AMERICAN
ASSOCIATION FOR THE
ADVANCEMENT OF
SCIENCE

SCIENCE

26 NOVEMBER 1993 $6.00
VOL. 262 • PAGES 1345–1484

Techniques in OPTICS

{*Cluckus Elasticus*}

WITH 1,000 *different* 10-MER OLIGOS, OPERON *can* HELP *you* MAP ANY *genome.*

Well, almost.

If you need 10-mer oligos for rapid mapping, you can now put all your eggs in one basket. Because you can now get 1000 different 10-mer primers from a single source. Operon.

Our 10-mer oligos are optimized for use in the genetic mapping method developed by Williams *et al.* (*Nucleic Acid Res., 18* 6531-6535). In this technique, single primers are used to amplify DNA polymorphisms, which are useful as genetic markers.

At just $150 per kit of 20 sequences, with free domestic delivery, our primers can be yours for chicken feed. We'll even deliver your order the very next day. So if you're using anyone else's 10-mers, isn't it time you crossed the road to Operon? With the greatest selection of primers in the world, we give your research a whole new level of flexibility.

For more information, or to place an order, call **1-800-688-2248.**

OPERON

WORLD'S LEADING SUPPLIER OF SYNTHETIC DNA

ISSN 0036-8075
26 NOVEMBER 1993
VOLUME 262
NUMBER 5138

SCIENCE

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

1364
Harold Varmus talks about his new job

NEWS & COMMENT

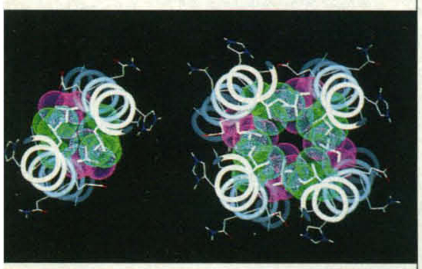
RESEARCH NEWS

TECHNIQUES IN OPTICS

NEWS

PERSPECTIVES

ARTICLES



1401
Changing partners

DEPARTMENTS

Board of Reviewing Editors

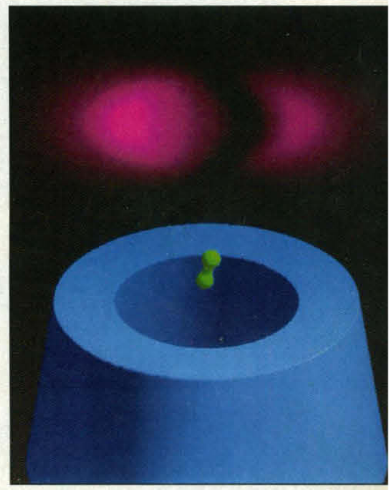
COVER

Resistance genes are widely used to control plant diseases caused by bacteria, fungi, viruses, and nematodes. A single gene, *Pto*, encoding a protein kinase, confers resistance in tomato to the bacterial pathogen *Pseudomonas syringae* pv. *tomato*, as shown by the healthy leaves from genetically modified plants (diseased leaves are from susceptible, wild-type plants). The presence of *Pto* homologs in many crop species may expedite the isolation of other plant resistance genes. See page 1432. [Photo: Gregory B. Martin]

RESEARCH ARTICLES

REPORTS

TECHNICAL COMMENTS



1382 & 1422

Scanning for singles

◩ Indicates accompanying feature

■ **SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1333 H Street, NW, Washington, DC 20005.** Second-class postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Copyright © 1993 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): $87 ($47 allocated to subscription). Domestic institutional subscription (51 issues): $205. Foreign postage extra: Mexico, Caribbean (surface mail) $50; other countries (air assist delivery) $95. First class, airmail, student and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. **Change of address:** allow 6 weeks, giving old and new addresses and 11-digit account number. **Postmaster:** Send change of address to *Science*, P.O. Box 2033, Marion, OH 43305-2033. **Single copy sales:** $6.00 per issue prepaid includes surface postage; Guide to Biotechnology Products and Instruments, $20. 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 the base fee of $1 per copy plus $0.10 per page is paid directly to CCC, 27 Congress Street, Salem, MA 01970. The identification code for *Science* is 0036-8075/83 $1 + .10. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

edited by PHIL SZUROMI

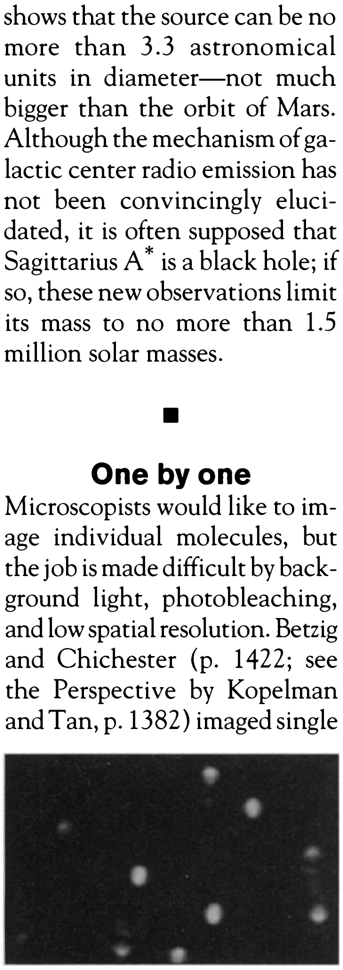
Search for the center

Sagittarius A^* is a prominent radio source that may mark the center of our galaxy. Observations by radio interferometry have so far failed to resolve its structure, and the latest such work, by Backer *et al.* (p. 1414), shows that the source can be no more than 3.3 astronomical units in diameter—not much bigger than the orbit of Mars. Although the mechanism of galactic center radio emission has not been convincingly elucidated, it is often supposed that Sagittarius A^* is a black hole; if so, these new observations limit its mass to no more than 1.5 million solar masses.

■

One by one

Microscopists would like to image individual molecules, but the job is made difficult by background light, photobleaching, and low spatial resolution. Betzig and Chichester (p. 1422; see the Perspective by Kopelman and Tan, p. 1382) imaged single



carbocyanine dye molecules with near-field optical scanning microscopy. By funneling the excitation light through an aperture smaller than the optical wavelength, the authors confined the detection volume; an image was then composed by scanning the aperture across the specimen. The orientation of each molecule was determined from the structure of the emitted radiation, and the electric field distribution near the aperture was mapped using the molecule as a probe.

DNA binding by the α subunit of RNA polymerase

In prokaryotes, promoter regions for transcription centered at sites 10 and 35 base pairs upstream of the start site interact with the σ subunit of RNA polymerase (RNAP). Ross *et al.* (p. 1407) have identified a third promoter element upstream of the *Escherichia coli* ribosomal RNA promoter *rrnB* P1; the UP element (the region 40 to 60 base pairs upstream) is rich in A and T nucleotides. This DNA promoter binds directly to the carboxyl-terminal region of the α subunit of RNAP. Mutations in this region diminished the activity of *rrnB* P1 and three other promoters, *rrnB* P2, RNA II, and *leuV*, which also have (A + T)-rich upstream regions. The underlying mechanism of transcriptional stimulation may share common features with certain transcriptional activator factors that are also inactivated by carboxyl-terminal α mutations.

On the double

Proteins might be very efficient frequency doublers, but because protein solutions are ionic and conduct electricity, it is not possible to apply a static electric field to orient the molecules and determine their electro-optic properties. Clays *et al.* (p. 1419) determined the nonlinear polarizabilities of ionic molecules by molecular orientation. They used the oscillating electric field present in an intense laser beam which, because of its high frequency and rapid phase changes, does not permit the molecules to move and give rise to conduction. The frequency doubling capacity of a protein solution is in fact large, and the authors give an idea for building supramolecular protein structures with very large optical nonlinearities.

■

Let it glow

The scanning tunneling microscope (STM) is normally used to record the location and geometry of a sample, but Berndt *et al.* (p. 1425) show that if the tunneling current at the STM tip is sufficiently large, luminescent photons can be excited and recorded to produce an optical image. They obtained a 4 angstrom spot of light from individual fullerene molecules on a gold surface. Spectroscopic studies of the luminescence may yield a useful diagnostic of the bond structure.

■

Avoiding attack

Insect parasitoids, those that parasitize and kill their hosts, have been used as biological control agents, largely on a trial and error basis. Hawkins *et al.* (p. 1429) have examined the application of refuge theory to the problem of biological control. These studies indicate that the size of refuges (the proportion of host population immune from attack by the parasitoid) is directly related to the success of the use of parasitoids for biological control. The greater the size of the refuge, the less susceptible was the host to attack by parasitoids.

■

Better organized and more presentable

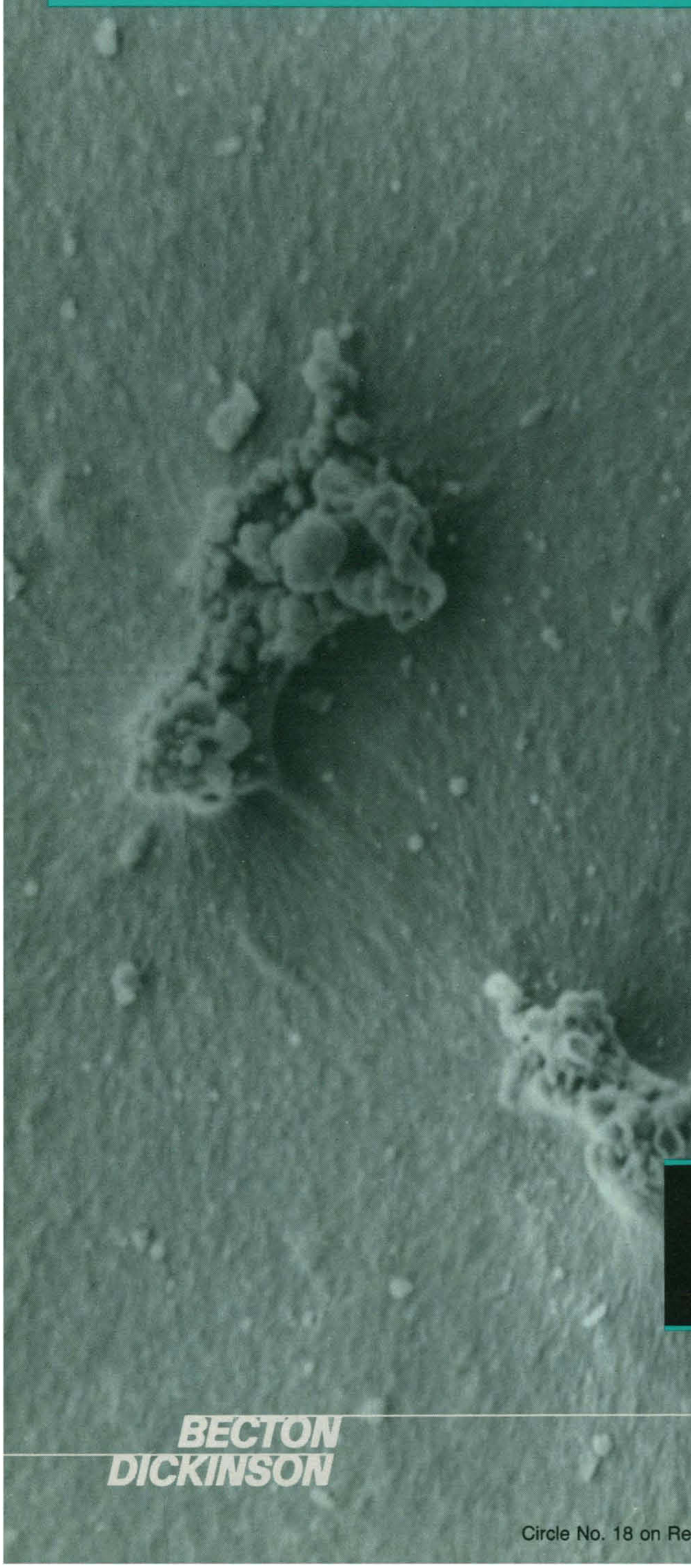
A B cell can become tolerized toward a particular antigen and not produce antibodies; this is especially important in avoiding the production of autoantibodies. Bachmann *et al.* (p. 1448) show that staying in this tolerant state depends on how the antigen is presented. They generated transgenic mice that expressed glycoprotein of vesicular stomatitis virus serotype Indiana [VSV-G (IND)]. The B cells of the transgenic mice were unresponsive to this soluble glycoprotein. However, immunoglobulin M antibodies were induced in these mice if they were challenged with either wild-type or inactivated VSV-IND. The responsiveness of the B cell to the glycoprotein was increased by presenting it in a more compact and organized form on the viral surface.

■

Ras-like proteins and Type II diabetes

Although the incidence of non–insulin-dependent or Type II diabetes mellitus (NIDDM) strongly suggests a genetic component, the gene or genes associated with this disease have not yet been identified. Skeletal muscle is a major site of insulin resistance in NIDDM; Reynet and Kahn (p. 1441) screened complementary DNA libraries from skeletal muscle of normal and diabetic individuals and identified a 29-kilodalton Ras-related protein that was overexpressed by almost a factor of 10 in NIDDM patients. The Rad protein (Ras associated with diabetes) has important sequence differences compared to other members of the Ras–guanosine triphosphatase superfamily, especially in the G2 and G3 domains that are involved in guanosine triphosphate binding and dissociation. Why Rad is overexpressed is unclear—possibilities include inhibiting normal Ras function or compensating for the blockade of signaling that leads to insulin resistance.

THE EVOLUTION IN CELL CULTURE CONTINUES...

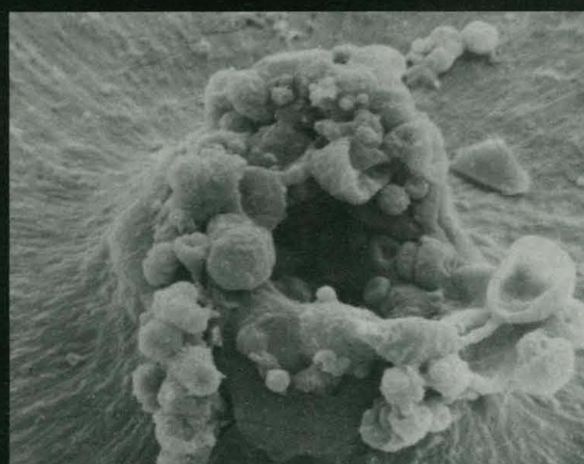


. . . with the development of BIOCOAT® Cell Environments. Now you can culture your cells under conditions which more closely approximate the physiological state of cells *in vivo*.

Whether you want your cells to rapidly adapt to culture conditions, grow in serum free medium, display enhanced gene expression, or exhibit higher levels of differentiation and biochemical function, there is a BIOCOAT Cell Environment appropriate for your needs.

BIOCOAT Cell Environments combine a wide variety of extracellular matrix proteins, such as laminin, fibronectin, collagens, EHS Natrix® and MATRIGEL® with FALCON® tissue culture plates, dishes, flasks, coverslips and cell culture inserts in ready-to-use culture systems.

For more biologically relevant results, use BIOCOAT Cell Environments in your experiments. Call or write today for further information.



Scanning electron micrographs of primary rat mammary epithelial cells at 24 hours (inset) and 36 hours (background) on MATRIGEL® Basement Membrane Matrix. Photo courtesy of Dr. Margaret Neville.

BIOCOAT®
CELL ENVIRONMENTS

Collaborative Biomedical Products
Becton Dickinson Labware
Two Oak Park, Bedford, MA 01730
800 343-2035 • (Fax) 617-275-0043

BECTON DICKINSON

New Transgenic Models For *In Vivo* Studies.

TIM™ RAG-2 Transgenic Mouse
Deficient in RAG-2 gene. Lacks mature T and B lymphocytes. Broadly immunodeficient. For gene function studies in chimeras and immune cell disorder research.

HLA-B27™ Transgenic Rat
Expresses HLA-B27 and human β2-microglobulin. Spontaneously exhibits signs of inflammatory bowel disease, psoriasis and arthritis. For inflammatory disease research.

C1D™ Transgenic Mouse
Inactivated β2-microglobulin gene. Deficient in mature cytotoxic T cells ($CD4^-8^+$). For basic immunology research.

C2D™ Transgenic Mouse
Disrupted A^b_β gene. Deficient in helper T cells ($CD4^+8^-$). For basic immunology research.

For technical information and availability of models, call 415-964-7024 or fax 415-964-3537.

GENPHARM
INTERNATIONAL

P. O. Box 568, Los Altos, CA 94023

1. *Cell* **68**, 855-867 (1992). 2. *Cell* **63**, 1099-1112 (1990). 3. *Nature* **344**, 742-746 (1990). 4. *Science* **253**, 1417-1420 (1991).
GenPharm is a registered trademark and C1D, C2D, HLA-B27 and TIM are trademarks of GenPharm International, Inc.

Circle No. 12 on Readers' Service Card

NEW FLUAR™ OBJECTIVES

THE ULTIMATE IN LIGHT TRANSMISSION FOR ALL FLUORESCENCE MICROSCOPY.

When Carl Zeiss develops a new line of objectives, you can be sure that they are special.

The new Fluar ICS (Infinity Color-corrected System) objectives deliver the brightest images possible over a wide spectral range by combining the highest numerical apertures with a minimum number of specially designed glass elements.

The high light transmission and large acceptance angle make Fluar objectives ideal for all fluorescence applications, from the measurement of intracellular calcium with FURA 2 to the observation of live cells where lowest light levels need to be detected.

Fluar ICS objectives also provide superior images with transmitted light, brightfield and DIC techniques.

Three types of Fluar objectives are currently available: Fluar 10X/0.5, Fluar 40X/1.3 oil and Fluar 100X/1.3 oil.

For further details contact your Zeiss representative or call
(800)233-2343
Fax (914)681-7446

Brightfield Microscopy
Darkfield Microscopy
Phase Contrast Microscopy
Fluorescence Microscopy
Differential Interference Contrast Microscopy
Polarizing Microscopy
Video Microscopy
Confocal Microscopy
Image Analysis
Microscope Photometry

Carl Zeiss, Inc.
Microscope Division
One Zeiss Drive
Thornwood N.Y. 10594

SEE WHAT YOU'RE MISSING

Circle No. 20 on Readers' Service Card

1994 SCHEDULE - NEW HAMPSHIRE AND RHODE ISLAND

Holderness School Plymouth, N.H.	Brewster Academy Wolfeboro, N.H.	Plymouth State College North Plymouth, N.H.	Plymouth State College South Plymouth, N.H.	New England College Henniker, N.H.	Salve Regina University Newport, R.I.
Molecular Cytogenetics	Basement Membranes	Nitrogen Fixation (NEW)	Cell Biology of the Neuron (NEW)	Neuroendocrinimmunology	
Fungal Metabolism	Solar Terrestrial Physics	Diamond Synthesis	(To be announced)	Periodontal Diseases	Stereochemistry
Physical Metallurgy	Microstructure Fabrication	Mutagenesis	Bioorganic Chemistry	Nondestructive Evaluation	Biopolymers
Tribology	Polymers	Meiosis	Thermosetting Hi-Performance Materials	(To be announced)	Neural Development
Postharvest Physiology	Bacterial Cell Surfaces	Motile and Contractile Systems	Reproductive Tract Biology	Immunochemistry & Immunobiology	Cardiac Regulatory Mechanisms
Drug Metabolism	Solid State Chemistry	Interaction of Water with Solid Surfaces	Chemical Senses: Taste and Smell	Magnetic Resonance in Bio. & Med.	Radiation Chemistry
Organometallic Chemistry	Tetrapyrrole Compounds	Microbial Stress Response (NEW)	Oxygen Binding Proteins (NEW)	Electron Spectroscopy	Calcium Phosphates
Dielectric Phenomena	Inorganic Chemistry	Particle-Solid Interactions	Point & Line Defects in Semiconductors		Polymer Physics
Water and Aqueous Solutions	Biomolecular Recognition & Immobilization	Hormonal and Neural Peptide Biosynthesis (NEW)	Foams		Oscillations & Dynamic Instability
Organic Geochemistry	Vibrational Spectroscopy				Electron Donor-Acceptor Interactions
					Origin of Life

FIXED CONFERENCE FEES, 1994

Fixed Fees (New Hampshire Sites)

Conferee (double occupancy)........................$500
($450 if postmarked 3 weeks prior to Conference)

Conferee (single occupancy-IF AVAILABLE)....$550
($500 if postmarked 3 weeks prior to Conference)

Non-Resident Conferee (meals, no room).........$460
($410 if postmarked 3 weeks prior to Conference)

Guest (double occupancy)............................$410
($360 if postmarked 3 weeks prior to Conference)

Guest (single occupancy - IF AVAILABLE).....$460
($410 if postmarked 3 weeks prior to Conference)

Fixed Fees (Rhode Island Site)*

Conferee (double occupancy).......................$515
($465 if postmarked 3 weeks prior to Conference)

Conferee (single occupancy-IF AVAILABLE)..$565
($515 if postmarked 3 weeks prior to Conference)

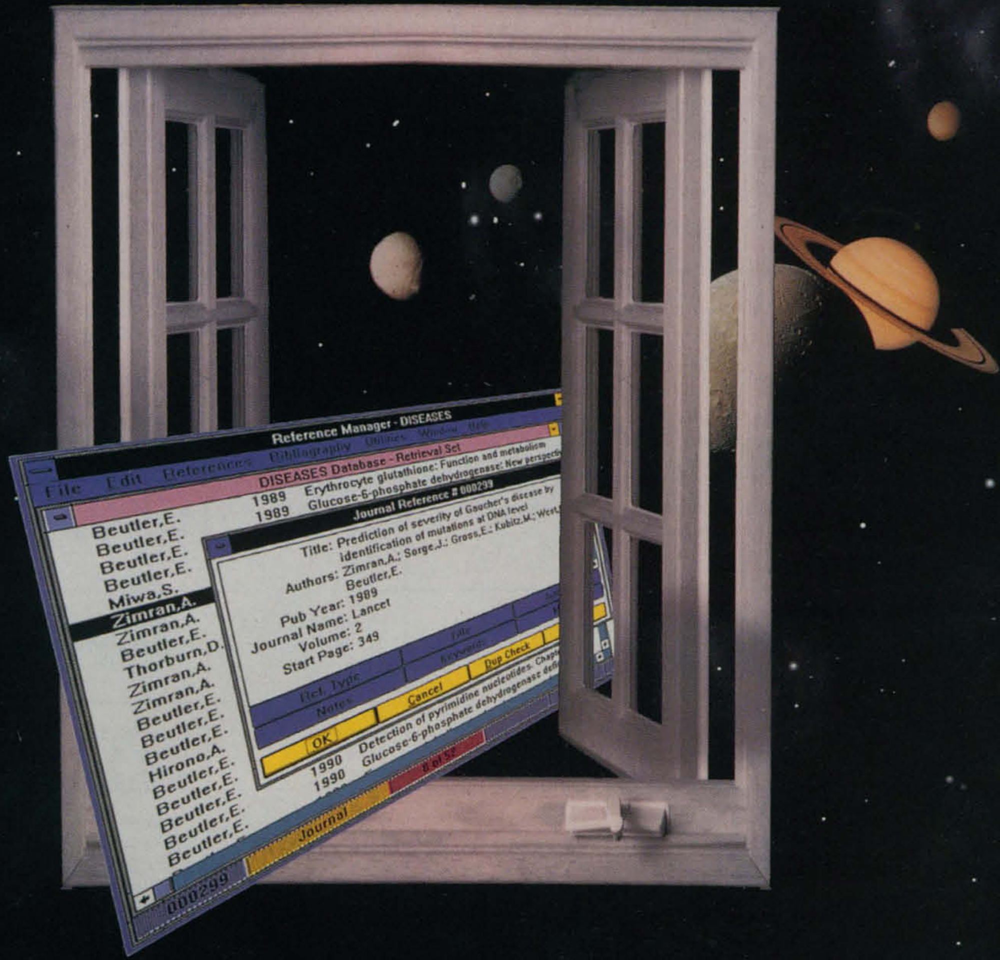
Non-Resident Conferee (meals, no room)........$460
($410 if postmarked 3 weeks prior to Conference)

Guest (double occupancy)...........................$425
($375 if postmarked 3 weeks prior to Conference)

Guest (single occupancy - IF AVAILABLE)....$475
($425 if postmarked 3 weeks prior to Conference)

*All rooms at the Rhode Island site are double with bath.
Children under 12 years of age are not permitted in the meeting rooms, dining rooms, or dormitories at any host sites.

1. Full fixed fee will be charged regardless of time conferee attends Conference. Please note fees.
2. Fixed fee cannot be prorated or reduced for anyone (speakers, discussion leaders, conferees).
3. Non-resident conferees are expected to eat all meals in the conference dining room and, therefore, the Fixed Fee for non-resident includes the full meal charge.



Reference Manager® Opens New WINDOWS

The leading bibliographic software is now available for Microsoft® Windows™ !

Since 1984, Reference Manager has been the leading bibliographic management software package for scientists, information professionals, and other scholars. Now Reference Manager is available for the Microsoft Windows operating system as well as for MS-DOS, Macintosh, and the NEC 9801.

In addition to the features found in its DOS and Macintosh counterparts, Reference Manager for Windows contains a number of enhancements, including greatly increased flexibility in bibliographic formatting and the ability to "cut and paste" entire references or their components using the standard clipboard function of Windows.

Reference Manager for Windows - The Best Bibliographic Management Software is now the only product of its kind for Microsoft Windows!

MICROSOFT® WINDOWS™ COMPATIBLE

RIS

Research Information Systems

2355 Camino Vida Roble, Carlsbad, CA 92009-1572

(800) 722-1227 • (619) 438-5526 • Fax: (619) 438-5573

Circle No. 5 on Readers' Service Card