9 March 2001

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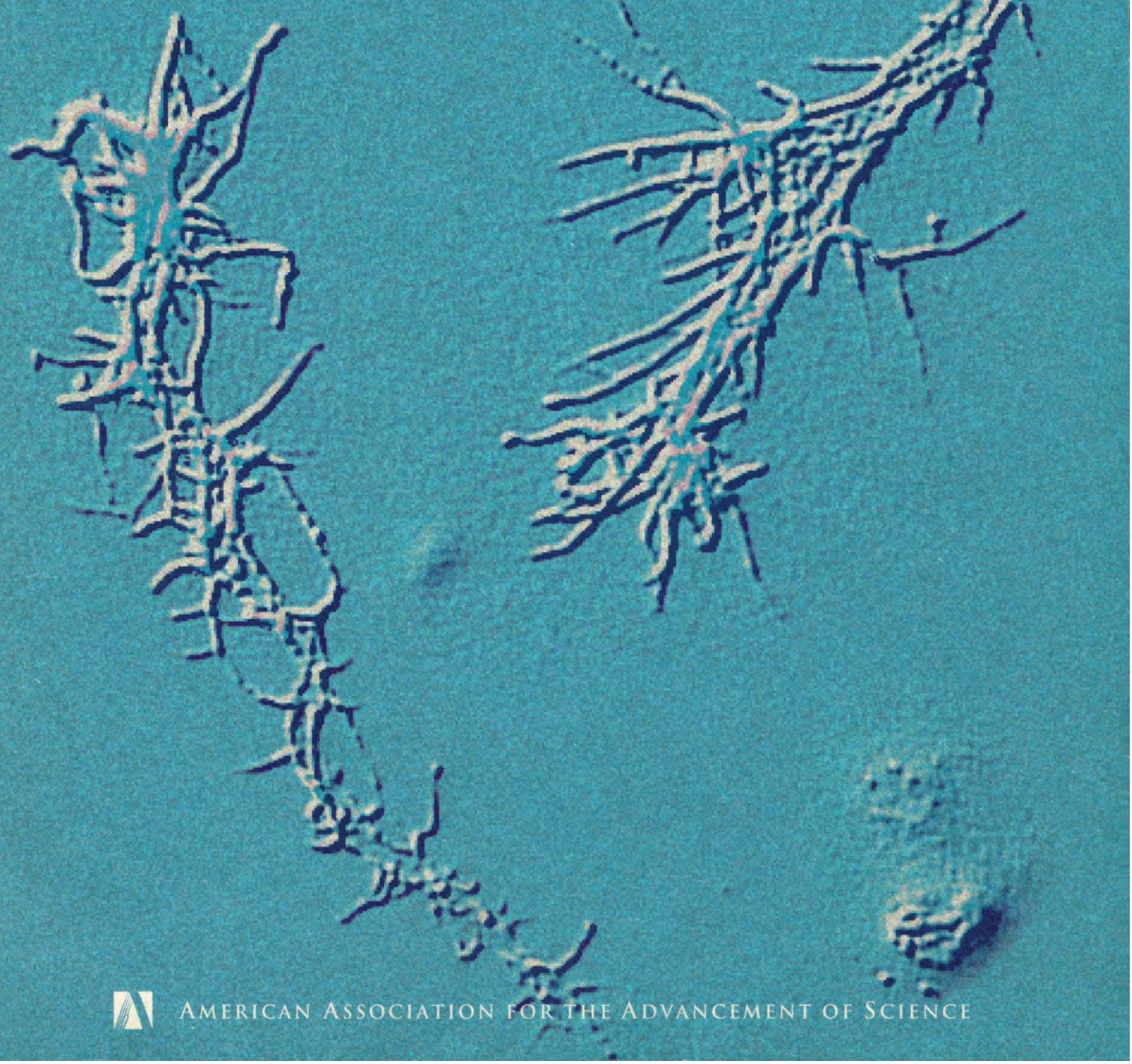
Pages 1847–2034 $9



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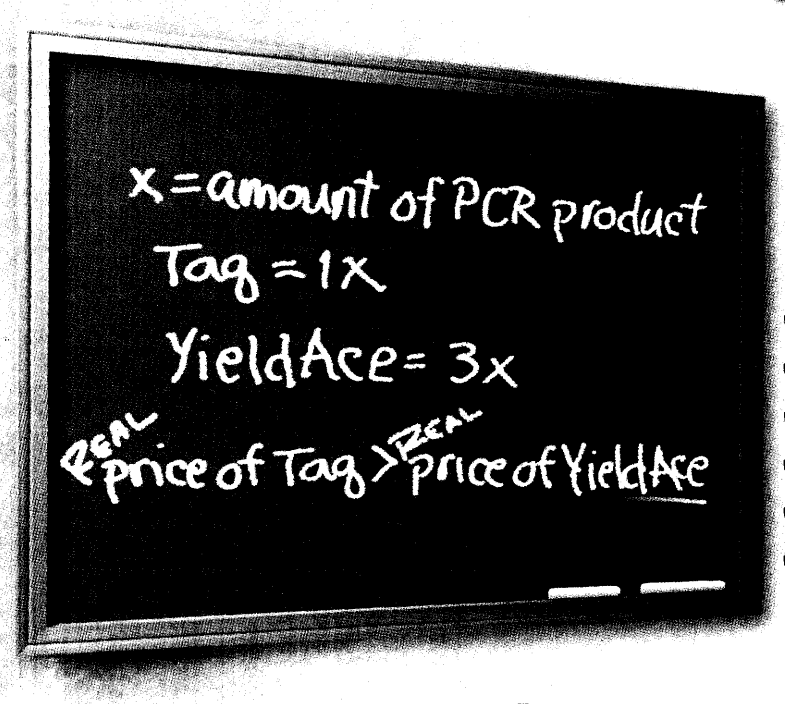

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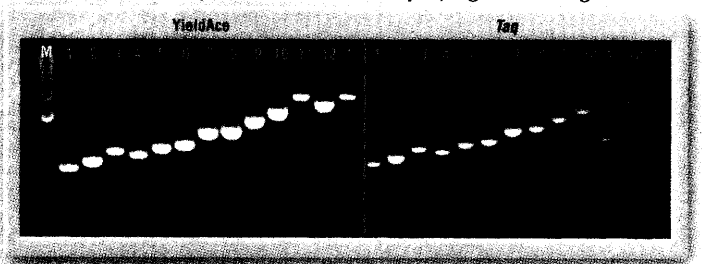

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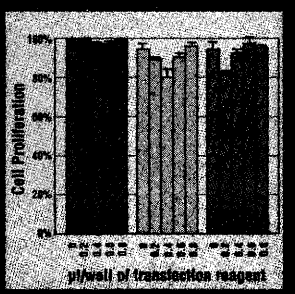
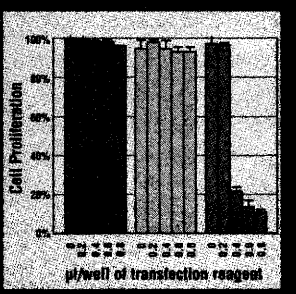


Effect of lipid X Concentrations on Antisense Delivery



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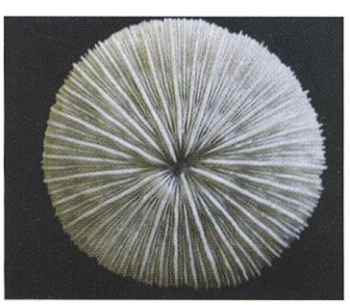
Science

Volume 291 9 March 2001 Number 5510

NEWS

1882
Unequal portions

SCIENCE'S COMPASS



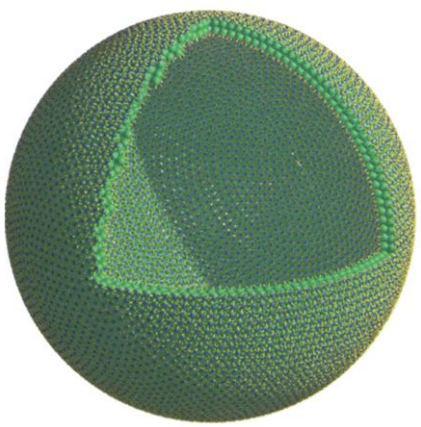
1913
Soft-bodied ancestors?

1909
Blasted by the solar wind

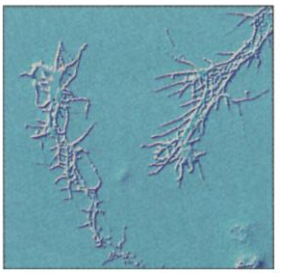
RESEARCH

RESEARCH ARTICLES

REPORTS

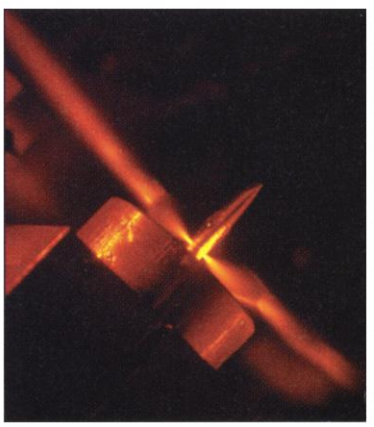


1944
Buckyball bilayer vesicle



COVER 1928

Two neuronal axons on a two-dimensional substrate, visualized by fluorescent staining of filamentous actin. One axon originates from a cell body beyond the top right and extends diagonally downward. The other, originating from a cell body beyond the bottom, is turning upward. The expanded tip of each axon, the growth cone, extends protrusions, filopodia, in search of proteins such as netrin and Slit, which guide axons to their destinations in the developing nervous system. (Image width, 120 μm; bottom right, nonneuronal cell.) [Image: E. Stein and M. Tessier-Lavigne]



1923
Experimental setup for ultrashort x-ray pulses

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Influence of Carbonic Anhydrase Activity in Vegetation on the ^{18}O Content of Atmospheric CO_2 J. Gillon and D. Yakir

PERSPECTIVE: **Discriminating Plants** F. I. Woodward

Variations in enzymatic activity among different types of land plants produce distinct modifications of the oxygen isotopic composition of atmospheric CO_2.

Pressure Dependence of the Superconducting Transition Temperature of Magnesium Diboride M. Monteverde *et al.*

Pressure and temperature measurements on MgB_2 help to elucidate the mechanism of superconductivity in this material.

Control of a Mucosal Challenge and Prevention of AIDS in Rhesus Macaques by a Multiprotein DNA/MVA Vaccine R. R. Amara *et al.*

Prolonged ability of a vaccine to delay or prevent disease progression after HIV infection is demonstrated in an animal model.

TECHNICAL COMMENTS

Examining Evidence for Reproductive Isolation in Sockeye Salmon

Hendry *et al.* (Reports, 20 Oct. 2000, p. 516) offered evidence of significant reproductive isolation in two salmon populations after only 13 generations of divergent selection. Howard *et al.*, in a comment, argue that the observed measures of genetic differentiation do not establish that the populations are indeed genetically divergent, that the migration estimates of the study are poorly supported, that Hendry *et al.* "have provided no evidence that observed phenotypic differences have a genetic basis," and that explanations for genetic differentiation other than reproductive isolation were not explored. Hendry *et al.* respond that "large genetic differences were neither expected nor crucial to our conclusions" given the brief time since the populations diverged. They also respond to the objection regarding migration estimates, provide indirect evidence that observed phenotypic differences "were at least partly genetic," and critically examine some alternative hypotheses. "We certainly do agree with Howard *et al.*," they conclude, "...that much work remains to be done."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/291/5510/1853a

science's stke www.stke.org

Perspective: Two Mammalian Mitotic Aurora Kinases—Who's Who? S. Descamps and C. Prigent

How aurora kinases regulate mitosis without getting in each other's way.

Protocol: Targeted Gene Repair in Mammalian Cells Using Chimeric RNA/DNA Oligonucleotides and Modified Single-Stranded Vectors H. Parekh-Olmedo, K. Czymmek, E. B. Kmiec

Gene-targeted repair using RNA-DNA hybrids can correct genetic mutations or be exploited to insert site-specific changes in genes of interest.

science's next wave www.nextwave.org

Germany: The Brain Gain? R. Metzke

You've read about "brain drain," the world's best and brightest fleeing their home countries for the U.S. Now, Germany is taking a concerted approach to turn the tide.

UK: A Temp-ting Offer K. Urquhart

Not all temps do shorthand; some can be found at the lab bench. And such a position can help you pay the bills, gain valuable experience, and get that all-important foot in the door.

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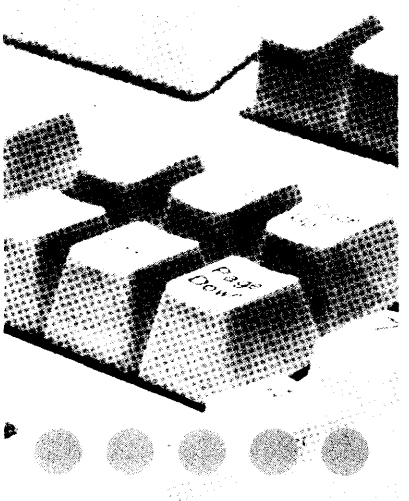

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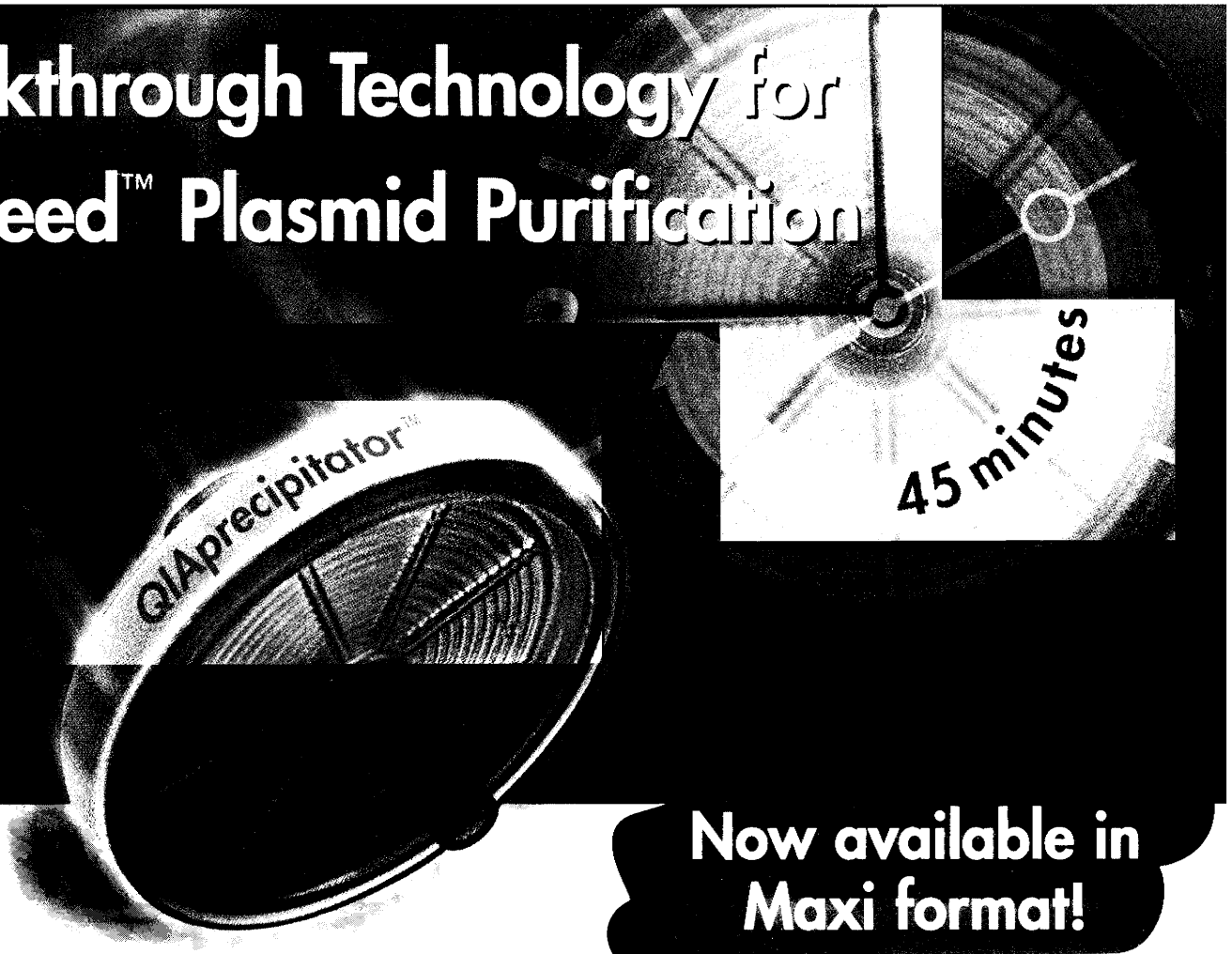

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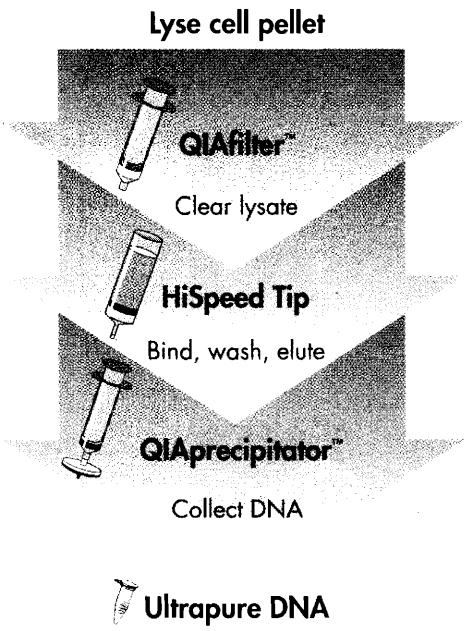

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THIS WEEK IN Science

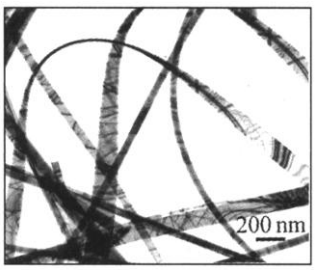
edited by Phil Szuromi

Toward Attosecond Optics

The development of femtosecond-scale optical pulses, comprising only a couple of cycles of the optical field, has opened the window on looking directly at atom and molecular dynamics. However, there are some other processes, electronic relaxation and ionization, that proceed on still shorter time scales. Observing the dynamics of these processes will require the development of yet shorter pulses and the ability to measure them. Drescher *et al.* (p. 1923; see the Perspective by Reid) now describe a technique for the generation and measurement of x-ray pulses 2.5 femtoseconds in duration that are shorter than the carrier field used for their generation.

1947 Oxide Nanobelts

Nanotube and nanowire morphologies are known for many materials. Pan *et al.* (p. 1947) have now found that several metal oxides (including zinc, tin, indium, and gallium) can form a "nanobelt" morphology after thermal evaporation the bulk oxide at high temperature and deposition of the vapor at lower temperatures on an aluminum oxide surface. The nanobelts are between 30 and 300 nanometer wide, have width-to-thickness ratios of 5 to 10, and can extend for several millimeters. These oxide semiconductors have several applications in sensing and electronics that could be enhanced by this high-area morphology.



CREDIT: Z. W. PAN *ET AL.*

The Quantum Mechanics of Micromechanics

In classical mechanics, a vacuum is a pretty dull place, but in quantum mechanics, it's quite busy. Quantum fluctuations of the electromagnetic field give rise to fleeting moments in which virtual photons are created and annihilated. If these events take place in the space between two uncharged plates, they cause a pressure differential that pushes the plates together—the Casimir effect. For large-scale separations, these events have little consequence, but as length scales are reduced, as in the case of microelectromechanical systems now being used as actuators, the effect could be significant. Chan *et al.* (p. 1941) demonstrate that as separations are reduced to the nanometer scale, quantum fluctuations do indeed play a significant role and must be considered in describing the operation of such microfabricated devices.

Losing Oxygen

The polar flux of O^+ out of Earth's atmosphere suggests that the atmosphere has lost an amount oxygen equivalent to 18% of its current oxygen content during the last 3 billion years. Seki *et al.* (p. 1939; see the Perspective by Lundin) estimated the amount of O^+ that is actually lost through four escape mechanisms in the magnetosphere. Their results suggest that only 2% of the oxygen has been lost during this period through these four escape routes. Either the oxygen is being recycled in the magnetosphere back into the ionosphere or a yet unknown escape mechanism lurks.

Extinction Clues in Space Dust

Interplanetary dust particles (IDPs) carry a higher abundance of ^{3}He than do terrestrial rock samples because this species is implanted by the solar wind. If small IDPs are not unduly frictionally heated by Earth's atmosphere, they will enrich the surface of minerals with ^{3}He when they are deposited. Thus, the measurement of ^{3}He normalized to ^{4}He in terrestrial sedimentary rocks can provide an estimate of IDP flux. Mukhopadhyay *et al.* (p. 1952) examined clays emplaced near the Cretaceous-Tertiary (K-T) boundary and found that the IDP flux was constant during this time period. No additional helium was added from the bolide impact, which is consistent with the interpretation that the bolide mostly vaporized. They also estimate a sedimentation rate of the K-T boundary clay layer of 11,000 years, which indicated that the K-T extinction event was rapid.

Switching Sides to Get Ahead

As the nervous system of the developing vertebrate embryo is laid down, the guidance molecule netrin attracts the growth cones of advancing axons to the embryo's midline. However, as soon as the growth cones cross the midline, they switch allegiance, ignoring netrin and instead responding to Slit, which repels the growth cones away from the midline. Two papers tackle how growth cones make their way through competing signals (see the Perspective by Dickson). Stein and Tessier-Lavigne (p. 1928– ; see the cover) show that this switch is the result of the cytoplasmic domain of the Slit receptor, Robo, binding to the cytoplasmic domain of the netrin receptor DCC. Thus, the dwindling effects of netrin on growth cones is directly linked to their increasing responsiveness to the repellent effects of Slit. This interlocked silencing mechanism prevents the growth cone from being trapped in a tug-of-war between the attractive and repellent activities of two opposing guidance molecules. Stein *et al.* (p. 1976) address the mechanism by which netrin exerts its effects. In contrast to a recent suggestion that netrin acts through the adenosine A2B receptor, the authors show that netrin binds directly to the DCC protein and that A2B activation is not required for netrin's effects on axon outgrowth or neuron attraction. Thus, DCC is the primary receptor responsible for netrin's actions.

Bypassing Checks and Balances

The hepatitis virus type C tricks the host's ribosomes into recognizing and initiating translation of its RNA even though its RNA lacks a 5′ cap, which is added to host messenger RNAs and is the usual prerequisite for initiation. It does so by utilizing an internal ribosome entry sequence (IRES) that lies directly upstream of the protein-coding region of its RNA. Spahn *et al.* (p. 1959) used electron microscopy to find that the IRES binds to the decoding sub-

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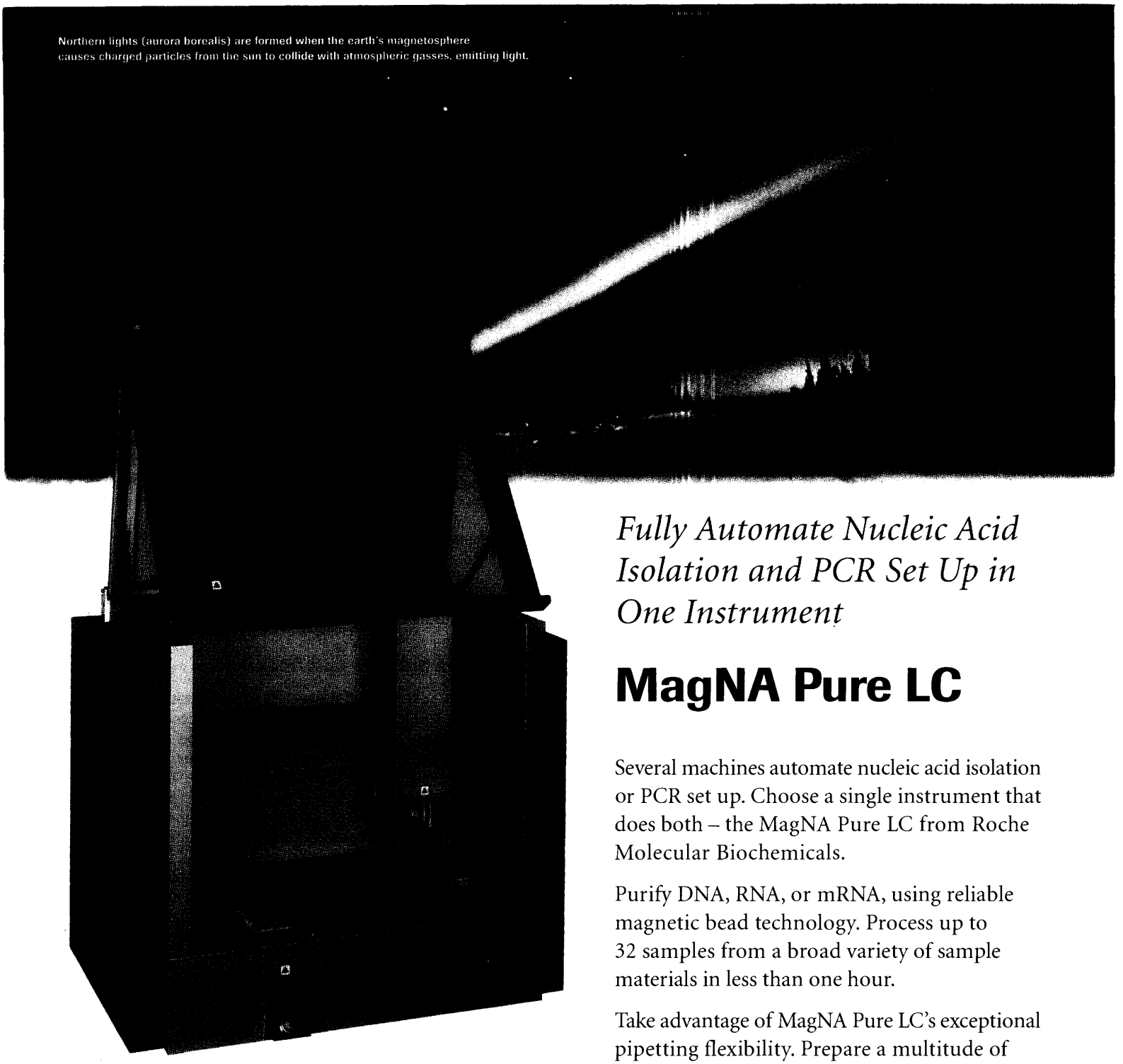

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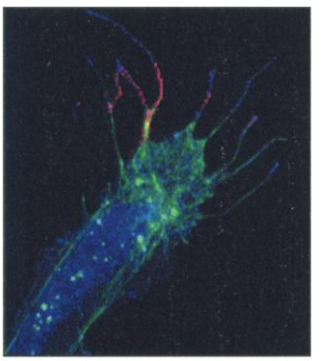
unit of the mammalian ribosome. Binding triggers a conformational change that brings the adjacent protein-coding region into the decoding site and locks it into place in preparation for initiating translation and protein synthesis.

Mysterious Resistance Revealed

Resistance against the penicillin family of antibiotics has almost become universal among clinically important strains of staphylococci bacteria. When penicillin binds to a sensor on the surface of bacteria, a signal is transmitted across the cell membrane to cause removal of a DNA repressor protein and to allow the transcription of the various regulatory genes for expression of β-lactamase or of low-affinity penicillin-binding protein substitutes. Zhang *et al.* (p. 1962; see the Perspective by Archer and Bosilevac) now show that penicillin binding to the sensor triggers self-proteolysis. The cleavage product then binds, either directly or via intermediates, to the DNA binding repressor protein. The repression is lifted in a second proteolytic step when the DNA binding protein is released and transcription of the antibiotic-resistance genes starts.

Turn Signals



Growth cones at the tips of extending neurites dictate axonal guidance by translating extracellular cues into intracellular signals that then determine the appropriate direction to turn. Gomez *et al.* (p. 1983) report that localized calcium transients occur in filopodia that extend from the growth cones. The frequency and amplitude of these calcium transients depend on the extracellular substrate, implicating the involvement of integrins in regulating the turning process. These calcium transients also appear to propagate back to the growth cone and affect global calcium dynamics.

Recovering Ebola Virus

Ebola virus, and its ally Marburg virus, are nonsegmented negative-strand RNA viruses and members of the family Filoviridae. They cause fatal hemorrhagic diseases, but so far their occurrence has been in fairly restricted localities, mostly in western and central Africa. The "wild hosts" for these viruses are currently unknown. Molecular tools are needed for therapeutic development and for responding appropriately to outbreaks of these and any new filoviruses. Volchkov *et al.* (p. 1965) have established a reverse-genetics system for rescuing Ebola virus from cloned DNA and generated mutants incapable of transcriptional editing of a key nonstructural glycoprotein. This mutant form of the virus expressed greater amounts of the envelope glycoprotein and was more cytotoxic. Further investigations should lead to insights into replication and pathogenicity of these viruses.

Do You Hear What I Hear?

The recognition of pitch is a two-part process in which the ear collects musical sounds, which are then extensively processed by the brain to produce pitch perception. To elucidate the contribution of genetics and environment to pitch perception ability, Drayna *et al.* (p. 1969; see the news story by Holden) applied the Distorted Tunes Test (DTT) to 284 monozygotic and dizygotic twin pairs. With the DTT, subjects have to recognize notes with incorrect pitch in simple popular melodies. There was a significantly higher correlation on DTT scores between monozygotic compared with dizygotic twin pairs, which indicates that there is a large inherited component to pitch perception.

Boosting Transmitter Release

In vertebrates, presynaptic neurotransmitter receptors are generally thought to inhibit transmitter release. However, Schmitz *et al.* (p. 1972) show that activation of high-affinity presynaptic kainate receptors at hippocampal mossy fibers facilitates glutamate release from the synaptic terminals. This mechanism contributes in part to the unusually large frequency facilitation during trains of stimuli seen at mossy fiber synapses.

Published online in *Science* Express

CREDIT: T. M. GOMEZ *ET AL.*

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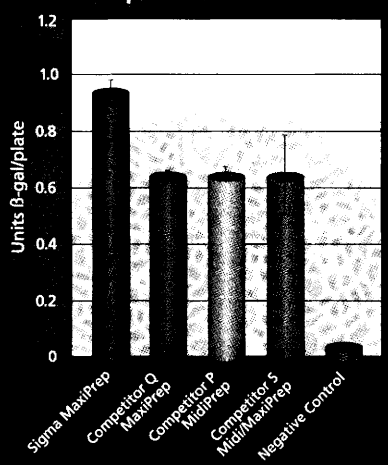

The data shows the average of six replicates for each named isolation method. All transfections were in CHO-K1 cells. The OD measurements were taken at 420 nm and the units of β-gal/plate were found using the Sigma β-Galactosidase Reporter Gene Activity Detection Kit. The cells were grown to ~60-75% confluency and transfected using 3µg of plasmid DNA/15µg of Escort IV. β-Gal activity was determined ~60-70 hour post-transfection.

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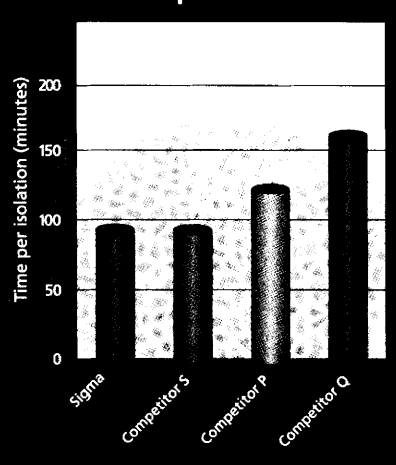

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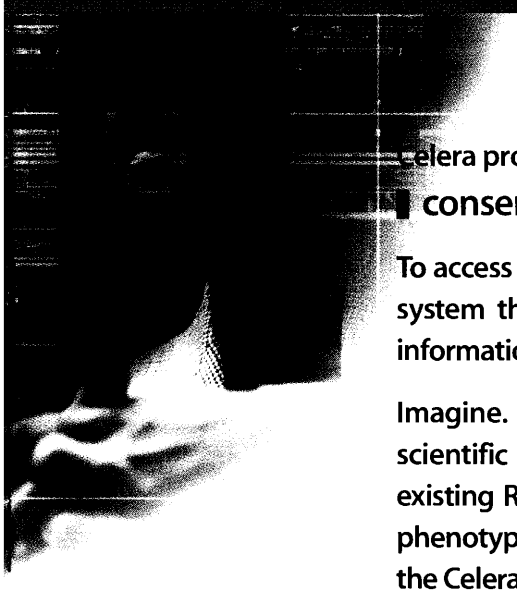

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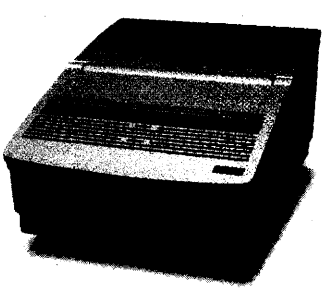

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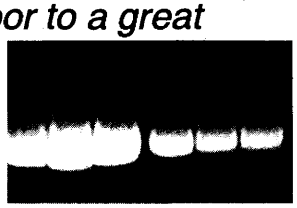

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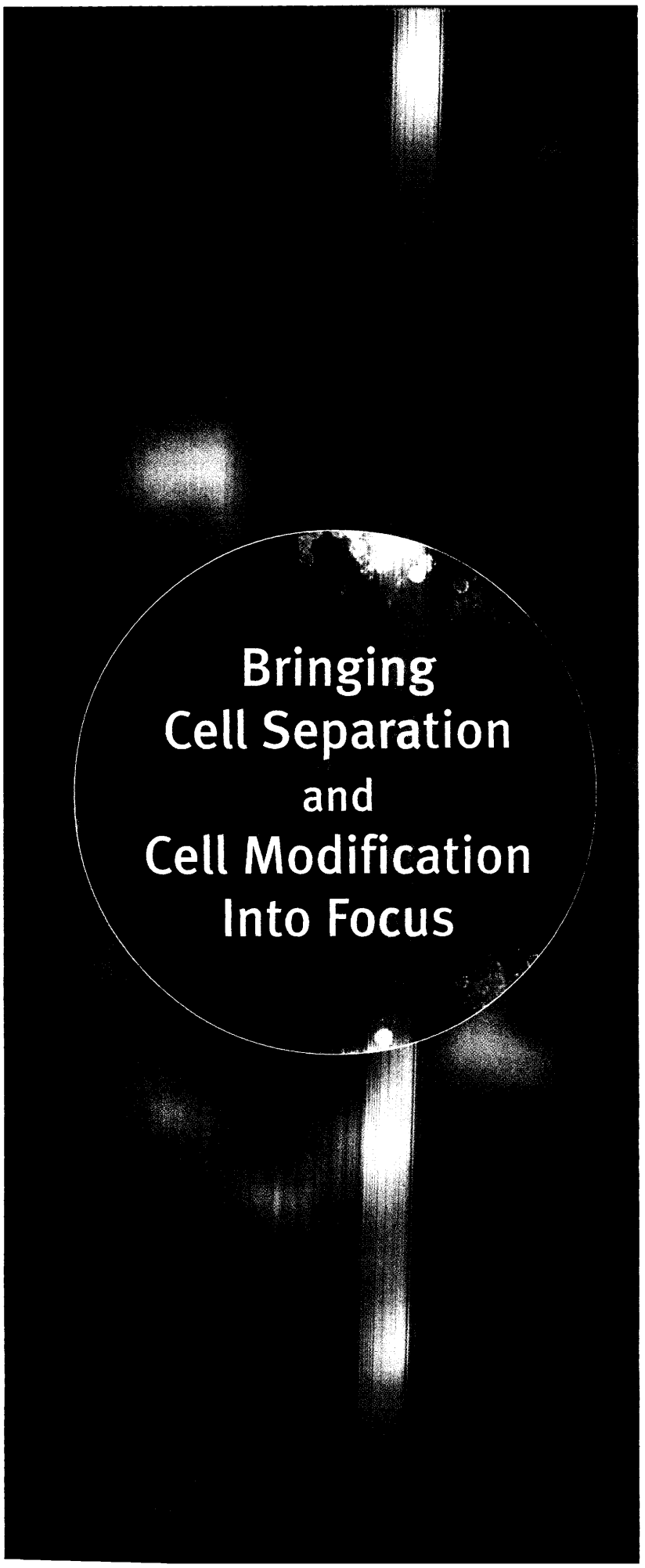

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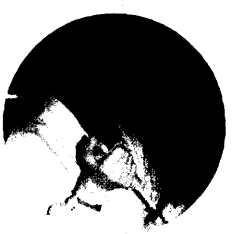

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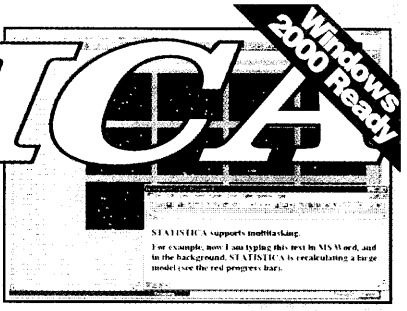

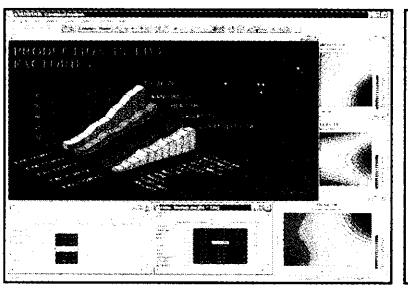

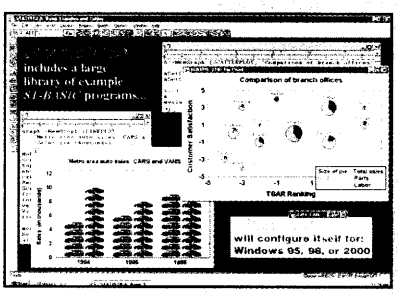

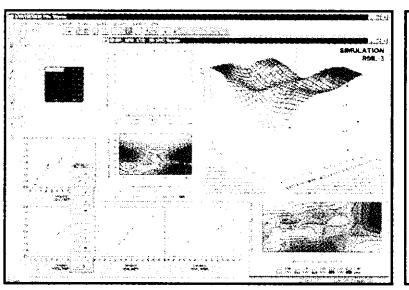

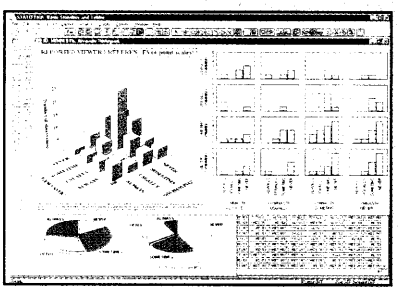

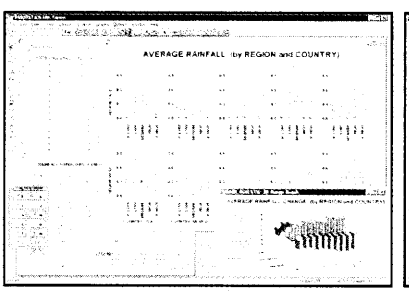

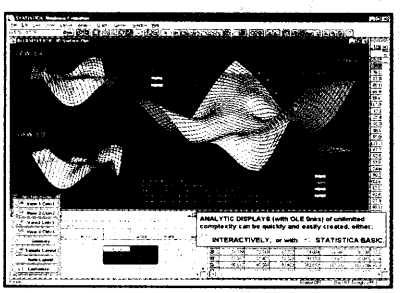

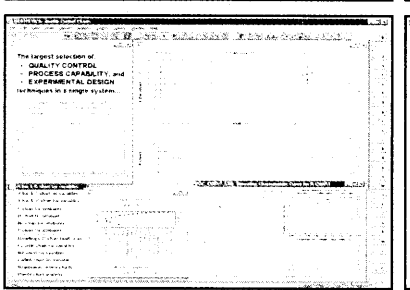

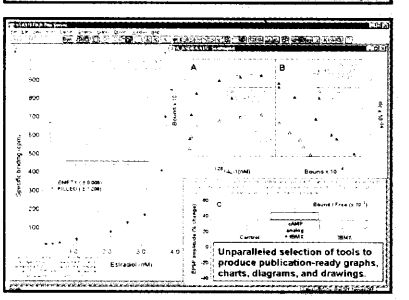

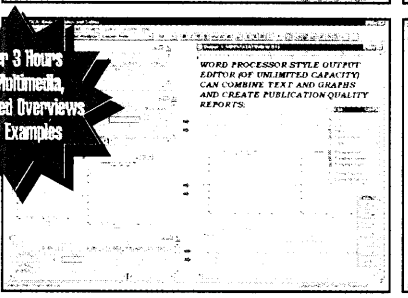

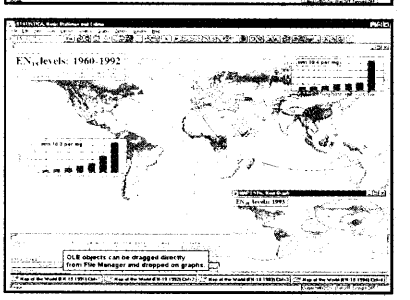

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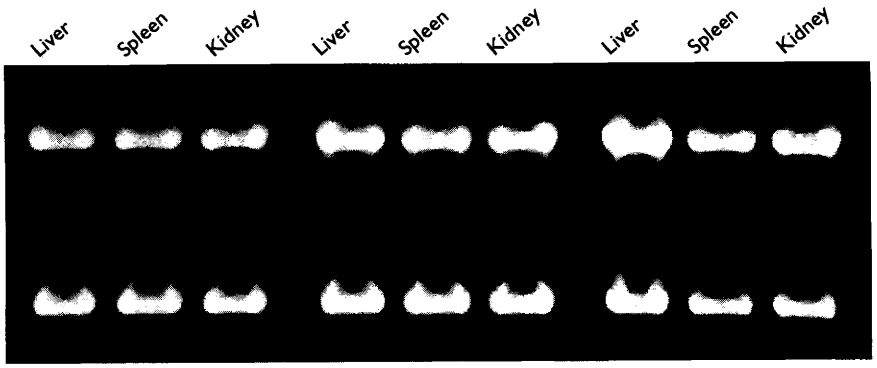

Figure 1a. Quality of RNA isolated from Tissue Stored in RNA*later*™ Solution. Fresh mouse tissues were dissected and stored in RNA*later*™ at 37°C for 1 day, room temperature for 1 week, or 4°C for 1 month. RNA was isolated using TRI Reagent® (MRC) and analyzed using denaturing agarose gel electrophoresis.

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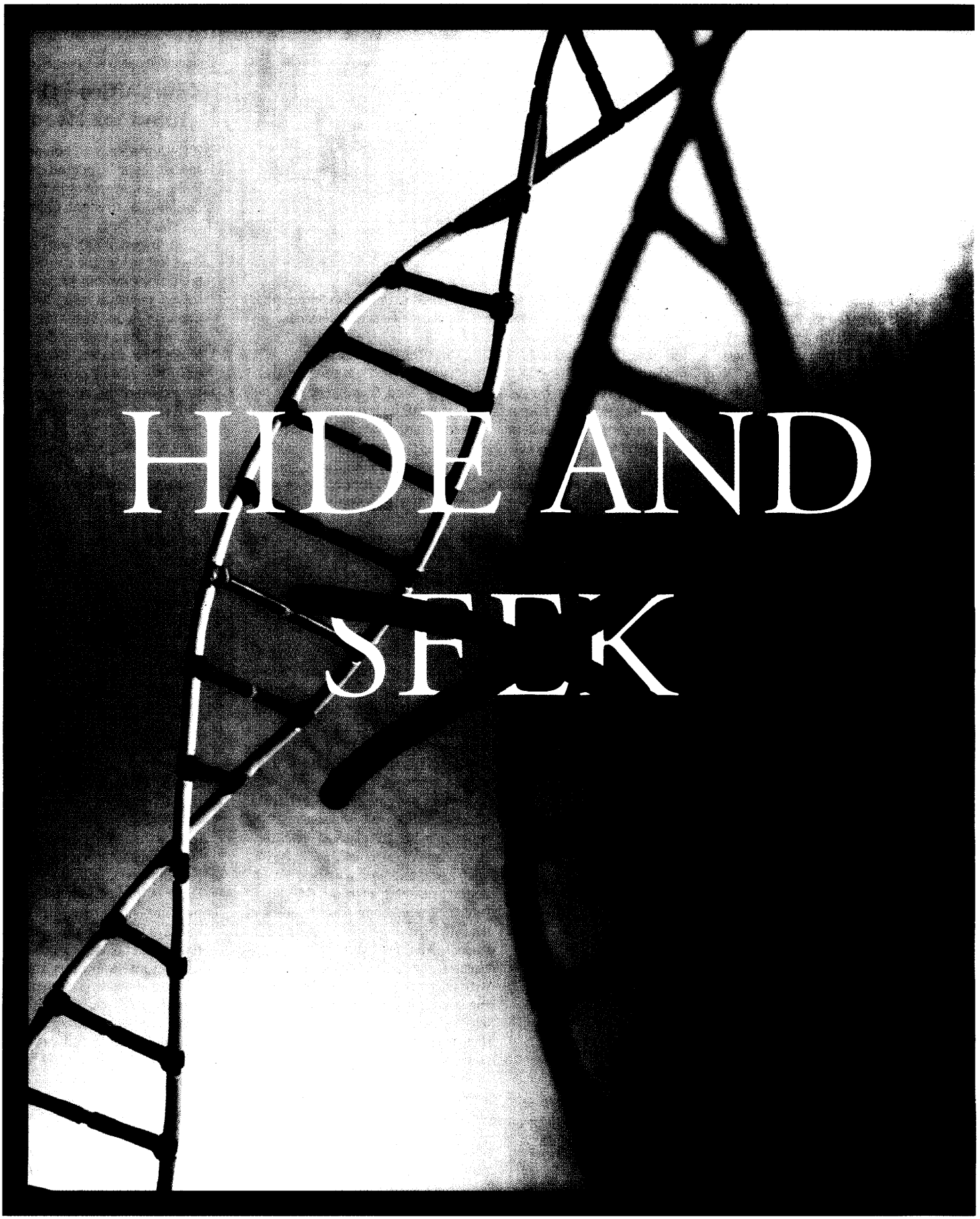
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* Yan H., et. al., Conversion of Diploidy to Haploidy, Nature, v. 403, 723, (2000)

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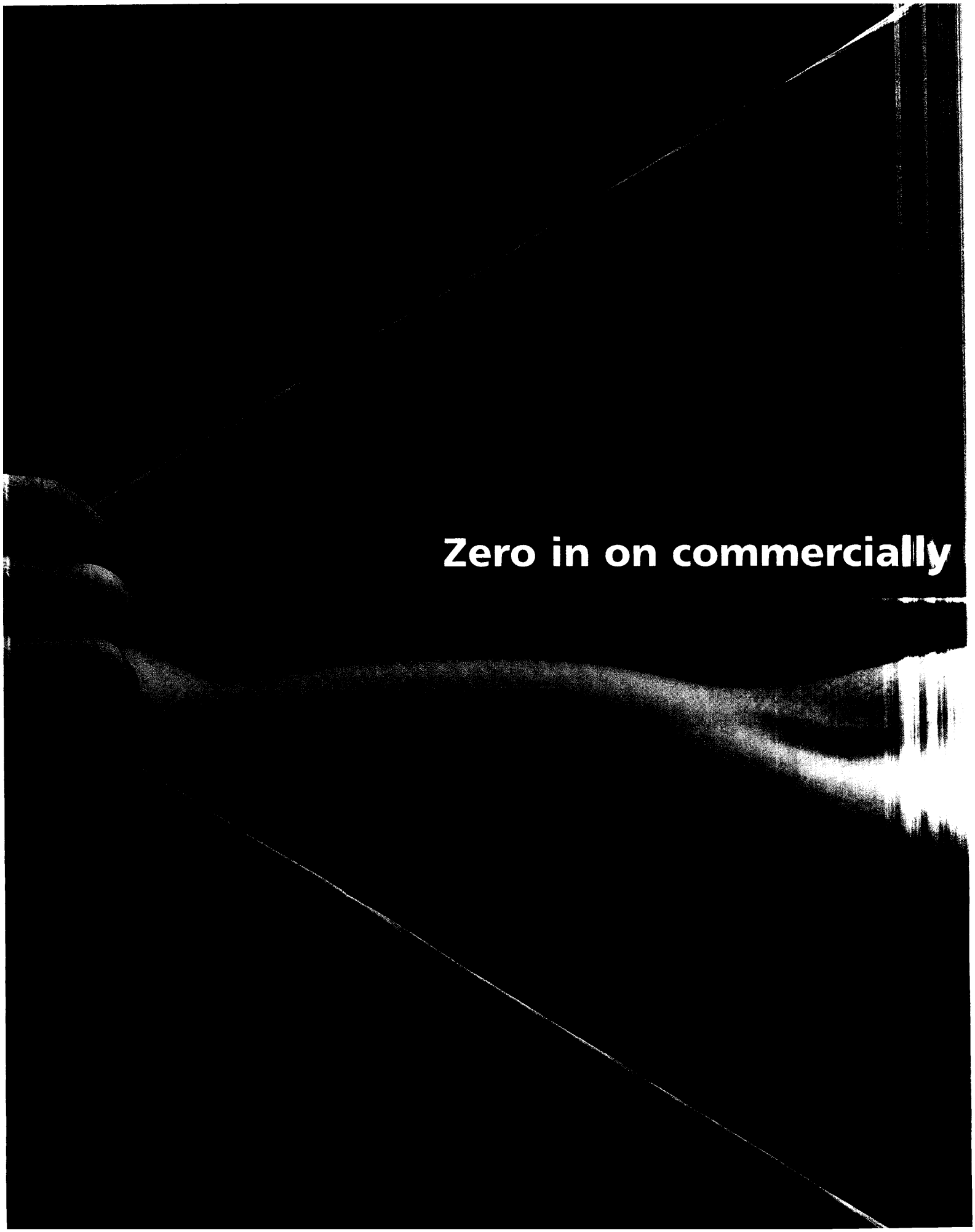
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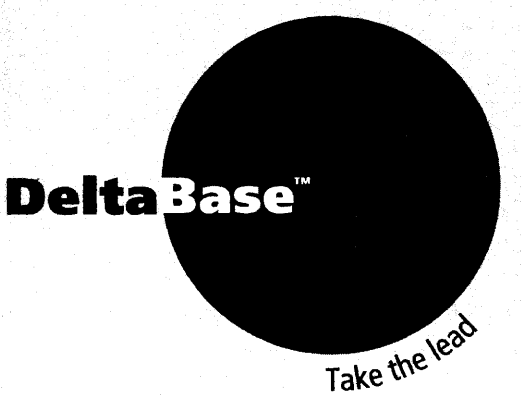

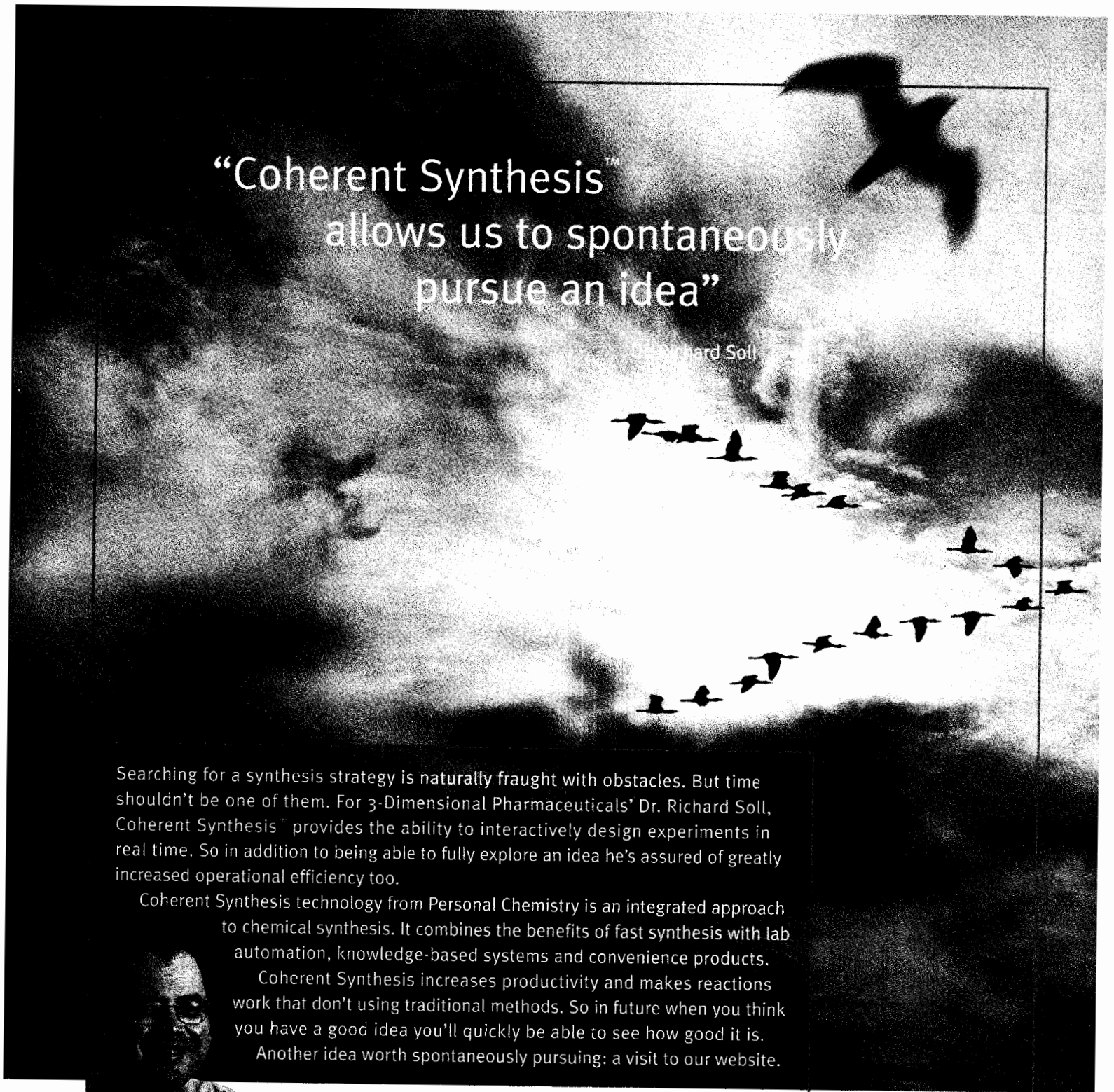

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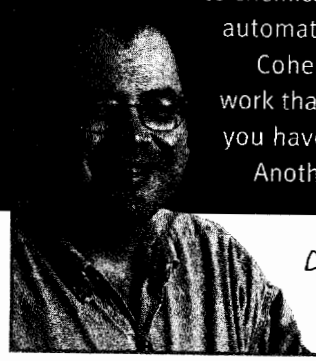

Dr. Richard Soll is Vice President, Chemistry at 3-Dimensional Pharmaceuticals, Inc.

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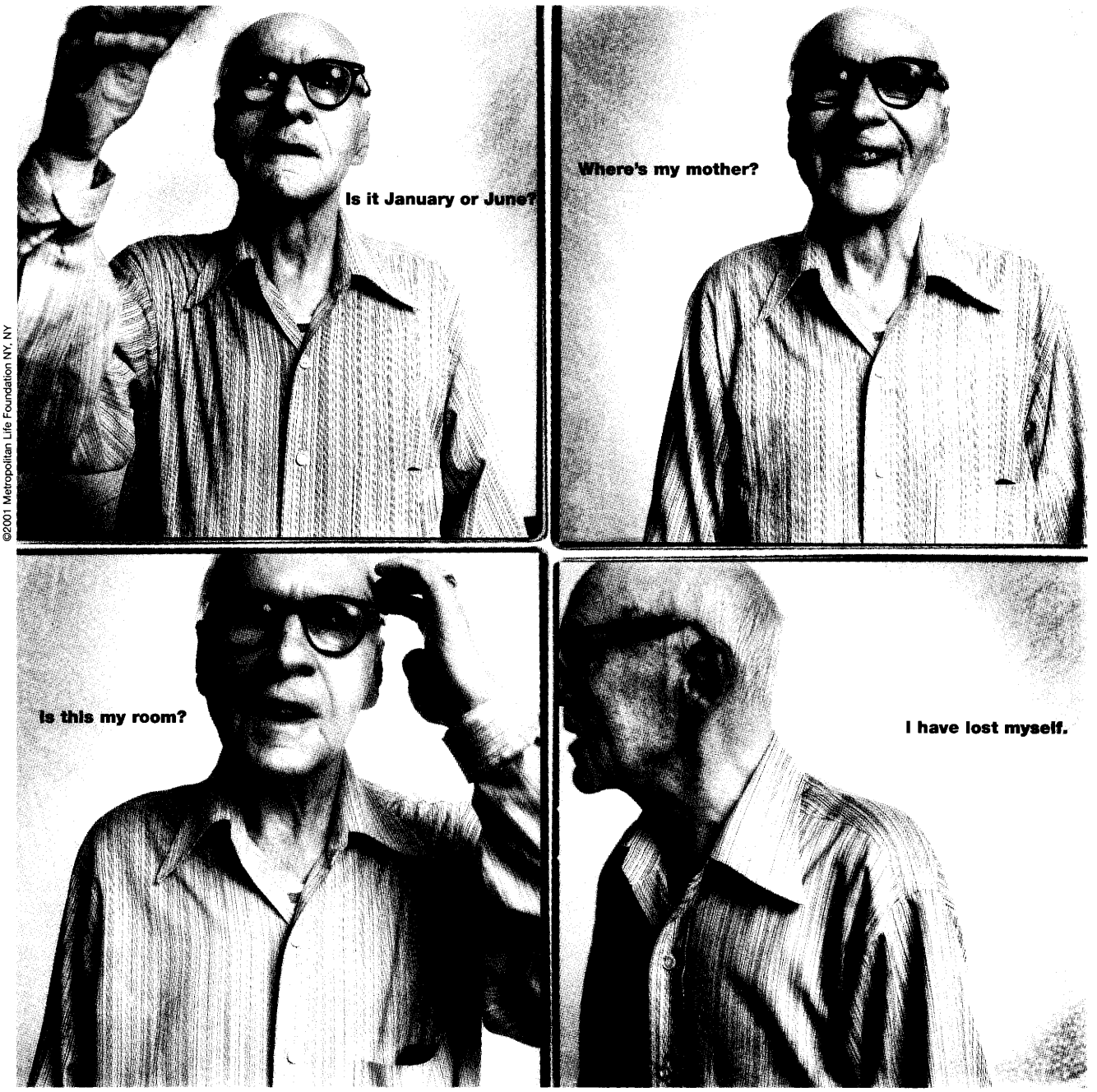

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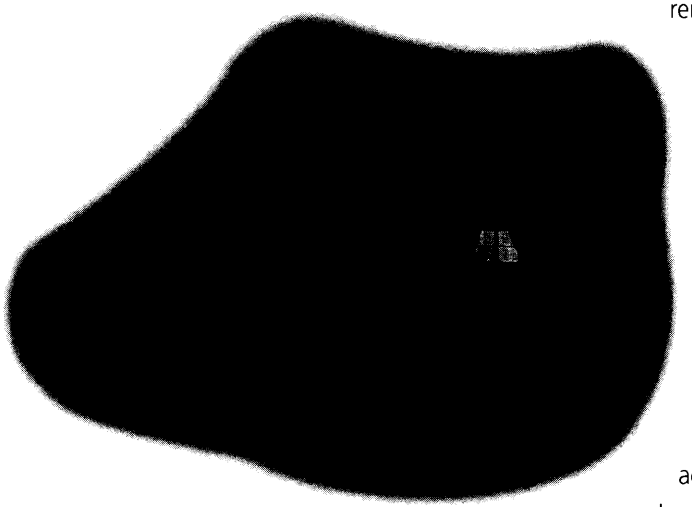

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