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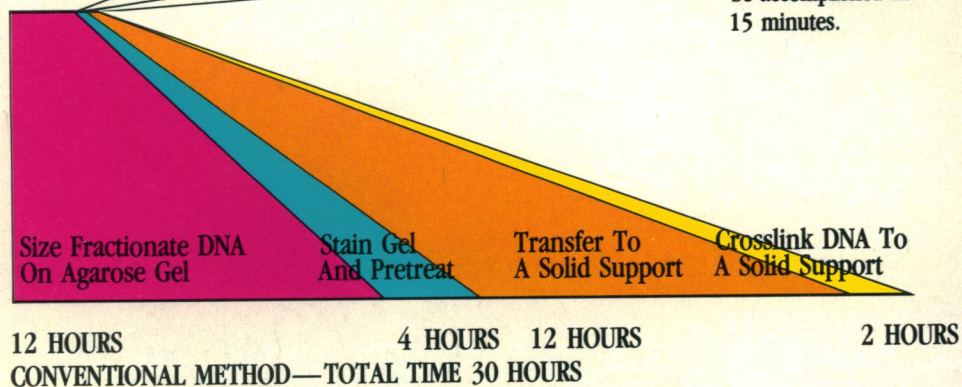
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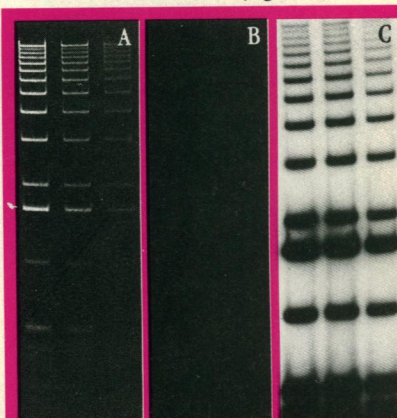
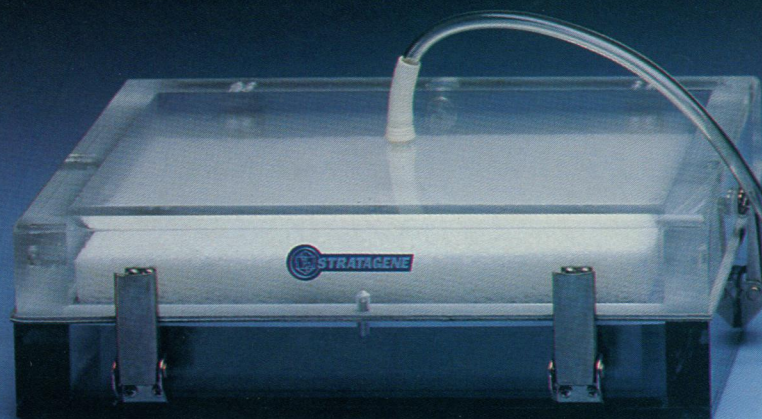
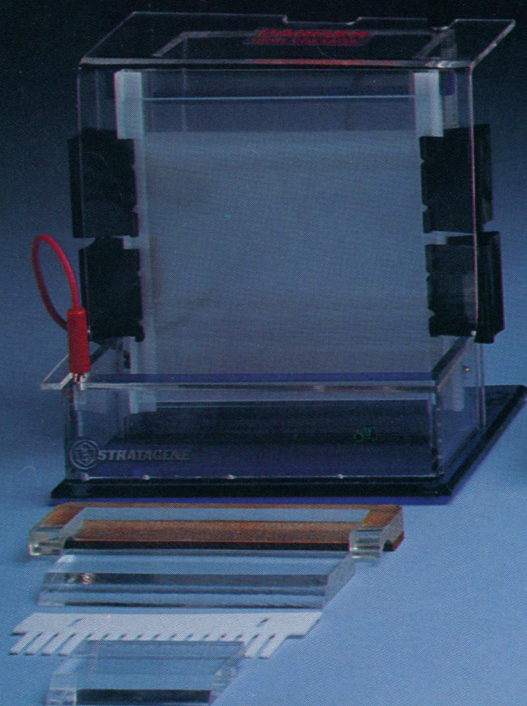


FIGURE 1:
Figure Legend: Fractionation of end labeled DNA markers on 3mm thick 0.8% agarose by the VAGE apparatus and transfer to Duralon—UV™ membranes using the PosiBlot pressure blotter.
A. Ethidium stained gel showing high resolution.
B. Same gel after pressure blotting.
C. Autoradiogram of membrane after pressure transfer.



PosiBlot™ Pressure Blotter

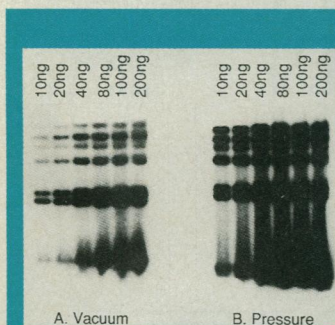


FIGURE 2:

Figure Legend: ^{32}P end-labeled lambda Hind III markers were electrophoresed in 0.8% agarose. The DNA was then transferred to a nylon membrane with a vacuum blotter at 30mm Hg below atmospheric or with the PosiBlot pressure blotter at 100mm Hg above atmospheric. Both transfers were carried out for 15 minutes. As can be seen, pressure blotting transferred significantly more DNA in the same period of time, especially in the higher molecular weight range (largest band is 23 kilobases).

The PosiBlot™ positive pressure blotter permits the transfer of nucleic acids in 1/3 the time of vacuum blotters and 1/50 the time of capillary blotting (Figure 2). Pressure blotting does not dehydrate gels as do other methods. This allows the use of substantially higher pressure differentials, compared with vacuum blotting, without gel collapse. The PosiBlot apparatus reduces blotting time to 15 minutes.

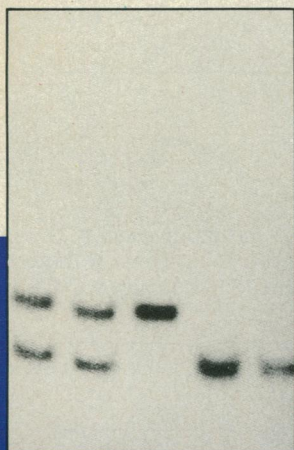


FIGURE 3:

Figure Legend: Autoradiogram showing the resolution of 2.8 and 1.3 Kb Msp I RFLP alleles revealed by a cystic fibrosis human DNA probe using the VAGE, PosiBlot and Stratalinker all in 2.5 hours.

Stratalinker™ UV Crosslinker

The Stratalinker™ UV Crosslinker fixes nucleic acids to solid supports such as nitrocellulose or nylon membranes, in less than one minute. This compares favorably to vacuum baking, which requires 2 hours. The Stratalinker actually monitors the ultra violet energy flux and deactivates the light source upon reaching the user-programmed energy level (Figure 4). Figure 3 shows an autoradiogram of a human genomic Southern blot performed using the VAGE, PosiBlot and Stratalinker all in 2.5 hours.

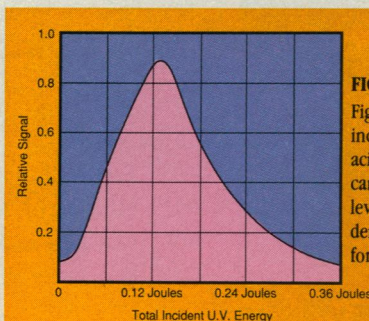


FIGURE 4:

Figure Legend: The effects of altering the incident energy for crosslinking nucleic acids to nylon membranes. The significant drop in signal intensity at energy levels below and above 0.12 Joules demonstrates the limited optimal range for UV treatment.

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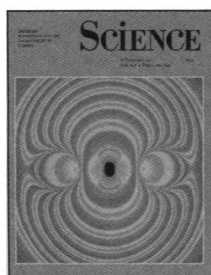
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COVER Graphical representation of the motion of satellite orbits in phase space (the space whose dimensions are position and momentum). Each point fixes the orbital eccentricity and argument of perigee; color bands correspond to constant energy levels. Rendered by contour "painting" on a massively parallel processor, the plot reveals a startling configuration of equilibria spawned by pitchfork and saddle node bifurcations. See page 833. [Computer graphics generated on a Thinking Machines Corporation CM-2 by Etienne Deprit and Liam Healy, Naval Research Laboratory, Washington, DC; photographic image by Mark Stucky]

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This Week in SCIENCE

Black holes

IT is possible that most galaxies harbor a massive black hole (page 817). But proof of a black hole's existence is tricky: with its greatly compressed mass and total absorption of light, a black hole is only really detectable through its effects on nearby stars and gases. Flares from disrupted stars that are being sucked into black holes may be the best diagnostic signs of a black hole's presence, but, if the hole's mass is much greater than 10^8 solar masses, some stars could be swallowed whole without releasing telltale gaseous debris. Rees reviews the evidence favoring black holes as end points in the evolution of active galactic nuclei and also assesses less attractive alternatives. Two to three billion years after the Big Bang, quasar activity peaked in galactic centers; now dead quasars may be at the centers of most galaxies. In part, then, galactic aging involves collapse of much of the galaxy's mass onto the black hole. Mergers of galaxies may be accompanied by hole mergers. And, in the very oldest quiescent galaxies, black holes may be so fuel-depleted that, though present at the galactic center, they will lurk undetected.

Philadelphia chromosome effects

THE Philadelphia chromosome is found in tumor cells of virtually all patients with chronic myelogenous leukemia (CML). This chromosome is a hybrid of chromosomes 9 and 22; the fusion of these two chromosomes produces a new gene that encodes a new protein, P210^{bcr/abl}, which is suspected of inducing CML. Daley *et al.* report that when P210^{bcr/abl} is inserted (on a retrovirus vector) into mouse bone marrow cells and the cells are transplanted into recipient mice, a disease is induced in some of the animals that exhibits features of human CML (page 824). The most characteristic changes observed in the diseased animals were enlarged spleens and granulocyte-rich blood. This system affords

opportunities for studying the cellular origins of P210^{bcr/abl}-induced tumors, for following the stages of disease progression, and for evaluating new therapies for CML.

Hominid scanning

TWO parameters used for inferring evolutionary relations among early hominids are brain size and cranial circulation pattern. With computed tomography (CT) technology, Conroy *et al.* studied the cranial anatomy of a specimen of the early hominid *Australopithecus africanus* (page 838). The CT scans indicated that the venous outflow pattern of specimen MLD 37/38 was like cranial circulation patterns of other *Australopithecus africanus* specimens and those of early *Homo*; accommodation was apparently being made for bipedalism and an upright body posture. The circulation pattern differed from what was characteristic of *Australopithecus robustus* and *Australopithecus afarensis*, two species that probably were not in the direct line to modern humans. The imaging technology allowed for "reconstruction" of a missing portion of the cranium of specimen MLD 37/38, and, from the reconstruction, the cranial capacity was calculated at 425 cubic centimeters, which is smaller than previous estimates. For comparison, modern human brains have capacities in the range of 1400 cubic centimeters.

Primacy of secondary structure

ONE of the regulatory genes of the AIDS virus is *rev*; it encodes the Rev protein, which facilitates the movement of messenger RNA molecules from the nucleus to the cytoplasm. Rev is essential for HIV replication and, therefore, might be a target for therapeutic intervention if its mechanism of action or structural requirements could be understood. Rev interacts with a region called RRE on messenger RNA molecules; RRE folds

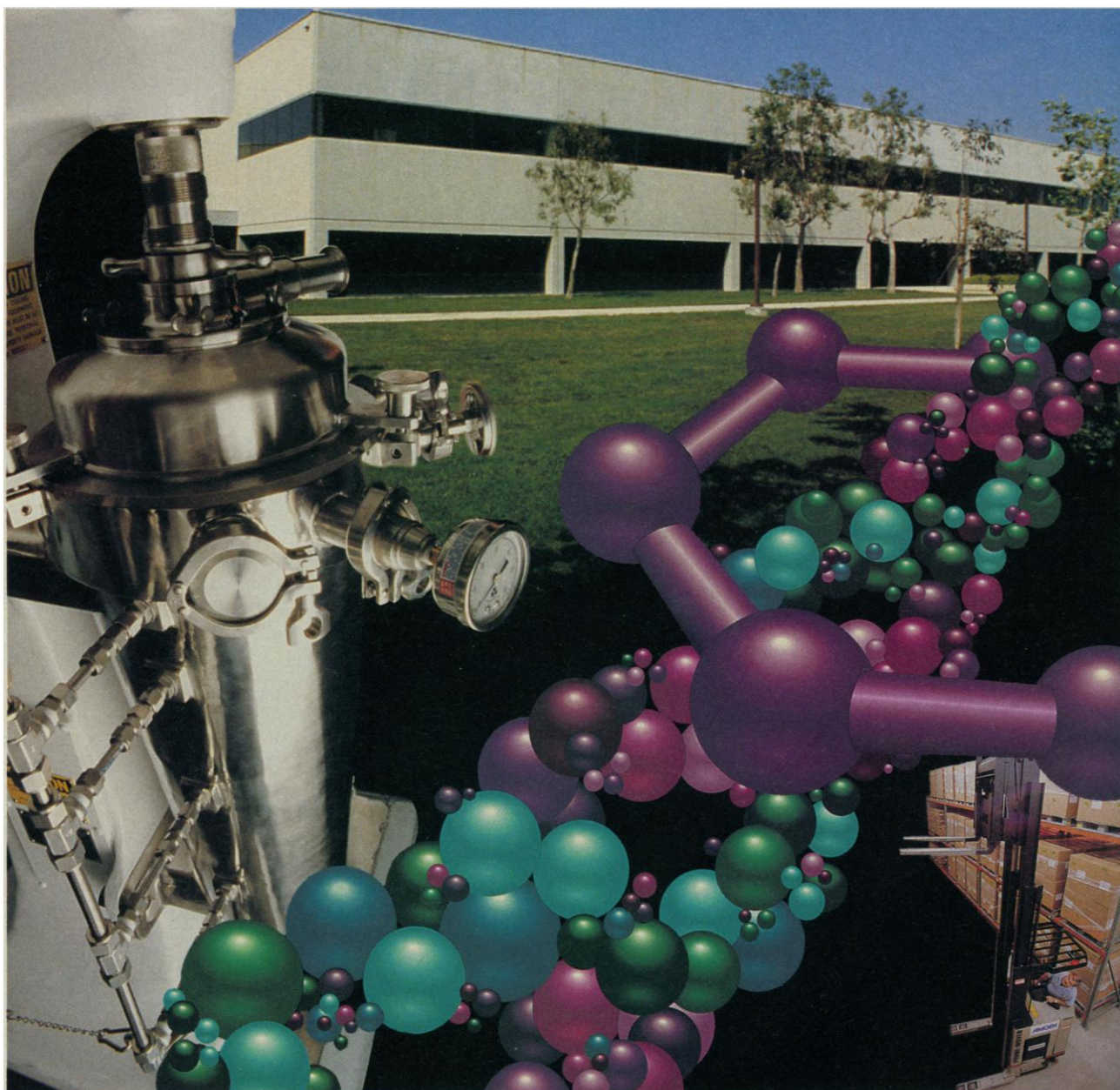
into a complicated flower-like structure. Olsen *et al.* show that the interaction between RRE and Rev is not altered when mutations are made in the nucleotide sequence of RRE's "stem structure" (page 845). In contrast, destruction of the stem abolishes the interaction of Rev and RRE; a second compensatory mutation that restores the secondary structure restores Rev-RRE binding and function, even though the RRE loop ends up with an entirely different sequence. While maintenance of secondary structure is key to the interaction of Rev with RRE, other protein-RNA interactions depend on the integrity of both primary and secondary structures and certain protein-DNA interactions depend only on intact primary structures.

Phenotypically mixed AIDS viruses

A warning flag is being raised regarding the suitability of certain model systems for realistic assessments of the normal behavior of the AIDS virus HIV-1 (page 848). Lusso *et al.* report that when HIV-1 is grown in human tumor cells that are also infected (as a result of passage through a mouse) with a murine leukemia virus, the time courses for HIV-1 infection, for antigen expression, and for evidence of the viruses' cytopathic effects are accelerated compared with time courses in cells not hosting the mouse virus. Although specific changes in the DNA and proteins of the two viruses could not be identified, phenotypically mixed viruses were apparently produced, and the "chimeric" HIV-1 viruses were able to infect a number of cell types that are not their natural hosts. Spurious conclusions about the biologic properties of HIV-1 could be drawn from experiments in which phenotypic mixing has occurred; furthermore, dangerous outcomes of such experiments could include production of more virulent organisms or organisms with expanded host ranges. The implications of these data are further discussed by Marx (page 809).

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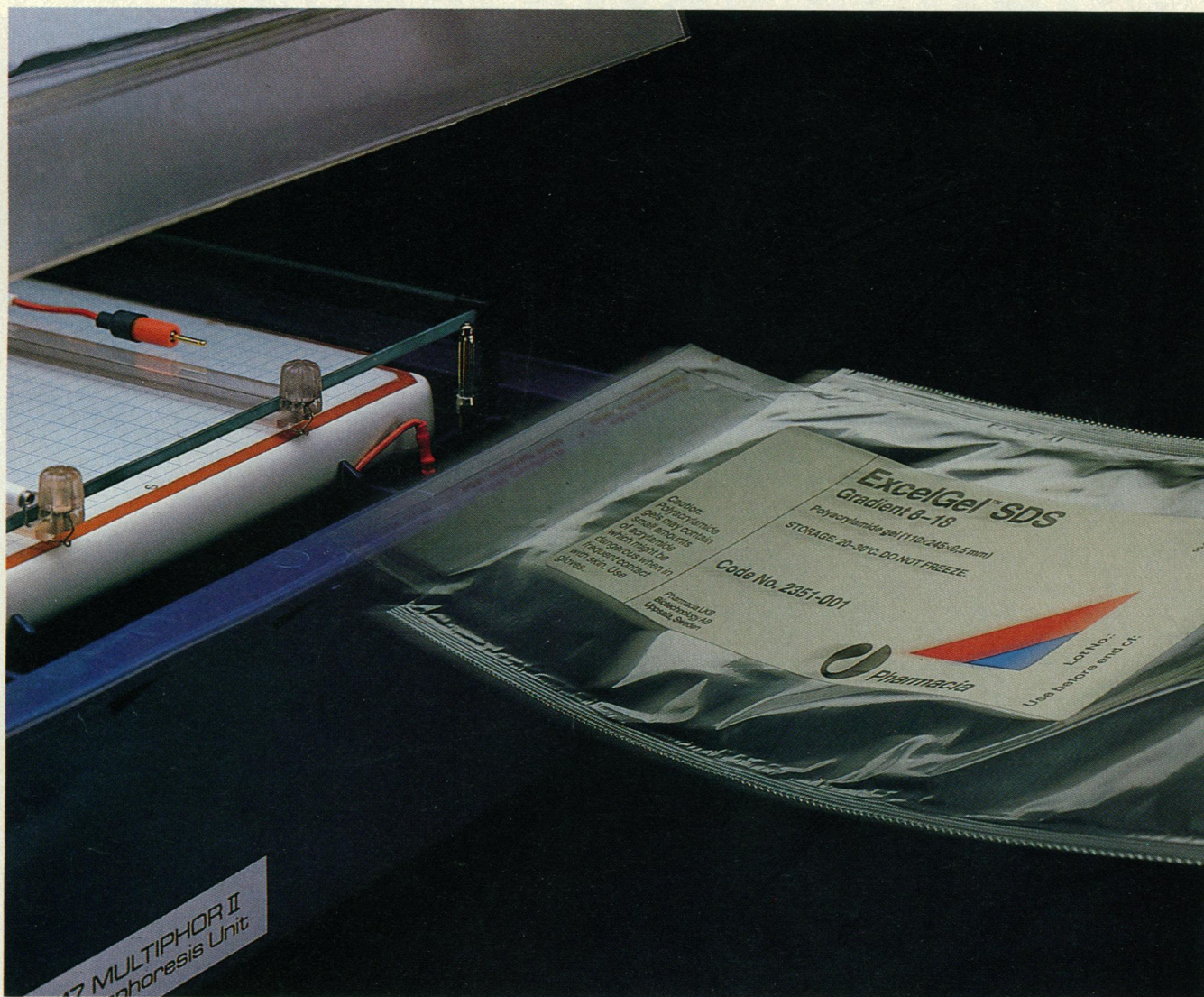
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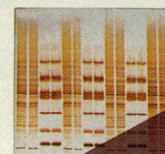
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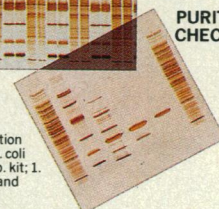
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ROUTINE ANALYSIS



PURITY CHECKING



Purity checking of a purification process, from left to right: E. coli starting material, LMW calib. kit; 1. purification, 2. purification and final purification.

SEPARATION CONDITIONS

Sample: Human growth hormone (kindly donated by KABI, Sweden). Samples are reduced and iodoacetamide treated.
Concentration: 0.1 mg/ml.
Application: 5 µl, as a droplet.
Conditions: 600V, 50 mA, 30W, 15°C, time, 80 min.
Detection: Silver staining, according to the J. Heukeshoven and R. Dernick method, with slight modifications.

Routine analysis of a large amount of samples, from left to right: Repeatedly: E. coli, HMW calib. kit; LMW calib. kit.

SEPARATION CONDITIONS

Sample: E. coli
Concentration: 0.1-0.2 mg/ml.
Application: 5 µl, with a sample applicator.
Conditions: 600V, 50 mA, 30W, 15°C, time, 80 min.
Detection: Silver staining, according to the J. Heukeshoven and R. Dernick method, with slight modifications.

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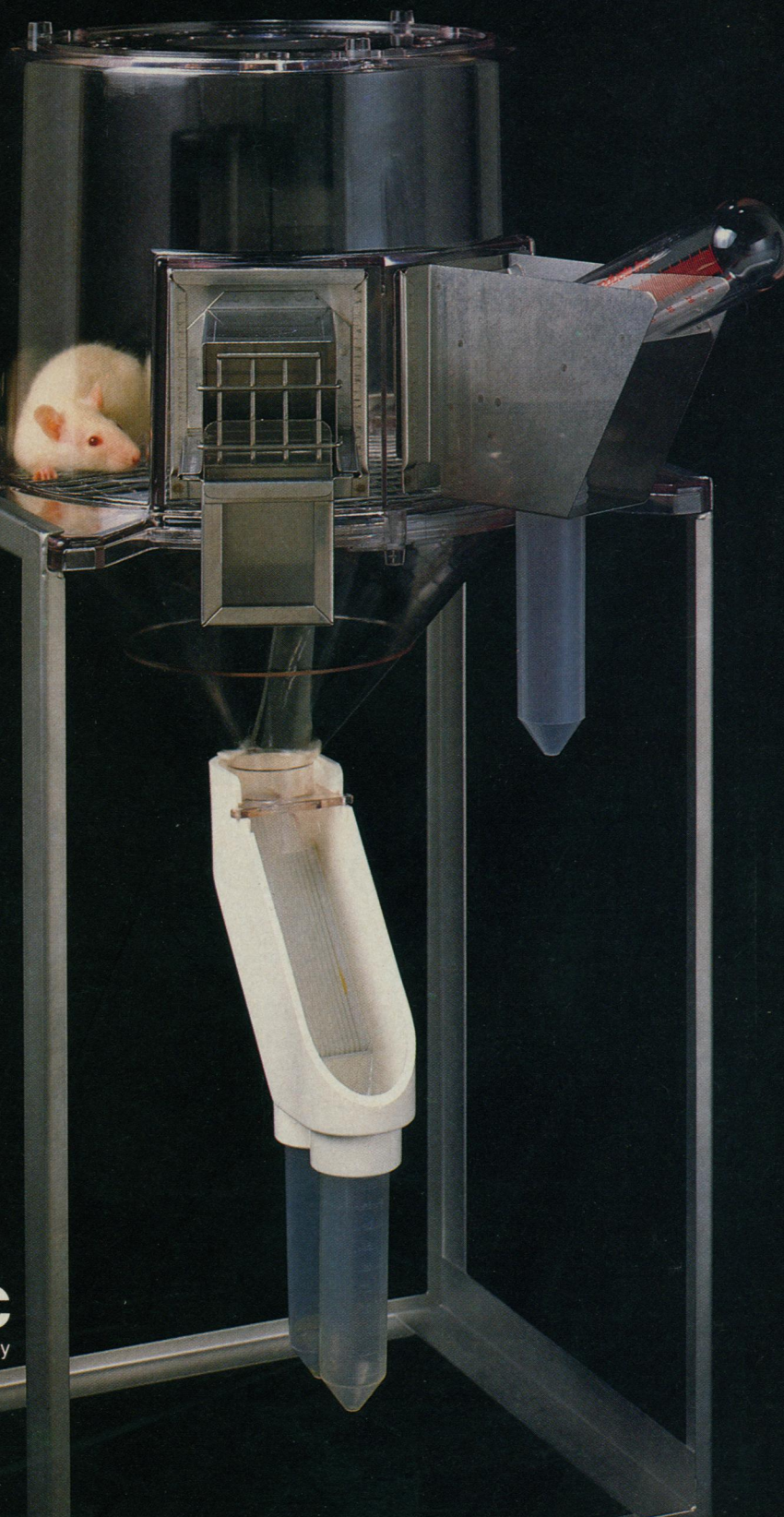
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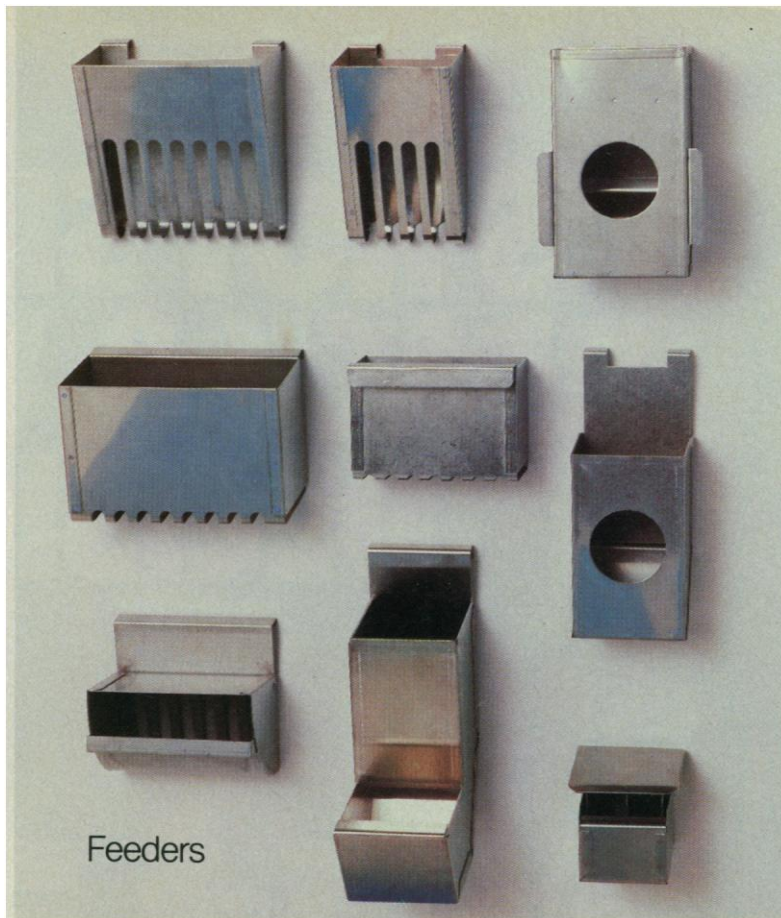


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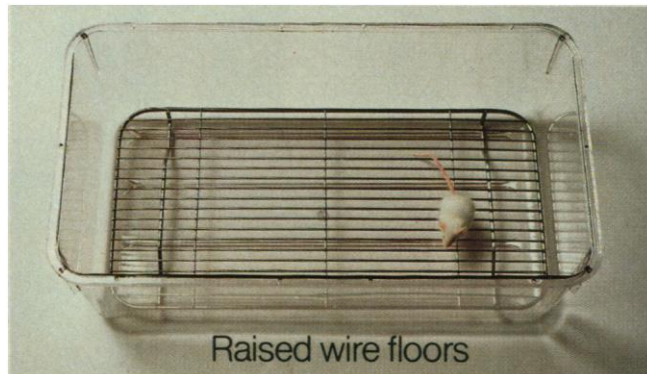


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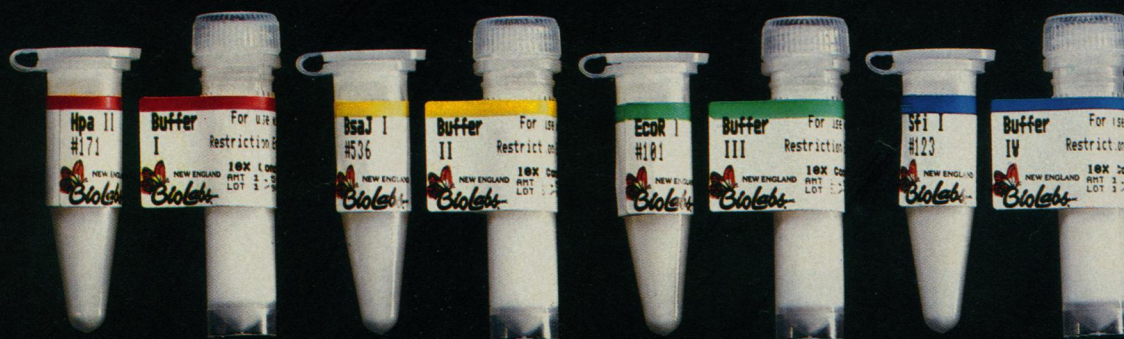
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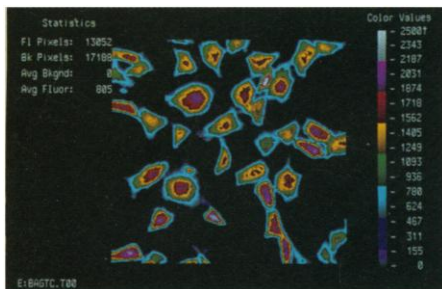
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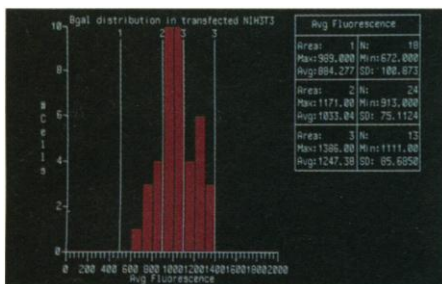
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Reason #7 “Cutting-Edge” Technology for Clonal Selection

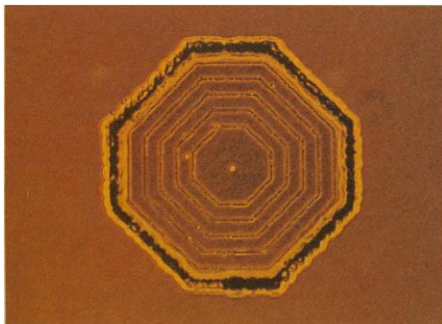
ACAS 570 Interactive Laser Cytometer... The Cytometer For All Reasons



Two-dimensional, pseudo-color fluorescence image of FDG-labeled, *lacZ*⁺, NIH3T3 cells.



Histogram display of β -galactosidase positive, NIH3T3 cells.



An example of ACAS cell sorting using the “Cookie-Cutter”™ technique to isolate single cells in culture while preserving their normal anchorage dependent growth state.

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- Screen cells,
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- Isolate sub-populations of cells for quantitative fluorescence analysis and,
- Automatically store cell locations for repeated scans of the same cells over time.

Meridian Instruments Inc., introduces a major breakthrough in cloning transfected cells with the ACAS 570. The ACAS was used for the screening, selection, and cloning of transfected mammalian cells carrying the *E. coli lacZ* gene.¹ The product of expression of the *lacZ* gene, β -galactosidase, was measured using the fluorescent probe fluorescein di- β -D-galactopyranoside (FDG).² Selected cells were easily isolated and

cloned using the patented ACAS “Cookie-Cutter”™ technique. The ACAS provided quantitative criteria to select *lacZ*⁺ and *lacZ*⁻ cells, and to distinguish between high and low expressers for cloning.

You can use this powerful interactive technique for the automated sorting and cloning of:

- Mutant cells
- Transfected cells
- Hybridomas
- Rare cells

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- #1 – Interactive Laser Cytometry
- #2 – Quantitative Fluorescence Measurements
- #3 – Sensitive Fluorescence Measurements
- #4 – Comprehensive Interactive Software
- #5 – Versatile Integrated Instrumentation
- #6 – Quantitative Confocal Microscopy

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¹ Courtesy of James M. Wilson, Howard Hughes Medical Institute, University of Michigan, and Asmina H. Jiwa, Meridian Instruments, Inc.
² Molecular Probes, Inc.

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ANNOUNCING THE DAWN OF A NEW ERA IN LABORATORY ANIMAL IDENTIFICATION

Simplicity itself: a programmable stand-alone system that doesn't require a computer hookup and uses *your* animal identification number.

Background

Some two years ago Bio Medic Data Systems revolutionized laboratory animal identification by introducing an implantable micro-identification device with an encoded number. An interrogation system activates the implantable chip which then transmits its number. In effect: a truly foolproof system akin to adding a unique electronic "universal product code" to each animal.

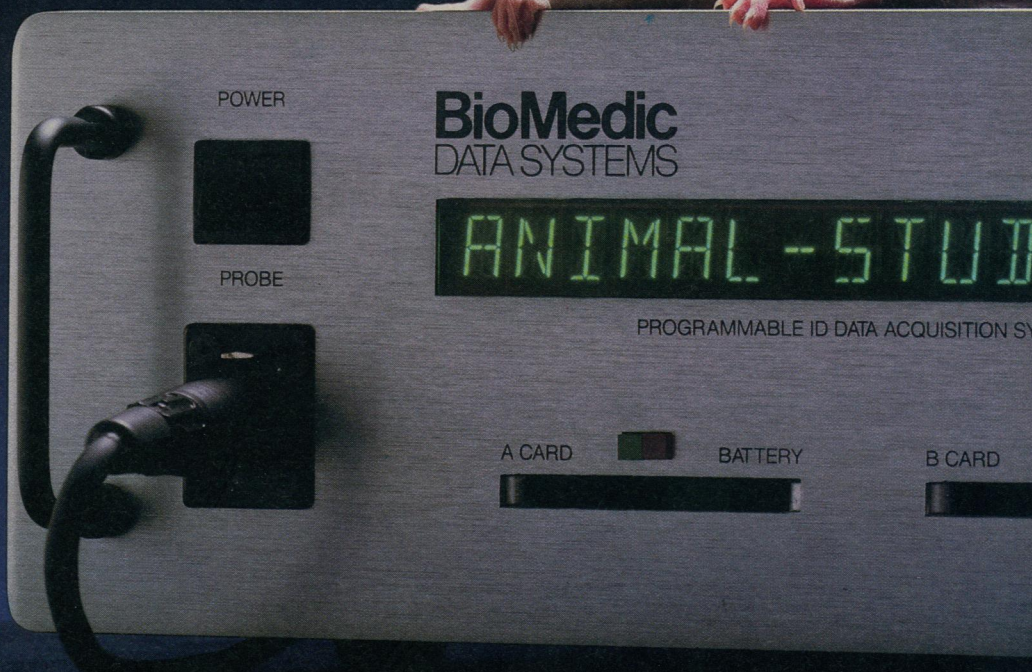
What are the Benefits?

This simple system obsoletes the traditional ear punching or tagging, toe clipping, and tail tattooing. As such, the age-old labor intensive techniques—in terms of the initial identification, the subsequent reading, and the inevitable re-dos—are replaced by a simple, easy, humane and remarkably efficient system. (A dramatic example: 200 animals can be identified in about 45 minutes.)

In addition: the imprecision of the conventional methods is replaced by *positive animal identification*. Animal misidentification or infection can indeed be catastrophic should they delay, impede, or destroy a crucial investigation. This simple foolproof system now converts ear punching or tagging, toe clipping, and tail tattooing into unacceptable risks... and who needs that when a positive animal identification system is now available!



Microchip implant shown at 8X magnification



What about Tissue Response?

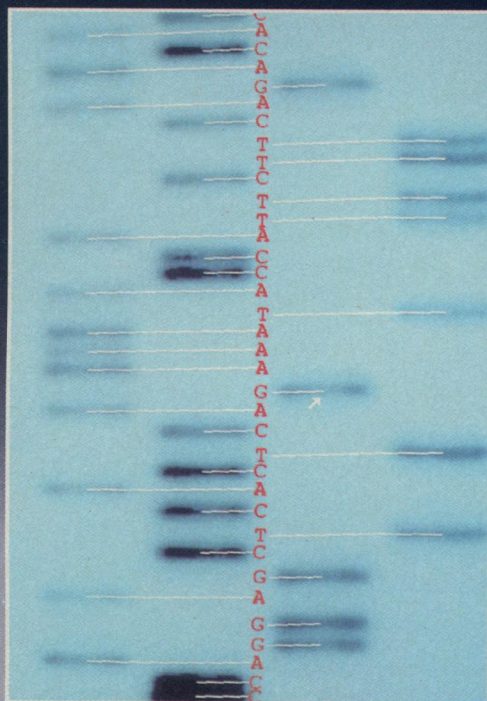
As a result of a 105-week subchronic evaluation in rats and mice, there have been:

- no significant effects on normal body weights.
- no palpable masses observed.
- no visible tissue reaction.

The tissue response to the implanted microchips is considered to be completely non-adverse.

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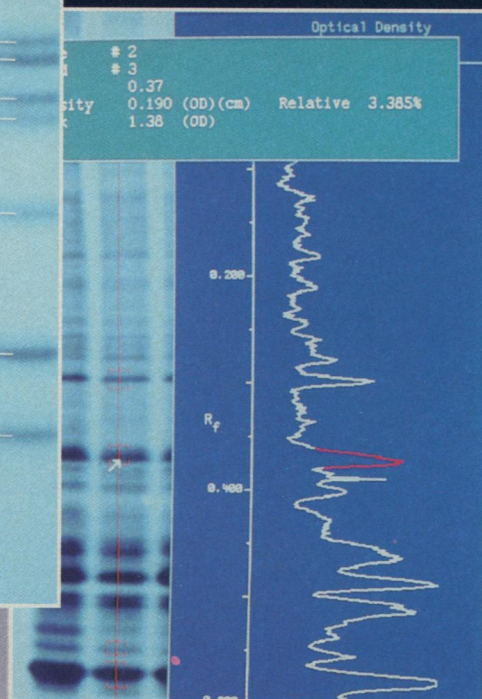
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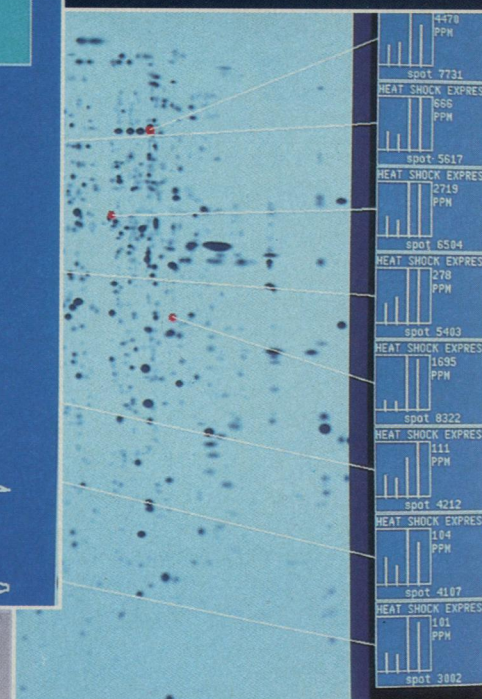
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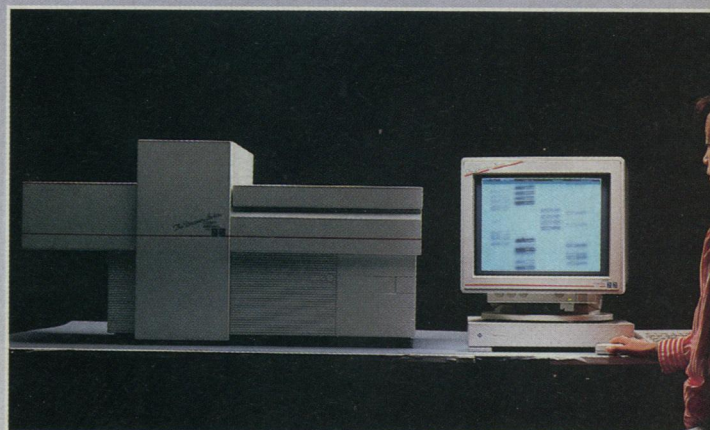
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Further: Since this system is not tied in to a computer, it can be used anywhere, even in hostile environments. However, should you choose, it can *easily* be coupled to a computer or a printer. For your additional protection, a back-up record can always be created in seconds. And this system works with *any* animal species.



Microchip is subcutaneously injected into the animal.

What about GLP Compliance?

ELAMS™ meets and exceeds the GLP guidelines providing a positive animal identification method that is cost effective and accurate.



Who is Using Bio Medic Data Systems' Implantable Micro Identification (IMI)?

More than 45 organizations now have the Bio Medic Data Systems Implantable Micro Identification including Sandoz Research Institute, Schering Plough, C.I.T., General Motors, N.S.I. Technical Services, Stanford University, University of Miami, M.I.T. (Note that the Sandoz Research Institute has submitted the results of the first year of a two-year study for publication.)

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WHEN:

Session I: June 3-June 16, 1990
Session II: June 19-July 2, 1990

WHERE:

Clark Science Center
Smith College
Northampton, MA

FACULTY:

Dr. Steven A. Williams
Dept. of Biological Sciences, Smith College, Northampton, MA; and Program in Molecular and Cellular Biology, University of Massachusetts.

Dr. Molly Fitzgerald-Hayes
Dept. of Biochemistry and Program in Molecular and Cellular Biology, University of Massachusetts.

Dr. John McCarrey
Division of Reproductive Biology
School of Hygiene & Public Health
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Dr. Barton Slatko
New England Biolabs, Inc.

TO APPLY

for this workshop, please submit a recent curriculum vitae and a brief statement of motivation to:

Dr. Steven A. Williams
Dept. of Biological Sciences
Smith College
Northampton, MA 01063

We are pleased to announce the fifth annual New England Biolabs' Molecular Biology and Biotechnology Summer Workshops to be held at Smith College, Northampton, MA.

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EXPERIMENTS WILL INCLUDE: Purification of DNA, restriction enzyme digestion, gel electrophoresis, construction of recombinant DNA molecules, cloning in plasmid and phage vectors, cloning strategies, bacterial transformation and transfection, Southern and Northern transfer and hybridization, radioactive and nonradioactive labeling of DNA, polymerase chain reaction, pulse-field gel electrophoresis, in situ hybridization, antibody screening of an expression library and DNA sequencing. Lectures and discussion sessions (at least three hours each day) will deal with all of the above topics and how these methods are applied in molecular biology research.

INTENDED FOR BEGINNERS IN MOLECULAR BIOLOGY. No previous experience in molecular biology is required or expected. Thirty participants will be selected from a variety of disciplines and academic backgrounds. Last year's participants included principal investigators, directors of programs, postdoctoral fellows and research assistants. Their fields of research included biochemistry, medical physiology, immunology, microbiology, plant biology and others. They came from large universities, small colleges, hospitals and industry.

FEE: \$2200 per participant includes lab manual, use of all equipment and supplies, and room and board (all rooms are singles). Fee includes the use of the libraries and all campus athletic facilities including indoor and outdoor tennis courts, pool, weight room, track, etc. Scientists living in developing countries with limited funds may apply for a scholarship to cover the cost of the workshop (travel not included).

APPLICATIONS MUST BE RECEIVED BY March 30, 1990. Notification of acceptance will be mailed by April 6, 1990. Payment in full will be due by May 11, 1990. Your application should include a C.V. and a statement of motivation. Please specify the session to which you are applying and indicate if you wish to be considered for the other session as a second choice. **For additional information, please contact Dr. Steven A. Williams at (413) 585-3826 (between 1PM and 5PM EST).**

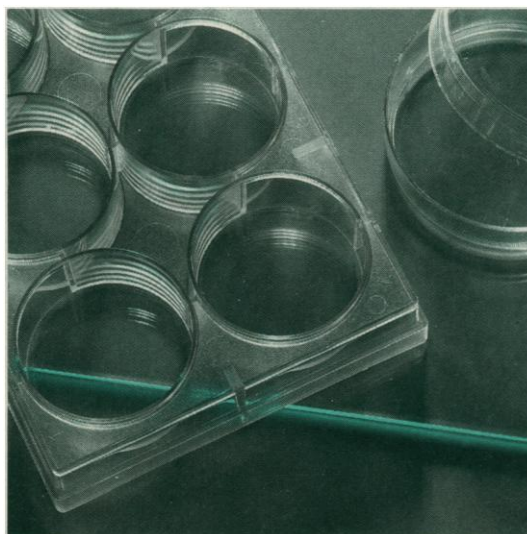


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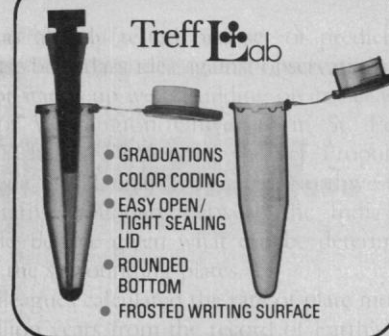
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Praglia Abbey, Bressio di Teolo, Padua, Italy
September 30–October 10, 1990

The second course of the International School of Neuroscience will concentrate on "Developmental Neurobiology," covering the following topics: Origins of Developmental Neuroscience; Molecular Neurogenetics; Intercellular Communication During Nervous System Development; Development of Sensory, Motor and Autonomic Systems; and Cognitive and Affective Aspects of the Developing Mind.

The course will open on September 30 with a plenary lecture given by Rita Levi Montalcini (Rome, Italy) on "The Origins of Trophic Interactions." On October 10 the course will conclude with a symposium on "Early Brain Damage."

Lecturers will include among others: Giorgi M. Innocenti (Lausanne, Switzerland), Daniel Jeanmonod (Zurich, Switzerland), Jacques Mallet (Gif-sur-Yvette, France), John G. Nicholls (Basel, Switzerland), Carla J. Shatz (Stanford, CA), Gunther S. Stent (Berkeley, CA), Colwyn Trevarthen (Edinburgh, Scotland), Hendrik Van der Loos (Lausanne, Switzerland), and Mario Wiesendanger (Fribourg, Switzerland).

Enrollment is limited to 50 students. Students will be selected on the basis of their scientific merit and will represent all countries from which applications have been received.

Application deadline: May 15, 1990.

Additional information about applications and travel grants can be obtained from Laura Linzi-P.O.B. 818-35100 Padua, Italy

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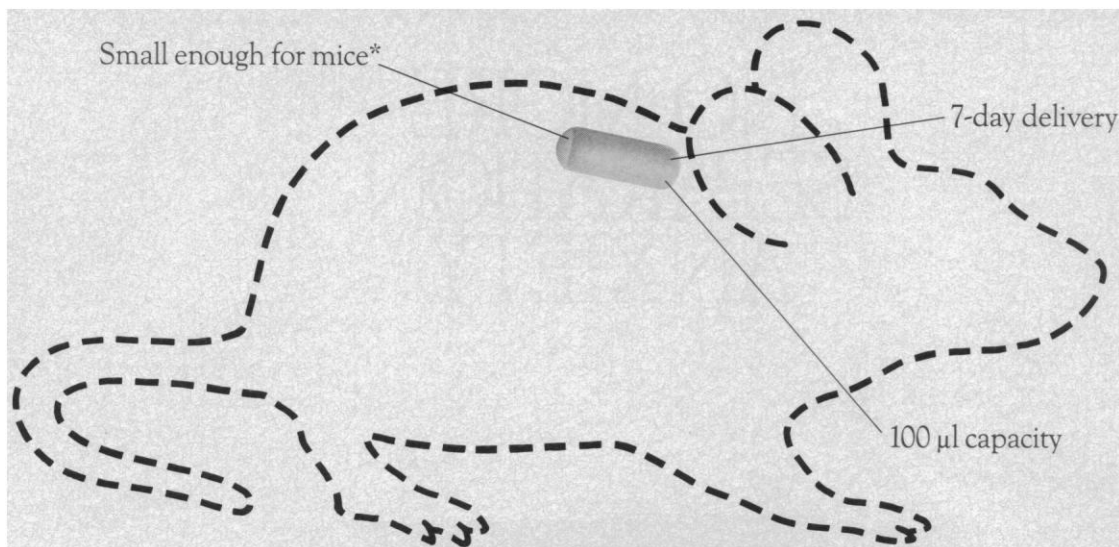
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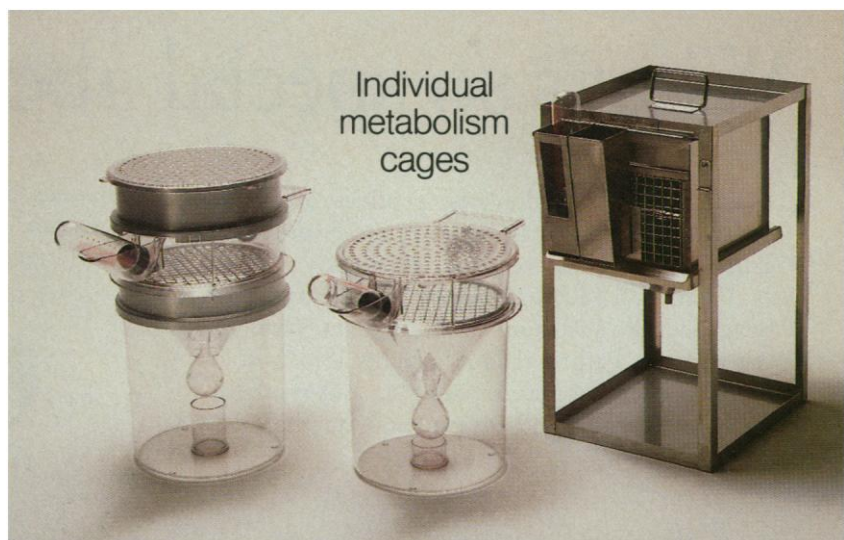
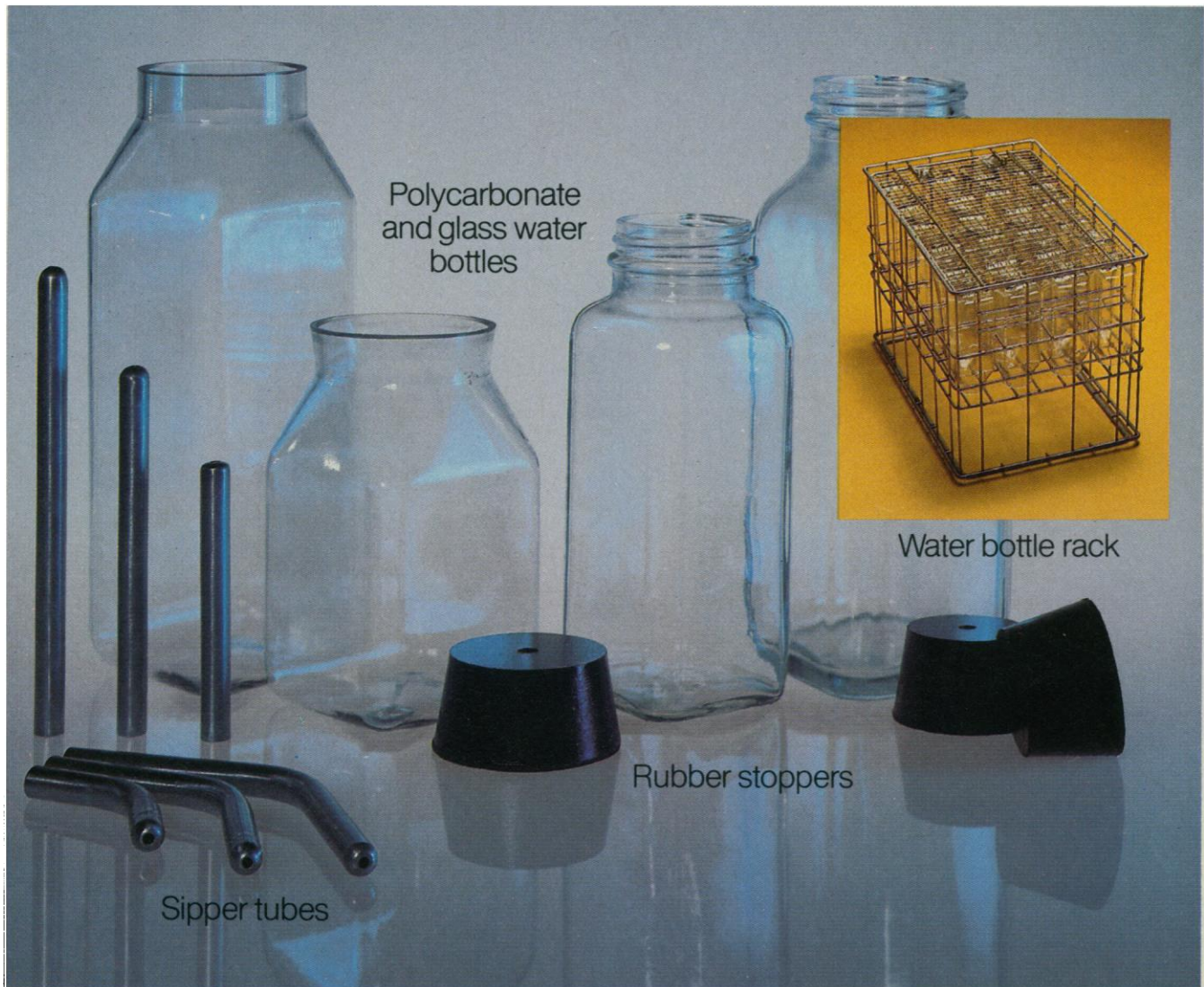
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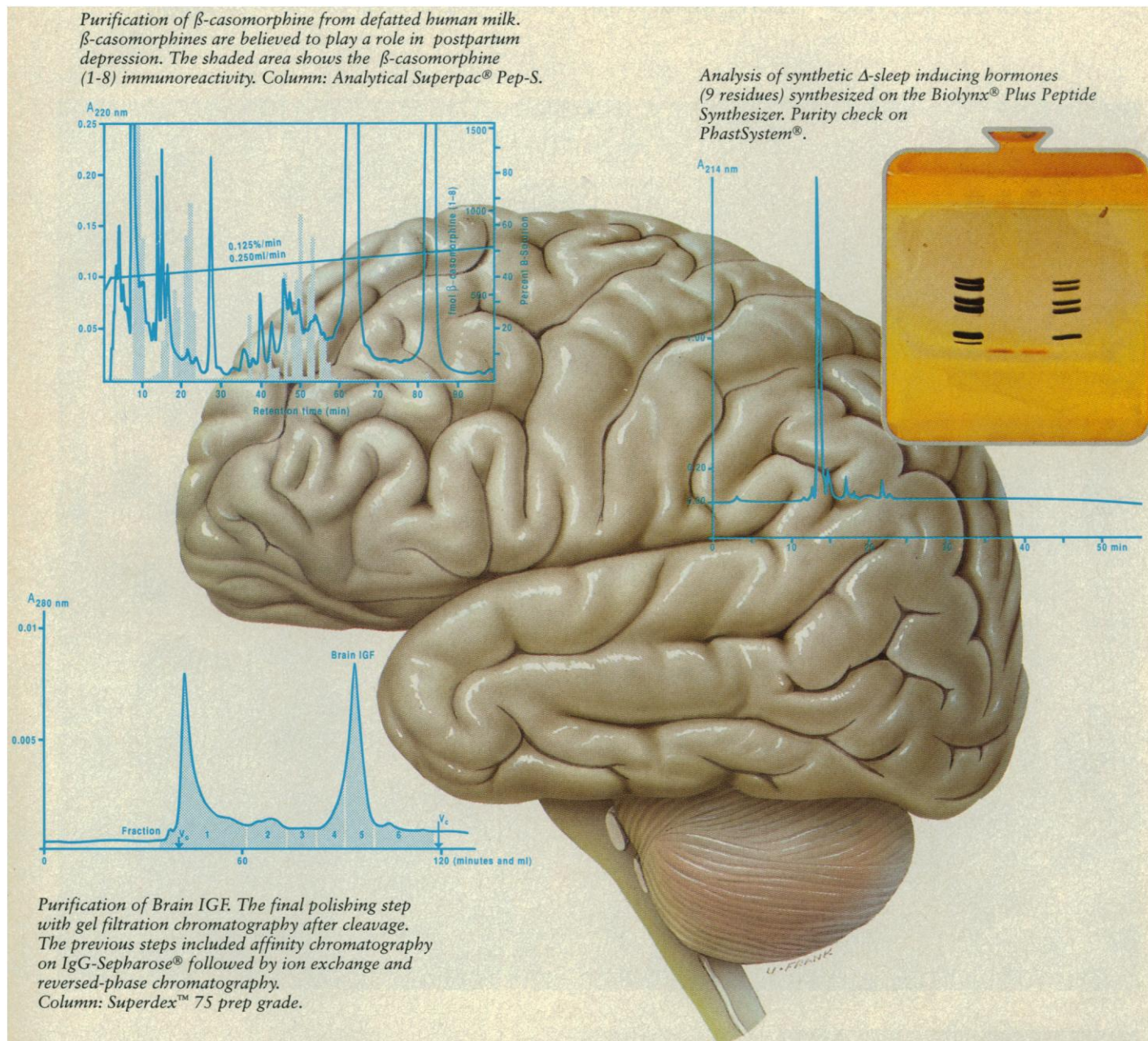
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BIOTECHNOLOGY: FUTURE DIRECTIONS, FUTURE POLICIES

Public Policy Program — Conference
The College of William and Mary
March 29-31, 1990
Williamsburg, Virginia

The "Biotechnologic Revolution" is well underway, but seems to have paused. Early successes have been impressive, but new knowledge and products are slower to emerge. This pause offers an opportunity to assess past progress and current directions to gain perspective on biotechnological developments, their uses, and the policy issues they raise. Session topics include: (1) Biotechnology in 1990: Looking Back, Looking Ahead; (2) Commercial Prospects: The Entrepreneurial Role; (3) Optimal Public Policy: Balancing the Promotion and Regulation of Biotechnological Progress; (4) The Mapping of the Human Genome: Implications For Health, Ethics, and Law.

Participants include: Lori B. Andrews, Am. Bar Foundation; Keith C. Boone, Denison U.; Samuel Broder, Natl. Cancer Inst.; Nancy L. Buc, Weil, Gotshal & Manges, OTA Adv. Panel; Frank Bullock, Schering-Plough Corp.; Steven Burrill, Ernst & Young; George deStevens, Drew U.; Bernard N. Fields, Harvard U. Med. School & Cambridge Bioscience; Robert A. Fildes, Cetus Corp.; Richard D. Godown, Ind. Biotech. Assoc.; Henry Hubbard, Biotech. Practice Group, Hill & Knowlton; Bruce F. Mackler, Mackler, Cooper, & Gibbs, PC, Gen. Council, Assoc. of Biotech. Cos.; Margaret Mellon, Biotech. Policy Inst., Natl. Wildlife Fed.; Stephen A. Merrill, Natl. Acad. of Sci.; Amal Kumar Naj, Wall St. J.; Richard J. Roberts, Cold Spring Harbor Lab.; Leonard G. Schiffrin, Col. of Wm. & Mary; Frank Young, Dept. of HHS; Norton Zinder, Rockefeller U.

For information contact David Finifter, Dir., Public Policy Prog., or Karen Dolan, Conf. Admin., Col. of Wm. & Mary, Williamsburg, VA 23185 (804) 221-2369. Cutoff for guaranteed hotel reservations is March 2.

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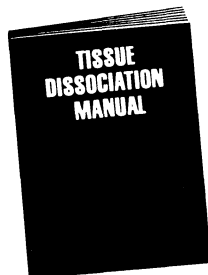


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