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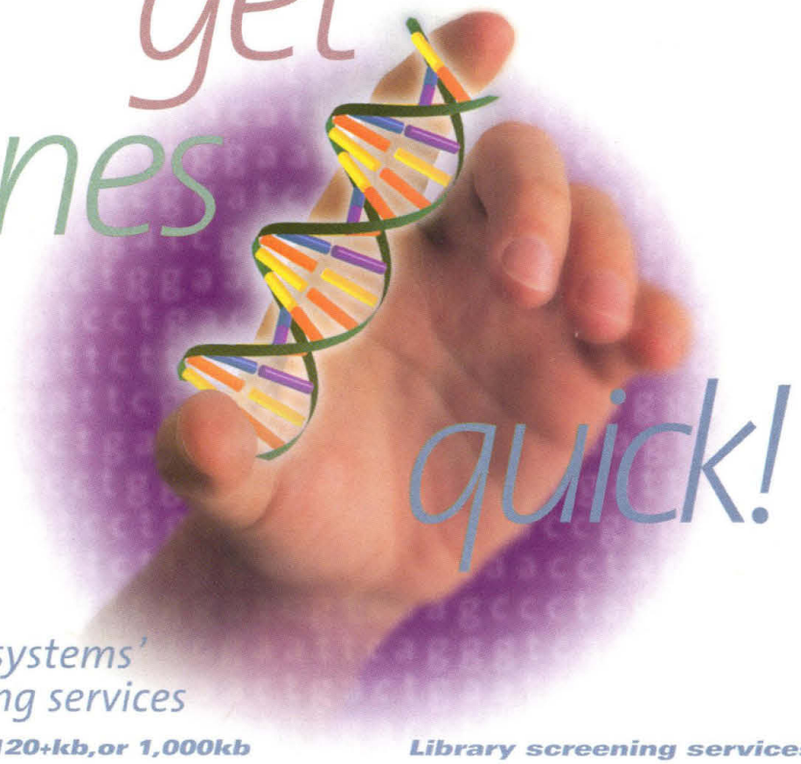

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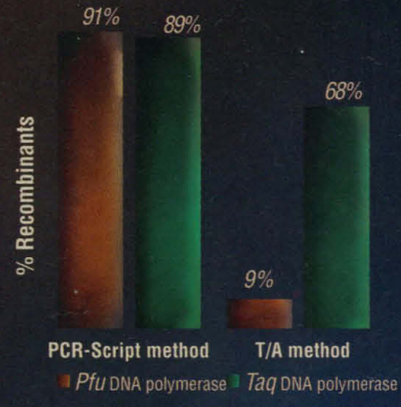

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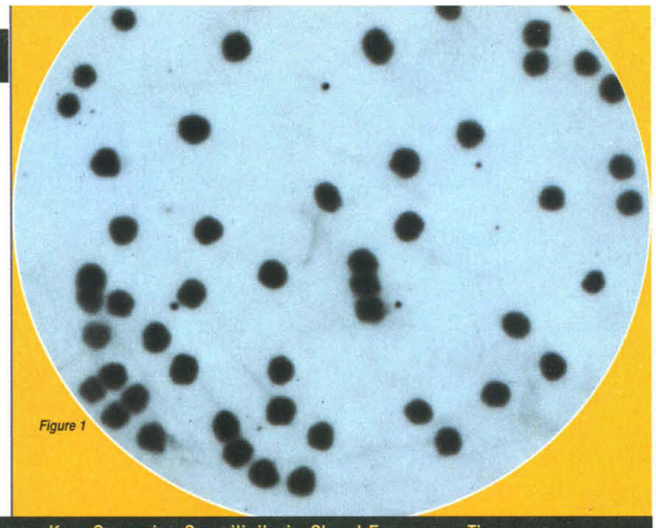

Figure 1

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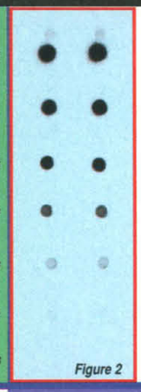

Figure 2

Figure 1. Colonies were screened for the TGF- ß1 gene with a fluorescein-labeled oligonucleotide probe and Enhanced Luminol. *This film demonstrates results obtained using the Renaissance 3'- End Labeling Fluorescein Kit with Antifluorescein-HRP (NEL823) and the detection substrate Enhanced Luminol (NEL201). Discs were exposed to Reflection film for 15 minutes.*

Figure 2. Mouse ß-actin was detected using a fluorescein-labeled ssRNA probe and ready-to-use CDP-Star. *This film demonstrates results obtained using Renaissance RNA Fluorescein Labeling Kit with Antifluorescein-AP (NEL633) in conjunction with ready-to-use CDP-Star (NEL601). Blots were exposed to Reflection film for 5 minutes.*

Whether your labeling method of choice is Random Priming, Nick Translation, 3'-End Labeling, or RNA Transcription, there is a convenient kit for use with our chemiluminescent or chromogenic substrates. For ultimate flexibility, versions of all kits are available to make hybridization probes labeled with either fluorescein or biotin and include either alkaline phosphatase or horseradish peroxidase conjugates. Once your DNA or RNA probes are labeled, detection is quick and simple on GeneScreen membrane with either ready-to-use CDP-*Star*™ or Enhanced Luminol and Reflection™ film or 4CN Plus.

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Figure 3. The v-Fos gene was detected in 125 ng of blotted mouse genomic DNA in less than 5 minutes using CDP-Star. *This film demonstrates results obtained using the Renaissance Random Primer Biotin Labeling Kit with Streptavidin-AP (NEL604) in conjunction with ready-to-use CDP-Star (NEL601). Blots were exposed to Reflection film for 5 minutes.*

Figure 3

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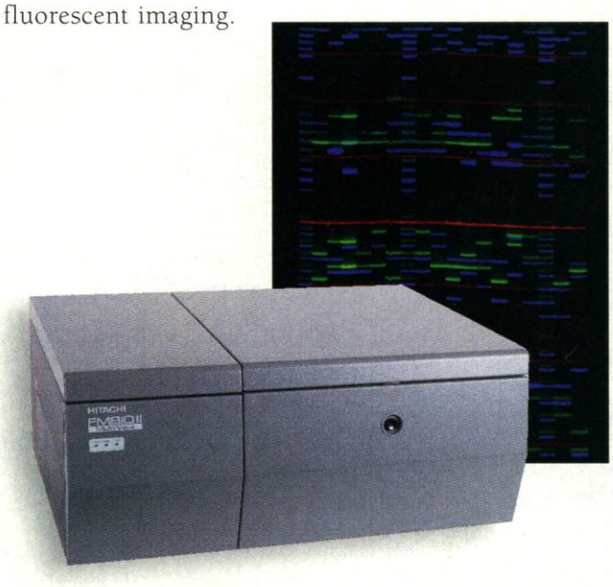

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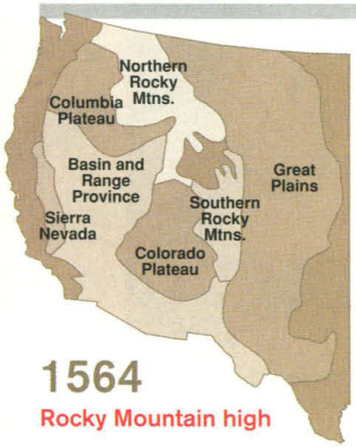

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NEWS

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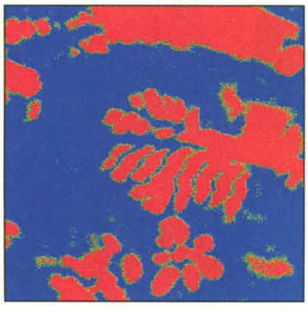

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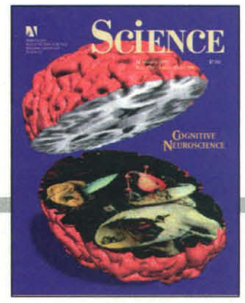
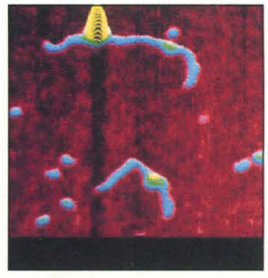
COVER

Mental illnesses arise from the brain but are expressed in the mind. Shown is a surface reconstruction of a schizophrenic patient's brain. The top half shows the internal anatomy, including ventricular enlargement often seen in schizophrenia, and the bottom shows the "The Garden of Earthly Delights" by Hieronymus Bosch, which suggests subjective features of the psychotic experience. See the special section (beginning on page 1579) and editorial (page 1547). [Image: T. Cizadlo, D. Heckel, G. Harris, N. Andreasen, Iowa MHCRC Image Processing Laboratory]



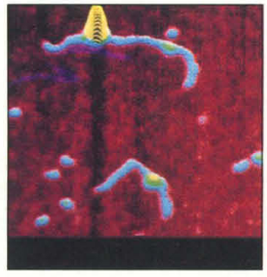
REPORTS

TECHNICAL COMMENTS



1614 & 1658

A buildup for enhanced transcription



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THE MJ RESEARCH NOTEBOOK

Volume VII...No. 2 *A Bulletin of Technological Advance in Molecular Biology* *Spring 1997*

DNA Engine with interchangeable Alpha™ blocks. The one mounted on the cycler has a motorized Power Bonnet™ heated lid; the other Alphas—both dual and single block models—have manual Hot Bonnet™ heated lids.

DNA Engine & Tetrad Set New Standards for Thermal Cyclers

UNPARALLELED PERFORMANCE, PARTICULARLY IN SOFTWARE

Intuitive Programming Especially Easy

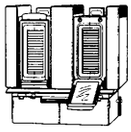
WATERTOWN, Mass. — In late 1994, MJ RESEARCH introduced a revolutionary new line of thermal cyclers for PCR* and cycle sequencing. Called the "DNA Engine™" line, this new design builds upon experience the company had gained manufacturing its pioneering PTC-100™ and MiniCycler™ instruments. Improvements included increased speed of ramping, higher precision and greater accuracy—as well as a new "swappable" block format. But perhaps the most significant advances were in the software, for these allowed easier user interface and better thermal control—as well as communication between cyclers and other digital devices.

The new software was the culmination of years of effort by engineers Joe Pacatte and Andrea Wolga. Building upon the intuitive concepts of PTC-100 software, they managed to create a powerful new system that allows for expansion, revision, and network communications via IEEE-488 or RS-232 ports—features that would impress any engineer. But they concentrated their efforts on the needs of users, creating a whole host of features to allow smoother functioning in the lab. These include the ability to store programs in individual folders, edit one program while another is running, choose from 3 different methods of thermal control, and calculate total run time from entered parameters. These and many other software features make DNA Engines a joy to use.

Other engineers did their jobs well too. In particular, the modular design of swappable blocks (called "Alphas") allows configuration for different vessels—96 or 384-well plates, 0.2 or 0.5ml tubes, for example. Last but not least, two available sizes of chassis—one holding 1 Alpha and the other 4—allows maximum flexibility in planning, purchase, and expansion.

Twin Tower *In Situ* Alpha Fits DNA Engines & Tetrads

The versatility of the DNA Engine system is well illustrated by the Twin Tower™ *in situ* Alpha. Two new methods of DNA amplification—*in situ* PCR* and PRINS—have recently come to common usage, but they usually require a specialty thermal cycler that processes only glass slides.



But not with the DNA Engine or Tetrad. Instead, a "swappable" dual block, called the Twin Tower, can be put into either chassis, and each Alpha cycles 2 x 16 glass slides rapidly, accurately, and precisely.

Accuracy & Data Export Needed for Diagnostics

Medicine is on the cusp of a new era when diagnosis of disease will be based increasingly upon the analysis of amplified DNA. But the thermal cyclers that actually do the amplification must be of specific and certifiable quality.

The College of American Pathologists and the NCCLS have chosen to focus upon two criteria for particular attention: accuracy and the recording of thermal data from every run. Each DNA Engine has NIST-traceable & field-verifiable accuracy. Thermal data may be continuously reported via serial or GPIB ports, or sent to a printer for hard copy, in order to record data.

Tetrads Lead the Charge into Genomics

High-Capacity Yet Compact—Cycler Holds Four 96 or 384-well Plates

A recent development in biology is an unrelenting surge of interest in genomics. Already increasing knowledge of the human and other genomes has had major influence upon the biotech, pharmaceutical, and medical industries, and Wall Street seems to be betting on further advances. According to a recent series of articles in *Science* (275, 767-782, 7 Feb 97) the pharmaceutical industry alone has invested at least $1 billion into genomics companies.

And what is the thermal cycler of choice among these companies? Why, the MJ RESEARCH Tetrad. This thermal cycler has all the features of the DNA Engine—and it also offers 4 independent blocks in one compact chassis. It fits easily inside robots, it can be controlled manually from its keypad or digitally through its ports, and when fitted with Power Bonnets, it can be operated without manual intervention.

Tetrad cycler with four swappable blocks

* PCR is covered by patents owned by Hoffmann-La Roche, Inc. & F. Hoffmann-La Roche Ltd. Users should obtain license to perform the reaction.

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edited by PHIL SZUROMI

Phonon squeezing

Heisenberg's Uncertainty Principle states that we cannot know simultaneously the values of conjugate variables (such as position and momentum) to arbitrary accuracy; the product of their errors must always exceed a certain value. However, experiments can be designed that reduce the error in one variable below the quantum limit—"squeezed states" of photons have been produced for some time. Garrett *et al.* (p. 1638; see the news story by Cleary, p. 1566) have created a nearly periodic squeezed state of acoustic-mode phonons (lattice vibrations) in crystals of $KTaO_3$. Femtosecond laser pulses induced counterpropagating phonons that select for a high density of phonon states. The variance in atomic displacements as the atoms vibrate dips below the quantum limit for half of each cycle.

■

Borehole baseline

One problem in interpreting currently observed global warming is that earlier temperature records for comparison are scarce. Harris and Chapman (p. 1618) show that temperature estimates from boreholes can provide a baseline that is also tied to the current observational record. Data from a borehole and meteorological network in Utah show that temperatures in the 19th century there were about 0.6°C below recent mean temperatures.

■

Sulfur in the core

Determination of the melting temperature of Earth's iron outer core requires a knowledge of how other elements such as sulfur can form stable phases with iron at high temperatures and pressures. Fei *et al.* (p. 1621) conducted multianvil experiments and found an additional phase, Fe_3S_2, near 14 gigapascals. The presence of Fe_3S_2 suggests that the temperature of the core may be overestimated by extrapolation from a simple Fe-FeS binary eutectic.

■

Off-site transcriptional activation

Activation of transcription requires proteins that bind DNA near the promoter sequence and recruit RNA polymerase (RNAP) and others that function at distant sites. Studies of bacterial transcription have begun to reveal the importance of protein-protein interactions. Wyman *et al.* (p. 1658) show that the transcriptional activator NtrC (nitrogen regulatory protein C) forms large oligomers at a distant DNA enhancer site. The non–DNA-binding components of these NtrC oligomers are essential for activation, possibly because they interact with RNAP at the promoter site. Miller *et al.* (p. 1655) show that bacteriophage N4SSB (single-stranded DNA binding protein) activates transcription not through its DNA binding domain but rather one that binds to RNAP β′. In a Perspective, Geiduschek (p. 1614) speculates that NtrC and N4SSB may both reconfigure the RNAP complex into a transcriptionally competent form.

Cooler carbonates

The temperature of formation of carbonate minerals precipitated on fracture surfaces in the martian meteorite ALH84001 has been controversial and is key for understanding the early evolution of Mars as well as whether the meteorite might contain traces of early life. Two reports provide evidence that the carbonates formed at low temperatures. Kirschvink *et al.* (p. 1629) show that the magnetic directions of pyroxene grains across a fracture are rotated. Magnetic directions should have been reset if the rock was heated above a few hundred degrees Celsius. The data also imply that early Mars had a substantial magnetic field. Valley *et al.* (p. 1633) show that the oxygen isotope compositions of the carbonate minerals are high and variable, suggesting that the minerals precipitated at low temperatures and in disequilibrium.

■

Under continents

The upper mantle beneath continents differs from that beneath ocean basins for reasons that have not been clear. Thybo and Perchuć (p. 1626) examined long-range seismic reflections profiles from several continents where the source and receiver were separated by at least 700 kilometers (8°). The sections imply that the mantle beneath the continents may be a region of partial melting; it is stratified to at least 100 kilometers above a zone of low seismic velocity.

■

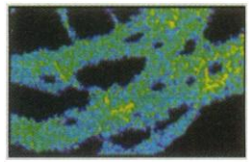
Reactive oxygen and cell proliferation

Reactive oxygen species (ROS) are produced by some cancer cells, and antioxidants appear to protect against some forms of cancer. However, the role of ROS in controlling cell proliferation is largely unknown. Irani *et al.* (p. 1649; see the news story by Pennisi, p. 1567) found that cells transformed by a constitutively active form of the Ras guanosine triphosphatase produced increased amounts of superoxide. Proliferation of Ras-transformed cells was inhibited by a chemical antioxidant or transfection of cells with catalase. The findings indicate that production of ROS is necessary for enhanced cell proliferation induced by an oncogenic form of Ras and also provide a hypothetical mechanism for some of the observed anti-proliferative actions of antioxidants.

■

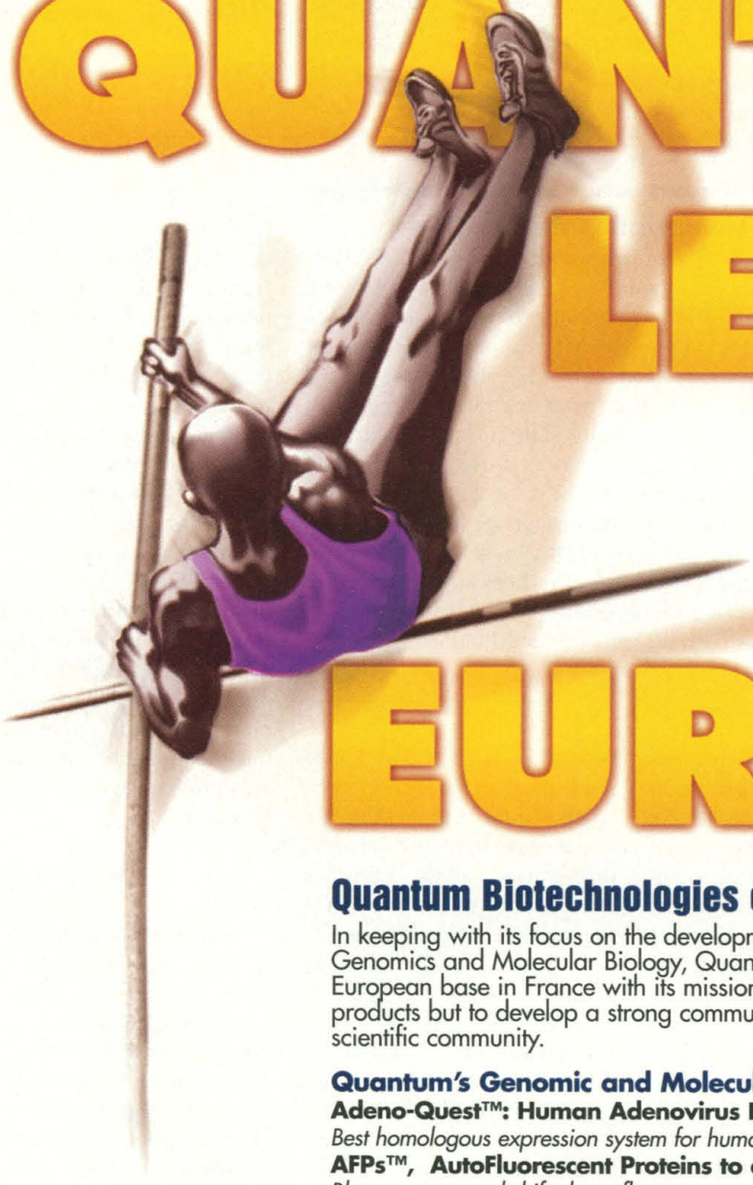
Calcium control

In many cells, release of calcium from intracellular stores is a critical step in regulating various processes. Golovina and Blaustein (p. 1643) used high-resolution imaging and calcium-sensitive fluorescent dyes to visualize calcium storage and release of calcium in stimulated



cells. Calcium exists in small spatially and functionally distinct compartments that can respond in distinct ways to physiological stimuli—the concentration of calcium in some stores even increased while others released calcium. Such local control of the concentration of intracellular calcium apparently allows calcium-dependent regulation of multiple processes within a single cell.

QUANTUM LEAPS TO EUROPE



Quantum Biotechnologies expands its activities in Europe

In keeping with its focus on the development of novel research reagents for Genomics and Molecular Biology, Quantum Biotechnologies has established a European base in France with its mission not only to promote and distribute its products but to develop a strong communication network with the European scientific community.

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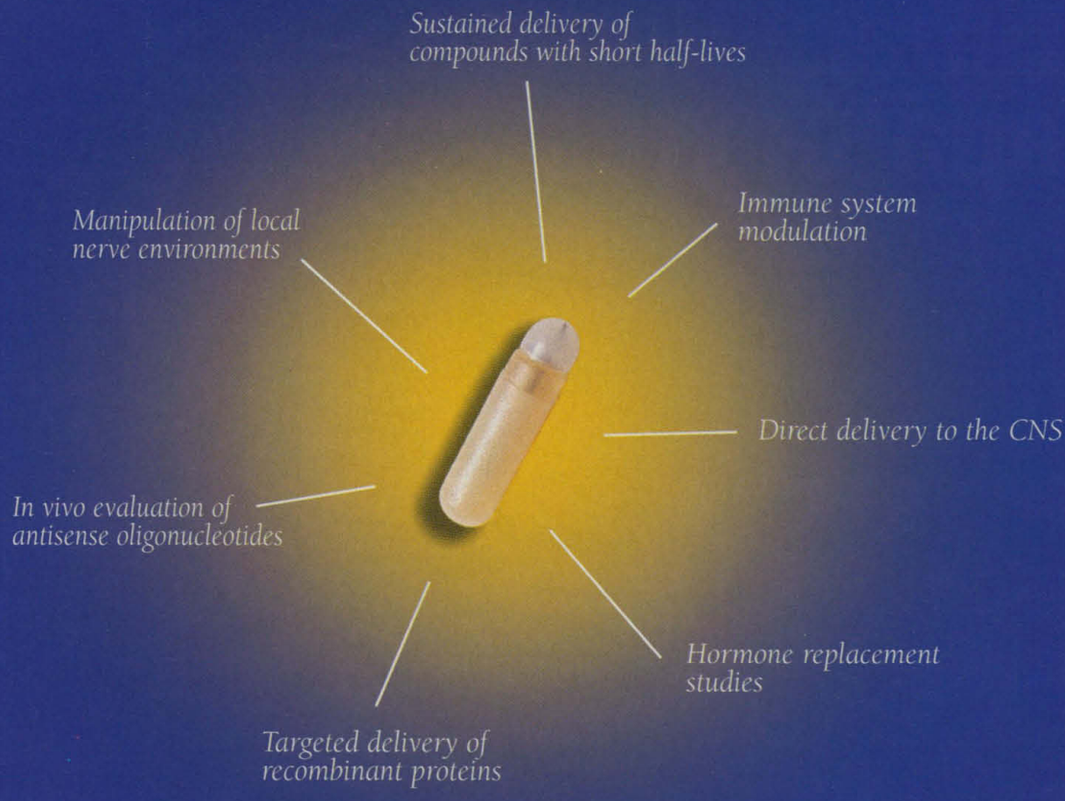

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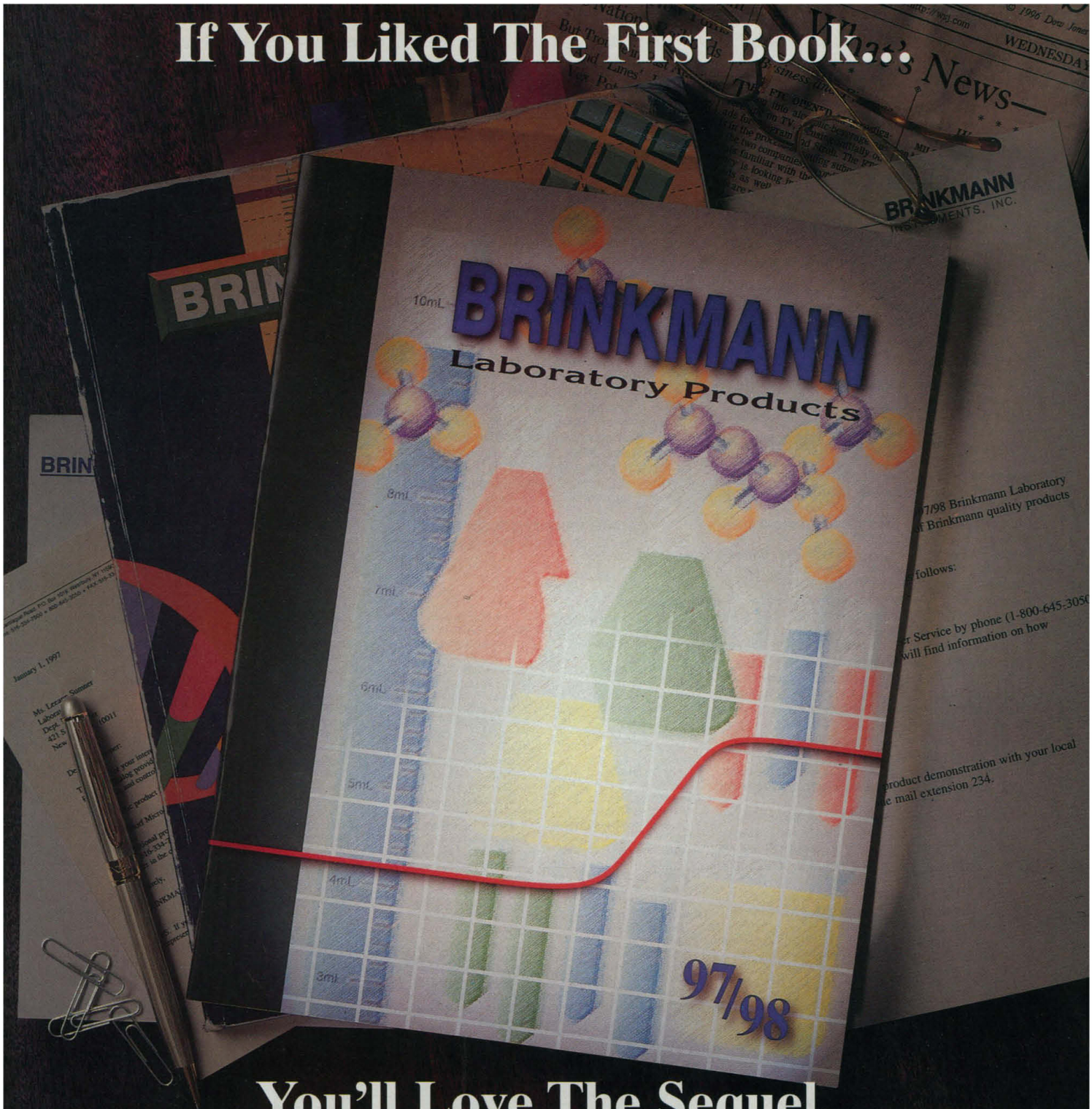

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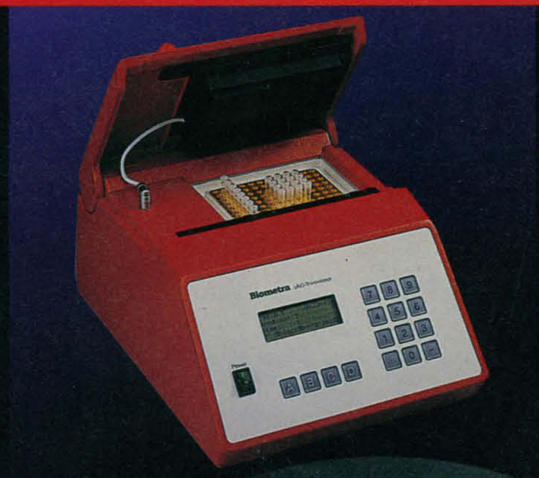

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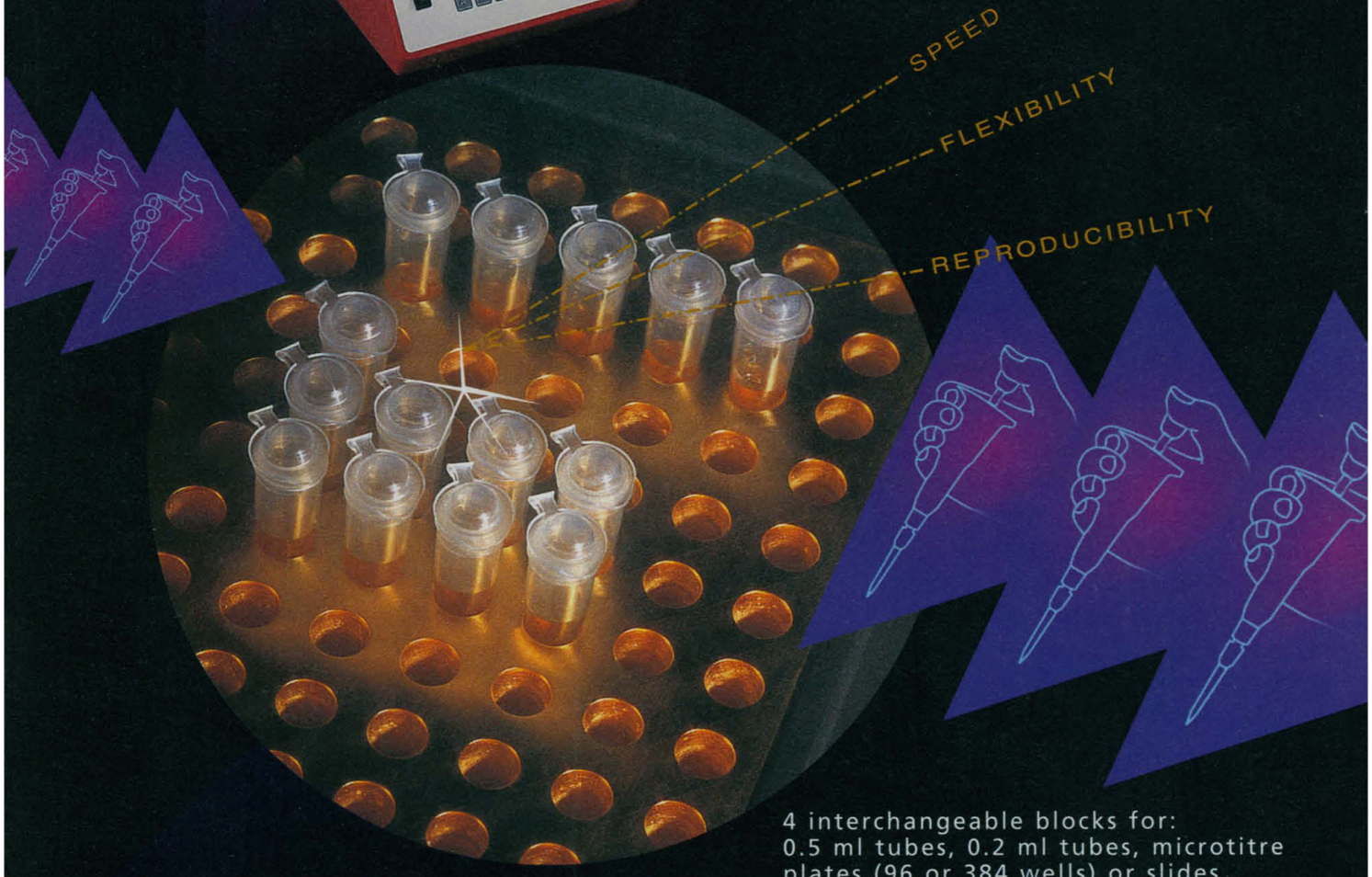

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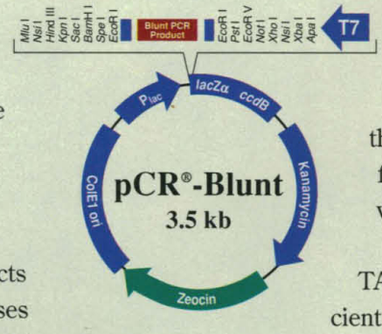

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