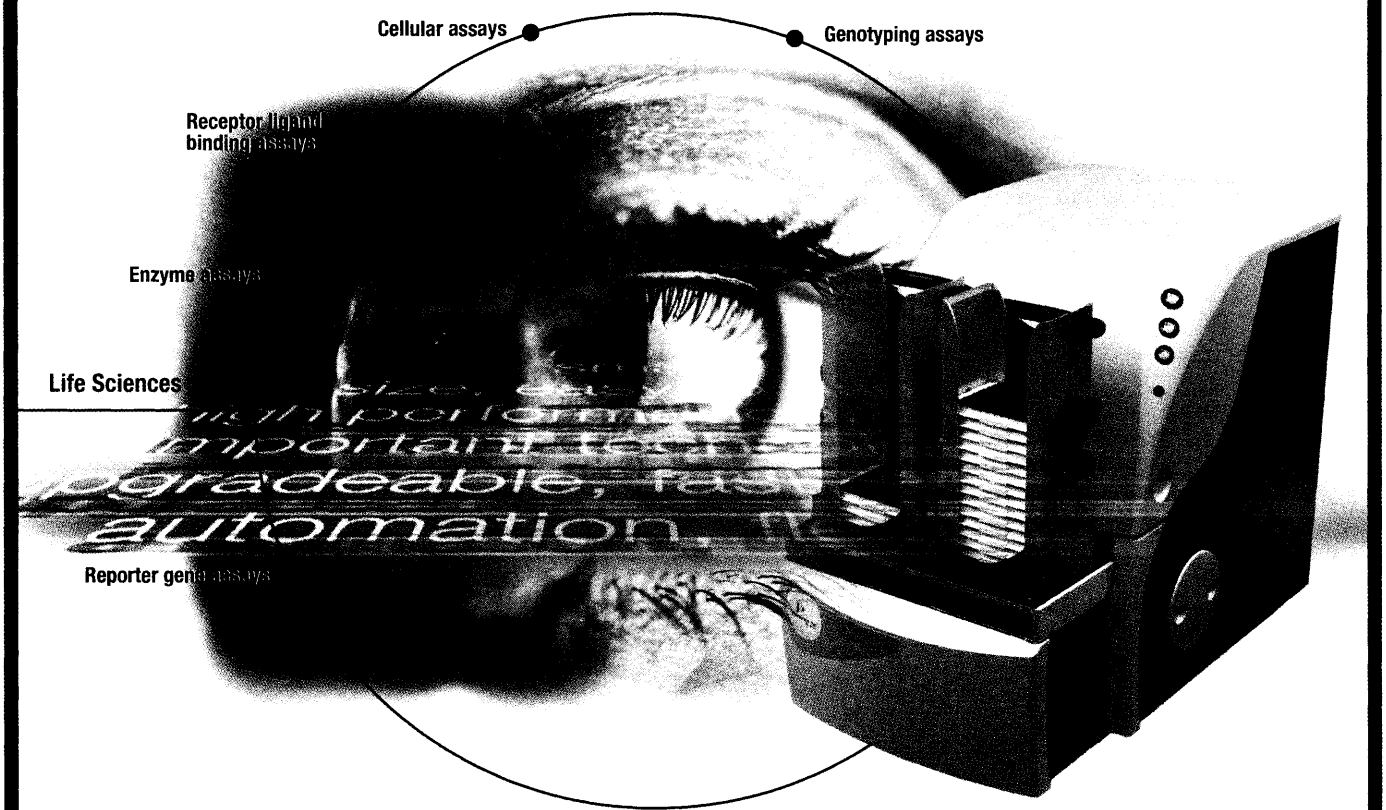

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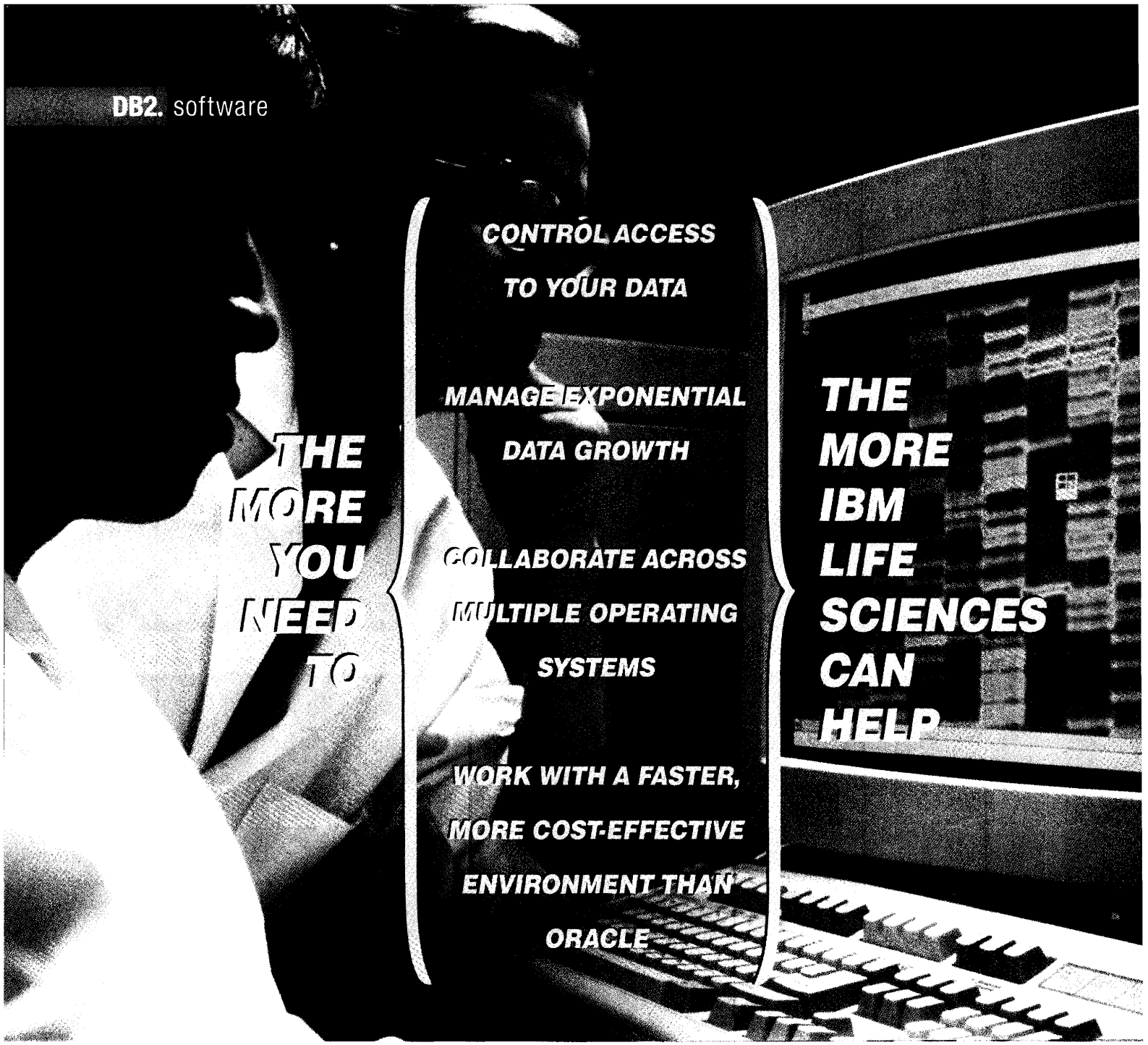

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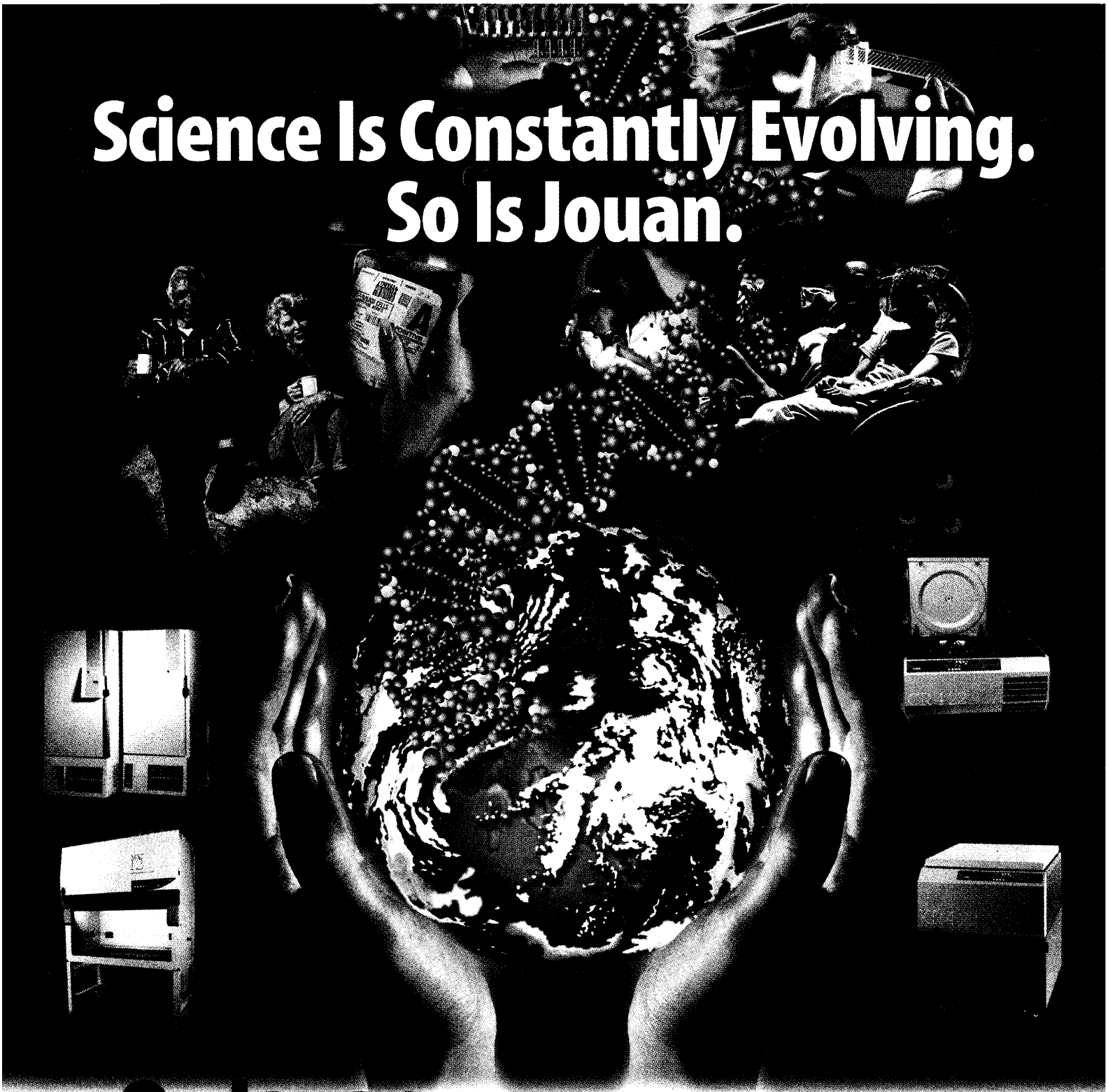

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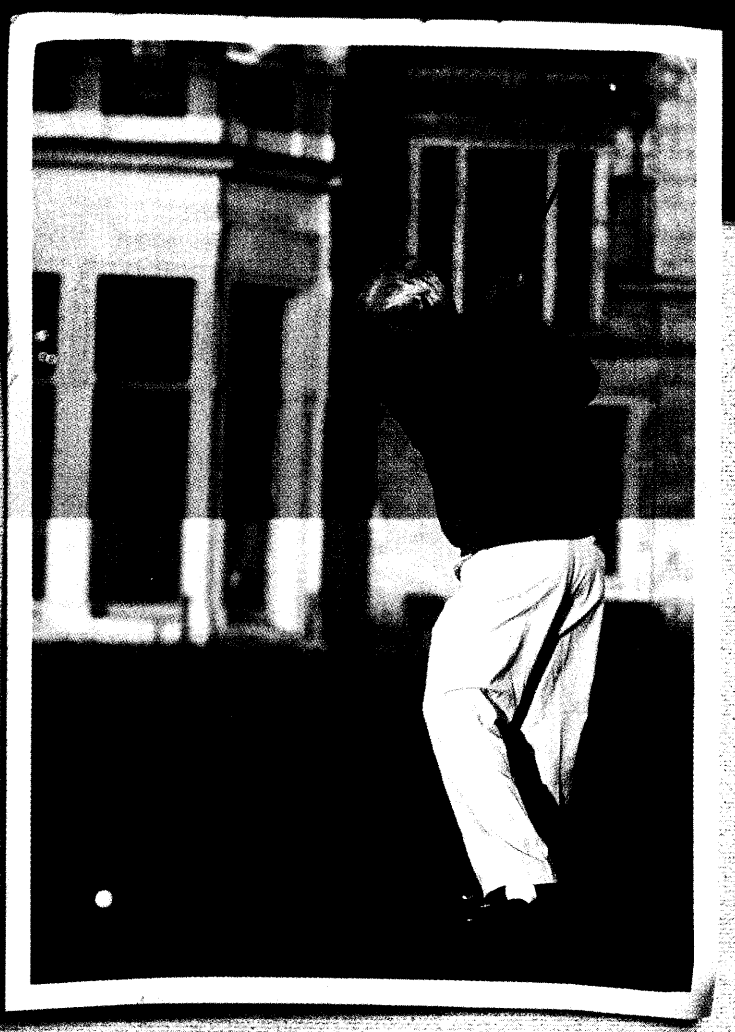

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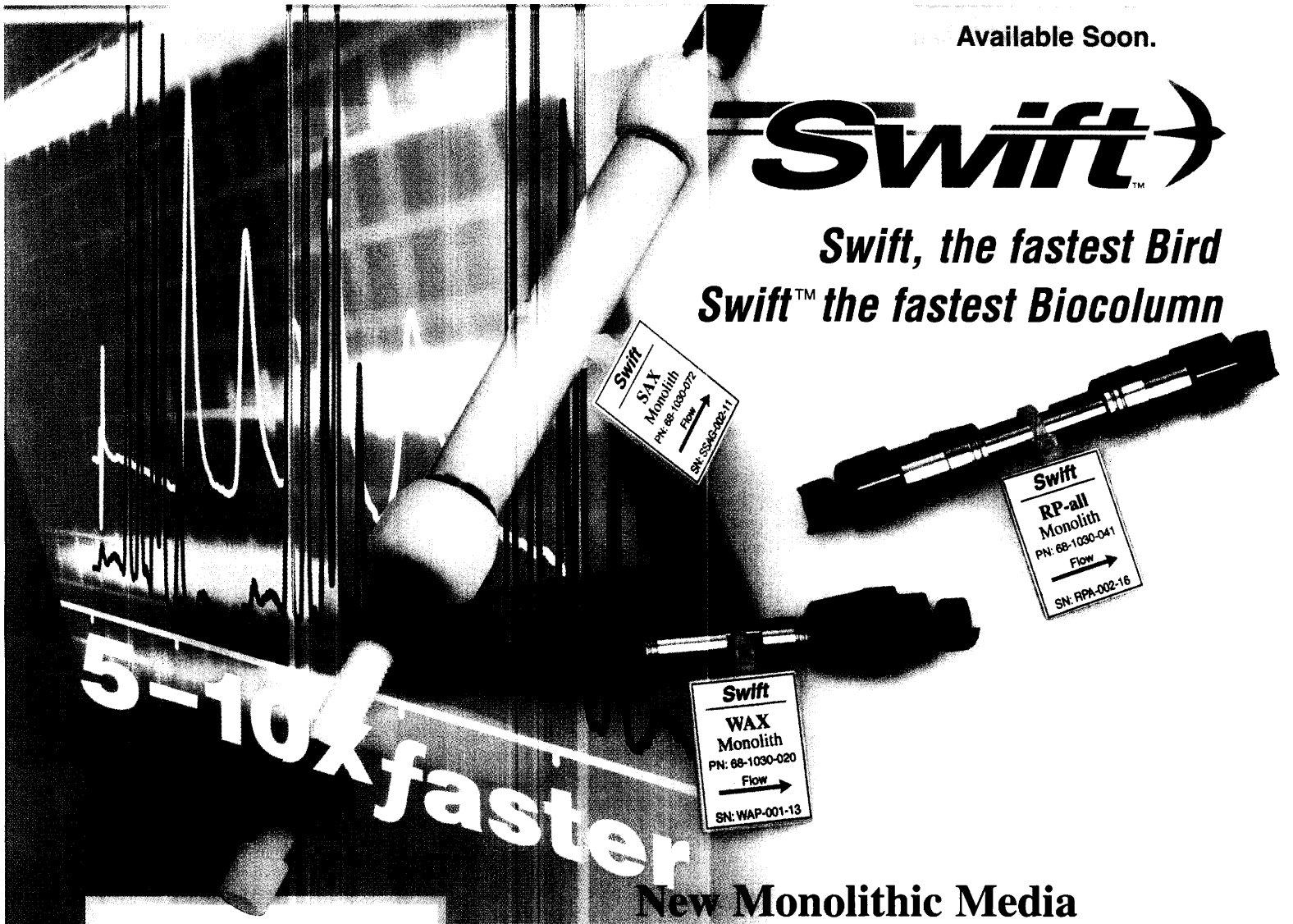

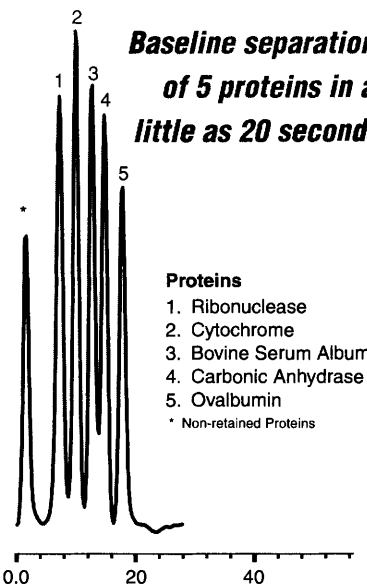

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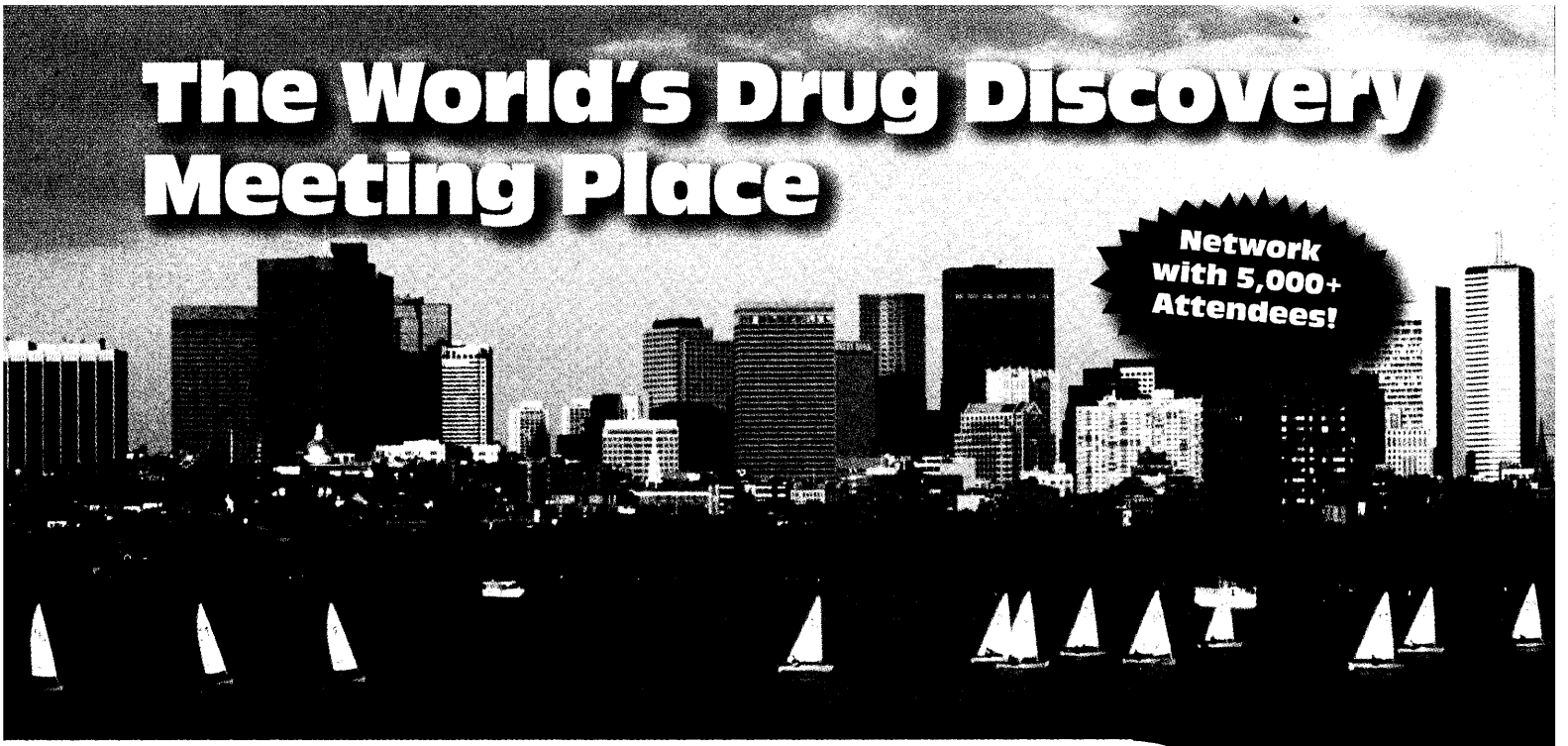

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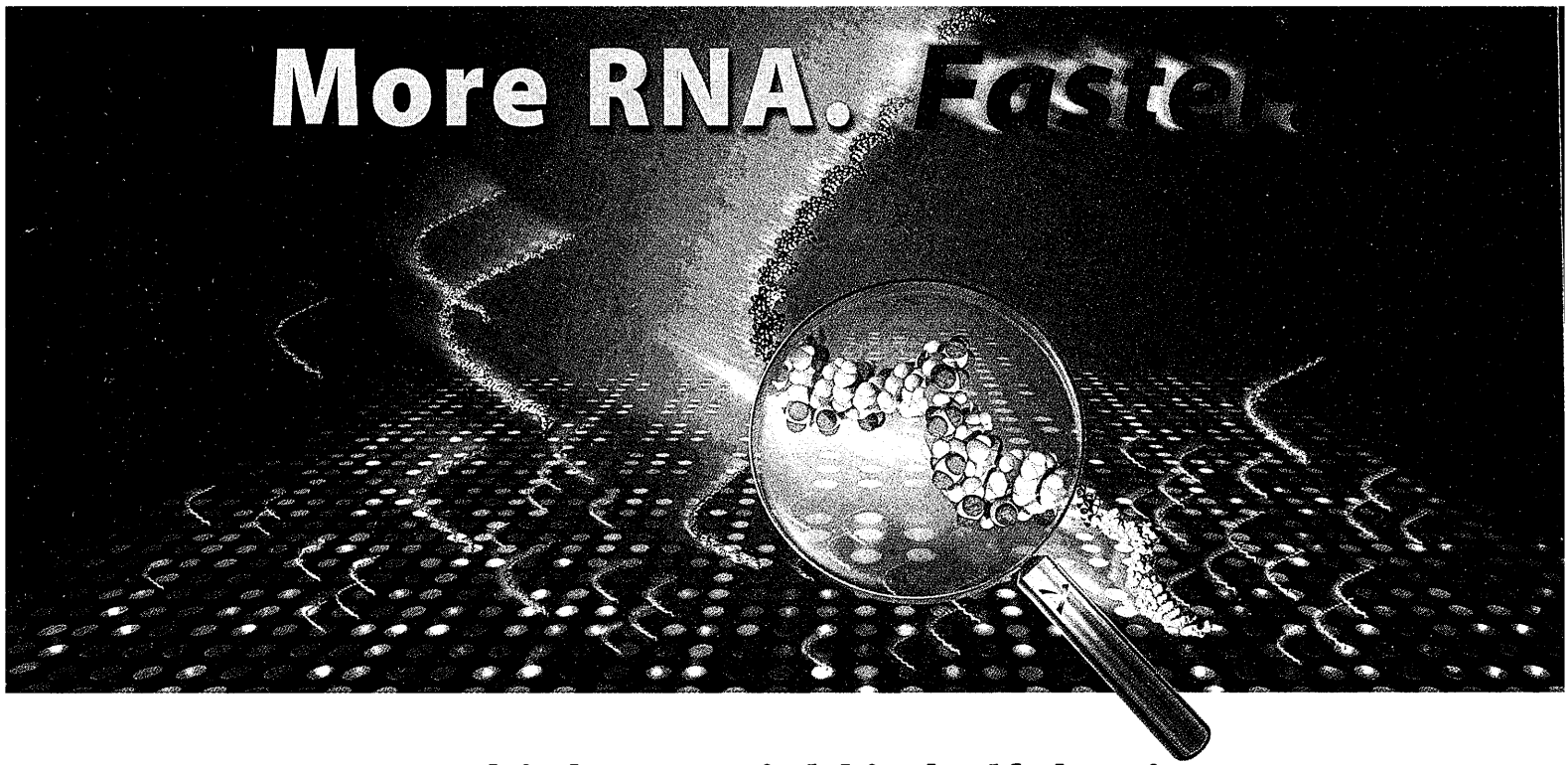

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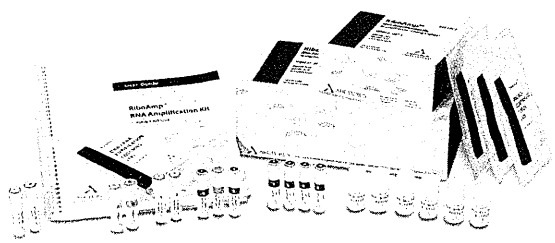

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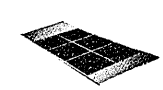

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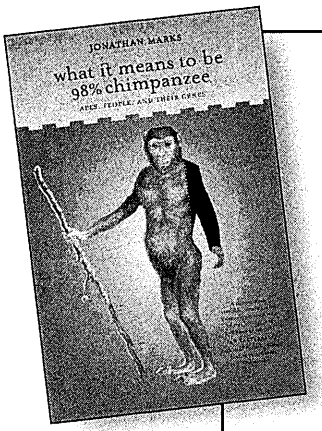

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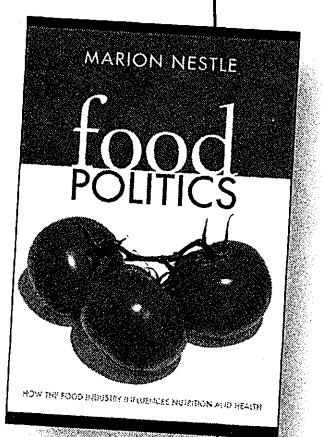

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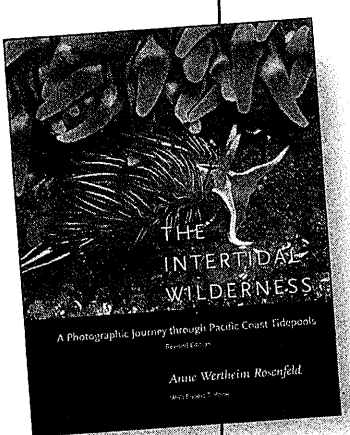

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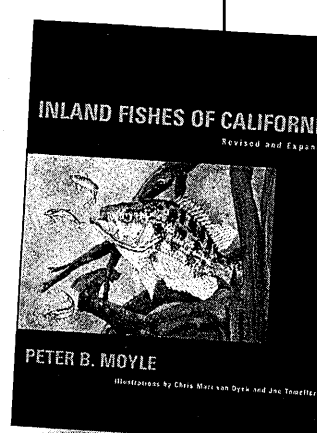

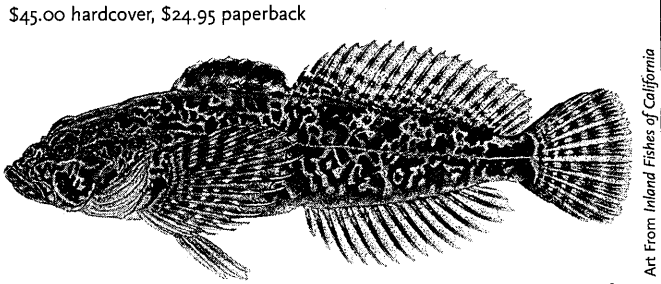

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