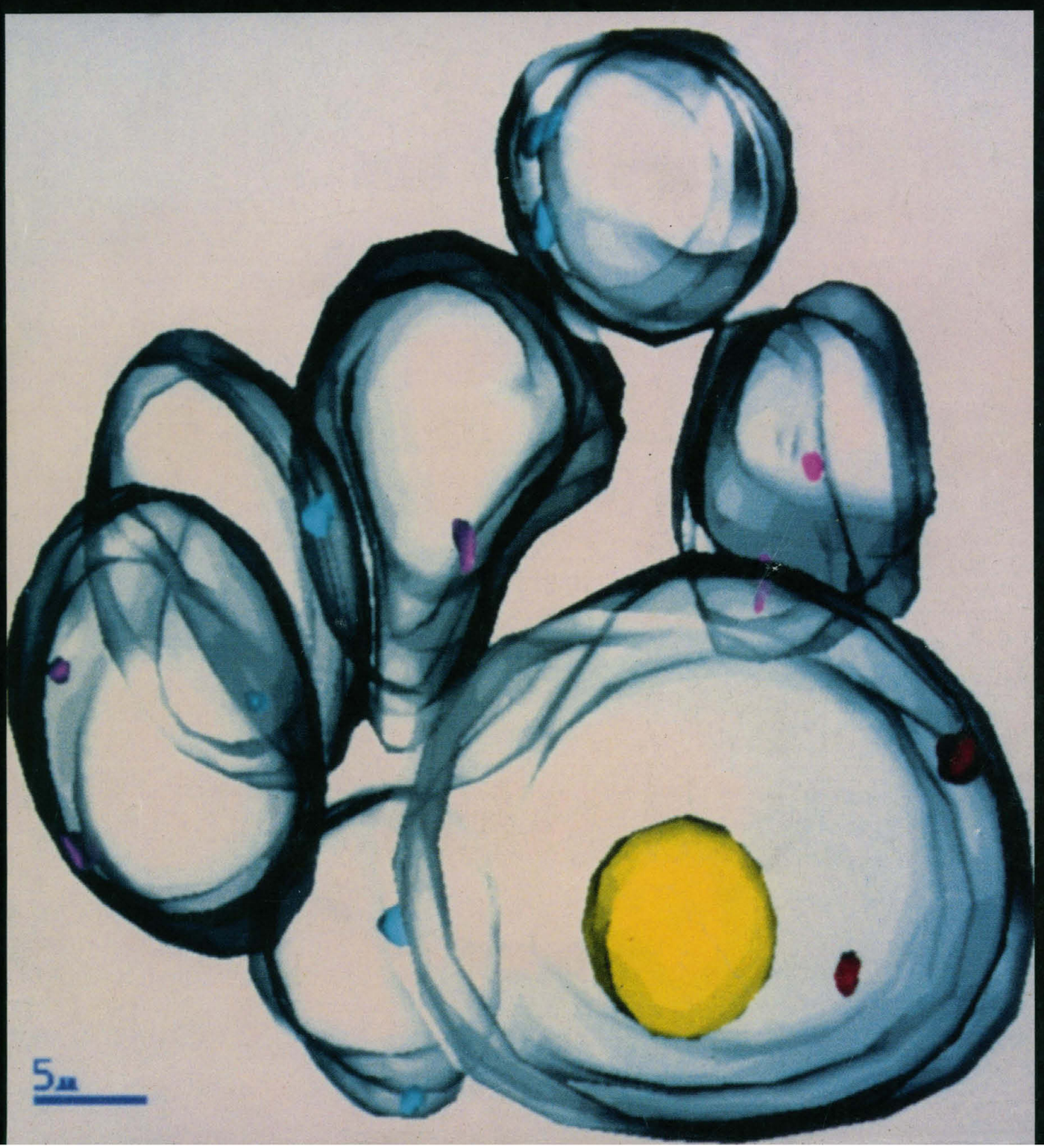
American Association for the Advancement of Science

SCIENCE

23 December 1988 $3.00
Vol. 242 ■ Pages 1613–1732



What a difference a J makes.

You'll really appreciate the difference a J Series high-speed or large-capacity centrifuge can make in your lab.

For one thing, they *are* different. They're designed that way. With a lot of attention to little details that make a big difference when you use a centrifuge day after day.

Like being able to set the controls in any order you want. Or attach the rotors with speed and ease.

And J Series centrifuges accept a full range of standard rotors, *plus* some very different ones. Counterflow centrifugal elutriation for living cell separation is a good example. So is our high-force rotor for mini-preps.

We've even made the J Series easier to live with. They're quieter, accelerate and decelerate faster, and put out less heat. Why less heat? Their efficient design means they don't have to work as hard to do the job.

All in all, we've done quite a lot to make the J Series friendly. And much more productive.

Find out what a difference a J makes. Contact Beckman Instruments, Inc., Spinco Division, 1050 Page Mill Road, Palo Alto, CA 94304. (800) 742-2345. Offices worldwide.

BECKMAN

A SMITHKLINE BECKMAN COMPANY

Circle No. 197 on Readers' Service Card

the care to meet, to know, to understand

Ares-Serono Symposia is an independent foundation, created in 1971, to promote scientific research in all disciplines which contribute towards improving human health. This aim is pursued by means of congresses, courses, seminars and specialized studies.

Some of the international meetings scheduled for 1989 are:

Unexplained Infertility: Basic and Clinical Aspects
Rome, Italy/March 7-8
Scientific Organization: G. Benagiano (I), K.J. Catt (USA) and G. Spera (I)

Symposium on the Pathogenesis and Control of Viral Infections
Beijing, Republic of China/April 24-26
Scientific Organization: F. Aiuti (I), Z. Zonghan (PRC) and S. Guoxian (PRC)

8th Workshop on Development and Function of the Reproductive Organs
Touraine, France/May 23-25
Scientific Organization: N. Josso (F)

1st International Congress on G.I.F.T.: from Basics to Clinics
Rapallo, Italy/June 8-10
Scientific Organization: R.H. Asch (USA) and L. De Cecco (I)

Membrane Technology in Clinical Pathology, Biochemistry and Pharmacology
L'Aquila, Italy/June 19-23
Scientific Organization: R. Verna (I), R.P. Blumenthal (USA), J.A. Hannover (USA) and R.P. Garay (F)

Cardiovascular and Neurological Function and Ovarian Secretions
Dubrovnik, Jugoslavia
Aug. 31-Sept. 1
Scientific Organization: F. Naftolin (USA)

Establishment of a Successful Human Pregnancy
Cambridge, U.K./September 21-23
Scientific Organization: R.G. Edwards (UK)

Developmental Endocrinology
Geneva, Switzerland/October 23-24
Scientific Organization: P.C. Sizonenko (CH) and M. Aubert (CH)

Advanced Course in Molecular Pathology and Biotechnology
Rome, Italy/November 6-10
Scientific Organization: L. Frati (I)

AS ARES SERONO SYMPOSIA

I would like to receive information about:
☐ All the Congresses
☐ In particular the Congress on .....
.....
.....
Name .....
Address .....
Institution .....
Please send to Ares-Serono Symposia, Via Ravenna 8 - 00161 Rome - Italy

No form of advertising or promotional activity by any pharmaceutical company is allowed at Ares-Serono Symposia Congresses.

swissair Official Carrier

PIETROSANTE RAY SUBIOLI - ROMA / SINTESI INFORMAZIONE - ROMA

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

SCIENCE

ISSN 0036-8075
23 DECEMBER 1988
VOLUME 242
NUMBER 4885

■ **SCIENCE is published weekly on Friday, except the last week in December, and with an extra issue in February by the American Association for the Advancement of Science, 1333 H Street, NW, Washington, DC 20005.** Second-class postage (publication No. 484460) paid at Washington, DC, and at an additional entry. Now combined with **The Scientific Monthly®** Domestic individual membership and subscription (51 issues): $70. Domestic institutional subscription (51 issues): $110. Foreign postage extra: Canada $32, other (surface mail) $32, air-surface via Amsterdam $85. First class, airmail, school-year, and student rates on request. Single copies $3.00; back issues $5.00; Biotechnology issue, $5.50 ($6 by mail); classroom rates on request; Guide to Biotechnology Products and Instruments $16 ($17 by mail). **Change of address:** allow 6 weeks, giving old and new addresses and seven-digit account number. **Postmaster:** Send Form 3579 to *Science*, 1333 H Street, NW, Washington, DC 20005. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

■ 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 Three-dimensional reconstruction of human epileptic cortex showing a large neuronal nucleus with a large nucleolus (yellow) and surrounded by multiple smaller astrocytic nuclei. The neuron shows an interior and abnormal position of one of the two chromosome 9 centromere signals (red). Astrocytic in situ hybridization signals are depicted either in magenta (pink) or cyan (turquoise) for each cell. See page 1687.

Reports

Book Reviews

Products & Materials

Author Index to Volume 242 is found on pages I–X.
Information for Contributors is found on pages XI–XII.

Preparing DNA?

QIAGEN

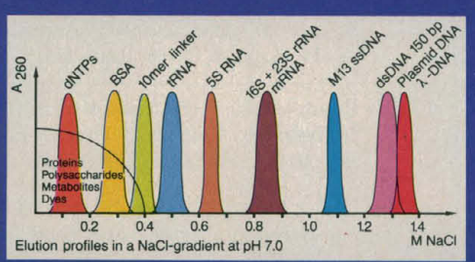
Single step purification

QIAGEN disposables transform cumbersome daily nucleic acid preparations into an easy, timesaving and inexpensive job. Picogram to milligram amounts of plasmid DNA, λ-DNA, genomic DNA or RNA can be directly isolated and purified from cleared cell lysates in one step due to QIAGENs extended separation range (see fig.).

QIAGEN-tips and -packs, which fit on conventional pipettes or syringes, contain an anion-exchange resin, patented to DIAGEN, for solid phase extraction of nucleic acids. Expensive equipment such as ultracentrifuges, HPLC/FPLC™ or reagents like CsCl and phenol are no longer required.

Very high purity, excellent yields and superior biological activity of nucleic acids are routinely achieved in 10 minutes:

1. Adsorb the lysate to QIAGEN.
2. Wash away impurities.
3. Elute the desired nucleic acid.



Elution profiles in a NaCl-gradient at pH 7.0

Biological activity

The quality of QIAGEN purified nucleic acids has been tested with more than 50 different restriction endonucleases, several polymerases, DNA ligases, phosphatases, kinases, and reverse transcriptases. Outstanding efficiency was obtained in all cases.

tips

QIAGEN-tip 5 and QIAGEN-tip 20 are prepacked pipette tips, with a capacity of 5 and 20 µg of nucleic acids respectively, which fit on variable volume pipettes. The entire procedure is performed simply by pipetting the appropriate solution in and out.

packs

QIAGEN-pack 100 and QIAGEN-pack 500 are small cartridges which fit on disposable syringes. The binding capacities are 100 and 500 µg of nucleic acids respectively.

tubes

QIAGEN-tube 20 is an Eppendorf™ tube containing resin sufficient to adsorb 20 µg of high molecular weight genomic DNA (50-200 kb) in a simple and gentle batch procedure.

For free samples and application protocols contact DIAGEN.

QIAGEN Inc.
11712 Moorpark Street
Studio City, CA 91604
P. O. Box 7401-737, USA
in CA call (818) 508-5258
toll-free (800) 426-8157
Fax (818) 508-5536

DIAGEN GmbH
Niederheider Straße 3
P. O. Box 13 02 47
4000 Düsseldorf 13 · FRG
Phone (0) 211 - 79 30 37
Telex 8 582 273 dia d
Telefax (0)211 - 79 04 44

DIAGEN

Circle No. 15 on Readers' Service Card

The 1988 drought

LAST summer, by mid-July, 43% of the continental United States was experiencing severe or extreme droughts; the magnitudes of the droughts were comparable to those of the devastating dust bowl droughts of the 1930s (page 1640). Two regional droughts had begun at different times, had been caused by different factors, but together were parching the nation. Trenberth *et al.* trace the roots of the 1988 West Coast drought back to the El Niño event of 1987 in the Pacific Ocean and show how subsequent oceanic events initiated the North American summer drought. They illustrate, with models, how changes in the jet stream that were responsible for setting up conditions favorable for the drought were associated with precipitation anomalies in the tropical Pacific and how these anomalies were, in turn, associated with temperature changes in the sea. Although many questions were raised during the drought as to the part played by greenhouse gases, the greenhouse effect did not cause the 1988 drought. The greenhouse effect has, however, been building and may slowly shift the balance toward more droughts and more heat waves in the years to come.

Superconductor's superstructure

IMAGES of bismuth-oxygen planes at the surface of cleaved crystals of the cuprate high-temperature superconductor $Bi_2Sr_2CaCu_2O_{8+\delta}$ show that every ninth or tenth row of bismuth atoms is missing; this irregularity can account for the incommensurate periodicity of bulk crystals that has previously been noted (page 1673). The high-resolution images were obtained with a scanning tunneling microscope operating under ultrahigh vacuum conditions and able to highlight single atoms in the plane. The bismuth-oxygen planes are buckled as are the copper-oxygen planes with which they share oxygen atoms. This buckling perturbs the electronic state of the copper-oxygen plane and, along with other features of the superstructure, may contribute to the superconducting properties of the crystal. Kirk *et al.* note that, despite the missing rows of bismuth, the crystal is slightly bismuth-rich; bismuth atoms may replace some strontium and calcium atoms in the crystal.

Mouse models and human diseases

SEVERAL new animal model systems have become available for studying human cells and human diseases. Immune-deficient mice that had received grafts of human lymphoid cells have now been infected with the AIDS virus HIV-1. The viruses replicated within the engrafted human cells. While normal mice do not support HIV-1 infections, the chimeras, described by Namikawa *et al.*, provide a system in which interactions of HIV-1 with human cells can be closely evaluated (page 1684). A very different system for studying the in vitro actions of the AIDS virus has been designed by Leonard *et al.* (page 1665). Transgenic mice, whose parents were a normal mouse and a transgenic mouse carrying the HIV-1 proviral genes in the germline, produced infectious viruses, developed some clinical symptoms that resemble those associated with AIDS, and died from AIDS-like disease within the first month of life. Such mice will be use for studying how HIV-1 exerts its pathogenic effects and for assessing the efficacy of drugs and other therapies in retarding or preventing the development of disease. Kamel-Reid and Dick report on chimeric mice that have been developed for use in studies of the human hematopoietic system (page 1706). Special immune-deficient triply mutant mice were engrafted with human bone marrow cells (a population that contains myeloid stem cells). With these mice, the normal developmental stages of human hematopoietic cells can be studied as well as the malignancies and infections of such cells. Further discussion of these models and of the misfortune that befell the transgenic mice is found on page 1638.

Split-brain monkeys

STUDIES of rhesus monkeys whose brain hemispheres had been separated surgically indicate that the left hemisphere is better than the right at discriminating differences in the orientations of straight lines, that the two hemispheres process information about geometric patterns equally well, and that the right hemisphere is better at discerning facial features, distinguishing (in photographs) two monkeys with the same expression or different expressions made by one monkey (page 1691). The pattern of hemispheric dominance versus hemispheric equivalence for specific tasks is like the pattern in the human brain (although the right not the left hemisphere of the human brain discriminates among tilted lines). Hamilton and Vermeire point out that hemispheric specializations thus predate rather than stem from language development. Hemispheric specialization may either be independent of language development or handedness, or it may be a precursor of one or both of them.

Repaired gene defect

SOME cases of hereditary emphysema are associated with the production of mutant α1-antitrypsin molecules that are encoded by Z alleles. The mutant molecules differ from normal molecules at amino acid position 342, where the standard amino acid glutamic acid is replaced by lysine. Brantly *et al.* propose that this change disrupts a salt bridge that normally forms between the glutamic acid at position 342 and the lysine at position 290; proper folding and further processing and secretion of the protein then are interrupted (page 1700). To reestablish the salt bridge, compensatory mutations were introduced, changing residue 290 from lysine to glutamic acid, thereby restoring the proper charge relationship. The salt bridge was apparently restored, and the molecules were secreted. The molecular repairs that have been made in vitro are a first step toward designing strategies for repairing defects in Z alleles in vivo.

The ingenuity of your research program depends on your vision. But the quality of your results hinges on the purity of materials you obtain from others. When you need peptides and proteins, come to a source you can trust.

The BACHEM Group has seventeen years of experience and offers an inventory of over 5,000 products. With our internal research and development, we add an average of two new products to our inventory each day. 96% of our catalog items are immediately available, with fast delivery. We guarantee the highest purity available, with high lot to lot consistency. Our products include: ▫ Peptides ▫ Enzyme substrates and inhibitors ▫ Neuropeptides ▫ Biochemicals ▫ Amino acid derivatives ▫ Lymphokines and cytokines.

We are happy to offer custom synthesis of peptides and proteins, specialty chemicals, solution phase synthesis and molecular biosynthesis (rDNA) services, as well as custom coupling and labelling. Our production plant in Switzerland can manufacture according to GMP requirements; and both our Swiss facilities and our research and development labs in the United States make bulk quantities of most of our products available.

Let us help you fulfill your vision. Call the BACHEM Group—one trusted source for all of your peptides, proteins and related chemicals.

BACHEM

BACHEM Feinchemikalien AG
Hauptstrasse 144
CH-4416 Bubendorf Switzerland
Tel 061 / 931 23 33
Tlx 966 081
Fax 061 / 931 25 49

BACHEM Bioscience Inc.
3700 Market Street
Philadelphia, PA 19104 U.S.A.
Tel (215) 387-0011
Tlx 910 250 2353
Fax (215) 387-1170

BACHEM Biochemica GmbH
Lessingstrasse 26
D-6900 Heidelberg West Germany
Tel 062 21/16 30 91
Fax 062 21/16 30 92

Circle No. 227 on Readers' Service Card

SCIENCE

23 DECEMBER 1988
VOLUME 242
NUMBER 4886

Federal Policies in Transition

During the past several months hundreds of groups have developed recommendations to present to President-elect George Bush and his transition team. Obviously some of the plans will receive more earnest attention than others. This is particularly true of two reports, one containing substantial contributions by collaborating authors Gerald Ford and Jimmy Carter, and a second sponsored by a distinguished Council on Competitiveness that includes leaders of industry, labor, and academia. The reports are mutually supportive in many ways, including a statement of the need for this country to improve its competitiveness. They note that the United States is not faring well in the global economy. For example, 15 years ago U.S. companies made 95% of telephones and 80% of television sets for U.S. homes. Today U.S. companies make 25% of telephones and 10% of television sets sold here. The U.S. share of world steel production in 1960 was 26%; now it is 11%.

The reports point to a relative paucity of U.S. investments directed at improving productivity. In turn, this lack is related to a poor national savings rate of 2% of gross national product (GNP). The average national savings rates of other industrial countries is about 10% of GNP. For Japan it is about 16%. The net national savings rate is defined as the sum of individual and corporate savings plus government surpluses or deficits. During the 1980s individuals have decreased their savings, and in 1987 U.S. consumers owed 85% of their year's after-tax income. The federal deficit also increased greatly.

There were few specific ideas about how to induce individuals to save more. (With plastic money so freely available, a downward trend in savings will probably continue.) Instead, the need to reduce the federal deficit was emphasized. A combination of budget cutting and increased taxes was recommended. The nondefense discretionary part of the budget is already so small that cuts must be found elsewhere, notably in the entitlements programs, which constitute 46% of the budget.

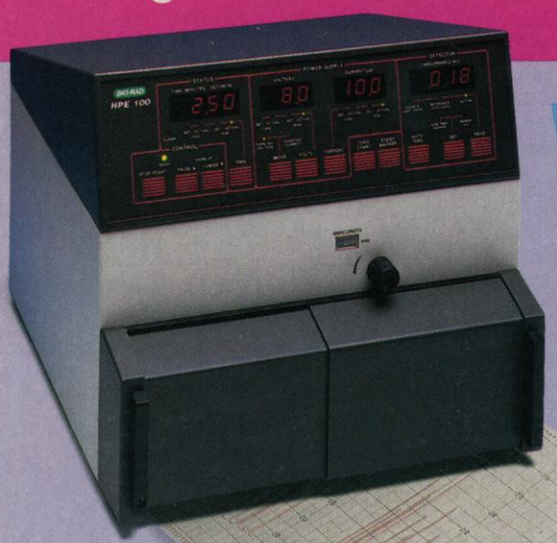
On the revenue side both reports cited cigarettes, alcohol, and gasoline as attractive targets for increases. In 1951 the excise tax represented 42% of the price of cigarettes; currently it amounts to only 15%. Similar remarks apply to beer, wine, and distilled spirits. The gasoline tax in some other countries amounts to $1 a gallon or more. Here, the federal tax is 9.1 cents per gallon. For every cent added, $1 billion of revenue would be obtained. The Council on Competitiveness, which made the most extensive studies of the deficit, also recommended consideration of moderate increases in the personal income tax, including a 33% rate on large incomes and a 5% surtax for all payers.

The reports recommended that more funds be made available to increase U.S. competence in science and technology. It was pointed out that although funds for federal R&D increased 100% during the past 7 years, 90% of this increase has been defense-related. In constant dollars civilian R&D is 14% below the 1980 level. In real terms National Science Foundation funds have been virtually unchanged for the past 20 years. During the past 20 years federal funding for university plants and facilities has declined 95% in real terms.

The Council on Competitiveness suggests that once the process of credible deficit reduction is under way, the following steps should be taken: strengthen the federal role in science and technology by doubling the NSF budget over 5 years, increase NSF funding for programs to encourage the development of science and engineering faculty, and provide additional federal resources to modernize university research facilities. The council would also make additional funding available for human resource development with emphasis on programs to serve the economically disadvantaged, to strengthen math and science education, and to provide training and employment services to dislocated workers.

The Council on Competitiveness says that the success of any deficit reduction effort will rest on the meshing of three basic principles. First, all sectors should contribute to the deficit-reduction initiative. Second, changes should be fair; they should not undermine the nation's historic commitment to equity. Third, attempts should be made to ensure that changes in either budget or tax policy increase economic efficiency and minimize any adverse impact on levels of private savings and investment.—PHILIP H. ABELSON

Quantitative electrophoresis in 10 minutes



Announcing the new HPE 100 High Performance Electrophoresis System from Bio-Rad.

Proven applications include:
■ purity checks on synthetic peptides ■ isoelectric focusing of proteins ■ pharmaceutical QC for FDA requirements ■ purity analysis of preparative HPLC ■ free zone, discontinuous or displacement electrophoresis ■ peptide fragmentation and degradation ■ detection of deamidation in recombinant proteins ■ DNA, bacterial, and viral analysis. And, astonishingly, these applications are only the tip of the iceberg.

The HPE 100 System is not only as simple to operate as any LC system, but it costs less as well. To find out just how much less, call **1-800-4BIO-RAD Ext. HPE.** You'll be pleasantly surprised.

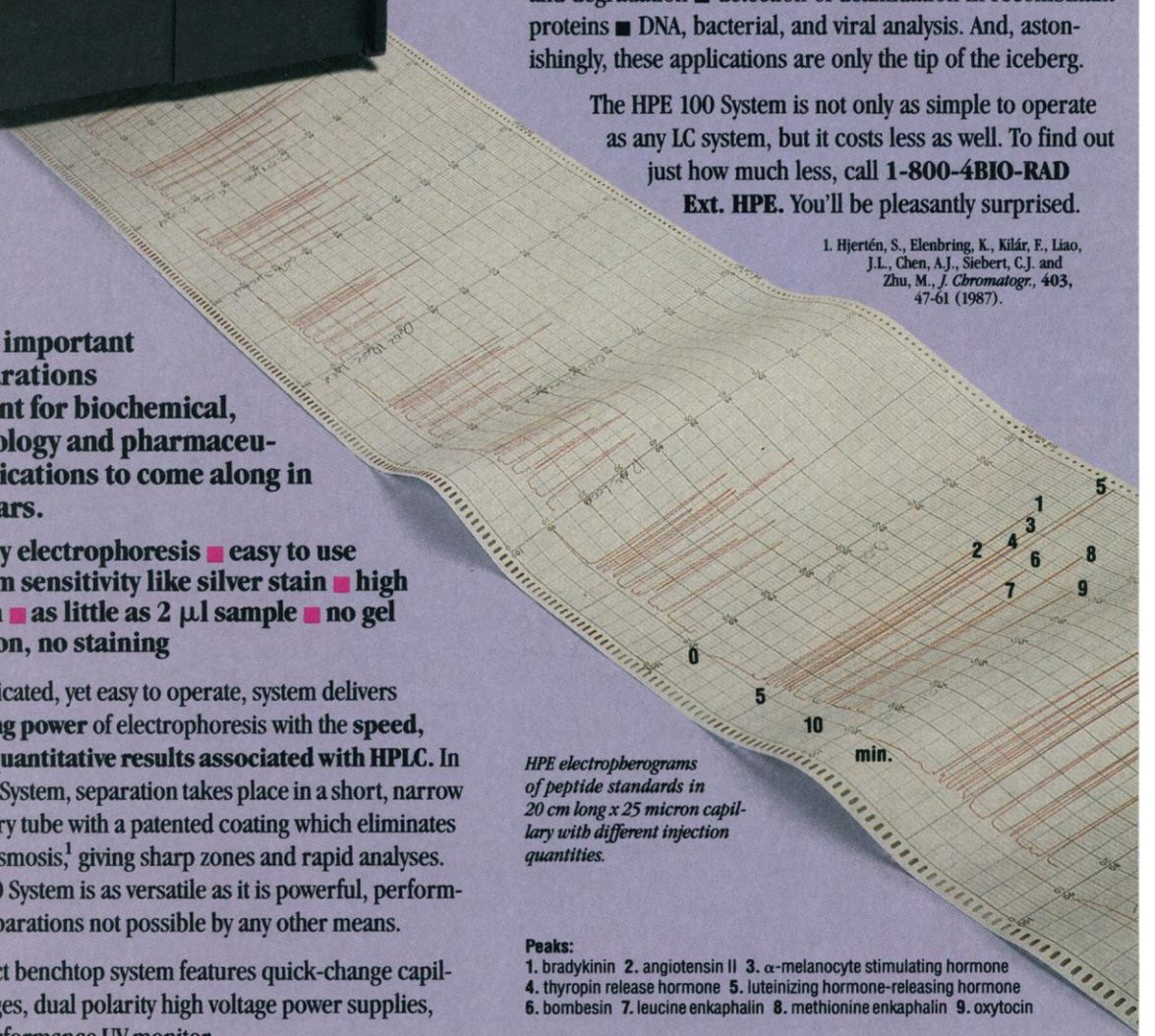
1. Hjertén, S., Elenbring, K., Kilár, F., Liao, J.L., Chen, A.J., Siebert, C.J. and Zhu, M., *J. Chromatogr.*, **403**, 47-61 (1987).

The most important new separations instrument for biochemical, biotechnology and pharmaceutical applications to come along in recent years.

■ Capillary electrophoresis ■ easy to use ■ picogram sensitivity like silver stain ■ high resolution ■ as little as 2 µl sample ■ no gel preparation, no staining

This sophisticated, yet easy to operate, system delivers the **resolving power** of electrophoresis with the **speed, ease, and quantitative results associated with HPLC.** In the HPE 100 System, separation takes place in a short, narrow bore capillary tube with a patented coating which eliminates electroendosmosis,[1] giving sharp zones and rapid analyses. The HPE 100 System is as versatile as it is powerful, performing some separations not possible by any other means.

This compact benchtop system features quick-change capillary cartridges, dual polarity high voltage power supplies, and high performance UV monitor.



HPE electropherograms of peptide standards in 20 cm long x 25 micron capillary with different injection quantities.

Peaks:
1. bradykinin **2.** angiotensin II **3.** α-melanocyte stimulating hormone **4.** thyropin release hormone **5.** luteinizing hormone-releasing hormone **6.** bombesin **7.** leucine enkaphalin **8.** methionine enkaphalin **9.** oxytocin

BIO-RAD ***Chemical Division***

1414 Harbour Way South
Richmond, CA 94804
(415) 232-7000
800-4-BIO-RAD

Also in Rockville Centre, NY; Hornsby, Australia; Vienna, Austria; Brussels, Belgium; Mississauga, Canada; Watford, England; Paris, France; Munich, Germany; Hong Kong; Milan, Italy; Tokyo, Japan; Utrecht, The Netherlands; and Glattbrugg, Switzerland.

Circle No. 211 on Readers' Service Card

53. V. Hamburger and M. Balaban, *Dev. Biol.* **7**, 533 (1963).
54. R. Llinás, in *Mind Waves*, C. Blakemore and S. Greenfield, Eds. (Basil Blackwell, Oxford, 1987), pp. 339–358.
55. G. M. Edelman, *Proc. Natl. Acad. Sci. U.S.A.* **81**, 1460 (1984).
56. K. Walton and R. Llinás, *Soc. Neurosci. Abstr.* **12**, 386 (1986).
57. ———, *Proc. Int. Physiol. Sci.* **16**, 118 (1986).
58. E. Carbone and H. D. Lux, *J. Physiol. (London)* **386**, 547 (1987).
59. Y. I. Arshazsky, M. B. Berkinblit, O. I. Fukson, I. M. Gelfan, G. N. Orlovsky, *Brain Res.* **43**, 272 (1972); *ibid.*, p. 472.
60. M. E. Greenberg, E. B. Ziff, L. A. Greene, *Science* **234**, 80 (1986); J. I. Morgan and T. Curran, *Nature* **322**, 552 (1986).
61. This might occur by a process of synaptic stabilization [J. P. Changeux and A. Danchin, *Nature* **264**, 705 (1976)].
62. W. J. Freeman, *Mass Action in the Nervous System* (Academic Press, New York, 1975). Cortical oscillatory events at 40 Hz have been encountered in relation to attention [J. J. Bouyer, F. Montaron, J. M. Vahnee, M. P. Albert, A. Rougeul, *Neuroscience* **22**, 863 (1987)]; these findings confirm reports of fast somatoparietal rhythms under similar behavioral conditions in different mammals [S. Rougeul, J. J. Bouyer, L. Dedet, O. Debray, *Electroenceph. Clin. Neurophysiol.* **46**, 310 (1979)].
63. During sleep the thalamic neurons do not respond to visual stimuli, although the visual pathway to that nucleus is not significantly altered by the sleeping state [L. Maffei, G. Moruzzi, G. Rizzolatti, *Science* **149**, 563 (1965)].
64. This notion becomes particularly relevant when considering, for instance, tremor in Parkinson's disease or enhanced physiological tremor. These abnormalities are related to the low-threshold Ca^{2+} action potentials. In the latter case, harmaline has been shown to generate tremor (*36*) and to increase rebound excitation (*112*). Similar increase in excitability probably related to other conductances may underlie epileptic activity. From a psychiatric point of view, the question of authorhythmic behavior becomes relevant when considering that dreaming is of necessity the product of intrinsic activity, as are the hallucinatory states in certain psychoses. This implies that intrinsic thalamo-cortical activity is paramount in the genesis of such forms of psychopathology. That intrinsic electroresponsiveness is relevant to such states is suggested by pharmacological studies of thalamic neurons in vitro. Haloperidol (an antipsychotic agent) decreases the low-threshold Ca^{2+} conductance, whereas dopamine, which is involved in psychotic conditions, has a potentiating effect on this conductance [E. Geijo-Barrientos and R. Llinás, *Soc. Neurosci. Abstr.* **13**, 1012 (1987)].
65. B. W. Connors, M. G. Gutnick, D. A. Prince, *Soc. Neurosci. Abstr.* **7**, 593 (1981).
66. ———, *J. Neurophysiol.* **48**, 1302 (1982).
67. C. E. Strafstrom, P. C. Schwindt, W. E. Crill, *Brain Res.* **236**, 221 (1982).
68. C. E. Stafstrom, P. C. Schwindt, M. C. Chubb, W. E. Crill, *J. Neurophysiol.* **53**, 153 (1985).
69. B. A. MacVicar, *Brain Res.* **333**, 378 (1985).
70. L. S. Benardo, L. M. Masukawa, D. A. Prince, *J. Neurosci.* **2**, 1614 (1982).
71. M. Sugimori and R. Llinás, *Soc. Neurosci. Abstr.* **6**, 468 (1980).
72. H. Jahnsen, *J. Physiol. (London)* **372**, 129 (1986).
73. A. Constanti, M. Galvan, P. Franz, J. A. Sim, *Pfluegers Arch.* **404**, 259 (1985).
74. R. K. S. Wong and D. A. Prince, *Brain Res.* **159**, 385 (1978).
75. D. Johnston, J. J. Hablitz, W. A. Wilson, *Nature* **286**, 391 (1980).
76. D. A. Brown and W. H. Griffith, *J. Physiol. (London)* **337**, 303 (1983).
77. A. R. Kay and R. K. S. Wong, *ibid.* **392**, 603 (1987).
78. B. H. Gahwiler and D. A. Brown, *Neurosci. Lett.* **76**, 301 (1987).
79. H. Kita, T. Kita, S. T. Kitai, *Exp. Brain Res.* **60**, 63 (1985).
80. V. Misgeld, P. Calabresi, H. U. Dolt, *Pfleugers Arch.* **407**, 482 (1986).
81. E. Cherubini and L. Lanfumey, *Neuroscience* **21**, 997 (1987).
82. A. Alonso and R. Llinás, *Soc. Neurosci. Abstr.* **13**, 536 (1987).
83. J. Lopez-Barneo and R. Llinás, *J. Neurophysiol.* **60**, 853 (1988); *ibid.*, p. 869.
84. J. T. Williams, R. A. North, S. A. Shedner, S. Nishi, T. M. Egan, *Neuroscience* **13**, 137 (1984).
85. R. Llinás, S. A. Greenfield, H. Jahnsen, *Brain Res.* **294**, 127 (1984).
86. K. Murase and M. Randic, *J. Physiol. (London)* **334**, 141 (1983).
87. B. P. Fulton and K. Walton, *ibid.* **317**, 25P (1981); V. Harada and T. Takahashi, *Proc. Jpn. Acad.* **57(B)**, 394 (1981); K. Walton and B. P. Fulton, *Neuroscience* **19**, 669 (1986).
88. P. C. Schwindt and W. E. Crill, *J. Neurophysiol.* **44**, 827 (1980).
89. Y. Yarom, M. Sugimori, R. Llinás, *Neuroscience* **16**, 719 (1985).
90. D. G. Owen, M. Segal, J. L. Barker, *Nature* **311**, 567 (1984).
91. O. Belluzzi, O. Sacchi, E. Wanke, *J. Physiol. (London)* **358**, 109 (1985).
92. M. Galvan and P. R. Adams, *Brain Res.* **244**, 135 (1982).
93. J. V. Halliwell, *J. Physiol. (London)* **341**, 10P (1983).
94. M. Deschenes, J. P. Roy, M. Steriad, *Brain Res.* **239**, 289 (1982).
95. T. M. Burlhis and G. K. Aghajanian, *Synapse* **1**, 582 (1988).
96. R. W. Greene, H. L. Haas, R. W. McCarley, *Science* **234**, 738 (1986).
97. C. S. Leonard and R. Llinás, *Soc. Neurosci. Abstr.* **13**, 1012 (1987).
98. R. Llinás and Y. Yarom, *ibid.* **12**, 174 (1986).
99. P. C. Schwindt and W. E. Crill, *J. Neurophysiol.* **43**, 1700 (1980).
100. K. Walton and R. Llinás, *Soc. Neurosci. Abstr.* **12**, 382 (1986).
101. B. Gustafsson, M. Galvan, P. Grafe, H. Wigstrom, *Nature* **299**, 252 (1982).
102. M. Segal, M. A. Rogawski, J. L. Barker, *J. Neurosci.* **4**, 604 (1984).
103. G. K. Aghajanian, *Nature* **315**, 501 (1985).
104. M. Segal, *Brain Res.* **359**, 347 (1985).
105. M. Galvan and C. Sedlmeir, *J. Physiol. (London)* **356**, 115 (1984).
106. O. Belluzzi, O. Sacchi, E. Wanke, *ibid.* **358**, 91 (1985).
107. H. Kasai, M. Kameyama, K. Yamaguchi, J. Fuduka, *Biophys. J.* **49**, 1243 (1986).
108. A. Constanti and M. Galvan, *J. Physiol. (London)* **335**, 153 (1983).
109. J. V. Halliwell and P. B. Adams, *Brain Res.* **250**, 71 (1982).
110. J. R. Hotson, D. A. Prince, P. A. Schwartzkroin, *J. Neurophysiol.* **42**, 889 (1979).
111. M. Segal and J. L. Barker, *ibid.* **51**, 1409 (1984).
112. Y. Yarom and R. Llinás, *J. Neurosci.* **7**, 1166 (1987).
113. A. Constanti and D. A. Brown, *Neurosci. Lett.* **24**, 289 (1981).
114. B. E. Alger and R. A. Nicoll, *Science* **210**, 1122 (1980).
115. D. A. Brown and W. H. Griffith, *J. Physiol. (London)* **337**, 287 (1983).
116. D. V. Madison and R. A. Nicoll, *ibid.* **372**, 221 (1986).
117. E. F. Barrett, J. N. Barrett, W. E. Crill, *ibid.* **304**, 251 (1980).
118. P. C. Schwindt and W. E. Crill, *J. Neurophysiol.* **46**, 1 (1981).
119. T. Kawai and M. Watanabe, *Br. J. Pharmacol.* **87**, 225 (1986).
120. D. Hughes, R. N. McBurney, S. M. Smith, R. Zorec, *J. Physiol. (London)* **392**, 231 (1987).
121. R. Llinás and Y. Yarom, unpublished data.
122. R. Llinás and M. Sasaki, unpublished data.
123. R. Llinás and H. Jahnsen, *Nature* **297**, 406 (1982).

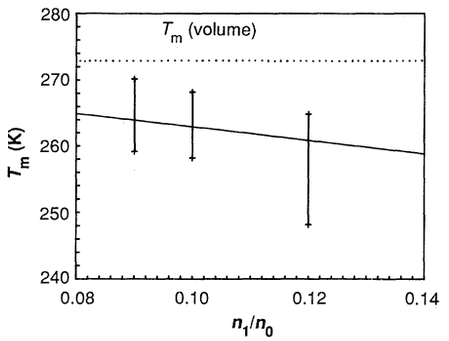


Fig. 3. Melting temperature versus molar ratio for water held between dipalmitoyl phosphatidyl choline bilayers (*6, 7*); the vertical bars indicate quasicontinuous melting over a wide T_m range; (——) Raoult (T_m = 273.15 K, see dotted line, L = 6019 J/mol).

agreement is accidental remains to be seen; we hope that our results will encourage future tests. Certainly, our use of Raoult's law for surface effects is not universally valid. Second-order phase transitions shift their critical temperatures by an amount proportional to $r^{-1/\nu}$ with a correlation length exponent ν that is different from unity. And for small liquid droplets in equilibrium with their vapor, Kelvin's law gives an increase of vapor pressure (proportional to the surface tension), whereas Raoult's law would predict a decrease of vapor pressure (proportional to the vapor pressure).

Our results suggest that certain mesoscopic systems represent binary solutions rather than a single-component material. The two components consist of atoms or molecules placed at the surface and those in the volume, respectively, and they have different physical characteristics. Raoult's law of dilute solutions can be used to describe the observed melting point depression in mesoscopic systems of gold or indium particles and of water held between lipid bilayers. This finding reveals the rivalry between surface and volume with decreasing size of the particles. We regard our observation as a suggestion for further checks in this direction.

REFERENCES AND NOTES

1. P. R. Couchman and W. A. Jesser, *Nature* **269**, 481 (1977).
2. P. Marquardt, G. Nimtz, B. Mühlschlegel, *Solid State Commun.* **65**, 539 (1988).
3. G. Nimtz, *Phys. Scr. T* **13**, 172 (1986).
4. Y. Imry, in *Directions in Condensed Matter Physics*, G. Grinstein and E. Mazenko, Eds. (World Publishing, Singapore, 1986), pp. 101–163.
5. P. Marquardt and G. Nimtz, *Phys. Rev. Lett.* **57**, 1036 (1986); ——, W. Weiss, *J. Phys. A Math. Gen.* **20**, L619 (1987).
6. W. Weiss, thesis, Universität Köln (1987).
7. M. Grünert, L. Börngen, G. Nimtz, *Ber. Bunsenges. Phys. Chem.* **88**, 608 (1984).
8. P. M. Ajayan and L. D. Marks, *Phys. Rev. Lett.* **60**, 585 (1988).
9. See for example: A. B. Pippard, *Elements of Classical Thermodynamics* (Cambridge Univ. Press, Cambridge, 1964), p. 111.
10. J. R. Sambles, *Proc. R. Soc. London Ser. A* **324**, 339 (1971).
11. Ph. Buffat and J. P. Borel, *Phys. Rev. A.* **13**, 2287 (1976).
12. J. F. Pócza, A. Barna, P. B. Barna, *J. Vac. Sci. Technol.* **6**, 472 (1969).
13. R. P. Berman and A. E. Curzon, *Can. J. Phys.* **52**, 923 (1974).

14. We thank M. Grünert, R. Zorn, and D. E. Wolf for helpful discussions.

23 August 1988; accepted 13 October 1988

Revised 23 December 1988

Information for Contributors

THE EDITORS OF *SCIENCE*

Manuscripts should be addressed to the Editor, *Science*, 1333 H Street, NW, Washington, DC 20005. Submit three copies together with a letter of transmittal giving

1) the names and telephone numbers of the authors;

2) the title of the paper and a statement of its main point;

3) three to eight keywords to be used for indexing;

4) the names, addresses, telephone numbers, and fields of interest of four to six persons outside your institution who are qualified to referee the paper;

5) the names of colleagues who have reviewed the paper;

6) the total number of words (including text, references, and figure and table legends) in the manuscript; and

7) a statement that the material has not been published and is not under consideration for publication elsewhere.

In addition, include with your manuscript:

(i) any paper of yours that is in press or under consideration elsewhere and includes information that would be helpful in evaluating the work submitted to *Science*;

(ii) written permission from any author whose work is cited as a personal communication, unpublished work, or work in press but is not an author of your manuscript;

(iii) for review of manuscripts based on crystallographic data, two copies of the coordinates;

(iv) the databank identifier codes for sequence or coordinate data.

It is assumed that all those listed as authors of a work have agreed to be so listed, have seen and approved the manuscript, and are responsible for its content.

Before being reviewed in depth, most papers are rated for their interest and overall suitability by a member of the Board of Reviewing Editors. Papers submitted in disciplines for which there is no appropriate member of the Board of Reviewing Editors may be screened by editorial staff members in consultation with outside experts. Papers that are not highly rated are returned to the authors within about 2 weeks; the title page and abstract from one copy are retained for our files. The others are reviewed in depth by two or more outside referees. Authors are notified of acceptance, rejection, or need for revision, usually within 6 to 10 weeks. Papers cannot be resubmitted, either after initial screening or after in-depth review.

Conditions of Acceptance

When a paper is accepted for publication in *Science*, it is understood by the editors that (i) any materials and methods necessary to verify the conclusions of the experiments reported will be made available to other investigators under appropriate conditions; (ii) sequence and crystallographic data will be offered for deposit to the appropriate data bank and the identifier code will be sent to *Science*; and (iii) the paper will remain a privileged document and will not be released to the press or the public before publication. If there is a need in exceptional cases to publicize data in advance of publication, the AAAS Office of Communications (202-326-6440) must be consulted.

Selection of Manuscripts

In selecting papers for publication, the editors give preference to those of general significance that are well written, well organized, and intelligible to scientists in different disciplines. An attempt is made to balance the subject matter in all sections of *Science*. Membership in the AAAS is not a factor in selection.

Accepted papers are edited to improve the accuracy and effectiveness of communication and to bring them within the specified length limits. When the author's meaning is not clear, the editor may consult the author by telephone; when editing is extensive, the manuscript may be returned for approval and retyping before the type is set.

Categories of signed papers include: general articles, research articles, reports, letters, technical comments, book and software reviews, perspectives, and policy forums.

General Articles. General articles (up to 5000 words) are expected to (i) review new developments in one field that will be of interest to readers in other fields; (ii) describe a current research problem or a technique of interdisciplinary significance; or (iii) discuss some aspect of the history, logic, policy, or administration of science. Readers should be able to learn from a general article what has been firmly established and what are unresolved questions; speculation should be kept to a minimum.

Many of the general articles are solicited by the editor, but unsolicited articles are welcome. Both solicited and unsolicited articles undergo review.

General articles should include a note giving the authors' names, titles, and addresses; a summary (50 to 100 words); an introduction that outlines for the general reader the main point of the article; and brief subheadings to indicate the main ideas. The reference list should not be exhaustive; a maximum of 50 references is suggested. Figures and tables should occupy no more than one printed page.

Research Articles. A research article (up to 4000 words) is expected to contain new data representing a major breakthrough in its field. The article should include an author note, abstract, introduction, and sections with brief sideheads. A maximum of 40 references is suggested. Figures and tables together should occupy no more than one printed page.

Reports. Reports (up to 2000 words) are expected to contain important research results. They should include an abstract (no more than 100 words) and an introductory paragraph. A maximum of 30 references is suggested. Figures and tables together with their legends should occupy no more than one printed page.

Letters. Letters are selected for their pertinence to material published in *Science* or because they discuss problems of general interest to scientists. Letters pertaining to material published in *Science* may correct errors; provide support or agreement; or offer different points of view, clarifications, or additional information. Personal remarks about another author are inappropriate. Letters may be reviewed by outside consultants. Letters selected for publication are intended to reflect the range of opinions received. The author of the paper in question is usually given an opportunity to reply.

All letters are acknowledged by postcard; authors are notified if their letters are to be published. Preference is given to letters that do not exceed 250 words. Letters accepted for publication are frequently edited and shortened in consultation with the author.

Technical Comments. Technical comments (up to 500 words) may criticize articles or reports published in *Science* within the previous 6 months or may offer useful additional information. Minor issues should

be resolved by private correspondence. The authors of the original paper are asked for an opinion of the comment and are given an opportunity to reply in the same issue if the comment is published. The comments, and sometimes the reply, are subject to the usual review procedures. Priority disputes undergo extensive review and are published only when action is recommended.

Book and Software Reviews. The selection of books and software packages to be reviewed and of reviewers is made by the editors. Instructions and length specifications accompany items to be reviewed when they are sent to reviewers.

Manuscript Preparation

Typing. Use double-spacing throughout the text, tables, figure legends, and references and notes and leave margins of at least 2.5 centimeters. Put your name on each page and number the pages starting with the title page.

Titles. Titles should be short, specific, and amenable to indexing. For general articles the maximum length is 80 characters and spaces; for research articles and reports the maximum is 100 characters.

Summaries or abstracts. These should include a sentence or two explaining to the general reader why the research was undertaken and why the results should be viewed as important. The abstract should convey the main point of the paper and outline the results or conclusions.

Text. A brief introduction should indicate the broad significance of the paper. The whole text should be intelligible to readers in different disciplines. Technical terms should be defined. All tables and figures should be cited in the text in numerical order.

Symbols and abbreviations. Define all symbols, abbreviations, and acronyms.

Units of measure. Use metric units. If measurements were made in English units, give metric equivalents.

References and notes. Number references and notes in the order in which they are cited, first through the text and then through the table and figure legends. List a reference only one time. References that are *always* cited together may be grouped under a single number. Use conventional abbreviations for well-known journals; provide complete titles for other journals. For references with up to five authors provide all the names; for more than five, provide the name of the first author only. See issues of the journal for examples.

Unpublished observations. Reference to unpublished data should be given a number in the text and placed, in correct sequence, in the references and notes.

Acknowledgments. Gather all acknowledgments into a brief statement at the end of the references and notes.

Informed consent. Investigations on human subjects must include a statement indicating that informed consent was obtained after the nature and possible consequences of the studies had been fully explained.

Animal welfare. Authors using experimental animals must state that their care was in accordance with institutional guidelines. For animals subjected to invasive procedures, the anesthetic, analgesic, and tranquilizing agents used, as well as the amounts and frequency of administration, must be stated.

Figures. For each figure submit three high-quality glossy prints or original drawings of sufficient size to permit relettering but not larger than 22 by 28 centimeters (8½ by 11 inches). On the back of every figure write the first author's name and the figure number and indicate the correct orientation. *Manuscripts with oversized figures will be returned to the author without review.* Photocopies of figures are not acceptable; transparencies, slides, or negatives cannot be used because they cannot be sent to reviewers.

On acceptance of a paper, authors requesting the use of color will be asked to supply slides or negatives of the color artwork and to pay $600 for the first color figure or figure part and $300 for each additional figure or figure part to help defray the cost of obtaining color separations.

Illustrations reprinted from other publications must be credited. It is the author's responsibility to obtain permission to reprint such illustrations in *Science*.

Tables. Tables should supplement, not duplicate, the text. They should be numbered consecutively with respect to their citation in the text. Each table should be typed, with its legend (double-spaced), on a separate sheet. Give each column a heading with units of measure indicated in parentheses. Do not change the unit of measure within a column.

Equations and formulas. Use quadruple-spacing around equations and formulas that are to be set off from the text. Define all symbols.

Uncertainties and reproducibility. Evidence that the results are reproducible and the conditions under which this reproducibility (replication) was obtained should be explicitly stated. The effect of limitations in experimental conditions on generalizability of results should be discussed. Uncertainties should be stated in terms of variation expected in independent repetitions of the experiments; they should include an allowance for possible systematic error arising from inadequacies in the assumed model and other known sources of possible bias. Probabilities from statistical tests of significance should be subordinated to the reporting of results and associated uncertainties.

Printing and Publication

Proofs and reprints. One set of galley proofs is sent to the authors. An order blank for reprints accompanies the proofs.

Scheduling. Papers are scheduled for publication after *Science* has received corrected galley proofs from the authors. Papers with tables or figures that present problems in layout, or with color figures or cover pictures, or that exceed the length limits may be subject to delay.

Cover Photographs

Particularly good photographs that pertain to a paper being submitted will be considered for use on the cover. Submit prints (not slides, negatives, or transparencies) with the manuscript.

fied by their ability to create mutations within the *lac* and *gal* operons of *Escherichia coli*, are known to be components of several transposable elements responsible for the dissemination of antibiotic resistance throughout the Enterobacteriaceae and their conjugal partners and to play a role in the organization of the R factors, which often contain nested sets of transposable elements. Transposable elements in yeast and higher eukaryotes are now important both as genetic tools and as clues to genome organization.

The present volume brings together current work on prokaryotic and eukaryotic transposable elements, and rapid publication has resulted in a book whose content is still timely. In it subjects not usually covered in current reviews figure prominently. It reports important data shortly in advance of journal publication (Clewell *et al.* on Tn*916*, a conjugative transposon in *Streptococcus*) or data from specialized systems (Chater *et al.* on the role of mobile antibiotic resistance determinants in genome flux in *Streptomyces*, Pays on DNA recombination and transposition in trypanosomes). There are general reviews on transposable elements in *Staphylococcus* (Murphy), the P elements in *Drosophila* (Rio), the yeast retrotransposons such as Ty (Kingsman *et al.*), and I-factors in *Drosophila* (Finnegan). Representative of the elegant in vitro analysis of transposition and resolution are papers on Mu transposition (Craigie *et al.*) and gamma-delta resolvase (Hatfull *et al.*). Phase and antigenic variation as a result of DNA rearrangements and the importance of such variation in the pathogenic properties of certain bacteria are reviewed by Meyer and Haas. The uses and properties of plant transposable elements are briefly treated by Schell (transfer of T-DNA from *Agrobacterium* into plants) and Schwarz-Sommer and Saedler. This important subject should have been covered in greater detail. Chapters with broader perspectives include those by Berg *et al.* on the mechanism and regulation of transposition and by Kuff and Leuders on the structure and evolution of retroviruses with homology to the transposable A-particle elements of mice.

The papers have numerous illustrations and references. For the reader who wants an introduction to the field, Shapiro's *Mobile Genetic Elements* is certainly more suitable (although an update of it is needed). But university and departmental libraries will want to have this current volume available for their faculty and graduate students.

MICHAEL MALAMY
Department of Molecular Biology, Tufts University School of Medicine, Boston, MA 02111

Lightning

The Lightning Discharge. MARTIN A. UMAN. Academic Press, San Diego, CA, 1987. xii, 377 pp., illus. $49. International Geophysics Series, vol. 39.

Our technologically based society is rapidly becoming more susceptible to the effects of lightning. In his preface to *The Lightning Discharge* Uman states that his goal is to provide a self-contained reference source on the subject. He has achieved this objective; the book also contains hundreds of references to the scientific research on lightning up to 1986, including an alphabetical list of books containing information on lightning that reveals the void this book fills.

This book represents a major departure from Uman's 1969 book *Lightning* in its organizational structure. This time he presents topics by physical process, not by diagnostic technique. There is not much detail on instrumentation, and experimental techniques are only summarized briefly in an appendix. I find the new organization more helpful. The book should be a useful reference for any comprehensive course on atmospheric electricity, and readers can easily glean from it general information about lightning. Each chapter has its own list of references, including some not cited in the text.

Topics covered by Uman include the components that make up a cloud-to-ground lightning flash, mostly related to the more common flash that lowers negative charge to the ground. In addition there is a chapter describing "positive lightning," that is, ground strikes that lower positive charge to ground, which are intriguing in their basic physics and have possible links with various weather phenomena, including severe storms and winter storms. In contrast to ground flashes, to which several chapters are devoted, cloud discharges are the focus of a single chapter, which adequately summarizes the historical data on the subject. Uman includes two chapters that cover relatively new areas of research, lightning on other planets and artificially initiated lightning. The latter phenomenon has recently become widely recognized as an operational problem for launch of all space vehicles and return to Earth of manned ones and is important in aviation because of the advent