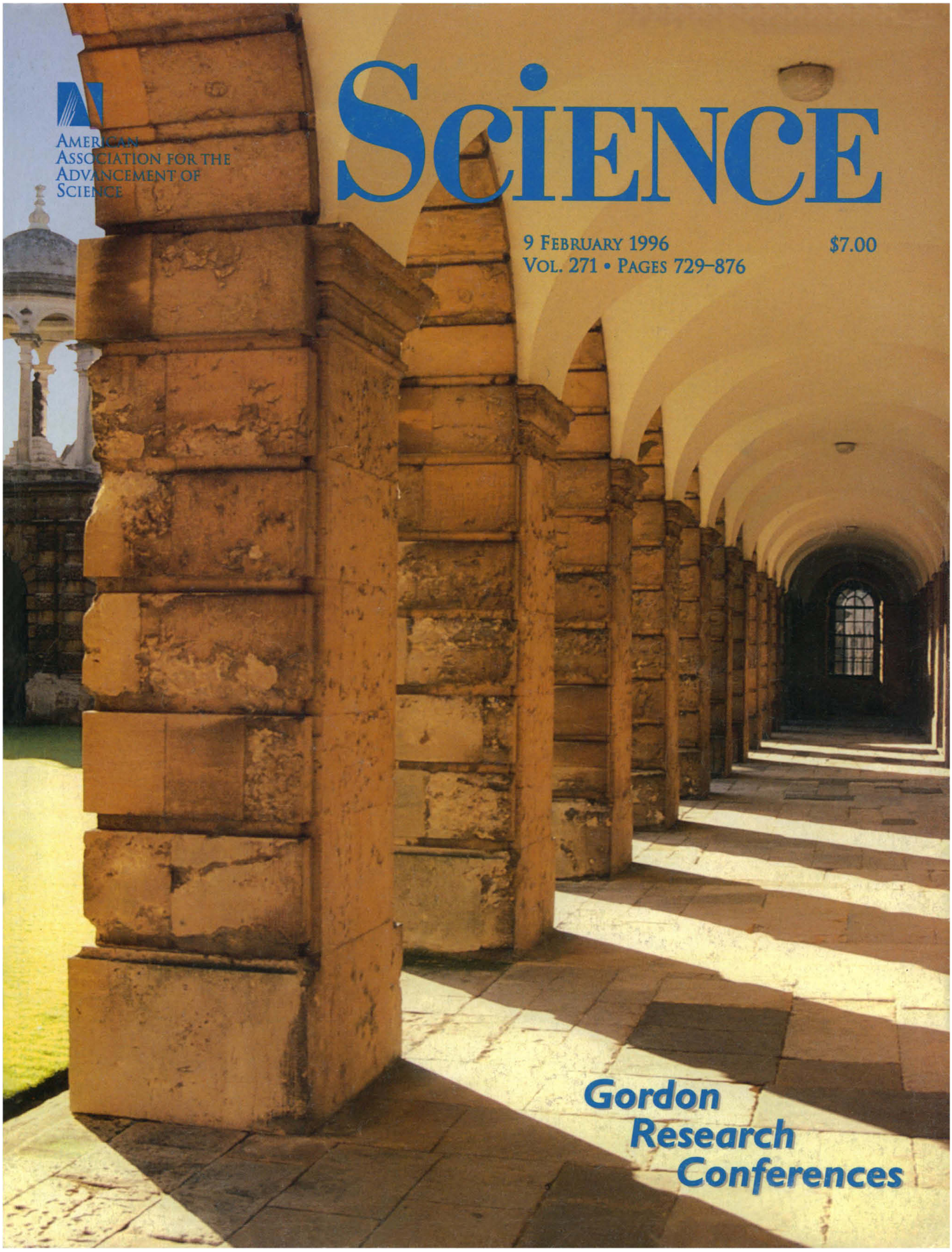

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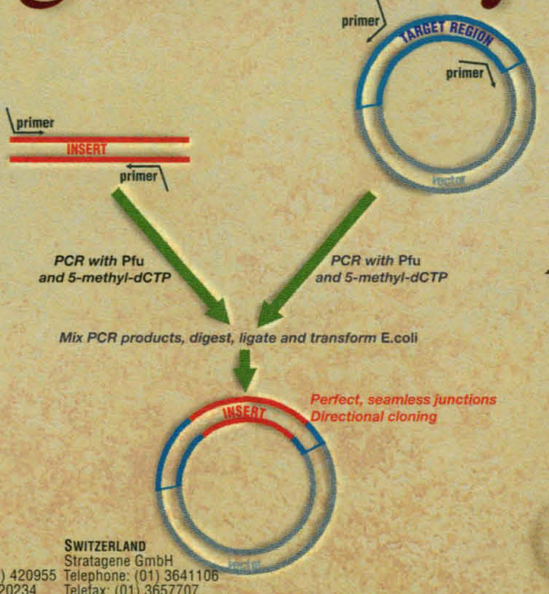

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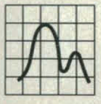

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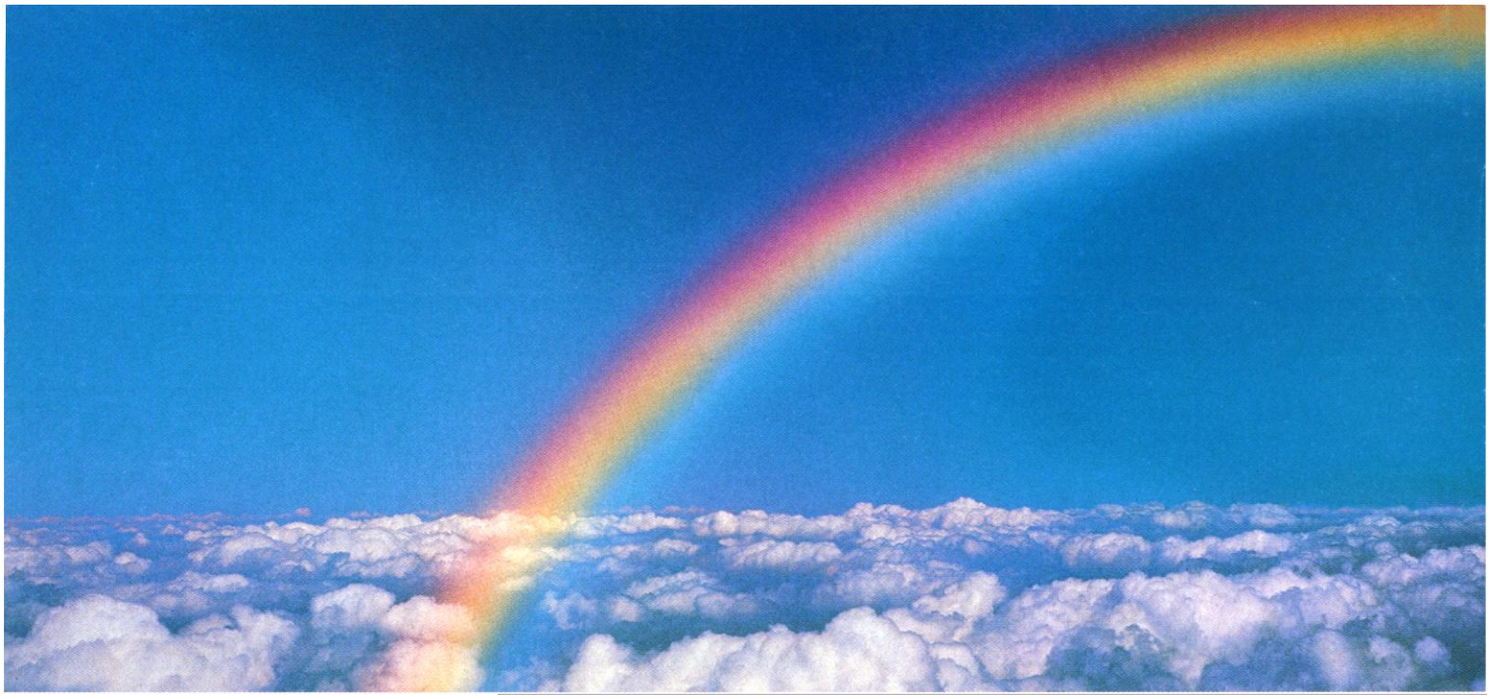

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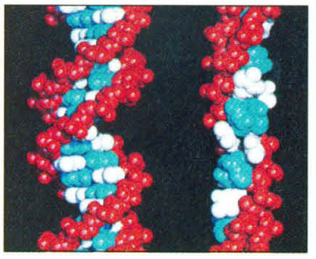
764

Move over, Gutenberg



778

DNA bending and transcription

NEWS

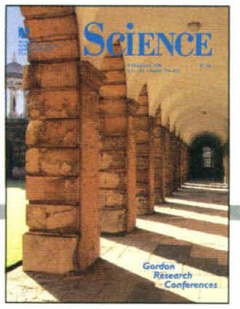
SPECIAL NEWS REPORT

PERSPECTIVES

DEPARTMENTS

COVER

The Gordon Research Conferences have been holding meetings in Europe since 1990. These meetings attract an international selection of scientists for discussions at the frontiers of fundamental science and technology in the biological, chemical, and physical sciences. In the fall of 1996, Gordon Conferences will convene at Queens College, Oxford (cover); Pruhonice in the Czech Republic; and two sites in Japan. See page 826 for scheduling information. [Photo: Chris Andrews, Oxford Picture Library]



ARTICLE

REPORTS

792 & 795

Stretching DNA to the limit

Indicates accompanying feature

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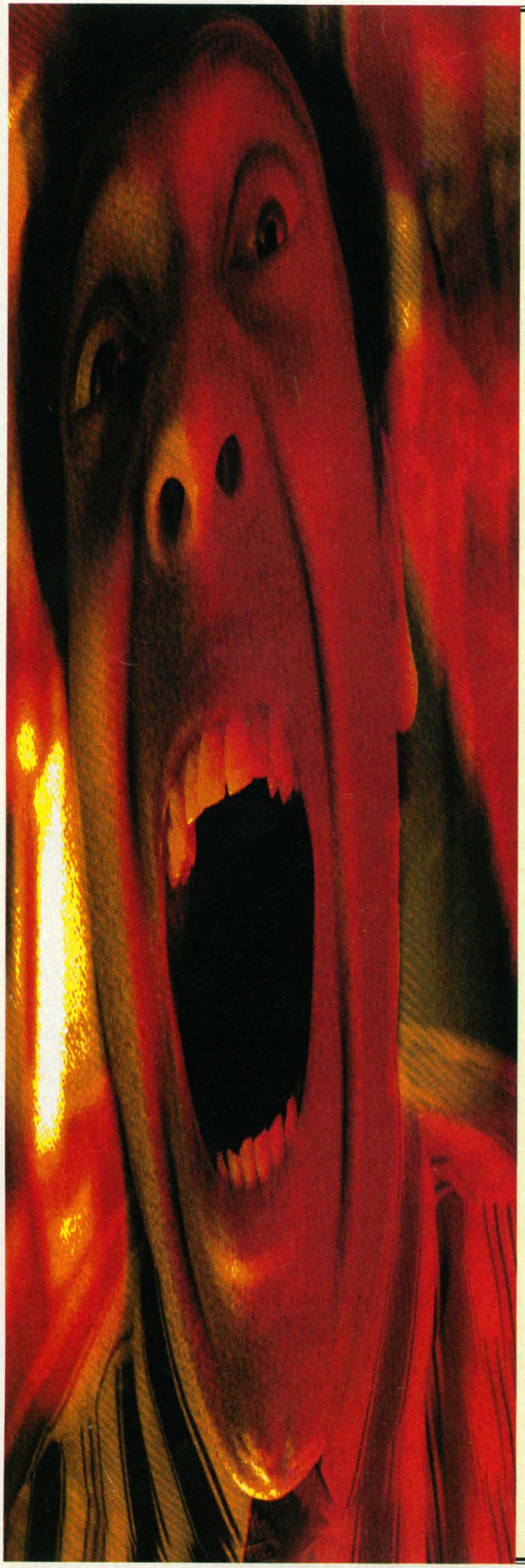
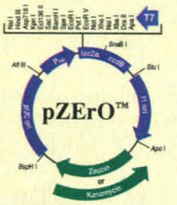


Scientists tormented by trying to clone DNA. On the next Oprah.

We know how you feel about complicated cloning methods. For years, we have all struggled with expensive, time-consuming vector manipulations such as linearization, dephosphorylation and repurification. Face it: selecting positive clones from a lawn of dark blue, light blue and white colonies can drive anybody crazy.



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1. Bernard, P. *et al.* (1994) *Gene* **148**: 71-74.

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edited by DAVID VOSS

Icy breakup

Recently, several large ice shelves in Antarctica have broken up or diminished in size. These ice shelves border large ice sheets. Rott *et al.* (p. 788) analyze radar images from the ERS-1 satellite and show that the Larsen Ice Shelf, which covered an area of 4200 square kilometers, fractured and disintegrated within a few days. In a Perspective, Fahnestock (p. 775) amplifies some of the possible implications for understanding the origin and dynamics of the larger ice shelves.

■

Pulling hard on DNA

Laser tweezer methods make it possible to manipulate large molecules in solution. Attachment of latex beads to the ends of DNA strands allows tension to be applied to the strand so that its mechanical properties (extension, given applied force) can be determined. Two reports by Cluzel *et al.* (p. 792) and Smith *et al.* (p. 799) show that at relatively high forces (70 piconewtons), there is a transition where the DNA suddenly stretches by 70 percent. Smith *et al.* show that the force plateau matches that for single-stranded DNA, suggesting that nicks along the double-strand lead to unraveling of the base pairs. These results may be relevant to recombination—such a transition may reduce the energy needed for proteins such as RecA to stretch DNA.

■

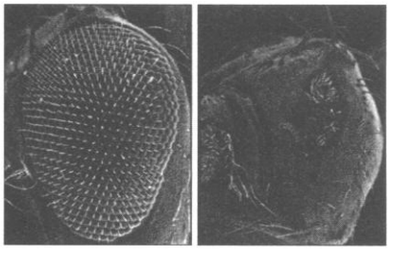
Water on acid catalysts

Solid acid catalysts, such as aluminosilicates and silicoaluminophosphates, are workhorses of industrial and petrochemistry, yet the nature of acidic species generated at their surfaces is difficult to determine experimentally. Water is often used as a probe for acidity—does it form the H_3O^+ cation, or is only hydrogen-bonded water present? Smith *et al.* (p. 795) used powder neutron scattering and infrared spectroscopy to study water bound to a microporous synthetic catalyst, HSAPO-34, that converts methanol to light alkenes. The ordered structure of the catalyst allowed both H_3O^+ and hydrogen-bonded water to be identified at two different sites. In a Perspective, Sauer (p. 774) discusses these results in relation to recent quantum chemical calculations.

■

Under the *reaper*

In *Drosophila*, the *reaper* gene (*rpr*) appears to play a major role in mediating apoptosis, and sequence data suggest similarities with mammalian apoptotic pathways. Two reports focus on mechanistic aspects of *reaper* expression. White *et al.* (p. 805) generated transgenic flies that allowed control of expression of the *rpr* gene. Overexpression of *rpr* in the fly retina resulted in compound eye ablation in a dosage-dependent manner. Pronk *et al.* (p. 808) induced expression of the RPR protein in *Drosophila* Schneider cells and showed that this increased ceramide production. In both reports, the apoptotic effects could be blocked by protease inhibitors. This result suggests that an interleukin-1β converting enzyme (ICE)–like protein plays a role in activating apoptosis.



Making mast cells

Understanding the origins and development of mast cells, which play a key role in allergic and inflammatory reactions, is of relevance to both basic and clinical science. Rodewald *et al.* (p. 818) report the identification of a committed mast cell precursor. It can be distinguished both morphologically, by the presence of cytoplasmic granules, and by its cell surface phenotype. It appears early in ontogeny, being found at day 15.5 of gestation in mice in the fetal blood; thus, commitment to the mast cell lineage can precede tissue emigration.

■

Insulin secretion

Diabetics are frequently treated with a group of drugs known as sulfonylureas. These compounds stimulate secretion of insulin from pancreatic β cells by inhibiting certain potassium channels. Eliasson *et al.* (p. 813) now show that in addition to the known indirect effects on plasma membrane channels, these drugs directly interfere with the cell's secretory machinery.

■

Cold comfort

To adapt to the cold, poikilothermic animals restore fluidity to cold-rigidified membranes by increasing the unsaturation of membrane phospholipids. Tiku *et al.* (p. 815) have cloned the enzyme, Δ^9-desaturase from carp that incorporates the first degree of unsaturation into saturated fatty acids. They also examined the enzyme's regulation in carp during the exposure to cold. Cold induced an increase in Δ^9-desaturase activity that was the result of increased transcription and the activation of latent desaturase.

■

B cell activation

Human X-linked agammaglobulinemia is caused by a defective signaling pathway involving Bruton's tyrosine kinase (BTK) in B cells that results in a drastic loss of γ-globulin and antibody production. Several studies have suggested that BTK interacts with SRC family kinases. Rawlings *et al.* (p. 822) now show that SRC kinases transphosphorylate BTK at one site and that autophosphorylation of BTK at a second site results in activation. These same sites are also phosphorylated when B cells are stimulated by immunoglobulin M. Certain mutations in BTK identified in patients map to the activation loop of BTK.

■

Following the flow

The hydrologic cycle of evaporation and precipitation on land provides nearly all of the fresh water used to sustain humanity and other life. Postel *et al.* (p. 785) provide an accounting of the use of this renewable fresh water by humans, including for agriculture, navigation, drinking, and other necessary activities. They conclude that humans appropriate 24 percent of evapotranspiration globally, and 54 percent of the runoff that is generally accessible (for example, flood waters are excluded).

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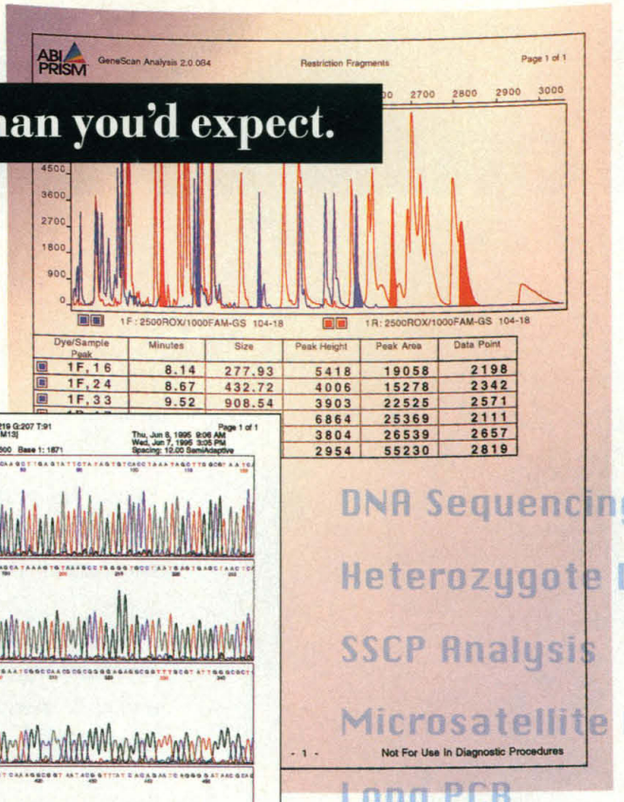

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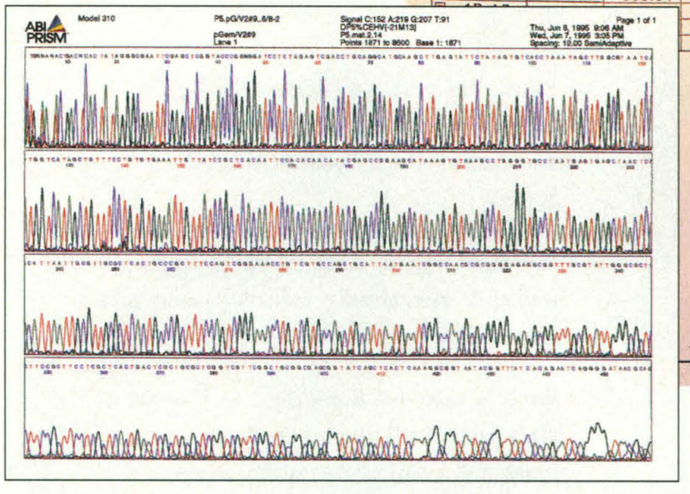
1F, 33	9.52	908.54	3903	22525	2571
			6864	25369	2111
			3804	26539	2657
			2954	55230	2819



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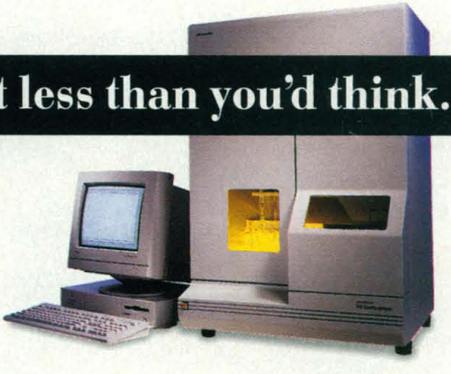

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1. Fodde, R., and Loosekoot, M., *Human Mutation*, **3**, 83, (1994).
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3. Borresen, A. L., *et al., Proc. Natl. Acad. Sci., U.S.A.*, **88**, 8405 (1991).

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THE MJ RESEARCH NOTEBOOK

Volume VI...No. 1 *A Bulletin of Technological Advance in Molecular Biology* *Winter 1996*

NEW TETRAD™ CYCLER OFFERS HUGE CAPACITY

FOUR INDEPENDENT BLOCKS

Fully Compatible With Earlier DNA Engine; Uses Same Interchangeable Alpha™ Blocks

WATERTOWN, Mass. – MJ RESEARCH proudly announces the introduction of an ultra-high-capacity model in its DNA Engine™ line of thermal cyclers. Called the PTC-225 DNA Engine Tetrad™, this speedy cycler has four fully-independent blocks, accurate and reliable Peltier-Joule heat pumps, and networking capabilities that make the cycler fully compatible with earlier DNA Engines—as well as with new automated systems.

In fact, the Tetrad cycler uses the same Alpha™ sample-block/heat-pump assemblies that fit the earlier PTC-200 DNA Engine. These interchangeable blocks deliver the same thermal precision and NIST-traceable accuracy no matter what machine they are plugged into—and swapping an Alpha takes just ten seconds. Eight different Alphas are currently available, and they fit 0.5ml or 0.2ml tubes, 96-well or 192-well plates—or even combinations of vessels in dual blocks. Two newer blocks fit 384-well plates *(see below)* and microscope slides for *in situ* reactions. These different Alphas can be mixed or matched in a single Tetrad, for a total capacity of up to 1536 simultaneous reactions. No cycler made by any other manufacturer offers such versatility or throughput.

This instrument is the latest in the long line of Peltier thermal cyclers offered by MJ RESEARCH. Since 1988, this innovative manufacturer has pioneered development of Peltier instrumentation for laboratories, having introduced its first PTC-100 cycler that year. This venerable instrument was later followed by three models of the portable PTC-150 MiniCycler™ as well as five more models of PTC-100. MJ RESEARCH is also the company that blazed the trail to *in situ* amplification, and its line of PTC-200 DNA Engines sets a standard against which all other cyclers are now judged.

FOR MORE INFO, PLEASE CALL OR E-MAIL: SALES@MJR.COM

MJ RESEARCH, INC.

Manufacturer of Peltier-effect Thermal Cyclers

149 Grove St. • Watertown, MA 02172 U.S.A.

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Distributors Worldwide—Please Fax or E-mail for List

The PTC-225 Tetrad™ with four independent blocks, each with its own Hot Bonnet™ heated lid.

Automated Systems

Slim Cycler Works Well With Robots

The Tetrad was designed to integrate easily with robotic and automated systems, and its hardware and software features were carefully crafted to make integrations straightforward and reliable.

For example, an important consideration with robots is geometry. Thus, the Tetrad has a compact footprint (37 x 55cm), low height (25cm), and front-back airflow—features that facilitate easy fit into a robot without excessive occupation of the work envelope. Further, motorized Power Bonnet™ heated lids are available, and these open a full 115° to allow easy access to the block area. They operate automatically and use variable-ratio, dual-overhead cams to seat the heated lid firmly and evenly.

NETWORKING SOFTWARE

Control Can be Effected Through Keypad or Computer

Perhaps the most impressive feature of the DNA Engine line of thermal cyclers (the PTC-200 & PTC-225) is the sophisticated networking software that is exclusive to MJ RESEARCH. Not only does the software offer three methods of thermal control, advanced editing and filing features, and multi-tasking capability—it also allows up to fifteen cyclers to operate on a single, computerized network. Full control can be effected by a central computer through either a RS-232 or an IEEE-488 port, or alternatively, the individual blocks can be programmed or controlled through use of a keypad and the LCD/LED displays on the cycler itself.

"What About the 384-Well Format?" Ask Scientists in the Human Genome Community

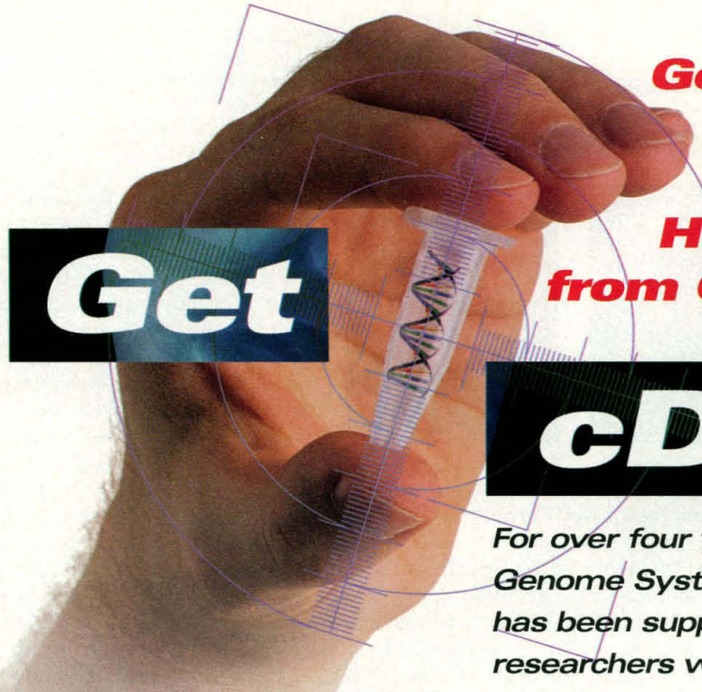
The Quest for Colossal Capacity

Now that thermal-cycle sequencing of M13 templates seems to have become the sequencing method of choice for the Human Genome Project (*Science* **267**, 783-4; *Nature* **375**, 93-4), investigators are faced with the engineering chore of scaling up equipment. Three billion bases in human DNA need decoding, and the older standard format of disposable vessel—96-well plates—is generally too small for this sort of large-scale investigation.

V-wells on 4.5mm centers *(actual size)*

Thus, a new 384-well format is in development. It shares the same basic V-well shape as the 0.2ml 96-well format, but the density has been multiplied four times by decreasing the well-to-well distance from 9mm to 4.5mm. This allows the use of the same multi-channel pipettors and automated dispensers/harvesters as with the 96-well format; the equipment merely accesses alternate wells in a back-and-forth fashion. MJ RESEARCH is working with others to establish standards for disposables, and although vessels (and the full utility of the system) are not yet available, 384-well Alphas for PTC-200 & 225 cyclers can be ordered. Reactions must now be conducted in 96-well plates; these vessels fit the 384 block adequately, but useful reaction volume is decreased to 20µl per well.

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



Get Access to the Arrayed I.M.A.G.E. Consortium (LLNL)[1] Human cDNA Library from Genome Systems.

Get cDNAs Now!

For over four years, Genome Systems, Inc. has been supplying researchers with high quality genomic clones and unequaled technical support. Our commitment to you has resulted in our being chosen as a distribution site for the I.M.A.G.E. cDNA clones.

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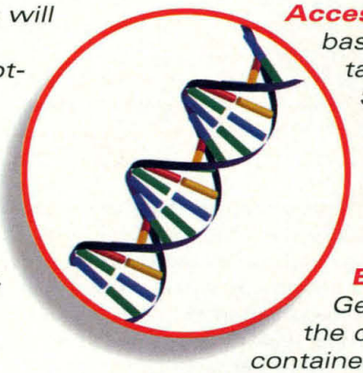
Technical Support: *The same high level of support we give our other services.*

Cost: *$17.50/clone. Individual clones will be shipped to you 24 hours after adequate growth. $14.00/plate for not-for-profit organizations, $40.00/plate for commercial entities. (Minimum order, 150 plates.)*

Characteristics of the Library

Tissue Source: *The I.M.A.G.E. cDNA clones are derived from ovary, retina, pineal gland, fetal spleen, liver, fetal liver spleen, breast, placenta, infant brain, adult brain and lung.*

Number of Clones: *200,000 clones are available.*



Database for Clones: *Over 180,000 5′ and 3′ sequences have been deposited in dbEST. Your clones can be easily accessed by computer sequence homology searches of the dbEST database (http://www.ncbi.nlm.nih.gov/dbEST/index.html).*

Access to Clones: *Choose your clone based upon your homology searches or take advantage of the Genome Systems cDNA products and services. We can screen the cDNA library for you.* ***Cost:*** *$1,995/screen. Or you can purchase our double spotted high density gridded filters.* ***Cost:*** *$2,450/filter set.*

Breakdown Your Genomic Clones: *Genome Systems will help you isolate the cDNA clones whose sequences are contained within your genomic clone.*

Related Services: *P1 or PAC/BAC™ library sreening services.*

1. *"The I.M.A.G.E. Consortium: An Integrated Molecular Analysis of Genomes and their Expression", Lennon, G.G., Auffray, C., Polymeropoulos, M., and Soares, M. B. [1995] Genomics.*

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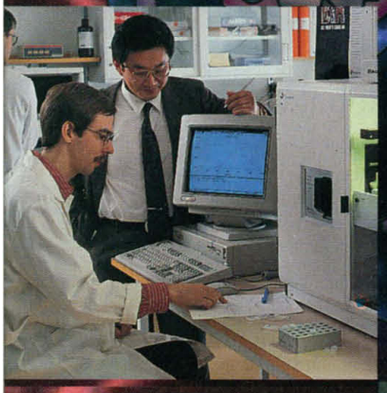

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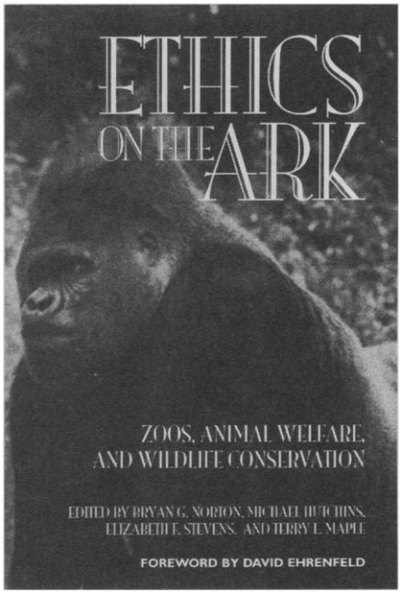
Individuals or species?
Animal rights or conservation?
Are zoos morally defensible?

ETHICS ON THE ARK

"Spendidly thought-provoking. . . . The writers for *Ethics on the Ark* (who include zoo directors, animal behaviorists, philosophers and others) grapple seriously and intelligently with the very real conflicts that lie between those who are, to be simplistic and heuristic, *for* zoos and those who are against. In turn, looming over the debate hang the huge questions of our duties to animals and of the disappearance of the natural world."
—**Martin Rowe, *Boston Book Review***



"This is the freshest look yet at the interwoven issues of animal conservation, welfare, and rights facing the North American and, indeed, global zoo community today. The authors work hard, using the most recent data and theory available from biology and ethics, and make a heroic effort to reach consensus. Achieved or not, the need to settle the differences is at crisis point, for the debate has become so fractious and fevered that the beleaguered animal kingdom is in danger of losing the best each side has to offer. The kingdom cannot now survive *any* lack of support."
—**Lee Durrell, Honorary Director, Jersey Wildlife Preservation Trust**

"Uncompromising honesty is the most striking feature of this book. If you are a reader accustomed to a televised diet of lies and deceptions, you may find yourself looking for the missing information, the stacked arguments, and the clever simplifications. You won't find any. You will find passionate and scientifically convincing essays."
—**David Ehrenfeld, Rutgers University**

"Both animal protection and zoo professionals need to have their heads knocked together more often until they recognize how much they share. This volume shows clearly that both groups have more in common than they, or others, believe and that, for the sake of the world's vanishing wildlife, both sides should build on what they share rather than spend their all too finite time and resources squabbling over real and imagined differences."
—**Andrew N. Rowan, Director, Tufts Center for Animals and Public Policy**

ZOOS, ANIMAL WELFARE, AND WILDLIFE CONSERVATION

Edited by Bryan G. Norton, Michael Hutchins, Elizabeth F. Stevens, and Terry L. Maple
Foreword by David Ehrenfeld

432 pp. Hardcover $32.50
Ethics on the Ark is the inaugural volume in the Zoo and Aquarium Biology and Conservation Series, published by Smithsonian Institution Press in conjunction with the American Zoo and Aquarium Association. Michael Hutchins, Terry Maple, and Chris Andrews, Series Editors.

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