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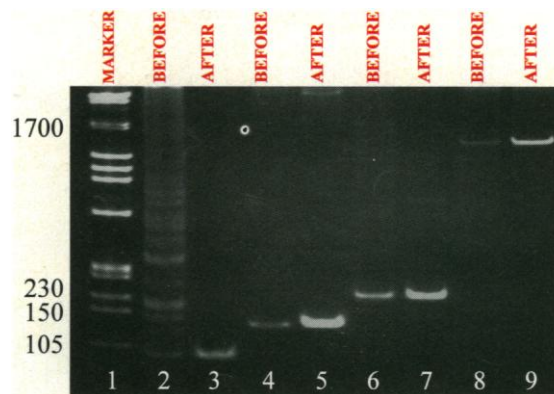
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PCR primers and DNA templates vary in purity, GC content and amount of secondary structure. In addition, DNA may have chemical modifications, nucleic acid analogs or other characteristics that can inhibit amplification efficiency. To improve the yield and specificity of the desired PCR products, the buffer components of a specific amplification reaction can be modified. But the process is tedious and time-consuming.

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*The PCR process is covered by patents owned by Hoffmann-La Roche Inc. Use of the PCR process requires a license.

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832, 850 & 914

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COVER

Tree rings and fire scars (dark areas) of a giant sequoia from the Sierra Nevada, California. Episodic fires that burned around the base of sequoias caused scars that were subsequently healed over by tree-ring growth. Composite records (spanning 2000 years) from many

fire-scarred trees in five sequoia groves document long-term changes in fire frequency and size associated with precipitation and temperature fluctuations. See page 885. [Photo: A. C. Caprio]



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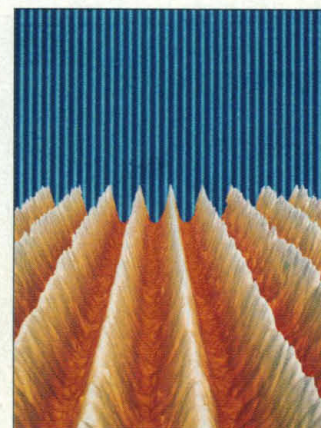
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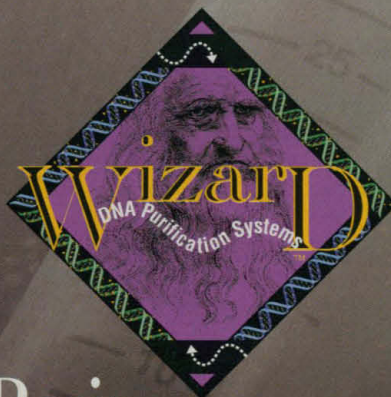
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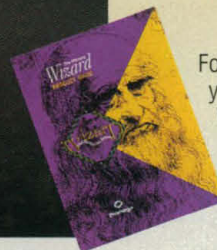
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Staying faithful

Every time RNA polymerase adds a nucleotide to a growing messenger RNA chain, the possibility for making an error in transcription arises. Erie *et al.* (p. 867) applied pre-steady state kinetics methods to a fully functional *Escherichia coli* RNA polymerase and found that the transcription complex can become "kinetically trapped" in alternative conformations when the appropriate nucleotide is absent or if the 3' terminal residue is incorrectly matched. They also show that the transcription factor GreA increases fidelity by preferentially cleaving elongation complexes that are an inactivated state.

Within the fold

Exchange of the amide proton of an amino acid residue can occur in a protein if that residue is exposed to solvent; thus mass spectrometry (MS) or nuclear magnetic resonance (NMR) spectroscopy or both can be used to follow changes in the folding of a protein (see the perspective by Englander, p. 848). Insights into protein folding gained with these methods are presented in a research article and two reports. Mayo and Baldwin (p. 873) used NMR methods to show that exchange of amide protons in ribonuclease A induced by a low concentration of a denaturant, guanidinium chloride, can occur through partial unfolding or through a "limited structural fluctuation." Jennings and Wright (p. 892) used NMR and circular dichroism methods to show that a molten globule intermediate that forms early in the kinetic folding pathway of apomyoglobin is similar to the equilibrium molten globule. Miranker *et al.* (p. 896) used MS methods to resolve a num-

New avenues for T cell costimulation

Proliferation of activated T cells requires costimulation by antigen-presenting cells (APCs), which include B cells; this process has been understood in terms of the pathway in which the B7 ligand on the APC surface binds to CD28 and CTLA-4 receptors on the T cell. Three reports show that molecules other than B7 participate in costimulation (see news story by Cohen, p. 844). Hathcock *et al.* (p. 905) screened for monoclonal antibodies that inhibited T cell activation and identified a cell-surface molecule, GL1, on activated B cells that is a CTLA-4 ligand. Freeman *et al.* (p. 907) found that mice that do not express B7 still exhibited a costimulatory response and that activated B cells express CTLA-4 ligands other than B7. Freeman *et al.* (p. 909) present the cloning of a second CD28-CTLA-4 ligand, which they term B7-2. This ligand is expressed in unstimulated B cells and may represent a critical early signal in costimulation.

ber of transient folding states of lysozyme and combined these results with data from NMR studies to map out protein folding pathways.

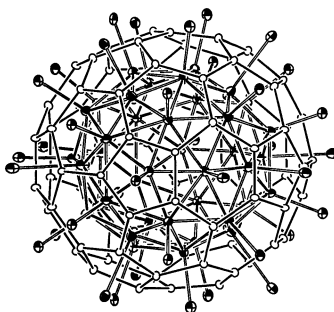
Building with lasers

Stable nanometer-scale structures have been fabricated by using lasers to direct the deposition of metal atoms. McClelland *et al.* (p. 877) used the strong oscillating electric field present in the standing wave set up by an intense laser beam as a template. Chromium atoms in a gas-phase atomic beam interact with the electric field and accumulate in areas of maximum field strength. The atoms are cooled by the continuous absorption and emission of photons and eventually form metallic structures on a silicon substrate. The parallel structures formed are spaced apart by one-half of the wavelength of the laser light.

Metallic buckyballs

Carbonaceous fullerenes now have some metallic cousins based on indium. Sevov and Corbett (p. 880) synthesized metal-

lic analogs, such as $\text{Na}_{96}\text{In}_{97}\text{Z}_2$, where Z is nickel, palladium, or platinum, by slowly cooling elemental mixtures that were



heated to 700°C. These materials contain nested clusters. For example, an outer cage of In_{74} has its inner faces capped by a Na_{39} cluster, inside of which is a disordered In_{10}Z cluster; the sodium atoms screen the inner cluster from the charges of the outer cage.

Tales of fire

Giant sequoias on the western slope of the Sierra Nevada in central California can survive fire damage and thus provide a history of fire occurrence during the past 2000 years. Swetnam (p. 885; cover) analyzed the relation of fire damage in five separate groves to climate

changes. Synchronous occurrence of fires in these groves was inversely related to yearly fluctuations in precipitation and directly related to longer term (decade to century) variations in temperature.

Geyser model

What are the special conditions controlling the periodicity of geysers and their apparent sensitivity to seismic events? Ingebritsen and Rojstaczer (p. 889) use a numerical model to investigate the sensitivity of eruption frequency to variations in permeability and recharge within the geyser conduit. Analysis indicates that periodic eruptions can be produced for a conduit with a high permeability, such as a fracture zone, surrounded by rock with low permeability. A difference in permeability of three to four orders of magnitude seems to be required to produce geysering, and the eruption frequency scales with permeability. Strain-induced changes in permeability could thus easily affect frequency.

Well expressed

Toxoplasma gondii is an intracellular mammalian parasite and is a prevalent opportunistic pathogen in AIDS patients. Stable transformants that either express introduced genes or that have genes selectively inactivated would allow the molecular biology of this parasite to be explored. Kim *et al.* (p. 911) have evidence that they were able to specifically replace or knock out *Toxoplasma* genes. Their system was based on the use of chloramphenicol acetyltransferase as a selectable marker.

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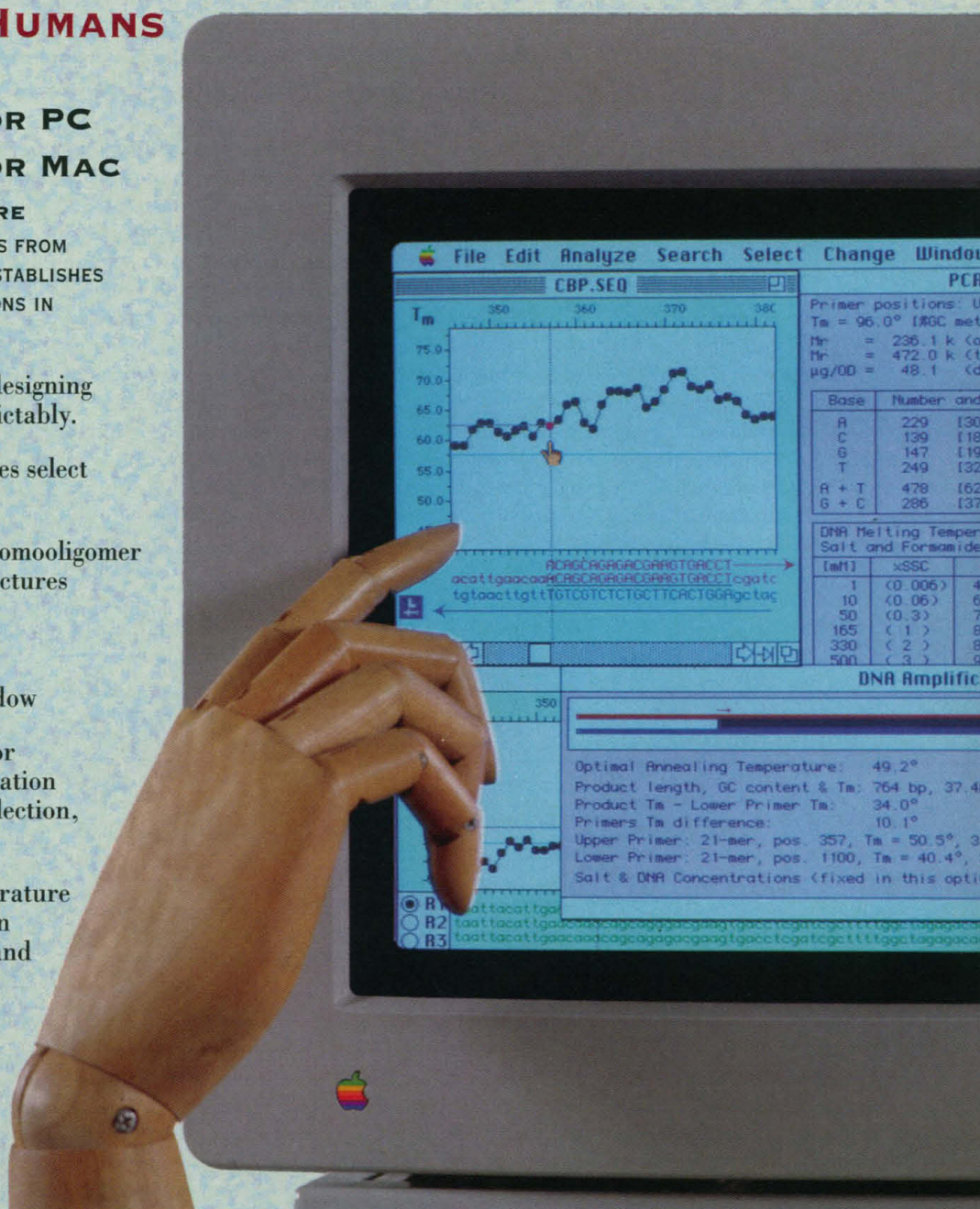
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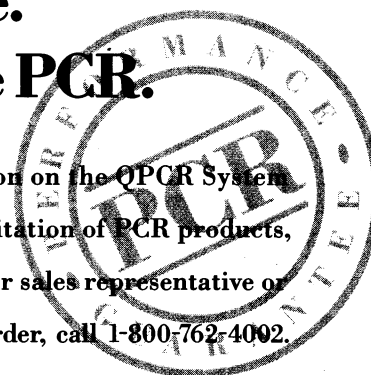
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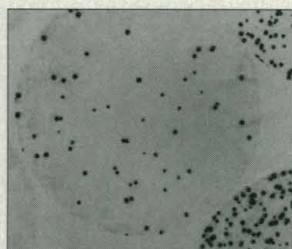


NEBlot Phototope Kit Catalog # 7550

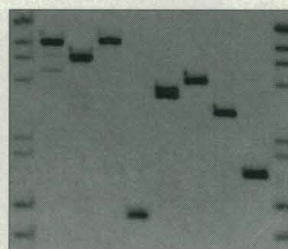
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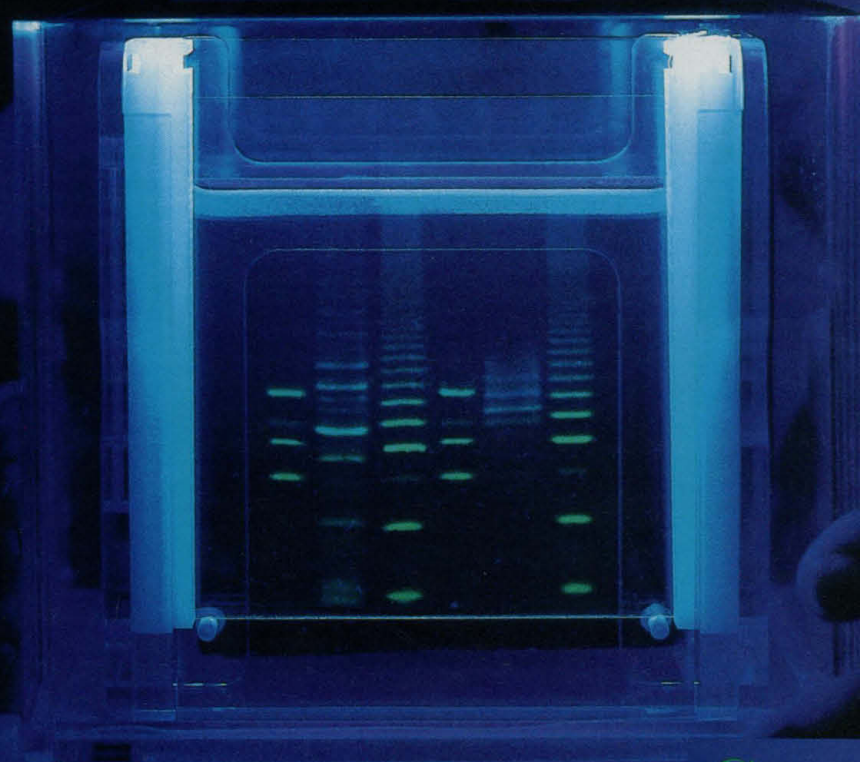


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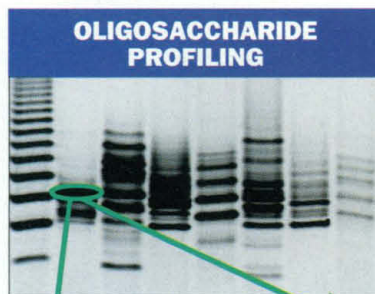
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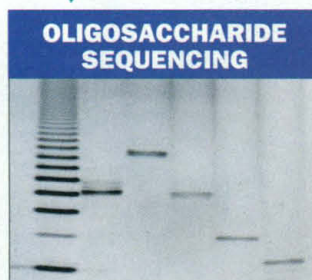
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Color-coded FACE kits make carbohydrate analysis easy and reliable

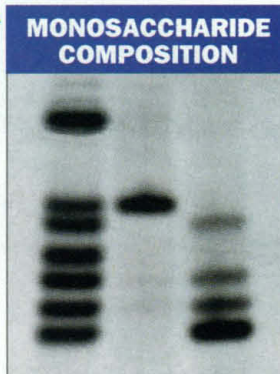
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FACE gel profile of N-linked oligosaccharides released from a number of different glycoproteins



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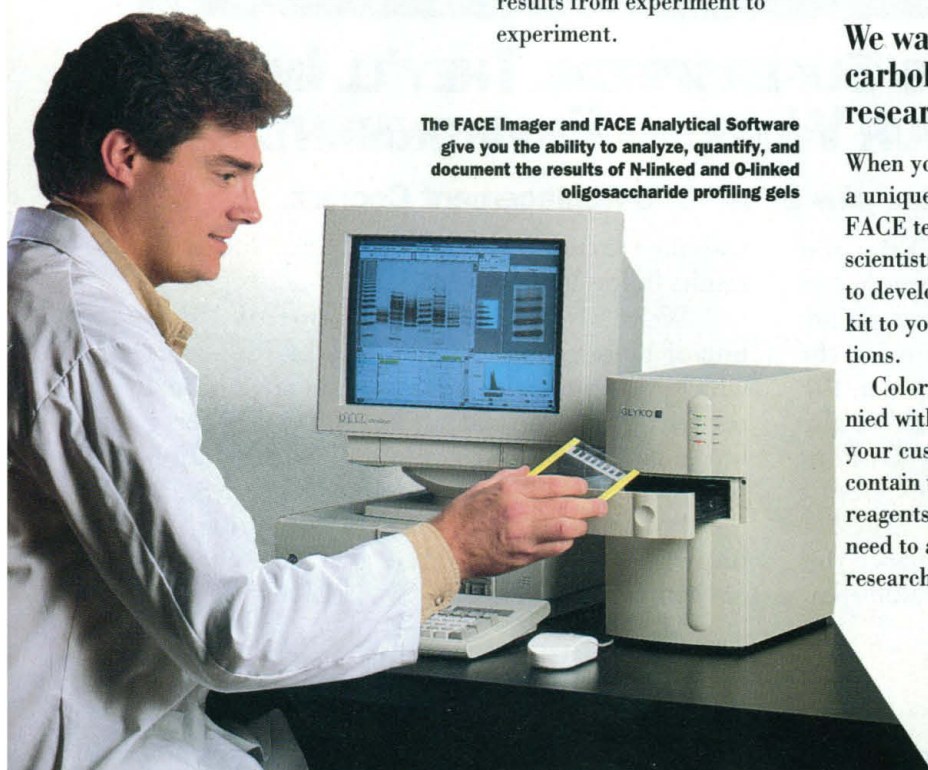
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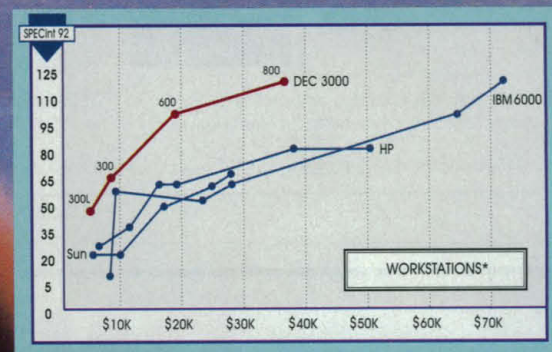
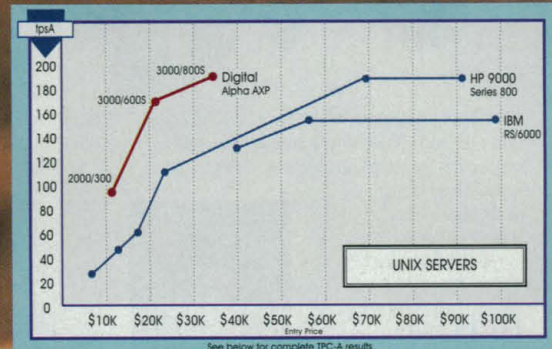
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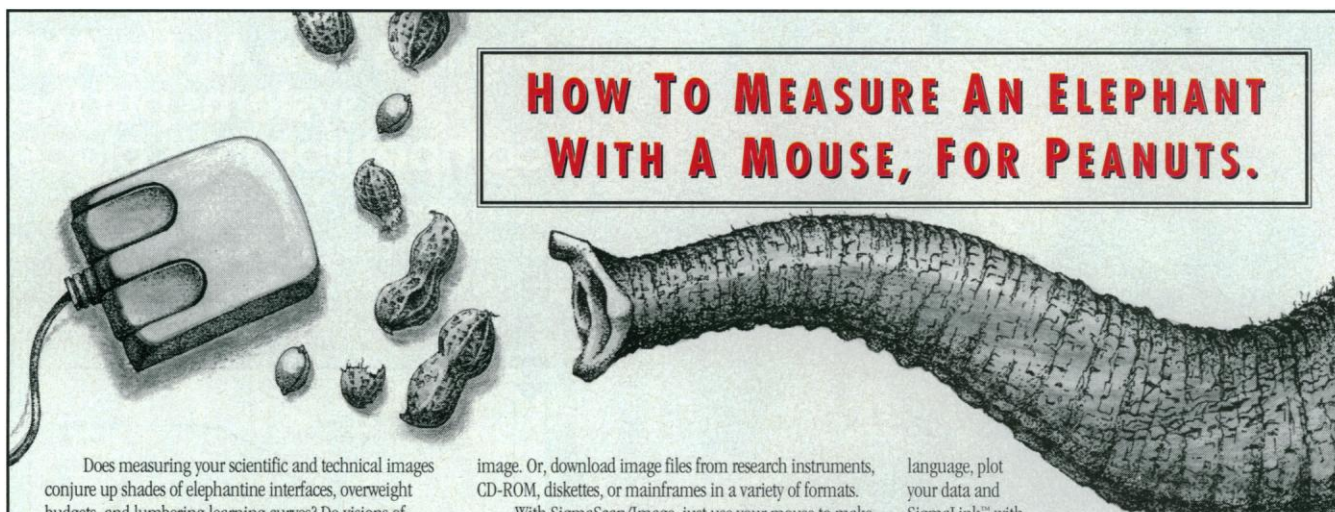
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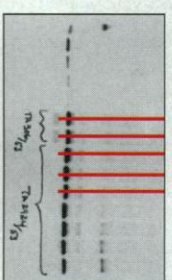
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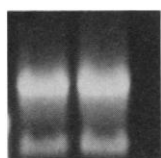
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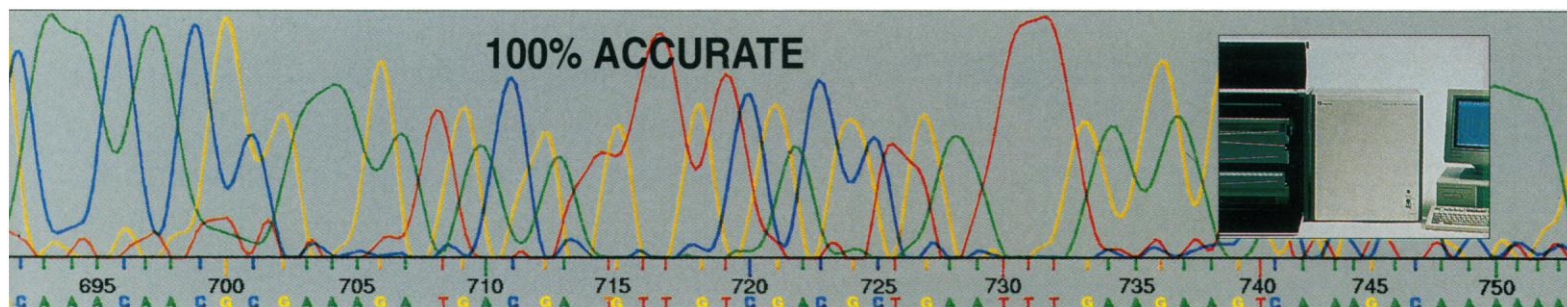
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1. Data supplied by M. Uhlén and T. Hultman from routine sequencing run at the Royal Institute of Technology, Stockholm, Sweden.

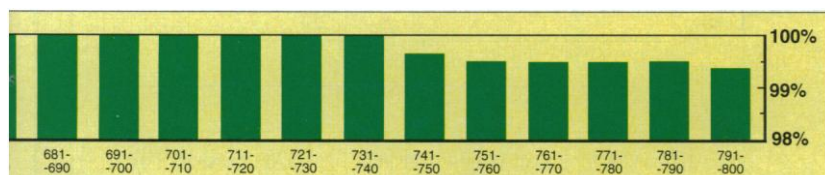
2. Comparison of three non-isotopic automated DNA sequence analysis systems. Poster presentation at the San Diego Conference on Nucleic acids, Nov. 20-22, 1991. Van Ranst, M., Fiten, P., Voet, M., Volckaert, G., Opdenakker, G.

3. Uniform scoring system for the assessment of DNA sequencing accuracy. *Meth. Mol. Cell. Biol.* 3 (1992) 243-245, Van Ranst, M., Fiten, P., Voet, M., Volckaert, G., Opdenakker, G.

4. Sequence length and error analysis of Sequenase and automated Taq cycle sequencing methods. *BioTechniques* 14 (1993) 442-447, Koop, B.F., Rowan, L., Chen, W.-Q., Deshpande, P., Lee, H., Hood, L.

5. An efficient low redundancy large scale DNA sequencing strategy: Primer walking on plasmid and cosmid DNA using T7 DNA polymerase and fluorescein-15'-dATP as internal label. Submitted for publication in *BioTechniques*, Voss, H., Wiemann, S., Zimmermann, J., Grothues, D., Sensen, C., Schwager, C., Stegemann, J., Erfle, H., Rupp, T., Sproat, B., Ansorge, W.

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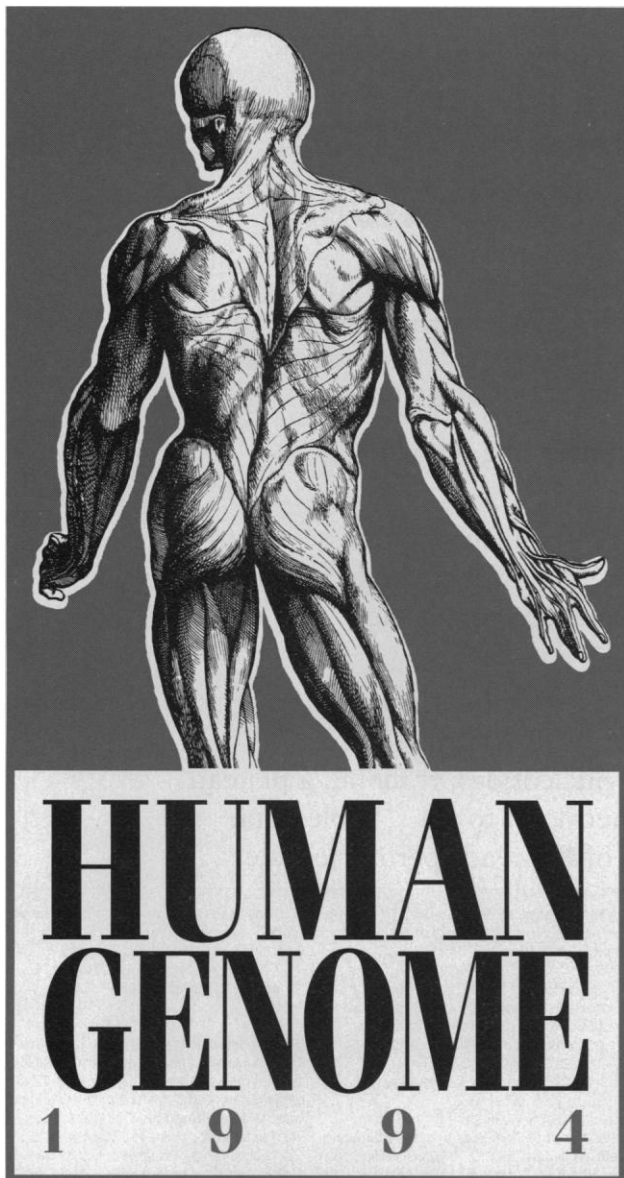
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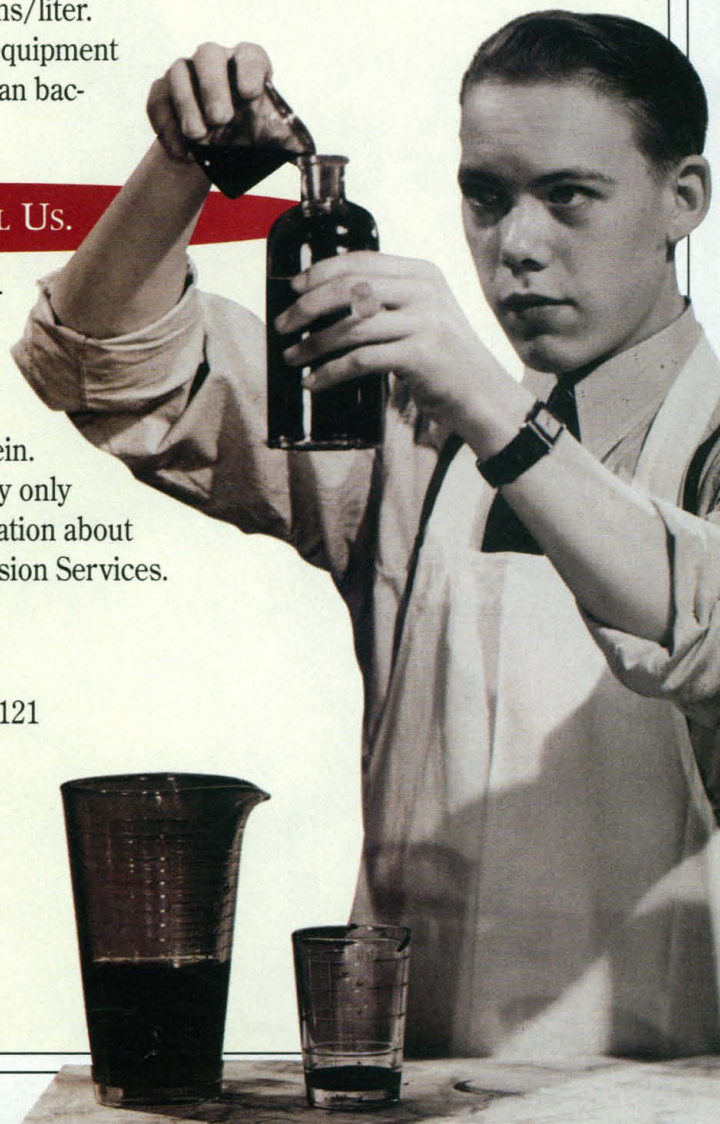


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1994-95

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*The current state of two-dimensional electrophoresis with immobilized pH gradients. *Electrophoresis* 9 (1988) 531-546, Görg, A., Postel, W., Günther, S.

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1994 CALENDAR OF EVENTS

Endocrinology

Endocrinology Under 35

Scientific Organization: A. De Bellis (I) • E. Schipani (USA)
Rome, Italy • May 25-27

Paracrine and Autocrine Signals in the Hypothalamic Pituitary Complex

Scientific Organization: L. Martini (I) • D. de Wied (NL) • S.M. McCann (USA)
Stresa, Italy • September 9-10

Endothelins in Endocrinology

Scientific Organization: I. T. Cameron (UK) • M. J. Dunn (USA) • M. Serio (I)
Florence, Italy • October 6-8

Immunology

Differentiation Therapy

Scientific Organization: A. Kimchi (IL) • G.B. Rossi (I) • S. Waxman (USA)
Herzlia, Israel • March 7-10

Cytokines: Basic Principles and Practical Applications

Scientific Organization: A. K. Abbas (USA) • S. Romagnani (I)
Florence, Italy • March 28-30

Primary Immunodeficiency Diseases

Scientific Organization: F. Aiuti (I) • M. D. Cooper (USA) • F. S. Rosen (USA)
Orvieto, Italy • June 18-21

New Horizons in Gynaecological Malignancies

Scientific Organization: D. Ayalon (IL)
Eilat, Israel • November 16-18

Reproduction

Puberty: Basic and Clinical Aspects

Scientific Organization: C. Bergadá (ARG)
Buenos Aires, Argentina • April 6-8

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Scientific Organization: J. Tesarik (F)
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Scientific Organization: O. Nilsson (S)
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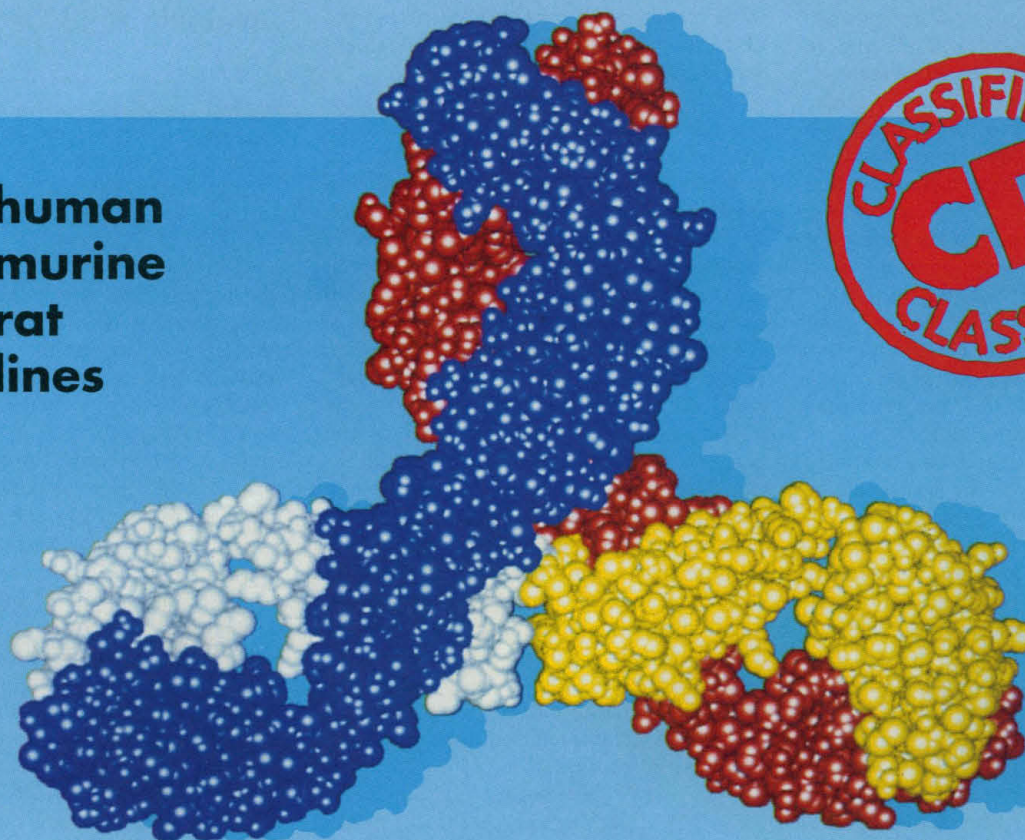
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Phone: 06221 / 163091
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