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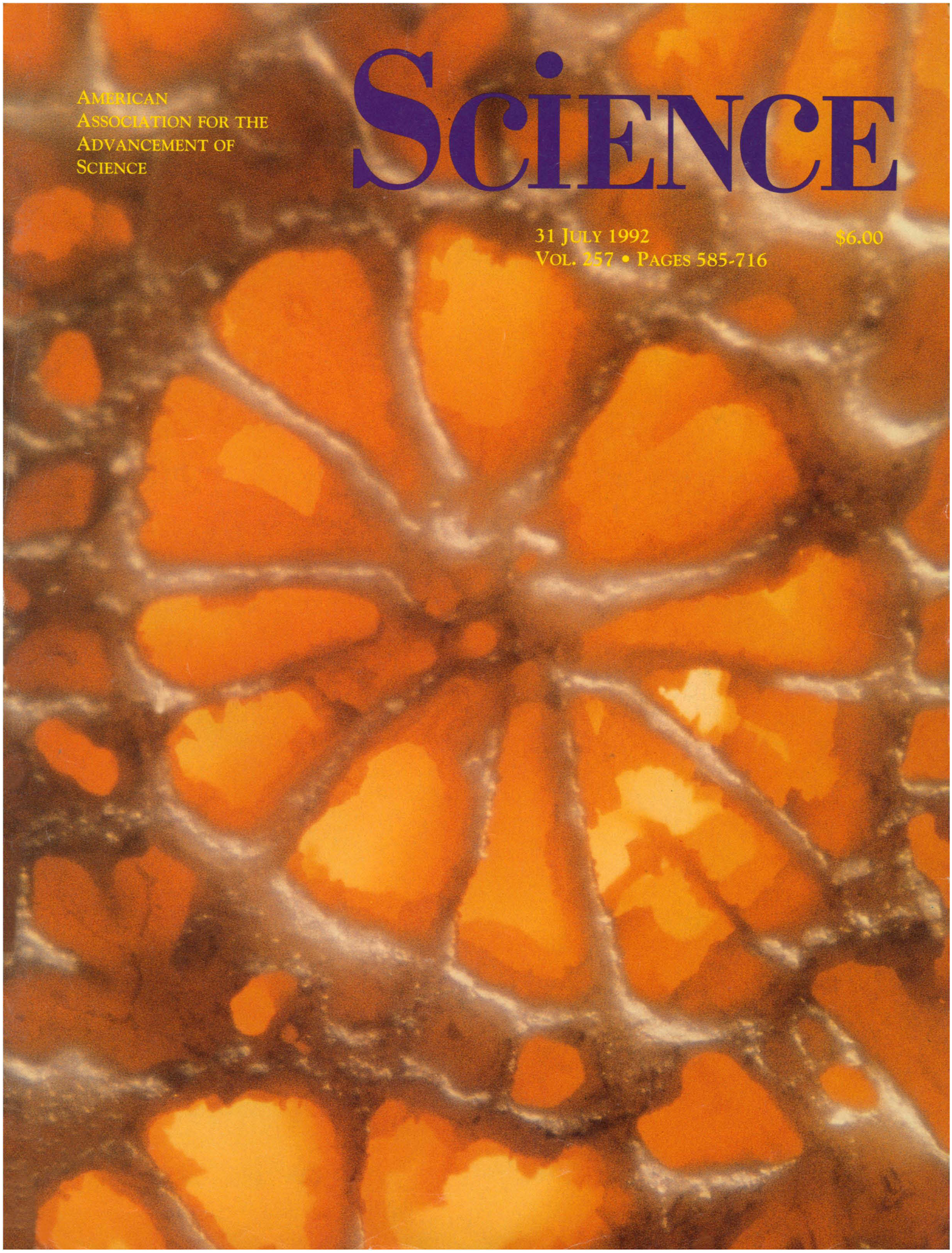

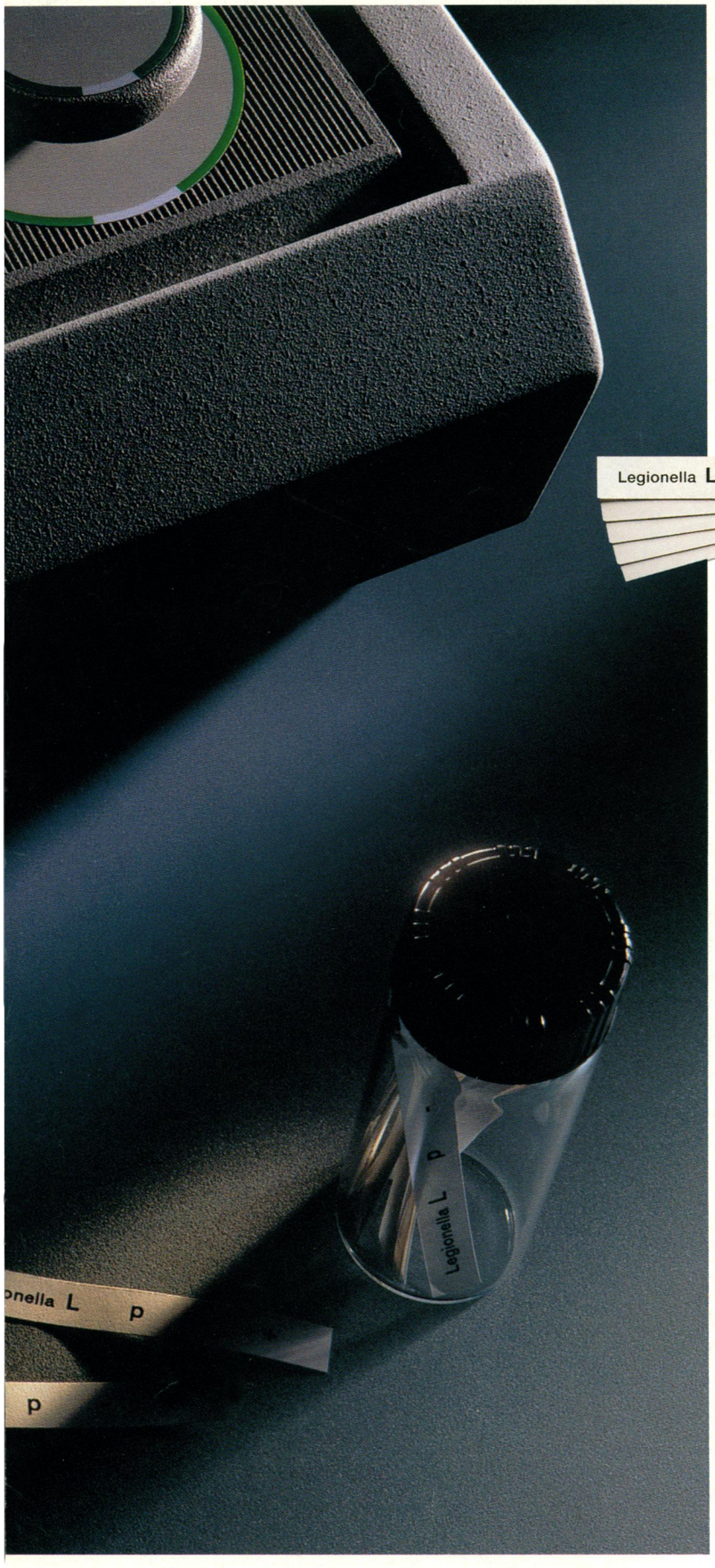

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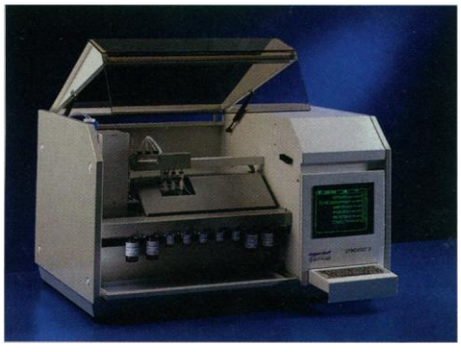

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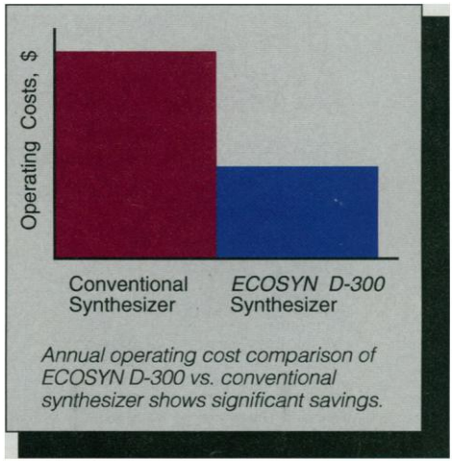

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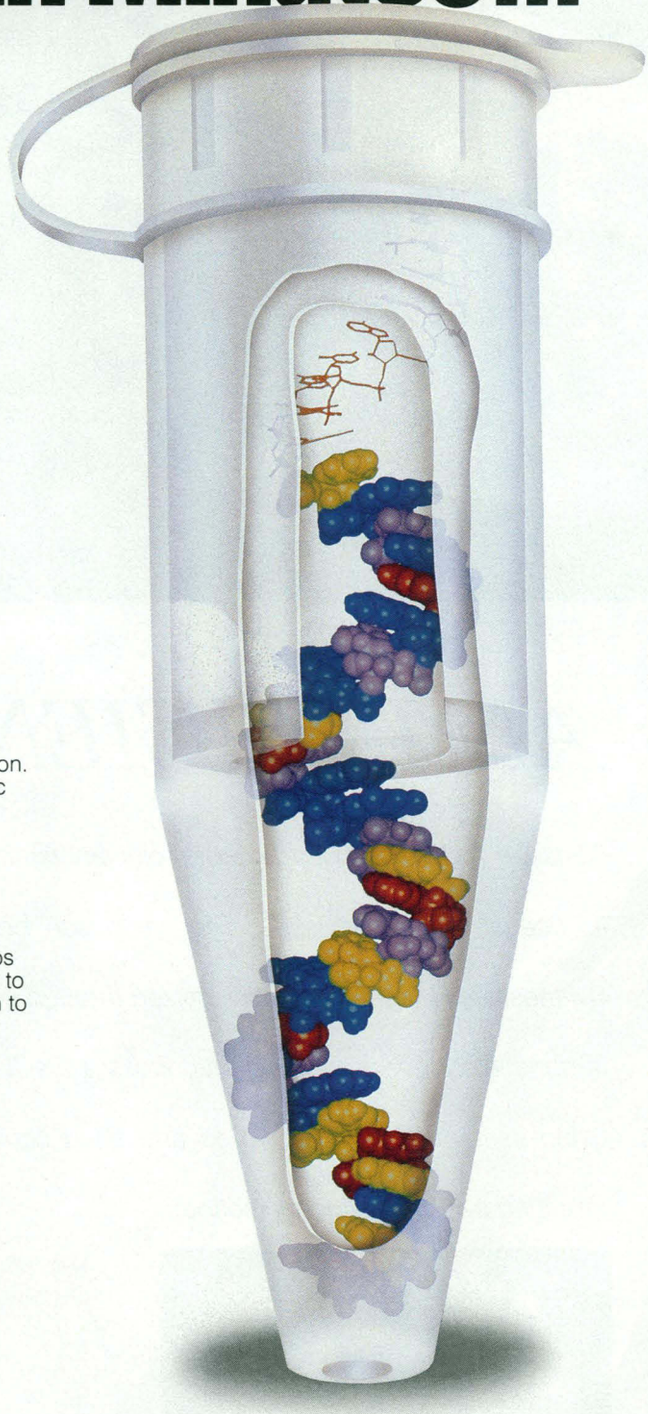

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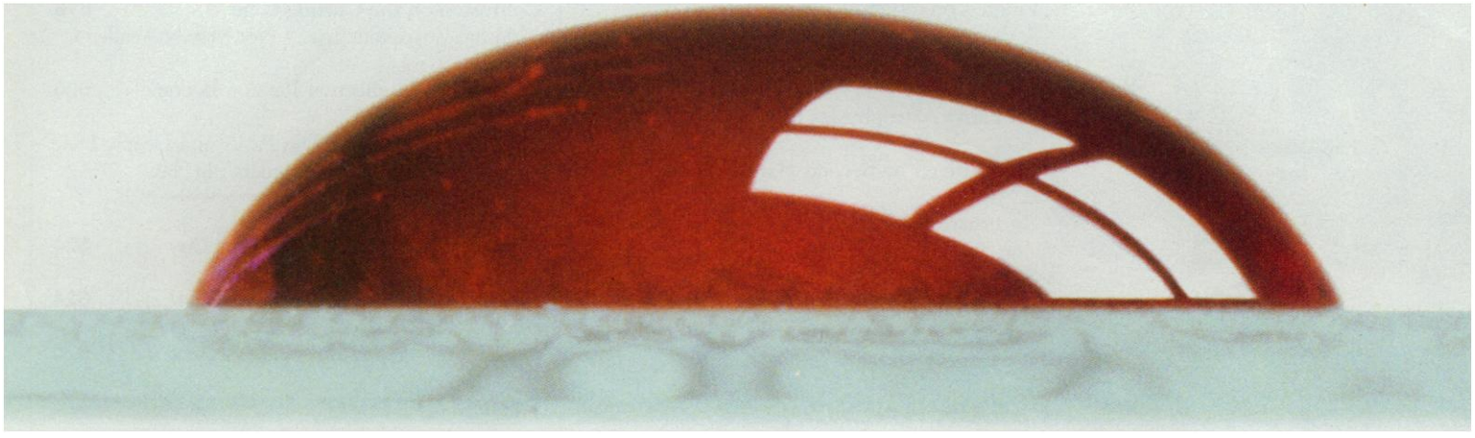

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Conflicts of interest in science

NEWS & COMMENT

RESEARCH NEWS

SPECIAL NEWS REPORT

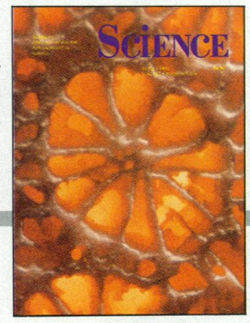
CONFLICTS OF INTEREST

PERSPECTIVE

ARTICLE

DEPARTMENTS

COVER



Coral skeleton of the genus *Favia*. Scleractinian corals secrete a hard skeleton composed of aragonite ($CaCO_3$), which incorporates strontium along with calcium in a ratio that depends on sea-surface temperature. Recent findings suggest that for corals of the genus *Porites* this dependence may be used to recover records of Pleistocene and Holocene sea-surface temperatures with an apparent accuracy of better than 0.5°C. See page 644. [Photomicrograph: J. W. Beck]

RESEARCH ARTICLE

REPORTS

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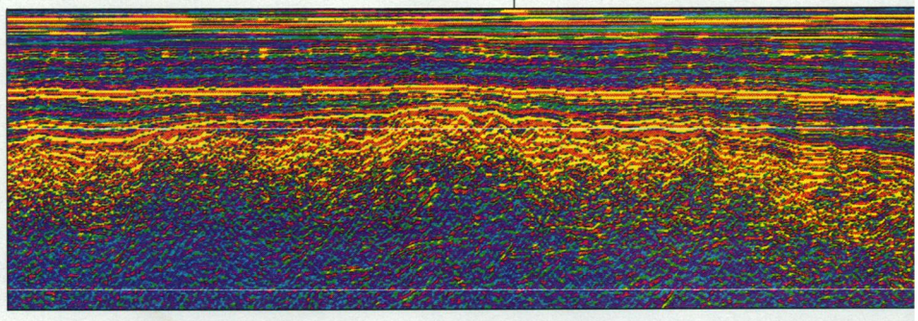
Dynamics of slow-spreading ridges



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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Pattern generator

Protein crystals have been used as templates for cutting nanoscale patterns into substrates. Douglas *et al.* (p. 642) used two-dimensional crystals of the S-layer from the bacteria *Sulfolobus acidocaldarius*, which form a lattice of holes with a periodicity of 22 nanometers. After the layers were deposited on graphite, they were coated with titanium metal, which oxidized to titania. The holes in the S-layer were uncoated, and thus ion milling could be used to cut holes into the exposed graphite substrate.

A superrotating atmosphere

The atmosphere of Venus rotates at speeds much faster than that of the planet; rotational speeds are greatest, 100 meters per second or more, at the cloud-top level at latitudes up to about 45 degrees. Some mechanism is thus required to induce such speeds and maintain them against friction. Newman and Leovy (p. 647) evaluated this problem with a numerical model of Venus' atmosphere. The results suggest that thermal tides, driven by the periodic daily absorption of solar energy primarily within the cloud layer, transfer momentum to low-latitude cloud-top regions and thus accelerate the flow there while decelerating the flow at higher levels.

Hydroxyproline in plant enzymes

Hydroxyproline (Hyp), which is formed through posttranslational modification of proline, is usually associated with secreted structural proteins. In animals, Hyp helps stabilize the triple-stranded structure of collagen, and in plants it is often found in secreted glycoproteins. Sticher *et al.* (p. 655) report that the type I tobacco chitinases, which are intracellular proteins found in plant vacuoles that help defend against pathogens such as fungi, also contain Hyp. In contrast to the other Hyp-containing plant proteins, the hydroxylation modification occurs only at a few residues in a short proline domain, and the Hyp residues are not O-glycosylated.

Temperatures from coral

Recovery of glacial age sea-surface temperatures (SSTs) from the $^{18}O/^{16}O$ ratio of fossil plankton has been difficult because the ratio also reflects the isotopic composition of seawater, which changed when much water was stored in large continental ice sheets. Beck *et al.* (p. 644 and cover) show that the Sr/Ca ratio incorporated by corals as they grow may provide a more direct measure of past SSTs than oxygen isotopes because the Sr/Ca ratio of the oceans likely did not change significantly during glacial times. The authors calibrated the method by using modern corals from islands where SST records are available. Analysis of a 10,200-year-old coral suggests that SSTs from the southwest Pacific were 5°C colder than those today.

Transmitter secretion and synaptophysin

Transmission of signals from one neuron to another depends on the calcium-triggered release of neurotransmitter molecules such as glutamate; synaptic vesicle proteins such as synaptophysin are thought to play a role in this process. Alder *et al.* (p. 657) show that glutamate secretion can be reconstituted in *Xenopus* oocytes by injection of total mRNA from rat cerebellum. Calcium-dependent glutamate secretion can be decreased by co-injection of antisense molecules for the synaptophysin message or antibodies to rat synaptophysin. These results suggest that synaptophysin is essential for transmitter secretion.

Neonatal neocortex

The cortex of the brain is organized as a modular structure consisting of radial columns of functionally interconnected cells. During development the neurons of each radial unit may coactivate simultaneously. Yuste *et al.* (p. 665) monitored calcium concentrations in these cells with the fura-2 indicator and found distinct domains of neurons that coactivated spontaneously. Slices parallel to the cortical layers revealed domains 50 to 120 micrometers in diameter that extended through several layers. These neurons are coupled by gap junctions and so can communicate without synaptic connections.

Regulating Ras

The guanine nucleotide-binding protein Ras is a critical component of signaling pathways that control cell growth. The activity of Ras can be regulated in two different ways. Ras is activated by cellular factors that stimulate guanine nucleotide exchange, whereas it is inactivated by guanosine triphosphatase-activating proteins (GAPs). Zhang *et al.* (p. 675) provide evidence that in cells cultured at high density, Ras is inactivated by enhanced GAP activity. However, activation of Ras in cells treated with serum or growth factors appears to result from increased guanine nucleotide exchange.

Recognizing pathogens

Recognition of foreign pathogens by the immune system is mediated by the major histocompatibility complex (MHC) molecules, which bind antigens and activate the T cell response. The role of nonclassical (class I-b) molecules has been unclear; these common class I genes are not as polymorphic as the "classical" class I gene. Kurlander *et al.* (p. 678) show that class I-b molecules bind to antigens from prokaryotes that are modified with *N*-formyl groups. This result clarifies previously recognized T cell responses to prokaryotes that were mistaken to be unrestricted by class I, and it also implicates these proteins in the first line of defense against common bacterial infections.

Finding protein substrates

Protein kinases participate in many regulatory pathways; however, it is often difficult to determine the physiological substrates of these enzymes. Yang *et al.* (p. 680) used a sensitive genetic method to scrèen for proteins that interacted with the SNF1 protein kinase from yeast, which regulates several aspects of cell growth. They isolated four genes, one of which encodes a substrate of SNF1. The method is applicable to any cloned protein kinase gene and can be used to identify substrates or other proteins that bind to such enzymes.

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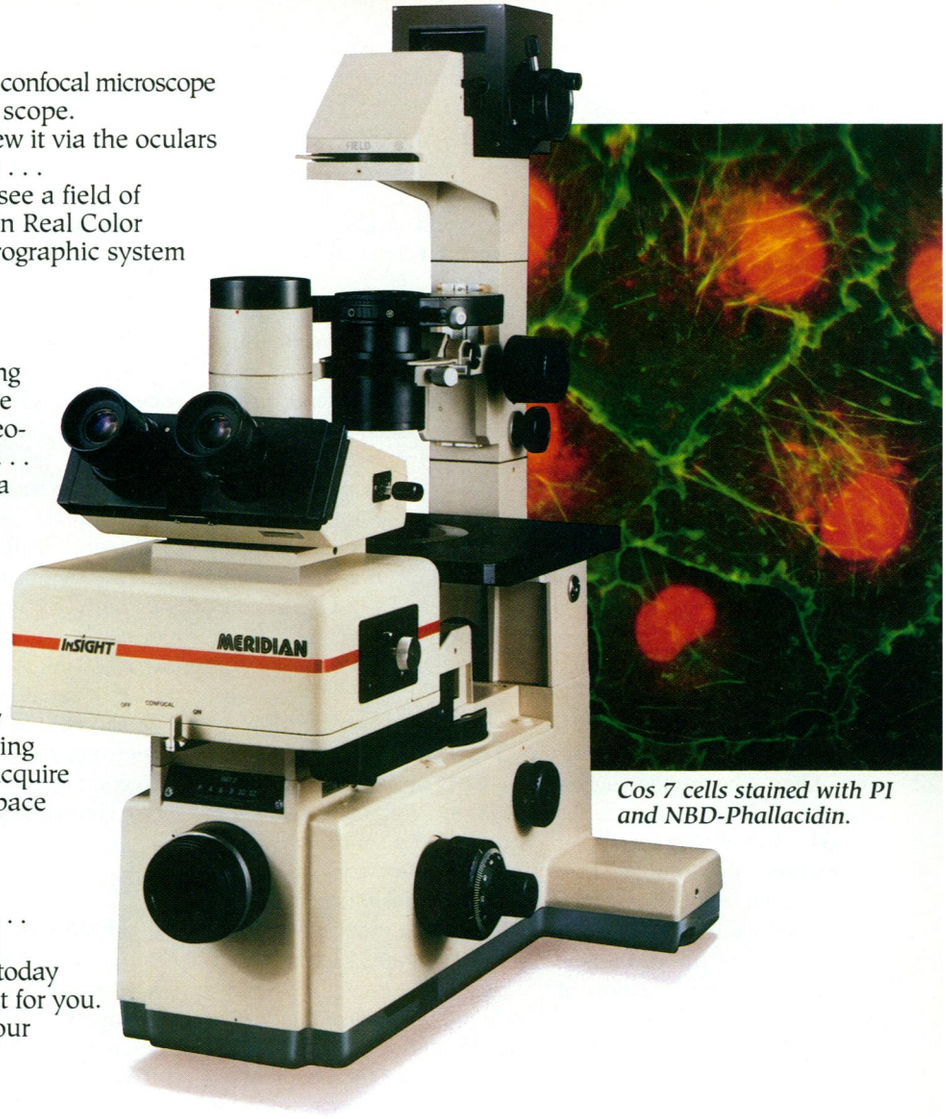

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- sequence and crystallographic data will be offered for deposit to the appropriate data bank and the identifier code will be sent to *Science* for inclusion in the published manuscript (coordinates should be released no later than 1 year after publication).
- the author or authors agree to transfer copyright of the paper to *Science*; and the paper will remain a privileged document and will not be released to the press or the public before publication.
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Authors may provide a copy of their manuscript on disc upon acceptance. Specific instructions will be provided when the manuscipt is returned for revision.

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Proofs and reprints. One set of proofs and an order blank for reprints are sent to the authors.

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SCIENCE STYLE SHEET

Acknowledgments, including funding information, should be gathered into a brief statement at the end of the references and notes and will be edited to conform to *Science* style.

Equations and formulas should be typed with quadruple-spacing if they are to be set off from the text. Define all symbols and number all equations.

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). Some illustrations (for example, bar graphs, simple line graphs, and gels) may be reduced to a smaller width. 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 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. The figure title should be given as the first line of the legend.

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*. Use heavy lines or boxes for emphasizing or marking off areas of the figure, and use black, white, hatched, and cross-hatched designs in place of stippling in bar graphs and 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 orginals (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 or laser proof. 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 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).

Sequences may be reduced considerably so make sure the typeface in the original is clear. 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 occupying two columns.

References and notes are numbered 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. Reference to unpublished data should be given a number in the text and placed, in correct sequence, in the references and notes. Use conventional abbreviations for well-known journals; provide complete titles for other journals. Do not use op. cit. See "Science Reference Style" (at right) for examples.

Symbols, abbreviations, and acronyms should be defined the first time they are used.

Tables should supplement, not duplicate, the text. They should be numbered in the order of their citation in the text. Each table should be generated on a separate page with its legend double-spaced above the table. The first sentence of the legend should be a brief descriptive title. Three horizontal lines are used in tables: at the top and 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 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 for use of italic type and uppercase letters.)

Footnotes should contain information relevant to specific entries or parts of the table. The sequence of symbols for footnotes is

*, †, ‡, §, ||, ¶, #, **, ††, ‡‡, ...

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

Science Reference Style

Journals

1. I. N. Tang, *Atmos. Environ.* **14**, 819 (1980). [one author]
2. J. C. Smith and M. Field, *Proc. Natl. Acad. Sci. U.S.A.* **51**, 930 (1964).
3. J. C. Cheeseborough III, S. Trajmar, J.-T. Yang, *EMBO J.*, in press. [three to five authors]
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]
6. J. Brown, ibid., p. 67.

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* **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 October 1984. [Sponsoring organization should be mentioned if it is not part of the meeting name.]

Theses and unpublished material

1. B. Smith, thesis, Georgetown University (1973).
2. J.A. Norton, unpublished material.

Books

1. A. M. Lister, *Fundamentals of Operating Systems* (Springer-Verlag, New York, ed. 3, 1984), pp. 7–11. [third edition]
2. J. B. Carroll, Ed., *Language, Thought and Reality: Selected Writings of Benjamin Lee Whorf* (MIT Press, Cambridge, MA, 1956).
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. *Principles and Procedures for Evaluating the Toxicity of Household Substances* (National Academy of Sciences, Washington, DC, 1977). [organization as author and publisher]