



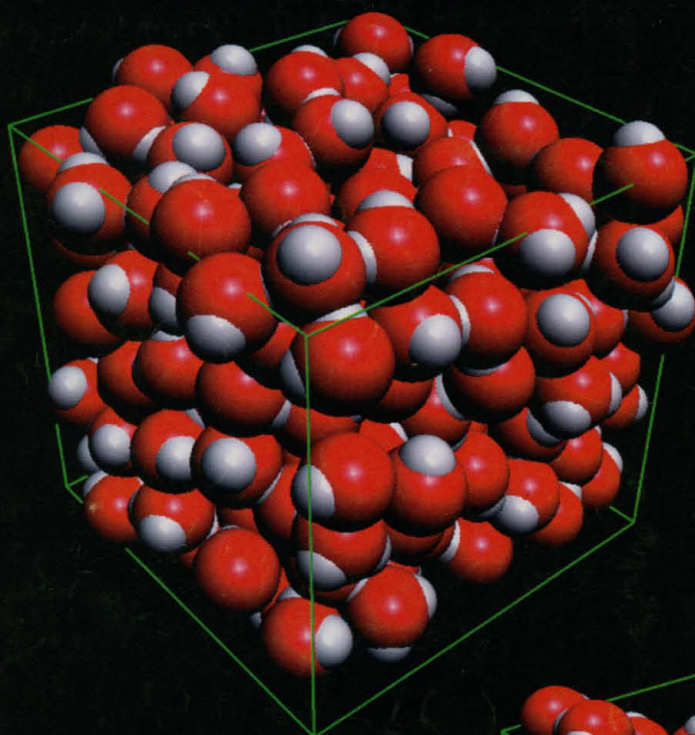
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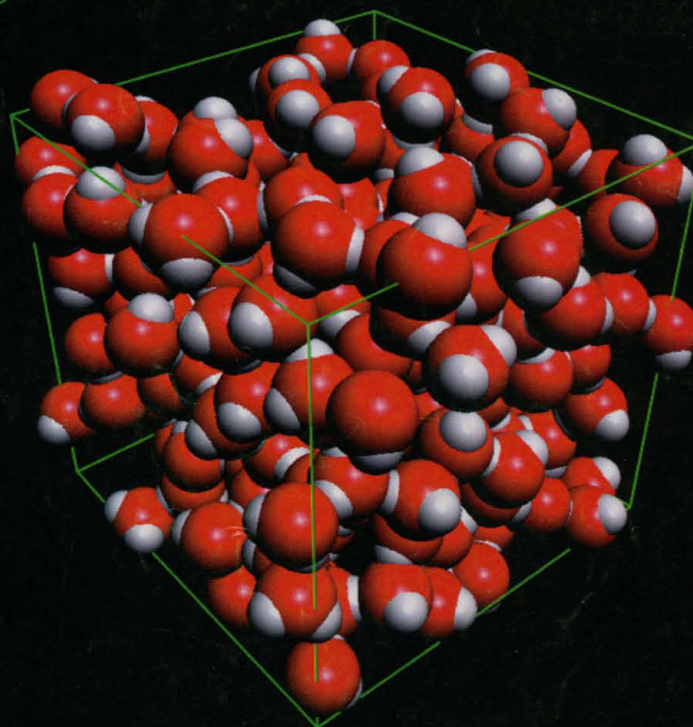
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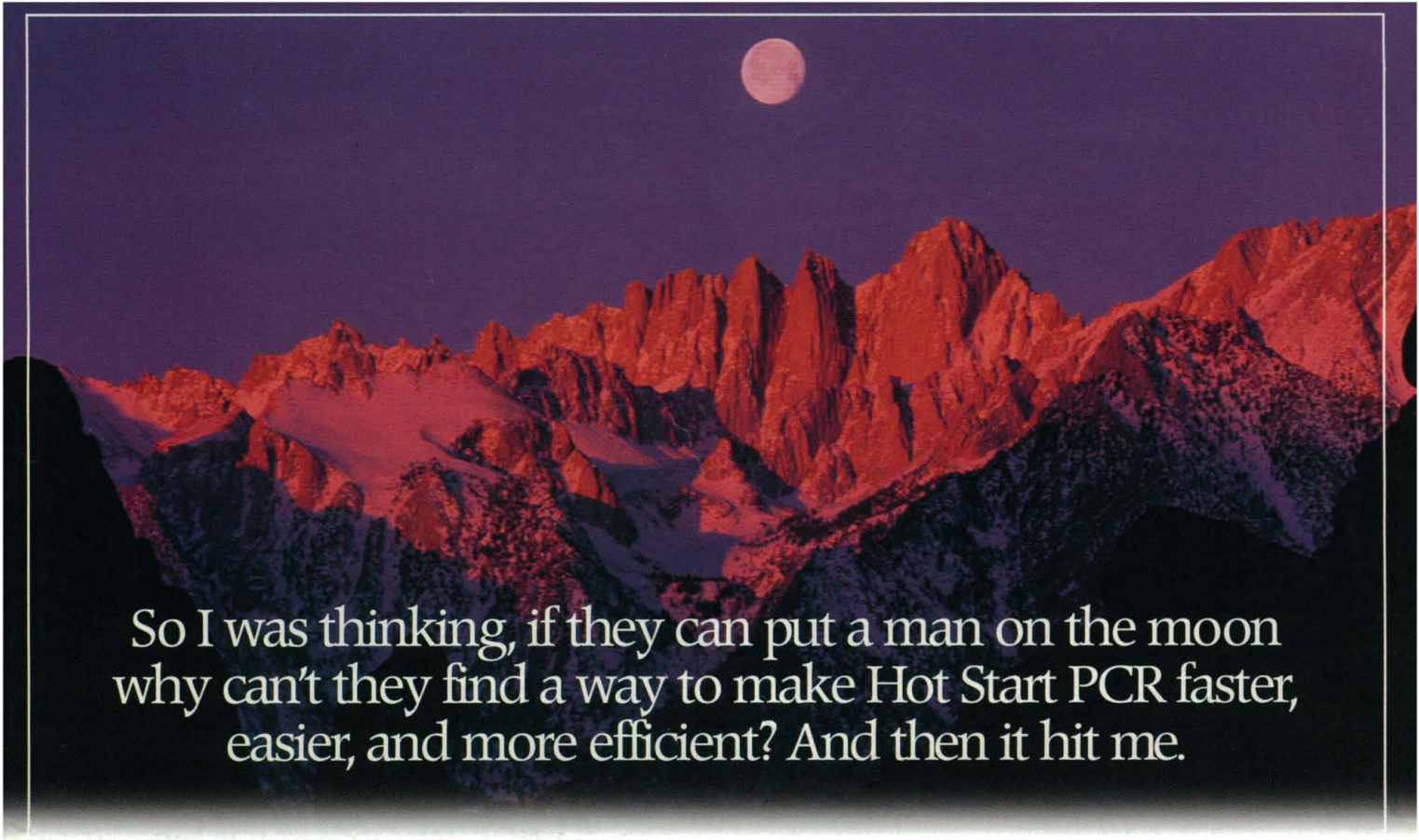
VOL. 267 • PAGES 1877-2056



Glasses & Amorphous Materials

Frontiers in Materials Science





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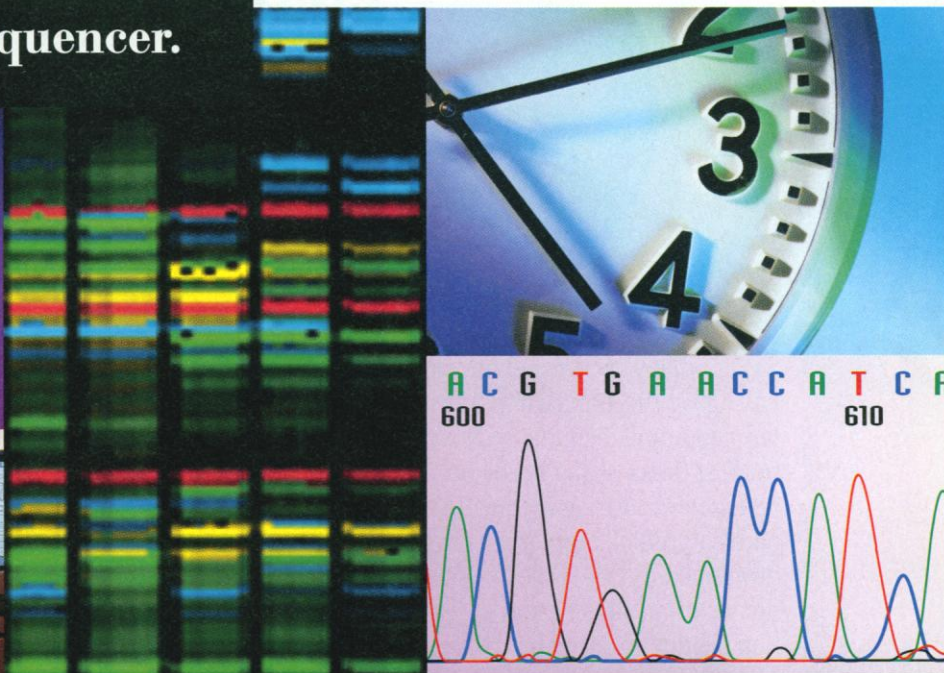
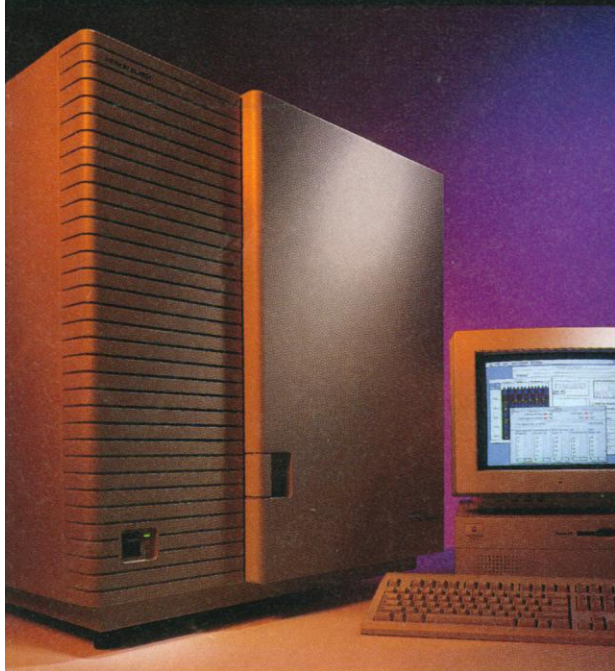
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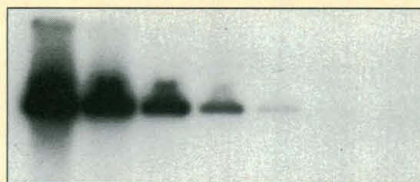
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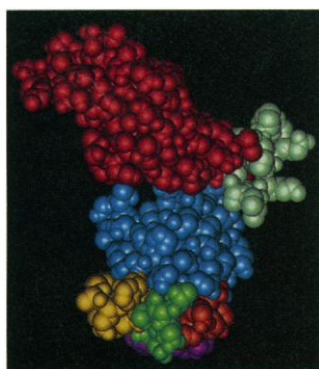
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1896

The biology of learning disabilities



1906 & 1984

T cell receptor β chain

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Patent Award Stirs a Controversy 1899

Commotion Over *E. coli* Project 1899

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Architectures of Class-Defining and Specific Domains of Glutamyl-tRNA Synthetase 1958
O. Nureki, D. G. Vassilyev, K. Katayanagi, T. Shimizu, S.-i. Sekine, T. Kigawa, T. Miyazawa, S. Yokoyama, K. Morikawa

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COVER

Molecular dynamics representations of two low-temperature amorphous states of water, which are characterized by different, incompatible short-range orderings of the molecules. The white spheres represent hydrogen and the red spheres oxygen. Polyamorphism, important in biopolymers, is one of the most recently

recognized features of the glassy state. See page 1939. Amorphous materials and glasses are the focus of a special section on Materials Science, which begins on page 1918. [Images: P. H. Poole, Dalhousie University, Halifax, Nova Scotia]



A Topographic View of Supercooled Liquids and Glass Formation 1935
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Physical Aging in Polymer Glasses 1945
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Metallic Glasses 1947
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Spatially Resolved Visible Luminescence of Self-Assembled Semiconductor Quantum Dots 1966
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Design and Application of Electron-Transporting Organic Materials 1969
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High-Pressure Elasticity of Iron and Anisotropy of Earth's Inner Core 1972
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Biogeological Mineralization in Deep-Sea Hydrothermal Deposits 1975
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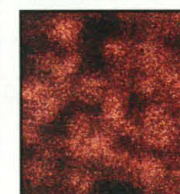
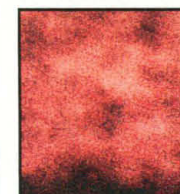
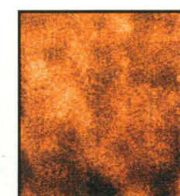
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Requirement for Phosphatidylinositol-3 Kinase in the Prevention of Apoptosis by Nerve Growth Factor 2003
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1966

Illuminating quantum dots

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Alike but not alike

Faithful translation of genetic information relies on the specificity with which the 20 aminoacyl-tRNA synthetases recognize and join their amino acids to tRNA. Nureki *et al.* (p. 1958) have resolved the crystal structure of glutamyl synthetase (GluRS) from the thermophilic archaeobacterium *Thermus thermophilus*. The amino-terminal half of this GluRS resembles that of the *Escherichia coli* glutaminyl-tRNA synthetase (GlnRS), the similarities occurring in domains that participate in the recognition of the D and acceptor stems of the glutamyl-tRNA. In contrast, the carboxyl-terminal half has a β -barrel structure in GlnRS but for GluRS has an α -helical structure, which was found to be important in anticodon recognition.

Stepping lightly

Quantum dots are small structures in which electrons can be confined in three dimensions much as they are in atoms: The electrons reside in discrete energy levels, and transitions between levels can lead to emission of light. Leon *et al.* (p. 1966) report the epitaxial fabrication and imaging of indium-aluminum-arsenide dots that luminesce at red wavelengths around 6600 angstroms. Spectroscopic analysis shows the discrete density of states of the quantum dots. Next steps may include fabrication of ordered 2D and 3D arrays of the tiny emitters.

Inner direction

Recent seismic data have suggested that Earth's solid iron inner core is seismically anisotropic. The origin and nature of the anisotropy—presumably re-

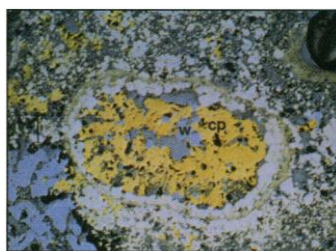
A partly open, partly shut case

The calcium release channels (ryanodine receptors, RyRs) on the sarcoplasmic reticulum open in response to an increased external concentration of Ca^{2+} , but then close or inactivate as they adapt to the higher concentration. The cycle repeats whenever Ca^{2+} concentration is increased. Cheng *et al.* (p. 2009) and Sachs *et al.* (p. 2010) offer models to explain these adaptative properties, while Valdivia *et al.* (p. 1997) provide new evidence for their physiological relevance. They show that the temporal pattern of cardiac RyR adaptation in vitro can approximate what occurs in vivo, and that phosphorylation of the RyR alters both its sensitivity to Ca^{2+} and its adaptation kinetics. Other signals within the cell can modulate the properties of the RyR, influencing the timing of Ca^{2+} release.

lated to preferential orientation of iron crystals—is unclear. Stixrude and Cohen (p. 1972) predict from theoretical arguments elastic constants for iron at the density of the inner core, and use these constants in models that account for the seismic anisotropy of the core. In a news story, Kerr (p. 1910) discusses how these results may relate to models of the geodynamo.

Formed by worms

The black smoker vents along mid-ocean ridges mark areas of active venting of hot hydrothermal fluids and extensive sulfide mineralization. Nutrients at these sites support a distinctive marine community, in-



cluding tube worms, and Cook and Stakes (p. 1975) show, through oriented drill cores into active vents, that the biologic tube structures exert a strong influence on the way mineralization proceeds at the vents.

Trapped atmosphere

Meteorites of the SNC (shergottite-nakhlite-chassignite) class are thought to be fragments of the surface of Mars. Marti *et al.* (p. 1981) found pockets of shock-melted glass in the shergottite meteorite Zagami, and determine that isotopic ratios of nitrogen and noble gases in them resemble ratios found by the Viking spacecraft for the martian atmosphere. In combination with earlier findings in another shergottite, these results point toward a systematic martian signature in all the SNC meteorites.

Recognizing structure

T cell receptors (TCRs) recognize antigens in the form of peptides bound to major histocompatibility complex (MHC) molecules. The crystal structure of a TCR β chain reported by Bentley *et al.* (p. 1984; see also news by O'Brien, p. 1906) offers some clues into how this recognition occurs. Conformational restrictions in the complementarity-determining regions (CDRs) on the variable part of the β chain appear to support models whereby the CDRs make contact with α -helical parts of the MHC molecules, and tight linkage between the constant

and variable regions indicate a fairly rigid structure that might facilitate signal transduction by responding to structural changes initiated by the TCR binding to the peptide-MHC complex.

ICE minus

Interleukin- 1β (IL- 1β), a key cytokine in inflammatory response, is generated from an inactive precursor by IL- 1β converting enzyme (ICE). Kuida *et al.* (p. 2000) created mice lacking the gene for ICE expression. The mice developed normally, but their monocytes failed to release IL- 1β when stimulated by the bacterial endotoxin lipopolysaccharide. Thymocytes from the mice were triggered into apoptosis by ionizing radiation and glucocorticoid, but stimulation by Fas antigen failed to induce the normal apoptotic response. These findings support the idea that apoptosis proceeds through many pathways.

Hearing the high notes

In the mammalian ear, outer hair cells respond to acoustic stimuli and transmit signals to auditory centers in the brain. Only a small number of the outer hair cells are activated by a particular frequency, and the response is amplified and sharpened by cochlear amplification, in which the hair cell shape changes in response to signals of the appropriate frequency. Dallos and Evans (p. 2006) propose a model in which cochlear amplification at high frequencies is attributed to extracellular potential gradients across the hair cell, explaining how shape-change behavior persists at high frequencies despite severe attenuation of the response by the cell membrane.

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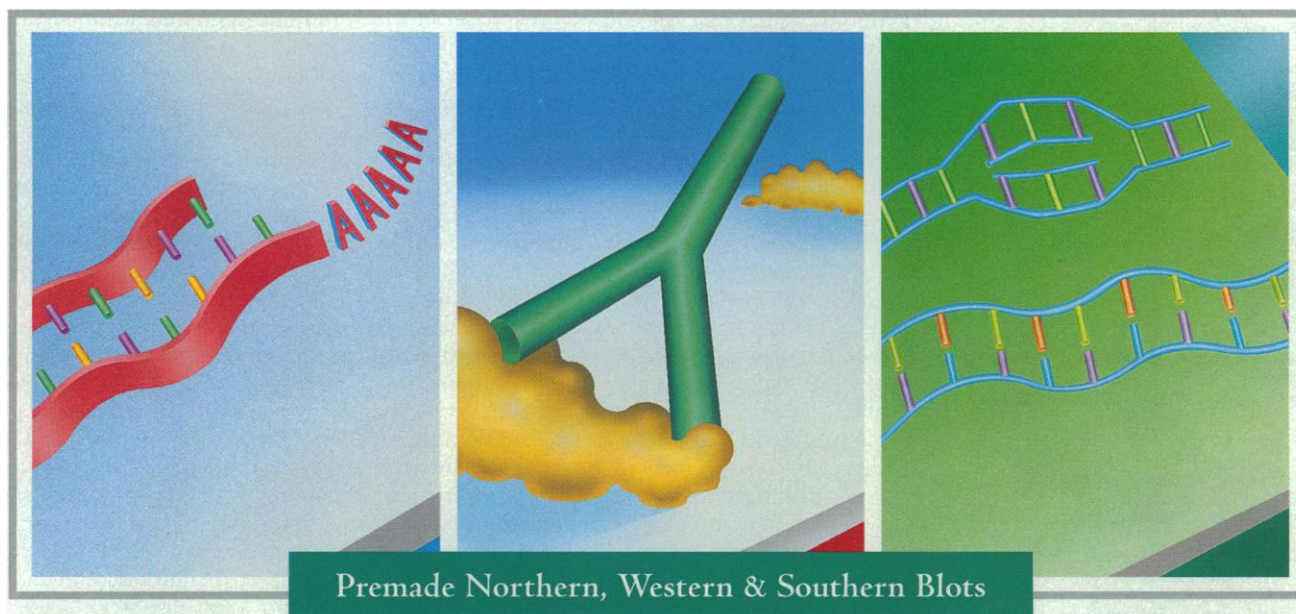
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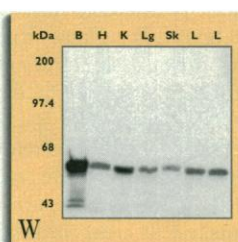
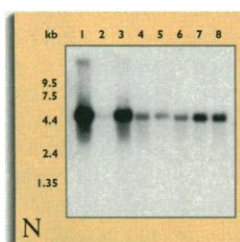
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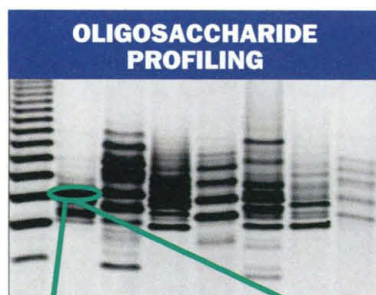
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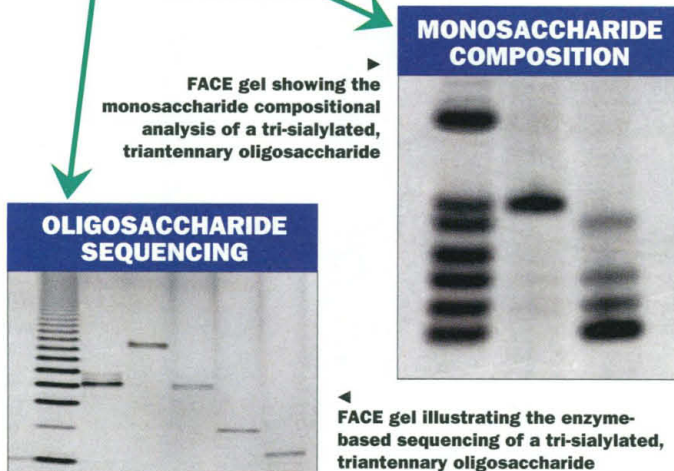
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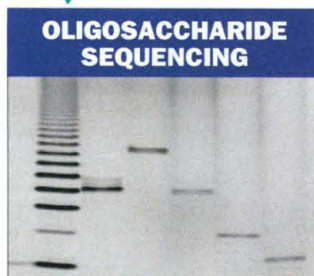
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FACE gel profile of N-linked oligosaccharides released from a number of different glycoproteins



FACE gel showing the monosaccharide compositional analysis of a tri-sialylated, triantennary oligosaccharide



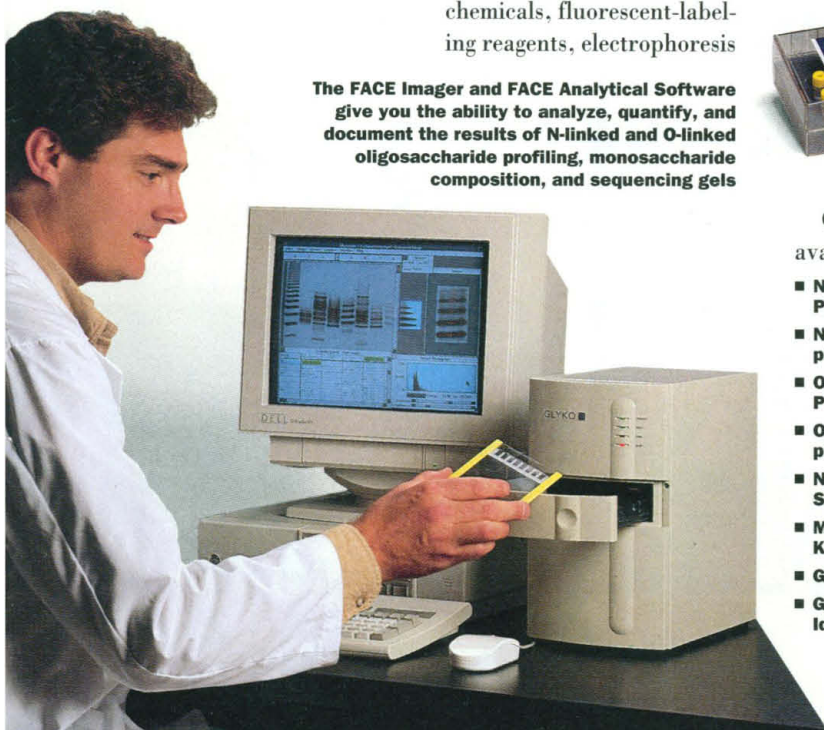
FACE gel illustrating the enzyme-based sequencing of a tri-sialylated, triantennary oligosaccharide

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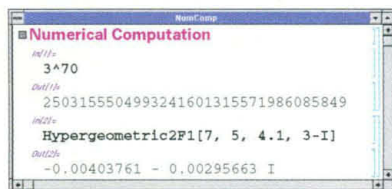
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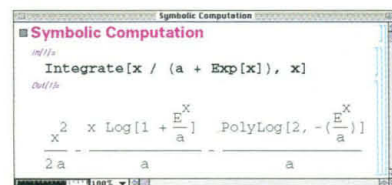
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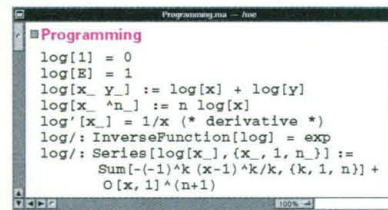


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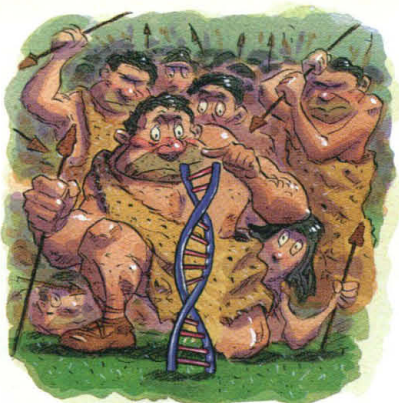
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Multiprobe Fluorescence Technique Finds Increasing Application in Research

Fluorescence *in situ* Hybridization (FISH), first introduced in the late 1970's, has played an important role in identifying chromosomes, detecting chromosomal abnormalities, and determining the number, size and location of specific DNA sequences in mammalian cells. Today, thanks to advances in probe technology and fluorescence microscopes, FISH is becoming increasingly important as a research tool and may eventually become a standard clinical diagnostic technique in areas such as cytogenetics, prenatal diagnosis and tumor biology.

As biomedical researchers continue to discover more and more human diseases with their causes rooted in genetic abnormalities, Fluorescence *in situ* Hybridization (FISH) has become an increasingly important tool for the analysis of genetic cellular characteristics. This highly sensitive technique is fast, easy to interpret, and yields statistically relevant data. It can be used to identify both normal and abnormal chromosomes and to determine the presence and location of specific genomic sequences with unprecedented detail and clarity.

In FISH, the hybridization reaction biochemically targets gene sequences so their location and size can be determined using fluorescence microscopy. DNA from a chromosome-specific probe is labeled by chemically modifying it to insert a reporter molecule that can be

observed via fluorescence. The labeled DNA is then hybridized to metaphase chromosomes or interphase nuclei for which chromosome-specific staining is desired. The technique is sufficiently sensitive to detect and characterize both numerical and structural aberrations, making it valuable for detection of a number of genetic disorders.

Multicolor probes permit simultaneous analyses

The FISH technique depends on the availability of probes that bind specifically to regions of genetic or cytogenetic interest. It is a powerful research tool because multicolor probe labeling permits simultaneous use of several different probes inside a single cell, allowing the researcher to analyze multiple genetic sequences and check for several genetic disorders at the same time.

In clinical studies, multicolor FISH analyses have shown striking differences in chromosome frequency in interphase cells from solid tumors, both from the same tumor and from tumors of different patients. Several of these studies are focused on relating tumor aggressiveness to specific chromosomal sequences to improve tumor prognosis beyond what is possible today.

New technology for new techniques

As FISH and other direct probe techniques have emerged, the need for more sophisticated fluorescence microscope systems has increased dramatically. Since individual sites on a chromosome are so minute, high numerical aperture, high transmission objectives are needed

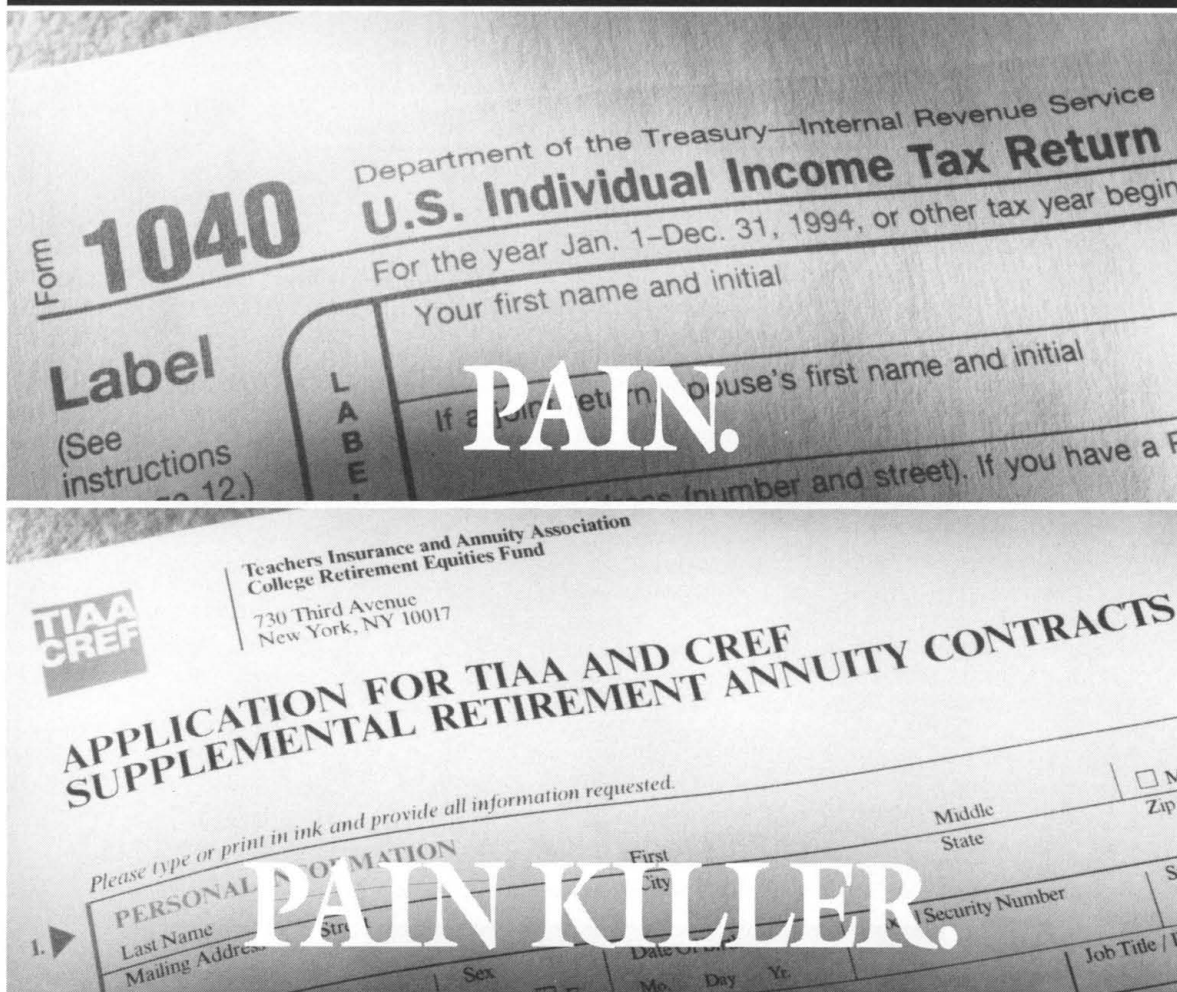
to image them. And simultaneous use of 2, 3 or 4 fluorescent probes necessitates multiple filters to image multiple sites.

In response to these needs, Nikon has introduced the new Quadfluor Epi-Fluorescence Illumination System, along with a series of higher numerical aperture objectives with higher transmission characteristics.

The new CF Plan Fluor objectives feature new optical cements and high transmission coatings to permit broader wavelength ranges (UV — Deep Red) and brighter images that are color aberration free with extremely high contrast and low background autofluorescence. The Quadfluor Illuminator offers expanded filter cube capacity and enhanced filter designs with even better signal to noise ratio performance. It accepts up to four filter cubes at once to separate different signals, or a multiband filter cube to image several fluorochromes simultaneously. The filters can be rapidly switched via an extremely smooth yet very precise linear slider, allowing excellent image registration and making the Quadfluor Illuminator ideal for today's multi-probe techniques.

For more information on Nikon's new Quadfluor Epi-Fluorescence Illumination System, call Nikon at (516) 547-8567, fax us at (516) 547-0306 or contact us on the Internet at nikonbio@aol.com.

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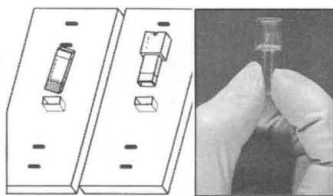
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Combined Radioisotope Detector

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Mutation Detection Agarose

MetaPhor XR agarose, which forms flexible gels for high resolution of small DNA conformers of <1 kb, is useful in mutation detection. This agarose, compatible with most horizontal and vertical electrophoretic equipment, combines the convenience and ease of agarose with the resolving power of polyacrylamide. **FMC BioProducts.** Circle 141.

Rapid DNA Ligation Kit

The Rapid DNA Ligation Kit can ligate blunt-ended or sticky-ended DNA fragments in 5 min at room temperature, reducing the cloning and transformation

procedure to 1 day and eliminating the need for special water baths. Extensive function tests and quality control procedures performed on each lot of kits guarantee optimal transformation efficiencies and ensure the validity of results. **Boehringer Mannheim.** Circle 142.

Hot Start PCR Beads

HotWax Mg^{2+} Beads are designed to make hot start polymerase chain reaction (PCR) easier, faster, and more efficient. The specially prepared wax beads contain MgCl_2 , which is released into the reaction when the wax bead melts during the first denaturation step. This simple system eliminates many of the manipulations required for a manual hot start. In addition, the melted bead forms an evaporation barrier making an oil overlay unnecessary. **Invitrogen.** Circle 143.

Streptavidin-Coated Plate

A streptavidin-coated, thin-wall polycarbonate plate for use in thermocyclers makes possible the simultaneous amplification and capture of the amplified product. The captured product can then be quantitated in a simple hybridization step. The immobilized strand can also be used as a template for sequencing. These plates make use of a special grade of streptavidin that is stable at the high temperatures of thermocyclers. The streptavidin is covalently attached to the surface through a proprietary chemistry that provides exceptional uniformity, extended shelf life, and maximum stability during high stringency washes. The plates are available to fit most thermocyclers. **Xenopore.** Circle 144.

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Sequence Assembly Software

AutoAssembler software automatically performs labor-intensive DNA sequence assembly tasks. Designed for Macintosh computers, AutoAssembler features automatic, batch-mode sequence clean-up and feature identification, automatic assembly of sequences, and easy viewing and editing of results. Designed for researchers performing small-to medium-size sequencing projects, the software can be easily upgraded for large-scale projects. **Perkin-Elmer.** Circle 145.

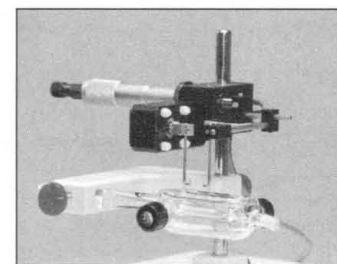
Lead Generation Software

Fast Clustering software can reduce the need for random screening of candidates for new drugs and conserve sample stocks. Many pharmaceutical organizations store vast quantities of structural data in chemical databases, including compounds available for testing. Through a novel algorithm, Fast Clustering can group databases in excess of 50,000 structures into subsets of similar compounds. Representative members of these subsets are then easily extracted to provide a further subset reflecting the diversity of the database screening. The algorithm groups molecules in the three-dimensional database based on the similarity of their pharmacophores. **Chemical Design.** Circle 146.

Micro Perfusion System

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lar design allows the micromanipulator, transducer, and tissue segment to be mounted from one support post while still having several axes of adjustment. The myograph assembly can be used easily with dissecting and inverted microscopes. The minimal spatial arrangement leaves ample area for other instruments such as



electrodes to measure action potential. **Kent Scientific.** Circle 147.

Literature

Fragment Analysis Software is a four-page brochure on this program for analyzing one-dimensional DNA and protein gel electrophoresis patterns. The brochure is illustrated with screen graphics that show how the software performs lane and band finding; size, mass, and isoelectric point calculation; and other restriction fragment length polymorphism analysis. **Molecular Dynamics.** Circle 148.

SynChroNotes is a technical newsletter. The most recent edition contains an article, "Hydrophobic Interaction—The 'Other' Hydrophobic Chromatography." **Synchrom.** Circle 149.

The Informed Choice for Protein Labelling and Detection is a 36-page catalog highlighting an extensive range of products, both radioactive and nonradioactive. Sections include Western blotting, total protein detection, and immunocytochemistry; cellular protein labeling; post-translational modification; and in vitro translation systems. **Amersham International.** Circle 150.