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4 January 1991
Vol. 251 ■ Pages 1–132

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1. Nielson, K. and Mathur, E.J. (1990) Strategies 3:17-19.
2. Nielson, K. and Mathur, E.J. Manuscript in preparation.
3. Nielson, K. and Mathur E.J. (1989) U.S. patents filed.
4. Mullis, K.B., and Faloona, F.A. (1987) Meth. Enzymol. 155:335-350.

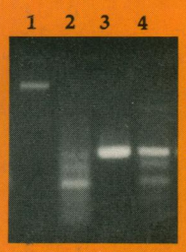

Figure Legend: A photograph of a 1% agarose gel stained with ethidium bromide representing reaction products from PCR amplifications using the GeneAmp™ Kit† from Perkin-Elmer Cetus according to manufacturer's instructions. The reactions were conducted with (lanes 1 and 3) and without (lanes 2 and 4) the inclusion of 1 unit Perfect Match polymerase enhancer. Lanes 1 and 2 represent 100 ng of human genomic DNA amplified with two 26-mer primers separated by 1400 nucleotides. Lanes 3 and 4 represent 100 ng of mouse genomic DNA amplified with two 23-mer primers separated by 550 nucleotides.

Figure 1 shows two examples of *in vitro* amplification reactions that are significantly enhanced by the addition of Perfect Match polymerase enhancer to the polymerase preparation. Note that in lanes 1 and 2, the desired PCR product cannot be detected unless Perfect Match polymerase enhancer is added to the amplification reaction. In lanes 3 and 4, Perfect Match polymerase enhancer not only increases the intensity of the desired amplification products, but dramatically reduces the background artifacts generated by non-specific priming events.

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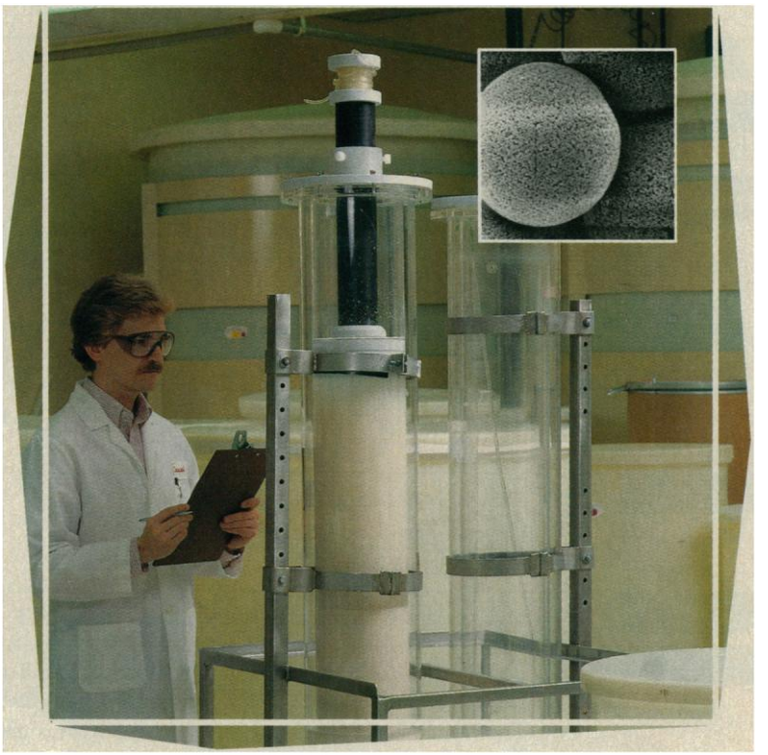

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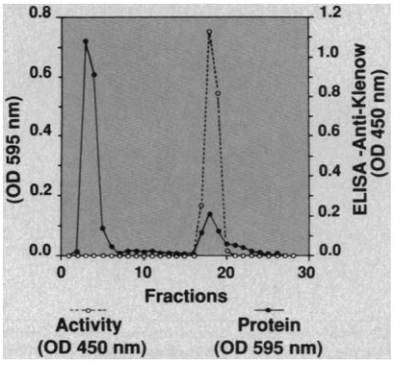

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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

SCIENCE

ISSN 0036-8075
4 JANUARY 1991
VOLUME 251
NUMBER 4989

■ **SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1333 H Street, NW, Washington, DC 20005.** Second-class postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Domestic individual membership and subscription (51 issues): $80. Domestic institutional subscription (51 issues): $150. Foreign postage extra: Canada $46, other (surface mail) $46, air mail via Amsterdam $85. First class, airmail, school-year, and student rates on request. **Change of address**: allow 6 weeks, giving old and new addresses and 11-digit account number. **Postmaster**: Send change of address to *Science*, P.O. Box 1723, Riverton, NJ 08077. **Single copy sales**: Current issue, $3.50; back issues, $5.00; Biotechnology issue, $6.00 (for postage and handling, add per copy $0.50 U.S., $1.00 all foreign); Guide to Biotechnology Products and Instruments, $20 (for postage and handling add per copy $1.00 U.S., $1.50 Canada, $2.00 other foreign). Bulk rates on request. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

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COVER Containment of elevated concentrations of the ClO free radical (shown in green) in the stratosphere above the Antarctic continent occurs within the wind jet generated by cooling during the austral winter night. Isolation of the vortex, that region poleward of the wind field maximum, is an important element in the case linking chlorofluorocarbon release to ozone destruction over Antarctica. See page 39. [Artwork by Joseph Spatola]

Reports

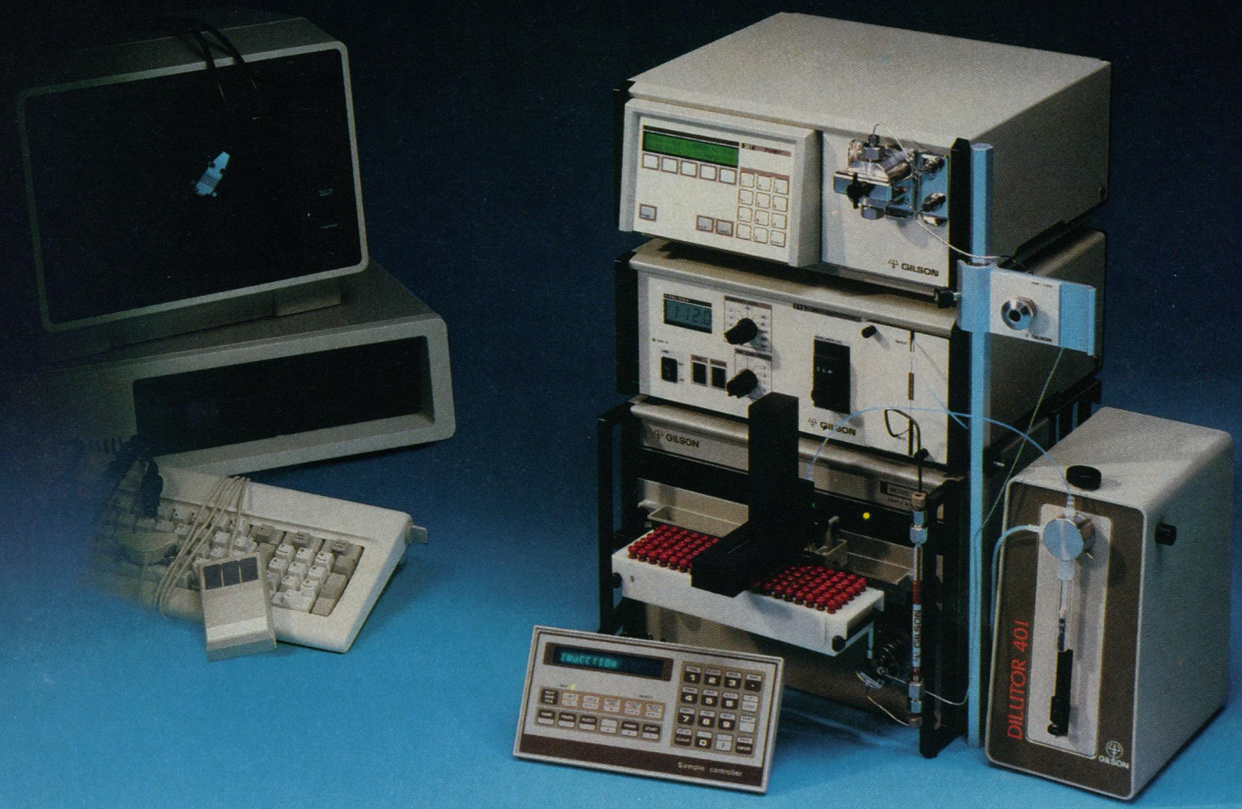
Technical Comments

Inside AAAS

Products & Materials

Information to Contributors is found on pages 35–37.

How we made a better HPLC system for QC/QA analysis



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Understanding ozone losses

COMPLEX chemical and physical changes in the stratosphere have caused severe losses of ozone over Antarctica each spring and less severe but still substantial ozone losses over the Arctic. Aircraft and satellites have been collecting a variety of chemical and dynamical data that are helping to define how stratospheric perturbations lead to the observed ozone holes (cover). Anderson, Toohey, and Brune review the chemical data that provide a stronger-than-ever case for chlorofluorocarbon release playing a causal role in the depletion of ozone in the stratosphere over Antarctica (page 39). Schoeberl and Hartmann describe how, within the stratospheric vortices that form each winter over the poles, cold conditions promote the formation of polar stratospheric clouds; it is these clouds that act as catalytic surfaces for the chemical reactions that destroy ozone (page 46). Improved understanding of ozone chemistry and global dynamical variables permits predictions of the likely limits of ozone losses and makes clear the case for stopping production and release of ozone-destroying compounds.

Maintaining B cells in culture

STUDIES of B lymphoid cells and of the antibodies that they produce have been hampered because of the difficulties that have been encountered in sustaining normal B lymphoid cells in culture. Only B cell tumor lines or cells experimentally transformed by a virus have been maintained successfully in culture for extended periods. Banchereau *et al.* have now achieved the long-sought goal (page 70). B cells from several sources—peripheral blood, cord blood, spleen, and tonsils—were stimulated with monoclonal antibodies that reacted with and cross-linked CD40 molecules on the cell surfaces. The proliferative responses of the B cells were enhanced if antibody stimulation was combined with exposure of the cells to interleukin-4, a growth factor for T lymphoid cells and apparently also for B cells. The cells grew in culture for up to 10 weeks. Besides making possible many types of studies on the growth and differentiation of normal B cells, these procedures could lead to the eventual production of antigen-specific B cell clones and human monoclonal antibodies.

Second messengers for interleukin-2 signals

INTERLEUKIN-2 binds to receptors on the surfaces of B lymphoid cells. It causes the cells to proliferate and to secrete antibodies of the IgM class. How the interleukin-2 message is relayed from cell membrane to cell nucleus has been unclear. Studies by Eardley and Koshland suggest that breakdown products of a membrane glycosylphosphatidylinositol (Gly-PI) may be the signal-transducing second messengers in the interleukin-2 system (page 78). The two hydrolysis products, myristylated diacylglycerol and inositol phosphate-glycan, have recently been implicated as possible second messengers for other protein factors—insulin and nerve growth factor—in other cellular systems. Exposure of a B lymphoma line of cells to interleukin-2 was quickly followed by hydrolysis of Gly-PI and proliferation of the lymphoma cells; both indicators were blocked when the cells were exposed to a second lymphokine (interleukin-4) that is known to counter the interleukin-2 effects.

Cell sorting from whole embryos

A TECHNIQUE has been developed for physically sorting embryonic cells on the basis of differential gene expression at a time in the development of the cells when the cells have no known morphologic differences. In prototype experiments described by Krasnow *et al.*, various subpopulations of cells were sorted out from whole *Drosophila* embryos (page 81). One example was the separation of cells of the stripes and interstripes (regularly spaced rows of cells along the embryo's axis) from each other. Those in the stripes had been genetically engineered to express the β-galactosidase gene, while those in the interstripe did not express this gene. A fluorescent substrate for the β-galactosidase gene product bound to the stripe cells, tagging them for sorting in a fluorescence-activated cell sorter. In theory, it should be possible to put β-galactosidase transgenes into most cell types of *Drosophila* embryos (as well as into the cells of the embryos of other manipulable organisms) with available genetic engineering techniques and then to sort subpopulations of cells that are expressing the transgene at different levels or at different times in their development.

Shape of fibroblast growth factors

FIBROBLAST growth factors (FGF) are proteins that have powerful effects on a variety of cell types. They bind to cellular receptors and then can stimulate cell differentiation, cell proliferation, angiogenesis, and chemotaxis; they also can bind to the serum protein heparin. Some of the members of this family are products of oncogenes. Zhu *et al.* present x-ray crystallographic data for two FGF proteins—human basic FGF and bovine acidic FGF—that have distinctive biologic activities (page 90). The two proteins have about 55% sequence identity, and they fold in much the same way. Interestingly their folding pattern is similar to that of some interleukin-1 molecules with which they share functional similarities (the interleukins also can stimulate cell differentiation and growth) but little sequence similarity. The crystallographic data will help in determining how specific portions (domains) of the FGF molecules participate in the various functions and activities of FGF, such as receptor binding, heparin binding, and nuclear translocation.

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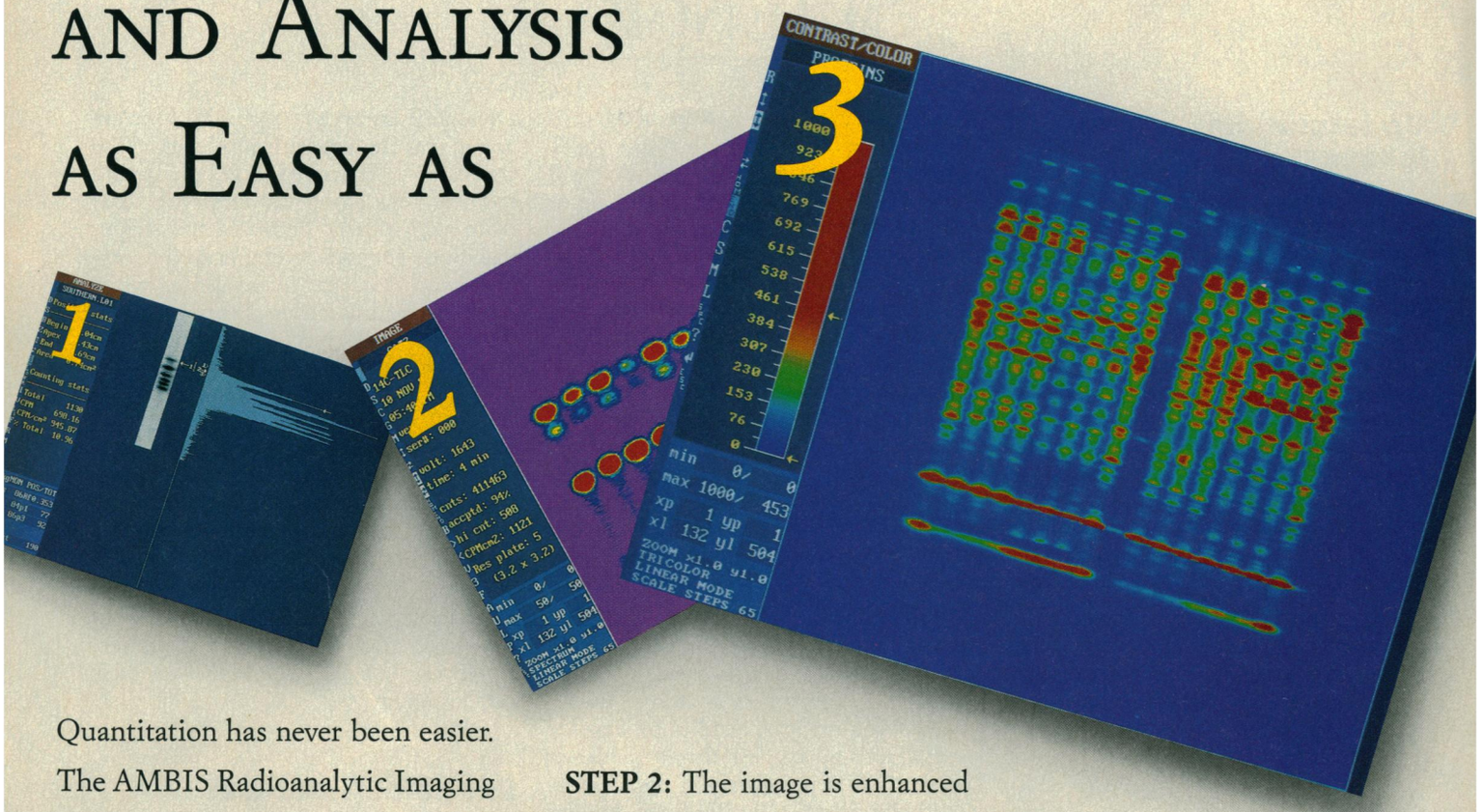

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AAAS Minority Scholars Workshop on Values and Ethical Issues in Science and Technology

The American Association for the Advancement of Science (AAAS) invites minority scholars in academic or other institutions to apply for participation in a workshop of intensive study on the values and ethical issues associated with science and technology. The workshop will be held from July 28 to August 4, 1991 near Washington, D.C.

Workshop participants will explore in depth various minority perspectives on science and technology, how they compare to prevailing perspectives, and the different influences that these perspectives can have on scholarship, individual practices, and policy decisions regarding science and technology. The workshop will also review important theoretical work and research methodologies in ethics and values research, as well as publishing outlets and resources that can help support scholarship in this field.

While persons of any minority group may apply, preference will be given to applicants from the following groups: Asian/Pacific Islander, Black/African-American, Hispanic/Chicano/Puerto Rican/Latino, or Native American/American Indian. Persons with an advanced degree in any field of science, engineering, medicine, law, or the humanities may apply. Participants will receive expenses for travel to and from the workshop, and for accommodations and meals.

For further information or to request an application form, contact A. Crumpton, Directorate for Science and Policy Programs, AAAS, 1333 H Street, N.W., Washington, D.C. 20005; (202) 326-6798.

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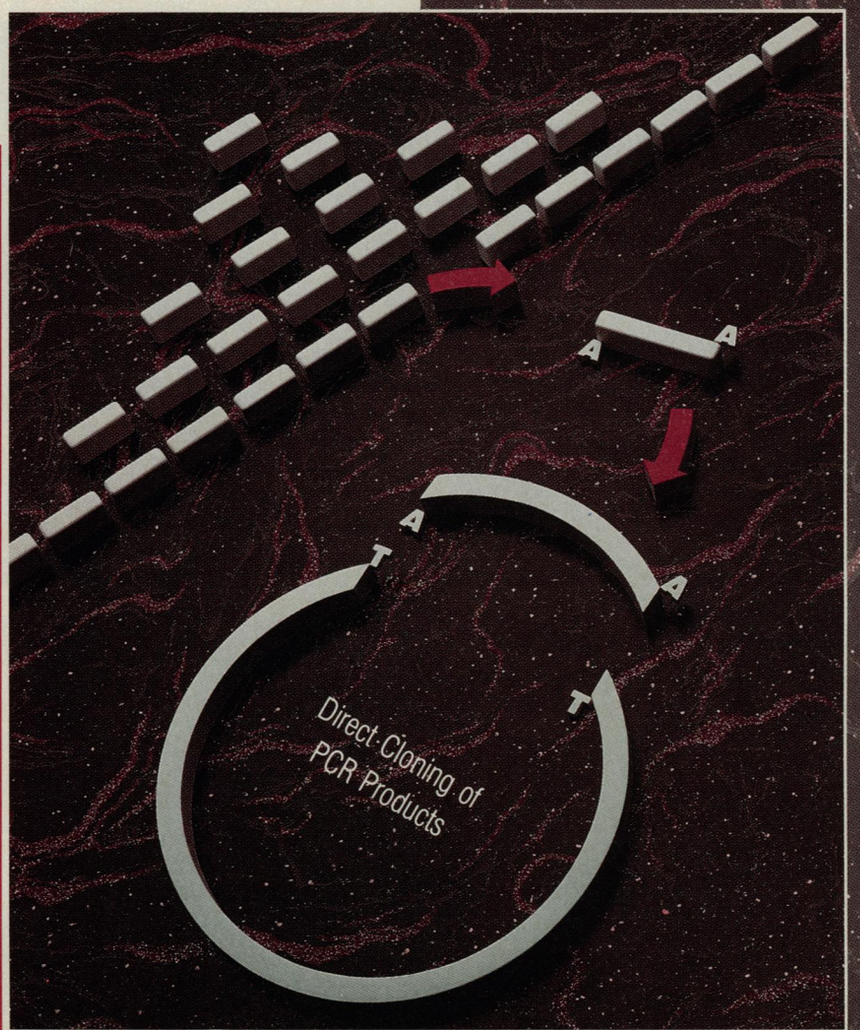

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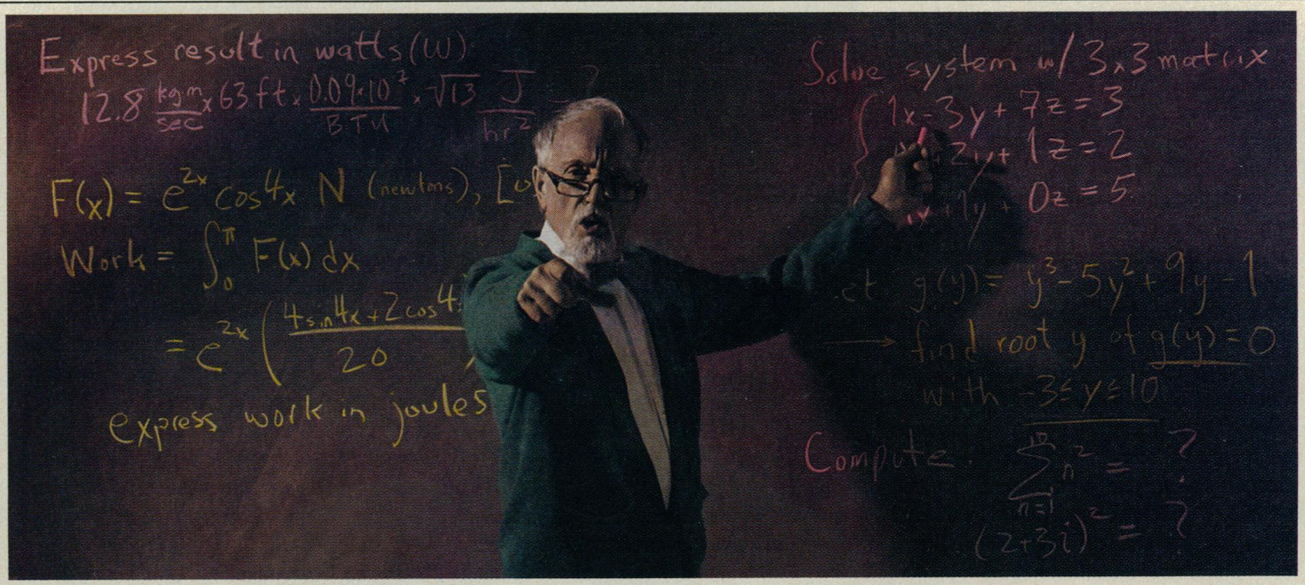

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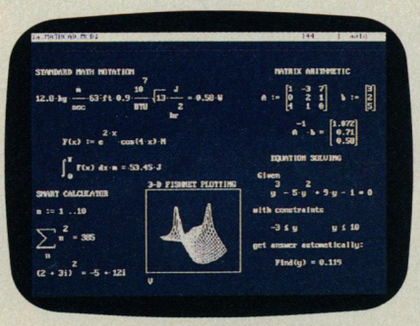

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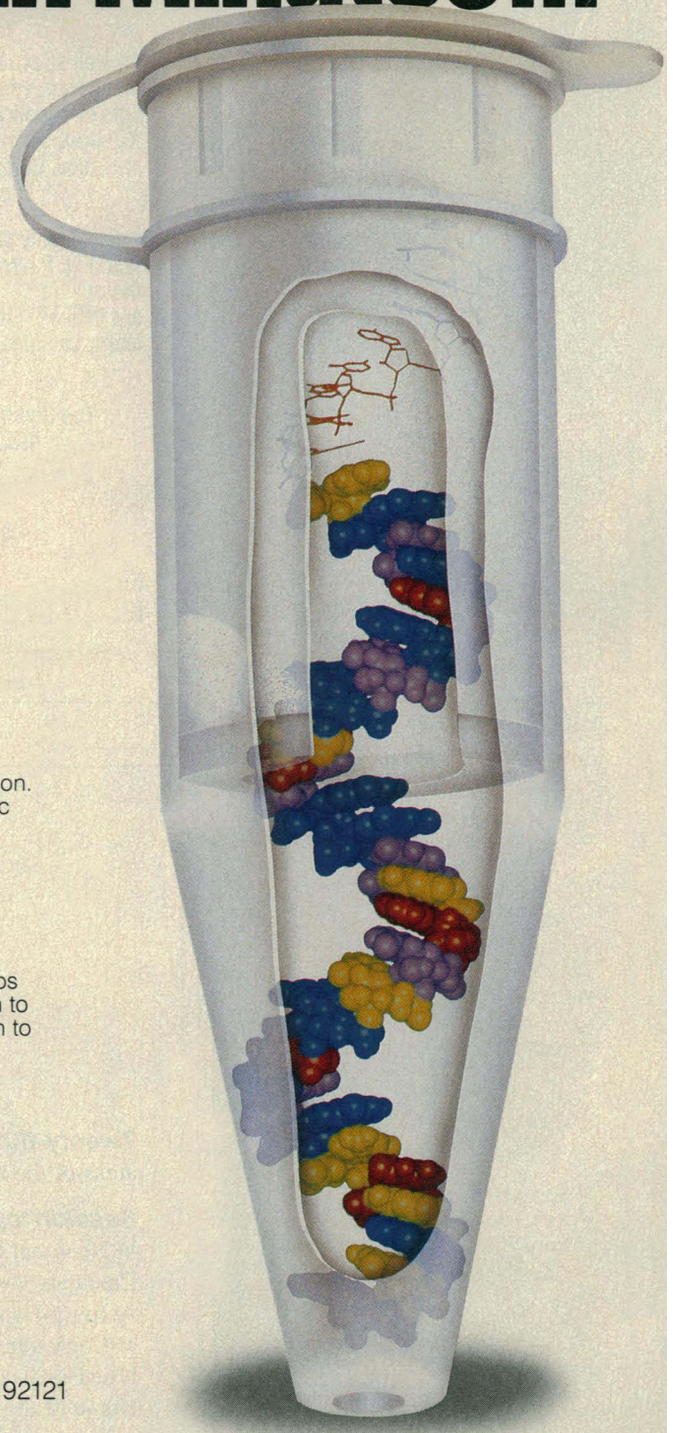

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Revised 1 January 1991

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In selecting papers for publication, the editors give preference to those of novelty and 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.

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 (3000 to 5000 words or three to five printed pages) 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 or future directions.

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 together with their legends should occupy about one printed page.

Research Articles. A research article (up to 4000 words or four printed pages) 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 subheadings. A maximum of 40 references is suggested. Figures and tables together with their legends should occupy about one printed page.

Reports. Reports (up to 2500 words or three printed pages) are expected to contain important research results. Addresses for all authors should be listed on the title page and the corresponding author should be indicated by an asterisk. Reports 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 of the pages.

Letters. Letters are selected for their pertinence to material published in *Science* or because they discuss problems of general

interest to scientists. Letters about 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 short letters (between 250 and 500 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. Comments and replies are subject to the usual reviewing and editing procedures. Priority disputes may 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 and subheadings should be a descriptive clause, not a declarative sentence or a question. 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 and 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 the first time they are used.

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. Do not use *op. cit.* See "*Science* Reference Style" (page 37) 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 were 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 prints, laser 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. See section on preparation of figures for details.

On acceptance of a paper, authors requesting the use of color will be asked 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. There will be an additional charge for color figures in the reprints.

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) above the table. 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 and number all equations.

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 not replace the reporting of results and associated uncertainties.

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Copyright law requires that we obtain copyright transfer from authors of each paper published in *Science*. Copyright forms are sent to all authors prior to acceptance and must be signed and returned to the editorial office immediately. U.S. government employees sign the section of the form stating exemption from copyright laws. Alterations to or substitutions for our form are not acceptable.

Printing and Publication

Proofs and reprints. One set of 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 proofs from the authors. Papers with tables or figures that present problems in layout, or with 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 can be considered for use on the cover. Submit prints (not slides, negatives, or transparencies) with the manuscript.

Figures

Most figures will be printed at a width of 5.9 cm (2.3 inches or 1 column) or 12.2 cm (4.8 inches or 2 columns) in reports and at a width of 9.1 cm (3.8 inches or 1 column) in articles. Some illustrations (for example, bar graphs, simple line graphs, and gels) may be reduced to a smaller width. Please provide figures that are about 50% larger than the expected final size but no larger than 22 by 28 cm (8.5 by 11 inches). Symbols and lettering should be large enough to be legible after reduction.

Composite figures should be labeled **A**, **B**, **C**,. . . . If mounting is necessary, use very flexible cardboard.

Legends should be typed double-spaced in numerical order on a separate page. No single legend should be longer than one page. Nomenclature, abbreviations, symbols, and units used in a figure should match those used in the text and should be consistent with those used in the other figures.

The figure *title* should be given as the first line of the legend rather than on the figure.

Line drawings should be labeled on the ordinate and abscissa with the parameter or variable being measured, the units of measure, and the scale. Scales with large or small numbers should be presented as powers of 10. Definitions of symbols should usually appear in the figure legend and not in the figure. Simple *symbols* (circles, squares, triangles, and diamonds, solid or open) will best survive reduction.

Recommended symbols at the size they should appear after reduction:

● ○ □ ▲ △

Avoid the use of *light lines, shading, and stippling*; light lines and gray shading may disappear when the figure is photographed at high contrast, and stippled areas may appear black when greatly reduced. Use heavy lines or boxes for emphasizing or marking off areas of the figure, and use black, white, hatched, and crosshatched designs in place of stippling (for example, in bar graphs or ball-and-stick molecular models). Authors using computer graphics should choose screens between 20 and 60%.

Halftones, such as electron micrographs, should be submitted as high-quality prints or originals (do not send irreplaceable artwork). If possible, use scale bars in place of, or in addition to, magnifications. In *gels*, the lanes should be numbered and identified by number in the figure legend.

For **color art** please provide a positive slide, if possible, and a print. Indicate positioning, lettering, and cropping limits on the print. For composite figures, send the original composite board rather than a print if the quality of the original is much better than that of the print. Do not send irreplaceable artwork.

Lettering in Helvetica or Times Roman font is preferable. Use boldface type for axis labels and for the labels **A**, **B**, **C**, . . . in composite figures; use italic type only as it would be used in the text (for example, for variables and genes). The first letter of each entry should be uppercase; otherwise, use uppercase letters as they would be used in the text (for example, for acronyms). Avoid wide variation in type size within a single figure. In the printed version of the figure, letters should be about 7 point (2-mm high).

This is 7-point type.

Sequences may be reduced to 5- or 6-point type, so clarity of the typeface in the original is essential. There should be about 130 characters (including spaces) per line for a sequence occupying the full width of the printed page and about 84 characters per line for a sequence (in a report) occupying two columns.

Tables

Tables should be typed double-spaced and numbered in the order of citation in the text; each table should be on a separate page and have a brief descriptive *title* as the first sentence of the legend. Three horizontal lines are used: at the top and at the bottom of the table and between the column headings and the table body. Vertical lines are not used between the columns.

Every vertical column should have a *column heading* consisting of a title with the unit of measure in parentheses. Units should not change within a column. Centered headings of the body of the table can be used to break the entries into groups. (See the section on lettering above for use of italic type and uppercase letters.)

The table *legend* should be typed above the table and should contain information relevant to the whole table.

Footnotes should contain information relevant to specific entries or parts of the table. The sequence of symbols for footnotes follows: *, †, ‡, §, ||, ¶, #, **, ††, ‡‡, ...

Science Reference Style

Journals

1. U. K. Laemmli, *Nature* **227**, 680 (1970). [one author]
2. J. C. Smith, Jr., and M. Field, *Proc. Natl. Acad. Sci. U.S.A.* **51**, 930 (1964). [without "Jr." = J. C. Smith and M. Field, . . .]
3. J. C. Cheeseborough III, S. Trajmar, J.-T. Yang, *EMBO J.*, in press. [three to five authors] [in press]
4. G. Sunshine *et al.*, *Lancet* **i**, 711 (1975). [more than five authors]
5. M. Schmidt, *Sci. Am.* **251**, 58 (November 1984). [journal paginated by issue]

Technical reports

1. D. E. Shaw, *Technical Report No. CUCS-29-82* (Columbia University, New York, 1982).
2. F. Press, "A report on the computational needs for physics" (National Science Foundation, Washington, DC, 1981). [unpublished or access by title]
3. "Assessment of the carcinogenicity and mutagenicity of chemicals," *WHO Tech. Rep. Ser. No. 546* (1974).

Proceedings

1. Proceedings of the *Fifth IEEE Pulsed Power Conference*, Arlington, VA, inclusive dates of meeting (publisher, publisher's location, year).
2. *Proc. IEEE (Inst. Elec. Electron. Eng.)* **88**, 452 (1968).
3. *Title of symposium published as a book*, sponsoring organization, location of meeting, dates (publisher, location, year).

Paper presented at a meeting (not published)

1. M. Konishi, paper presented at the 14th Annual Meeting of the Society for Neuroscience, Anaheim, CA, 10–15 October 1984. Sponsoring organization should be mentioned if it is not part of the meeting name.

Theses

1. B. Smith, thesis, Georgetown University (1973).

Books

1. A. M. Lister, *Fundamentals of Operating Systems* (Springer-Verlag, New York, ed. 3, 1984), pp. 7–11. [third edition] [Note: Springer Publishers, New York, is a different press.]
2. J. B. Carroll, Ed., *Language, Thought and Reality: Selected Writing of Benjamin Lee Whorf* (MIT Press, Cambridge, MA, 1956). [subtitle]
3. R. Davis and J. King, in *Machine Intelligence*, E. Acock and D. Michie, Eds. (Wiley, New York, 1976), vol. 8, chap. 3.
4. D. Curtis *et al.*, in *Clinical Neurology of Development*, B. Walters, Ed. (Oxford Univ. Press, New York, 1983), pp. 60–73. [*et al.* = more than five authors]
5. F. R. Sabier, *Contributions to Embryology* (Publ. 18, Carnegie Institution of Washington, Washington, DC, 1917), p. 61.
6. M. Ptashne, *A Gentle Switch* (Cell/Blackwell, Cambridge, MA, in press). [joint publication] [in press]
7. *Principles and Procedures for Evaluating the Toxicity of Household Substances* (National Academy of Sciences, Washington, DC, 1977). [organization as author and publisher]