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Science

Vol. 292 No. 5515
Pages 157–384 $9

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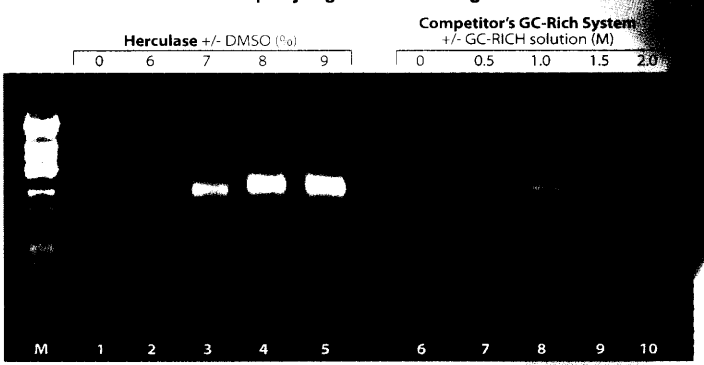

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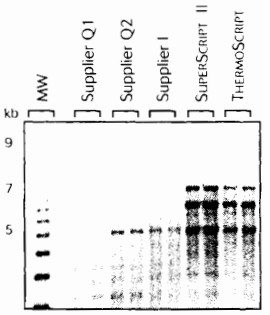

Comparison of yields of cDNA synthesis using various reverse transcriptases.

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Science

Volume 292 13 April 2001 Number 5515

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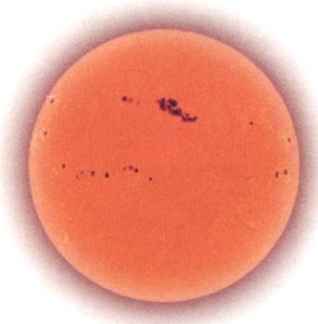

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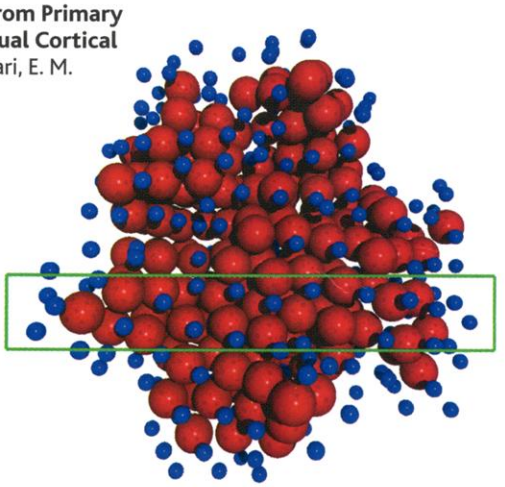
REPORTS

COVER 249

Barn owls can pinpoint prey by sound in the dark. The differences in arrival time and intensity of sound between the two ears of the owl indicate the target's position. Separate neural pathways process these two cues and converge on neurons that combine the time and intensity signals by multiplication. [Photo: Ben Arthur]



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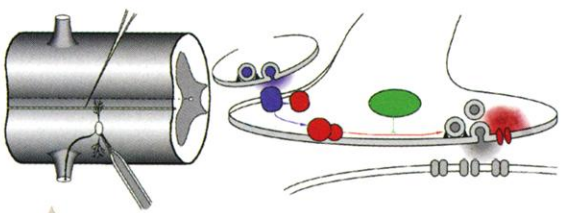
Watching crystals nucleate and grow



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G proteins control neurotransmitter release

Combinatorial genetic regulation of wing development **163**

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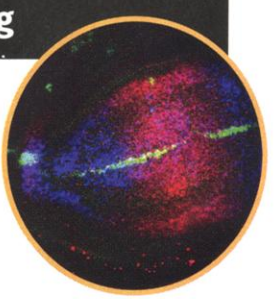

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SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices.

Domestic individual membership and subscription (51 issues): $115 ($64 allocated to subscription). Domestic institutional subscription (51 issues): $370; Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $87. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Publications Mail Agreement Number 1069624. **Printed in the U.S.A.**

Change of address: allow 4 weeks, giving old and new addresses and 8-digit account number. **Postmaster:** Send change of address to *Science*, P.O. Box 1811, Danbury, CT 06813–1811. **Single copy sales:** $9.00 per issue prepaid includes surface postage; bulk rates on request.

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MgB_2 Superconducting Thin Films with a Transition Temperature of 39 Kelvin W. N. Kang, H.-J. Kim, E.-M. Choi, C. U. Jung, S.-I. Lee

High-quality thin films of the superconductor magnesium diboride, prepared with a pulsed laser deposition technique, exhibit a sharp transition at 39 K.

Spermiogenesis Deficiency in Mice Lacking the *Trf2* Gene D. Zhang, T.-L. Penttila, P. L. Morris, M. Teichmann, R. G. Roeder

In contrast to the embryonic lethal phenotype observed in the worm and frog, eliminating TRF2 protein (a TBP-related factor) in the mouse results in male sterility.

Control of a Genetic Regulatory Network by a Selector Gene K. A. Guss, C. E. Nelson, A. Hudson, M. E. Kraus, S. B. Carroll

As shown for the *Drosophila* wing, specific responses to signaling pathways in a developmental field require the combined DNA-binding activities of selector proteins and signaling proteins.

The Foot-and-Mouth Epidemic in Great Britain: Pattern of Spread and Impact of Interventions N. Ferguson, C. Donnelly, R. Anderson

An epidemiological model confirms that ring-culling of livestock adjacent to infected farms is the most effective treatment for the U.K. foot-and-mouth epidemic.

TECHNICAL COMMENTS

Object Processing in the Infant Brain

Csibra *et al.* (Reports, 24 Nov. 2000, p. 1582) found that 8-month-old infants showed electroencephalogram responses in the gamma band (40 Hz) when presented with Kanizsa figures, illusory-square diagrams known to be perceived by infants of that age, but that 6-month-olds, who do not perceive the squares, did not show such gamma-band activity (GBA). The study thus underscored the link between GBA and the process by which "the brain 'binds' together separately coded stimulus features to form unitary representations of objects." Comments by Müller and by Herrmann and Friederici point out significant differences between the Csibra *et al.* infant study and studies in adults—particularly with respect to the location of the GBA increase in the brain and the detailed patterns of event-related potential (ERP) data presented by Csibra *et al.*—and question the proposed relation between the ERPs and perceptual binding. Csibra and Johnson respond that "in light of . . . variable findings in adults, we need to keep an open mind when interpreting the data from infants."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/292/5515/163a

SPECIAL FEATURES

Quarterly Author Index www.sciencemag.org

science's stke www.stke.org

Connections Maps: Wnt/beta-Catenin Pathways Pathway Authorities: R. T. Moon (canonical, *Xenopus*); M. Boutros and N. Perrimon (*Drosophila*); B. Bowerman (*C. elegans*)

Recently updated Wnt signaling cascades include the canonical pathway and the specific Wnt pathways in three model organisms.

science's next wave www.nextwave.org

UK: A Friendly Network J. Parkinson

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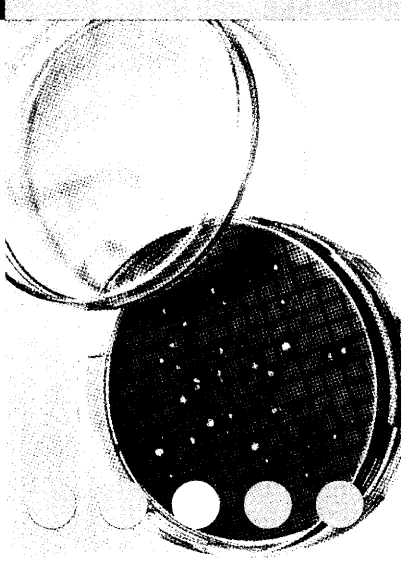

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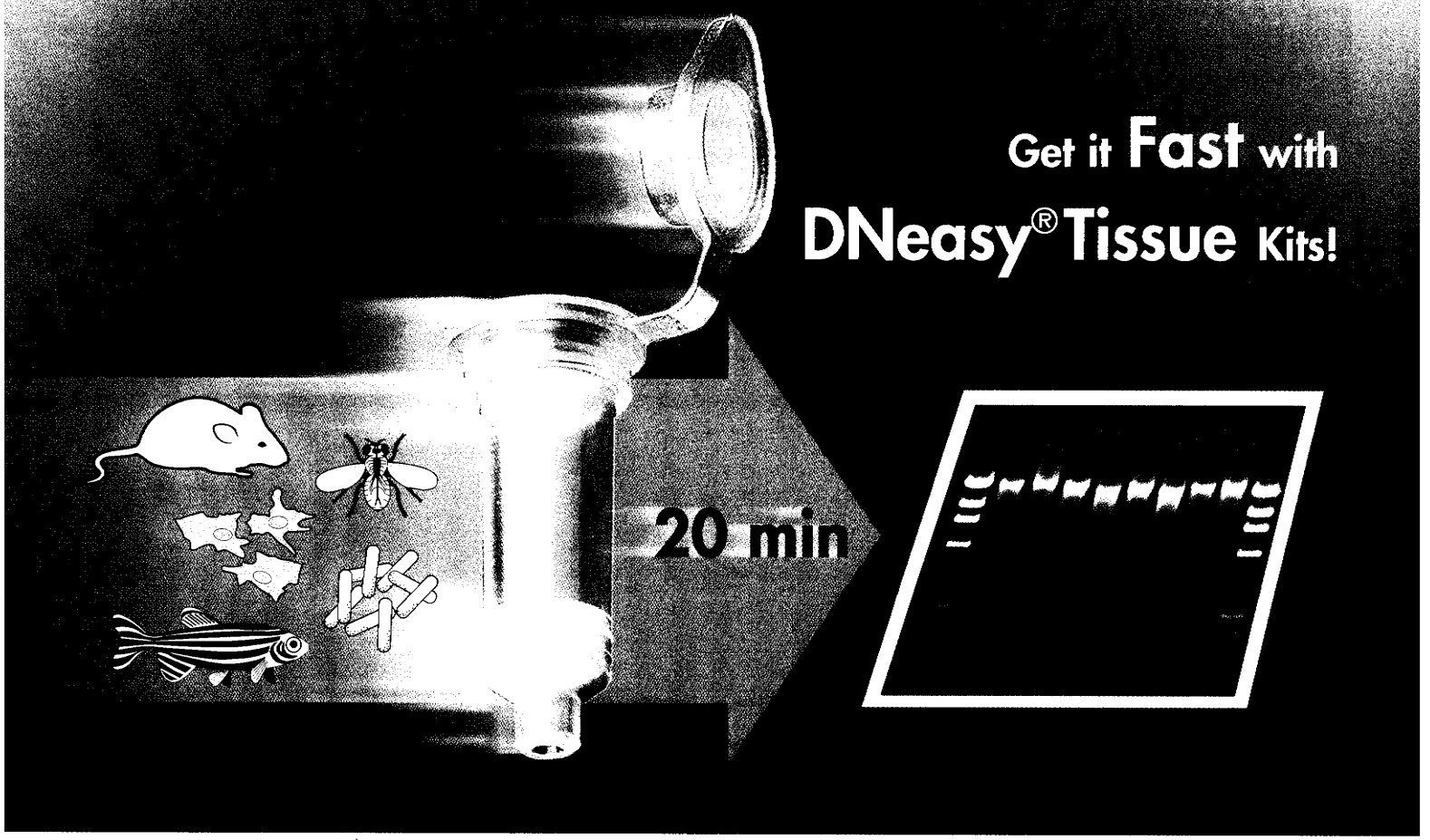

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THIS WEEK IN Science

edited by Phil Szuromi

Tuning Josephson Junctions

In a Josephson junction, superconducting Cooper pairs of electrons cross a narrow insulating region barrier between two superconductors even at zero bias. Josephson junctions are one of the keystone structures for new superconducting devices, but one limitation has been that the properties of the junctions are more or less fixed once they have been fabricated. Schön *et al.* (p. 252; see the Perspective by Wendin and Shumeiko) now describe the fabrication of tunable Josephson junctions in organic materials in which the superconductivity can be induced by the application of an electric field.

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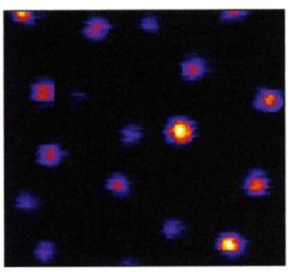
Single-Molecule Moves in Melts

A critical issue in understanding the dynamics of glassy states is the origin of nonexponential relaxation of molecular motion. Such nonexponential kinetics could be inherent or could arise from a population of molecules that relax with exponential kinetics along a distribution of time scales. Deschenes and Vanden Bout (p. 255; see the Perspective by Ediger and Skinner) examined the rotational orientation of individual dye molecules in polymer films just above their glass transition temperature. They find that heterogeneous dynamics result from dye molecules diffusing first on one time scale and then abruptly switching their relaxation time scale in response to changes in the glassy medium.



CREDIT: L.A. DESCHENES AND D.A. VANDEN BOUT

The Ice Sheets Cometh

The recent dramatic changes in Earth's climate, marked by the growth and retreat of large ice sheets about every 100,000 years, are thought to have been driven by small changes in Earth's orbit through a yet-unknown amplification mechanism. Such orbital variations have occurred throughout Earth's history—not just during recent glacial times—but clear climatic effects have been difficult to resolve. Zachos *et al.* (p. 274; see the news story by Kerr) now present a detailed deep-sea record of climate change from about 23 million years ago that seems to show such an effect. A major glaciation corresponds with a time when cycles in the obliquity and eccentricity of Earth's axis were synchronized, and the record over several million years shows an orbital pacing. This congruence may have had a longer lasting effect, as it is about the time that large and persistent ice sheets appeared in Antarctica.

Egging-on Crystallization

Crystal nuclei will spontaneously form in a liquid when molecular fluctuations cause a local set of atoms to associate temporarily. The stability of the nuclei is highly temperature dependent because the surface energy, which drives shrinkage of the nuclei, competes with the bulk energy, which drives their growth. The size and length scale associated with the initial stages of crystallization prevents direct observation in most materials. Gasser *et al.* (p. 258) used confocal microscopy in a colloidal system to observe the size, shape, and dynamics of nuclei. The nuclei that formed were ellipsoidal, as opposed to the spherical shape assumed by most theories, and the lattice packing of the grown crystal matched that of the nuclei.

Twin Peeks at Ocean Warming

Although global warming is often framed in terms of atmospheric temperature, the atmosphere contains only a small fraction of the heat supplied by the sun. From an energetic point of view, the oceans are far more important, and it has been shown recently that the heat content of the upper 3000 meters of the ocean has increased during the past 50 years. Two studies show that this observation agrees quite well with what we should expect for an Earth warmed by greenhouse gas emissions (see the news story by Kerr). Using different climate models, Levitus *et al.* (p. 267) and Barnett *et al.* (p. 270) show that changes in the distribution of heat in the world ocean are accurately reproduced when forcing by anthropogenic greenhouse gases and sulfate aerosols are incorporated. The agreement between these different models, which have both successfully simulated observed changes in the climate system that have not been reproduced previously, lends greater confidence to these approaches.

Be Subthreshold and Multiply

The auditory system of the barn owl has provided numerous valuable models for neurobiology. Peña and Konishi (p. 249; see the cover and the news story by Helmuth) used intracellular recording from many identified space-specific neurons in the inferior colliculus of the barn owl to determine what computational processes could account for the emergence of space specificity. They compared multiplication and addition in the space-specific cells and present clear evidence in favor of multiplication of subthreshold inputs. The need for multiplicative combination was predicted by previous modeling studies but not shown conclusively. The results in this study will allow the mechanisms in those models to be tested experimentally.

Chip Off the Old Clock

The main circadian clock in mammals is located in the brain, but the cells of many peripheral tissues also contain clocks. Yagita *et al.* (p. 278) report that the molecular components that make up these peripheral clocks, at least those in fibroblasts, are the same as those that form the brain's master clock in the mouse. Transcriptional and translation feedback loops consisting of *Per2*, *Bmal1*, *Clock*, and *Cry1* and their respective proteins interact to produce a circadian 24-hour rhythm in cultured fibroblasts. The oscillations and period length are dependent on the presence of *Cry1*, as in the brain. Thus, the causes of the distinctive features of peripheral oscillators—a tendency to damp and insensitivity to light—must be sought elsewhere.

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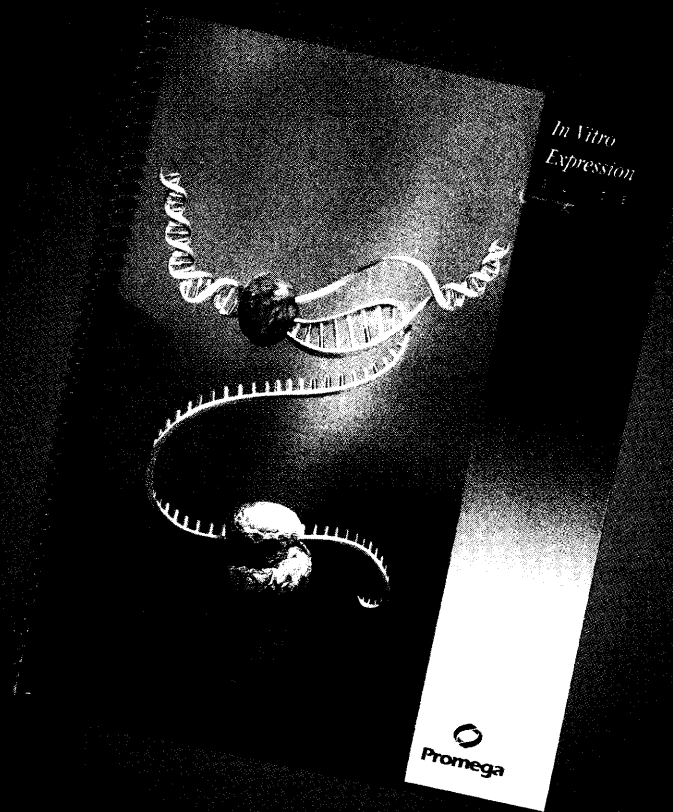
Hidden Identities. Secret Relationships. Drug Use.



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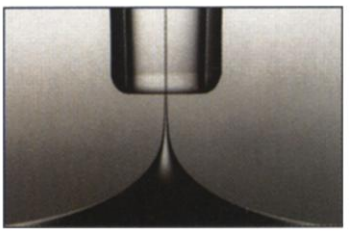

The coating or encapsulation of microparticles is a critical step in developing drug delivery vehicles and in protecting cells, tissues, or catalysts. Current methods tend to produce particles of the same final diameter, so that particles of different diameter have a non-uniform coat thickness or produce uniform coats but are restricted in the choice of polymers and their further processing. Cohen *et al.* (p. 265) can coat particles uniformly by selectively withdrawing them from a water-oil interface, and they can cure the coatings via light, heat, or chemical reaction.

Molecular Trigger of Infectivity

The protozoan parasite *Leishmania* causes severe and disfiguring diseases and is transmitted between humans and companion or wild animals by insect (sand fly) vectors. The factors that regulate the parasite's exit and entry between the various life cycle stages in the different hosts have been difficult to pinpoint. Cunningham *et al.* (p. 285) show that tetrahydrobiopterin (H_4B), through control of pteridine metabolism, restrains the differentiation of noninfective procyclic forms of the parasites within the sand fly into highly infective metacyclic forms. Mutant *Leishmania* that lack the key enzyme pteridine reductase 1 had low levels of H_4B and were hypervirulent in mice.

Insulin-Like Pathways and Aging

In the nematode *Caenorhabditis elegans*, mutations in the *daf* pathway, which normally regulates an inactive hibernation-like life phase, can prolong life-span dramatically. The *daf* pathway is homologous to the insulin pathway of higher organisms, and the ability of caloric restriction to increase the life-span of rodents suggests further links. Fabrizio *et al.* (p. 288; see the news story by Strauss, 6 April) take this demonstration a step further by screening for mutants that control life-span in nonreplicating yeast. They identify Sch9, a kinase similar to the Akt/PKB kinase in the insulin signaling pathway of mammals, as well as the yeast homolog of adenylate cyclase. The insulin-like signaling pathway appears to be a prime regulator of life-span, likely through its control of whole-organism metabolism.

"What" and "Where" in What We Hear

Compared to other sensory modalities, our understanding of the organization of primate auditory cortex is still rather incomplete. Tian *et al.* (p. 290) analyzed neuronal responses in the lateral belt of the auditory cortex and found evidence for distinct processing pathways. Different areas of the lateral belt respond with different degrees of specificity for location and range of monkey calls. There may be different processing streams in the auditory cortex similar to the pathways described in the visual system.

G Proteins and Presynaptic Inhibition

Several neurotransmitters modulate synaptic release from presynaptic terminals by activating G protein–coupled receptors. Blackmer *et al.* (p. 293) investigated the basic mechanisms underlying this modulation of the exocytotic machinery in neurons. Microinjection of G-protein βγ-subunits (Gβγ) into lamprey reticulospinal axons inhibited synaptic transmission without decreasing the action potential–dependent influx of Ca^{2+}. This result suggests a potentially new effector role for Gβγ through directly modulating the vesicle fusion machinery in the synaptic terminal.

Functional Segregation of Visual Processing Streams

Whether separate functional streams connect the magno- and parvocellular retino-geniculocortical pathways to different cortical systems, particularly the dorsal and ventral cortical stream of the visual processing system, is still not resolved. Yabuta *et al.* (p. 297; see the Perspective by Levitt) combined laser scanning photostimulation and whole-cell voltage clamp recordings in slices of macaque visual cortex to identify neurons providing excitatory input to layer 4B of area V1. Layer 4B pyramidal neurons receive inputs from both 4Cα and 4Cβ, whereas spiny stellate cells receive input from 4Cα but not 4Cβ.

CREDIT: I. COHEN *ET AL.*

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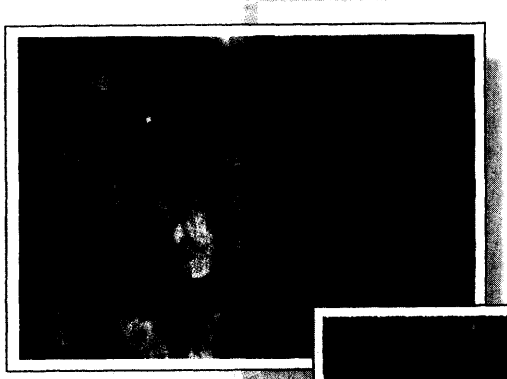

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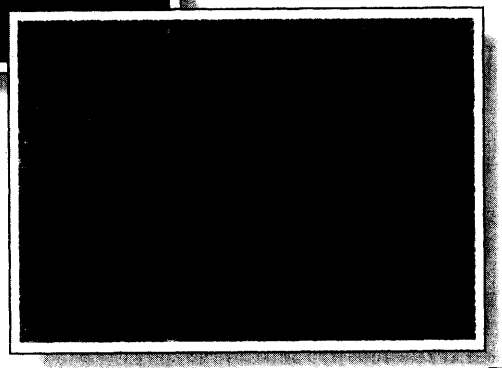

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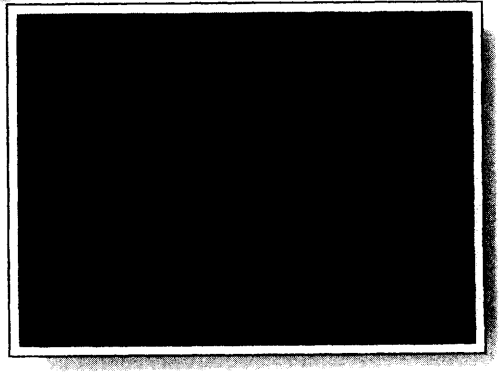

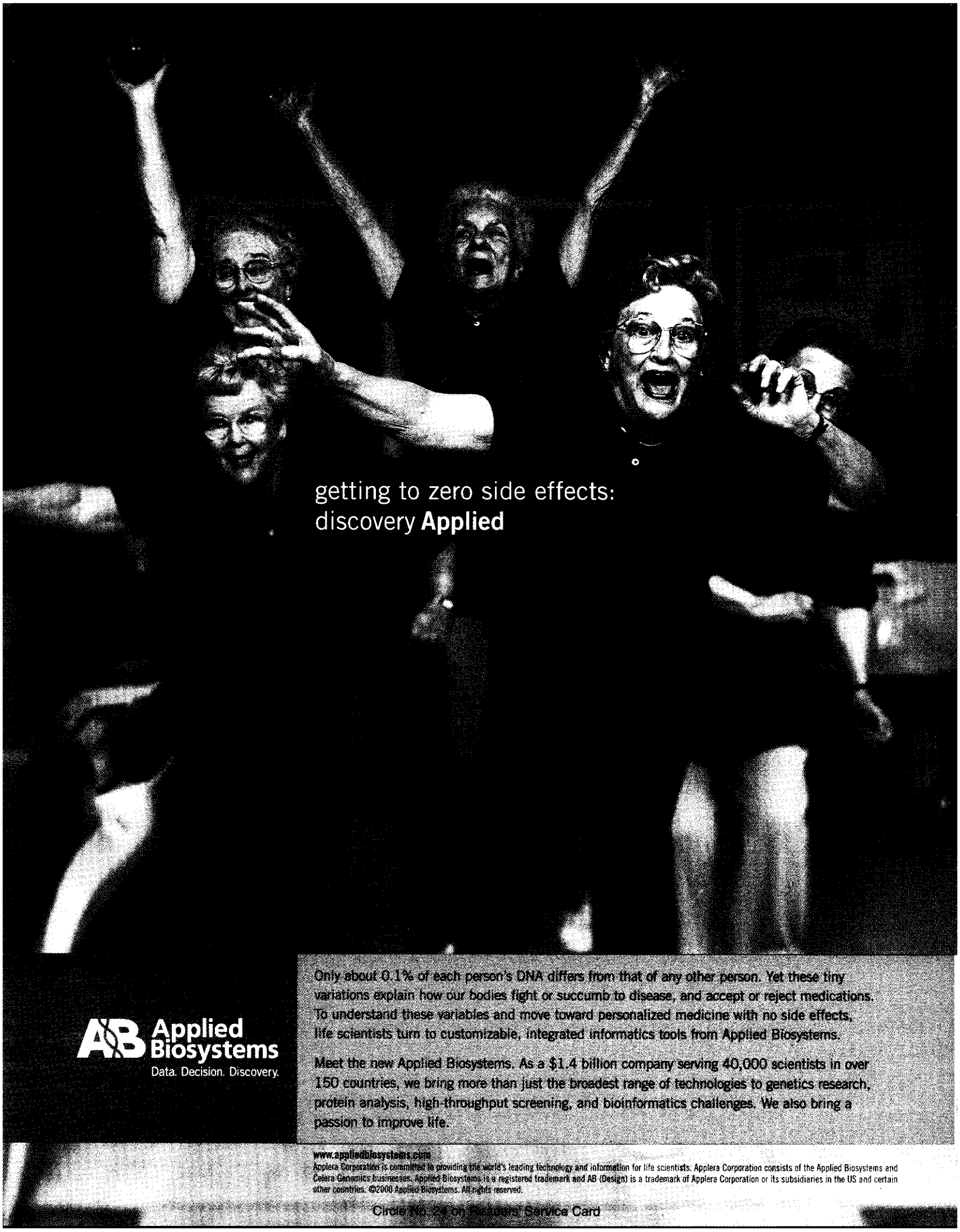

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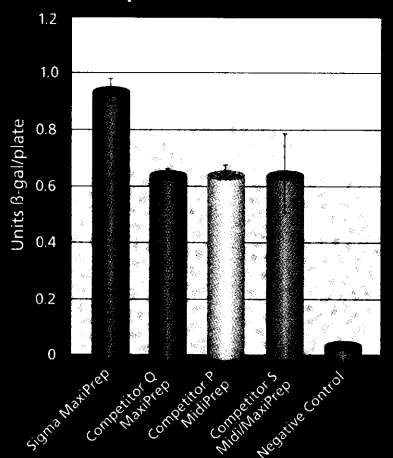
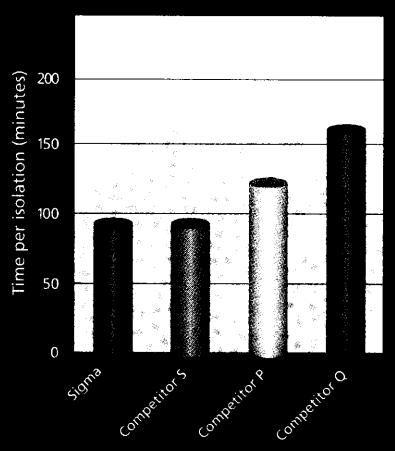


The data shows the average of six replicates for each named isolation method. All transfections were in CHO-K1 cells. The OD measurements were taken at 420 nm and the units of ß-gal/plate were found using the Sigma ß-Galactosidase Reporter Gene Activity Detection Kit. The cells were grown to ~60-75%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

Time Required Per Isolation



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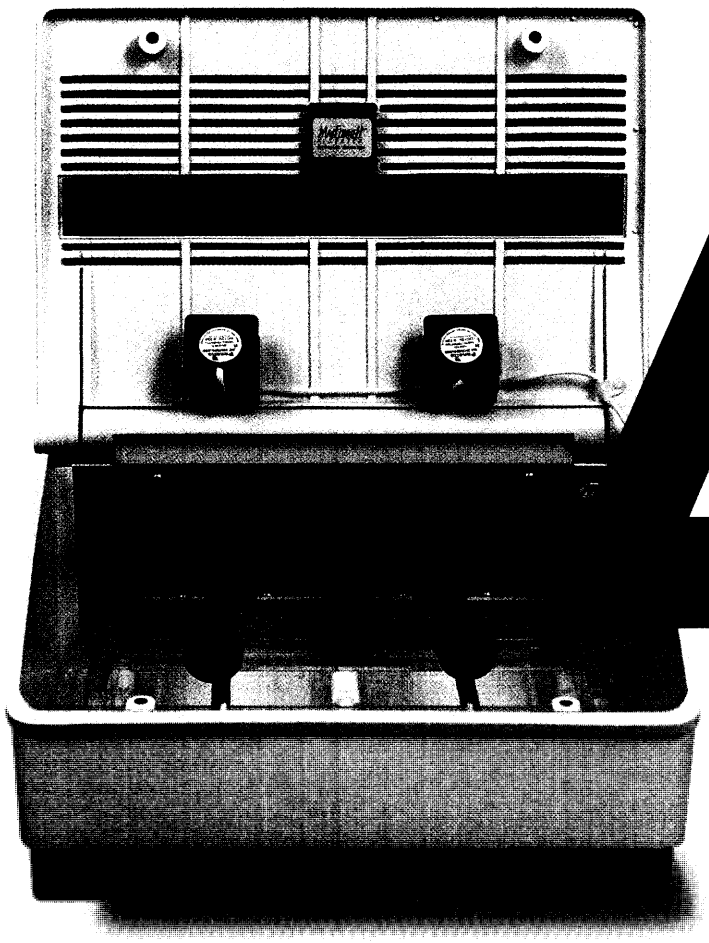

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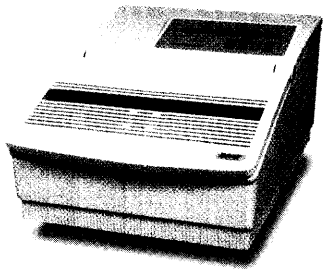

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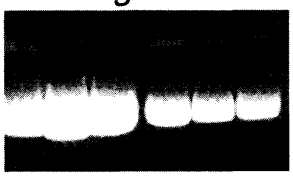

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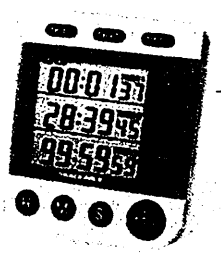

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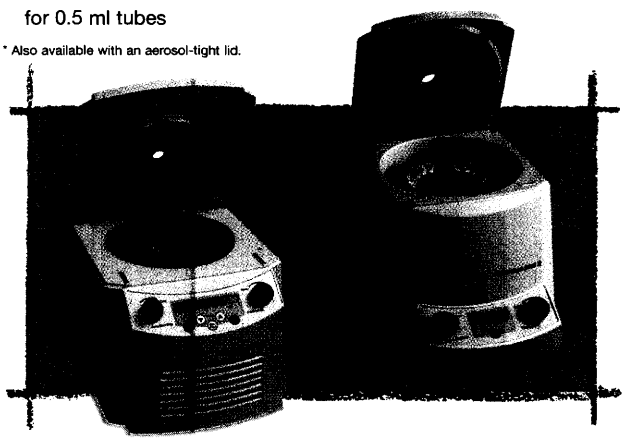

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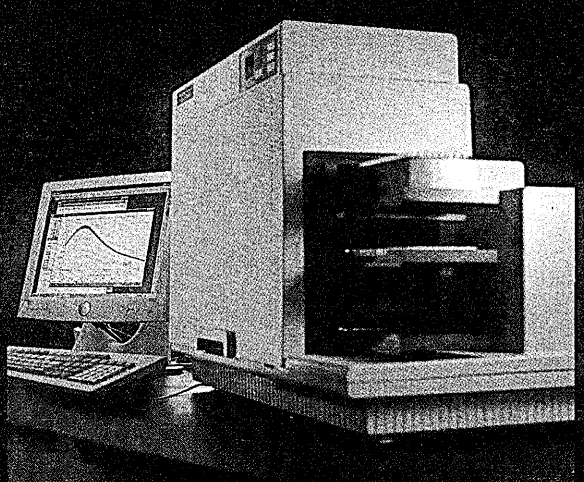

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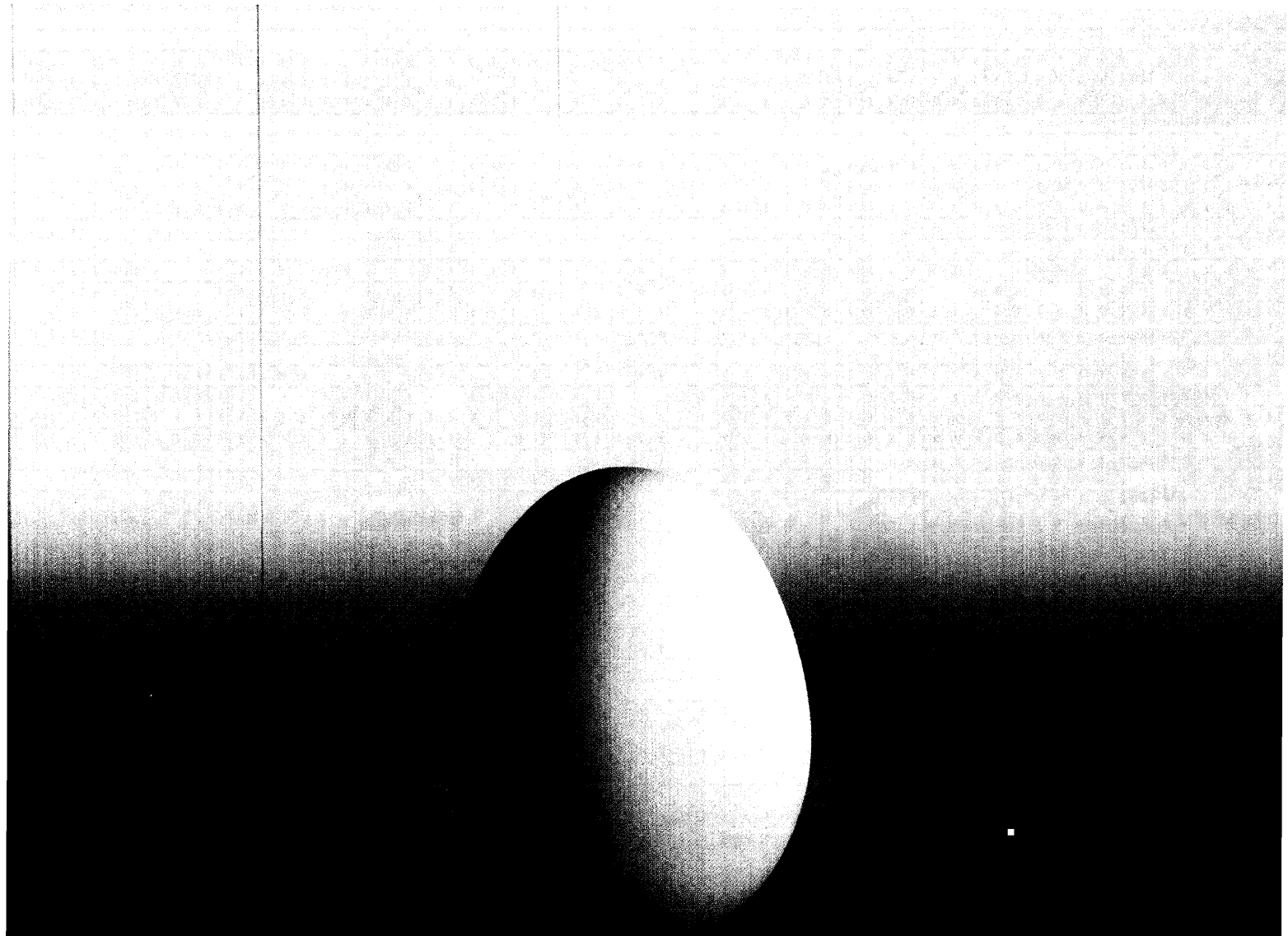

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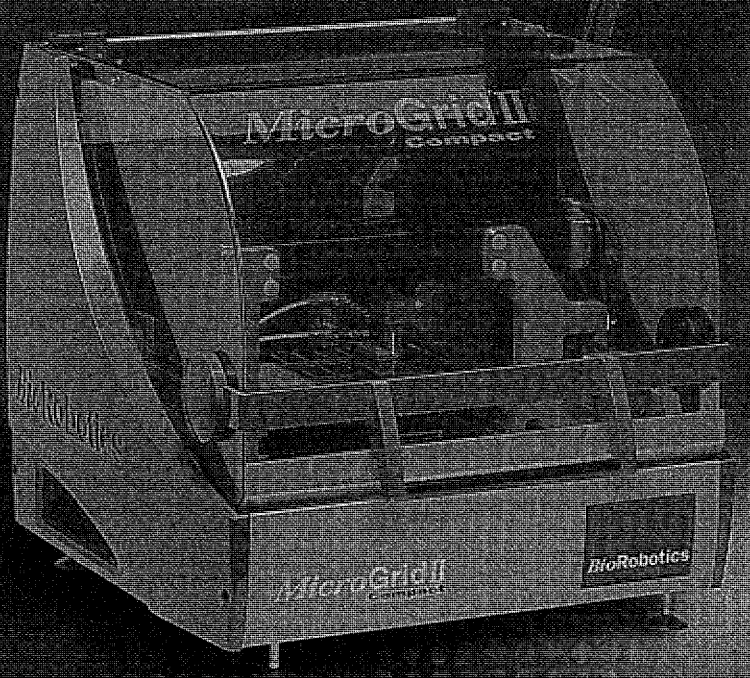

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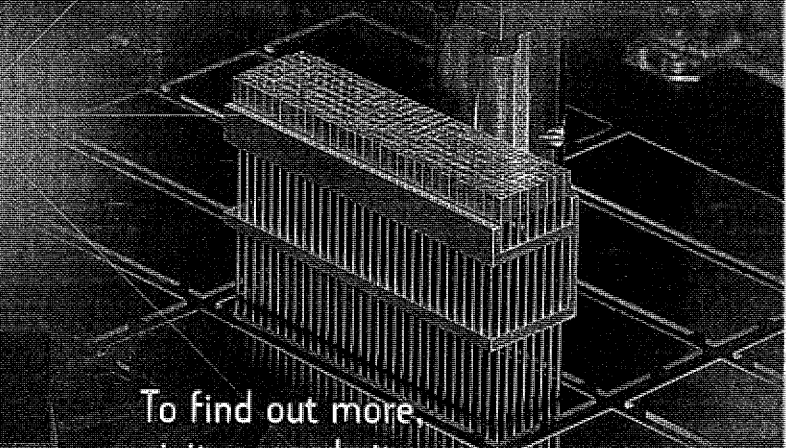

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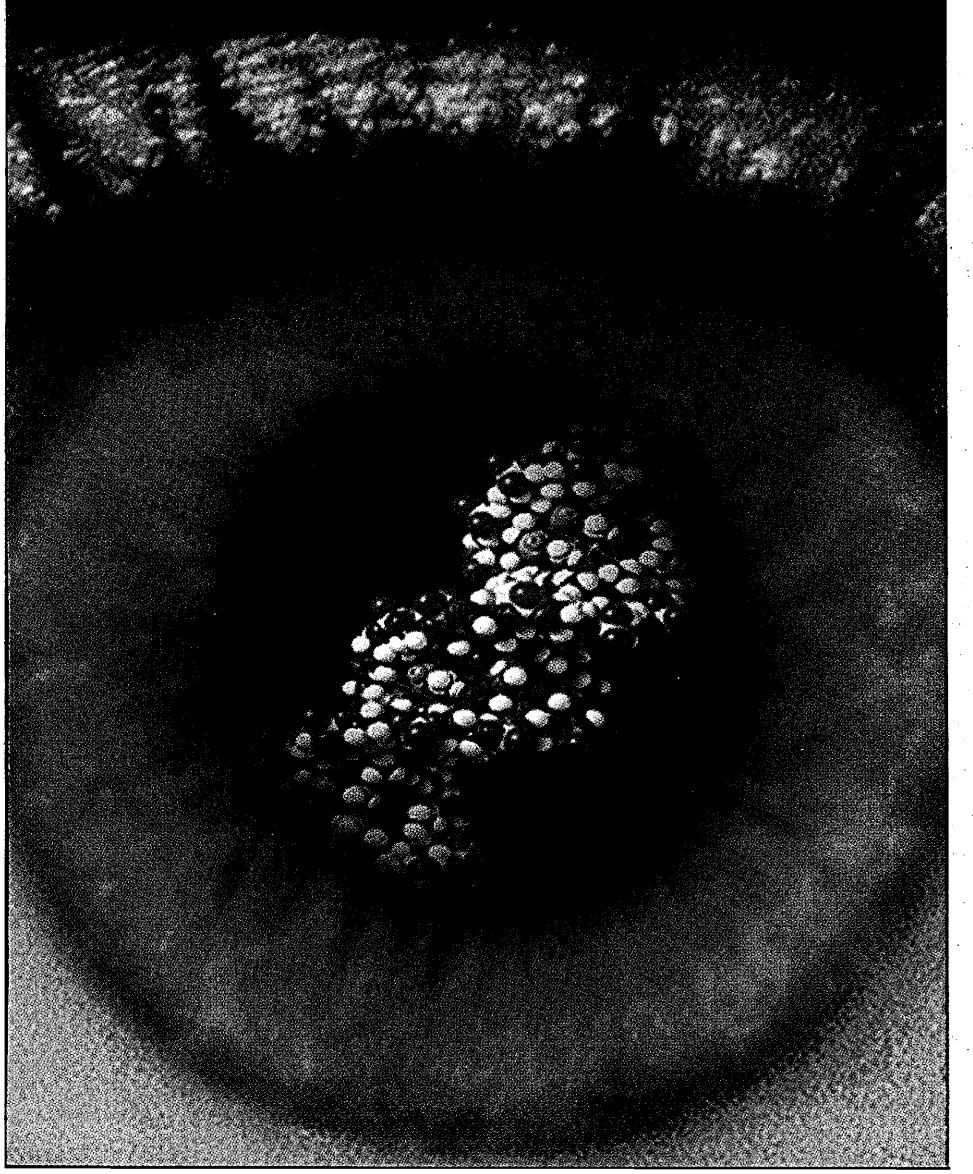

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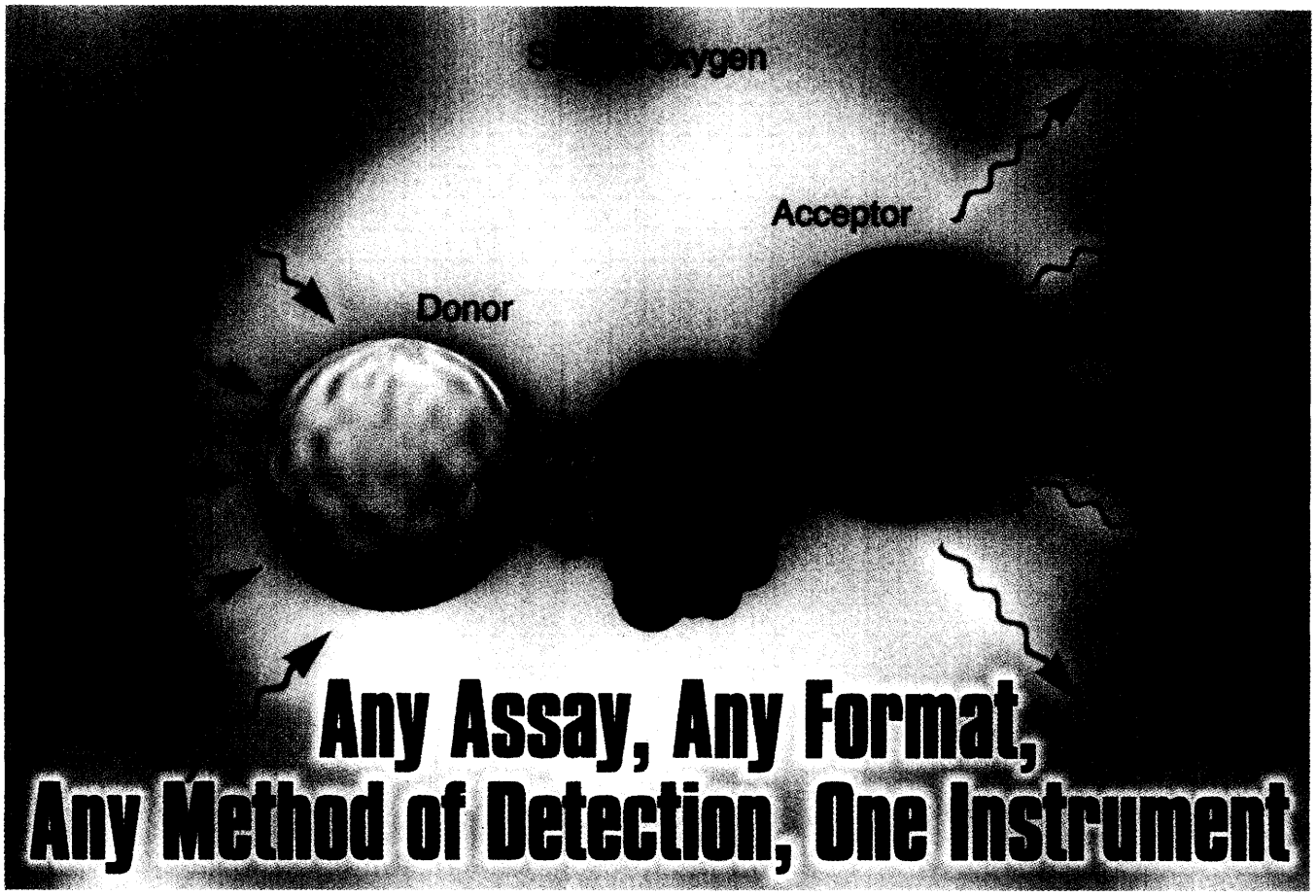

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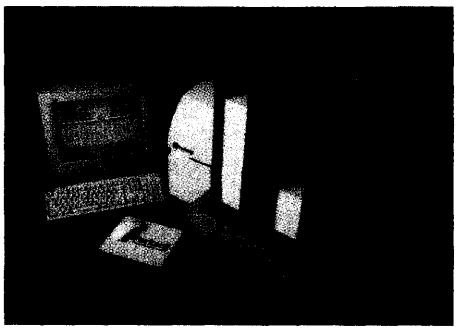

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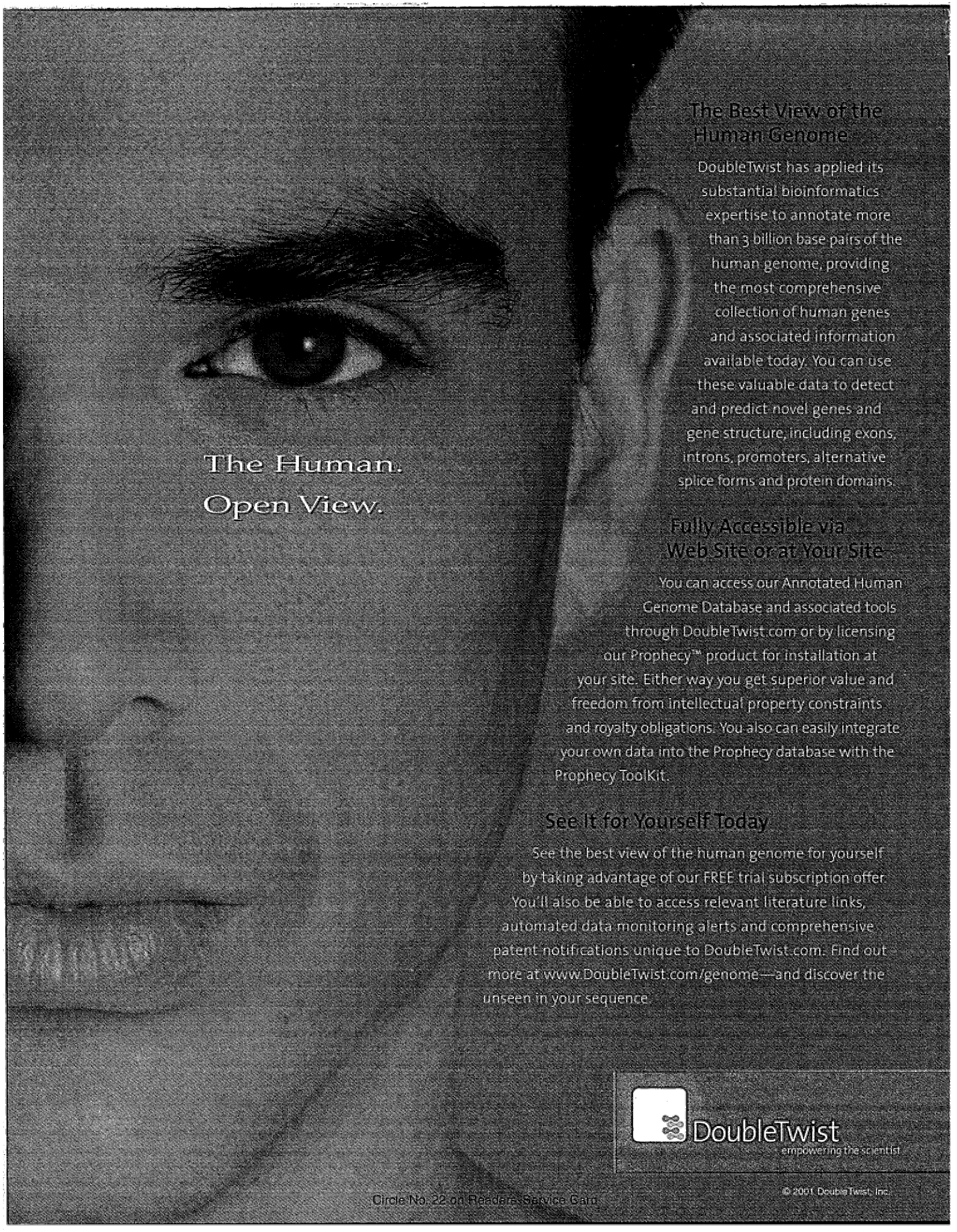

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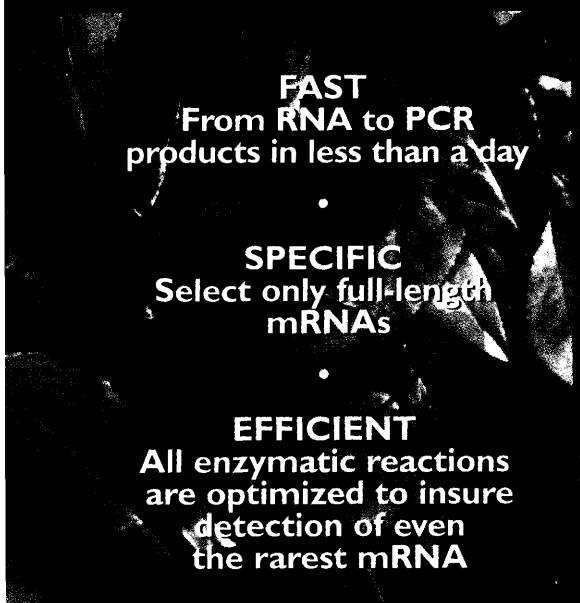

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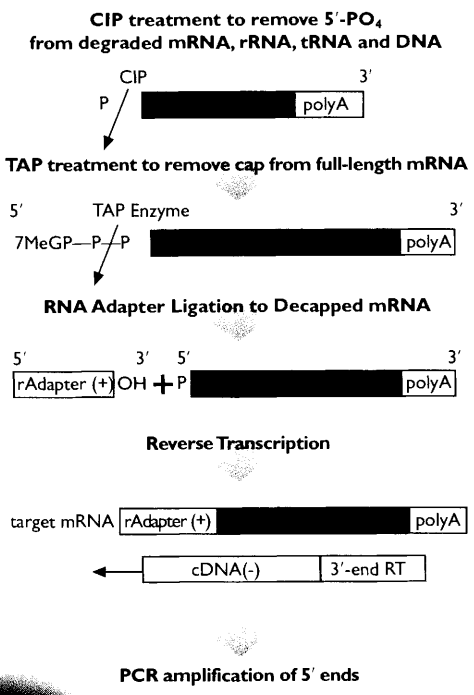

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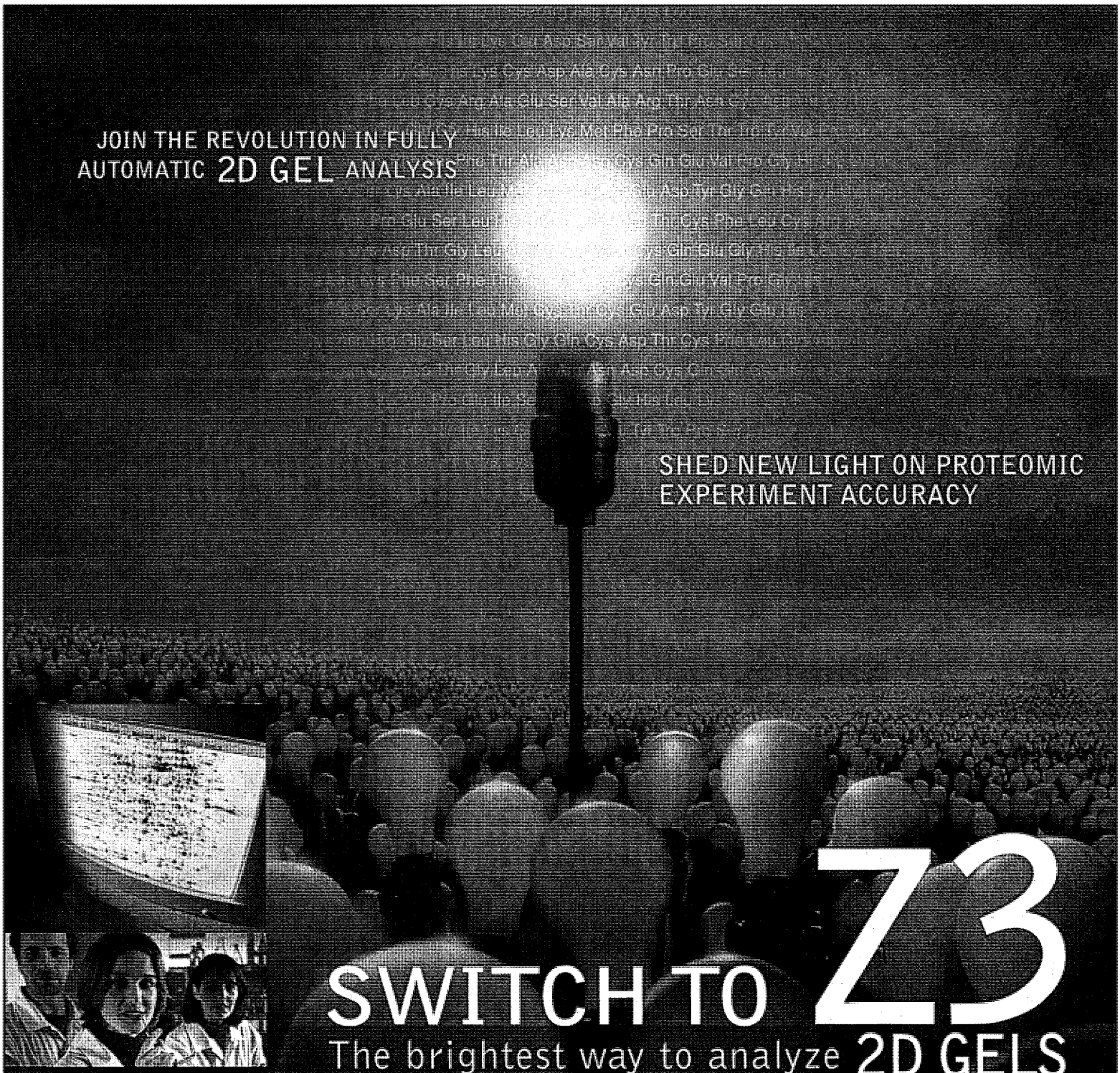

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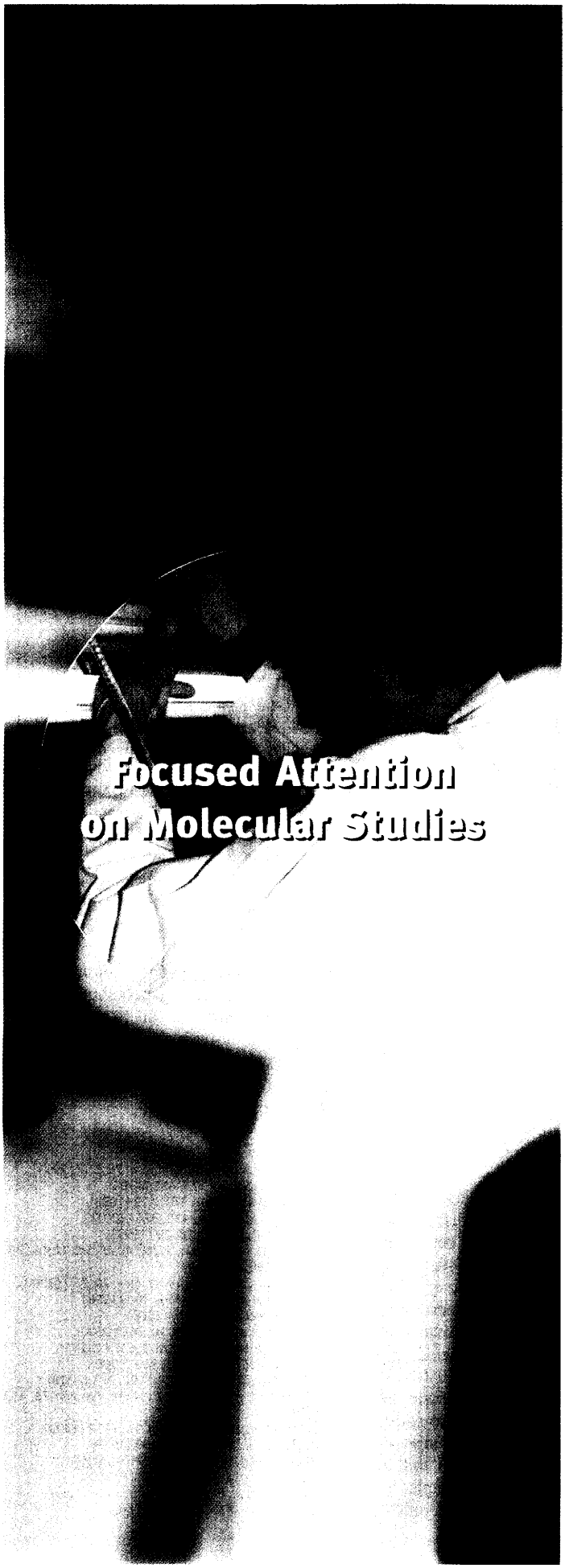

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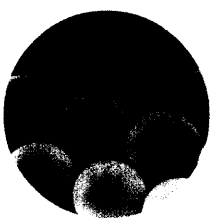

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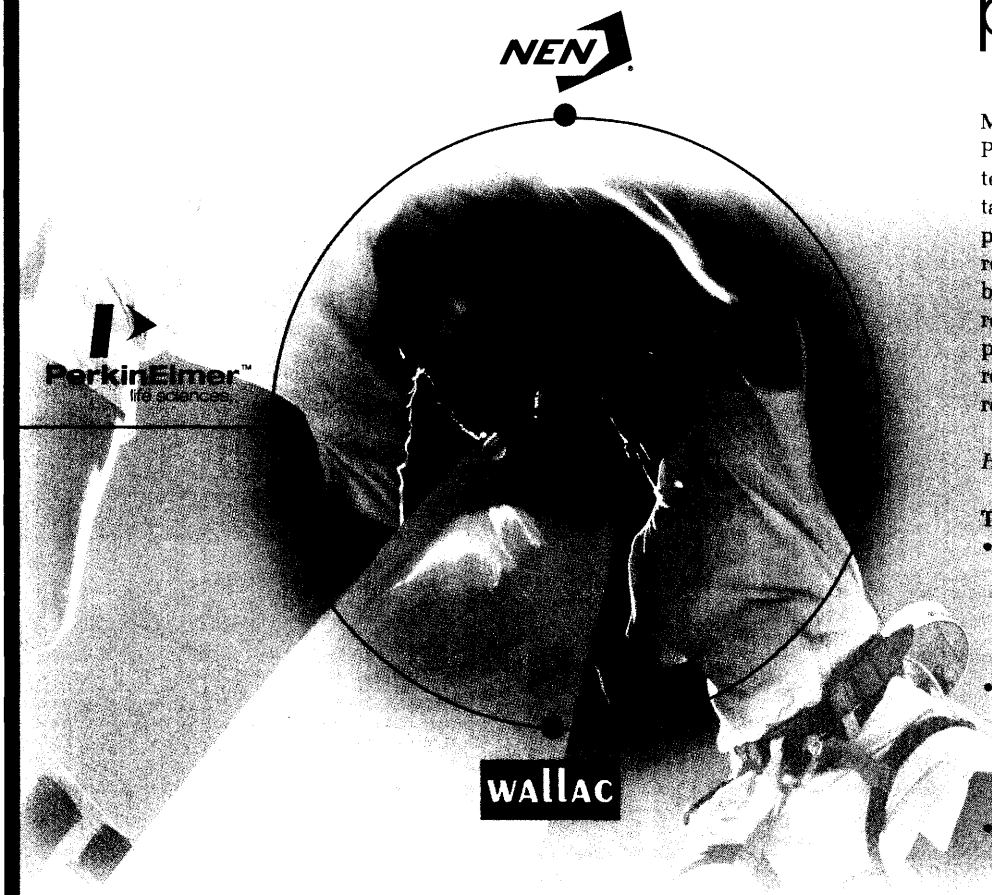

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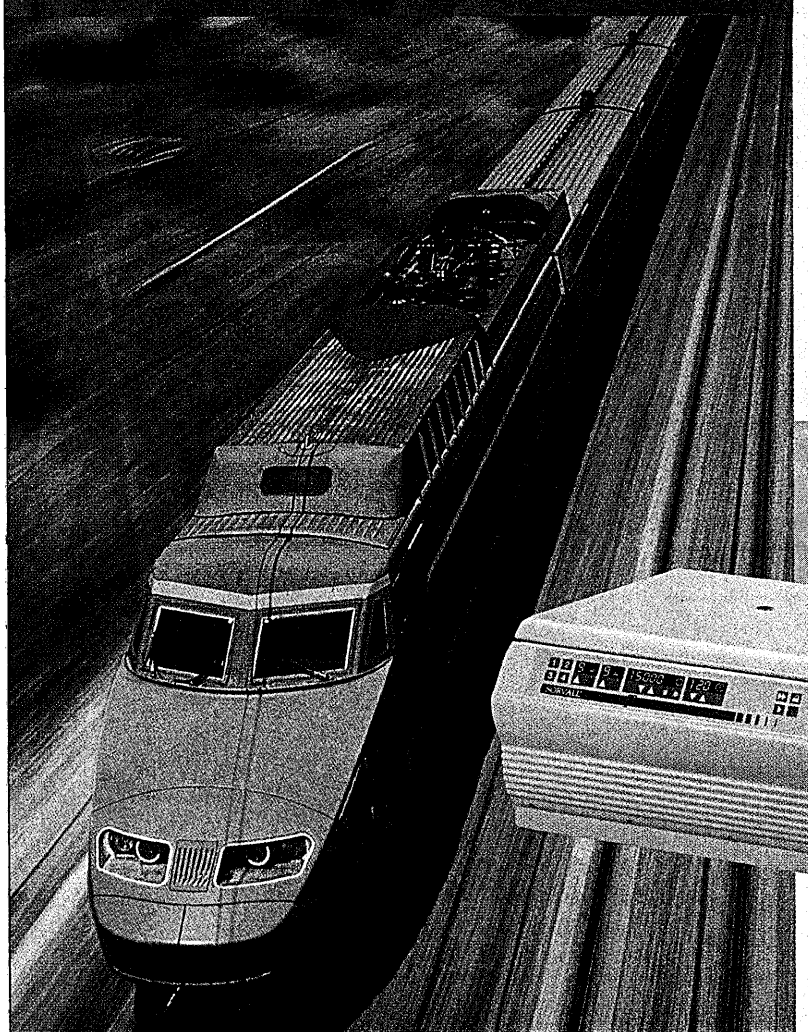

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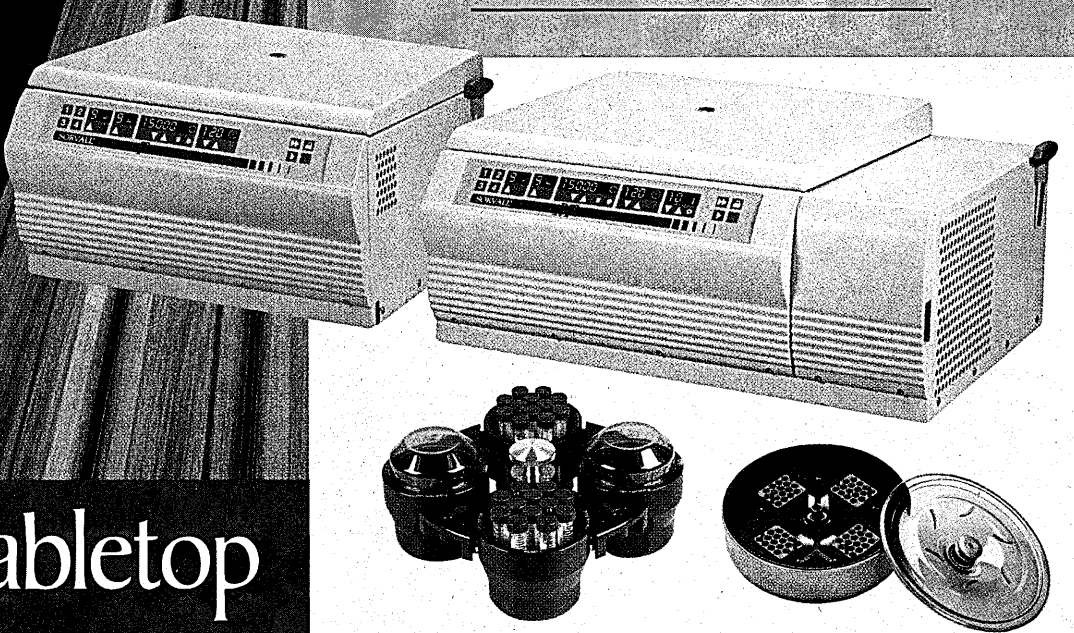

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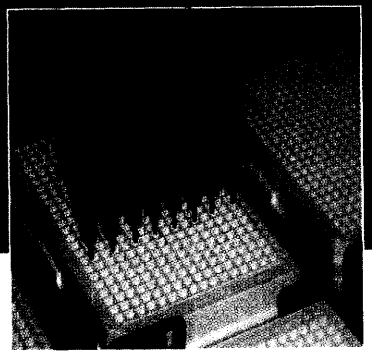

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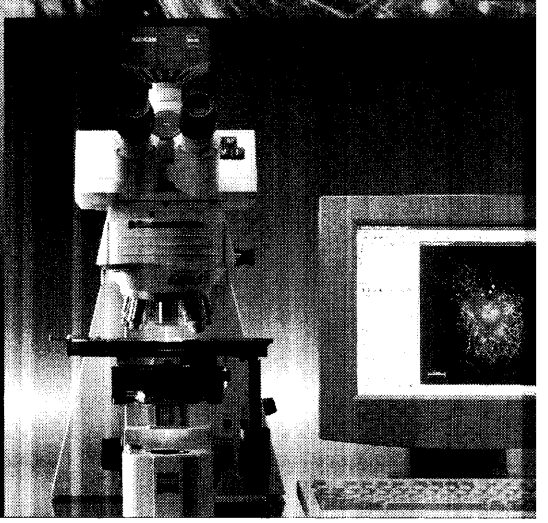

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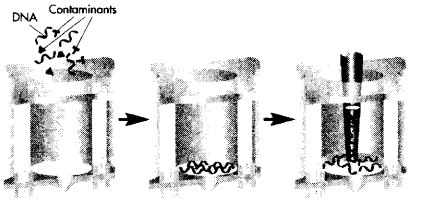

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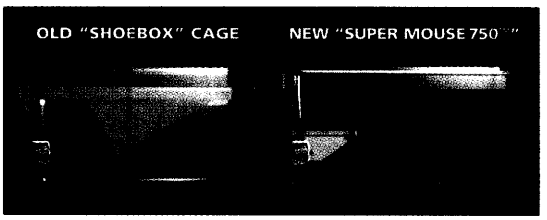
You asked for it and like our One Cage™ System, Super Mouse 750™ was designed to incorporate the same modular features into a cage exclusively for mice.



Our new Super Mouse 750™ cage is designed to do just that, while increasing the overall efficiency of housing laboratory mice. We've eliminated the wire bar lid... creating greater volume using the same space. The interior cage height is increased to over 5-3/4 inches. Combined with a floor area of over 75 square inches, the new inner space allows you to house 5 adult mice weighing over 25 grams each, exceeding the ILAR Guide*.

When removing the Micro-Isolator SP™ Filter Top, you have immediate access to your animals, saving your valuable time during animal manipulations and cage changes. In addition, the clear plastic Modular Diet Delivery System allows enhanced visibility of food, water and animals. Designed with removable stainless steel food and water bottle attachments, the delivery system may be placed at either end of the cage. Our new water bottle and time-saving 1/2 twist One Cap,™ provide full usage of the 15 ounce water capacity.

The new Super Mouse 750™ cage represents such a brand new view of animal housing, we think you'll like what you see. The time and space savings clearly allow you to perform more work in less time.

SUPER MOUSE 750™

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*Guide for the Care and Use of Laboratory Animals. Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, National Academy Press, 1996.

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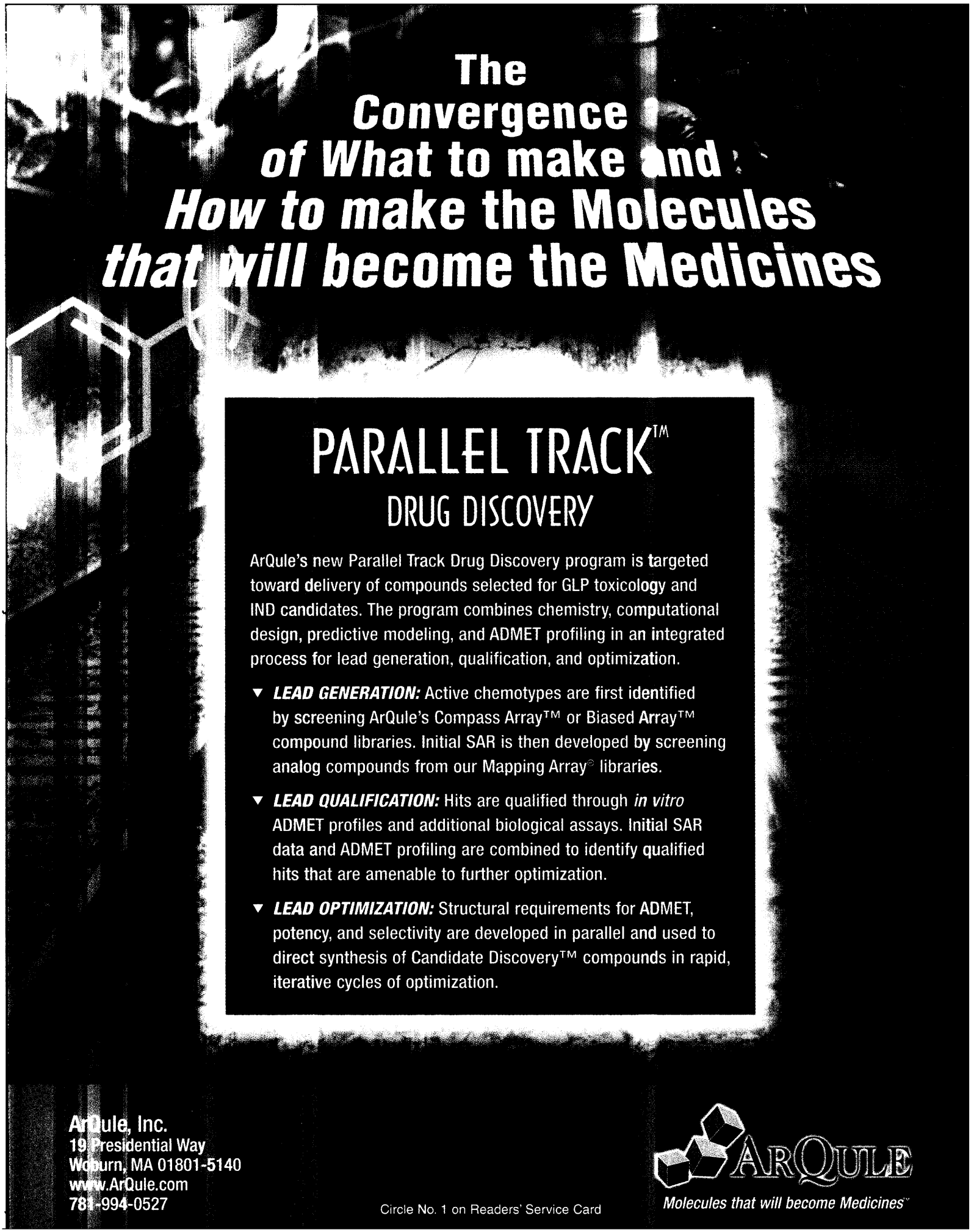
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PCR clean-up.

Why waste time with it when you can

Fig. 1. Fluorescent sequencing results of a 100 bp pUC18 PCR fragment sequenced with a -20 Fwd primer using the DYEnamic ET Terminator Cycle Sequencing Kit (Amersham Pharmacia Biotech). Data generated for USB by Cleveland Genomics (clevelandgenomics.com), a research service company. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up. Base miscalls in (b) are due to inherently low yields of short PCR products when using columns.

Fig. 2. Autoradiograms of a 20.7 kb Lambda PCR fragment sequenced with MBL202 Fwd primer using USB's Thermo Sequenase Radiolabeled Terminator Cycle Sequencing Kit. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up.

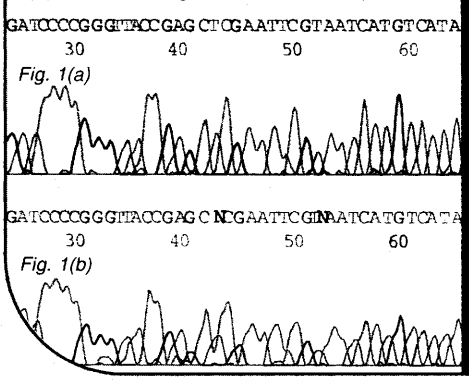

Fig. 1(a)

Fig. 1(b)

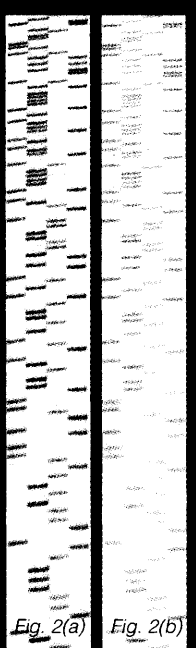

Fig. 2(a) *Fig. 2(b)*

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- Less hands-on time than other methods
- Scaleable to handle large volumes

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Need an easy way to clean-up PCR† products, especially before sequencing? Without using a column or beads? And, without losing product? USB has a solution. Just ExoSAP-IT™‡ using Exonuclease I to degrade primers, and Shrimp Alkaline Phosphatase to degrade the dNTPs - both enzymes in one tube. A single pipeting step is all it takes to treat the PCR template. Just add ExoSAP-IT to your PCR product and within 30 minutes, sequence with either fluorescent or radioactive reagents.

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† The Polymerase Chain Reaction (PCR) is covered by patents owned by Roche Molecular Systems and F. Hoffmann-La Roche Ltd. ‡Patent pending on product. The method of use is covered by the following patents: 5,756,285 and 5,741,676.

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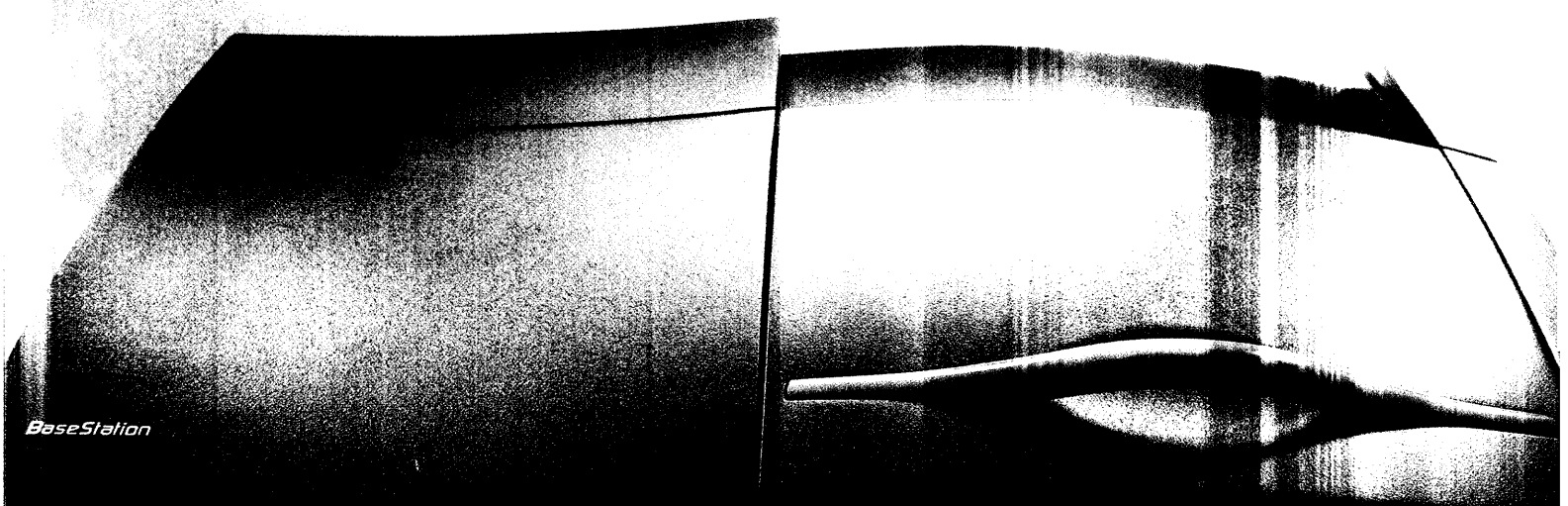

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