



AMERICAN
ASSOCIATION FOR THE
ADVANCEMENT OF
SCIENCE

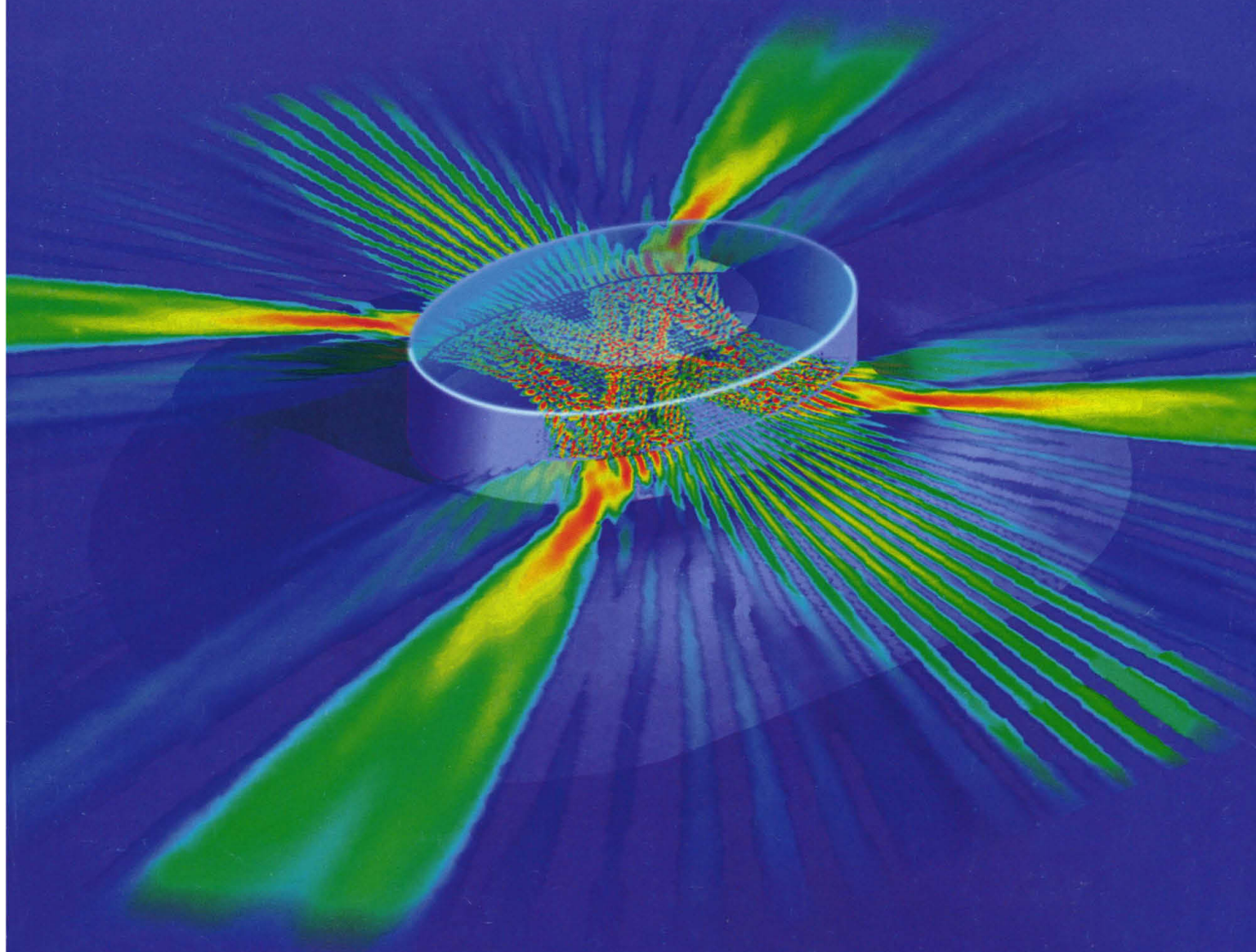
150 YEARS • 1848-1998

SCIENCE

5 JUNE 1998

\$7.00

VOL. 280 • PAGES 1493-1656



QuikChange™

SITE-DIRECTED MUTAGENESIS KIT*

The fast, easy and efficient non-PCR site-directed mutagenesis method.

Near 100% Efficiency

- ▶ Highest efficiency method
- ▶ Eliminates background
- ▶ Mutations in virtually all transformants

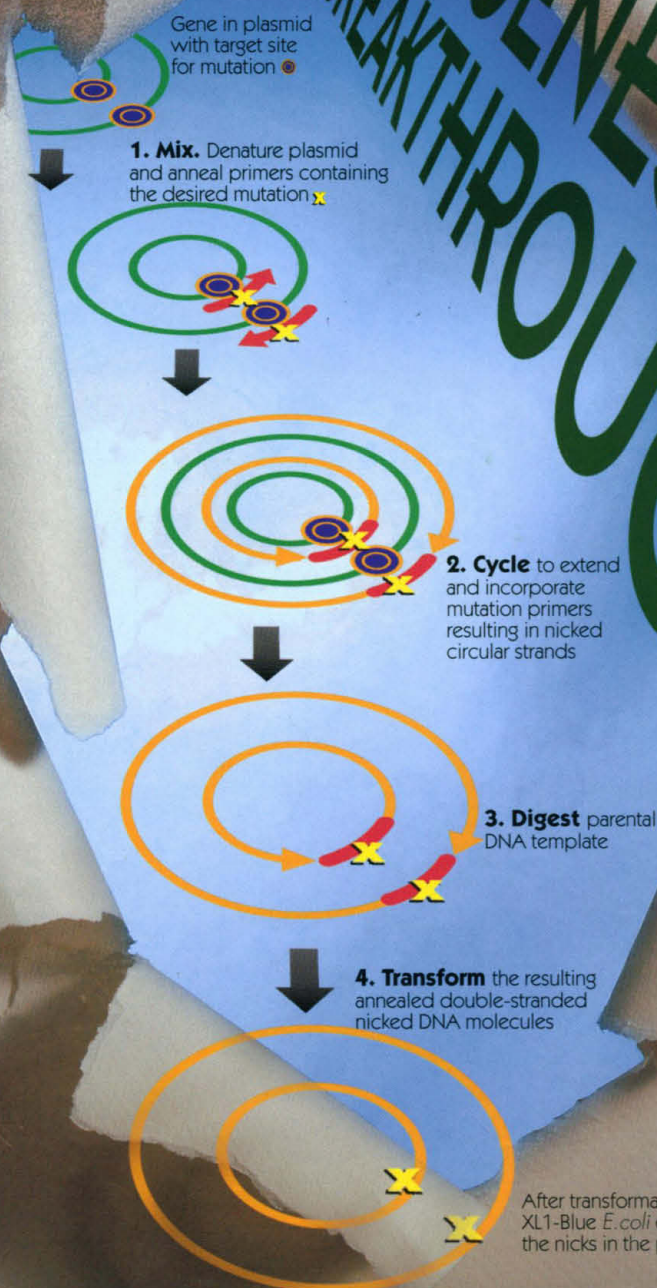
150 Times More Accurate

- ▶ Extends without PCR
- ▶ Uses high-fidelity *Pfu* DNA polymerase
- ▶ Replicates only parental DNA
- ▶ Reduces second-site mutations 150-fold

Simple One-Day Procedure

- ▶ Eliminates single-stranded DNA templates, subcloning into specialized vectors, unique restriction sites and multiple transformations
- ▶ Cuts screening time in half

1-DAY METHOD



Change the
Way You Do
Mutagenesis!

UNITED STATES:
Stratagene Cloning Systems
(800) 424-5444
INTERNET MAIL:
techservices@stratagene.com

AUSTRALIA: (02) 9417 7866
AUSTRIA: (0222) 3 68 99 51
BRAZIL: 11 5561-1771
CANADA: 905-713-1201
DENMARK: 86 10 10 55
FRANCE: (01) 34 60 24 24
GERMANY: (0130) 84 09 11
HONG KONG: 578-5839
ISRAEL: 03-5761520
ITALY: 02-58.01.34.09
JAPAN: (Funakoshi) (03)5684-1622
(Toyobo) (03)3660-4819
KOREA: (02)-556-0311
MALAYSIA: 3-7031888
NETHERLANDS: 033 495 00 94
NEW ZEALAND: 9 443-5867
NORWAY: 22 20 01 37
PORTUGAL: 01-441 06 84
SINGAPORE: 2730898
SPAIN: 1 729 03 33
SWEDEN: (8) 6800845
SWITZERLAND: (061) 6 93 05 40
THAILAND: (662) 308-0611
UNITED KINGDOM: 0800 585370

OTHER COUNTRIES CALL:
STRATAGENE USA: (619) 535-5400

*Patent pending

QuikChange™ Site-Directed Mutagenesis Kit catalog #200518



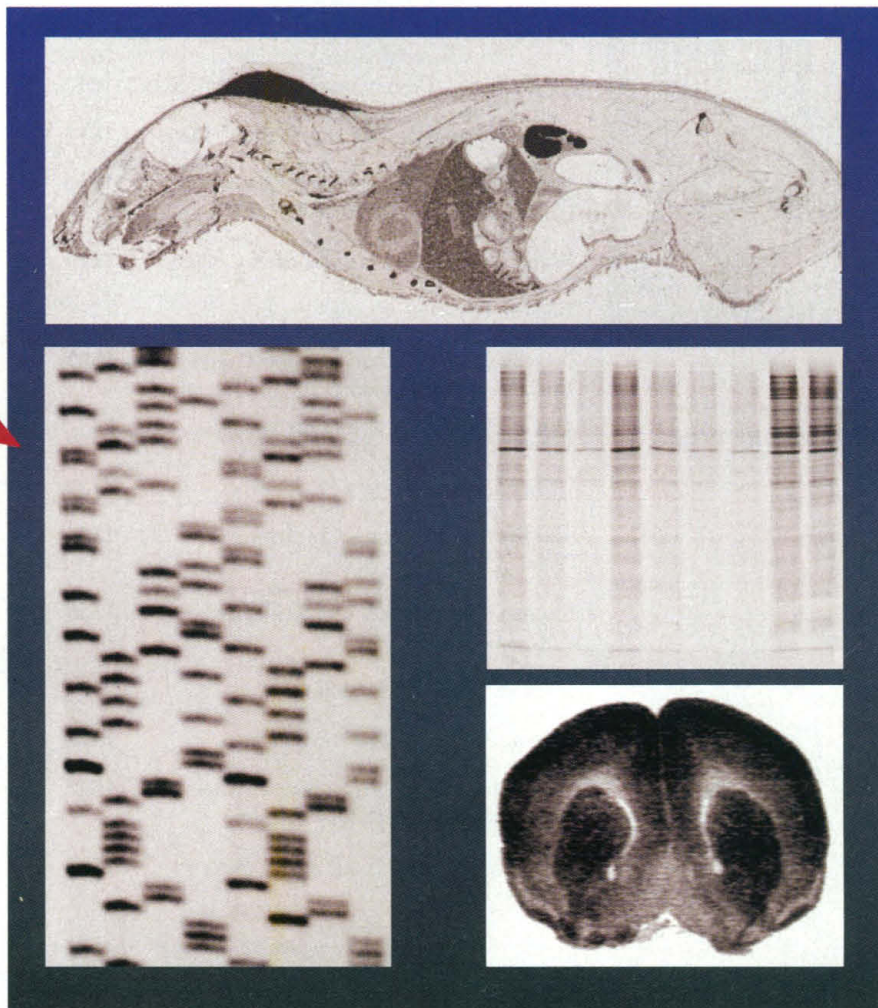
STRATAGENE®

Circle No. 35 on Readers' Service Card

Highest Performance, Lowest Price

\$17,995* USD

Cyclone Storage Phosphor System



Packard Instrument Company

800 Research Parkway
Meriden, CT 06450 U.S.A.
Tel: 203-238-2351
Toll Free: 1-800-323-1891
FAX: 203-639-2172
Web Site: <http://www.packardinst.com>
Email: webmaster@packardinst.com

Packard International Offices:

Australia 03-9543-4266 or 1 800 335 638;
Austria 43-1-2702504; Belgium 32(0)2481.85.30;
Canada 1-800-387-9559; Central Europe 43 456 2230 015;
Denmark 45-43909023 or 45-43907151;
France (33) 1 46.86.27.75; Germany (49) 6103.385-151;
Italy 39-2-33910796/7/8; Netherlands 31-50-549 1296;
Russia 7-095-259-9632; Switzerland (01) 481 69 44;
United Kingdom 44 (0)118 9844981

The Cyclone™ utilizes a state-of-the-art confocal optical design in a helical scanning system. This unique design optimizes efficiency of detection, resolution and sensitivity with a long linear dynamic range. This compact system enables the Cyclone to take advantage of the best phosphor screens and to get the highest performance for every sample.

- 42 micron pixel resolution
- Up to 10 to 100 times faster than film
- Choice of 11 phosphor screens to suit any application
- Cyclone fits your lab and your budget

Contact Packard today for more information about the new Cyclone Storage Phosphor System.

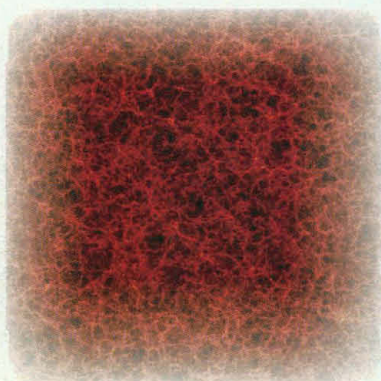
*Prices will vary outside the U.S.A. due to exchange rates, freight, duties, and local service. Offer expires September 30, 1998.

Circle No. 34 on Readers' Service Card





1527
10 years after the
Yellowstone fires



1522
Silicon universe

NEWS & COMMENT

- NIH Plans Bioengineering Initiative **1516**
Biology by Design: From Software to Skin **1517**
- Ousted Kenya Parks Head Gets Job Back **1518**
- Ireland: Peace Process Set to Boost Collaboration **1519**
- India: New Budget Boosts 'Secret' Science **1520**
- Biggest Telescope Opens One Eye **1520**
- New Rules on Human Subjects Could End Debate in Canada **1521**

RESEARCH NEWS

- Cosmos in a Computer **1522**
- Tau Protein Mutations Confirmed as Neuron Killers **1524**
- Human Origins: Old, Old Skull Has a New Look **1525**
- A Giant Snare for Monopoles **1526**
- Putting Antimatter on the Scales **1526**
- Yellowstone Rising Again From Ashes of Devastating Fires **1527**
- One-Eyed Animals Implicate Cholesterol in Development **1528**

SCIENCE'S COMPASS

- Policy**
- Shotgun Sequencing of the Human Genome **1540**
J. C. Venter, M. D. Adams, G. G. Sutton, A. R. Kerlavage, H. O. Smith, M. Hunkapiller
- Books and New Media**
- Palaeobiography **1542**
P. Copper
- Research**
- Not Noticed by Darwin? **1543**
D. Bowers
- Geometrical Shaping of Microlaser Emission Patterns **1544**
E. Gornik
- Deuteronomy?: A Puzzle of Deuterium and Oxygen on Mars **1545**
Y. L. Yung and D. M. Kass
- Glutamate Receptor Activation: A Four-Step Program **1547**
C. Miller
- An End in the Beginning **1548**
J. Dunlap
- Review**
- Dynamics of Glasses and Glass-Forming Liquids Studied by Inelastic X-ray Scattering **1550**
F. Sette, M. H. Krisch, C. Masciovecchio, G. Ruocco, G. Monaco

DEPARTMENTS

- NETWATCH** **1499**
- THIS WEEK IN SCIENCE** **1501**
- EDITORIAL** **1507**
It's Not Rocket Science—But It Can Save Lives
- LETTERS** **1507**
Wildlife Conservation in Kenya: D. Western; K. Benirschke, J. Berger, D. H. Janzen, W. Hallwachs, G. K. Meffe, N. Myers, W. D. Newmark, D. S. Woodruff, J. Bradbury; P. H. Raven; Response: C. Norman
- SCIENCESCOPE** **1515**
- RANDOM SAMPLES** **1531**
An Exo-Jupiter? • Pain at Georgetown Medical Center • Earth Joins Fossil Record • Labor Scholar Lawsuit Thrown Out
- ESSAYS ON SCIENCE AND SOCIETY** **1532**
Presidents, Experts, and Asteroids
A. Clarke
- TECH.SIGHT: PRODUCTS** **1621**

AAAS Board of Directors

Mildred S. Dresselhaus
Retiring President, Chair
M. R. C. Greenwood
President
Stephen Jay Gould
President-elect

Robert D. Goldman
Alice S. Huang
Sheila Jasanoff
Sally Gregory Kohlstedt
Marcia C. Linn
Michael J. Novacek
Neena B. Schwartz
Jean E. Taylor

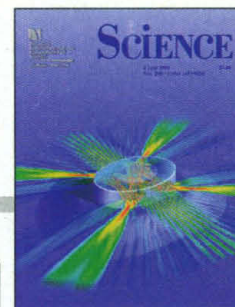
William T. Golden
Treasurer
Richard S. Nicholson
Executive Officer

■ **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. Copyright © 1998 by the American Association for the Advancement of Science. The title **SCIENCE** is a registered trademark of the AAAS. Domestic individual membership and subscription (51 issues): \$108 (\$60 allocated to subscription). Domestic institutional subscription (51 issues): \$295. Foreign postage extra: Mexico, Caribbean (surface mail) \$55; other countries (air assist delivery) \$90. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. IPM #1069624. Printed in the U.S.A.

COVER

A cylindrical semiconductor microlaser has been deformed from circular symmetry. The deformation in general leads to a chaotic behavior of the light rays in the resonator. For the laser shown the deformation results in a "bow-tie"-shaped intensity pattern inside the

microresonator, strongly directional light emission (yellow-green "beams"), and 1000 times the light output that would be achieved from the corresponding undeformed laser. See p. 1556 and the Commentary on p. 1544. [Illustration: K. D. Drake, Bell Labs, Lucent Technologies]



RESEARCH ARTICLES

High-Power Directional Emission from Microlasers with Chaotic Resonators

C. Gmachl, F. Capasso, E. E. Narimanov, J. U. Nöckel, A. D. Stone, J. Faist, D. L. Sivco, A. Y. Cho

Role of the CLOCK Protein in the Mammalian Circadian Mechanism

N. Gekakis, D. Staknis, H. B. Nguyen, F. C. Davis, L. D. Wilsbacher, D. P. King, J. S. Takahashi, C. J. Weitz

REPORTS

Coupled ^{186}Os and ^{187}Os Evidence for Core-Mantle Interaction

A. D. Brandon, R. J. Walker, J. W. Morgan, M. D. Norman, H. M. Prichard

Distribution of Rock, Metals, and Ices in Callisto

J. D. Anderson, G. Schubert, R. A. Jacobson, E. L. Lau, W. B. Moore, W. L. Sjogren

Detection of Atomic Deuterium in the Upper Atmosphere of Mars

V. A. Krasnopolsky, M. J. Mumma, G. R. Gladstone

Atmosphere-Surface Interactions on Mars: $\Delta^{17}\text{O}$ Measurements of Carbonate from ALH 84001

J. Farquhar, M. H. Thiemens, T. Jackson

Localization of Metastable Atom Beams with Optical Standing Waves: Nanolithography at the Heisenberg Limit

K. S. Johnson, J. H. Thywissen, N. H. Dekker, K. K. Berggren, A. P. Chu, R. Younkin, M. Prentiss

Silicalix-[n]-phosphaarenes: Macrocyclic Ligands Based on Dicoordinate Phosphoric Centers

N. Avarvari, N. Mézailles, L. Ricard, P. Le Floch, F. Mathey

High- T_c Superconductors in the Two-Dimensional Limit: $[(\text{Py}-\text{C}_n\text{H}_{2n+1})_2\text{HgI}_4]\text{-Bi}_2\text{Sr}_2\text{Ca}_{m-1}\text{Cu}_m\text{O}_y$ ($m = 1$ and 2)

J.-H. Choy, S.-J. Kwon, G.-S. Park

Ribozyme-Mediated Repair of Sick β -Globin mRNAs in Erythrocyte Precursors

N. Lan, R. P. Howrey, S.-W. Lee, C. A. Smith, B. A. Sullenger

The Tetrameric Structure of a Glutamate Receptor Channel

C. Rosenmund, Y. Stern-Bach, C. F. Stevens

Closing the Circadian Loop: CLOCK-Induced Transcription of Its Own Inhibitors *per* and *tim*

T. K. Darlington, K. Wager-Smith, M. F. Ceriani, D. Staknis, N. Gekakis, T. D. L. Steeves, C. J. Weitz, J. S. Takahashi, S. A. Kay

Teratogen-Mediated Inhibition of Target Tissue Response to *Shh* Signaling

M. K. Cooper, J. A. Porter, K. E. Young, P. A. Beachy

Inhibition of a *Mycobacterium tuberculosis* β -Ketoacyl ACP Synthase by Isoniazid

K. Mdluli, R. A. Slayden, Y. Zhu, S. Ramaswamy, X. Pan, D. Mead, D. D. Crane, J. M. Musser, C. E. Barry III

Axonal Swellings and Degeneration in Mice Lacking the Major Proteolipid of Myelin

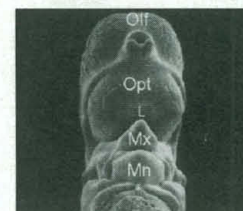
I. Griffiths, M. Klugmann, T. Anderson, D. Yool, C. Thomson, M. H. Schwab, A. Schneider, F. Zimmerman, M. McCulloch, N. Nadon, K.-A. Nave

Inhibition of Cell Migration, Spreading, and Focal Adhesions by Tumor Suppressor PTEN

M. Tamura, J. Gu, K. Matsumoto, S.-i. Aota, R. Parsons, K. M. Yamada

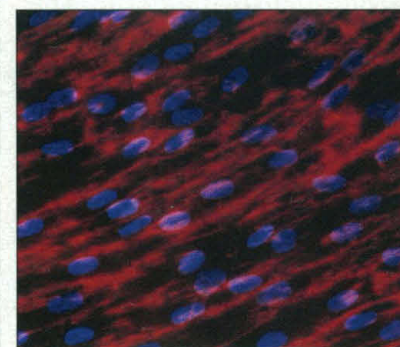
Entry of Alphaherpesviruses Mediated by Poliovirus Receptor-Related Protein 1 and Poliovirus Receptor

R. J. Geraghty, C. Krummenacher, G. H. Cohen, R. J. Eisenberg, P. G. Spear



1528 &
1603

Teratogens and
Sonic hedgehog



1614

PTEN tumor suppressor
regulating adhesion


Indicates accompanying feature

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: \$7.00 per issue prepaid includes surface postage; bulk rates on request.
Authorization to photocopy: material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that \$4.00 per article is paid directly to CCC, 222 Rosewood Drive, Danvers, MA 01923. The identification code for *Science* is 0036-8075/93 \$4.00. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

On the Web

This week's **Enhanced Research Commentary** describes how lasers can benefit from chaos
www.sciencemag.org





Are your blotting signals getting blurred in the background noise? Are your tests as DNA-sensitive as they should be? Clearly, you could do with a little help.

Hybond™

The advanced performance formula of Hybond-XL nylon membranes has been specifically designed to give you more information per gel.

You can look forward to outstanding signal-to-noise ratio: up to five times better than other membranes. You can detect minor bands more reliably and with shorter exposure times. So you get better results in even less time.

If you're already using a radioactive detection method for nucleic acid blotting and hybridisation, why compromise with the membranes you're using?

All clear? Now try Hybond-XL for free! Contact us today for your free sample of Hybond-XL or for more information about other Hybond products call 1-800 526 3593 in the USA; in Europe (+44) (0) 1494 544550; from the rest of the world (+44) (0) 1494 544100. Or visit us on the web: www.apbiotech.com/hybond

Let's get a
few things
clear about
Hybond-XL

Amersham Pharmacia Biotech UK Limited, Amersham Place, Little Chalfont, Buckinghamshire, England HP7 9NA. All goods and services are sold subject to the terms and conditions of sale of the company within the Amersham Pharmacia Biotech group which supplies them. A copy of these terms and conditions of sale is available on request.

Circle No. 22 on Readers' Service Card



amersham pharmacia biotech



Replaced by the copy machine.



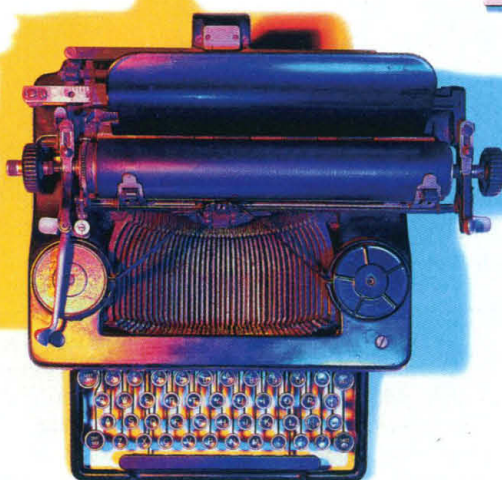
Replaced by the compact disc.



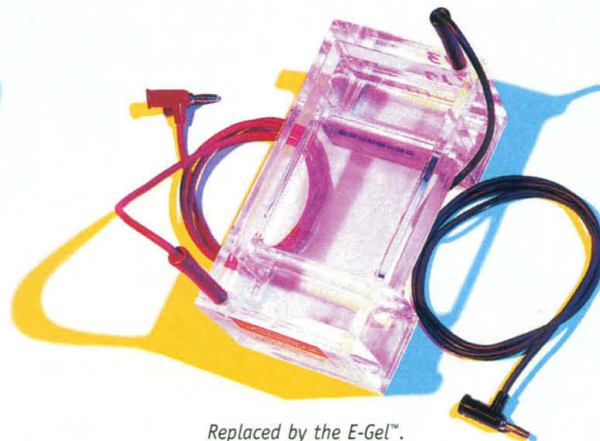
Replaced by the boom box.



Replaced by the calculator.



Replaced by the personal computer.



Replaced by the E-Gel™.

E-Gel™. The innovation that's replacing conventional electrophoresis.

There comes a time when every technology is replaced by a new innovation. For agarose gel electrophoresis that time is now! E-Gels™ from Invitrogen represent a breakthrough in agarose gel electrophoresis technology. E-Gels™ make electrophoresis faster, easier, and more convenient than ever before.

E-Gels™ are bufferless, precast agarose gels that allow you to perform electrophoresis at least two-times faster than conventional methods. Each E-Gel™ contains all of the elements you need for high resolution electrophoresis—agarose, an ion exchange matrix for proper buffering



conditions, ethidium bromide, and electrodes—all packaged into a convenient UV transparent cassette.

Simply snap the cassette into the unique E-Gel™ base, plug it into your power supply, and go.

With E-Gels™ you don't have to prepare buffers; weigh, melt, and pour agarose; or wait for your gel to solidify.

Simplify and accelerate your electrophoresis with E-Gels™.

Call Invitrogen today and order a Starter Pak of 1.2, 2, or 4% E-Gels™. See for yourself why E-Gels™ are the innovation that's replacing conventional agarose gel electrophoresis.

Circle No. 27 on Readers' Service Card

European Headquarters:

Invitrogen BV
De Schelp 12, 9351 NV Leek
The Netherlands
Tel: +31 (0) 594 515 175
Fax: +31 (0) 594 515 312
Email: tech_service@invitrogen.nl

Toll Free Phone Numbers:

Belgium 0800 111 73
Denmark 800 188 67
Finland 990 31 800 5345
France 00 31 800 5345
Germany 0130 8100 43
The Netherlands 0800 022 88 48
Norway 800 113 70
Sweden 020 795 369
Switzerland 0800 551 966
United Kingdom 0800 96 61 93

Distributors:

Australia 1 800 882 555
China 010 6255 3477
Hungary 01 280 3728
India 91 80 839 1453
Israel 02 652 2102
Italy 02 38 19 51
Japan 03 5684 1616
Korea 82 2 569 6902

Malaysia 03 432 1357
Poland 058 41 42 26
Portugal 01 453 7085
Singapore 65 779 1919
Slovak Republic 07 3707 368
Spain 03 450 2601
Taiwan 080 231 530
Thailand 246 7243

From all other countries, contact our European headquarters at +31 (0) 594 515 175.

United States Headquarters:

Invitrogen

1600 Faraday Avenue
Carlsbad, California 92008
Tel: 1-800-955-6288
Fax: 760-603-7201

Email: tech_service@invitrogen.com
<http://www.invitrogen.com>

THIS WEEK IN SCIENCE

edited by BROOKS HANSON

Glass dynamics

The dynamics of disordered systems differ inherently from those of crystalline materials, and many fundamental questions have remained unanswered because of experimental limitations. In a review, Sette *et al.* (p. 1550) examine recent progress at the European Synchrotron Radiation Facility, a third-generation radiation source, where inelastic x-ray scattering experiments with millielectron volt energy resolution have been performed on a range of glass-forming liquids, primarily glycerol. The data reveal how the microscopic dynamics of these materials, especially collective excitations at short wavelengths, are related to structural relaxation processes and other properties.

Expanded superconductors

The layered high-temperature (high- T_c) superconductors are made up of CuO_2 planes separated by other cations. Choy *et al.* (p. 1589) show that the layers of the $\text{Bi}_2\text{Sr}_2\text{CuO}_y$ and $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_y$ can be exfoliated by intercalation, first with HgI_2 and followed by alkylpyridinium iodides. Even though this process separated the planes by distances of tens of angstroms, magnetization measurements indicate that there was little or no change in T_c . These results suggest that interlayer coupling effects are not critical for superconductivity. Such exfoliated superconducting layers may also have thin-film applications.

Cored plumes

The origin and evolution of hot upwellings (hot spots) in Earth's mantle can only be remotely

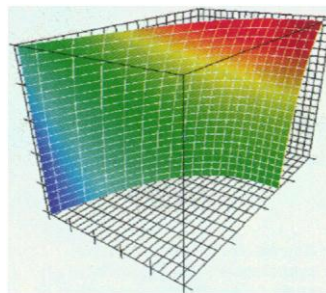
High laser output from chaotic resonators

At the heart of a laser is its resonator, which allows light to pass back and forth through the active material and provides the feedback for stimulated emission. Recently, microdisk semiconductor lasers have been developed in which light, trapped by total internal reflection inside a circularly symmetric cavity, exhibits "whispering gallery modes." Although their small size is attractive for device applications, their output is low. Gmachl *et al.* (p. 1556; see the cover and the commentary by Gornik, p. 1544) now demonstrate that devices with an asymmetric resonant cavity exhibit an increase in far-field power of up to three orders of magnitude because of the formation of "bow-tie" resonances. The effects of refraction at high deformations in these high-index semiconductors lead to chaotic behavior of the light rays as they circulate in the resonant cavity.

detected by chemical tracers in rocks sampled at or near the surface or by the behavior of seismic waves. One model is that the hot spots are produced by plumes rising from the core-mantle boundary. Brandon *et al.* (p. 1570) measured the osmium isotopic abundances in lavas from the classic hot spot, Hawaii. They found that the lavas were enriched in ^{186}Os and ^{187}Os , which are produced by decay of rhenium and platinum isotopes that are now concentrated in Earth's core. The data suggest that the Hawaiian plume originated at the core mantle boundary. Thus, the coupled isotopic enrichments may be used to distinguish a deep plume from a shallow plume.

Callisto's layers

Callisto is the outermost of the four Galilean satellites that orbit Jupiter. One close flyby of the Galileo spacecraft had yielded radio doppler data suggesting that Callisto was not differentiated (that is, a homogeneous mixture of ice, rock and metal from the surface to the center). Now, Anderson *et al.* (p. 1573) have refined this model based on more accurate radio doppler data from a third



flyby. Callisto may be partially differentiated into an outer layer of ice, a middle layer of mixed rock and ice, and a rocky, metallic core.

The Mars cycle

Mars probably had liquid water flowing on its surface soon after its formation. Measuring the hydrogen and oxygen isotopic abundances in martian materials provides one of the best methods for determining how much water Mars started with, how much has been lost, and how much remains frozen or trapped beneath the surface. Krasnopolsky *et al.* (p. 1576) have used the Hubble Space Telescope to estimate the fractionation of hydrogen and deuterium, which could be explained by a planetwide reservoir of water ice about 5 meters thick. Farquhar *et al.* (p. 1580) have measured the oxygen isotopic

abundances of carbonate grains in martian meteorite ALH 84001 and found that the isotopes are fractionated in the carbonates independently of their mass, unlike previous measurements of other silicate minerals. This suggests that the oxygen may be exchanged between ozone and carbon dioxide, requiring two exchange reservoirs: ozone from the atmosphere and carbon dioxide from the crust. Where the oxygen is stored in the crust remains unresolved as discussed in the accompanying commentary by Yung and Kass (p. 1545).

Rhythm mechanism

Circadian rhythms maintain organismal physiology through the daily light-dark cycle. Molecular details of the regulation of clock components are described in mammals by Gekakis *et al.* (p. 1564) and in *Drosophila* by Darlington *et al.* (p. 1599). Both reports describe how a clock component and a transcription factor subunit interact to regulate transcription of other clock components. A commentary by Dunlap (p. 1548) explains the importance of the findings in completing our picture of how rhythmic cycles are established and maintained.

Nanopatterns with infrared gratings

One approach to nanoscale lithographic patterning of surfaces is to use excited, metastable rare gas atoms, such as argon, or other compounds to chemically alter an overlayer; for example, adsorbed hydrocarbons can form a carbonaceous material that can be used to resist etching. Normally, the

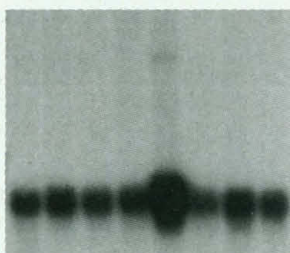
(Continued on page 1503)

Quality. Selection. Results.

Multiple Tissue Northern Blots

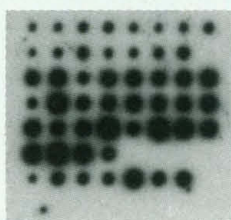
Illustration inspired by the art of René Magritte (1898–1967).

kb
9.5
7.5
4.4
2.4
1.35



Human MTN Blot II (#7759-1) hybridized with the **Human HPRT cDNA Control Probe (#9807-1)**. Lane 1: spleen. Lane 2: thymus. Lane 3: prostate. Lane 4: testis. Lane 5: ovary. Lane 6: small intestine. Lane 7: colon. Lane 8: peripheral blood leukocyte.

[Look for our new 12-lane MTN Blots!](#)



Hybridization of an MHC cDNA probe to the Human Master Blot (#7770-1). Hybridization signals vary in intensity between tissues, indicating differential expression. The blot consists of 50 different poly A⁺ RNAs arrayed on a membrane. Each RNA is normalized using eight housekeeping genes.

Find the latest MTN Blot citations with **CLONTECH's Citation Search** at www.clontech.com/clontech/Citations.html

Circle No. 31 on Readers' Service Card

In Germany please contact **CLONTECH GmbH** • Tel: 06221 34170 Fax: 06221 303511

In the UK please contact **CLONTECH UK Ltd.** • Tel: 01256 476500 Fax: 01256 476499

In Japan please contact **CLONTECH Japan Ltd.** • Tel: 03 5643 3251 Fax: 03 5643 3252

Australia: 61 2 9417 7866 ■ Austria and Eastern Europe: 43 1 889 1819 ■ Belgium/Luxemburg: 0 800 1 9815 ■ Canada: Now call CLONTECH direct • 800 662 2566 ■ China: BEIJING YUANGPING BIOTECH • 86 10 68187551; GENE CO. LTD. • 86 21 64748700; HW SCIENCE & TECHNOLOGY DEVELOPMENT CO., LTD. • 86 22 26647265; SINO-AMERICAN BIOTECH CO. • 86 21 6402 2371; WATSON BIOMEDICALS, INC. • 86 21 65572386 ■ Czech Republic: 420 19 65214 ■ Egypt: 202 349 8311 ■ Finland: 9708 596 19 ■ France: 33134 602424 ■ Germany: CLONTECH GmbH • 49 6221 34170 ■ Greece: 30 1 483 1190 ■ Hong Kong: 852 2646 6101 ■ India: 091 11 54 21714 ■ Israel: 972 4 9960595 ■ Italy: 55 5 001871 ■ Japan: CLONTECH Japan Ltd. • 81 3 5643 3251 ■ Korea: 82 2 556 0311 ■ Malaysia: 603 777 2608 ■ Mexico: 525 281 4718 ■ The Netherlands: 31 33 495 00 94 ■ Scandinavia: 46 8 749 5940 ■ Singapore: 65 775 7284 ■ Spain/Portugal: 34 1 630 0379 ■ Switzerland: 41 61 272 3924 ■ Taiwan: 886 2 27202215 ■ Thailand: 662 530 3805 ■ Turkey: 90 216 385 8321 ■ United Kingdom: CLONTECH UK Ltd. • 44 1256 476500 rev. 4/22/98

CLONTECH's MTN™ Blots have been cited in more than 1,600 journal articles—you can depend on them to provide consistent, reliable results. What separates MTN Blots from others is that each is made from **Premium RNA™**, poly A⁺ RNA of the highest quality. Human, Mouse, and Rat MTN Blots are available featuring from four to twelve tissues or cell lines each. CLONTECH also offers **Human and Mouse Master Blots™**, also made with Premium RNA, for high-throughput expression profiling. Call and order today!

CLONTECH
NOW YOU CAN.

1020 East Meadow Circle, Palo Alto, California 94303 USA

Tel: 800-662-2566 (CLON) 650-424-8222 • Fax: 800-424-1350 650-424-1088

E-mail: products@clontech.com orders@clontech.com • Internet: www.clontech.com

© 1998, CLONTECH Laboratories, Inc.

(AD85419)



(Continued from page 1501)

patterning is achieved with physical masks to block the metastable atoms or with optical gratings that steer the atoms into lines. Johnson *et al.* (p. 1583) have taken a different approach by using an infrared optical grating to pump a de-excitation transition. Atoms are de-excited everywhere except at the nodes of the grating, thus forming lines of metastable atoms with nanometer-scale widths that impinge on the surface.

Macrocyclic phosphorus ligands

Phosphorus is one of the main ligating atoms in transition metal chemistry. However, few macrocycles containing phosphorus are known; the ones that are known contain tricoordinate phosphorus and many consist of mixtures of conformational isomers. Avarvari *et al.* (p. 1587) have synthesized macrocycles containing three or four bicoordinate phosphorus atoms that coordinate transition metal ions. Such macrocyclic ligands may prove important in catalysis involving transition metals and because of their potential reducing properties.

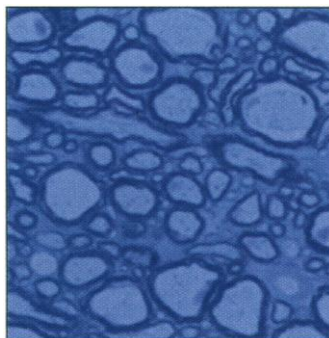
The FAKs of tumor suppression

Alterations of the putative tumor suppressor gene PTEN occur in a wide range of human cancers, particularly endometrial cancer and glioblastoma. The PTEN protein shares sequence motifs with the cytoskeletal protein tensin and is a phosphatase, but its cellular function and substrates are unknown. In experiments with fibroblasts, Tamura *et al.* (p. 1614) show

that wild-type PTEN inhibits cell migration, spreading, and adhesion, most likely through dephosphorylation of the focal adhesion kinase FAK. This cell surface role of PTEN distinguishes it from other tumor suppressors, which typically function in the nucleus.

Axonal degeneration

Mutations in proteolipid protein (PLP) are responsible for neurological problems in humans and mice. The PLP is thought to help to stabilize myelin in the central nervous system but is not required for the production of the myelin sheath itself. Griffiths *et al.* (p. 1610) now



report that axon degenerate locally in aging mice lacking PLP. Their data point to a previously unsuspected role for the oligodendrocytes that wrap myelinated axons in maintaining axonal integrity.

Therapeutic regulation

One of the problems of gene therapy is that the transferred gene needs to be brought under the same cellular regulation as the original one. This problem is especially severe in the regulation of globin gene expression needed to have successful gene therapy for sickle cell anemia. Lan *et al.* (p. 1593) circumvent-

ed this problem by targeting the β -globin transcripts themselves. They used a group I ribozyme to convert the mutant β -globins into γ -globins, which retard the development of sickling in red blood cells. These experiments were done in erythrocyte precursors isolated from people with the disease; future experiments will be needed to determine efficacy in actual patients.

Receptor stoichiometry

Glutamate receptors are the most abundant neurotransmitter receptors in the brain. These receptors evidently malfunction in a large number of neurological diseases, including, for example, stroke and epilepsy. By drawing an analogy from other ligand gated receptors it was often assumed that glutamate receptors were made of five subunits. Rosenmund *et al.* (p. 1596; see the commentary by Miller, p. 1547) present evidence that they are made up of only four subunits from single-channel recordings, kinetic analysis, electrophysiological recordings, and clever antagonist application experiments.

Teratogen target

Certain steroidal alkaloids in plants are classified as mammalian teratogens because they induce cyclopia, a developmental defect characterized by the absence of median facial structures and an undivided forebrain. Cooper *et al.* (p. 1603; see news story by Strauss, p. 1528) show that these teratogens, which include cyclopamine and jervine, inhibit the response of target tissues to Sonic hedgehog (Shh), a secreted signaling protein that has a crucial role in the

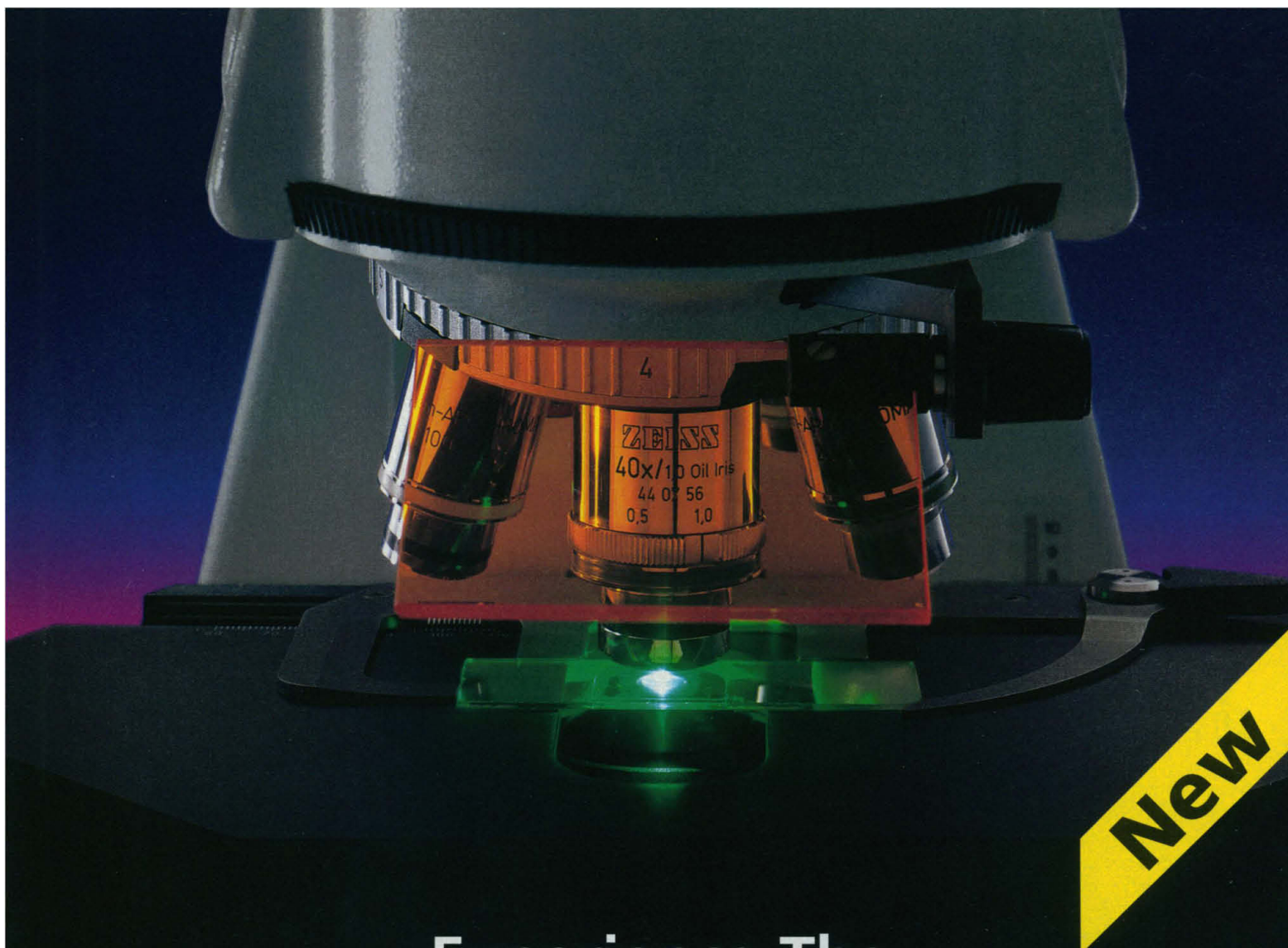
patterning of the head and brain. These compounds resemble cholesterol in structure and alter cholesterol biosynthesis, but notably they do not affect the autoproteolytic cleavage of Shh, a reaction that requires cholesterol and is essential for Shh's biological activity.

Isoniazid-resistance in tuberculosis

Resistance to the tuberculosis drug isoniazid has become a significant problem. In some cases, resistance has been traced to mutations in two genes *katG* and *inhA*, but they cannot account for all clinical isolates or the accumulations of a saturated fatty acid that is associated with sensitivity. Mdluli *et al.* (p. 1607) found that an enzyme in the pathway of mycolic acid synthesis, β -ketoacyl ACP synthase (a product of the *kasA* gene), is inhibited by isoniazid. Mutations in this enzyme were found as isoniazid-resistant clinical isolates in the absence of changes in other genes.

Common entry

Geraghty *et al.* (p. 1618) find that poliovirus receptor-related protein 1 (which they call Hve-C) is a general mediator of alphaherpesvirus entry into the host cell. Although other coreceptors have been found, this is the first to mediate entry of both herpes simplex virus types 1 and 2. Thus, two very different types of viruses (herpesviruses and picornaviruses) use the same receptors. This finding may help design therapies or vaccines that will prevent infection of mucosal surfaces and the spread of the virus to the nervous system.



Experience The Pleasure Of Routine

Wishes come true

The **Axioskop 2** is the routine microscope you have always longed to have. Its ICS optics provide top-quality images, and its operating convenience adds extra efficiency to your work. The microscope that turns routine into a pleasure.

Fluorescence four-fold

The **Axioskop 2** is excellently equipped to provide the flexibility and optimal illumination required in fluorescence work: Reflector turret for 4 fluorescence modules, 6-place excitation filter slider, plus the power of 100 watts.

Motorized comfort

There is no need any more to memorize every detail. In the **Axioskop 2 MOT**, both stage focusing and universal condenser setting (including Koehler) are motorized and can be automated. Contact your Zeiss representative today for the full story.

ZEISS

Extreme Accuracy

SeqMan™ II Sequence Assembly Software

When you're leading edge, you can't afford mistakes.

Only SeqMan™ II has DNASTAR's unique trace analysis algorithm. So SeqMan™ II generates the consensus sequence with greater accuracy than other sequence assemblers. And that's not all. SeqMan™ II:

- Displays all six translation frames and multiple trace alignments in one editing window.
- Assembles up to 32,000 sequences per project.
- Automatically screens out contaminating sequences.
- Delivers expert performance on Win95/NT and Mac.

There's more. The demo's free. Go to the extreme. Call DNASTAR for a free demo.

SeqMan™ II
expert sequence analysis software



© DNASTAR, Inc.

DNASTAR, Inc. (USA) 1228 S. Park St., Madison, WI 53715
Phone: 608•258•7420 FAX: 608•258•7439 email: info@dnastar.com www.dnastar.com

IN GERMANY: GATC GmbH, Fritz-Arnold-Str. 23, D-78467 Konstanz, Germany
Phone: 49•7531•81600 FAX: 49•7531•816081 email: sales@gatc.de

IN JAPAN: Teijin Systems Technology Ltd., 2-38-16 Hongo, Bunkyo-ku, Tokyo 113-0033 Japan
Phone: 3•3818•3176 FAX: 3•3818•3518 email: sales@mlg.co.jp

Circle No. 39 on Readers' Service Card

DNASTAR
DNASTAR

www.sgi.com/go/workstations

Performance measured in Breakthrough Discoveries.

THE POWER TO EXPLORE, DISCOVER AND SIMULATE THE POSSIBILITIES.

Transforming data into powerful information is the key to success for every discovery research organization. Silicon Graphics® workstations are the most powerful means of doing just that through visualization. Our systems combine outstanding performance, industry-leading graphics and the broadest range of applications for today's leading pharmaceutical, chemical and biotech companies.

Silicon Graphics O2™, OCTANE™ and Onyx2™ workstations comprise the broadest range of scalable high-performance platforms. Enhanced CPUs offer greater applications performance so you can tackle more complex designs and analyses, handle bigger data sets, create powerful models and generate remarkable images. Focus more clearly on any problem. Turn data into understanding, turn understanding into insight. Reach the breakthroughs that only Silicon Graphics workstations can help you discover.

© 1998 Silicon Graphics, Inc. All rights reserved. Silicon Graphics and Onyx are registered trademarks, and O2, OCTANE, Onyx2 and the Silicon Graphics logo are trademarks, of Silicon Graphics, Inc. Images courtesy of MSI and Tripos.

* Price quoted is valid for U.S. only.

Circle No. 19 on Readers' Service Card



Desktop Performers.

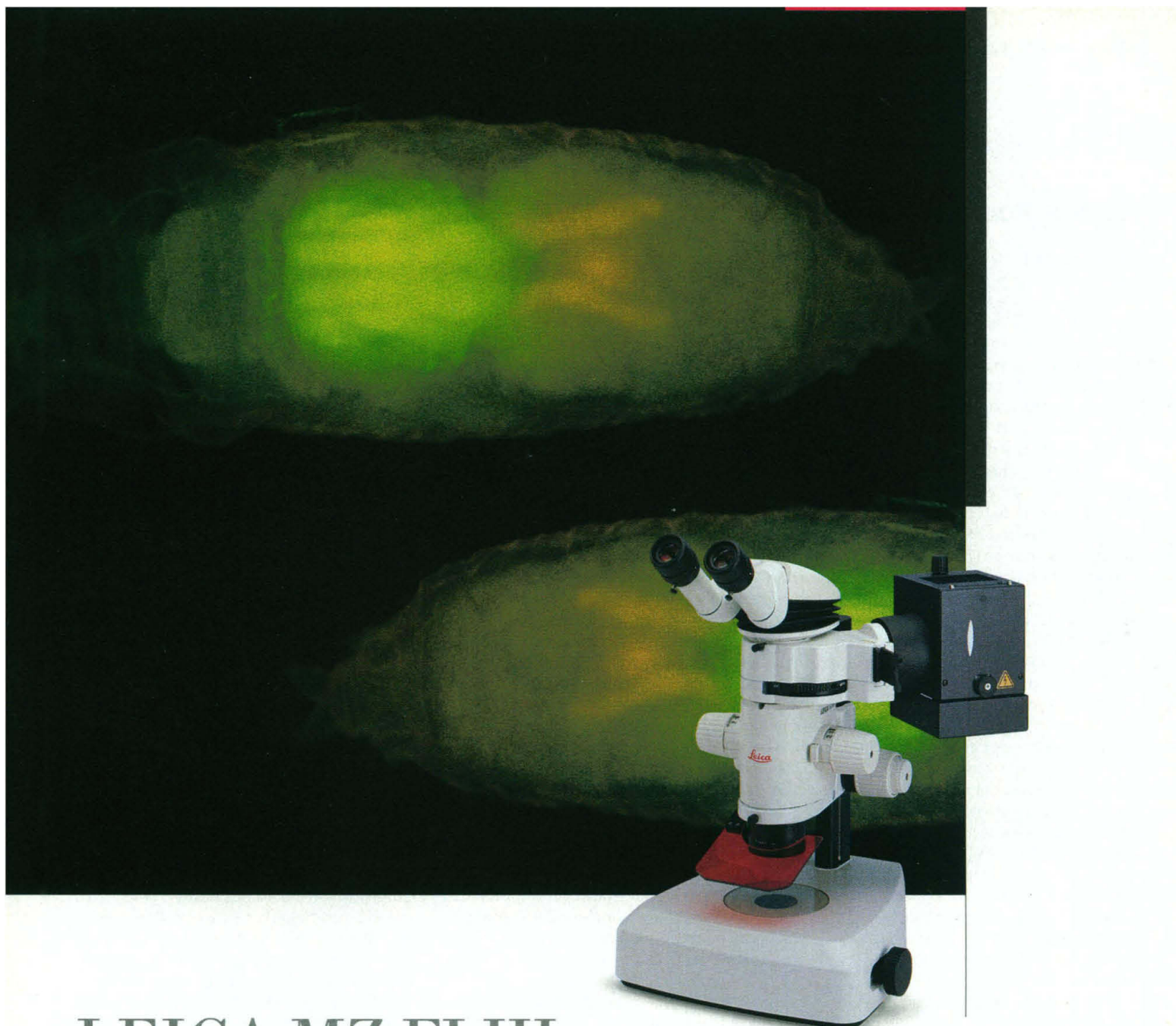
The O2 and OCTANE workstation solutions starting at \$5902*.

at the core of

science



SiliconGraphics



LEICA MZ FLIII

Shining advantages

The new LEICA MZ FLIII opens up interesting new perspectives in 3D viewing. It is the first fluorescence stereomicroscope with patented separate beam path (TripleBeam™) for the fluorescence illuminator. It offers other advantages, such as the patented filter system (FLUOIII™), the comprehensive range of filters, and the made-to-measure program of modular ergonomic accessories. Internet, or Leica itself, will give you more information about this new dimension in stereomicroscopy. The innovative technology of the LEICA MZ FLIII brings shining advantages. <http://www.leica.com/stereomic-ch/product/mzfl.htm>

Leica Microscopy Systems Ltd
Business Unit SM
CH-9435 Heerbrugg (Switzerland)

Telephone +41 71 727 31 31
Fax +41 71 727 46 76
For local agencies: www.leica.com

Leica

Circle No. 20 on Readers' Service Card

Missing

Is the Reader Service card missing from this issue of SCIENCE? Then use our new Online Reader Service to receive information on products and services advertised in this or any issue of SCIENCE. Online Reader Service requests are sent instantly via the Internet to all the companies you select. This means you receive detailed product information... fast.

www.sciencemag.org

Go to Electronic Marketplace & select Reader Service Card.

SCIENCE
Online Reader Service

www.sciencemag.org SCIENCE

Editorial

Assistant Managing Editor: Dawn McCoy; **Senior Editors:** Gilbert J. Chin, R. Brooks Hanson, Pamela J. Hines, Barbara Jasny, Paula A. Kiberstis, Linda J. Miller, L. Bryan Ray, Phillip D. Szuromi; **Associate Editors:** Beverly A. Purnell, Linda R. Rowan; **Letters and Technical Comments:** Christine Gilbert, Editor; Steven S. Lapham, Associate Letters Editor; Charlene King, Assistant; **Science's Compass:** Katrina L. Kelner, David F. Voss, Senior Editors; Sherman J. Suter, Associate Book Review Editor, Brent Gendelman, Jeffrey Hearn, Assistants; Janet Kegg, Information Specialist; **Tech.Sight:** Richard Peters, Robert Sikorski, Contributing Editors; **Editing:** Cara Tate, Supervisor; Harry Jach, Jason Llewellyn, Christine M. Pearce, Senior Copy Editors; Jeffrey E. Cook, Etta Kavanagh, Joshua Marcy; **Copy Desk:** Ellen E. Murphy, Supervisor; Joi S. Granger, Abigail Hollister, Monique Martineau, Beverly Shields; Jessica Moshell, Assistant; **Editorial Support:** Carolyn Kyle, Editorial Assistant; Candace Gallery, Amy Herda, Josh Lipicky, Patricia M. Moore, Anita Wynn, Manuscript Assistants; **Administrative Support:** Sylvia Kihara; **Computer Specialist:** Roman Frillarte

News

News Editor: Colin Norman; **Features Editor:** Tim Appenzeller; **Deputy News Editors:** Elizabeth Culotta (contributing editor), Jean Marx, Jeffrey Mervis, Richard Stone; **News & Comment/Research News Writers:** Constance Holden, Jocelyn Kaiser, Richard A. Kerr, David Kestenbaum, Andrew Lawler, Eliot Marshall, Elizabeth Pennisi, Robert F. Service, Gretchen Vogel; **Bureaus:** Berkeley, CA: Marcia Barinaga (contributing correspondent); San Diego, CA: Jon Cohen; Chicago, IL: James Glanz; **Copy Editors:** Linda B. Felaco, Daniel T. Helgerman; **Contributing**

Editor-in-Chief: Floyd E. Bloom
Editor: Ellis Rubinstein
Managing Editor: Monica M. Bradford
Deputy Editors: Philip H. Abelson (*Engineering and Applied Sciences*); John I. Brauman (*Physical Sciences*); Thomas R. Cech (*Biological Sciences*)

Correspondents: Barry A. Cipra, Ann Gibbons, Charles C. Mann, Anne Simon Moffat, Virginia Morell, Gary Taubes, Ingrid Wickelgren; **Administrative Support:** Scherraine Mack, Fannie Groom

Production & Art

Production: James Landry, Director; Wendy K. Shank, Manager; Elizabeth A. Harman, Assistant Manager; Clarence A. Foules, Vicki J. Jorgensen, Cynthia M. Penny, Kameaka Williams, Associates
Art: Amy Decker Henry, Design Director; C. Faber Smith, Art Director; Elizabeth Carroll, Associate Art Director; Katharine Sutliff, Scientific Illustrator; Holly Bishop, Preston Morrighan, Darcel Pugh, Patricia M. Riehn, Graphics Associates; Leslie Blizard, Photo Researcher
Technology Manager: Christopher J. Feldmeier

Science International: Europe Office

Editorial: Richard B. Gallagher, Office Head and Senior Editor; Stella M. Hurtle, Peter Stern, Julia Uppenbrink, Associate Editors; Belinda Holden, Editorial Associate; **News:** Daniel Clery, Editor; Nigel Williams, Correspondent; Michael Balter (Paris), Contributing Correspondent; **UK Editor, Science's Next Wave:** John MacFarlane; **Administrative Support:** Janet Mumford, Liz Ellis; **Asia Office:** Japan News Bureau: Dennis Normile, Contributing Correspondent; China Representative: Hao Xin

ScienceNOW: www.sciencenow.org
Editor: Erik Stokstad

Science's Next Wave: www.nextwave.org

Managing Editor: Wendy Yee; **Associate Editor:** Nicole Ruediger; **Writer:** Melissa Merti; **Canada Editor:** Charles Boulakia

Richard S. Nicholson
Publisher

Beth Rosner
Associate Publisher

Michael Spinella
Membership/Circulation Director

Membership/Circulation

Deputy Director: Marlene Zendell
Member Services: Michael Lung, Manager; Mary Curry, Supervisor; Pat Butler, Laurie Baker, Jonathan Keeler, Jantell Smith, Representatives
Marketing: Dee Valencia, Manager; Lauri Sirois, Coordinator; Jane Pennington, Europe Manager; Ben Holland, Representative
Research: Renuka Chander, Manager
Business and Finance: Susan Maxim, Assistant
Computer Specialist: Charles Munson

Finance and Advertising

Business and Finance: Deborah Rivera-Wienhold, Business Manager; Randy Yi, Senior Analyst; Connie Dang, Financial Analyst
Permissions: Lincoln Richman, Administrator; Emilie David, Assistant
Marketing: John Meyers, Director; Chris Harbaugh, Allison Pritchard, Associates
Electronic Media: David Gillikin, Manager; Wendy Green, Computer Specialist; Mark Croatti, Crystal Young, Production Associates

Product Advertising: Carol Maddox, Traffic Manager; Sheila Myers, Sandra Walls, Associates
Assistant to Associate Publisher: Jessica Tierney

Sales

Product Advertising: Richard Teeling, Acting National Sales Manager/E. Coast and E. Canada: 973-904-9774, FAX 973-904-9701 • **Midwest/Southeast:** Elizabeth Mosko: 773-665-1150, FAX 773-665-2129 • **West Coast/W. Canada:** Neil Boylan: 415-673-9265, FAX 415-673-9267 • **U.S. Inside Sales:** Christopher Breslin: 202-326-6544, FAX 202-682-0816 • **UK/Scandinavia/France/Italy/Belgium/Netherlands:** Andrew Davies: (44) 1-457-871-073, FAX (44) 1-457-877-344 • **Germany/Switzerland/Austria:** Tracey Peers: (44) 1-260-297-530, FAX (44) 1-260-271-022 • **Japan:** Masah Yoshikawa: (81) 3-3235-5961, FAX (81) 3-3235-5852
Recruitment Advertising: Terri Seiter Azie, Sales and Production Operations Manager • **U.S. Sales:** Gabrielle Boguslawski, Sales Manager: 718-491-1607, FAX 202-289-6742; Daryl Anderson, Sales Supervisor; Beth Dwyer, Bren Peters-Minnis, Eric Banks, Troy Benitez, Sales Representatives; Erika Bryant, Kathleen Clark, Angela Panton, Assistants • Ellen McGuire, Jennifer Rankin, Production Associates; Chris Filatreau, Copy Editor/Proofreader • **U.K./Europe:** Debbie Cummings, Sales Manager; Sabine Lenud, Sales Executive; Michaela Heigl, Assistant: (44) 1-223-302-067, FAX (44) 1-223-576-208
Australia/New Zealand: Keith Sandell: (61) 02-9922-2977, FAX (61) 02-9922-1100 • **Japan:** Masah Yoshikawa: (81) 3-3235-5961, FAX (81) 3-3235-5852

Published by the American Association for the Advancement of Science (AAAS), Science serves its readers as a forum for the presentation and discussion of important issues related to the advancement of science, including the presentation of minority or conflicting points of view, rather than by publishing only material on which a consensus has been reached. Accordingly, all articles published in Science—including editorials, news, and comment, and book reviews—are signed and reflect the individual views of the authors and not official points of view adopted by the AAAS or the institutions with which the authors are affiliated.

The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objectives are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of human welfare, to advance education in science, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

INFORMATION RESOURCES

SUBSCRIPTION SERVICES

For change of address, missing issues, new orders and renewals, and payment questions, please contact AAAS at Danbury, CT: 800-731-4939 or Washington, DC: 202-326-6417, FAX 202-842-1065. Mailing addresses: AAAS, P.O. Box 1811, Danbury, CT 06813 or AAAS Member Services, 1200 New York Avenue, NW, Washington, DC 20005 • **Other AAAS Programs:** 202-326-6400

MEMBER BENEFIT CONTACTS

Credit Card: MBNA 1-800-847-7378; Car Rentals: Hertz 1-800-654-2200 CDP#343457, Dollar 1-800-800-4000 #AA1115; AAAS Travels: Betchart Expeditions 1-800-252-4910; Life Insurance: Seabury & Smith 1-800-424-9883; Other Benefits: AAAS Member Services 1-202-326-6417.

REPRINTS & PERMISSION

Reprints: Ordering/Billing/Status, 800-407-9190; Corrections, 202-326-6501 • **Permissions:** 202-326-7074, FAX 202-682-0816

INTERNET ADDRESSES

science_editors@aaas.org (for general editorial queries); science_news@aaas.org (for news queries); science_letters@aaas.org (for letters to the editor); science_reviews@aaas.org (for returning manuscript reviews); science_bookrevs@aaas.org (for book review queries); science@science-int.co.uk (for the Europe Office); membership@aaas.org (for member services); science_classifieds@aaas.org (for submitting

classified advertisements); science_advertising@aaas.org (for product advertising)

INFORMATION FOR CONTRIBUTORS

See pages 108 and 109 of the 2 January 1998 issue or access www.sciencemag.org/misc/con-info.shtml.

EDITORIAL & NEWS CONTACTS

North America

Address: 1200 New York Avenue, NW, Washington, DC 20005

Editorial: 202-326-6501, FAX 202-289-7562

News: 202-326-6500, FAX 202-371-9227 • **Bureaus:** **Berkeley, CA:** 510-841-1154, FAX 510-841-6339, **San Diego, CA:** 760-942-3252, FAX 760-942-4979, **Chicago, IL:** 312-360-1227, FAX 312-360-0537

Europe

Headquarters: 14 George IV Street, Cambridge, UK CB2 1HH; (44) 1223-302067, FAX (44) 1223-302068
Paris Correspondent: (33) 1-49-29-09-01, FAX (33) 1-49-29-09-00

Asia

News Bureau: Dennis Normile, (81) 3-3335-9925, FAX (81) 3-3335-4898; dnormile@twics.com

• **Japan Office:** Asca Corporation, Eiko Ishioka, Fusako Tamura, 1-8-13, Hirano-cho, Chuo-ku, Osaka-shi, Osaka, 541 Japan; (81) 6-202-6272, FAX (81) 6-202-6271; asca@os.gulf.or.jp

• **China Office:** Hao Xin, science@public3.bta.net.cn

BOARD OF REVIEWING EDITORS

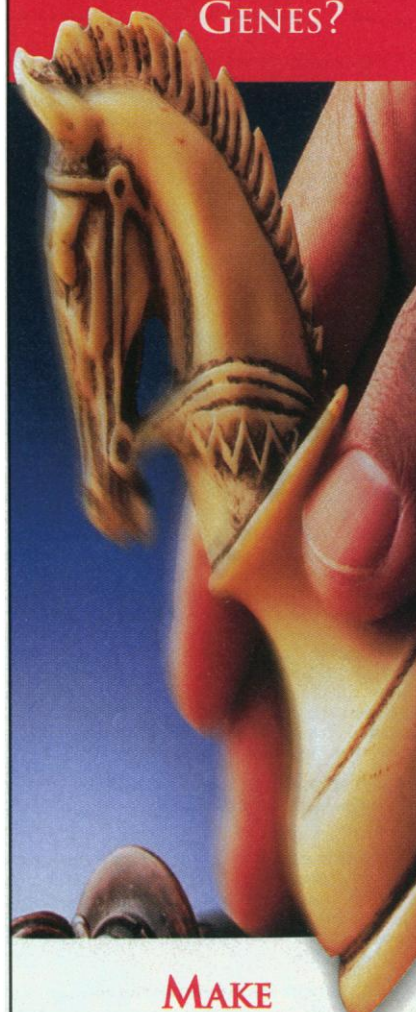
Frederick W. Alt
Children's Hospital, Boston
Don L. Anderson
California Institute of Technology
Michael Ashburner
Univ. of Cambridge
Frank S. Bates
Univ. of Minnesota, Minneapolis
Stephen J. Benkovic
Pennsylvania State Univ.
Alan Bernstein
Mount Sinai Hospital, Toronto
Michael J. Bevan
Univ. of Washington, Seattle
Seth Blair
Univ. of Wisconsin, Madison
David E. Bloom
Harvard Institute for International Development
Piet Borst
The Netherlands Cancer Institute
Henry R. Bourne
Univ. of California, San Francisco
James J. Bull
Univ. of Texas at Austin
Kathryn Calame
Columbia Univ. College of Physicians & Surgeons
Dennis W. Choi
Washington Univ. School of Medicine, St. Louis
David Clapham
Children's Hospital, Boston
Adrienne E. Clarke
Univ. of Melbourne, Parkville
F. Fleming Crim
Univ. of Wisconsin, Madison
Paul J. Crutzen
Max-Planck-Institut für Chemie
James E. Dahlberg
Univ. of Wisconsin Medical School, Madison
Robert Desimone
National Institute of Mental Health, NIH
Hans Eklund
Swedish Univ. of Agricultural Sciences, Uppsala
Paul T. Englund
Johns Hopkins Univ. School of Medicine
G. Ertl
Max-Planck-Gesellschaft
Richard G. Fairbanks
Lamont-Doherty Earth Observatory
Douglas T. Fearon
Univ. of Cambridge

Harry A. Fozzard
The Univ. of Chicago
Roger I. M. Glass
Centers for Disease Control
Peter N. Goodfellow
SmithKline Beecham, UK
Jack F. Greenblatt
Univ. of Toronto
Peter Gruss
Max Planck Institute of Biophysical Chemistry
Philip C. Hanawalt
Stanford Univ.
Paul Harvey
Univ. of Oxford
M. P. Hassell
Imperial College at Silwood Park
Nobutaka Hirokawa
Univ. of Tokyo
Tomas Hökfelt
Karolinska Institutet
Tasuku Honjo
Kyoto Univ.
Susan D. Iversen
Univ. of Oxford
Eric F. Johnson
The Scripps Research Institute
Hans Kende
Michigan State Univ.
Elliott Kieff
Harvard Univ.
Jeffrey T. Kiehl
National Center for Atmospheric Research, Boulder
Judith Kimble
Univ. of Wisconsin, Madison
Stephen M. Kosslyn
Harvard Univ.
Michael LaBarbera
The Univ. of Chicago
Antonio Lanzavecchia
Basel Institute for Immunology
Nicole Le Douarin
Institut d'Embryologie Cellulaire et Moléculaire du CNRS
Norman L. Letvin
Beth Israel Hospital, Boston
Harvey F. Lodish
Whitehead Institute for Biomedical Research
Richard Losick
Harvard Univ.
Seth Marder
California Institute of Technology

Diane Mathis
Institut de Chimie Biologique, Strasbourg
Susan K. McConnell
Stanford Univ.
Anthony R. Means
Duke Univ. Medical Center
Stanley Meisel
Univ. of California, Davis
Douglas A. Melton
Harvard Univ.
Andrew Murray
Univ. of California, San Francisco
Elizabeth G. Nabel
The Univ. of Michigan Medical Center
Shigetada Nakanishi
Kyoto Univ.
Kim Nasmyth
Research Institute of Molecular Pathology, Vienna
Roger A. Nicoll
Univ. of California, San Francisco
Staffan Normark
Swedish Institute for Infectious Disease Control
Kiyotaka Okada
Kyoto Univ.
Bert W. O'Malley
Baylor College of Medicine
Roy R. Parker
Univ. of Arizona, Tucson
Stuart L. Pimm
The Univ. of Tennessee, Knoxville
Yeshayau Pocker
Univ. of Washington, Seattle
Ralph S. Quatrano
Univ. of North Carolina, Chapel Hill
Martin Raff
Univ. College London
Douglas C. Rees
California Institute of Technology
T. M. Rice
ETH-Hönggerberg, Zürich
David C. Rubie
Universität Bayreuth
Erkki Ruoslahti
The Burnham Institute, CA
Gottfried Schatz
Biozentrum, Basel
Jozsef Schell

Max-Planck-Institut für Züchtungsforschung
Ronald H. Schwartz
National Institute of Allergy and Infectious Diseases, NIH
Terrence J. Sejnowski
Salk Institute
Edward E. Smith
Univ. of Michigan, Ann Arbor
Christopher R. Somerville
Carnegie Institute of Washington
Michael P. Stryker
Univ. of California, San Francisco
Cliff Tabin
Harvard Medical School
John Jen Tai
Academia Sinica, Taiwan
Tomoyuki Takahashi
Univ. of Tokyo
Masatoshi Takeichi
Kyoto Univ.
Keiji Tanaka
RIKEN Institute
David Tilman
Univ. of Minnesota, St. Paul
Robert T. N. Tjian
Univ. of California, Berkeley
Yoshinori Tokura
Univ. of Tokyo
Derek van der Kooy
Univ. of Toronto
Geerat J. Vermeij
Univ. of California, Davis
Bert Vogelstein
Johns Hopkins Oncology Center
Gerhard Wegner
Max-Planck-Institut für Polymerforschung
Arthur Weiss
Univ. of California, San Francisco
Zena Werb
Univ. of California, San Francisco
George M. Whitesides
Harvard Univ.
Ian A. Wilson
The Scripps Research Institute
Alan P. Wolfe
National Institute of Child Health and Human Development, NIH
Martin Zatz
National Institute of Mental Health, NIH

DOES YOUR
RESEARCH REQUIRE
CUSTOM
GENES?



MAKE
THE SMART MOVE.



For fast, low-priced
design and
assembly of your
custom genes, check
out Genosys. Our

Masterpiece™ Custom Gene

Synthesis Service ensures
you get the highest quality
product—guaranteed to meet
your needs—quickly and inex-
pensively. It's simply unbeatable!

GENOSYS

(281) 363-3693 • www.genosys.com

1-888-400-GENE

STATISTICA

STATISTICA (automatically configures itself for Windows 95, NT, or 3.1) ■ A complete data analysis system with thousands of on-screen customizable, presentation-quality graphs fully integrated with all procedures ■ Comprehensive Windows support, OLE (client and server), DDE, customizable *AutoTask* toolbars, pop-up menus ■ Multiple data-, results-, and graph-windows with *data-graph* links ■ The largest selection of statistics and graphs in a single system; comprehensive implementations of: Exploratory techniques with advanced brushing; multi-way tables with banners (presentation-quality reports); nonparametrics; distribution fitting; multiple regression; general nonlinear estimation; stepwise logit/probit; general ANCOVA/MANOVA; variance components; stepwise discriminant analysis; log-linear analysis; confirmatory/exploratory factor analysis; cluster analysis; multidimensional scaling; classification trees; canonical correlation; item analysis/reliability; correspondence analysis; survival analysis; a large selection of time series modeling/forecasting techniques; structural equation modeling with *Monte Carlo* simulations; and much more ■ On-line *Electronic Manual* with comprehensive introductions to each procedure and examples ■ Hypertext-based *Stats Advisor* expert system ■ Workbooks with multiple *AutoOpen* documents (e.g., graphs, reports) ■ Extensive data management facilities (fast spreadsheet of unlimited capacity with long formulas, *Drag-and-Drop*, *AutoFill*, *Auto-Recalculate*, split-screen/variable-speed scrolling, advanced Clipboard support, DDE links, hot links to graphs, relational merge, data verification/cleaning) ■ Powerful *STATISTICA BASIC* language (professional development environment) with matrix operations, full graphics support, and interface to external programs (DLLs) ■ Batch command language and editable macros, flexible "turn-key" and automation options, custom-designed procedures can be added to floating *AutoTask* toolbars ■ All output displayed in *Scrollsheets*™ (dynamic, customizable, presentation-quality tables with instant 2D, 3D, and multiple graphs) or word processor-style report editor (of unlimited capacity) that combines text and graphs ■ Extremely large analysis designs (e.g., correlation matrices up to 32,000x32,000, virtually unlimited ANOVA designs) ■ Megafile Manager with up to 32,000 variables (8 Mb) per record ■ Unlimited size of files; extended ("quadruple") precision; unmatched speed ■ Exchanges data and graphs with other applications via DDE, OLE, or an extensive selection of file import/export facilities (incl. ODBC access to virtually all data bases and mainframe files) ■ Hundreds of types of graphs, incl. categorized multiple 2D and 3D graphs, ternary 2D/3D graphs, matrix plots, icons, and unique multivariate (e.g., 4D) graphs ■ Facilities to custom-design new graph types and add them permanently to menus or toolbars ■ On-screen graph customization with advanced drawing tools (e.g., scrolling and editing of complex objects in 32x real zoom mode), compound (nested) OLE documents, *Multiple-Graph AutoLayout Wizard*, templates, special effects, icons, page layout control for slides and printouts; unmatched speed of graph redraw ■ Interactive rotation, perspective and cross-sections of 3D displays ■ Large selection of tools for graphical exploration of data: extensive brushing tools with animation, fitting, smoothing, overlaying, spectral planes, projections, layered compressions, marked subsets ■ Price \$995.

Quick STATISTICA (for Windows) ■ A subset of *STATISTICA*; comprehensive selection of basic statistics and the full analytic and presentation-quality graphics capabilities of *STATISTICA* ■ Price \$495.

STATISTICA Industrial System (requires *STATISTICA* or *Quick STATISTICA*) ■ The largest selection of industrial statistics in a single package; quality control charts (real-time data acquisition options), process capability analysis, R&R, Weibull Analysis, sampling plans, and an extremely comprehensive selection of experimental design (DOE) methods ■ Flexible tools to customize and automate all analyses and reports (incl. "turn-key" system options, and tools to add custom procedures) ■ Price \$995.

NEW STATISTICA Neural Networks (interfaces with, but does not require *STATISTICA*) ■ The most comprehensive, universal, and user-friendly NN application available on the market, featuring unique, automatic (AI) algorithms to find the best NN architecture and best subsets of variables; supports multiple networks and designs of practically unlimited sizes ■ Price \$795.

STATISTICA/Mac (for Macintosh) ■ Price \$695 (Quick - \$395).

Overseas prices vary. Domestic sh/h \$12; 30-day money back guarantee.

STATISTICA has received the highest rating in EVERY comparative review of statistics software in which it was featured, since its first release.

Circle No. 3 on Readers' Service Card

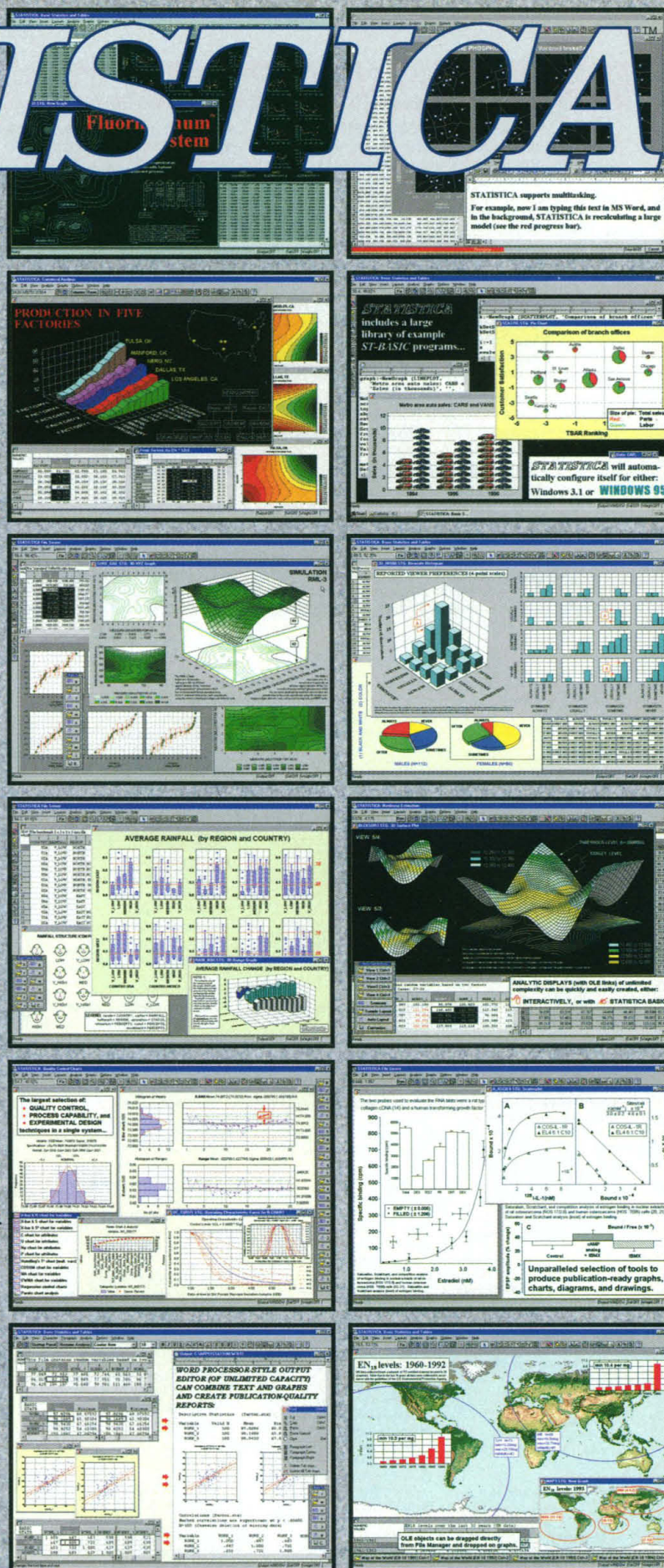


StatSoft®

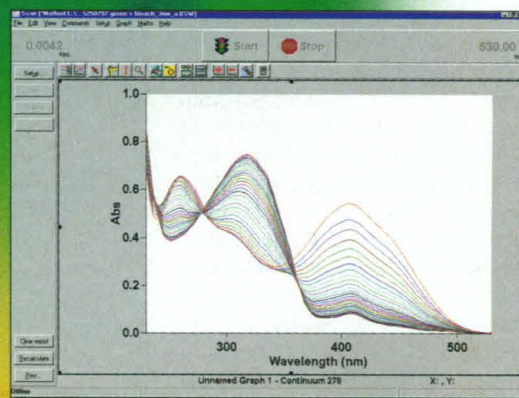
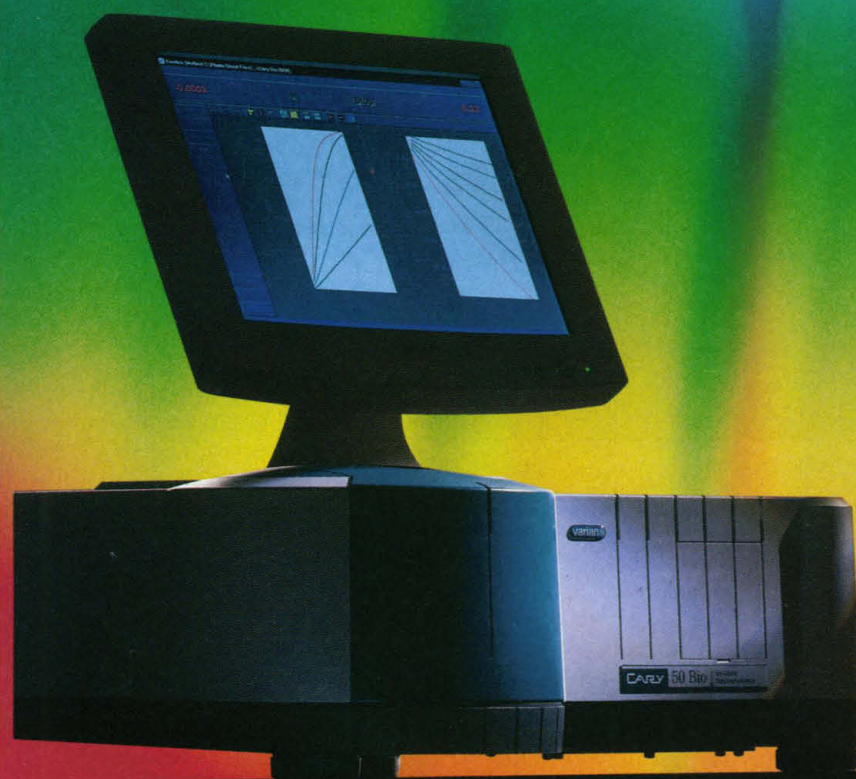
2300 East 14th Street • Tulsa, OK 74104 • (918) 749-1119
Fax: (918) 749-2217 • WEB: <http://www.statsoft.com>
e-mail: info@statsoft.com

- StatSoft Ltd. (London, UK), ph: +44 1234 341226, fax: +44 1234 341622
- StatSoft GmbH (Hamburg, Germany), ph: +49 40/468866-0, fax: +49 40/468866-77
- StatSoft France (Paris, France), ph: +33 01-45-185-999, fax: +33 01-45-185-285
- StatSoft Polska Sp. z o.o. (Krakow, Poland), ph: +48 12-391120, fax: +48 12-391121
- StatSoft Italia (Padova, Italy), ph: +39 49-893-4654, fax: +39 49-893-2897
- StatSoft Pacific Pty Ltd. (Australia), ph: +613 9521 4833, fax: +613 9521 4288
- StatSoft Japan (Tokyo, Japan), ph: +813 3667 1110, fax: +813 3668 3100
- StatSoft Taiwan (Taipei, Taiwan, R.O.C.), ph: +886 2 5786587, fax: +886 2 5793179

The complete line of StatSoft products and training/consulting services are available from authorized representatives worldwide, including: Austria, Belgium, Brazil, Chile, Czech Republic, Denmark, Finland, Greece, Hungary, India, Korea, Malaysia, Mexico, The Netherlands, New Zealand, Norway, Portugal, Russia, South Africa, Spain, Sweden, Switzerland, Turkey. Please contact your nearest StatSoft office for the authorized representative nearest you. StatSoft, the StatSoft logo, STATISTICA, and Scrollsheet are trademarks of StatSoft, Inc.



Want Real Results? Get a Cary.



Why dream about a UV-Vis spectrophotometer that always delivers the right results when you can own a Cary?

With Cary, super stable and precise temperature control is a reality, and probes accurately monitor the temperature of your samples—not the block they sit in. And Cary's smooth magnetic stirring for 12 cuvettes is fast and uniform for reproducible results.

Ever wished for more speed? Cary collects data at 80 points per second, and you can pause data collection at any time to add reagents without affecting performance.

For Life Science imaginations, there's more: extend collection times if you

guess incorrectly during set-up; use multiple temperature ramp rates and directions during a single denaturation run; and even conduct annealing and thermal melt experiments in the same cuvette.

And Cary WinUV software makes it all easier. Even infrequent users will find it simple to load the right application and method by clicking a single icon and just pressing Start to begin measurements.

When it's a Cary instrument from Varian, nothing else measures up in overall quality and value. After all, we have 50 years experience providing innovative solutions in spectrophotometry.

Austria 1.699.9669
Belgium 2.721.4850
Canada 1.800.387.2216
France 1.6986.3838
Germany 06151.7030
Italy 11.997.9111
Netherlands 30.635.0909
Russia 95.937.4280
Spain 1.472.7612
Sweden 8.445.1620
Switzerland 61.295.8000
UK 1932.898.000
USA 1.800.926.3000

www.varian.com/cary

GC • GC/MS/MS • HPLC • AAS • ICP-MS • UV-Vis-NIR • NMR • Sample Preparation • Vacuum Products

Circle No. 24 on Readers' Service Card

varian 50 YEARS

The **New** ABI PRISM® 377 Genetic Analysis System



Worldwide, laboratories of all sizes have standardized their genetic analysis methods on the ABI PRISM 377 system. The reason? The ABI PRISM 377 system delivers the performance they need now—and in the future.

Fact. The new ABI PRISM 377 system offers enhanced performance with ongoing technical innovations such as:

- BigDye™ Terminators
- New Neural Net Tracker
- 96 Lane Upgrade
- 900 Base Reads

Fact. You can configure the ABI PRISM 377 system to meet your throughput and budget requirements today, with models from 18 to 96 lanes, and easily add capability as needed.

Fact. The new ABI PRISM 377 system is so versatile, you can automate applications from genome sequencing, to heterozygote detection, to microsatellite and STR analysis, and more.

Fact. A broad range of convenient application kits and fully integrated software packages optimized for the ABI PRISM 377 system ensure accurate results.

Fact. The ABI PRISM 377 system streamlines data analysis with BioLIMS™, an open database management system.

Fact. Worldwide customer service and support ranked best in the industry.*

Fact. The ABI PRISM 377 system was developed and is supported by a single organization—PE Applied Biosystems, the world leader in genetic analysis.

There has never been a better time to buy an ABI PRISM 377 system. Because now, the ABI PRISM 377 system gives you all the performance you need, with the throughput you want, and the value you've been waiting for.

So, if you're looking for performance, look into the new ABI PRISM 377 system. Call your local PE Applied Biosystems sales representative today, or visit our web site.

www.perkin-elmer.com/377

PE Applied Biosystems

United States Foster City, California Tel: 1-800-345-5224 Fax: 650-638-5884

Europe Langen, Germany Tel: 49 (0) 6103 708 301 Fax: 49 (0) 6103 708 310

Japan Tokyo, Japan Tel: (047) 380-8500 Fax: (047) 380-8505

Latin America Mexico City, Mexico Tel: 52-5-651-7077 Fax: 52-5-593-6223

Australia Melbourne, Australia Tel: 1-800-033-747 Fax: (03) 9212-8502

ABI, the ABI PRISM Design, Applied Biosystems, PE, PE Applied Biosystems, BigDye, and BioLIMS are trademarks of The Perkin-Elmer Corporation.

ABI PRISM and Perkin-Elmer are registered trademarks of The Perkin-Elmer Corporation.

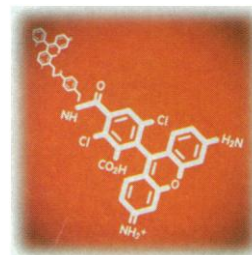
* Based upon an independent industry survey.

Circle No. 46 on Readers' Service Card

New Neural Net Tracker



Accurate, Robust BigDye™ Terminators



Linkage Mapping Set Version 2



Expert Worldwide Service and Support

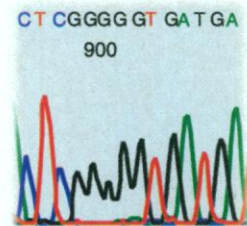


Performance. Not Promises.

From The World Leader
In Genetic Analysis



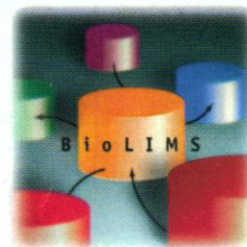
900 Bases
Per Template



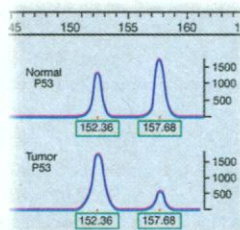
96 Lane Upgrade



BioLIMS™—Automated
Data Management



Versatility—Sequencing,
Genotyping, Mutation Detection...



no one is immune to being first.

Ask Christine Jacobs.

As the 1997 prize winner, she discovered that being published in *Science*, winning US\$20,000, a free trip to Stockholm and appearing in this ad can be quite a shot in the arm.

If you are a recent Ph.D. graduate in the field of molecular biology, you are eligible to enter the 1998 Amersham Pharmacia Biotech & Science Prize for Young Scientists. Just send us an essay based on your graduate thesis, and we'll take it from there.

What's in it for you.

The grand prize is US\$20,000 with an additional seven runners-up winning US\$5,000 and being announced in *Science*. The winning essay will be published in full. The award ceremony will be held in Sweden in early December. The Grand Prize winner will feature in next year's Amersham Pharmacia Biotech & Science Prize for Young Scientists advertisement. As an additional bonus, all winners and finalists receive a free subscription to *Science*.

Call for entries.

To be eligible, you must have received your Ph.D. between January 1 and December 31, 1997. Your thesis has to be in the field of molecular biology and submitted to us in the form of a 1,000-word essay which describes your work and places it in perspective with regard to the field of molecular biology. The essay can be written in English, French, German, Spanish, Japanese or Chinese (Mandarin).

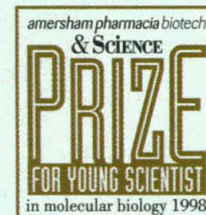


Christine Jacobs discovered the mechanism that bacteria use to defend themselves against antibiotics.

MMC Stockholm

The closing date is June 15, 1998. All prizes will be presented in Sweden in December 1998. Full details, and the required entry form can be collected from:

- * the administrator of the award committee at the address below
- * from the *Science* homepage at <http://www.aaas.org/science/prize.htm>
- * from the Amersham Pharmacia Biotech homepage at <http://www.apbiotech.com>



Amersham Pharmacia Biotech and Science Young Scientist Prize Selection Committee

Enquiries in Europe should be addressed to: Science International/Thomas House 14 George IV Street Cambridge CB2 1HH UK
Tel: +44 1223 302067. Fax: +44 1223 302 068

Enquiries in the United States and other regions should be addressed to: Science 1200 New York Avenue, N.W., Room #1053 Washington, DC 20005 USA
Tel: +1 202 326 6553. Fax: +1 202 289 7562

Circle No. 17 on Readers' Service Card



The Next Step. The Virtual Laboratory.

A new way to manage science through computation

Imagine every scientist in your organization using their desktop PC to apply simulation tools, search corporate and third-party databases, create knowledge out of data, interactively communicate and access that knowledge, and make informed decisions...faster.

If you are interested in new ways for your company to manage its scientific research, talk to MSI. We are developing enterprise-wide solutions that integrate advanced computation with chemical communications software and the power of the Web.

Today, MSI's simulation products help you focus experiments and identify productive new research pathways. Our informatics tools process and analyze your chemical and biological information.

MSI's vision for the future is a Virtual Laboratory where computational tools complement every aspect of experiment and maximize return on your corporate knowledge.

Take the next step.

Call MSI today or visit us at <http://www.msi.com/virtual-lab>.

U.S.: 1-888-249-2292 U.K.: (44) 1223 413300 France: (33) 1 69353232 Germany: (49) 8106 35 93 0 Asia/Pacific: (61) 2 9954 4322 Japan: (81) 3 3663 8615



Circle No. 40 on Readers' Service Card

EXCELLENCE IN SCIENCE SCHOLARSHIP

Now in paperback...

Improving Nature?

The Science and Ethics of Genetic Engineering

Michael Reiss and Roger Straughan

"The book includes ethical concerns for the whole spectrum of life...and is rich with extended examples..."

—Science

Written in a clear, nontechnical style, this book delves thoroughly into the biological and ethical considerations we must confront in the face of genetic engineering technology. In every chapter, the authors tackle hot-button issues such as the possible consequences of genetic engineering of plants, animals, and humans, and the justification for improving upon nature.

1998 304 pp.

0-521-63754-6 Paperback \$15.95

Bioarchaeology

Interpreting Behavior from the Human Skeleton

Clark Spencer Larsen

This is the first comprehensive synthesis of the emerging field of bioarchaeology. A central theme of this book is the interaction between biology and behavior, particularly the dynamic nature of skeletal and dental tissues, and the influences of environment and culture on human biological variation. It discusses research findings, covering paleopathology, physiological stress, skeletal and dental growth and structure, the processes of aging and biodistance.

Cambridge Studies in Biological Anthropology 21

1998 474 pp.

0-521-49641-1 Hardback \$85.00

Animal Vocal Communication

A New Approach

Donald H. Owings and Eugene S. Morton

Animal Vocal Communication explicitly avoids human-centered concepts and approaches and links communication to fundamental biological processes instead. Written by a psychologist and a zoologist, it offers a new conceptual framework—assessment/management—that integrates detailed studies of communication with an understanding of evolutionary perspectives.

1998 296 pp.

0-521-32468-8 Hardback 64.95

Available in bookstores or from

CAMBRIDGE
UNIVERSITY PRESS

Ecology and Biogeography of Pinus

David M. Richardson, Editor

This book presents a definitive review of pine ecology and biogeography written by forty of the world's leading authorities on this important genus. In the face of increasing human pressure and global climate change, this book provides an essential source of reference for all those concerned with the management of natural and planted pine forests.

1998 546 pp.

0-521-55176-5 Hardback \$155.00

Medical Harm

Historical, Conceptual and Ethical Dimensions of Iatrogenic Illness

Virginia A. Sharpe and Alan I. Faden

This book integrates history, philosophy, medical ethics and empirical data to examine the concept and phenomenon of medical harm. Issues covered include appropriateness of care, acceptable risk and practitioner accountability, and recommendations for limiting iatrogenic harm.

1998 292 pp.

0-521-63490-3 Paperback \$27.95

Facilitating Sustainable Agriculture

Participatory Learning and Adaptive Management in Times of Environmental Uncertainty

Niels Röling and Annemarie Wagemakers, Editors

Through case studies taken from around the world, this book examines the implications of adopting more ecologically sound agricultural practices, both at the level of individual farmers and at the level of larger-scale agroecosystems such as water catchments.

1998 344 pp.

0-521-58174-5 Hardback \$80.00

Fractals, Scaling and Growth Far from Equilibrium

Paul Meakin

This book describes the progress that has been made toward the development of a comprehensive understanding of the formation of complex, disorderly patterns under far from equilibrium conditions. It describes the application of fractal geometry and scaling concepts to the quantitative description and understanding of structure formed under nonequilibrium conditions.

Cambridge Nonlinear Science Series 5

1998 688 pp.

0-521-45253-8 Hardback \$125.00

Principles of Animal Design

The Optimization and Symmorphosis Debate

Ewald F. Weibel, C. Richard Taylor, and Liana Bolis, Editors

This book discusses the controversial issue of whether animals are designed according to the same rules that engineers use in building machines, namely that materials and energy are used economically while attempting to achieve a high level of performance. There is considerable scientific controversy surrounding this question because, although there is much evidence suggesting that animals are indeed well designed, evolutionary biology tells us that animals are not "engineered" but result from evolution by natural selection.

1998 314 pp.

0-521-58667-4 Paperback \$32.95

Photosynthesis

A Comprehensive Treatise

A.S. Raghavendra, Editor

This is the first advanced-level treatment to cover the broad range of the topic within a single volume, providing a uniquely comprehensive, authoritative and self-contained sourcebook. Written by an international team of experts, the volume opens by considering the cell and molecular biology of chloroplasts, followed by a section that presents the latest information on the biochemistry and physiology of photosynthesis. These chapters are then complemented by coverage of more ecological and applied aspects, such as photosynthesis and global climate change, and crop productivity.

1998 394 pp.

0-521-57000-X Hardback \$115.00

Ethics in Engineering Practice and Research

Caroline Whitbeck

Engineers encounter difficult ethical problems in their practice and in research. In many ways, these problems are like design problems: they are complex, often ill-defined; resolving them involves an iterative process of analysis and synthesis; and there can be more than one acceptable solution. This book offers a real-world, problem-centered approach to engineering ethics, using a rich collection of open-ended scenarios and case studies to develop skill in recognizing and addressing ethical issues.

1998 350 pp.

0-521-47944-4 Paperback \$27.95

40 West 20th Street, New York, NY 10011-4211 Call toll-free 800-872-7423.

The Edinburgh Building, Shaftesbury Road, Cambridge CB2 2RU, U.K.

Web site: <http://www.cup.org> MasterCard/VISA accepted. Prices subject to change.

Circle No. 1 on Readers' Service Card

TSA™ IS THE DIFFERENCE

See Clearly.

Now you can enhance both chromogenic and fluorescent signals up to 1000 times with Renaissance® Tyramide Signal Amplification (TSA), a powerful new technology from NEN™ Life Science Products. TSA is easily integrated into standard immunohistochemistry (IHC) or *in situ* hybridization (ISH) protocols, providing Horseradish Peroxidase (HRP) is present in the system.

Fig. 1. Multicolor detection using TSA-Direct.
Courtesy of Kevin Roth, M.D., Washington University
School of Medicine, St. Louis, Missouri.

Fig. 1.

How does it work?

This technology uses HRP to catalyze the deposition of biotinyl or fluorescent tyramide onto tissue-section or cell-preparation surfaces that were previously blocked with protein. This reaction is quick (less than 10 minutes) and results in the deposition of numerous biotin or fluorochrome labels.

These labels can then be detected directly or indirectly by standard techniques. The deposition occurs right at the enzyme site, resulting in minimal loss of resolution. This easy-to-use signal amplification technique may be applied to both IHC and ISH.

Fig. 2

a. Standard fluorescent detection.

b. TSA-Enhanced fluorescent detection.

c. Standard chromogenic ISH.

d. TSA-Enhanced chromogenic ISH.

Enhance signal up to 1000-fold.

Figs. 2 a-b. Fluorescent detection of chromosome centromere probes in metaphase spreads.
Figs. 2 c-d. *In situ* chromogenic detection of oxytocin in rat brain tissue sections.

Care to Jump?

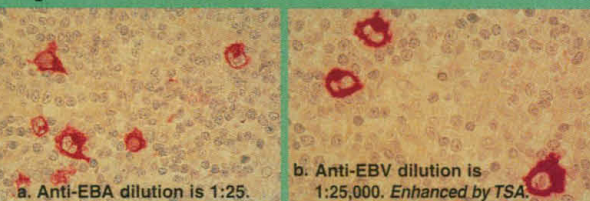
Call today to learn more about TSA and our complete line of Renaissance labeling and detection products for nucleic acids and proteins. To order call your local NEN office.

© NEN™ Life Science Products, 1997.

TSA is a registered trademark of NEN™ Life Science Products. Renaissance products are manufactured under an ISO 9002 Quality System registered by UL.

Circle No. 36 on Readers' Service Card

Fig. 3



Figs. 3 a-b. IHC of EBV antigen in Hodgkin's Lymphoma of mixed cellularity.
Courtesy of R. Von Wasielewski and S. Gignac, Pathologisches Institut de
Medizinischen Hochschule, Hannover, Germany.

Reduce use of valuable reagents.

The use of TSA allows you to conserve your precious antibodies while maintaining the same level of sensitivity.

Fluorescent or chromogenic, it's your choice.

TSA-Direct deposits numerous fluorochromes that can be directly visualized immediately after amplification. TSA-Direct kits are available in a variety of colors: Fluorescein (Green), Tetramethylrhodamine (Red), and Coumarin (Blue).

TSA-Indirect deposits numerous biotins which are then detected by streptavidin conjugated to an enzyme (followed by chromogenic detection) or a fluorochrome (for fluorescent detection).

NEN™ Life Science Products

Boston, MA 02118-2512 USA
1-800-551-2121 • 617-482-9595
Fax: 617-482-1380
Web: <http://www.nenlifesci.com>

Products available worldwide.
Consult the NEN home page for your
local sales office or distributor.
<http://www.nenlifesci.com>