American Association for the Advancement of Science

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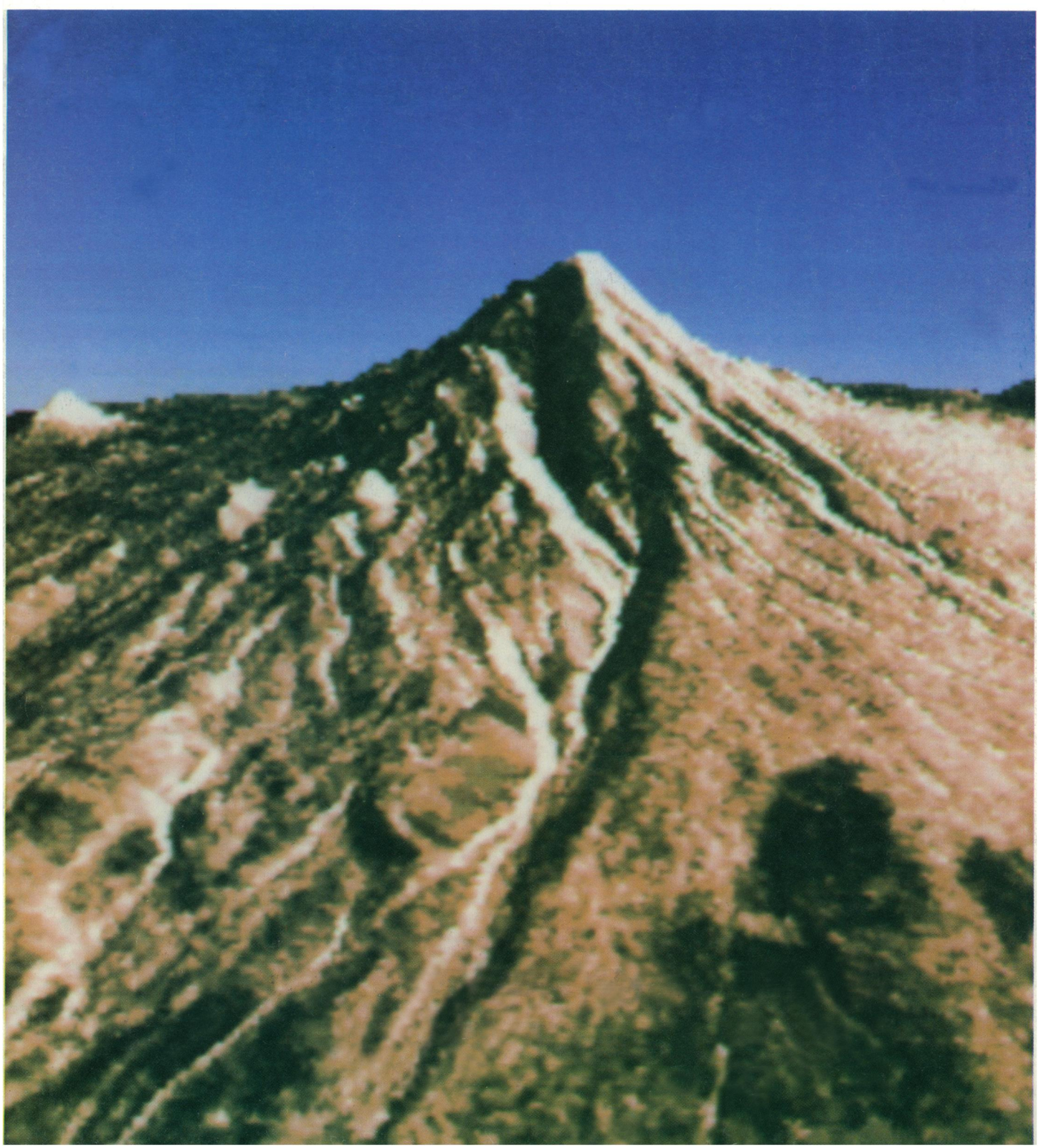

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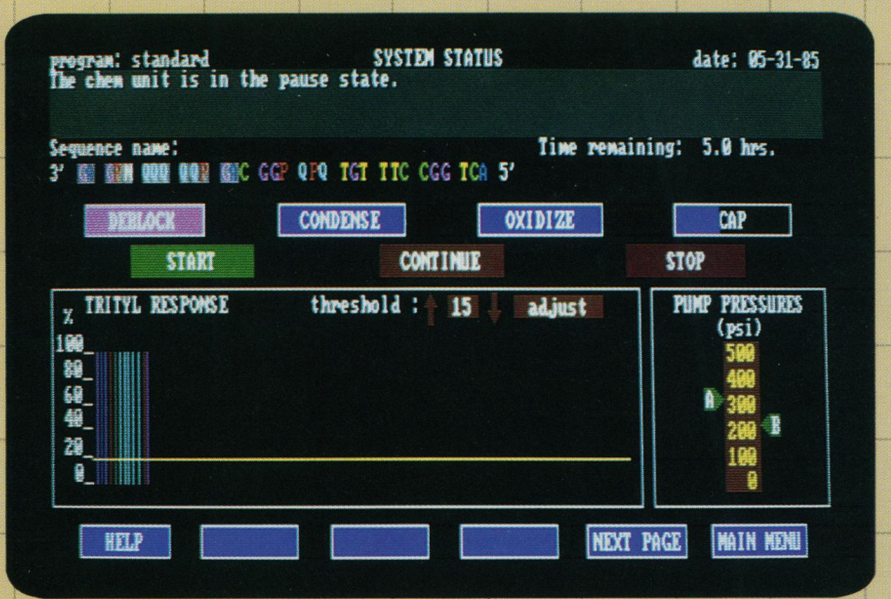

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BASIC BIOLOGY AND STRATEGIES FOR CLINICAL APPLICATION

AUGUST 10-13, 1986

BOSTON MARRIOTT COPLEY PLACE, BOSTON

Organized by

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This meeting will focus mainly on interleukins, interferons, and cytotoxic cytokines, highlighting their potential importance in human disease. This meeting is timely because many of these agents are available in pure form as a result of advances in conventional protein purifications and molecular biologic techniques. An attempt will be made to integrate studies of the mechanism of actions of these agents and their application in the treatment of disease.

The symposium will take place Monday and Tuesday from 8:30 am – 6:00 pm and Wednesday until 12 noon. Discussion groups based on poster sessions will be held Monday and Tuesday evenings. Table top exhibits will also be presented.

CO-CHAIRMEN

Stanley Cohen, Professor of Pathology, University of Connecticut Health Center, Farmington
Jan T. Vilcek, Professor of Microbiology, New York University Medical Center, New York

TENTATIVE PROGRAM

SUNDAY EVENING, AUGUST 10

KEYNOTE ADDRESS: MECHANISMS OF CELL PROLIFERATION

Speaker: *Renato Baserga*

MONDAY, AUGUST 11

TUMOR NECROSIS FACTOR AND OTHER CYTOTOXIC MEDIATORS

Chairman: *P. Henkart*
Comparison of TNF and Lymphotoxin: *B.B. Aggarwal*
Cachetin: *B. Beutler*
Interplay of TNF, IL 1, and Interferons in Monocyte Cytotoxicity: *Lois B. Epstein, M.D.*
Soluble Factors in Cell-Mediated Cytotoxicity: *P. Henkart*
Regulation of Hematopoietic Cells by Cytotoxins: *G. Trinchieri*

INTERFERONS AS REGULATORY AGENTS

Chairman: *M. Revel*
Regulation of Interferon Gene Expression: *John D. Stobo, M.D.,*
Regulation of Data Interferon: *T. Maniatis*
Beta$_2$ Interferon: *M. Revel*
Interferon Receptors: *S. Pestka*
Regulations of Oncogenes Expression by Interferons: *R.M. Friedman*

TUESDAY, AUGUST 12

INTERLEUKIN 2 AND OTHER GROWTH FACTORS

Chairman: *T.A. Waldmann*
The Nature of IL 2 Receptor: *T.A. Waldmann*
IL 2 Ligand-Receptor Interactions: *K.A. Smith*
Intracellular Transduction Pathways in IL 2 Stimulation: *S. Cohen*
Protein Kinase C in IL 2 Action: *W.L. Farrar*
B Cell Growth Factor: *A.L. Maizel*

INTERLEUKIN 1, COLONY STIMULATING FACTORS

Chairman: *C.A. Dinarello*
Structural Studies of IL 1: *C.A. Dinarello*
The Role of IL 1 in the Central Nervous System: *L.B. Lachman*
IL 1 and Rheumatoid Arthritis: *E. Amento*
Biologic Effects of Colony Stimulating Factors: *M. Moore*
Growth Factors as Interferon Inducers: *J. Vilcek*

WEDNESDAY, AUGUST 13

POTENTIAL CLINICAL APPLICATIONS

Chairman: *C.F. Nathan*
LAK and IL 2 in Cancer Therapy: *M.T. Lotze*
Adoptive Transfer of Interferon-Activated Macrophages: *H.C. Stevenson*
Interferon in Malaria: *Victor Nussenzweig, M.D.,*
Inhibition of Intracellular Micro-organism by Cytokines: *Christine W. Czarniecki*
Gamma Interferon in Leprosy and AIDS: *C.F. Nathan*

SUMMARY AND OVERVIEW

Nancy H. Ruddle, Ph.D.
B. Sehgal, M.D., Ph.D.
K. Welte, M.D.
F.E. Wheelock, M.D., Ph.D.

CONCLUDING REMARKS: *S. Cohen, J. Vilcek*

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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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

COVER Perspective view from the southeast with 50% vertical exaggeration of Mount Shasta, a 14,000-foot Cascade chain volcano in northern California. A digital topographic map generated by F. Leberl (Vexcel Corp.) and J. Raggam (Graz Technical University, Graz, Austria) from a SIR-B stereo image pair was used to rectify and reproject one of the images into this view, in which colors from dark green through pink to white are proportional to 23-centimeter radar brightness. See page 1511. [M. Kobrick, Jet Propulsion Laboratory, Pasadena, CA]

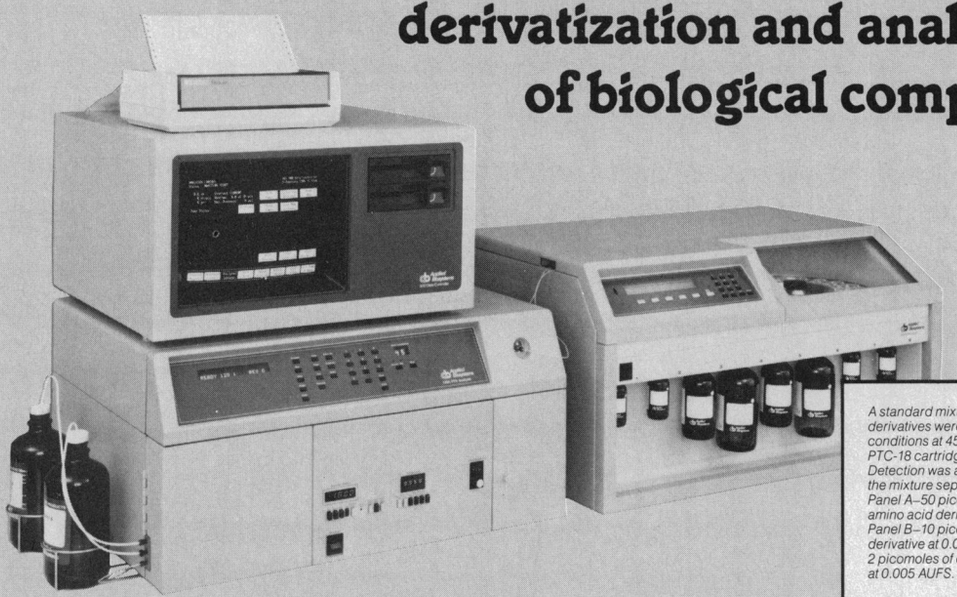
Reports

Book Reviews

Products & Materials

BIOSYSTEMS UPDATE

A new, multi-method system for the derivatization and analysis of biological compounds



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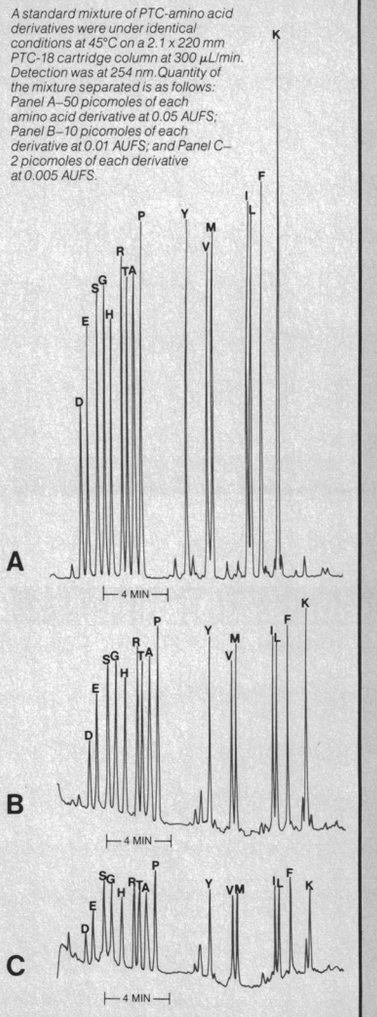
A standard mixture of PTC-amino acid derivatives were under identical conditions at 45°C on a 2.1 x 220 mm PTC-18 cartridge column at 300 µL/min. Detection was at 254 nm. Quantity of the mixture separated is as follows: Panel A–50 picomoles of each amino acid derivative at 0.05 AUFS; Panel B–10 picomoles of each derivative at 0.01 AUFS; and Panel C–2 picomoles of each derivative at 0.005 AUFS.



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This Week in

SCIENCE

Radar imagery of the earth

SHUTTLE imaging radar, launched on the space shuttle Challenger in 1984, has provided a new and better look at the earth from space (page 1511). Equipped with a pointable antenna, the sensor was able to provide digitized data at a range of incidence angles and had the capacity to generate radar stereo images of features on the ground. Elachi *et al.* provide an overview of the results, and Beal *et al.* (page 1531) and Gasparovic *et al.* (page 1529) give detailed results from two of the experiments. The radar successfully mapped ocean wave patterns and verified the theory that the wave spectrum is rotated in the radar image. Data from a low-altitude orbiting radar can now be used with confidence for accurate global surface wave prediction. Although a number of problems during the mission allowed acquisition of only about 20% of the planned data, capabilities were also confirmed in geologic mapping, detection of buried landforms in the desert, classification of forest cover, and imaging of the ground through forest canopies. A new generation instrument will be launched about 1990 and will have the capability to image the earth's surface at three frequencies and all polarizations.

Water vapor in Halley's comet

COMET Halley has made 29 trips around the sun in recorded history, and vaporization causes the nucleus to lose on average several meters of thickness each perihelion passage (page 1523). By use of infrared resonance fluorescence, Mumma *et al.* have studied the vaporized material in the coma and have detected the presence of water vapor. Although it has long been assumed that H_2O was present, and species such as H_2O^+, the hydroxyl radical OH, and atomic hydrogen have been observed, molecular water has not been unambiguously detected. The high-resolution Fourier transform instrument was flown at 41,000 feet aboard the NASA-Kuiper Airborne Observatory last December, when Halley was in favorable position for observation. Nine spectral lines for H_2O were identified, and their characteristics allowed estimation of an H_2O production rate of 10^{29} molecules per second. The ratio of H_2O molecules in ortho configuration to those in the para configuration was 2.66. This ratio may reflect the aphelion temperature of the nucleus of the comet and yields a temperature estimate of 32 K. Infrared resonance fluorescence can be applied to the detection and study of parent molecular species in other comets and may help unravel the problems of their origin and evolution.

Virus evolution in vivo

AIDS virus (HTLV-III/LAV) has been serially isolated from three infected patients over a period of 1 to 2 years (page 1548). Hahn *et al.* found that the virus isolates from a single patient over time change rapidly but are more related to each other than to viruses isolated from other patients. The virus isolates have been molecularly cloned, and genes sequenced and compared. Evolution of the viruses was rapid, especially in the gene encoding the extracellular envelope glycoprotein. The changes detected were nucleotide point mutations, short deletions or insertions, and duplications. In contrast, sequenced portions of the *gag* gene were highly conserved. The changes indicate parallel evolution of virus variants within a patient. In addition, the close relation among sequential virus isolates suggests that each patient has been infected with only one or a limited number of viral forms. An initial infection perhaps leads to protection from subsequent viral infections.

Orchid flowers force pollen on bees

ORCHIDS of the genus *Catasetum* have strongly sexually dimorphic flowers borne on unisexual plants. Plants that produce male flowers are more numerous and have more blossoms than female plants (page 1538). Romero and Nelson observed that when a bee seeking perfume enters a male flower a trigger mechanism causes a mass of pollen to be shot onto the bee. The male flower then wilts within a day and cannot be entered by another bee. The experience of having pollen forcibly emplaced on it is aversive, and the bee avoids entering other male flowers. The pollen-loaded bee will still visit the different looking female flowers of *Catasetum* and may leave behind its pollen mass in the stigmatic cleft of the reproductive structure. The pollinated cleft will quickly swell shut, and the female flower thus receives pollen from only one bee and one male flower. The unusual competition among male flowers for the opportunity to have their pollen transferred to a female flower may account for the widespread sexual dimorphism in this genus of orchids.

Phototransduction cascade

THE cascade of events in phototransduction in the invertebrate photoreceptor has been clarified by use of a blocking agent that halts the chain of events at an early stage and leaves later events unaffected (page 1543). In Fein's model of transduction in the horseshoe crab *Limulus*, information flows from the visual pigment rhodopsin, which is isomerized by illumination, to a guanine nucleotide–binding protein (G protein or transducin), which activates phospholipase C, causing the production of an intracellular messenger. The intracellular messenger causes the release of calcium, thereby inducing current to flow. A blocking agent was used to inhibit the activity of the nucleotide–binding protein. Visual excitation was blocked, but later events of the cascade could still be activated by injection of the intracellular messenger. Vertebrate phototransduction seems to work the same way, and these experiments show that the interaction between rhodopsin and guanine nucleotide–binding protein is fundamental to phototransduction.

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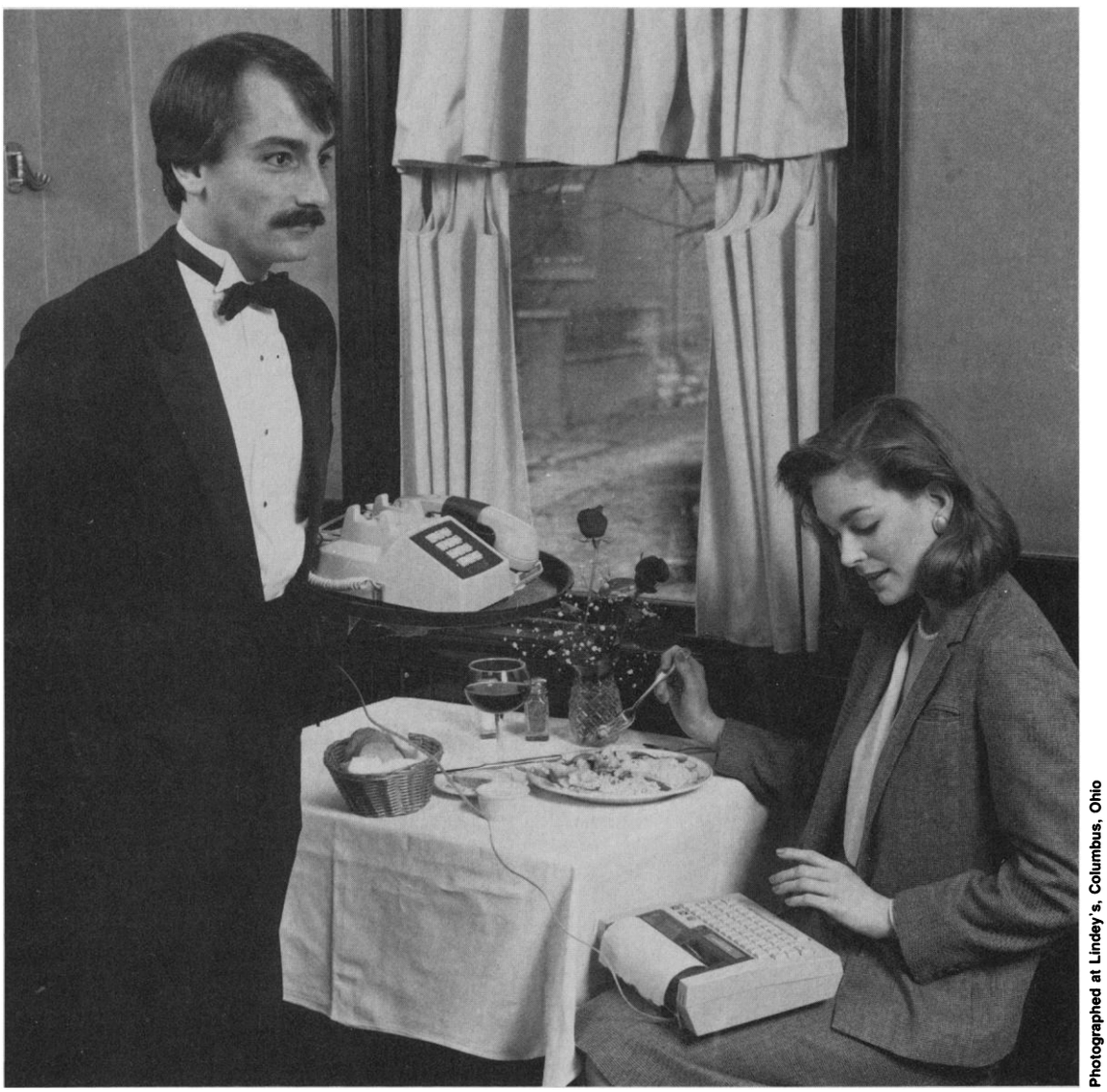

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SCIENCE

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Materials Science and Engineering

Given high-quality materials and superior designs for function and for manufacturing, superior products can be created at minimal cost. The Japanese have been more vigorous than we in exploring the potentials of materials, but activity in the United States is expanding. A symposium at the recent AAAS meeting in Philadelphia permitted a glimpse into some of the activities in progress.* Major fields of materials include polymers, composites, magnetic materials, semiconductors, fiber optics, and ceramics. In general, while new materials are still being discovered, major emphasis now is on processing.

New insights were presented about the behavior of mixtures of polymers and especially the behavior of composites containing strengthening fibers. Highly complex shapes and structures can be made by injection moulding, and this technique will be used increasingly in automobiles and in making other items. The strength of such items in any given direction is highly dependent on the placement of fibers. Computer modeling of fiber orientation would permit improved designs. Computer analysis of many facets of behavior of polymers and mixtures of polymers under stress is now beginning. Increasingly composites are being used in airplanes and their large-scale adoption would be hastened were they better conductors of electricity and thus less susceptible to lightning strikes. Graphite fibers used in composites can be made nearly as conductive as copper through incorporation of substances such as $CuCl_2$ between the layers of the graphite structure.

For most applications involving semiconductors, silicon will continue to be the prime choice. But gallium arsenide can emit light. Silicon cannot. Gallium arsenide circuits have speeds 10 to 100 times those of silicon. The drawbacks are many, including difficulty of creating perfect single crystals. Experiments on the space shuttle indicate that perfection can be achieved in a microgravity field. Precise conductor connections between semiconductor circuits can be made by laser irradiation of organometallic films. This process is being improved through research.

An increasing number of techniques are available for rapid solidification of metals. These permit production of very fine grained metals and alloys that can be sintered together to create objects with superior strength and resistance to creep. The fast cooling techniques and subsequent metal forming of powders can be used to construct turbine blades with internal air cooling. These blades can function in gases at temperatures 500°C higher than the melting point of the metal.

Advances in ceramics were also discussed. The current technology for transmission of information through SiO_2 fibers involves repeater stations required at roughly 100-kilometer intervals. A goal worth achieving is transmission from London to New York without a repeater. Such a goal is theoretically possible with the use of fluoride-containing glasses—for example, a mixture of ZrF_4, BaF_2, LaF_3, AlF_3, and NaF. Good progress is being made toward the goal. A powder of Al_2O_3 can be sintered at temperatures approaching its melting point of 2050°C to form a very strong and transparent glass for use in high-pressure sources of light. The process now in use requires hours. By sintering in a plasma (at temperatures on the order of 5000°C) the time required can be reduced to some seconds.

For detecting changes in pressure or pressure waves, single crystals of substances such as lead zirconium titanate (PZT) have long been employed. However, for undersea applications single crystals are not very sensitive. A design methodology has been found that combines ceramics and polymers in composite piezoelectric transducers highly sensitive to pressure changes. The new transducers have potential applications in medical ultrasonics and will allow robots to "feel" the objects they grip.

The dominant materials of a decade ago are being supplemented or replaced by new superior combinations. Computer modeling is improving designs. A materials science and engineering revolution is under way that will be a key factor in determining the outcome of global economic competition.—PHILIP H. ABELSON

*The symposium, "The Changing World of Materials," was organized by Witold Brostow of Drexel University in Philadelphia. The speakers and topics are listed in the meeting program.

60-centimeter telescope will be equipped with four complementary and versatile focal plane instruments, which will permit imaging, photometric, spectroscopic, and polarimetric observations. Consortia of national scientific institutes, in close conjunction with ESA, are already building these instruments, which will be delivered to the Agency for launch and operations in orbit.

It would seem that in the area of infrared astronomy after IRAS, the Europeans are now building what Rieke *et al.* are dreaming of.

R. M. BONNET
Scientific Programme,
European Space Agency,
8-10, rue Mario-Nikis,
75-738 Paris Cedex 15, France

Response: We welcome Bonnet's letter and thank him for bringing to the U.S. scientific community a more complete picture of the capabilities of the Infrared Space Observatory (ISO) than we presented in our article. Astronomers on both sides of the Atlantic have recognized the scientific importance of the infrared band and the tremendous gains that can be made with modern infrared detectors on cooled telescopes in space. These gains are vividly demonstrated by the Infrared Astronomy Satellite (IRAS), surely a dramatic advance in the exploration of the universe.

Within this country, the importance of a coordinated program to exploit these unparalleled sensitivity gains was recognized in a recommendation in 1974 by the Space Science Board that NASA proceed with the Space Infrared Telescope Facility (SIRTF) promptly after IRAS. The National Academy of Sciences' study on priorities for astronomy in the 1980's, the Field report, was written on the assumption that SIRTF would move ahead early in this decade. Unfortunately, this assumption has proved incorrect.

When the proposal for ISO was made by the European Space Agency (ESA) in 1979, attempts were made to join the two projects, but these attempts foundered for a variety of reasons. The SIRTF team has continued to explore this issue, most recently at the International Society for Optical Engineering (SPIE) conference in November 1985. At that time, the uncertain schedule for SIRTF appeared to make collaboration impossible.

Detailed descriptions of both projects were presented in a joint ISO-SIRTF session at that conference, available as *SPIE Proceedings*, volume 589, "Instrumentation for optical remote sensing from space." It was apparent from these presentations that SIRTF will be much more capable than ISO in sensitivity, image quality, and pointing stability; ISO was described by members of its team as an intermediate step between IRAS and SIRTF. Nonetheless, ISO will be a powerful facility for more detailed study of many IRAS sources. Given the richness of the infrared sky revealed by IRAS, ISO can be expected to make additional discoveries not anticipated in IRAS. However, SIRTF will be required to answer many of the scientific questions posed in our article.

The performance that ISO will ultimately achieve will depend on the rapidity with which European engineers and infrared astronomers assimilate the requisite technology and adjust the plans for ISO to accommodate it. In a field pioneered for many decades in the United States, it is with some regret that American astronomers must now step aside while ESA has the first pick of the exciting and tantalizing IRAS findings.

GEORGE RIEKE*
Steward Observatory,
University of Arizona, Tucson, AZ 85721

*For the SIRTF Science Working Group.

The Normalization Pairing

The Normalization Pairing

A scientist at the General Motors Research Laboratories has developed a new method for accurately determining the effectiveness of safety belts in preventing traffic fatalities. The approach may be used to answer a wide variety of questions using data bases that lack conventional measures of exposure.

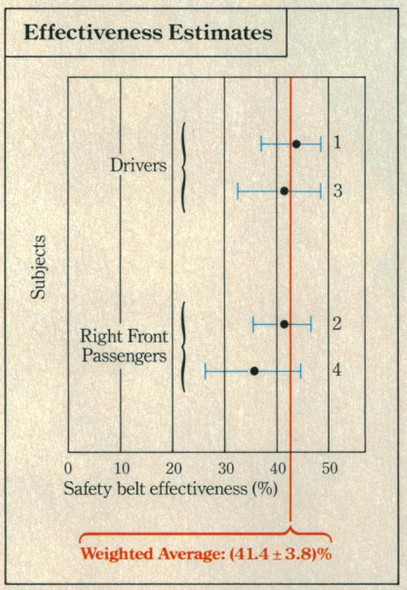


Figure 1: Weighted estimates of safety-belt effectiveness by subject, with standard error. Estimate 1 pairs subjects with right-front passengers; 2 pairs subjects with drivers; 3 and 4 pair subjects with occupants of all other seating positions.

THERE IS A serious problem that researchers often encounter when trying to analyze large collections of information. It is the problem of measuring exposure. Though a collection of data may contain a large number of cases, and though the facts in each case may be highly detailed, there may be no way of comparing events selected for inclusion in the collection against the normal occurrence of similar events in the world at large.

One such data base is the Fatal Accident Reporting System (FARS) maintained by the U.S. Department of Transportation's National Highway Traffic Safety Administration. FARS details all fatal accidents in the U.S. since January 1, 1975—more than 300,000 crashes. However, it lacks an explicit measure of exposure.

FARS contains, for example, the number of fatalities classified by safety belt use. But fatalities among users depend on two considerations: first, the effectiveness of safety belts; and second, the crash involvement differences between users and non-users—that is, the exposure of belt users to crash involvement. If crash involvement were independent of belt use, it would be a simple matter to calculate the effectiveness of safety belts in preventing fatalities. However, belted drivers have fewer crashes, and the crashes they do have tend to be of lower average severity than those of unbelted drivers.

Now a scientist at the General Motors Research Laboratories has developed an approach to drawing inferences from FARS using only the information contained in the file. Dr. Leonard Evans has designed a method for comparing the effects of isolated characteristics by using two sets of crashes. In each set, a *subject* occupant is paired with an *other* occupant. In the first set, the subject exhibits the characteristic to be studied; in the second, the subject does not. The *other* occupant is chosen to have similar characteristics in both sets of crashes (e.g. always unbelted), and thereby acts as a measure of exposure.

To illustrate the workings of the method of double-pair comparison, Dr. Evans first applied it to a study of the effects of safety belt use on fatality risk. He could define the effectiveness of safety belts in terms of the ratio:

$$R_{true} = \frac{N_b}{N_u} = \frac{N' \int q_{D,b}(s) f_u(s) ds}{N' \int q_{D,u}(s) f_u(s) ds}$$

where N' is the number of crashes per year by unbelted drivers, s is crash severity, $f_u(s)$ is the probability that a crash involving an unbelted driver has a severity s, $q_{D,u}(s)$ is the probability that an unbelted driver will become a fatality in a crash of severity s, and $q_{D,b}(s)$ is the probability that a belted driver will become a fatality in a crash of severity s. R_{true} is a ratio of new to

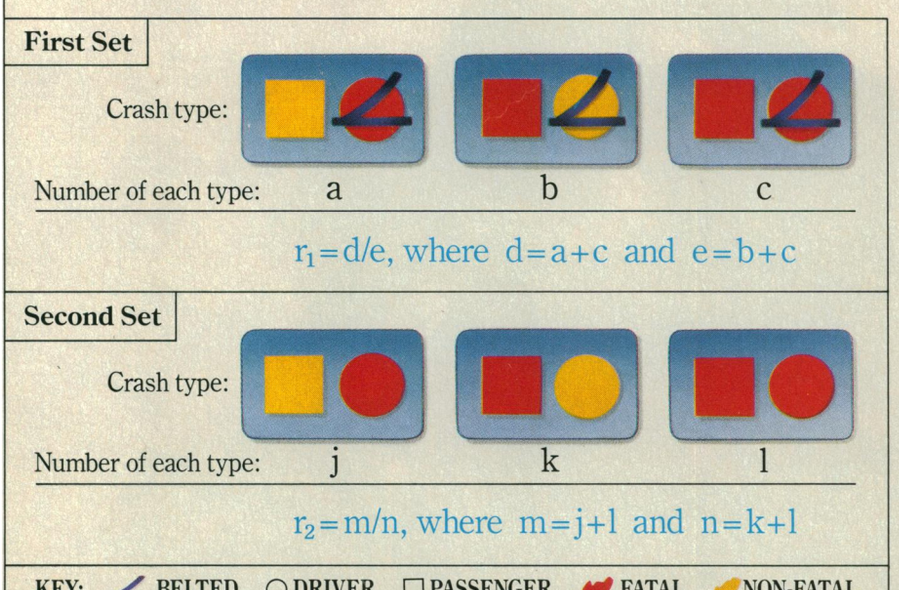


Figure 2: Schematic representation of a sample double-pair comparison.

old fatalities—assuming a formerly unbelted population became a belted population, with nothing else changing. But while N_u, the number of unbelted driver fatalities, can be determined from the FARS data, N_b, the number of these who would still have been fatalities had they been wearing safety belts, clearly is not coded in the data base.

Dr. Evans applied the double-pair comparison method to determine a quantity, R, that would, under plausible assumptions, accurately estimate R_{true}. Figure 2 shows the pattern of the first application. In it, one set of crashes paired belted drivers and accompanying unbelted front-seat passengers, generating a ratio, r_1, of belted driver fatalities per unbelted passenger fatality. The second set paired unbelted drivers with unbelted front-seat passengers, leading to a ratio, r_2, of unbelted driver fatalities per unbelted passenger fatality. This yields a value of $R = r_1/r_2$ as a measure of safety-belt effectiveness.

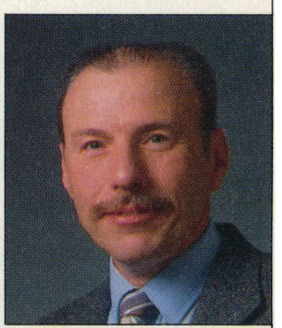
IN ADDITION to calculating R for driver *subjects* using front-seat passenger *others,* effectiveness was also calculated for right-front passenger *subjects* using driver *others.* Additional calculations were made pairing driver or right-front passenger *subjects* with passengers in any other seating position. Figure 1 reflects the synthesis of these estimates. Estimates 1 and 2 represent *subject* and *other* occupants disaggregated into three age categories and averaged. Estimates 3 and 4 represent pairings of *subjects* with occupants in other seating positions and averaged.

In all, Dr. Evans calculated 46 estimates of R. The weighted average of these gives a safety-belt effectiveness of (41.4 ± 3.8)%. This should be an accurate estimate whenever the distribution of severities is the same for both sets of crashes in each double-pair comparison.

Moreover, a formal analysis showed r_1/r_2 to be an accurate estimate of R_{true} under much less stringent restrictions. Even when the distributions of crash severity differ for belted and unbelted drivers, Dr. Evans concluded that the simple ratio $R = r_1/r_2 = nd/me$ is indeed an accurate estimate of safety-belt effectiveness.

Dr. Evans' confidence in the method rests on some key assumptions. But, as he points out: "One of the beauties of the method is its ability to remove the biasing effects of confounding interactions that may undermine those assumptions. It is necessary only to disaggregate occupants into different categories of the suspect variable.

"Because of bias elimination, and the ability to create a measure of exposure, the method of double-pair comparison lends itself to a broad range of investigations. We can estimate, for example, fatality risk as a function of helmet use by motorcyclists, or safety-belt effectiveness in different accident types. More broadly, we can estimate fatality risk as a function of age, sex, or alcohol use. We may even have revealed a trend in trauma response, in general, as a function of sex and age."



THE MAN BEHIND THE WORK

Dr. Leonard Evans is a Senior Staff Research Scientist in the Operating Systems Research Department at the General Motors Research Laboratories.

He received his undergraduate degree in physics from The Queen's University of Belfast, and holds a D. Phil. in the same discipline from Oxford University. He was a Post-Doctorate Fellow at the National Research Council of Canada in Ottawa.

Since joining GM in 1967, Dr. Evans has published research on such diverse topics as atomic physics and trauma analyses. His current area of concentration is traffic safety research.

He is a member of the Human Factors Society and is a Past President of the Society's Southeastern Michigan Chapter. In 1985, Dr. Evans received the Society's A. R. Lauer Award "for outstanding contributions to the human factors aspects of highway safety."

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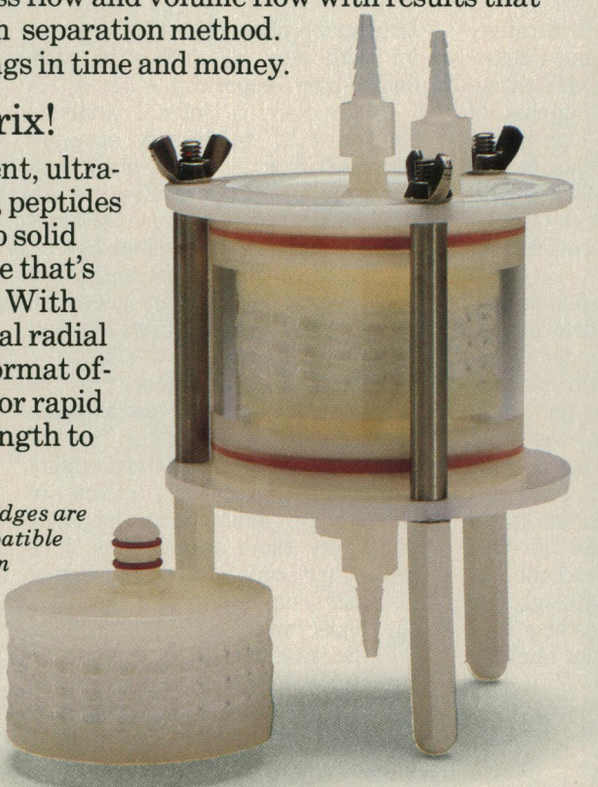

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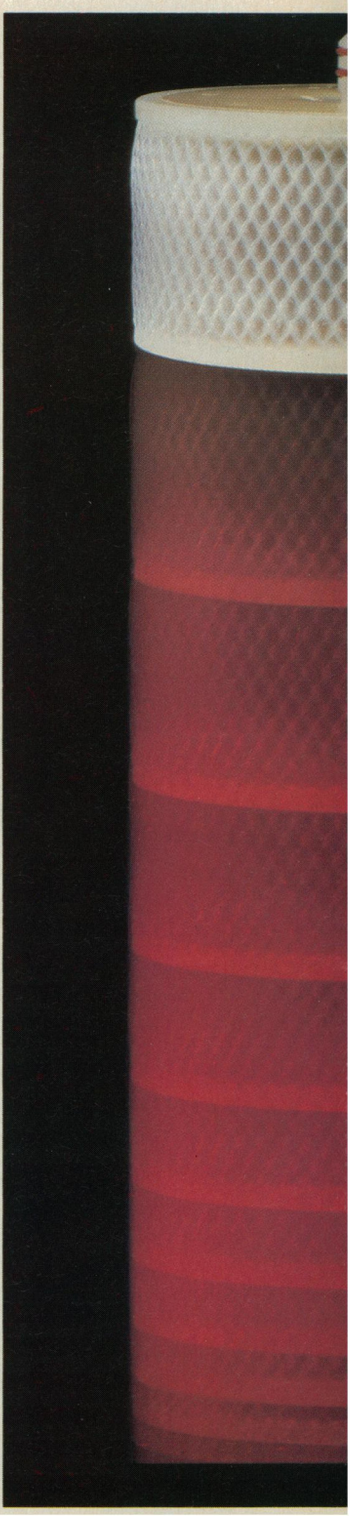

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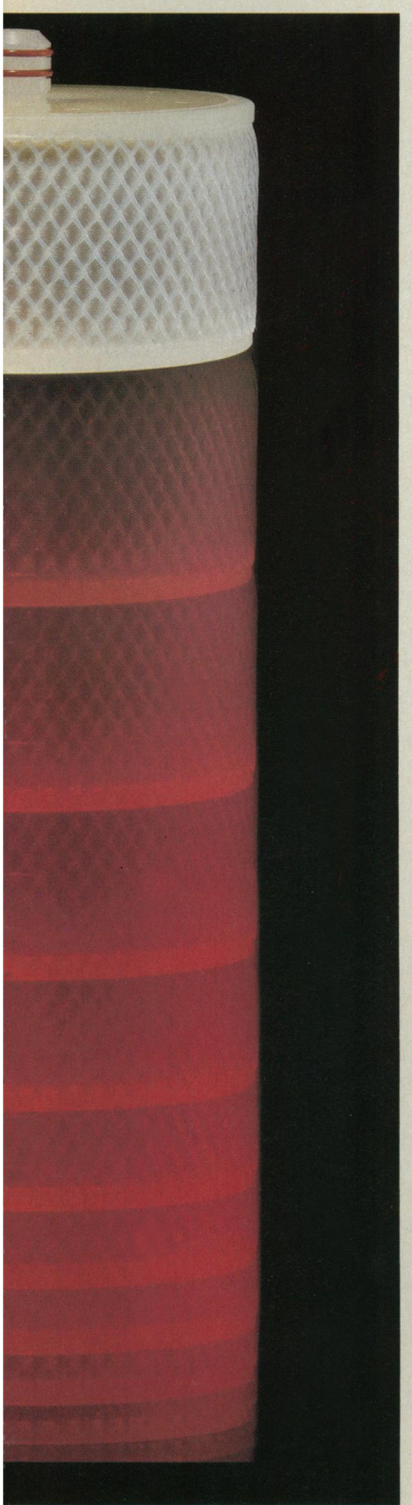

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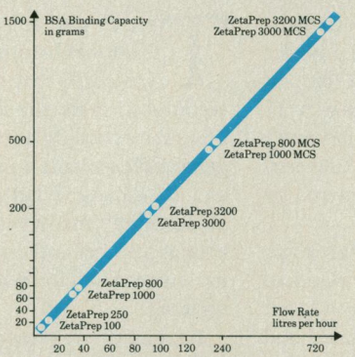

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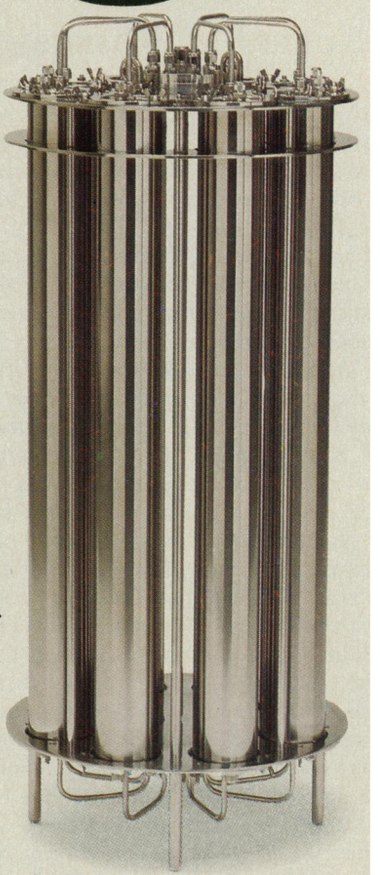

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