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CNTF R α	IL-2	MIP-1 α
Eotaxin	IL-2 R α	MIP-1 β
FGF basic	IL-2 R β	MK
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FGF-7	IL-3	PDGF-AA
FGF-9	IL-4	PDGF-BB
Flt-3 Ligand	IL-4 R	PDGF R α
G-CSF	IL-5	PIGF
G-CSF R	IL-5 R α	PTN
GM-CSF	IL-6	RANTES
sgp 130	IL-6 R	SCF
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HCC-1	IL-8	TGF- β 1
HRG- α	IL-10	TGF- β RII
I-309	IL-10 R	TGF- β RIII
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IGF-IR	IL-13	VEGF
IGF-II	IL-17	

MOUSE

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IL-4	MIG	VEGF
IL-5		

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Immunofluorescent localization of active TGF- β 1 and latent TGF- β 1 complex in normal and irradiated mouse mammary gland sections using TGF- β 1 affinity purified chicken anti-TGF- β 1 antibody (Cat. # AF-101-NA and goat anti-LAP (TGF- β 1) affinity purified antibody (Cat. # AF-246-NA), respectively.

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Mouse mammary gland cryosections were fixed with 4% para-formaldehyde and dual stained using chicken anti-TGF- β 1 antibody detected with Texas Red labeled secondary antibody and goat anti-LAP (TGF- β 1) antibody detected with fluorescein labeled secondary antibody. Nuclei were counterstained with DAPI. Normal mammary gland (LEFT) - shows abundant LAP (TGF- β 1) immunostaining (green) reflecting the presence of latent TGF- β 1. Mammary gland taken from animals exposed to whole body irradiation with 5Gy 24 hours prior to processing. (BELOW - exhibits predominantly active TGF- β 1 immunoreactivity (pinkish-red). This shift is due to the loss of LAP concomitant with increased access to active TGF- β 1 and is consistent with activation of latent TGF- β 1.

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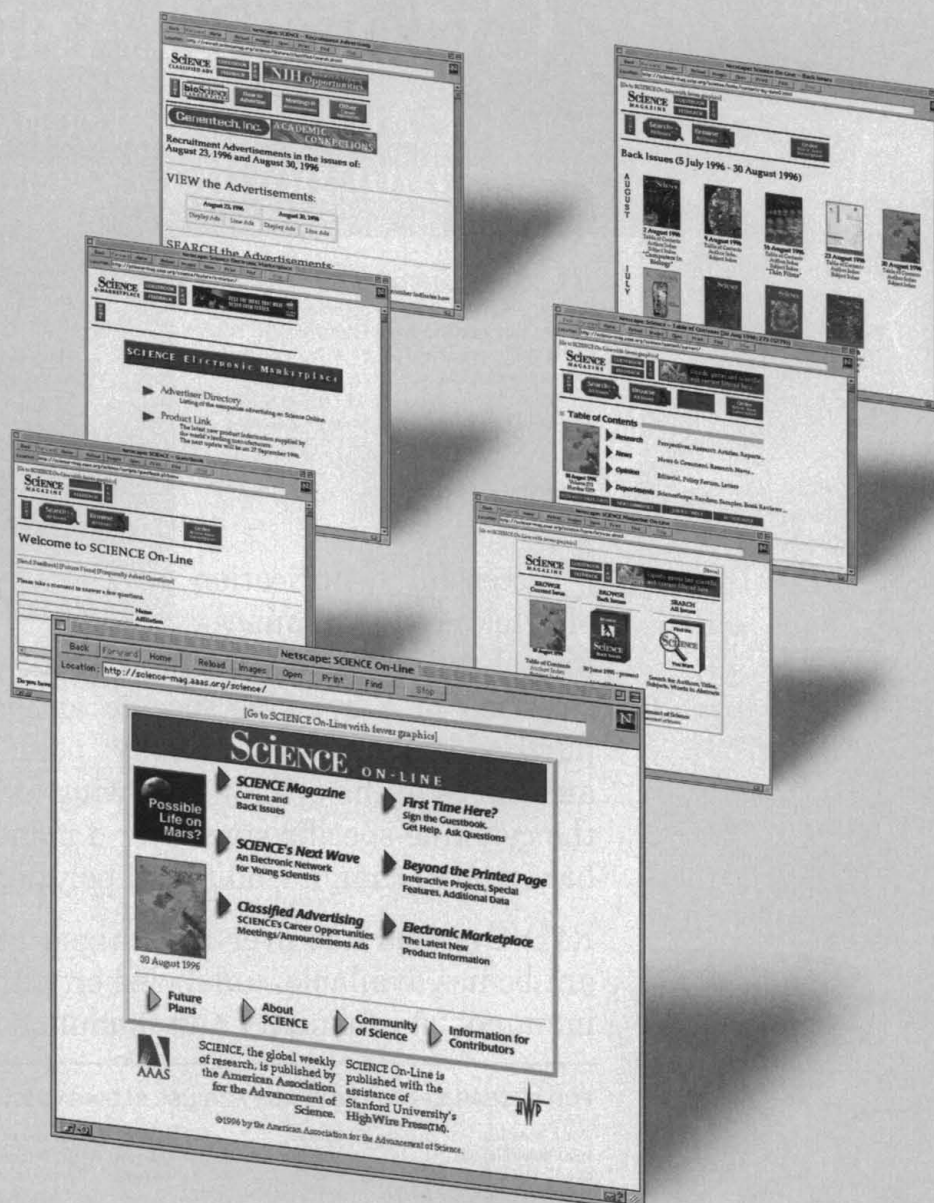
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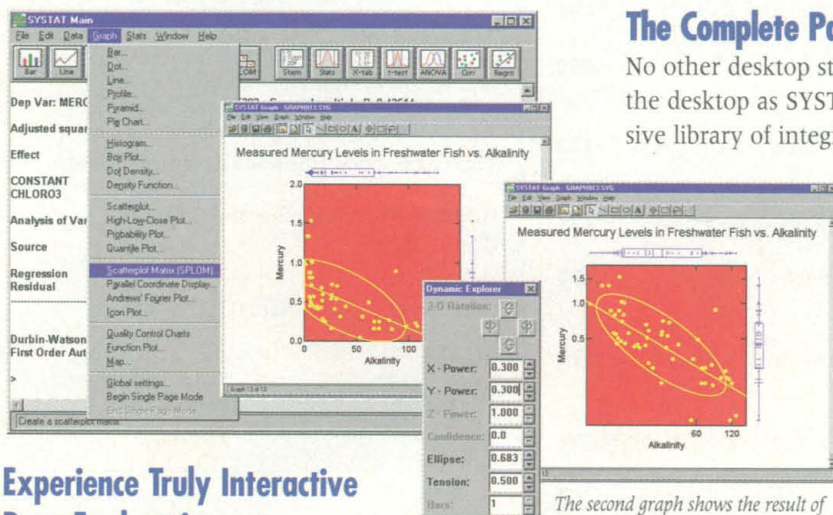


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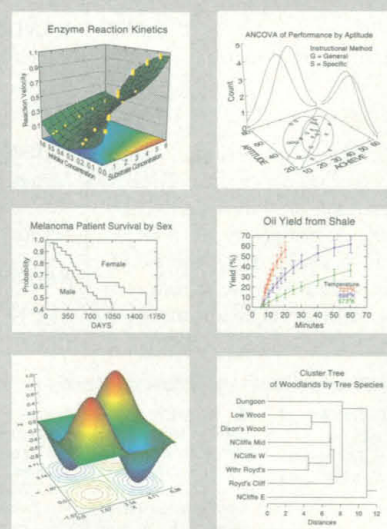
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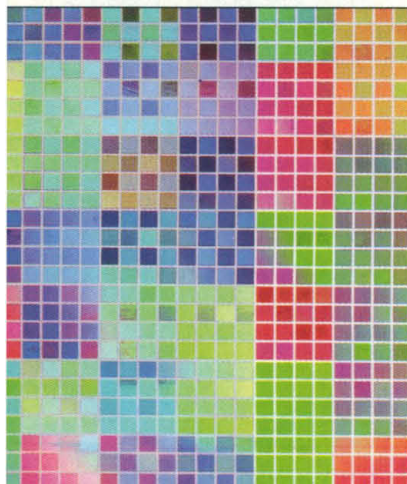
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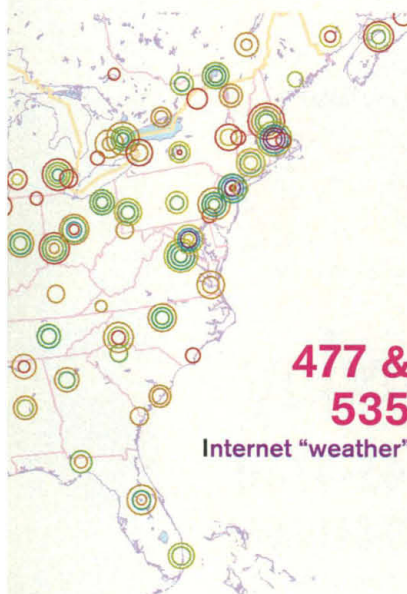
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COVER

Humankind casts a large shadow over the whole planet, with the structure and function of virtually every ecosystem being affected by pervasive human activity. The special section beginning on page 485 pulls together our current scientific understanding of the topic and

examines science-led measures to optimize resource management and protect the environment. Also see the related Editorial on page 457. [Photo illustration: Tracy Keaton Drew]



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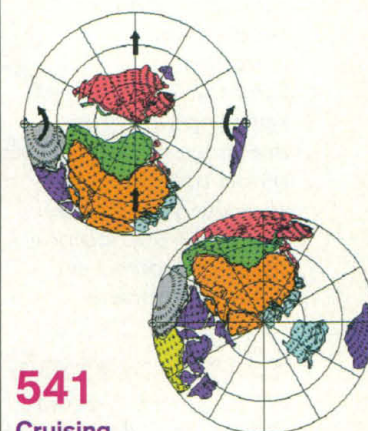
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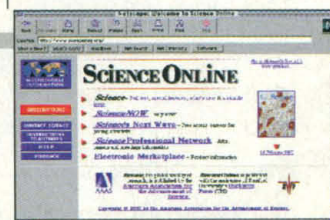
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Cruising continents in the Cambrian

Indicates accompanying feature

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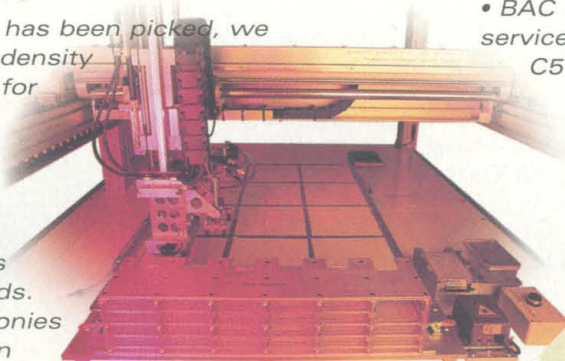
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Cosmic markings

Records of the past abundance of cosmogenic nuclides can be used to infer the history of the sun and geodynamo and are necessary to use cosmogenic nuclides, such as carbon-14, for dating, as discussed in a Perspective by Bard (p. 532). Plummer *et al.* (p. 538) infer the production history of one cosmogenic isotope, chlorine-36, over the past 40,000 years from chlorine in rat urine preserved in pack rat middens. The middens provide a useful record of production at low latitudes and may imply that production rates decreased abruptly at the end of the Pleistocene.

Supercharged plates

The beginning of the Cambrian, about 540 million years ago, was a time when animal life seems to have exploded, perhaps associated with or following changes in the composition of Earth's atmosphere and oceans. Kirschvink *et al.* (p. 541) compiled paleomagnetic data from several continents and suggest that this was also an unusual time for plate tectonics. The data imply that all of the major continental plates rotated and moved rapidly during the Early and Middle Cambrian. For example, Australia evidently traversed about 90 degrees in latitude within 30 million years. The authors suggest that the motion can be explained by rapid rotation of Earth's mantle and lithosphere.

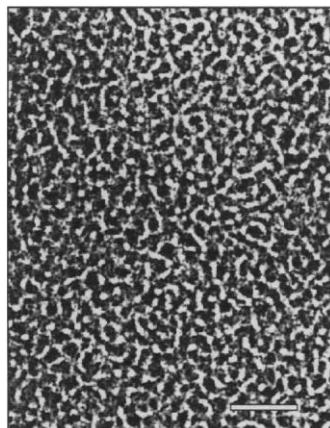
Pores to order

Mesoporous silicate materials contain networks of channels with widths on the nanometer scale. McGrath *et al.* (p. 552) show how to tune the channel diameters over a wide range by using the lyotropic L_3 phase as the template. The L_3 phase is a multiply connected bilayer that divides water into two compartments, and its pore size varies

Gaining light with polymers

Photorefractive (PR) materials can perform two-beam coupling, in which the energy from one laser beam can be transferred to another. This process can result in an optical gain, so the material acts as an optical transistor. High gain coefficients are normally associated with inorganic PR materials, but Grunnet-Jepsen *et al.* (p. 549; see the Perspective by Anderson, p. 530) show that by stacking thin films of PR polymers on transparent electrodes, gain coefficients can exceed unity and be as high as five. They also constructed an optical cavity that allowed a single beam to produce spontaneous oscillations. This configuration can be used to produce "time-reversed" images, which could be run back through an optical train to eliminate any introduced distortions.

continuously with surfactant concentration. The materials formed large, optically transparent monoliths, and the surfac-



tant does not have to be removed to access the pores. Possible applications include filters, optical materials, and nanocomposites.

Tragedy of the electronic commons

Internet users are not directly charged for the amount of time or bandwidth they consume on the net. This situation can lead to greedy behavior and excessive demand for Web resources. Cases of extreme localized congestion have been observed, so called "packet storms," in which Internet nodes are inundated with streams of data. Huberman and Lukose (p. 535; see the news story by Seife, p. 477) report observations of congestion and model the properties of this

congestion. Such modeling may help in deciding how best to allocate resources to accomplish load leveling and bandwidth management.

Delayed start

The most common motor neuron disease in people is amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. In a mouse model of the human disease, in which the mice contain a mutation in copper-zinc superoxide dismutase, Kostic *et al.* (p. 559) tried to prevent the loss of motor neurons by crossing the mice with animals that overexpress the proto-oncogene *bcl-2*. The onset of the disease was delayed in offspring, and neurodegeneration was less. These results suggest that therapeutic approaches that interfere with cell death pathways may be useful in ameliorating the symptoms associated with ALS.

Insulin A,B,C's

Human insulin is synthesized as part of a larger proinsulin molecule that consists of an A chain and a B chain linked by a connecting peptide (C-peptide). The C-peptide was thought to have little if any biological activity. Ido *et al.* (p. 563) show that C-peptide can prevent or attenuate vascular and neural dysfunction in diabetic rats. These actions

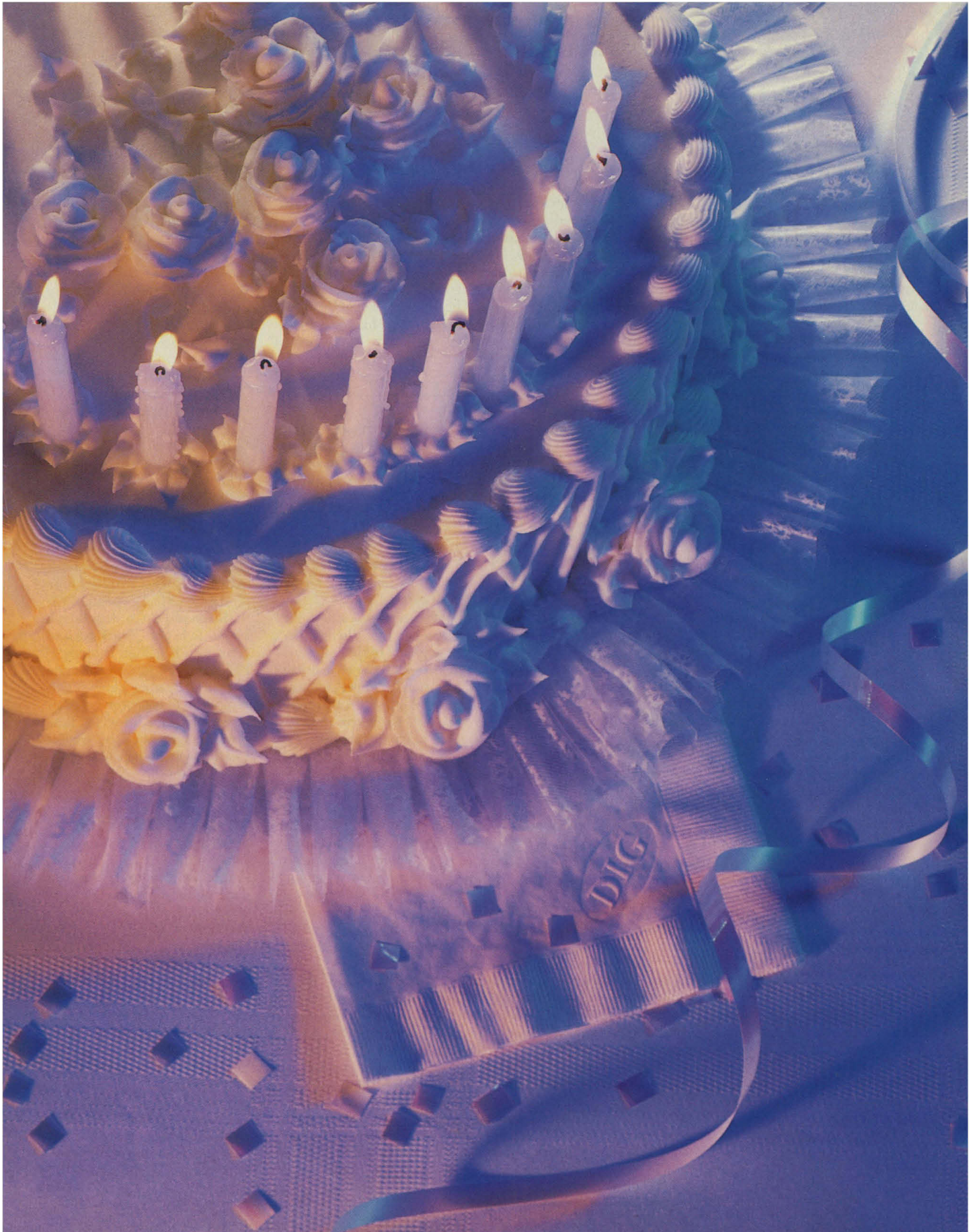
appear to be mediated by non-chiral interactions (L and D amino acids are equipotent) and therefore do not involve receptors or binding sites. The ability of C-peptide to correct the abnormalities in diabetes suggests that the peptide may be used in the treatment of diabetic complications.

Doubly controlling

The proto-oncogene protein kinase B (PKB) participates in cellular signaling through growth factor receptors. PKB is known to be activated as a consequence of increased activity of the phosphoinositide 3-kinase (PI3K), but how it was regulated has been unclear. Stokoe *et al.* (p. 567) report that the product of the PI3K enzyme—phosphatidylinositol 3,4,5 trisphosphate [PtdIns(3,4,5)P₃]-regulates PKB in two ways. First, it stimulates a kinase that phosphorylates and activates PKB; then it binds to PKB to make a suitable substrate for the activating kinase. This complicated regulatory mechanism presumably provides close control of PKB at the correct location within the cell.

Hepatitis C clone

Hepatitis C virus (HCV), which can cause hepatitis and cirrhosis, infects more than 1 percent of the world's population. Studies of this virus have been hampered by the need to rely on patient samples, which are heterogeneous and thus cannot be used for genetic studies. Kolykhalov *et al.* (p. 570) have identified a consensus sequence representing a full-length clone of the virus that is infectious and disease-causing in the chimpanzee. No additional sequences or factors were required for infectivity. The ability to infect with molecularly defined material will facilitate studies of viral variation and immune selection.




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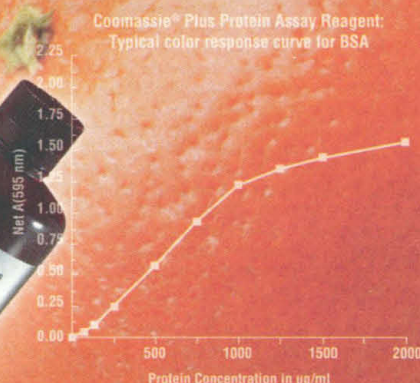
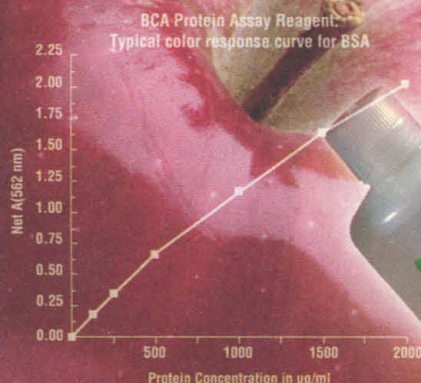
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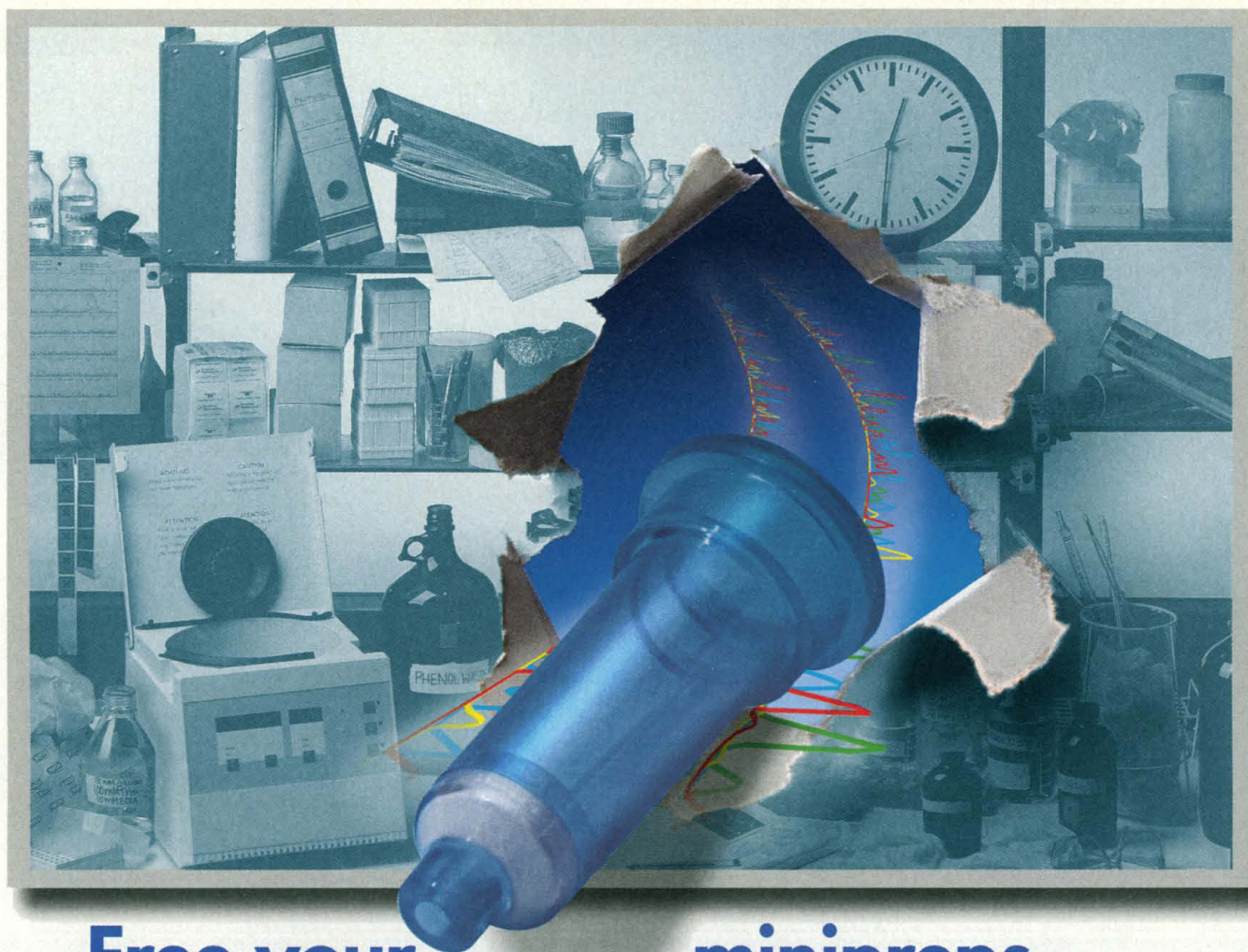


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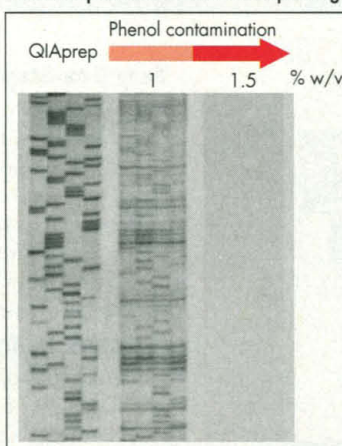
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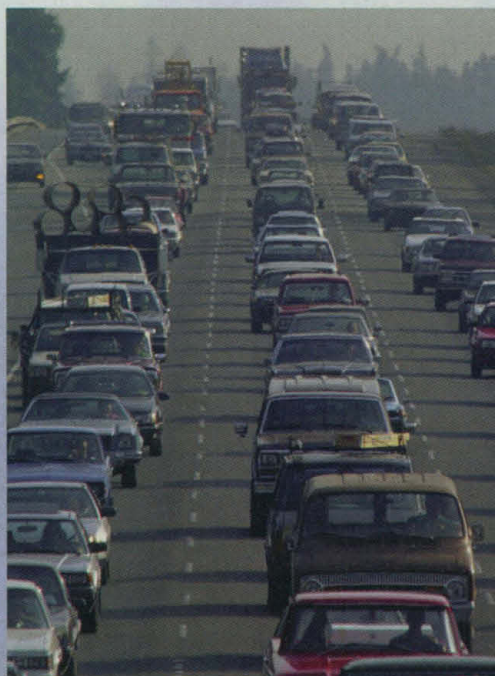
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Pre-Congress Workshop on Peer Review

One full day of
interactive teaching
on attracting,
commissioning,
selecting, and
improving papers
for publication in
biomedical
journals.

Space for this
workshop is
limited.

**Thursday-Saturday
September 18-20**

Third International Congress on Peer Review in Biomedical Publication

Following the success of 2 previous
Congresses, we aim to further the
science of editorial peer review
through this third congress. More
than 80 reports of new research will
be presented on all aspects of peer
review and scientific publication.

**Friday Evening
September 19**

Inaugural Meeting of the World
Association of Medical Editors

**Sunday
September 21**

Conference on Peer Review and Global Communications

Plenary sessions
on how digital
technologies are
affecting peer
review, scientific
publication, and
the worldwide
dissemination of
biomedical
information.

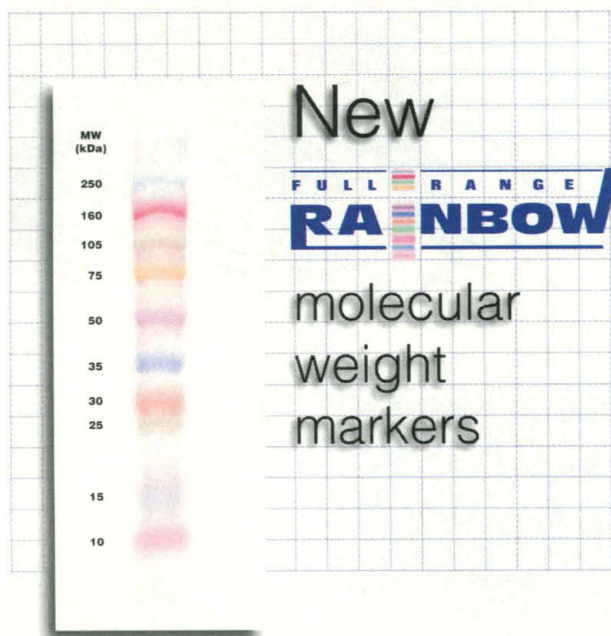
For more information, contact Annette Flanagan, JAMA, 515 N State St, Chicago, IL 60610 USA
Tel: 312-464-2432; Fax: 312-464-5824; E-mail: jama-peer@ama-assn.org

VISIT THE CONGRESS WEB SITE AT <http://www.ama-assn.org/peer>

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