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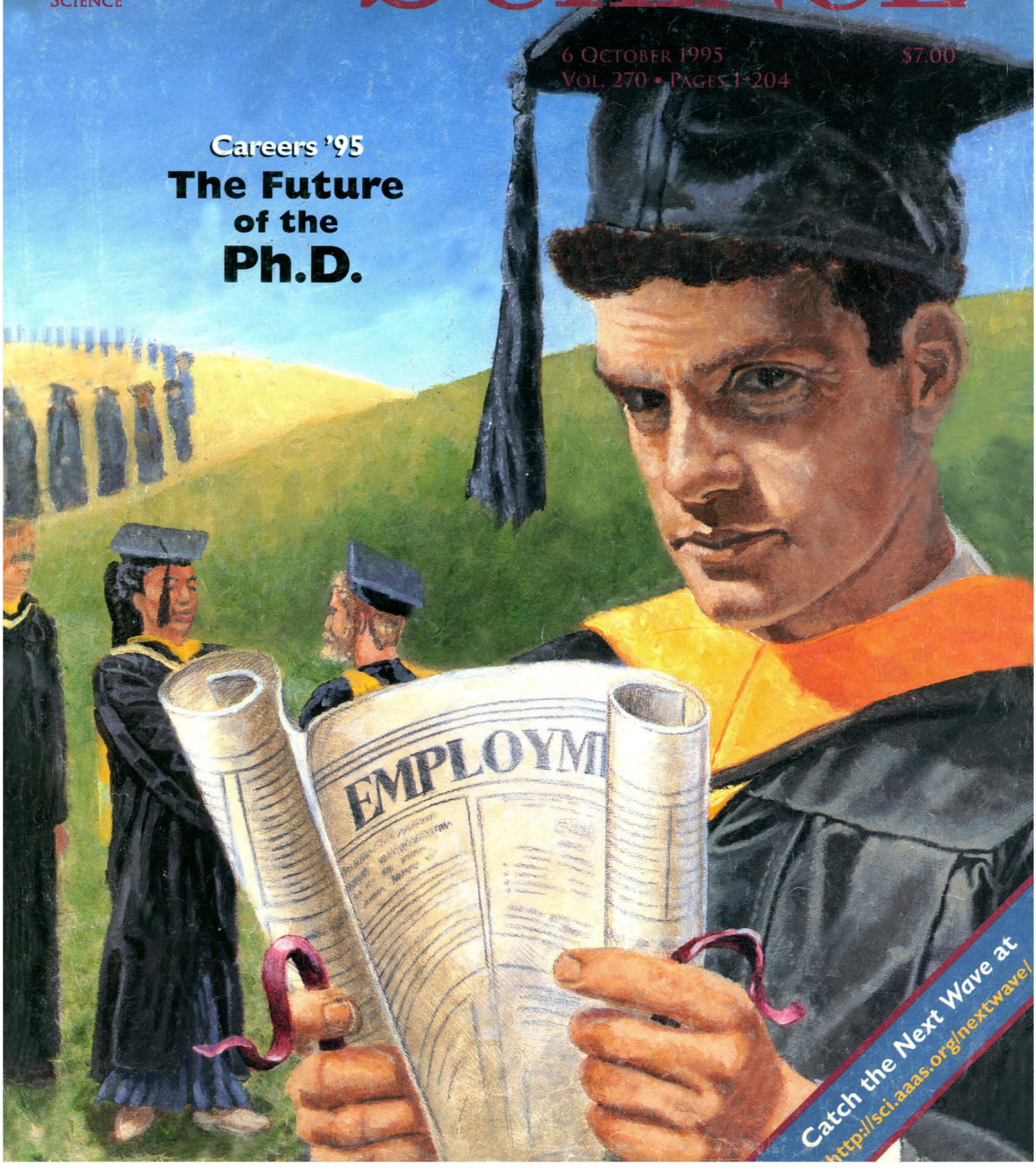

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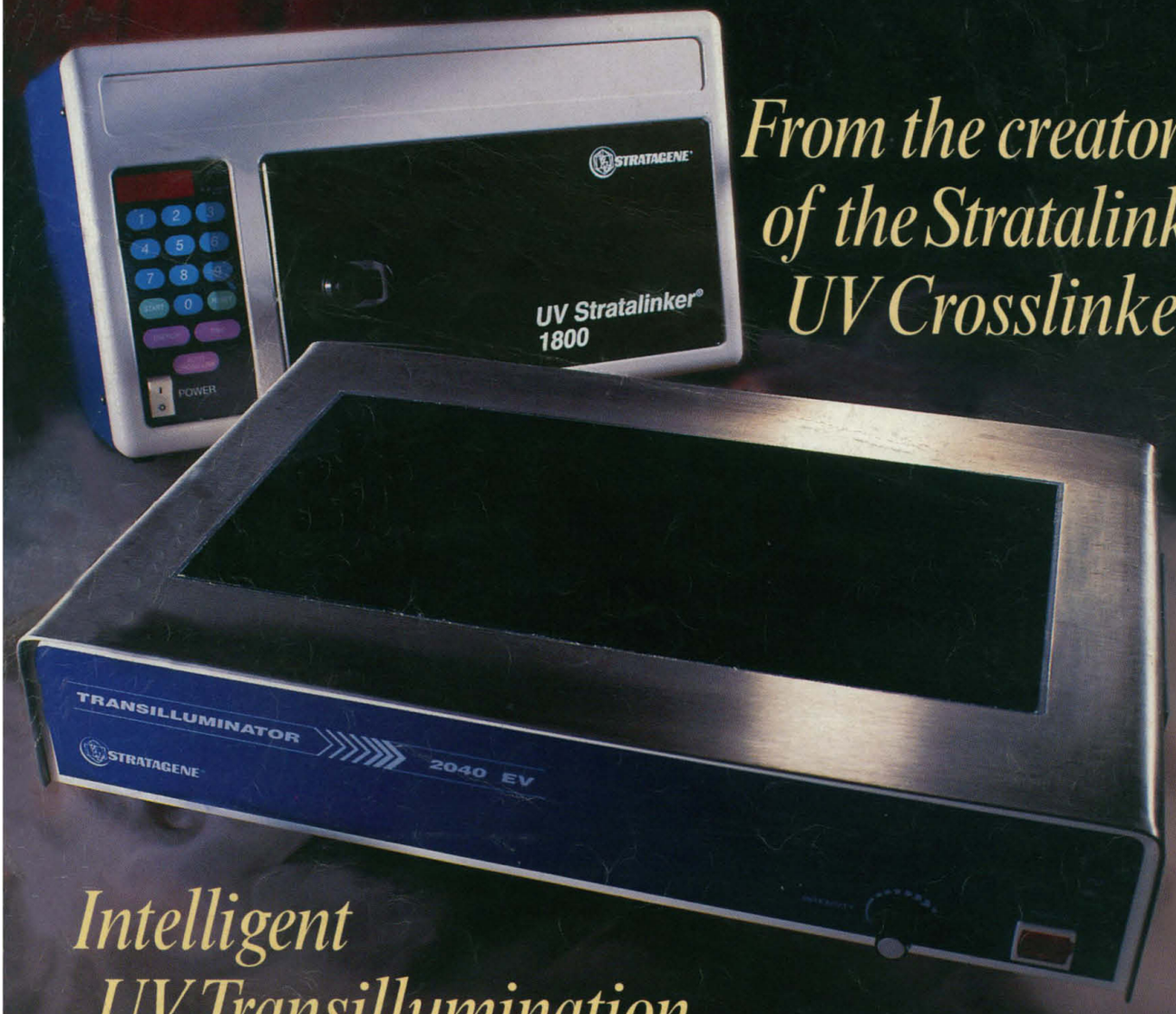

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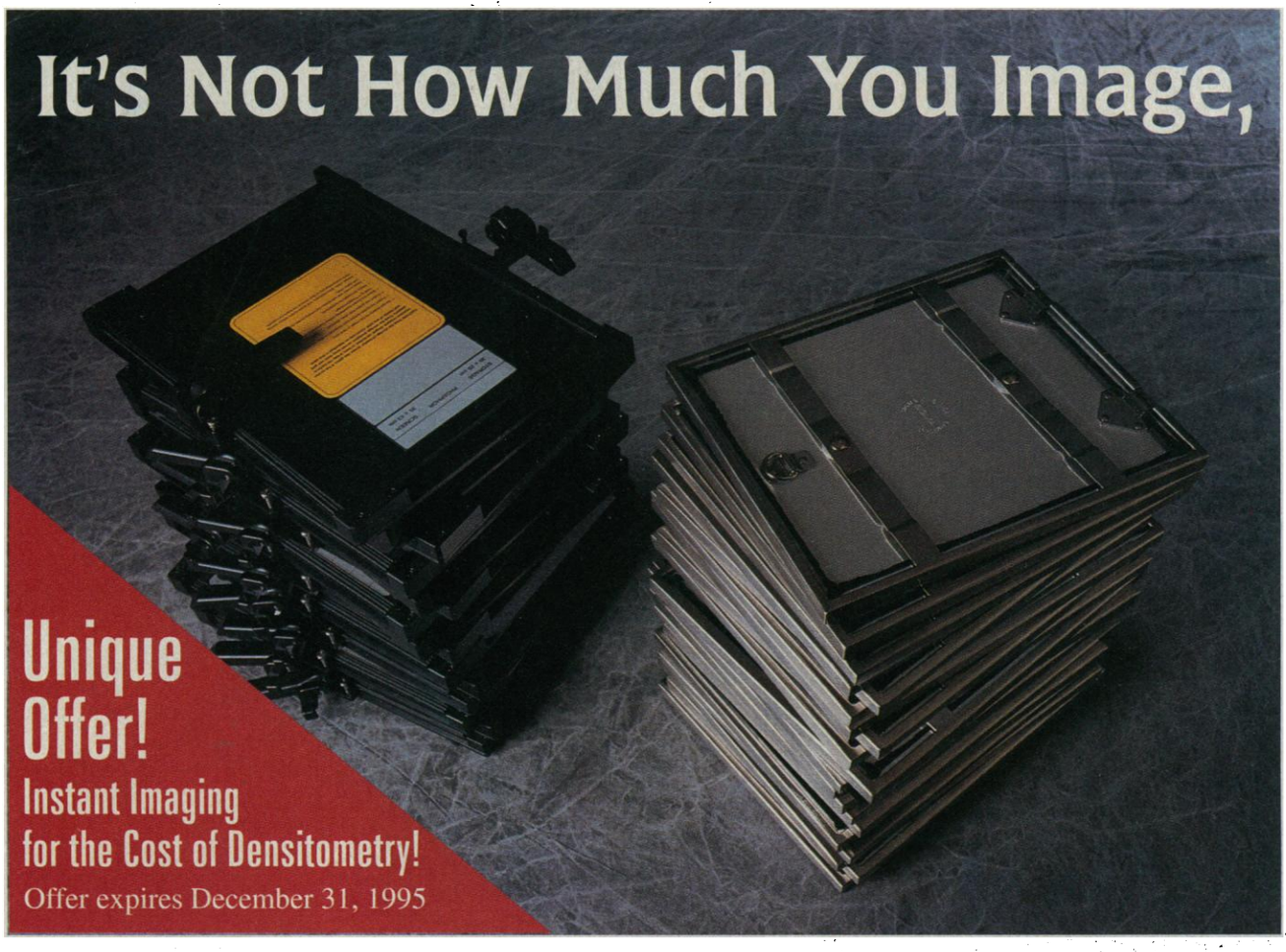

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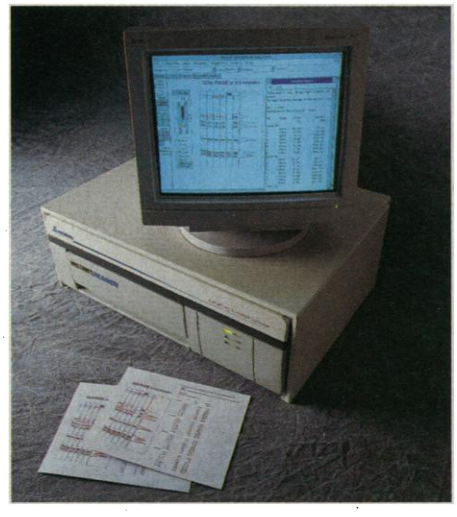

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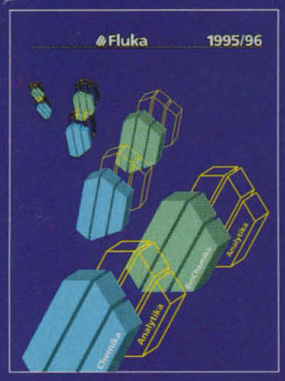

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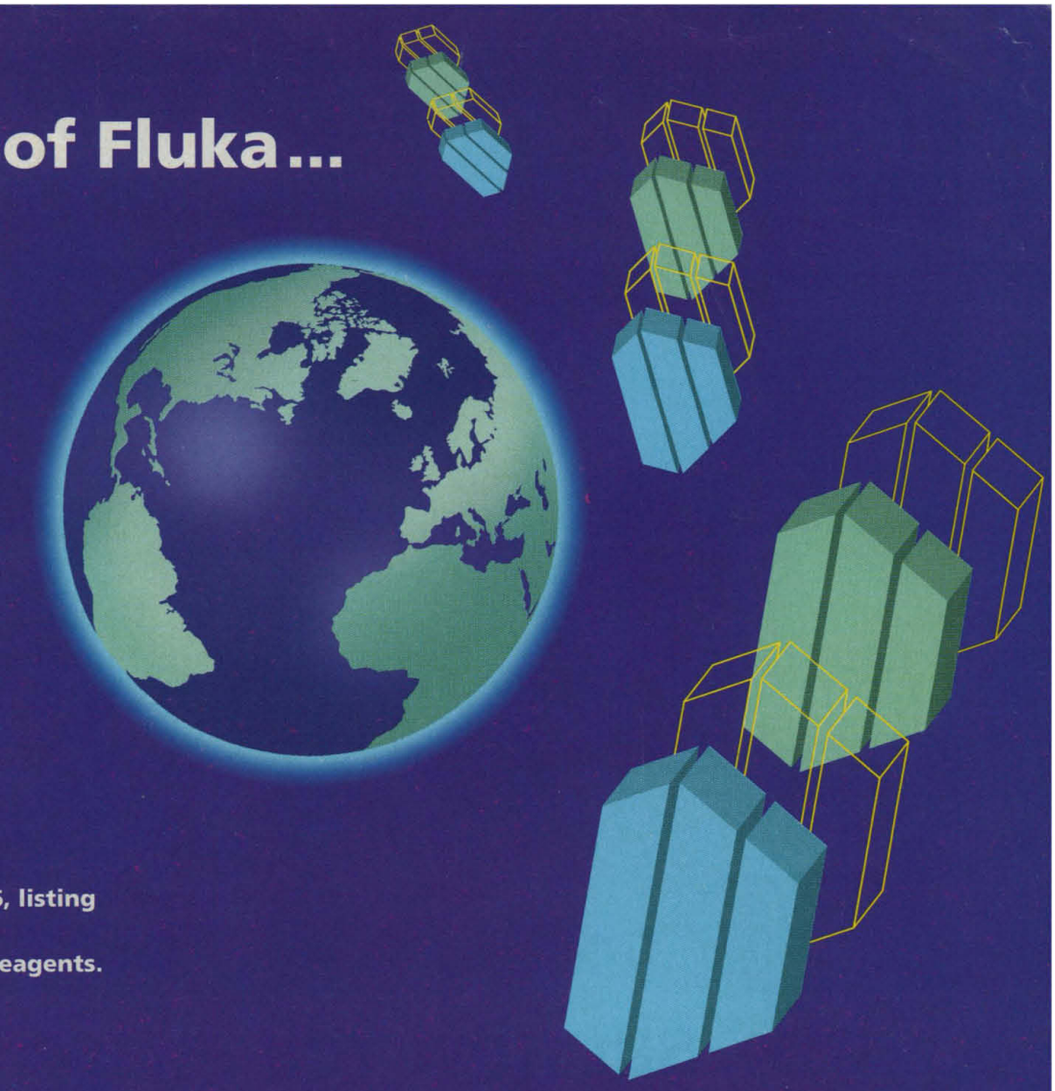

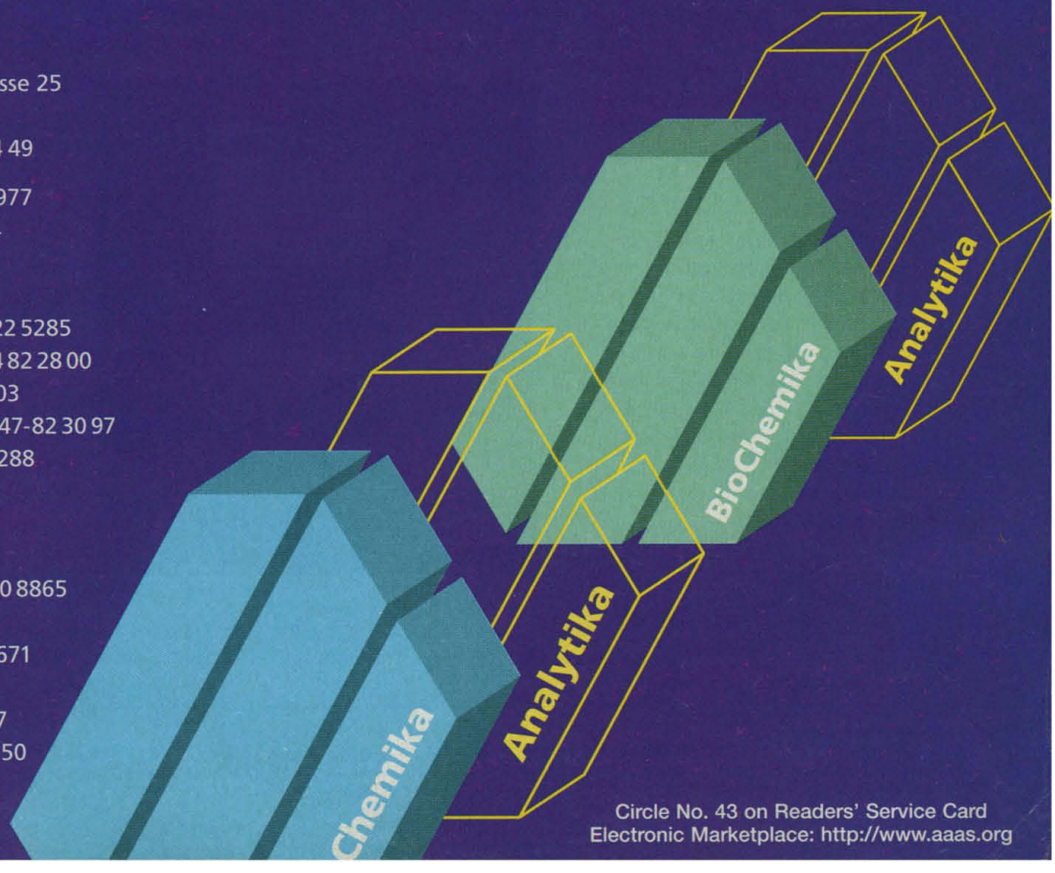

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NEWS & COMMENT

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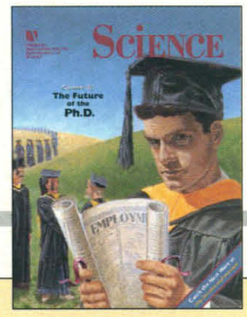
COVER

The future of the science doctorate goes under the microscope in this special issue of *Science*. And the most pressing question new graduates pose about that future, as illustrated in this image, is, Will I get a job? To adapt to a shrinking job pool, many are proposing Ph.D. population control, curriculum changes, and altering the research university in very basic ways. See the special News section "Careers '95: The Future of the Ph.D." beginning on page 121. [Illustration: Jody May]



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Careers '95:
The Future of the Ph.D.

Is It Time to Begin Ph.D. Population Control? • Foreign Competition • Grad Schools Preview the Shape of Ph.D.s to Come • A Marketable Master's • A Business Blueprint: How to Build a Better Ph.D. • The Future University: Leaner and Meaner? • Scientists Enjoy Life in the Not-So-Fast Lanes • Young Scientists Voice Hopes and Fears for the Future

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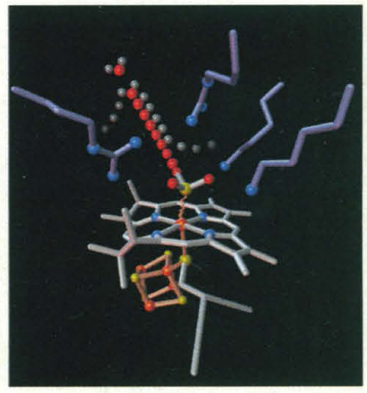

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Multielectron reduction in the soil

◩ Indicates accompanying feature

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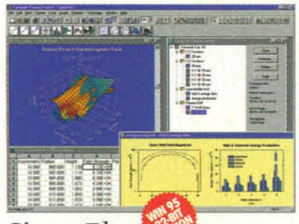

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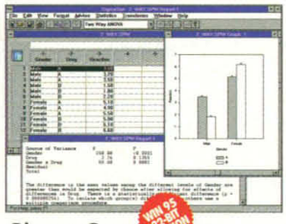

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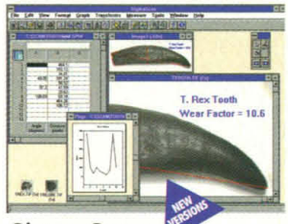

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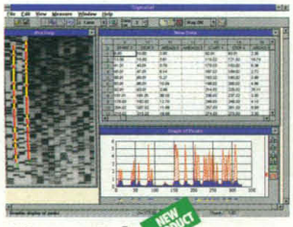

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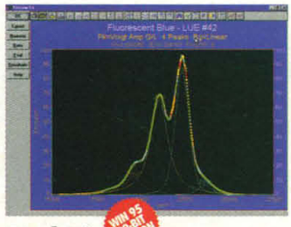

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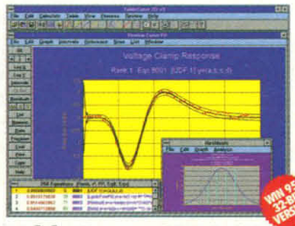

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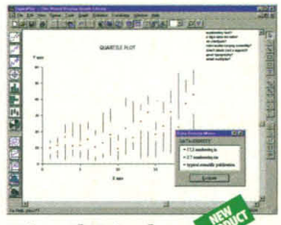

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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

African paleoclimate

Prominent changes in the climate in Africa have occurred during the past several million years and may have influenced the evolution and migration of hominids. DeMenocal (p. 53) presents detailed marine records (particularly of dust transport) off the east and west coasts of Africa and overviews the climate changes and relations to the fossil record. A prominent transition to a cooler and drier climate in Africa is seen at about 2.8 million years ago, coincident with the onset of Northern Hemisphere glaciation.

■

Flying high

New fleets of commercial supersonic aircraft are being planned, and the design of their engines must take into account possible effects of their emissions on stratospheric chemistry. Fahey *et al.* (p. 70) sampled emissions from the Concorde during a supersonic cruise in the stratosphere. Their results indicate that gas emissions can be extrapolated from ground-based tests, whereas the large numbers of particles in the emissions are not yet understood satisfactorily. The increased aerosol surface area of these particles may lead to further ozone losses.

■

Deep reflections

Two prominent seismic reflectors are recognized in Earth's mantle, at depths of about 440 and 670 kilometers, and are thought to be associated with changes in the mineralogy of the mantle with increasing pressure. Evidence for reflectors in the lower mantle, which is thought to have a more constant mineralogy, have been sparse and seem to be associated primarily with subduction zones. Le Stunff *et al.* (p. 74) now present evidence for two reflectors in the lower mantle, at depths of 785 and 1200 kilometers, beneath Africa. They examined seismic waves emanating from the recent deep earthquake in Fiji using stations in Africa and California.

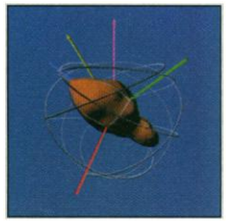
Laser control of a chemical reaction

Molecules can be excited and photodissociated with lasers, but it is often difficult to manipulate the course of the reaction with lasers so that the products formed can be controlled. Zhu *et al.* (p. 77) now report that the outcome of the photoexcitation of hydrogen iodide (HI) can be controlled by how the energy is deposited (either as three ultraviolet photons or as one vacuum ultraviolet photon with the same energy). By modulating the phase difference between the two lasers, quantum mechanical interference was used to control the relative amounts of HI^+ and I^+ produced.

■

Asteroid portfolio

Imaging asteroids that come close to Earth orbit is made difficult by their small optical size. Radar observations, however, can be synthesized to produce



detailed images of these objects. Ostro *et al.* (p. 80) and Hudson *et al.* (p. 84) describe images of 4179 Toutatis, an Earth-orbit–crossing asteroid that came as close as 3,600,000 kilometers, or about 9.4 lunar distances. Radar data from two stations were combined to produce high-resolution images of Toutatis, which is several kilometers long, has a bifurcated shape, and is heavily cratered. A collision may have imparted its unusual rotation state.

Off and on

The cyclin-dependent kinases (CDKs) are critical regulators of cell cycle progression and are thus subject to multiple levels of control. One of these is phosphorylation at distinct sites, which can either activate or inhibit the enzymes. Two reports describe new insights into control of CDKs. Mueller *et al.* (p. 86) identified a protein kinase from *Xenopus* that inactivates Cdc2 by phosphorylating it on threonine-14 and tyrosine-15. The kinase, designated Myt1, is active during interphase and inactive during mitosis. Poon and Hunter (p. 90) describe the activity of a phosphatase, KAP, that dephosphorylates threonine-160 on Cdk2, a residue that must be phosphorylated for Cdk2 to be active. KAP can dephosphorylate Cdk2 only in absence of its regulatory subunit cyclin A.

■

TAP lessons

Class I major histocompatibility complex (MHC) molecules bind to cytosolic peptide antigens and present them on the cell surface. Grandea *et al.* (p. 105) have studied a human mutant lymphoblastoid cell line that is impaired in the surface expression of class I molecules. Immature heterodimers of class I heavy chain and β_2-microglobulin form in these cells but fail to associate with TAP, the transporter associated with antigen processing. Thus another gene is necessary for efficient association and peptide loading.

■

Words in thought and action

Distinct areas of the human brain are specialized for processing aspects of visual stimuli, such as color and motion, but where do the results of processing reside and how are they retrieved? Martin *et al.* (p. 102) present a brain imaging study in which subjects were required to generate words describing the color of a viewed object or an action associated with the object. The brain areas that were activated during these tasks overlapped or were near parts of the brain previously shown to be involved in color and motion processing. The authors suggest that the distribution of stored knowledge may parallel the organization of cortical processing in the brain.

■

Yeast prions

Prions—a type of infectious protein responsible for causing several neurodegenerative disorders in mammals—have recently been identified in yeast. Masison and Wickner (p. 93) now show that the propagation of the prion phenotype in yeast requires a specific domain of the prion precursor protein, Ure2p, which normally plays a role in controlling nitrogen catabolism. After induction of the prion phenotype, it becomes resistant to proteolysis. The prion-inducing domain could be deleted from Ure2p, which left the nitrogen control function intact but abolished the susceptibility of the yeast cells to express the prion phenotype.

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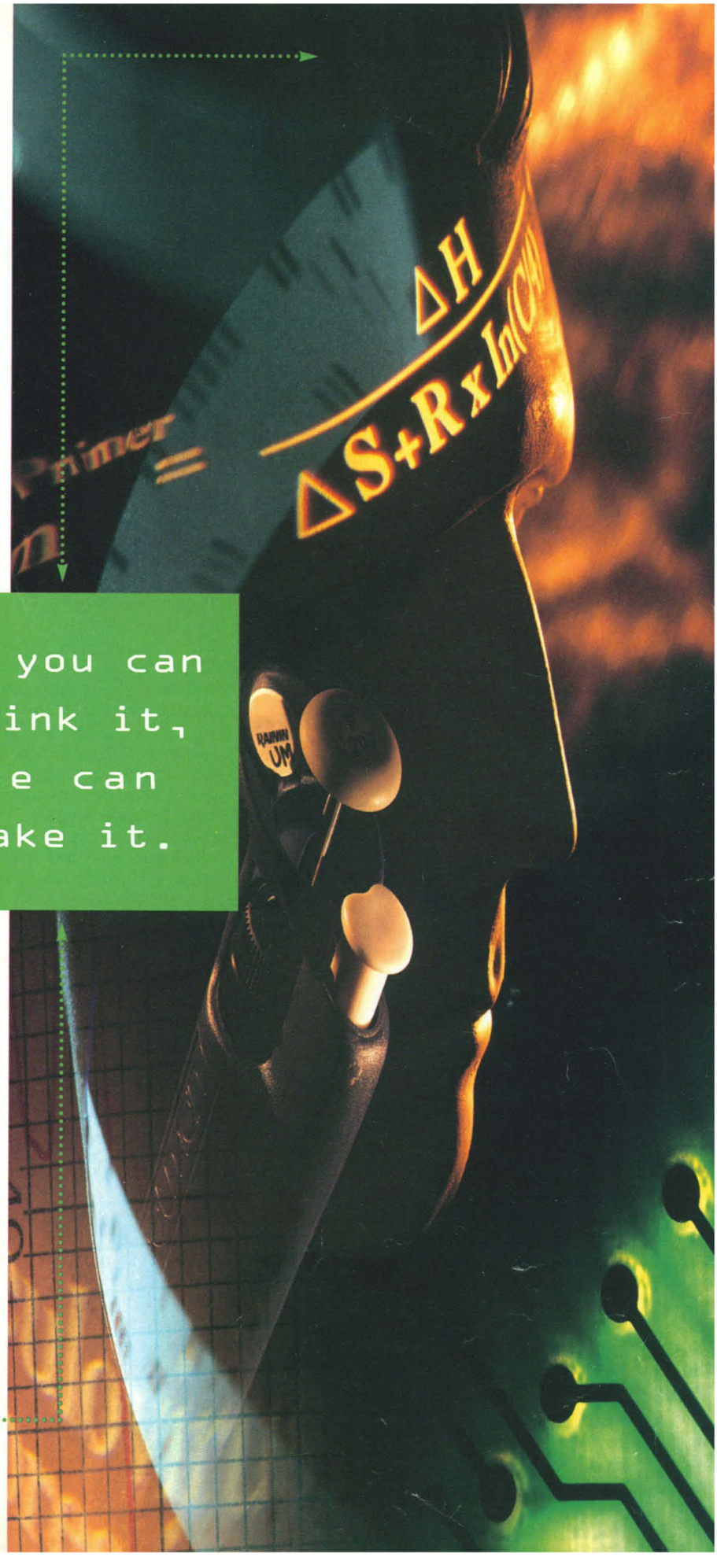

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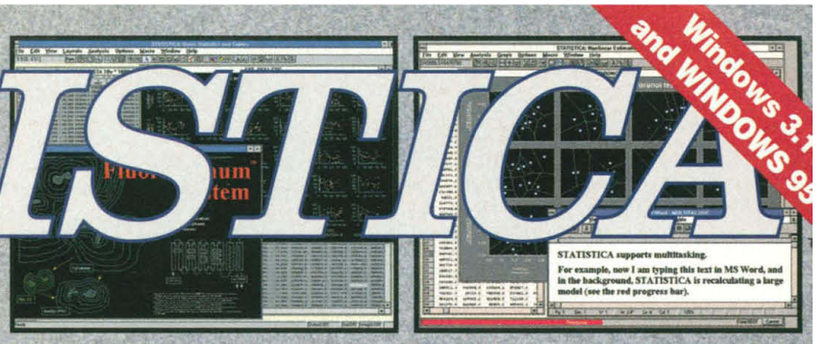

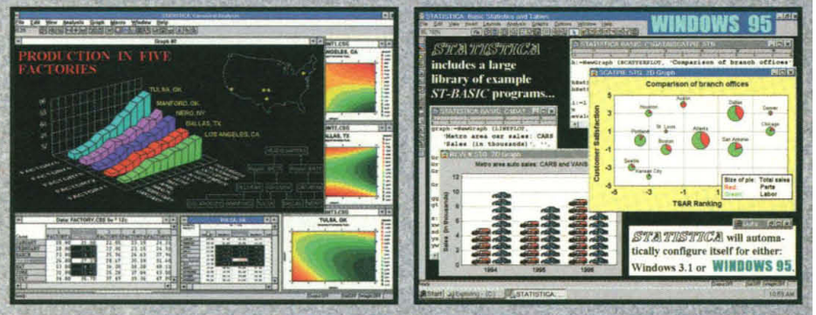

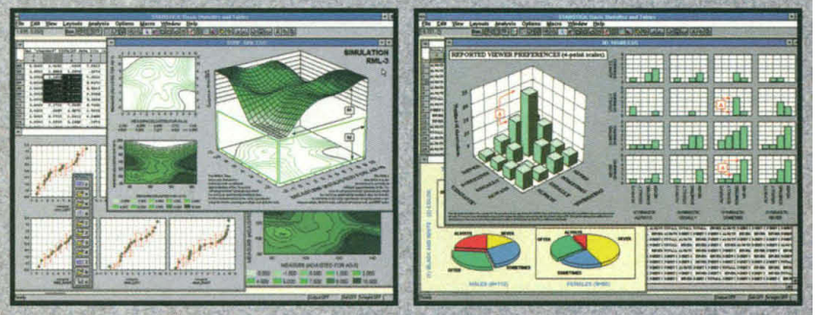

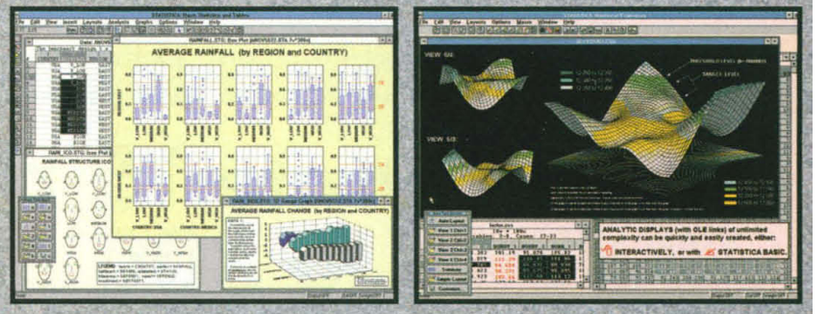

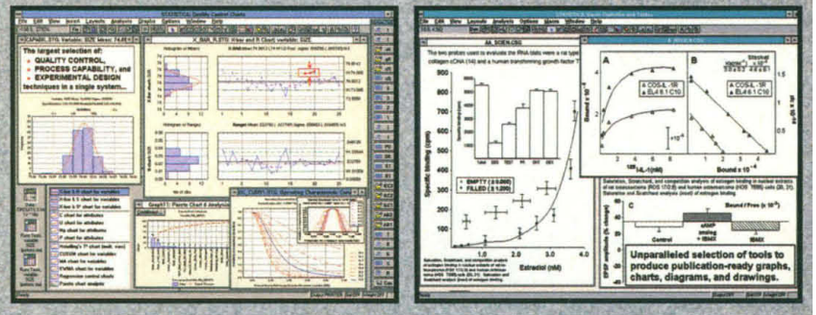

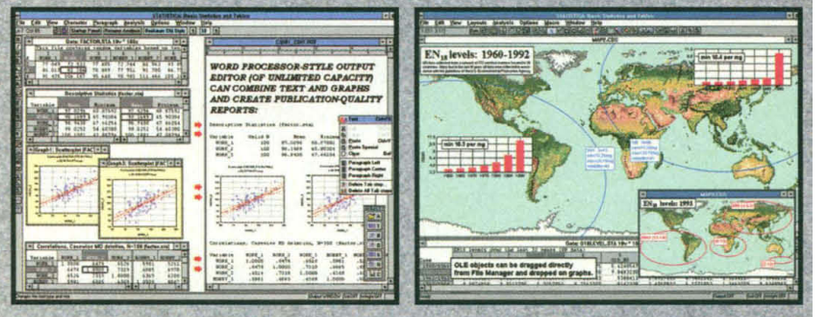

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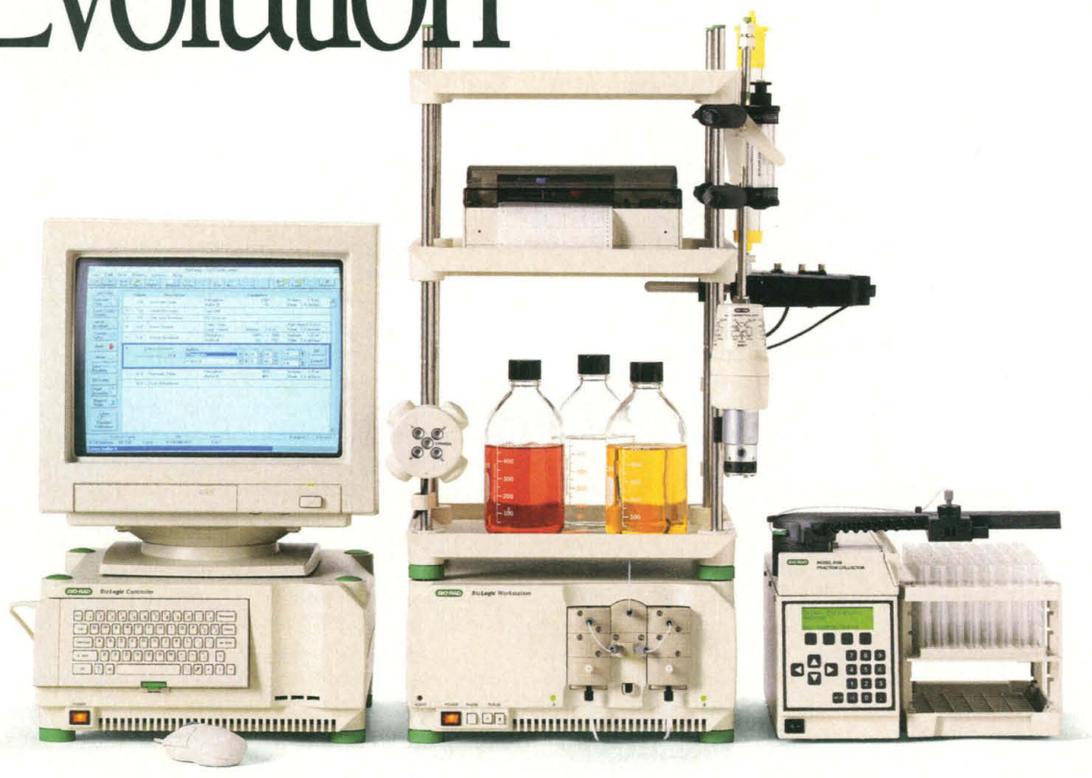

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- Presently directing research activities and product development for Sigma BioSciences.
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- Prior to Sigma, worked five years in a molecular biology group in the pharmaceutical industry.
- Also worked in academia at the Wistar Institute of Anatomy and Biology and at the University of Medicine and Dentistry of New Jersey.
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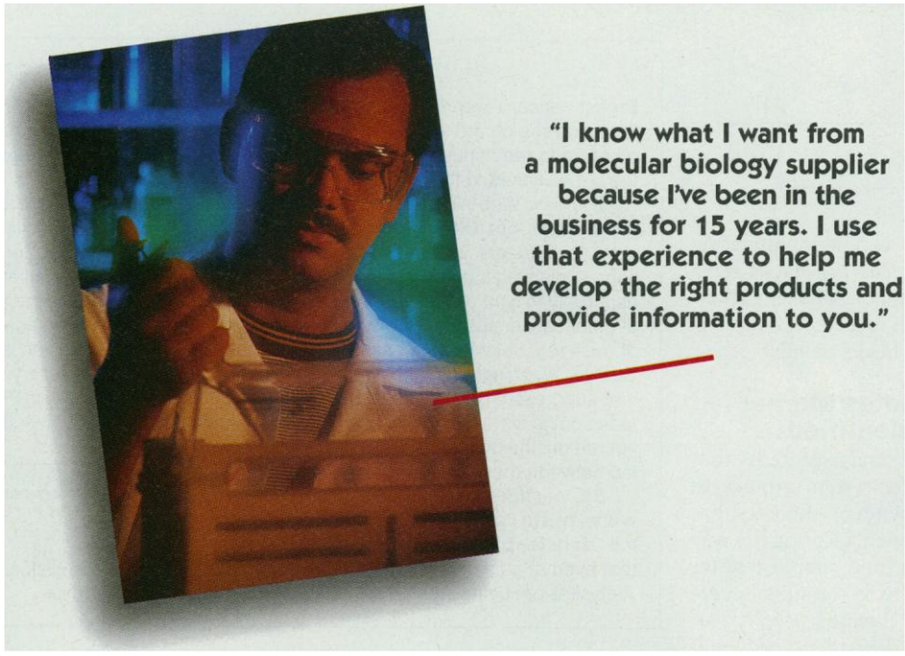

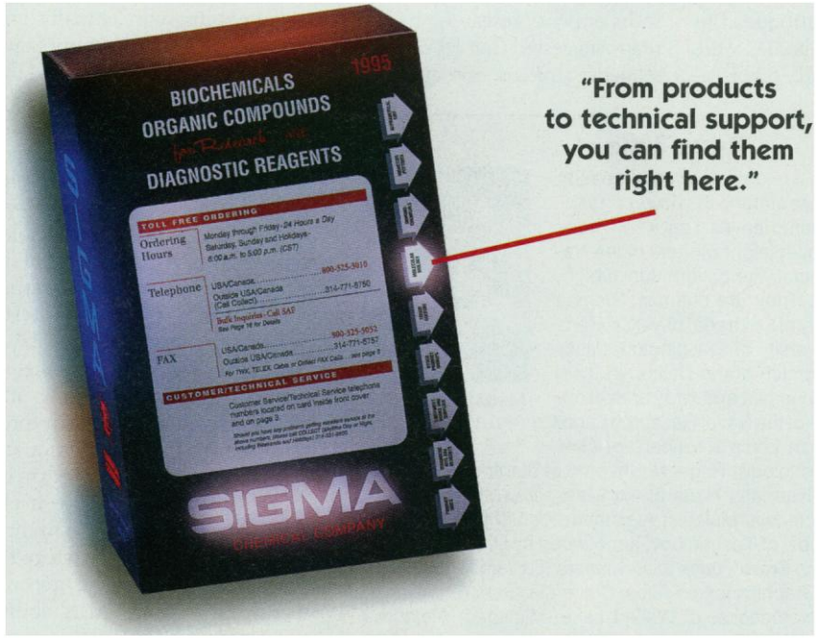

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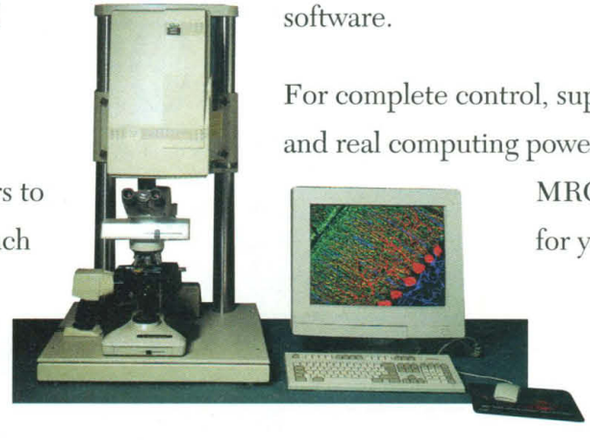

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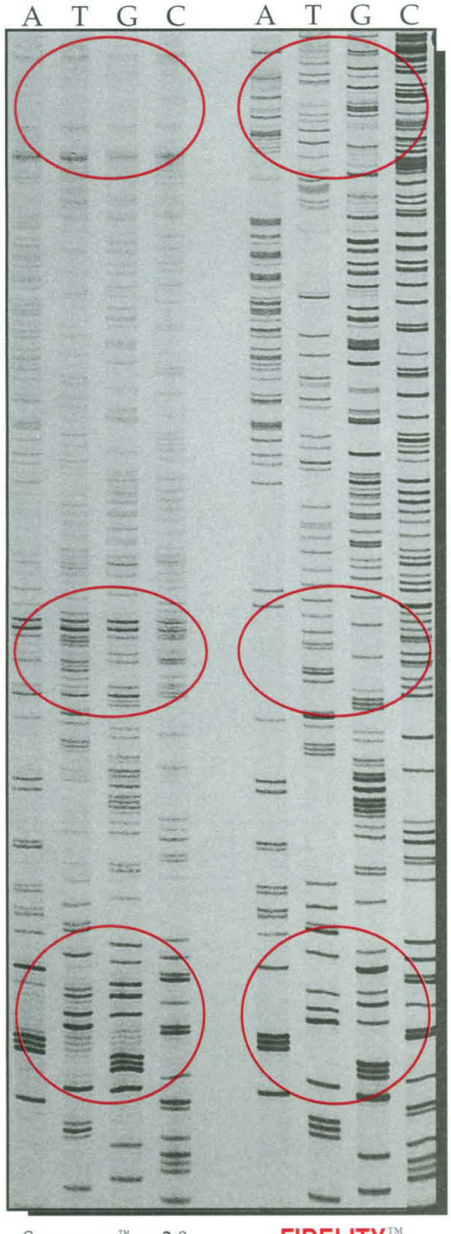

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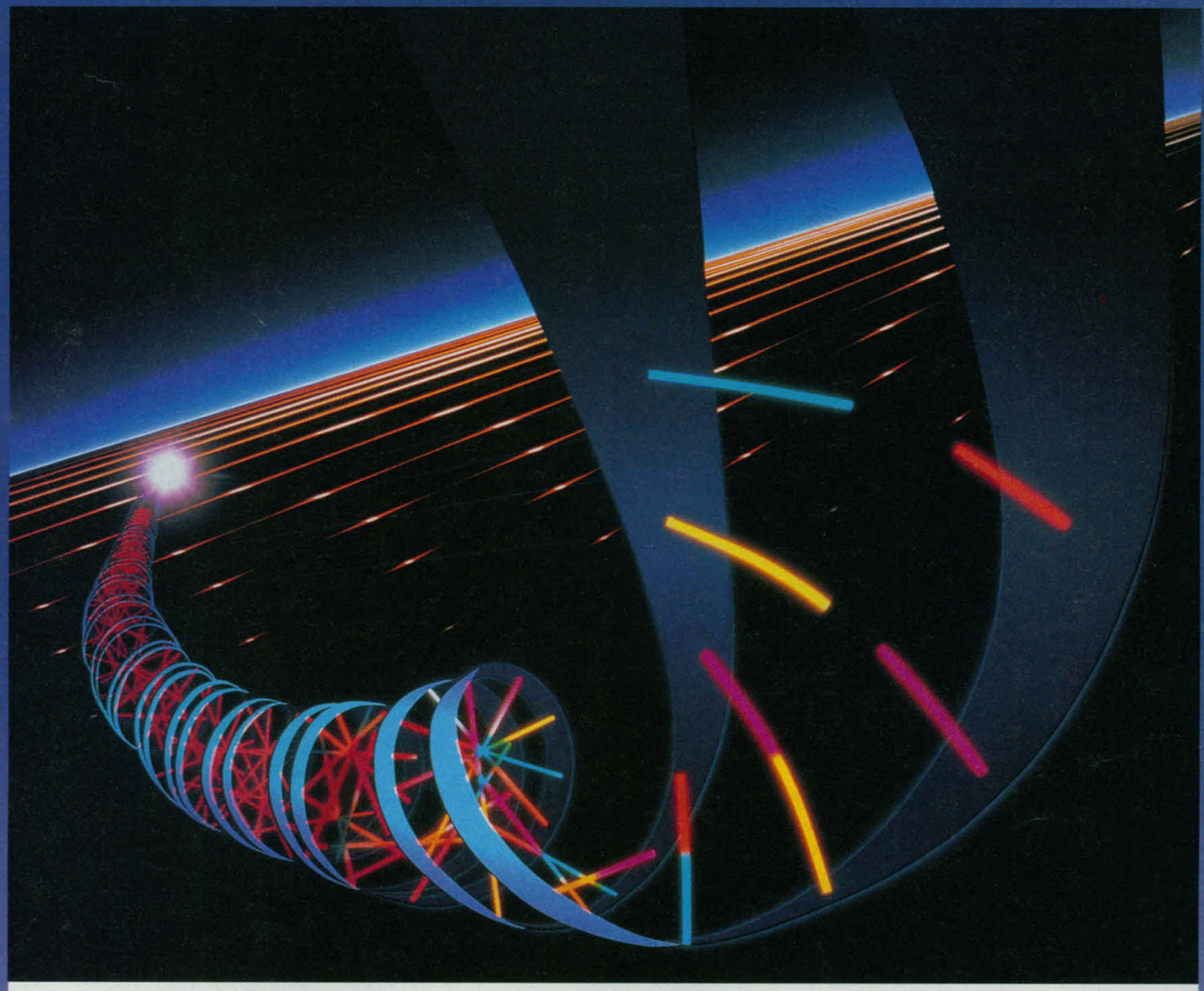

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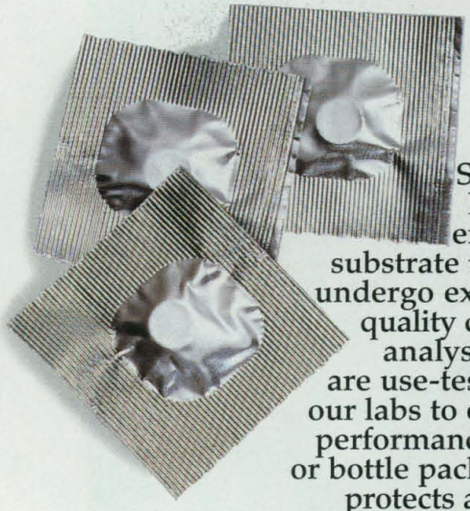

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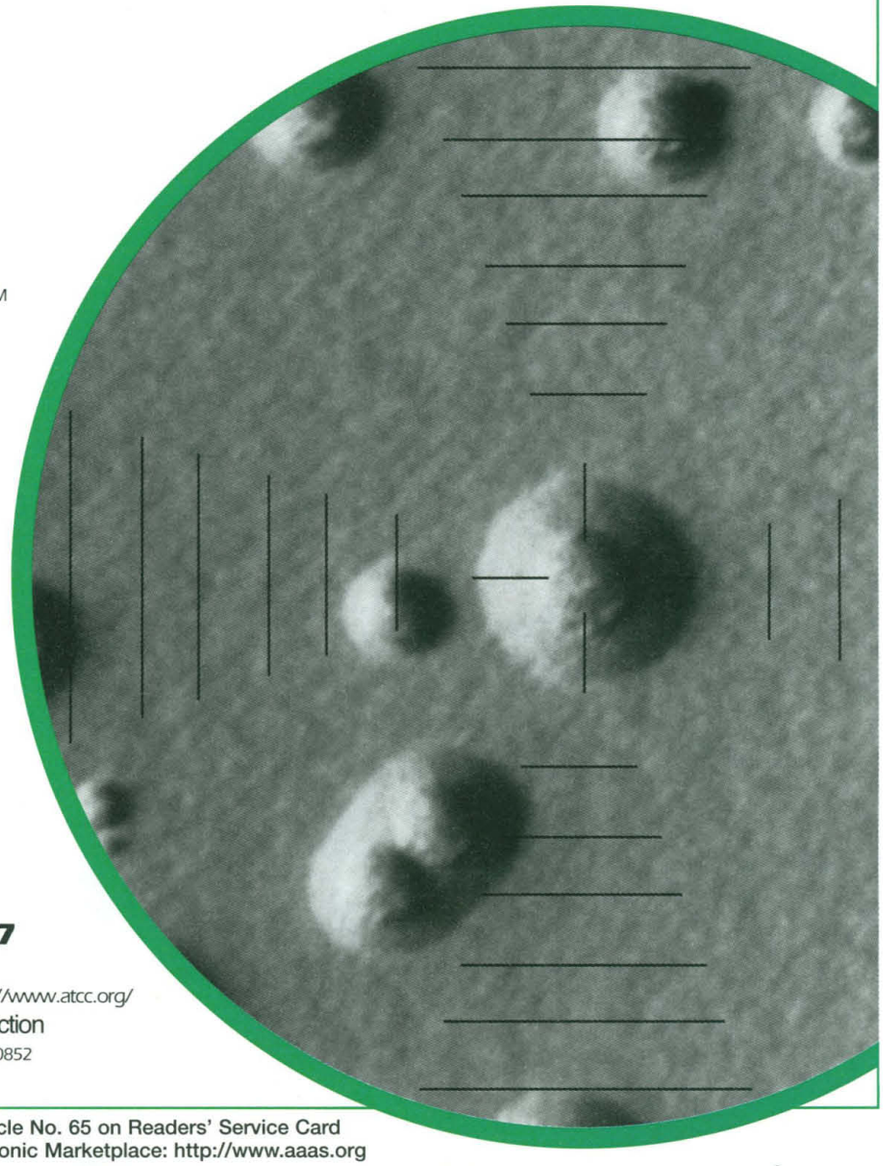

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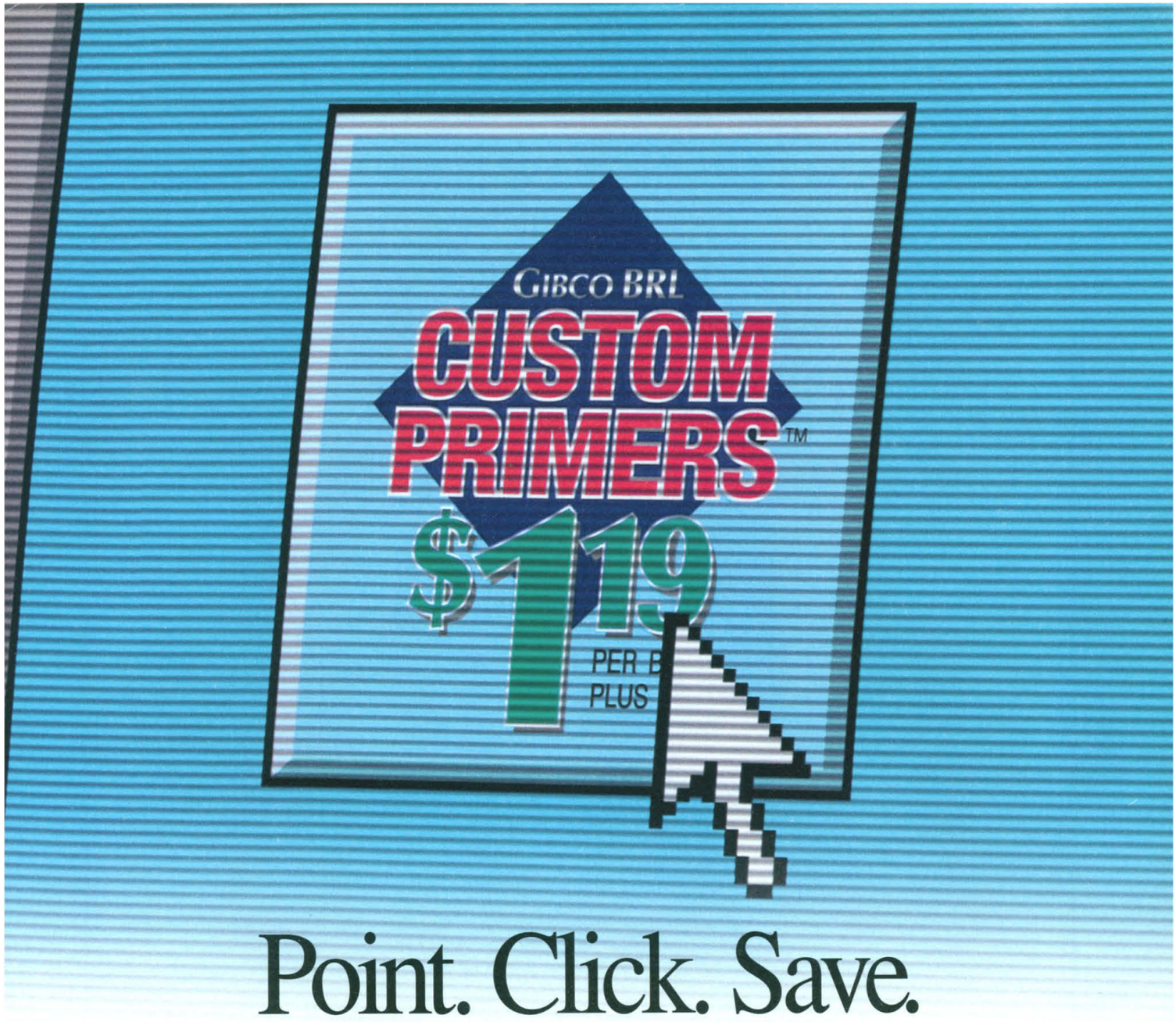

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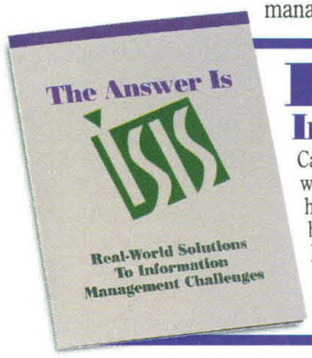

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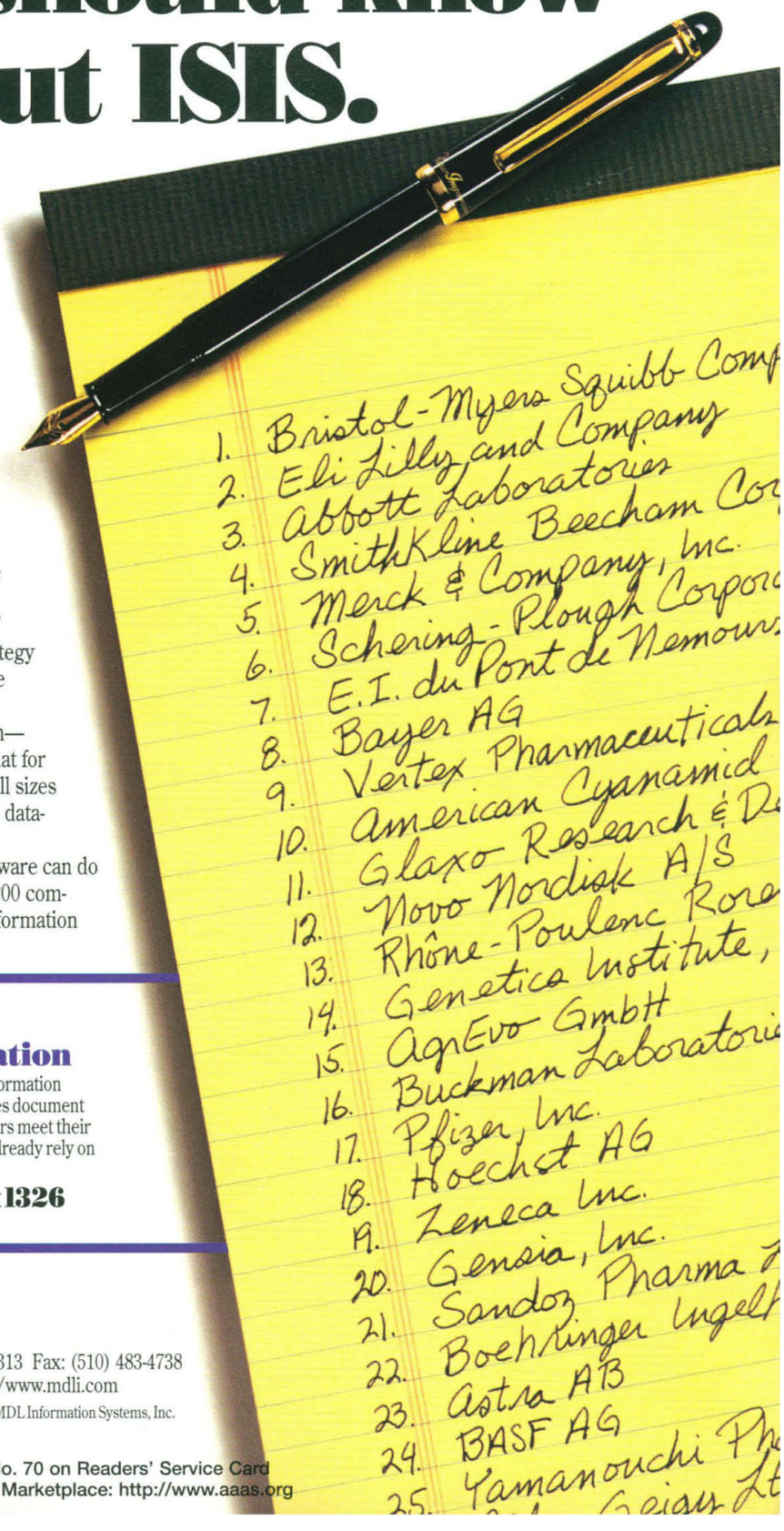

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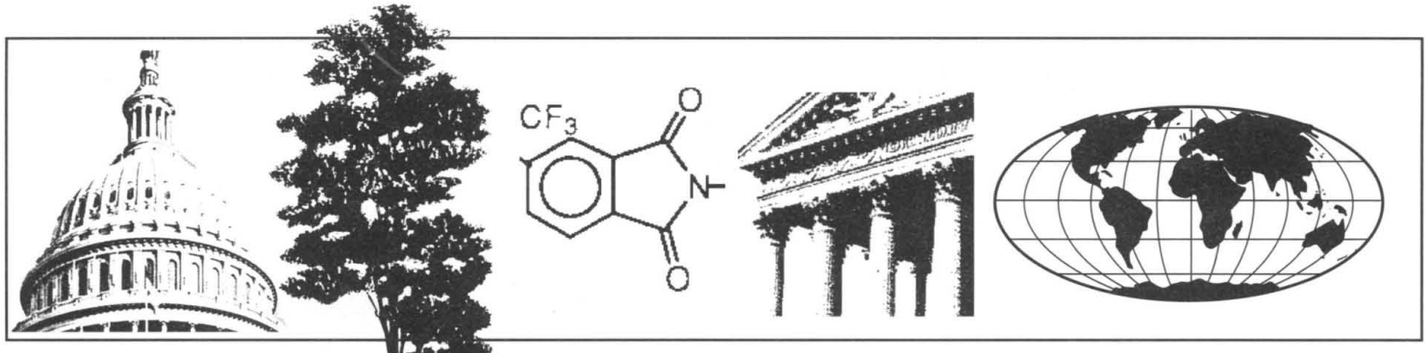

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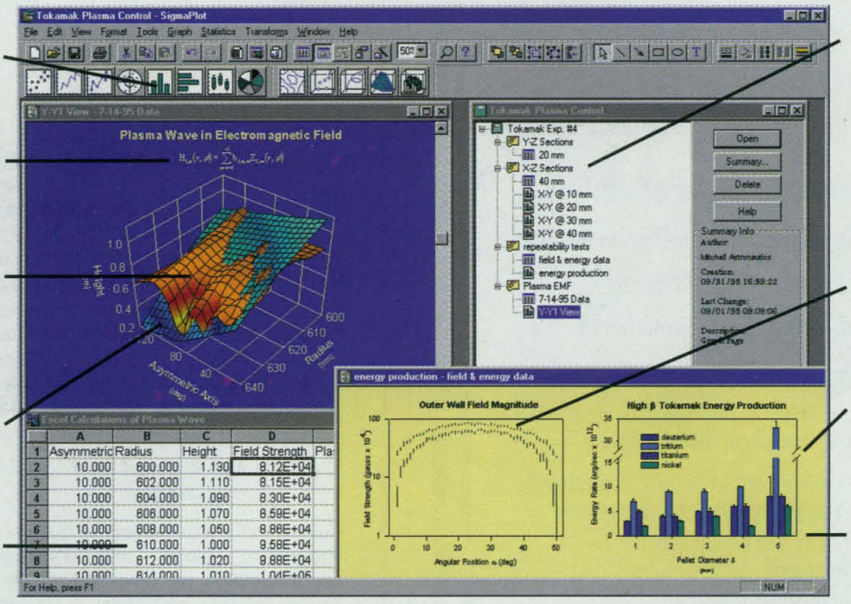
Embed images into SigmaPlot or embed SigmaPlot graphs into your documents with OLE 2 container and server

NEW! Visualize 3D
Multiple, intersecting 3D graphs with hidden line removal, discrete and continuous shading, and light source • Scatter, trajectory, mesh, and 3D bar charts

Robust multidimensional nonlinear curve fitting
10 independent variables, 25 parameter • Piecewise continuous, multifunctional, weighted, and boolean functions

NEW! Excel® inside SigmaPlot
Use Excel as your spreadsheet and pick data from it to create SigmaPlot graphs



NEW! Jandel Notebook
Organize multiple data worksheets and multiple graph pages effectively

NEW! Time-saving transforms
Create quick and powerful mathematical analysis routines to use again and again, including FFT functions

NEW! Visual Display Graph Library
Edward Tufte's templates and style guidelines • The Visual Display of Quantitative Information book *• Data density meter*

NEW! Control axes completely
Linear, semi-log, log, logit, probit, probability, polar, and category and custom axes • Offset axes • Axis breaks

NEW! Flexibility of multiples
Multiple pages per worksheet Multiple graphs per page • Multiple curves per graph • Multiple axes per graph

Create and customize *the exact* scientific graph you want

You've spent months collecting and analyzing data. Don't spoil your work now! Maximize the impact of your research with *new* SigmaPlot. When you want to document, present, and publish your work, financial spreadsheets and business graphing software can't do what SigmaPlot *already does* for tens of thousands of researchers worldwide.

AWARD-WINNING SIGMAPLOT

Since 1985, scientists and engineers have chosen award-winning SigmaPlot for the technical analyses and graphing they *want* – and for the total flexibility they *need*. Clear, precise technical graphs provide new insights into your data and allow you to present your results better.

POWERFUL DATA ANALYSIS

The best scientific graphs begin with powerful data analysis. SigmaPlot has what you need – huge data worksheets, FFTs, mathematical transform language, automatic regressions, nonlinear curve fitter, and much more.

CREATE GRAPHS EASILY

Click on a graph toolbar icon, pick your data with the new Graph Wizard, and you have your graph! Double click on any graph element and customize it with the new Graph Properties Dialog – everything's in one easy-to-use dialog.

CUSTOMIZE GRAPHS YOUR WAY

Create multiple technical axes per graph, control error bars, and choose from a variety of new 3D graphs. Don't settle for "canned graphs" software. Make the graphs you want.

EASY EXCEL AND OLE 2 INTEGRATION

Annotate your SigmaPlot graph with Word®'s Equation Editor. Embed your graph in PowerPoint® or Word. Analyze your data with an Excel worksheet *right inside of SigmaPlot – Excel's menus actually merge with SigmaPlot's!*

ANNOUNCING THE VISUAL DISPLAY GRAPH LIBRARY

Dr. Edward Tufte designed The Visual Display Graph Library using the unique flexibility of SigmaPlot. This graph library includes: the book *The Visual Display of Quantitative Information*, style guidelines, data density meter, fonts, and templates.

To get started with SigmaPlot's graphing flexibility and to create the graphs you want,

CALL 1-800-4-JANDEL (1-800-452-6335)

OTHER JANDEL PRODUCTS

SigmaPlot®: DOS Macintosh
SigmaStat®: Advisory statistical software
SigmaScan™: Image measurement software
SigmaScan™ Pro: Automated image analysis software
SigmaSuite™: Integrated graphing, statistics & image measurement software
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TableCurve™ 2D: Equation generator & curve fitting software
TableCurve™ 3D: Equation generator & surface fitting software
PeakFit™: Automated peak analysis software

FOR MORE INFORMATION PLEASE CALL, FAX OR E-MAIL:

Jandel Scientific: 2591 Kerner Blvd., San Rafael, CA 94901 415-453-6700 Fax 415-453-7769 **Internet:** sales@jandel.com
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Jandel
SCIENTIFIC SOFTWARE

TRAVEL FELLOWSHIP PROGRAM

for

Scientists of East Central Europe and the former Soviet Union

The United States Department of Energy (DOE) and the American Association for the Advancement of Science (AAAS) seek to recognize the research accomplishments of mid-career scientists from East Central Europe (ECE) and the countries of the former Soviet Union (FSU) in the area of environment and health, especially as it relates to problems of radiation contamination and health. A program has been established to award young ECE and FSU scientists travel grants to attend the AAAS Annual Meeting in the United States and be able to present their research findings to conference attendees during poster sessions.

The 1996 AAAS Annual Meeting will be held February 8 – 13 in Baltimore, Maryland.

Fellows will be given economy class travel support to the conference along with lodging and per diem reimbursement for food and incidental expenses. The fellows will also participate in site visits to local agencies and institutes directly related to their research.

ELIGIBILITY

Applications by ECE and FSU graduate students and post-doctoral scientists (within five years of completing their degree) *who currently are actively conducting research* in the areas of environmental contamination and health in geographic regions identified as being contaminated by radiation will be accepted. This would include researchers in these regions specializing not only in the effects of radiation contamination on health but also other possible contributory causes of negative health effects in these regions. These individuals must be working at recognized scientific research institutions; must be able to speak, read, and write English with a moderate degree of fluency; and must be able to gain the permission of their governments to travel.

APPLICATION AND NOTIFICATION PROCEDURES

Application materials should include all of the following: 1) a letter of intent by the applicant including name, affiliation, address, telephone, and e-mail address, if any, where he/she can be reached; 2) an abstract of the proposed poster session including a brief description of the research question, design, methods, results, discussion, and conclusions reached; 3) a curriculum vitae; and 4) two letters of support from professors or colleagues familiar with the applicant's research.

These materials must be submitted to AAAS by mail or fax no later than October 31, 1995. No late or incomplete applications will be considered. Send materials or inquiries to: Ms. Beth Boswell, Project Coordinator, AAAS, 1333 H Street, NW, Washington, DC 20005; Tel: (202) 326-6427; Fax: (202) 289-4958; bboswell @aaas.org.

PRODUCTS & MATERIALS

Sensitive Immunostaining Kits

A selection of biotin-streptavidin detection systems optimized for mouse, rat, and rabbit tissues is now available. The Super Sensitive Animal Detection Kits contain secondary antibodies treated by solid-phase adsorption to animal tissue to provide excellent results by minimizing cross-reactivity. These kits provide accurate, dependable staining of formalin-fixed, paraffin-embedded tissues. Each kit includes mouse-, rat-, or rabbit-adsorbed biotinylated secondary antibody and peroxidase-conjugated streptavidin label. There are four choices for the secondary antibody: rat-adsorbed goat antibodies to mouse immunoglobulin (anti-mouse Ig), rabbit-adsorbed goat anti-mouse Ig, mouse-adsorbed goat anti-rat Ig, and mouse- and rat-adsorbed goat anti-rabbit Ig. **BioGenex. Circle 138.**

■

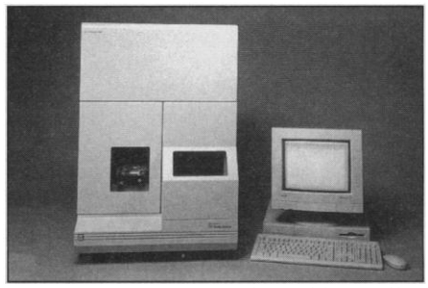
Fluorimetric and Luminescence Analysis

BioFluor is a complete system for quantitative cuvette-based fluorimetry and luminescence measurements down to the single photon level. It includes all the software and hardware needed for intracellular ion measurements with the latest fluorochromes as well as luminescent probes for biotechnology and molecular biology. BioFluor enables fast dual and single wavelength fluorescence ratio measurements from cell suspensions and monolayers on cover slips in cuvettes. It can be used with virtually all conventional fluorescence probes for biological activity of living cells. The system is also well suited to work with luminescent probes such as aequorin and other light-emitting reporters of gene expression. **Life Science Resources. Circle 139.**

■

Genetic Analyzer

The low-cost ABI PRISM 310 Genetic Analyzer is designed to bring automated sequencing, sizing, and quantitation to more life science laboratories than ever before. The system integrates multicolor fluorescent labeling, capillary electrophoresis, and software for the collection and analysis of fluorescent signal. Every function, from sample and gel loading to data collection and analysis, is automated. The analyzer is aimed at small



laboratories that previously could not afford sophisticated fluorescent technology. The analyzer eliminates the need to pour conventional acrylamide and agarose slab gels or to load samples onto the gel for electrophoresis. Users can begin receiving data in less than half an hour. **Perkin-Elmer. Circle 140.**

■

Data Analysis Software

StatView 4.5 for the Macintosh has been released in English, Japanese, French, and German versions. The data analysis program includes survival analysis, quality control Microsoft Excel read and write capabilities, more than 20 new analysis and graphing templates, criteria labels, and speed enhancements. **Abacus Concepts. Circle 141.**

■

Molecular Modeling Software

SCULPT is an interactive molecular modeling application that lets one use a mouse to select atoms, secondary structures, and ligands and move them around while other atoms move in response to the changed atom's position. SCULPT couples the user's manipulations of the structure to a novel algorithm that is orders-of-magnitude faster than conventional methods. Applications include exploring alternative side-chain packing, determining how an active site accommodates a ligand, designing proteins and peptides,

Newly offered instrumentation, apparatus, and laboratory materials of interest to researchers in all disciplines in academic, industrial, and government organizations are featured in this space. Emphasis is given to purpose, chief characteristics, and availability of products and materials. Endorsement by *Science* or AAAS is not implied. Additional information may be obtained from the manufacturers or suppliers named by circling the appropriate number on the Readers' Service Card and placing it in a mailbox. Postage is free.

packing secondary structures, and understanding molecular behavior. **Interactive Simulations. Circle 142.**

■

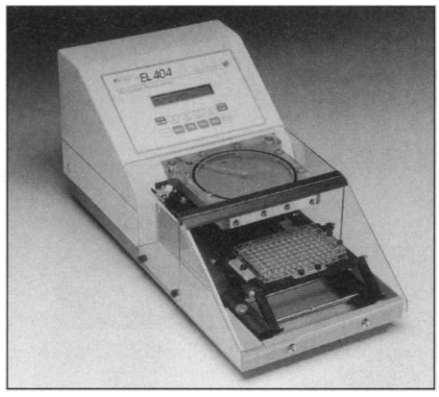
Total RNA Kits

Qiagen Total RNA kits streamline large-scale total RNA purification by replacing tedious organic extractions and cesium chloride ultracentrifugation with gravity flow anion-exchange technology. The kits are designed to purify as much as 200 μg of RNA with Qiagen-tip 100 and up to 1 mg of total RNA with Qiagen-tip 500 from animal cells or tissues, yeast, and Gram-positive or Gram-negative bacteria. The kits can also be used to isolate cytoplasmic RNA, purify large amounts of in vitro transcripts, clean up RNA after enzymatic reactions, and desalt RNA samples. **Qiagen. Circle 143.**

■

Universal Microplate Reader

The ELx800 Universal Microplate Reader can be programmed for up to 75 complex assays (qualitative or quantitative) via a new Windows software package or via the reader



keyboard. The unique optical system is capable of reading 24-, 48-, 96-, and 384-well plates. **Bio-Tek Instruments. Circle 144.**

■

Protein Assay

The dotMETRIC protein assay shows no protein-to-protein variation and is not affected by the presence of common chemicals such as reducing agents, detergents, chelating agents, drugs, and cobalt. The 10-min test produces a permanent record. **Geno Technology. Circle 145.**

Literature

HPLC Tips and Traps is an application note for chromatographers on selecting and working with tubing and fittings. **Phenomenex. Circle 146.**

Biological Activity Reaction Tests Reaction Comparator Chart describes a set of self-contained tests to detect specific algae and bacteria in water. The tests can be incubated at room temperature and so can be used in the field or in the lab. **Hach. Circle 147.**

Laboratory CO_2 Incubators describes a line for critical culture applications with features such as thermal and infrared CO_2 sensing, water- and air-jacketed design, microprocessor environment control, seamless interior construction, and single- or double-chambering. **Queue Systems. Circle 148.**

Microfiltration and Laboratory Products Catalog contains 146 pages of filters and other products. **Poretics. Circle 149.**

Vacuum Accessories is a catalog that features fittings, flanges, construction components, compact gauges, residual gas analyzers, and valves. **Balzers. Circle 150.**

TIGR HCD
A New Resource for Genomics Research.

The Institute for Genomic Research is making its Human cDNA Database (TIGR HCD) of more than 345,000 complementary DNA (cDNA) sequences (and certain associated clones) available to scientists conducting basic research at non-profit institutions. These data were the basis for the paper, "Initial assessment of human gene diversity and expression patterns based upon 83 million nucleotides of cDNA sequence,"[1] published in *Nature* on September 28, 1995.

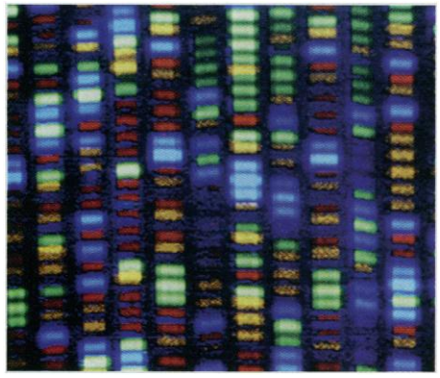
TIGR HCD is a curated relational database of cDNA fragments and assemblies, including tissue-specific expression data and (where possible) positive or tentative gene identifications.

The Institute for Genomic Research created the HCD — with scientific and financial support from Human Genome Sciences (HGS) and SmithKline Beecham (SB) — to offer researchers Internet access (via e-mail and the World Wide Web) to sequence and related data generated by privately financed studies carried out at TIGR and HGS[2].

Access •There is no charge for access to the TIGR Human cDNA Database. •Clones for TIGR sequences are available from the American Type Culture Collection at a nominal charge. •TIGR HCD is open to employees of non-profit or governmental orgnizations. •There are no restrictions on access to some 300,000 EST sequences substantially identical to whole or partial gene sequences already published. •An additional 45,000 unpublished ESTs and assemblies (and associated clones) are available under terms that reflect provisions common in academic and industrial material transfer agreements.

Queries: TIGR HCD users can search the database by protein or gene name (putative identification), by nucleotide or peptide sequence, or by TIGR accession number (as listed in reference 1). Results can range from a list of entries with specified similarity to full sequences of matching entries.

Data: The data in HCD have been generated by the expressed sequence tag (EST) method, which provides rapid characterization of expressed genes by partial DNA sequencing[3]. IICD data include nucleotide sequences, putative sequence identifications, and tissue-based expression information derived from a large-scale EST survey of human tissues. The data set includes 40,000 assemblies, constructed by combining overlapping ESTs. And all nucleotide data are searched in six-frame translation — that is, the database contains searches all reading frames for both the sequence and its antisense strand.



For more information regarding TIGR HCD (including user application forms), or contact the TIGR Database Manager at:

e-mail: info@hcd.tigr.org
fax: (301) 838-0218
mail: Manager, TIGR Database
The Institute for Genomic Research
9712 Medical Center Drive
Rockville, MD 20850

world wide web: http://www.tigr.org(TIGR Database)

[1] *Adams MD, et al. 1995. Nature, 377:250-330*

[2] *Of TIGR HCD's 345,000 expressed sequence tags, approximately 105,000 were generated at TIGR and 55,000 at HGS; the remainder derive from sources in the public domain.*

[3] *Adams MD, et al. 1991. Complementary DNA sequencing; Expressed sequence tags and the Human Genome Project. Science, 252:1651-1656*

SB
SmithKline Beecham
Pharmaceuticals

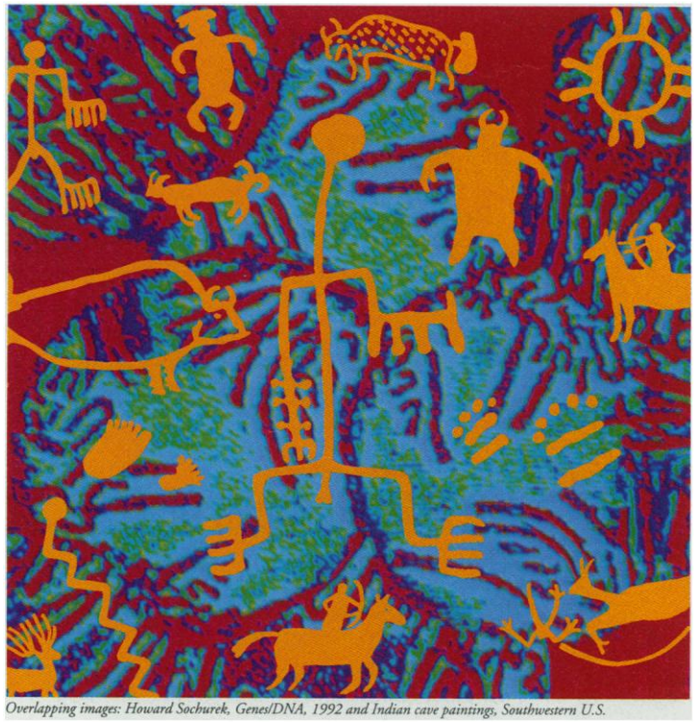
This notice is sponsored by SmithKline Beecham, the international human healthcare company

Securing a healthy future, one gene at a time.

Analysis of the structure, function and regulation of genes in health and disease has yielded profound insight into the origin and progression of major diseases and is creating unprecedented opportunities to discover innovative drugs, vaccines and new diagnostic tests based on a rational understanding of molecular pathology.

Genomics now joins the diverse array of other scientific and clinical skills needed for innovation in healthcare research. SmithKline Beecham is at the forefront of genomics research in the healthcare industry. In seeking to forge new advances in genetic medicine, we build on a strong heritage of innovation that has discovered some of the world's most important medicines, to become the world's number one vaccine company and a leader in diagnostic clinical laboratory services.

If you have research experience in genomics, microbiology, protein engineering, macromolecular and combinatorial chemistry, mechanistic enzymology, high-resolution analytical chemistry, computational chemistry, structural biology, bioinformatics or the analysis of non-linear systems and would like to work in an environment dedicated to being a leader in genetic medicine, please send your resume to: SmithKline Beecham Pharmaceuticals, Research and Development, Dept. N10/95, P.O. Box 2646, Bala Cynwyd, PA 19004. We are an Equal Opportunity Employer, M/F/D/V.



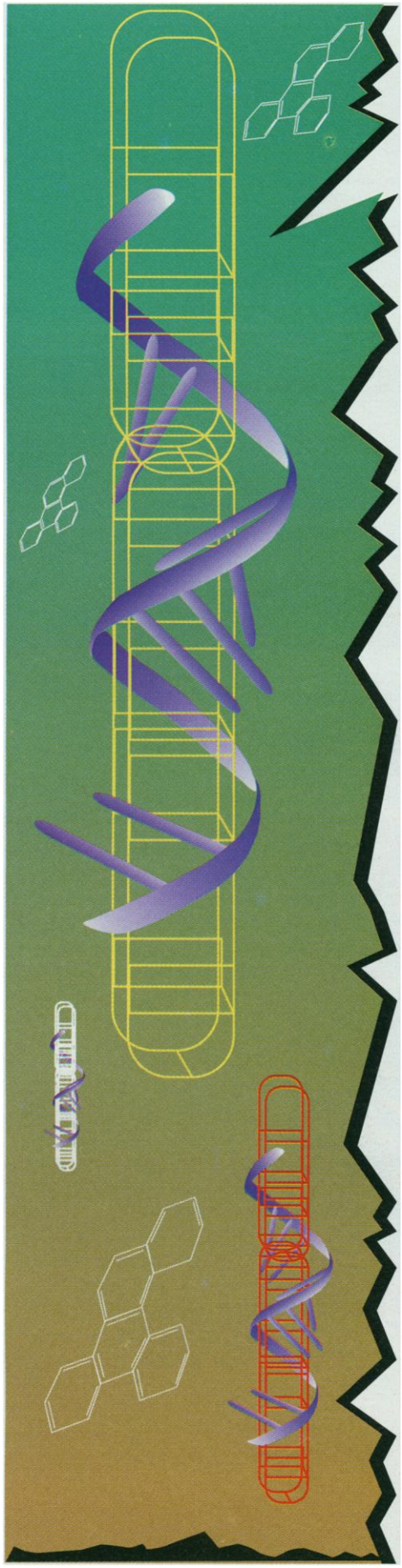
Overlapping images: Howard Sochurek, Genes/DNA, 1992 and Indian cave paintings, Southwestern U.S.

SB

SmithKline Beecham

Pharmaceuticals

Challenging the natural limits.



SEQUANA

THERAPEUTICS

Sequana Therapeutics Inc., a leading genomics company dedicated to the discovery of genes associated with common human diseases, is seeking senior-level scientists for our gene discovery programs. We currently have strategic alliances with Glaxo Wellcome, Boehringer Ingelheim and Corange, and we have research programs in the areas of NIDDM, asthma, osteoporosis, obesity, schizophrenia, CNS, CVD and cancer. We are presently seeking the following talented individuals to contribute to these and other programs:

DIRECTOR - GENOMICS

The selected candidate will lead the effort to simultaneously map several disease loci. The applicant should have several years of experience directing molecular genetics groups in the search for human disease genes and should be familiar with a range of gene identification techniques.Code: SCI-DIR.

GROUP LEADER - BIOINFORMATICS

The selected candidate will direct a team of bioinformatics scientists responsible for generating information critical to our gene discovery programs. Sequana has state-of-the-art bioinformatics and engineering capabilities and requires an experienced biologist with high-grade computer skills. The ideal candidate will have an M.S. or Ph.D. or equivalent, and several years of relevant experience. Code: SCI-BIO.

GROUP LEADER AND SCIENTISTS - GENOTYPING

The selected candidates will join our world-class genotyping operation as we expand our capacity for isolating disease genes. The ideal candidate for the Group Leader position will have several years of relevant laboratory experience, ideally in a high-throughput, fluorescent-based sequencing or genotyping operation, and be familiar with robotic sample processing and automated data analysis tools. The ideal candidates for the scientist positions will have at least one year of experience in fluorescent-based genotyping and/or sequencing. Code: SCI-GEN.

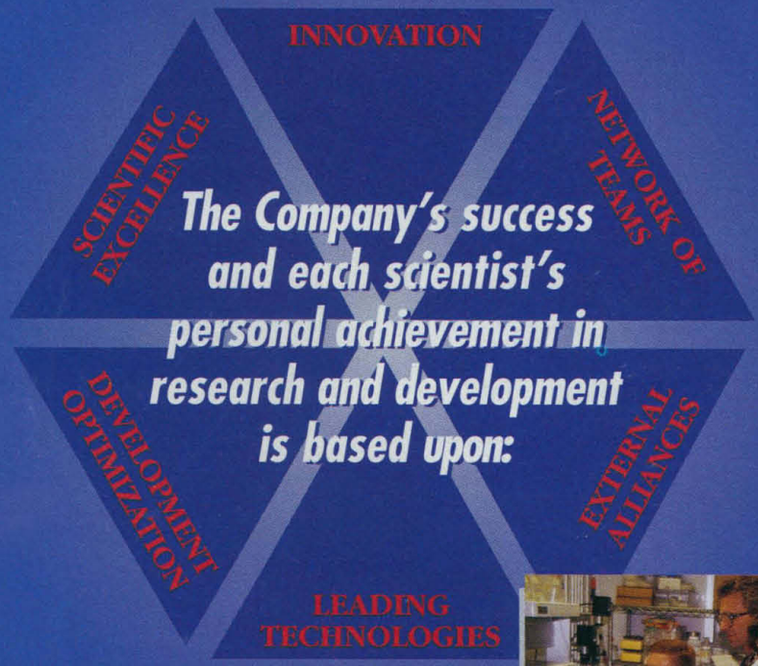
SCIENTISTS - PHYSICAL MAPPING

The selected candidates will join a team of scientists with the goal of mapping and cloning common disease genes. The ideal candidates will have substantial experience in molecular genetics and genome analysis tools, including large insert cloning vectors (YACs, BACs and P1s), contig assembly and gene identification techniques. The position requires an M.S. or Ph.D. or equivalent in molecular biology or a related field, and at least three years of postdoctoral experience in mammalian genome analysis. Code: SCI-PM.

Sequana Therapeutics is a publicly-held corporation headquartered in La Jolla, CA. Our executive offices and laboratory facilities are located in a science park across from the Scripps Research Institute, about one mile from UCSD and The Salk Institute. We offer a highly competitive salary plus stock options, and relocation assistance where appropriate. Please mail or fax resume to: Sequana Therapeutics, Inc., Att: HR/ Code (see above), 11099 North Torrey Pines Road, Suite 160, La Jolla, CA 92037. Fax: (619) 452-4378. We are an equal opportunity employer.

SEQUANA THERAPEUTICS

Uncompromising Science at Bristol-Myers Squibb Leads to Diverse Opportunities in R&D



CENTRAL NERVOUS SYSTEM

Neurodegenerative Disorders

PROTEIN CHEMISTS. CNS Drug Discovery has a challenging opportunity for an innovative scientist to join a multidisciplinary team developing novel therapeutics to treat Alzheimer's Disease. Candidates must have a Ph.D. and at least 3 years postdoctoral experience, and have experience in Protein Biochemistry including chromatography (FPLC, HPLC) and electrophoresis, and Cell Biology including cell culture and immunological methods (ELISA, immunoprecipitation, western blot). Experience with quantitative enzyme analysis and protein purification of endogenous cellular proteins is required. Knowledge of membrane biology is desirable. (Dept. HD-0373)

Psychobiological Disorders

RESEARCH SCIENTISTS. CNS Drug Discovery has positions available in behavioral pharmacology for scientists to be involved with in vivo work on drug-induced changes in circadian rhythms and eating behavior. Candidates must have a B.S./M.S. degree and a minimum of 2 years experience, which includes expertise in the area of animal behavior, particularly in the use of models in CNS research. We require skills in performing stereotaxic procedures and experience with data management and statistical analysis. Proficiency in experimental design, data analysis software (i.e. SAS, SPSS), and computer programming is desired. (Dept. HD-0286)

For positions within CNS, forward/fax resume with Dept. # to: Human Resources, P.O. Box 5101, 5 Research Parkway, Wallingford, CT 06492-7661. FAX: 203-284-7762.

VIROLOGY

VIROLOGISTS. Successful candidates are expected to conduct research to evaluate targets for the therapeutic intervention of viral diseases. Experience in the isolation, assay and characterization of viruses from cell culture and clinical samples, and hands-on familiarity with antiviral research are required. Positions require either an M.S. or Ph.D. in Biology or related field. (Dept. HD-0257)

BIOORGANIC CHEMIST/BIOCHEMIST. The candidate should be well-versed in bioorganic chemistry. Knowledge of organic synthesis is required in addition to having some experience in biochemistry and/or molecular biology. Experience with chemical modification of nucleic acids and proteins is a plus. This position requires an M.S. in chemistry or biochemistry with 1-2 years of experience. (Dept. HD-0333)

For positions within Virology, forward/fax resume with Dept. # to: Human Resources, P.O. Box 5101, 5 Research Parkway, Wallingford, CT 06492-7661. FAX: 203-284-7762.

COMBINATORIAL CHEMISTRY

PRINCETON, NJ AND WALLINGFORD, CT. We seek all levels of scientists with expertise in the following areas:

- Synthetic Organic Chemistry, automated and/or solid phase synthesis strongly preferred
- Combinatorial libraries
- Computational methods for managing molecular diversity
- Robotics, instrument design and automation
- Design and application of database systems for integrated chemical/biological data management.

For positions within Combinatorial Chemistry, forward/fax resume to: Human Resources, Dept. BM-132, P.O. Box 11279, Trenton, NJ 08620-0279. FAX: 609-581-8841.

Bristol-Myers Squibb Company

Equal Opportunity Employer, M/F/D/V

Research and Development Is The Foundation of Our Business

Johnson & Johnson, with over $15 billion in annual sales, is the world's largest and most comprehensive health care products company serving the consumer, professional, diagnostic and pharmaceutical markets. We believe that our worldwide commitment of over a billion dollars annually ranks us among the top American-based corporations in R&D expenditure. Key to maintaining leadership throughout our entire family of companies is our demonstrated ability to turn R&D investments into significant new products, particularly in the pharmaceutical business.

While openings vary by company, we are interested in hearing from candidates with health care industry or academic experience and a degree (BS, MS, PhD) in Biology, Biochemistry, Biochemical Engineering, Biostatistics, Chemistry, Immunology, Medicine, Microbiology, Molecular Biology, Pathology, Pharmacy, Toxicology or equivalent, for involvement in the following areas:

Pre-Clinical R&D

- Chemical Development
- Drug Discovery
- Drug Safety Evaluation
- Pharmaceutical Development
- Drug Metabolism

Clinical Drug Development

- Clinical R&D
- Clinical Trials
- Medical Biostatistics
- Medical Writing
- Regulatory Affairs

In addition to an excellent compensation and benefits package, Johnson & Johnson offers a LIVE FOR LIFE Wellness Program with on-site fitness centers, smoke-free work places in campus-like settings, and programs that can help you balance your work life with your family life. To apply for these openings or to be considered for future opportunities, send your resume suitable for scanning into our state-of-the-art database (i.e., clean/clear, no graphics, and preferably unfolded). Forward to: Dept. 413, Johnson & Johnson Recruiting, Employment Management Center, P. O. Box 16597, New Brunswick, NJ 08906-6597.

We are an equal opportunity employer and support diversity in the workplace.

Johnson & Johnson

"Leadership Beyond Compliance"

Postdoctoral Opportunities In The Biomedical Sciences.

The following research training opportunities are currently available at the National Institutes of Health.

Behavioral Genetics
Dean Hamer, PhD

The role of genes in human behavior is studied by gene mapping, molecular approaches and psychometrics. The main interests are cancer risk-related behaviors, such as smoking and excess alcohol consumption, and other complex psychological traits and diseases. Positions are open for geneticists, molecular biologists, statisticians and psychologists. Applicants must have less than five years of postdoctoral experience. Laboratory of Biochemistry (OE-101), NCI/DCBDC, Building 37, Room 4A13, 37 CONVENT DR MSC 4813, BETHESDA MD 20892-4813.

Differentiation and Signal Transduction
Ira O. Daar, PhD

Studies are aimed at understanding the cellular interactions and signal transduction events elicited by a member of the Eph family of receptor tyrosine kinases as well as candidate ligands. Emphasis is placed on their function during *Xenopus laevis* embryogenesis. Candidates should have less than five years of postdoctoral experience and a strong background in molecular, developmental or cell biology. Laboratory of Leukocyte Biology (OE-101), NCI-BRMP FCRDC, Building 567, Room 227, Frederick MD 21702.

HIV Gene Regulation
Sundararajan Venkatesan, MD

Research efforts are focused on 1) the functional mechanisms of HIV-1 Rev transactivator protein and associated cellular co-factors and HIV-1 RNA binding cellular protein(s); and 2) the mechanisms of receptor down-regulation and cell signaling modulation induced by HIV-1 Nef protein. Applicants must be well trained in molecular and cell biology. Training and experience in virology and immunology are highly desired. Laboratory of Molecular Microbiology (OE-101), NIAID, Building 10, Room 6A05, 10 CENTER DR MSC 1576, BETHESDA MD 20892-1576.

Immunology
Kathryn E. Stein, PhD

Antigen processing and presentation of polysaccharide-protein conjugate vaccines are being investigated. Experience in working with cell fractionation and lysosomes/endosomes or other relevant experience is desirable. Applicants must have less than five years of postdoctoral experience and must be a US citizen or permanent resident. Laboratory of Molecular and Developmental Immunology (OE-101), FDA/CBER, (HFM-555), Building 29B, Room 5E08, 1401 Rockville Pike, Rockville, MD 20852-1448.

Molecular Biology and Immunology
Michael A. Steller, MD

Novel peptide epitope-based vaccine therapies are being developed aimed at the prevention or treatment of human papillomavirus associated cervical cancer. Future studies will involve immunologic and molecular techniques to optimize HPV epitope recognition by cytotoxic T-lymphocytes and lysis of target tumor cells harboring the virus. Investigations are also ongoing to examine if HPV-induced malignant transformation involves corruption of apoptotic molecular pathways. Applicants must have less than five years of postdoctoral experience. Surgery Branch (OE-101), NCI/DCT, Building 10, Room 2B42, 10 CENTER DR MSC 1502, BETHESDA MD 20892-1502, Fax 301-496-0011.

Molecular Biology and Protein Traffic
Stephen Shears, PhD

The inositolpolyphosphate phosphatase compartmentalized in the lumen of endoplasmic reticulum has been cloned. A molecular biologist is required to modify levels of enzyme expression, perform mutagenesis and generate truncated clones in order to: characterize the enzyme's active site; study targeting and retention of this protein in endoplasmic reticulum; investigate inositol polyphosphates' contributions to protein traffic and to signal transduction. Applicants must have less than five years of postdoctoral experience. Laboratory of Cellular and Molecular Pharmacology (OE-101), NIEHS, P.O. Box 12233, Research Triangle Park, NC 27709.

Molecular Mechanisms of Cellular Senescence
J. Carl Barrett, PhD

The molecular mechanisms of cellular senescence are being investigated. Candidates should have experience in studying the mechanisms of cellular senescence as documented by outstanding publications in this area and must have less than five years of postdoctoral experience. Laboratory of Molecular Carcinogenesis (OE-101), NIEHS, Mail Drop C2-15, P.O. Box 12233, Research Triangle Park, NC 27709.

Additional Opportunities

The NIHEDNET Bulletin Board **POSTDOC** (fellowship positions) and **TENURE** (tenure track positions) conferences are accessed via a modem (***301-402-2221 or 800-358-2221*** with parameters set at ***7,Even,1***) or the Internet using Telnet (***wylbur.cu.nih.gov***) or the World Wide Web (URL: ***telnet://wylbur.cu.nih.gov***). When connected to NIH, key in ***,vt100*** for terminal emulation, ***F5E*** for initials, and ***AJL1*** for account number. To view tenure track positions, ***quit*** the **POSTDOC** conference and ***join*** the **TENURE** conference.

An electronic version of the *Postdoctoral Research Fellowship Opportunities* catalog is accessed via the Internet using either the Gopher Information System (***gopher.nih.gov***) or the World Wide Web (URL: ***http://www.nih.gov***). When connected with Gopher, select ***Grants and Research Information*** and then ***NIH Office of Education***. When connected with WWW, select ***Grants and Contracts*** and then ***NIH Office of Education***. If you have further questions, please contact the NIH Office of Education, Building 10, Room 1C129, 10 CENTER DR MSC 1158, BETHESDA MD 20892-1158, Phone 301-496-2427, Fax 301-402-0483.

To Apply

If you hold a graduate doctoral degree (e.g., PhD, MD/PhD) or a professional degree (MD, DO, DDS, DMD or DVM) accompanied by previous laboratory research experience, and would like to be considered for one of these positions, please send a cover letter, *curriculum vitae*, bibliography, and statement of research interests to the address listed with each position. In addition, please arrange to have letters of recommendation sent from three scientists who can provide an evaluation of your qualifications.

National Institutes Of Health

Office Of Education

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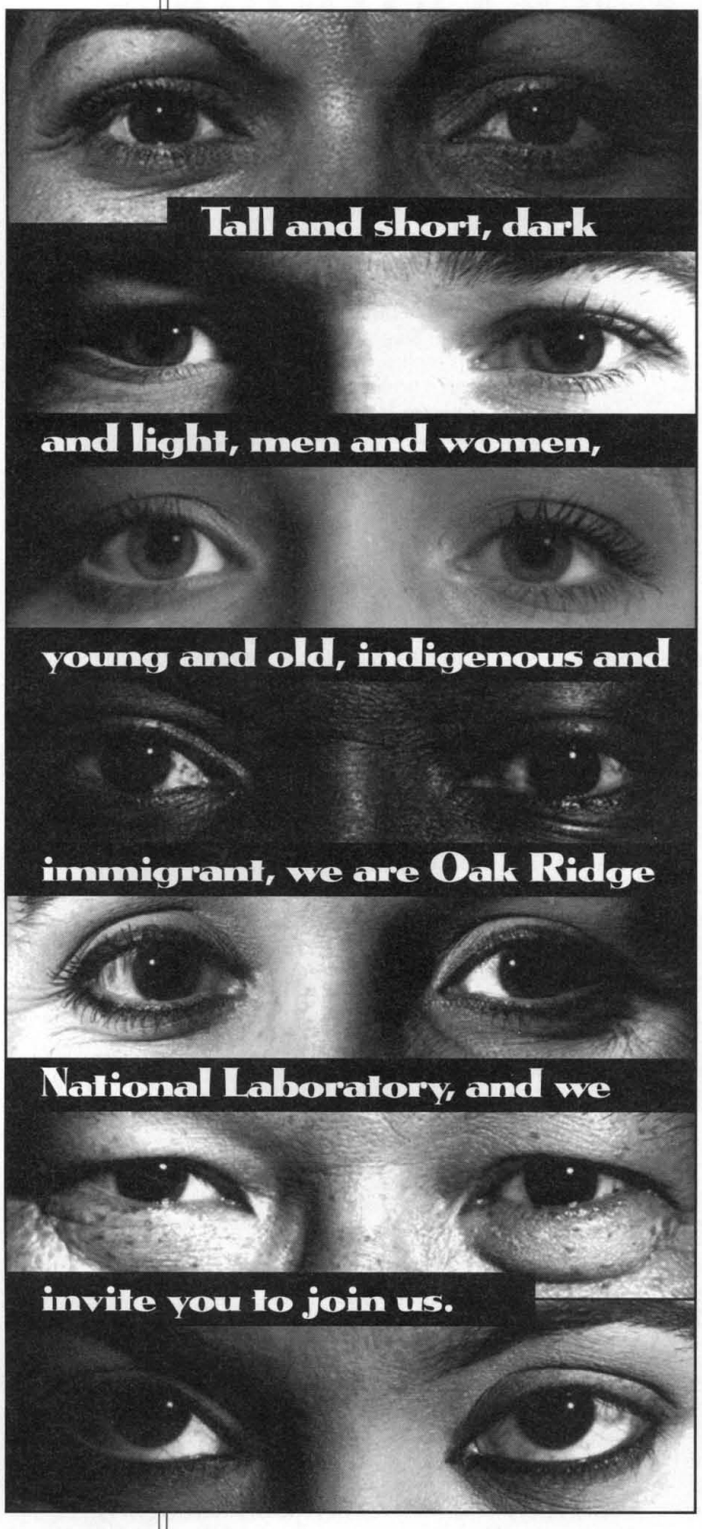

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Cold Spring Harbor Laboratory

1996 Courses

Spring Application Deadline: January 15, 1996

Advanced Genome Sequence Analysis
March 20 - April 2
Ellson Chen, Richard Gibbs, W. Richard McCombie, Richard Wilson

Cloning & Analysis of Large DNA Molecules
April 10 - 23
Hadi Abderrahim, Bruce Birren, Harold Riethman

Protein Purification and Characterization
April 10 - 23
Richard Burgess, Al Courey, Sue-Hwa Lin, Sheenah Mische

Early Development of *Xenopus Laevis*
April 12 - 21
Robert Grainger, Hazel Sive

Summer Application Deadline: March 15, 1996

Advanced Bacterial Genetics
June 7 - 27
Bonnie Bassler, Colin Manoil, Nancy Trun

Molecular Approaches to Ion Channel Structure, Expression & Function
June 7 - 27
John Caldwell, Rock Levinson, Robert Maue

Molecular Embryology of the Mouse
June 7 - 27
Richard Behringer, Virginia Papaioannou

Genetic-Epidemiologic Studies of Complex Diseases
June 11 - 18
Neil Risch, Elizabeth Squires-Wheeler

Neurobiology of Human Neurological Disease
June 20 - 26
Sam Gandy, William Mobley, Stan Prusiner

Computational Neuroscience: Vision
June 28 - July 11
David Heeger, Michael Shadlen, Eero Simoncelli

***Arabidopsis* Molecular Genetics**
July 1 - 21
Xing-Wang Deng, Robert Last, Daphne Preuss

Molecular Cloning of Neural Genes
July 1 - 21
Instructors to be announced

Neurobiology of *Drosophila*
July 1 - 21
Nipam Patel, Barbara Taylor, Tim Tully

Molecular Neurobiology: Brain Development & Function
July 14 - 27
Ronald McKay, Erin Schuman

Advanced Molecular Cloning & Expression of Eukaryotic Genes
July 24 - August 13
Kenneth Burtis, Marc Learned, Stephen Smale

Imaging Structure & Function in the Nervous System
July 24 - August 13
Arthur Konnerth, Fred Lanni

Yeast Genetics
July 24 - August 13
Allison Adams, Daniel Gottschling, Chris Kaiser

Advanced *Drosophila* Genetics
July 30 - August 12
Michael Ashburner, Scott Hawley

Tentative 1996 Fall Courses Dates and Instructors to be announced

Macromolecular Crystallography

Analysis & Genetic Manipulation of Yeast Artificial Chromosomes

Advanced *In Situ* Hybridization & Immunocytochemistry

Computational Genomics

Monoclonal Antibodies from Combinatorial Libraries

1996 Meetings

Zebrafish Development Genetics
April 24 - 28
Nigel Holder, Nancy Hopkins, Philip Ingham, Christiane Nusslein-Volhard, Monte Westerfield
Abstract Deadline, February 7, 1996

Molecular Chaperones and the Heat Shock Response
May 1 - 5
Costa Georgopolos, Susan Lindquist Rick Morimoto
Abstract Deadline, February 14, 1996

Genome Mapping & Sequencing
May 8 - 12
David Bentley, Eric Green, Philip Hieter
Abstract Deadline, February 21, 1996

The Cell Cycle
May 15 - 19
Fred Cross, Jim Roberts
Abstract Deadline, February 28, 1996

Retroviruses
May 21 - 26
Ron Desrosiers, Anna Marie Skalka
Abstract Deadline, March 6, 1996

61st Symposium: Function & Dysfunction in the Nervous System
May 29 - June 5
Bruce Stillman
Abstract Deadline, March 13, 1996

Cancer Genetics & Tumor Suppressor Genes
August 14 - 18
Anton Berns, Terri Grodzicker, Ed Harlow, David Livingston, Carol Prives, Bert Vogelstein
Abstract Deadline, May 29, 1996

Molecular Genetics of Bacteria & Phages
August 20 - 25
Carol Gross, Jeff Roberts, Marion Russel
Abstract Deadline, June 5, 1996

Mouse Molecular Genetics
August 28 - September 1
Rosa Beddington, Allan Bradley, Rob Krumlauf, Liz Robertson
Abstract Deadline, June 12, 1996

Translational Control
September 4 - 8
Richard J. Jackson, Michael Mathews, Marvin Wickens
Abstract Deadline, June 19, 1996

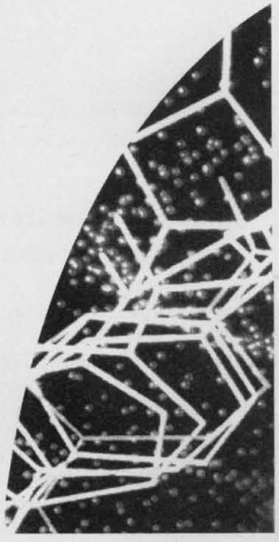
Molecular Approaches to the Control of Infectious Diseases
September 9 - 13
Fred Brown, Dennis Burton, John Mekalanos, Erling Norrby
Abstract Deadline, June 26, 1996

Molecular Biology of Hepatitis B Viruses
September 18 - 22
Robert Lanford, Michael Nassal
Abstract Deadline, July 3, 1996

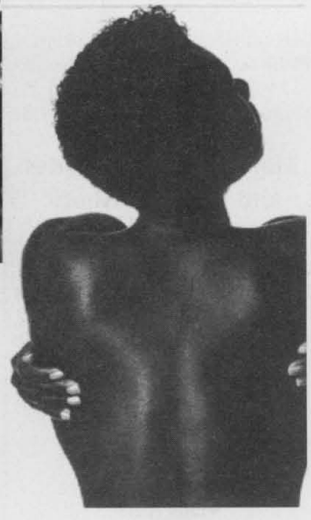
Gene Therapy
September 25 - 29
Theodore Friedmann, Richard Mulligan, Gary Nabel, David Weatherall
Abstract Deadline, July 10, 1996

Learning & Memory
October 2 - 6
Per Anderson, Eric Kandel, Richard F. Thompson, Susumu Tonegawa
Abstract Deadline, July 17, 1996

Meetings and Courses Office
Cold Spring Harbor Laboratory
1 Bungtown Road, PO Box 100
Cold Spring Harbor, N.Y. 11724-2213
Email:meetings@cshl.org Fax:516-367-8845
Phone:516-367-8346 w³ site *http://www.cshl.org/*



Expanding Minds



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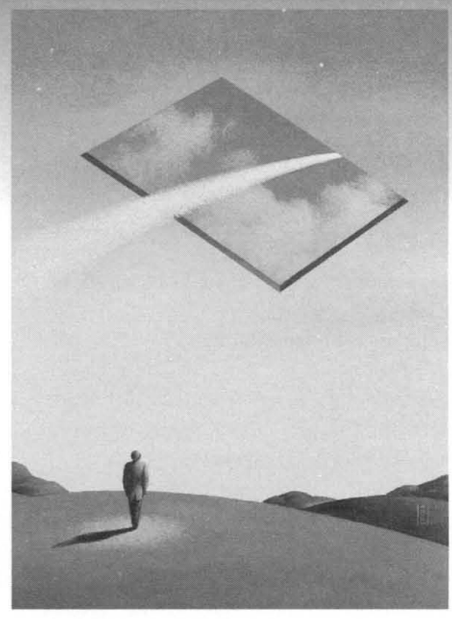

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Postdoctoral Fellow

The Postdoctoral Fellow will conduct studies on the maternal and fetal effects of a novel cytokine during embryonic development and gestation. This program provides a unique opportunity to combine *in vivo* pharmacology with molecular biology techniques. Additional responsibilities include the conduct of studies of the cytokine in animal models of pathologic pregnancy and *in vitro* with human trophoblast cultures. Additionally, this person will investigate the role of this cytokine in potential new indications. Requirements includes PhD, and previous experience in *in situ* hybridization, immunohistochemistry, and light and electron microscopy. **Job Code: 95-PDF-SCI**

Toxicologist

This person will design and implement drug safety programs for novel recombinant protein therapeutics. The individual will work in close collaboration with toxicology contract laboratories to design, monitor, and report safety studies conducted in a variety of animal species and serve as toxicology representative on multidisciplinary Preclinical and Development project teams. The toxicologist will establish an investigative experimental toxicology laboratory. Requirements include a PhD, D.V.M., or equivalent and at least two years' industry experience in product safety evaluation. Previous experience in interacting with contract research labs, training in experimental pharmacology, and working with recombinant protein products is preferred. **Job Code: 95-TOX-SCI.**

To be considered for current or future job openings, please only forward original resumes, suitable for scanning, indicating job code, to: Human Resources Department, Genetics Institute, Inc., 87 CambridgePark Drive, Cambridge, MA 02140. Fax: (617) 498-8089 or (617) 876-8847.

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Special Plenary Session

Twenty-fifth Anniversary of the National Cancer Act: Progress and Promise (Joseph R. Bertino)

Symposia

Apoptosis: Manipulating Programmed Cell Death in Cancer (David E. Fisher)

Matrix Metalloproteases and Inhibitors (Lynn M. Matrisian)

Cell Cycle: Targets for Therapy (Stephen H. Friend)

Endogenous DNA Damage: Detection and Biological Significance (John M. Essigmann)

Cell Signalling

Recent Developments in Gene Therapy (Drew M. Pardoll)

Cancer Chemoprevention in Humans (Thomas W. Kensler)

Genetic Predisposition to Cancer (Mark H. Skolnick)

Cell Responses to DNA Damaging Agents (Nathan A. Berger)

Drug Resistance: Transcriptional and Translational Mechanisms (Kathleen W. Scotto)

Monoclonal Antibodies: Clinical Mechanisms and Effectiveness

Targeting Growth Factor Receptors for Therapy (John Mendelsohn)

Melanoma as a Clinical Model (Alan N. Houghton)

Thymidylate Synthetase and Its Inhibitors

Nutrition and Cancer (Walter C. Willett)

Aberrant Transcription Factors and Malignancy (Lorraine J. Gudas)

Steroid Hormones: Breast and Prostate Cancer (Myles A. Brown)

Viral Mechanisms of Carcinogenesis (Harald zur Hausen)

Tumor Suppressor Genes (Bert Vogelstein)

Ovarian Cancer: From the Laboratory to the Clinic (Robert F. Ozols)

Drug Metabolizing Enzymes in Cancer Prevention and Therapy (Cecil B. Pickett)

Cell Adhesion Molecules and the Cytoskeleton (Jun-Lin Guan and Rudolph L. Juliano)

Tumor Angiogenesis (Judah Folkman and Mark A. Goldberg)

Neuroblastoma: Recent Advances in Diagnosis and Treatment (Garrett M. Brodeur)

Telomeres, Cell Senescence, and Cancer (Calvin B. Harley)

Pre-Meeting Methods Workshops

Quantitative Biology and Pharmacodynamics (Robert C. Jackson)

Animal Models: Transgenic and Knockout Mice in Cancer Investigations

Controversy Sessions

Does Regional Chemotherapy Work? (David S. Alberts)

Is Beta-Carotene Useful in Cancer Prevention? (Waun Ki Hong)

In Studies of Drug Resistance, Have Preclinical Models Provided Accurate Predictions for Clinicians? (Bruce A. Chabner)

Is p53/Rb Important for Therapeutic Outcome? (William F. Benedict)

Should Genetic Testing Be Done on Patients to Assess Cancer Risk? (Judy E. Garber)

Meet-The-Expert Sunrise Sessions

Quantitative PCR As a Tool to Detect Minimal Residual Disease in Lymphoma and Leukemia (John Gribben)

Inhibition of Tobacco-induced Carcinogenesis (Stephen S. Hecht)

Cell Cycle (Peggy J. Farnham)

Drugs Which Interact with Microtubules: An Update (Eric K. Rowinsky)

Culturing Normal and Neoplastically Transformed Human Epithelial Cells (Martha R. Stampfer)

Mammary Carcinogenesis (Daniel Medina)

Radiation Sensitization (Theodore S. Lawrence)

NMR As a Prognosticator (Jerry D. Glickson)

Antiestrogens (V. Craig Jordan)

DNA Topoisomerases and Their Inhibitors (Yves G. Pommier)

Estrogens and Breast Cancer (Lovell A. Jones)

Tumor Physiology (Rakesh K. Jain)

Protein Kinase C in Cell Transformation (Susan Jaken)

Environmental Carcinogens: Their Impact in Cancer (John A. McLachlan)

Lung Cancer: A Primer

Chromosomal Deletions and Cancer: Recent Advances in Mapping Techniques (Funmi I. Olopade)

Tumor Vaccines (Jeffrey Schlom)

Challenges in Bone Marrow Transplantation (William S. Dalton)

Immunologic Features of AIDS Pathogenesis (Jay A. Levy)

Natural Killer Cells (Ronald B. Herberman)

Interferons and Cancer (Ernest C. Borden)

Transcription Factors As Therapeutic Targets (Richard A. Heyman)

Chemokines and Leukocyte-specific Chemotactic and Activating Factors (Barrett J. Rollins)

Bcl and Cell Death (Stanley J. Korsmeyer)

Prodrugs (Peter D. Senter)

Reconstruction of Complex Tissues in Culture

Diet and Tumorigenesis (Diane F. Birt)

Childhood Leukemias: The Latest in Treatment (Steven E. Sallan)

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