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23 JUNE 1995 $7.00
VOL. 268 • PAGES 1669–1816

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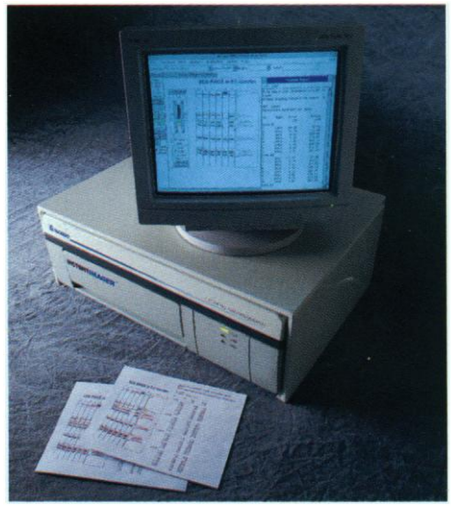

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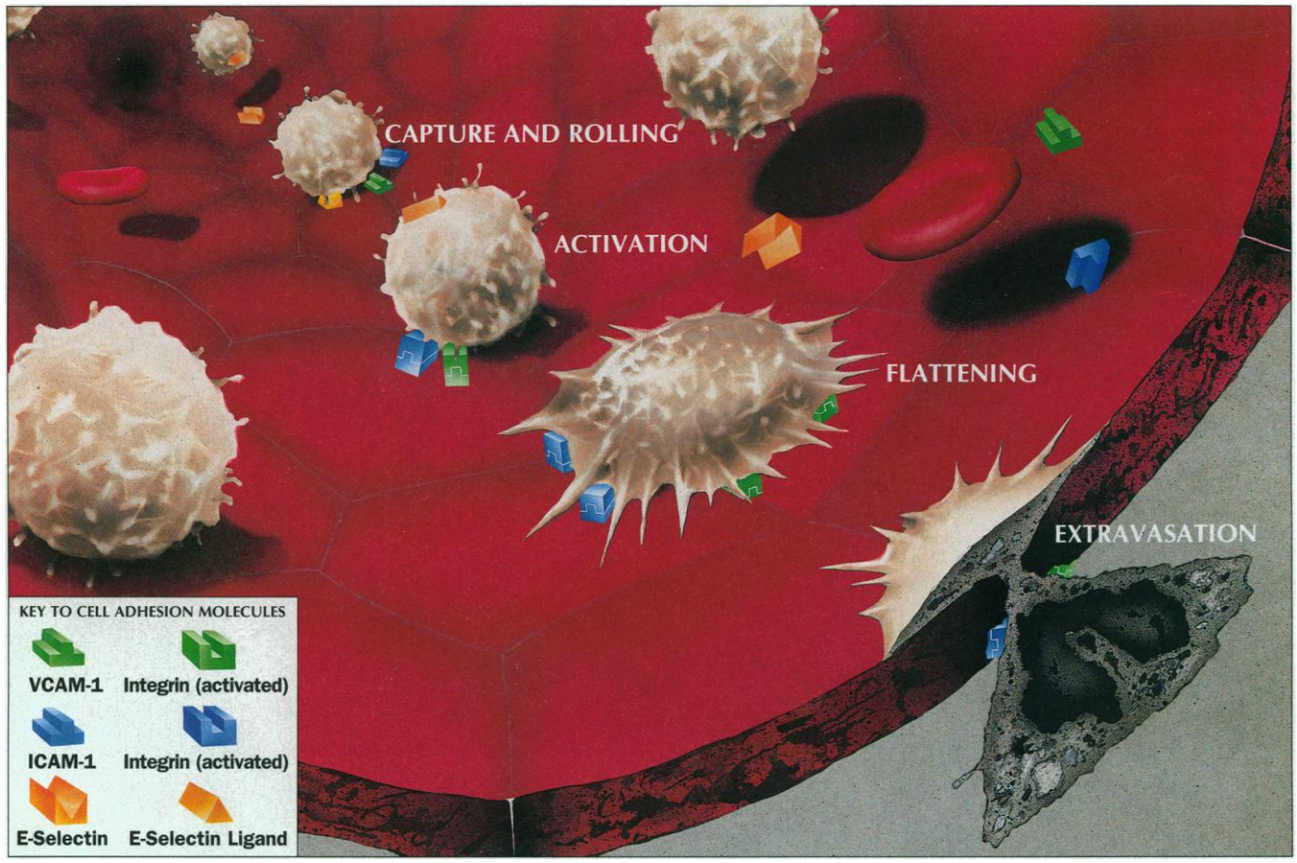

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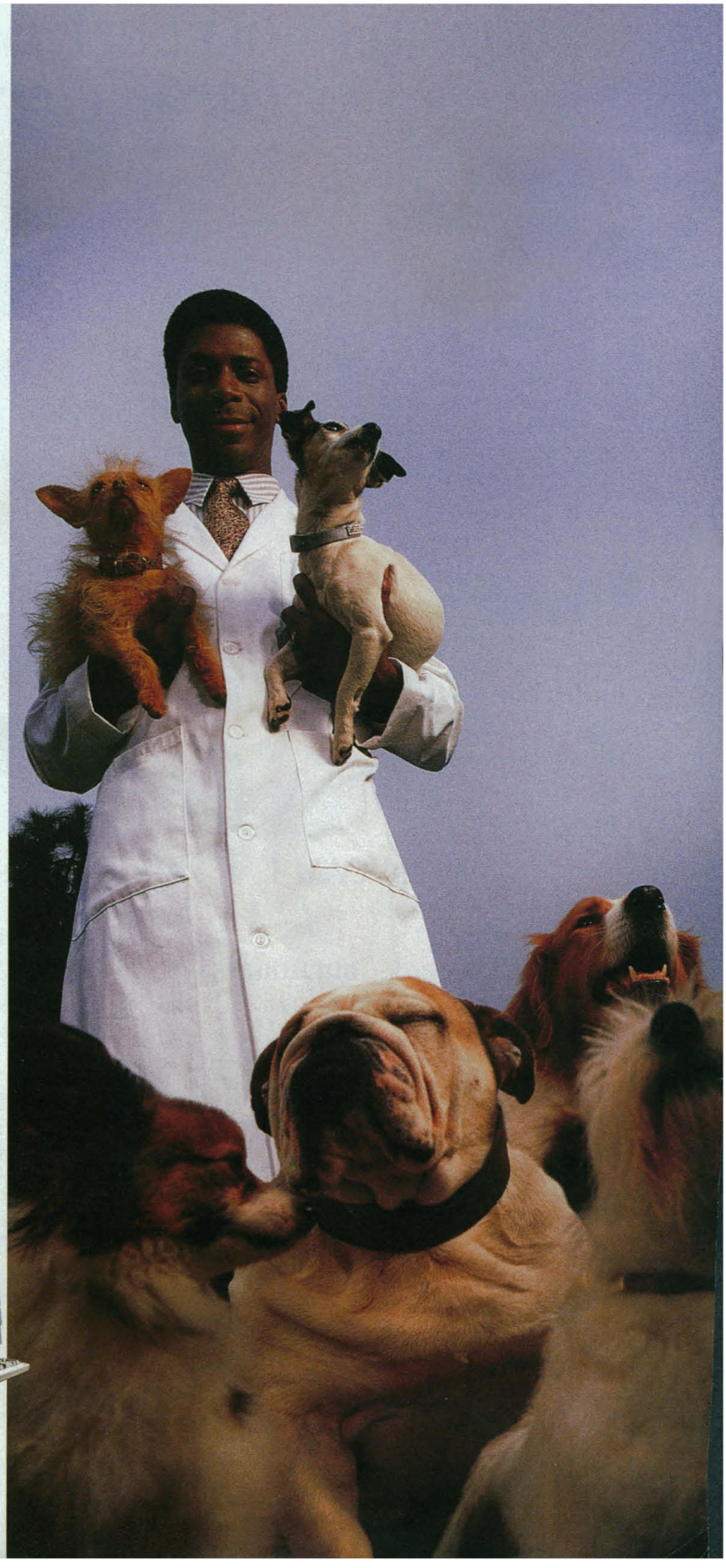
Like the time they went off and optimized a deprotonization on a Mac™ instead of building a pilot plant. And saved $30 million. That made the whole group look good. And bred a new kind of loyalty between Ben and his Mac. The kind usually reserved for someone named Spot.



Benjamin W. Sallard, Jr.
Chemist
Network Administrator
Process Technology Group
Sandoz Agro, Inc.
Des Plaines, Illinois

As part of a multinational life sciences company with more than 1,200 employees in the U.S. and Canada, Sandoz Agro specializes in the development and manufacture of environmentally sensitive biological, biochemical and chemical pest control products.

"If all you want to do is data acquisition, sure, you can do it on a Windows PC. But if you want to connect to a Novell server and a VAX and an AS/400, and you want to run business apps, and you need to do it now, then you need a Power Mac. Anyone who thinks there is a faster or easier way to accomplish all that is, well, barking up the wrong tree."

Process Tech scientists at Sandoz Agro are charged with finding the fastest, easiest and most cost-efficient ways to produce everything from herbicides and fungicides to flea control products for the family pet. Their latest finding? "Power Mac has the power we need to stay competitive."

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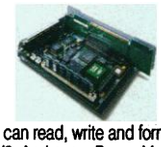
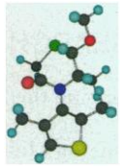


Every Power Mac can read, write and format disks for DOS, Windows and OS/2. And every Power Mac lets you open and work with DOS and Windows files. If you need more compatibility than that, the Power Macintosh 6100/66 DOS Compatible includes both a 66 MHz 486DX2 and a PowerPC 601 microprocessor in one PC.



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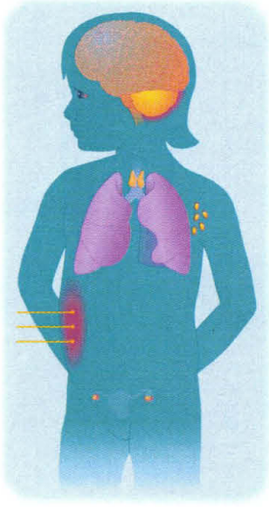


1700 & 1749
AT gene—Cancer and radiation risk

NEWS & COMMENT

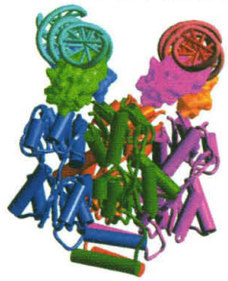
RESEARCH NEWS

SPECIAL NEWS REPORT

CONDUCT IN SCIENCE

PERSPECTIVE

1721
Close encounters of the Lac kind



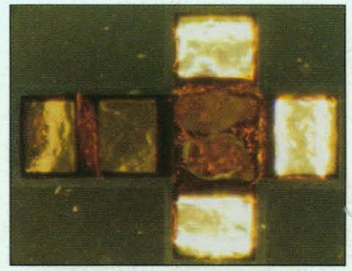
DEPARTMENTS

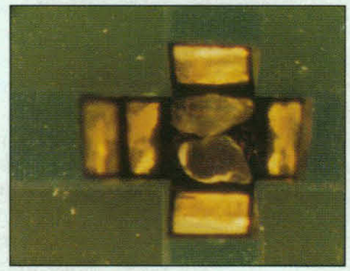
COVER

A combination of thin film deposition and physical masking techniques was used for the parallel synthesis of a spatially addressable library containing high-temperature cupric oxide superconductors. The color of each site is the natural color of reflected light of the library before being heated in air to form oxides. Each site is 1 millimeter by 2 millimeters. See page 1738. [Image: X.-D. Xiang and P. G. Schultz]

RESEARCH ARTICLE

REPORTS





1735
Beyond the hinge

◩ Indicates accompanying feature

■ **SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1333 H Street, NW, Washington, DC 20005.** Second-class postage (publication No. 484460) paid at Washington, DC, and additional mailing offices.

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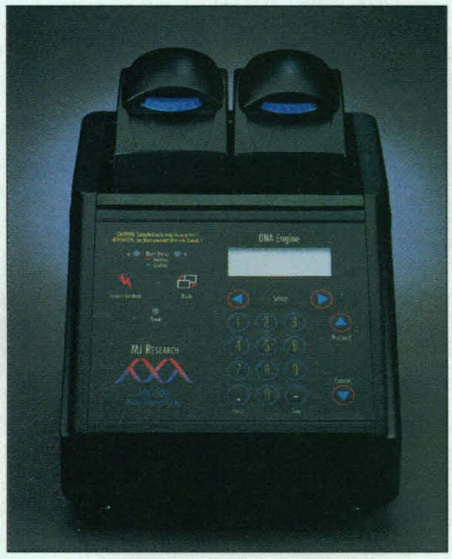
THE MJ RESEARCH NOTEBOOK

Volume V...No. 2 *A Bulletin of Technological Advance in Molecular Biology* *Spring 1995*

DNA Engine Helps Power Era of PCR* Diagnostics



The PTC-200 DNA Engine™

ENGINES REVVING FOR LARGE-SCALE SEQUENCING

Human Genome Project Advances Towards Actual Sequencing Phase

The Human Genome Project has now reached a crossroads where existing technology—based upon thermal cycle sequencing of M13 templates—has achieved a level of development where the actual sequencing of the three-billion bases in human DNA can now begin. As reported in *Science (10 Feb 95 (267) p 783-784)*, two leaders of the project have proposed a plan to begin the sequencing phase immediately. They argue that existing technology could allow the project to be completed as soon as 2001—a full five years ahead of schedule.

MJ RESEARCH has been working with teams—both in the U.S. and the U.K.—to use the DNA Engine system to help drive this accelerated schedule. The extremely speedy nature of its cycling—combined with the ease with which the instrument integrates into automated robotic systems—has made the DNA Engine the cycler of choice for thermal cycle sequencing. Higher-density formats are in development, as are pre-engineered systems that will feature robotic fluid handling.

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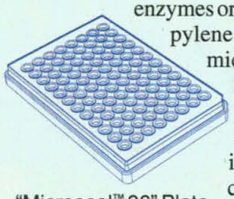

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Perhaps the most powerful tool yet invented for the diagnosis of infectious and genetic disease—the polymerase chain reaction (PCR)*—is now poised to enter the clinical arena. A decade has passed since the original conception of this enormously specific and sensitive technique, and now PCR promises to be helpful not only for the diagnosis of disease, but also for the prognosis of cancer, heart disease, and other conditions as well.

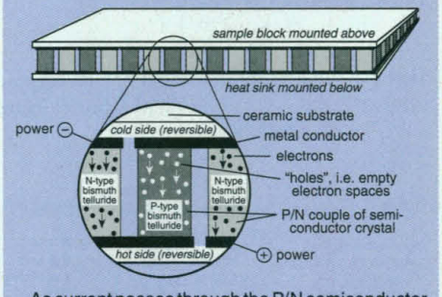
Many companies have been working to bring PCR to clinical pathology laboratories, but limitations had lain with the thermal cyclers that drive the reaction, which had not yet fully met the special needs of the clinical market. Now, MJ RESEARCH has used its eight years of manufacturing experience to construct the PTC-200 DNA Engine™, the highest-performance thermal cycling system ever. Its Peltier-Joule heat pumps outperform every competing technology, its adjustable Hot Bonnet™ heated lids make oil-free operation easy and reproducible, and its networking and digital export capabilities can make documentation automatic. The various methods of control are compatible with existing systems, easy-to-use software allows protected protocols, and swappable blocks can accommodate virtually any vessel (soon even slides for *in situ*). In short, this system is the perfect clinical platform.

PCR Process Patents—How to Get License

Licenses to conduct PCR for human and veterinary diagnostic use are available from Roche Molecular Systems in the U.S. and F. Hoffmann-La Roche Ltd. worldwide. Standard terms exist that are independent of the thermal cycler to be used, and hundreds of licenses have been granted to date. For more information, contact: Director of Licensing; Roche Molecular Systems; 1145 Atlantic Avenue; Alameda, CA 94501 U.S.A.

License for other research and forensic uses can be obtained by use of reagents carrying a label license, which currently states they must be used in conjunction with an "authorized" thermal cycler. Any MJ RESEARCH cycler can be "authorized"—contact: Director of Licensing; P-E/ABD; 850 Lincoln Drive; Foster City, CA 94404 U.S.A.

How A Peltier Heat Pump Works



As current passes through the P/N semiconductor couples, charge carriers (electrons or "holes") absorb energy at one of the metal/semiconductor interfaces and deposit energy at the other, generating a thermal gradient of up to 70°C across the crystals. The rate of heat pumping is proportional to current, and the direction is reversible by switching polarity.

* PCR is covered by patents owned by Hoffmann-La Roche, Inc. and F. Hoffmann-La Roche Ltd. *(see note for info on licensing).*

■

edited by PHIL SZUROMI

Block party

Block copolymers string together alternating stretches of different monomer units. Zhang and Eisenberg (p. 1728) have found that polystyrene polymers that contain much shorter poly(acrylic acid) (PAA) blocks exhibit a wide range of morphologies that depends on the length of the PAA block. In aqueous solution, they see spheres, rods, lamellae, and a new phase of micrometer spheres filled with aggregates resembling reverse micelles. In organic solvents a reverse micelle is seen. Upon drying, the spherical micelles form highly birefringent needles.

■

Stormy weather

An unexpected finding during the Voyager 2 flyby of Neptune was the Great Dark Spot (GDS), a large atmospheric storm in the southern hemisphere that rivals Jupiter's Great Red Spot, which has been seen for hundreds of years. Recent Hubble Space Telescope images of Neptune presented by Hammel *et al.* (p. 1740) show that the GDS has disappeared and that a new storm has now appeared in the northern hemisphere.

■

Structural costs

Adsorption of small molecules can cause some crystal faces to adopt a different surface structure. Quantitative measurements of the energy difference between such phases have in the past suffered from large uncertainties. Surface calorimetry now allows direct measurements of the energetic cost of such rearrangements with unprecedented precision, as Yeo *et al.* (p. 1731) show for two surface phases of platinum. Such high-quality experimental data can serve as a test for the theoretical treatment of metal surfaces.

■

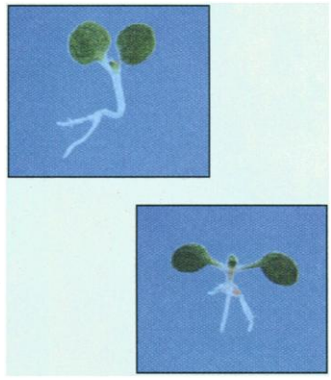
Small folding boxes

The fabrication of microdevices such as microrobots requires a combination of rigid and flexible elements on a micrometer scale. As Smela *et al.* (p. 1735) show, volume changes that are associated with cation uptake in conducting polymers can be used to make such complex microdevices. The polymers undergo larger volume changes than inorganic materials, and require smaller voltages for operation. The principle is illustrated with a box of micrometer dimensions, which automatically and reversibly folds around two grains of sand when a small voltage is applied.

■

Cut loose

In plants, almost all of the growth regulator indole-3-acetic acid (IAA) present is in an inactive, conjugated form. Enzymes remove amino acid, peptide, or carbohydrate groups to activate IAA locally and stimulate growth, but few such enzymes have actually been identified. Positional cloning studies in plants unable to activate certain conjugates allowed Bartel and Fink (p. 1745) to clone the *ILR1* gene, whose product cleaves IAA–amino acid conjugates.



■

In the beginning

Conversion of hydroxylmethylglutaryl–coenzyme A (HMG-CoA) to mevalonic acid is catalyzed by HMG-CoA reductase, and is the first committed step in the biosynthesis of isoprenoids, including cholesterol. Cholesterol's role in cardiovascular disease has led to the development of enzyme inhibitors such as lovastatin. Lawrence *et al.* (p. 1758) present a high-resolution structure of *Pseudomonas* HMG-CoA reductase, which is functionally and structurally similar to the mammalian enzyme. The structure analysis locates conserved residues and suggests conformational changes that may occur during catalysis.

■

Single gene in ataxia telangiectasia

Patients with ataxia telangiectasia (AT), an autosomal recessive disorder, suffer from neuromuscular and cerebellar disorders and immunological deficiencies and usually die in early adulthood, and individuals heterozygous for AT are predisposed to cancer. At the cellular level, high radiation sensitivity, cytoskeletal defects, and cell cycle abnormalities are seen. Although the disease is genetically heterogeneous (four complementation groups are known), Savitsky *et al.* (p. 1749; see news story by Novak, p. 1700) identified a mutation in a single gene (*ATM*) on chromosome 11 in patients from all four groups. Partial gene products from *ATM* show similarities to proteins involved in cell cycle control.

■

Exerting control

A system for concise regulation of gene expression in vivo in mammalian cells has been developed that could prove useful in transgenic animals and in gene therapy. Gossen *et al.* (p. 1766) used mutants of Tet repressor protein and the VP16 activation domain to construct a transcriptional transactivator that requires the addition of tetracycline derivatives for specific DNA binding. Upon addition of a tetracycline derivative, this protein rapidly induced gene expression in mammalian cells from a reporter gene controlled by tet operator by more than a thousandfold.

■

In the mind's eye

When the travel ads ask us to "picture a sandy beach," it is not clear which parts of our cerebral cortex that are devoted to visual processing help us produce visual imagery, or "daydreams." Previous experiments have discovered activity in visual cortical areas during imagery, and other workers have found that imagery interferes with the perception of external stimuli. Ishai and Sagi (p. 1772, see the Perspective by Miyashita, p. 1719) present evidence from human subjects in which recalled stimuli decreased the threshold for detection of a subsequent stimulus. Because the improvement was specific for the orientation of the remembered stimulus and for the eye with which that stimulus was first viewed, they suggest that the earliest part of the visual cortical pathway is reactivated during imagery.

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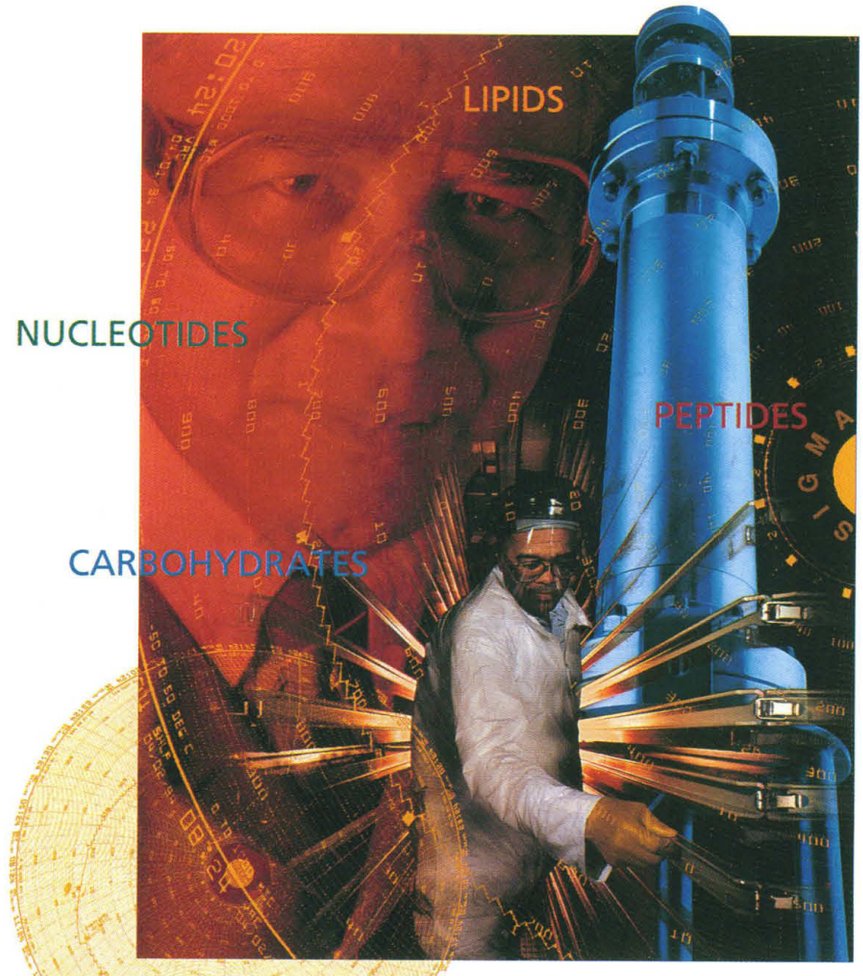

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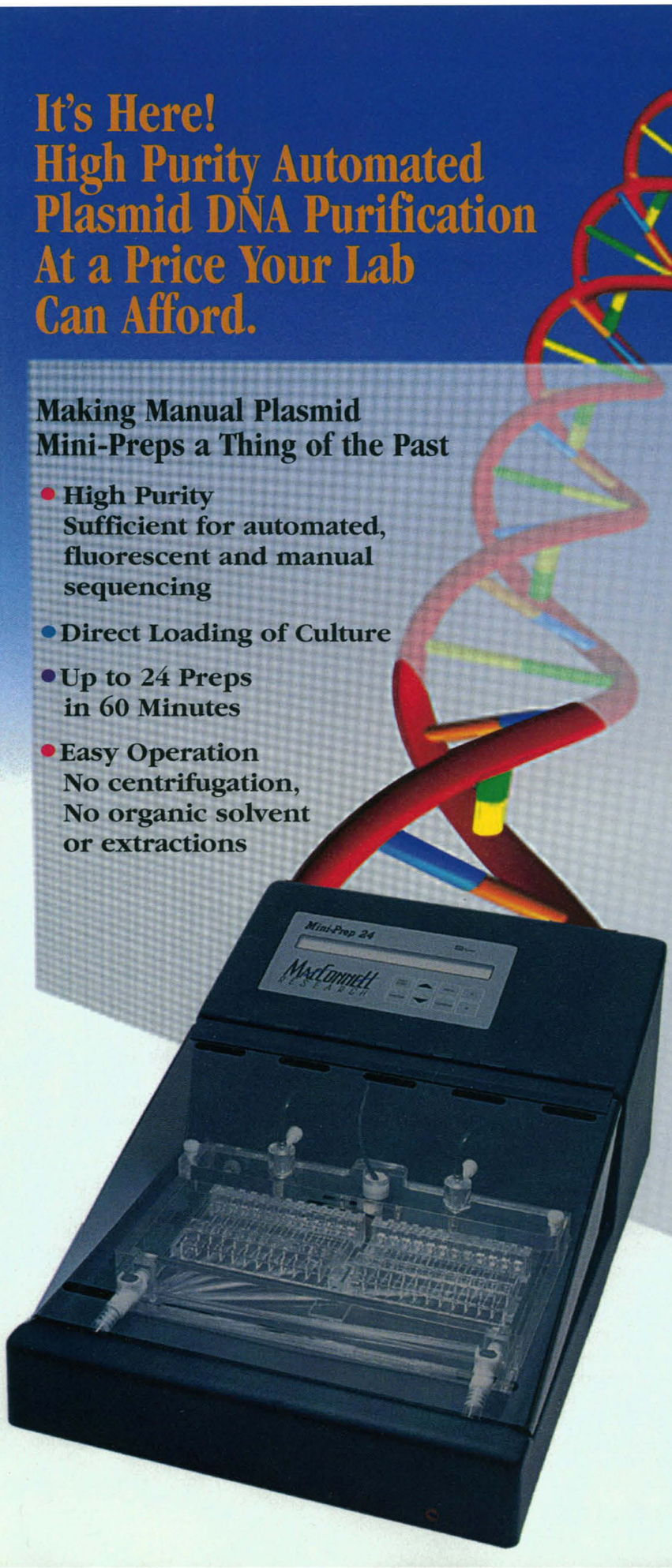

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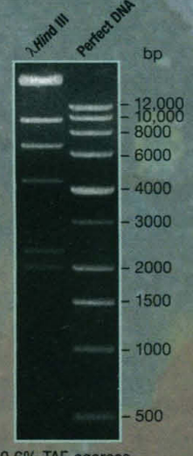

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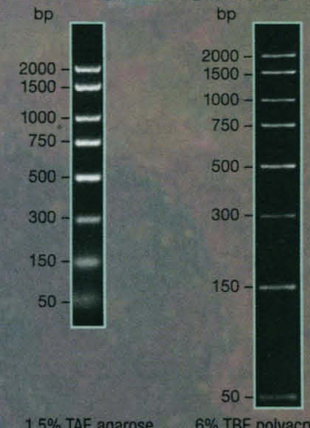

1.5% TAE agarose 6% TBE polyacrylamide

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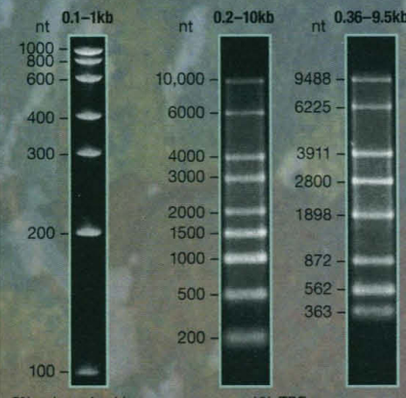
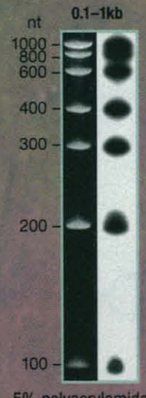
Perfect RNA™ Markers



5% polyacrylamide-urea 1% TBE agarose

Perfect RNA Markers come in two size ranges: 0.1–1kb and 0.2–10kb. Novagen's original RNA markers—0.36–9.5kb—are also available.

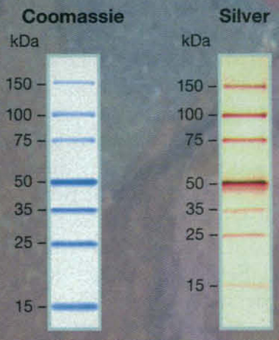
Perfect RNA™ Marker Template Mix



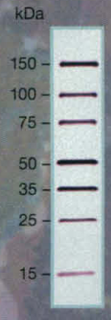
5% polyacrylamide-urea

Radiolabeled markers are generated by transcribing the plasmids in the Perfect RNA Marker Template Mix (0.1–1kb) with T7 RNA polymerase in the presence of labeled nucleotides.

Perfect Protein™ Markers



Perfect Protein™ Western Blot



All markers carry the S•Tag™ peptide for one-step detection using Novagen's S-Protein Alkaline Phosphatase Conjugate. These tagged proteins can be used with any alkaline phosphatase-based detection method.

Novagen

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