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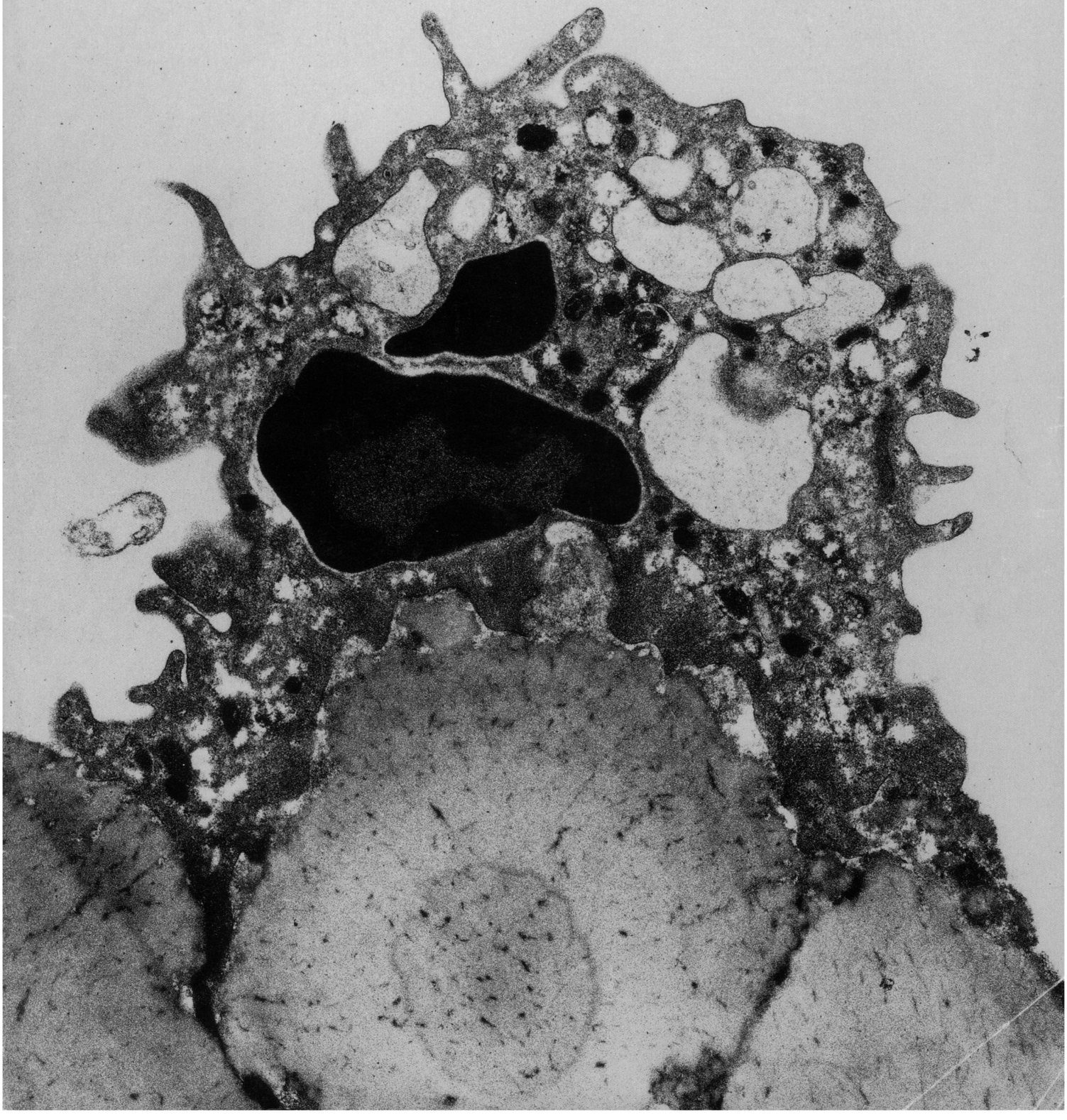
13 JULY 1990 $3.50
VOL. 249 ■ PAGES 101–216



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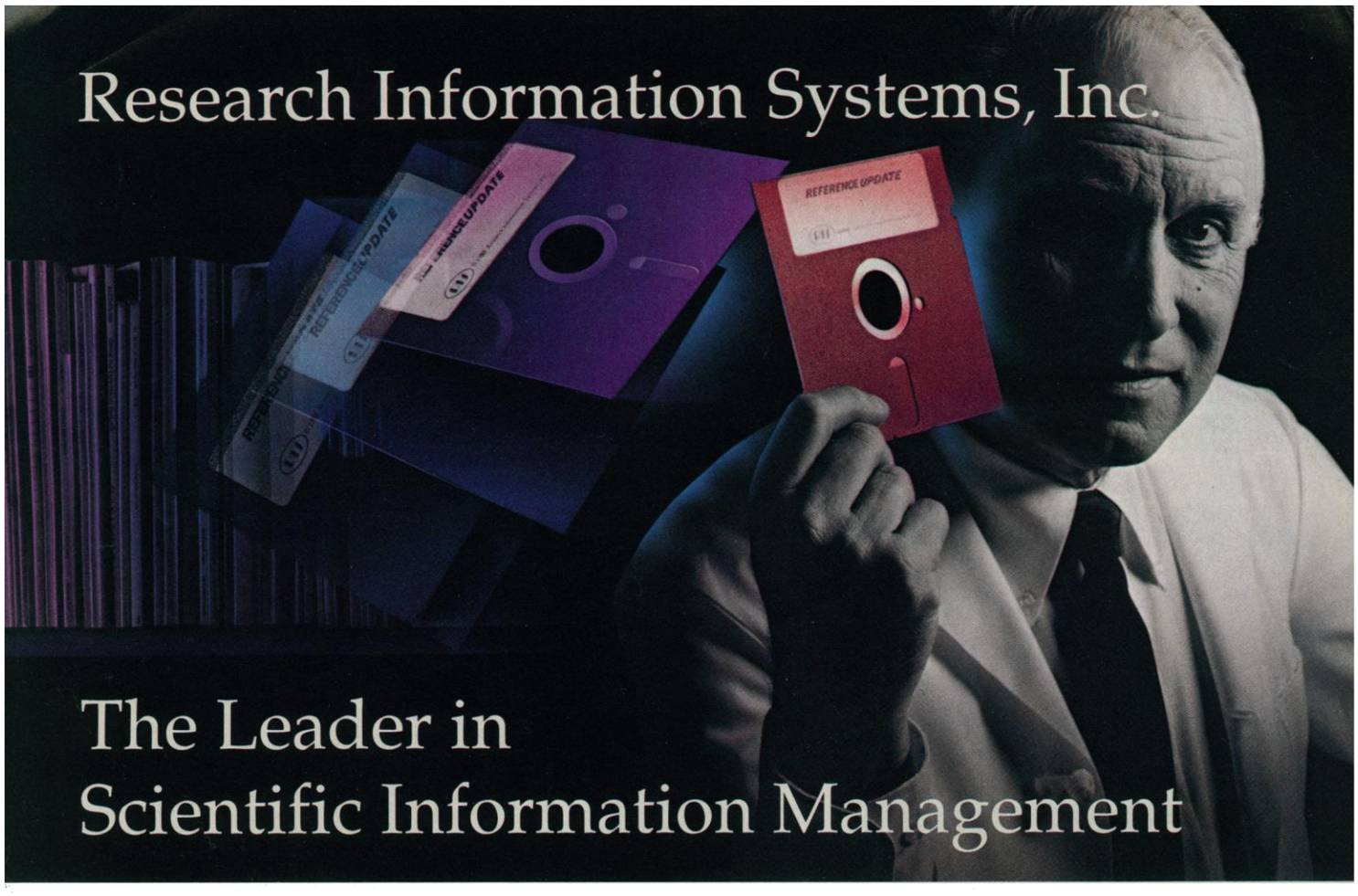

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SCIENCE

ISSN 0036-8075
13 JULY 1990
VOLUME 249
NUMBER 4965

■ **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 non-profit 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.

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COVER A transmission electron micrograph (magnification ×16,000) of a human neutrophil that is degrading particles of antibody-coated, insoluble elastin in the presence of human plasma. Although endogenous plasma proteinase inhibitors cannot regulate neutrophil-mediated proteolysis at sites of tight cell-substrate contact, subjacent substrates can be protected from the attacking neutrophils by secretory leukoprotease inhibitor, a structurally unique proteinase inhibitor normally concentrated in human mucous secretions. See page 178. [Photograph by Andreas R. Huber, Sandra Regiani, Bruce Donohoe, and Stephen J. Weiss]

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Splat and hammer chemistry

In many chemical reactions involved in industrial catalysis and in producing electronic devices, molecules at the surface must be activated. It has been thought that the energy for activation came from the surface. Ceyer discusses molecular beam experiments that show that, in addition, translational energy of the incident molecule can help activate molecules (page 133). Only faster molecules distort themselves—splat—in colliding with the surface. In addition, fast-moving incident molecules from the gas phase can hit adsorbed molecules—hammer—and activate them. Such processes expose and weaken bonds so that reactions with surface atoms can take place. Insights provided by these experiments have made possible new types of surface chemical reactions; reactions that would only occur under high-pressure conditions are now being carried out at low pressure in the ultrahigh vacuum conditions used to probe surface reactions.

Inhibiting inflammation

Inflammation is a common complication of many diseases and injuries; it can be triggered by the "complement cascade" (a complex network of interacting proteins) acting in conjunction with leukocytes. Any inhibitor of the complement system might therefore be a candidate agent for countering complement-induced tissue damage. The protein CR1 has inhibitory effects on complement components, but it is naturally bound to membranes of a few cell types. Weisman *et al.* prepared a soluble truncated form of CR1 (page 146); it lacked transmembrane and cytoplamic domains and thus had no membrane affiliation. "Liberated" CR1 was a highly effective inhibitor of complement activation in vitro. More important, in an experimental disease model, it reduced the size of myocardial infarcts, which are complement-dependent lesions. Because burns, ischemia, autoimmunity, and inflammation are complement-dependent, they might be successfully alleviated with CR1 or similar agents.

Receptor structure

Glucocorticoid receptors belong to a superfamily of related proteins that also includes receptors for thyroid hormone, retinoic acid, and vitamin D_3. These proteins have a conserved 70–amino acid DNA-binding domain (DBD) that mediates binding of the receptor to hormone response elements on DNA. Detailed three-dimensional structural data for the glucocorticoid receptor DBD have now been obtained (page 157), and a melding of the data with previously obtained genetic and biochemical information has led to a better definition of the structure, folding, and interactions of this protein fragment. DBD is globular with two tetrahedrally coordinated zinc atoms held in "zinc fingers." The locations of regions of hydrophobicity and hydrophilicity were identified as were individual residues in contact with zinc, bases, and amino acids. Härd *et al.* point out that, whereas members of the superfamily probably all interact with DNA in the same way, other zinc finger-containing DNA-binding proteins that are in different coordination classes probably use different structural motifs in their interactions with DNA.

Methyl halides

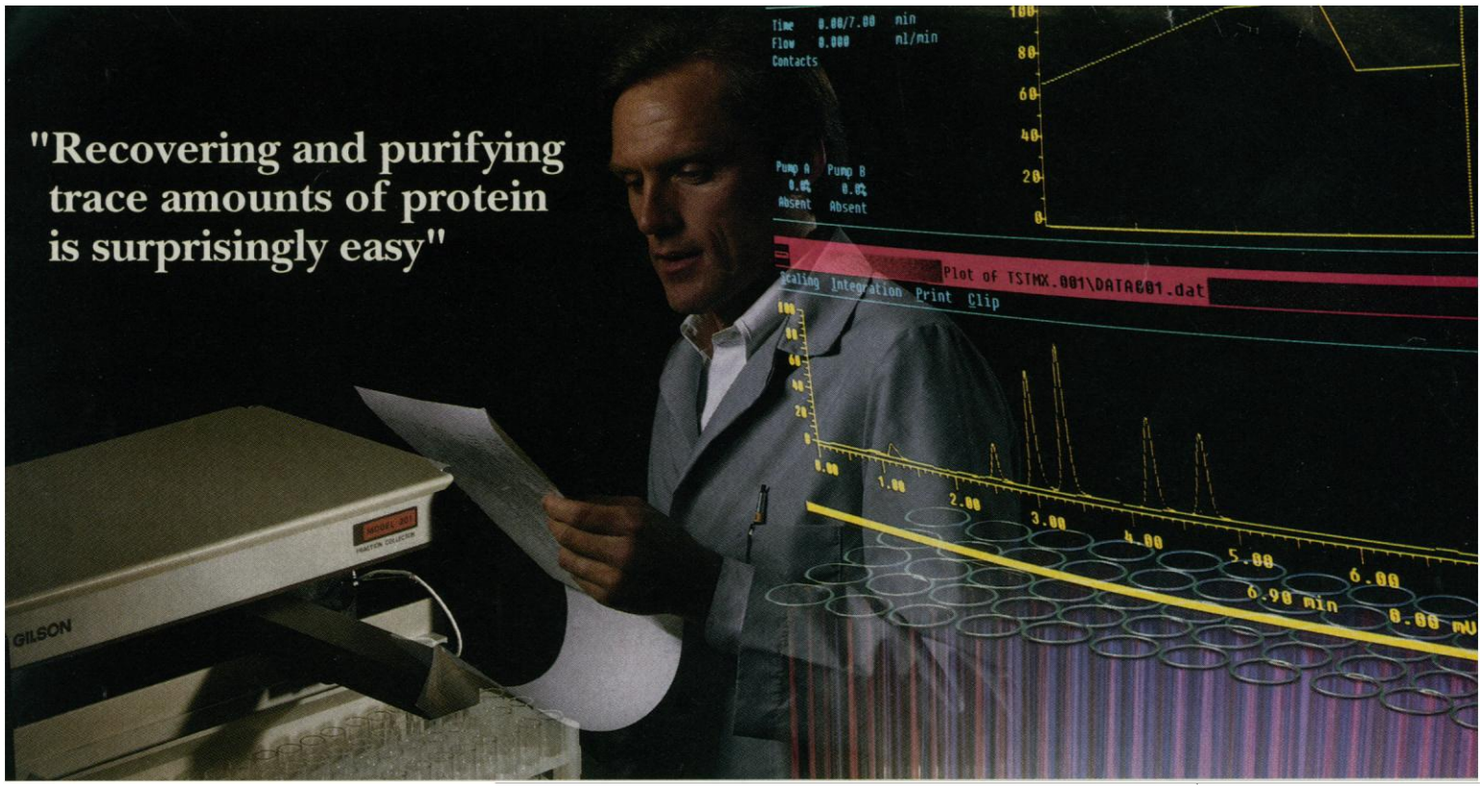
Five million tons of methyl chloride find their way into the upper atmosphere each year. The compound is synthesized by a range of organisms—wood rot fungi, phytoplankton, and ice plants. Wuosmaa and Hager have now examined its production in marine red algae (page 160). They partially purified an enzyme, a methyl chloride transferase, that catalyzes the methylation of halogen ions. Methylation rates for the different halogens varied but were consistent with the known nucleophilicities of the acceptor anions. A survey of marine algae in Monterey Bay indicated that 50% could produce methyl chloride. Because both marine and terrestrial organisms that produce methyl chloride have broad global distributions, it is now possible to understand the enormous annual output of this compound.

Inhibiting inflammation

Neutrophils can participate in tissue inflammation by releasing proteolytic enzymes that degrade substrates in the local tissue matrix. The neutrophils bind closely to the tissue and create a "privileged" environment in which their proteases can work; access to the site by inhibitors from blood is blocked. When actions of neutrophils and their enzymes are intense, acute inflammatory disease can result. Rice and Weiss report that it is possible to block the proteolytic action of neutrophil enzymes with a recombinant inhibitor, secretory leukoprotease inhibitor (page 178). The natural enzyme is normally only found in mucous secretions. This type of inhibitor might be an effective in vivo modulator of acute inflammatory reactions.

Neurofibromatosis gene

Von Recklinghausen neurofibromatosis is a common inherited disease that affects about 1 in 3000 people. Benign neurofibromas are hallmarks of the disease and there is increased risk of certain malignancies, especially neurofibrosarcomas. The gene responsible for the disease is known to be on human chromosome 17 in the q11.2 band; positional cloning experiments have now more precisely defined its location (page 181). The newly described gene, called *NF1LT*, is large and expressed in many tissues; it was found to be altered by an insertion in a patient with the disease and is positioned such that it is interrupted by translocations that are associated with the disease. Wallace *et al.* discuss these and other data that convincingly tie this gene to the disease and describe various mechanisms by which alterations in the gene could produce the disease phenotype. ■ Ruth Levy Guyer



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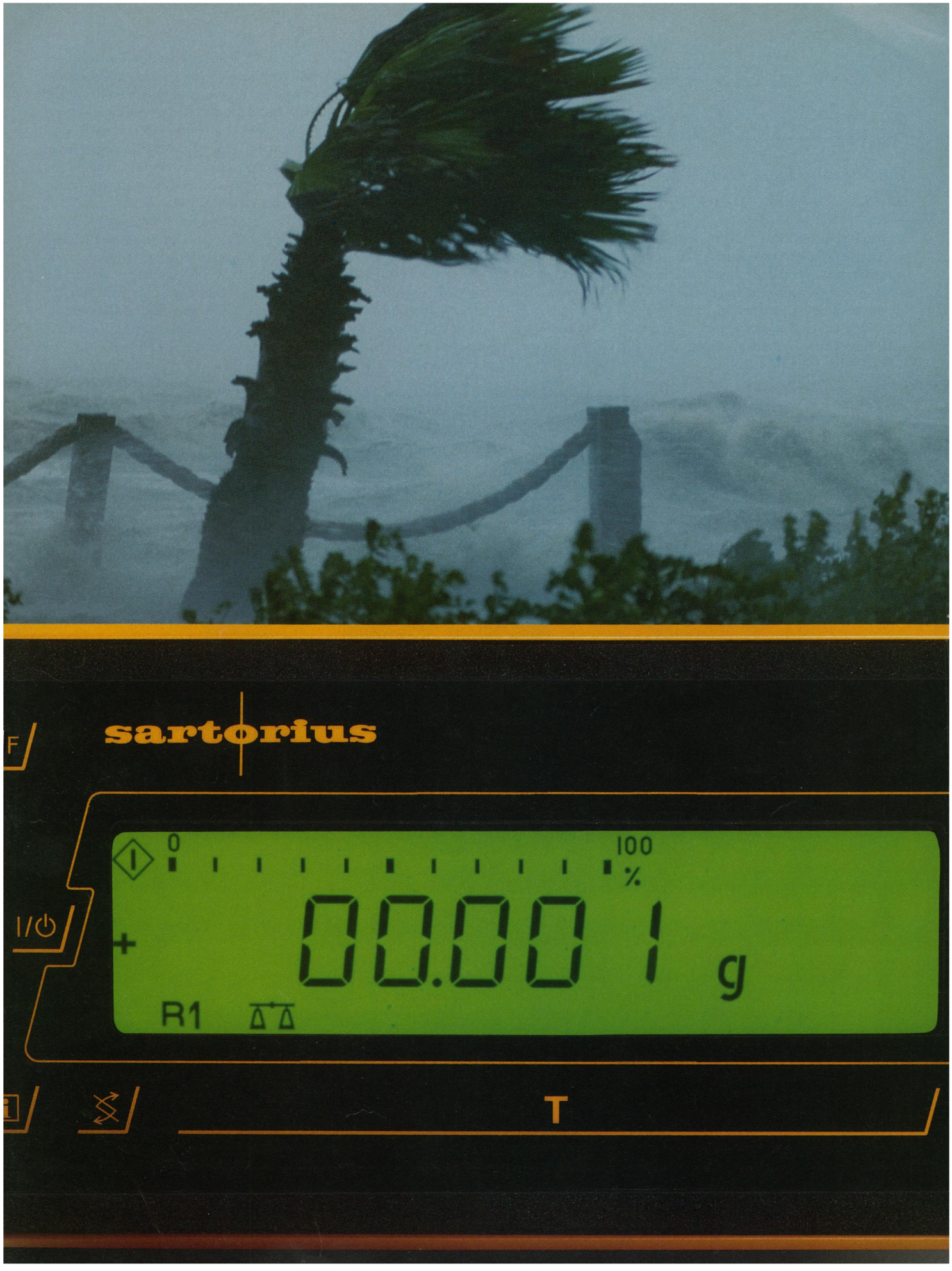
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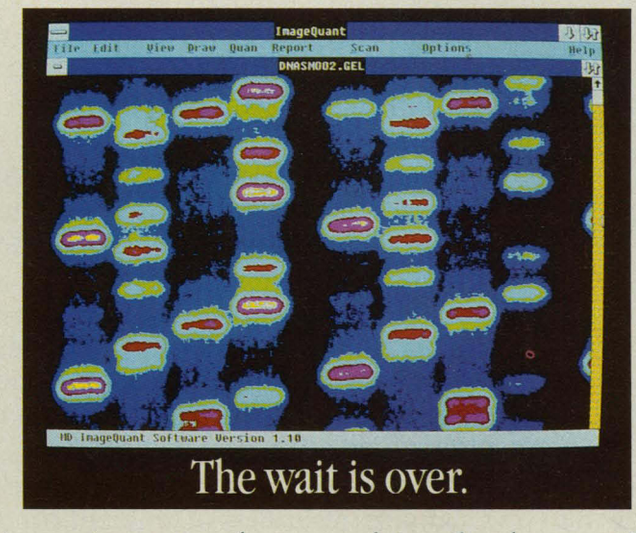

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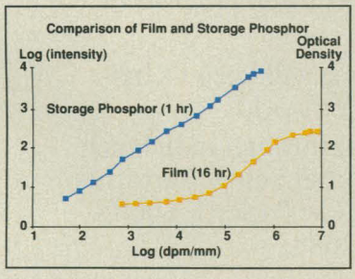

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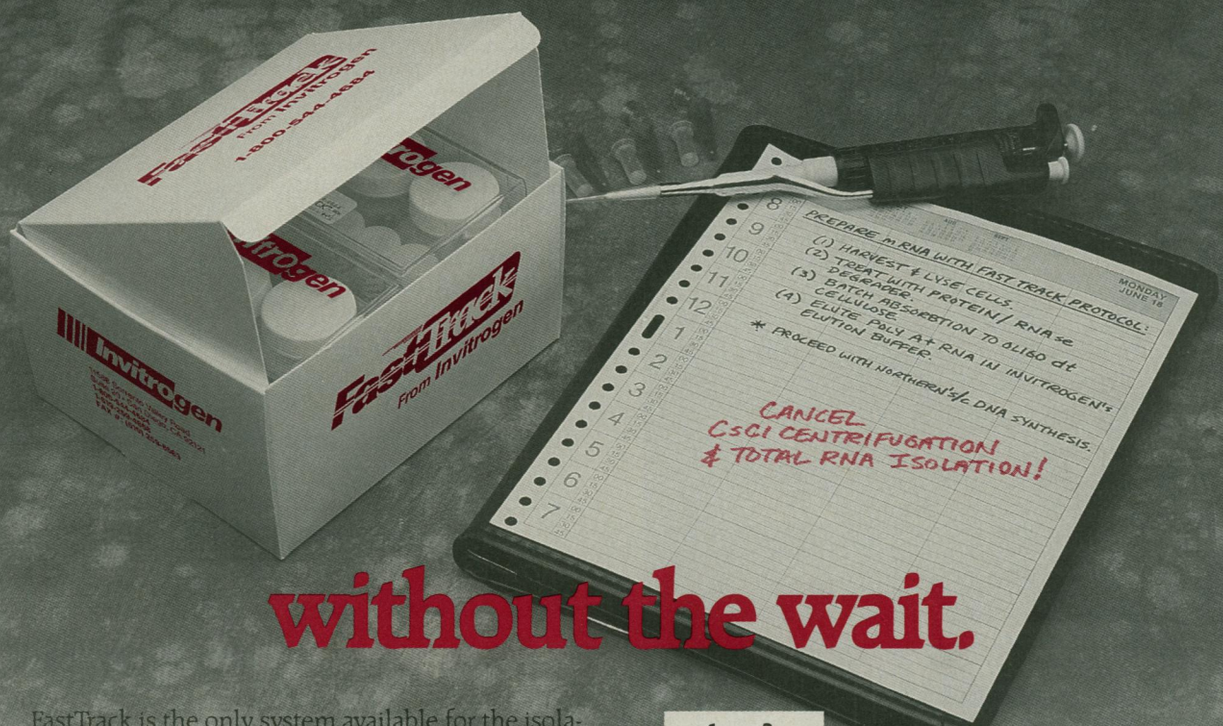

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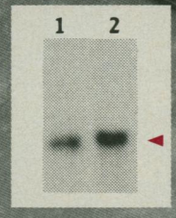

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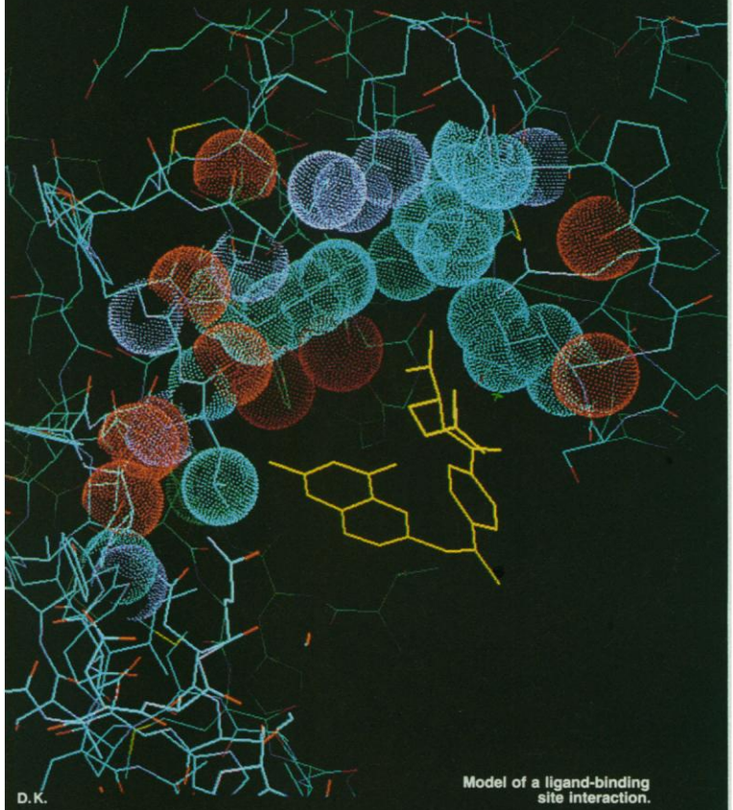

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Model of a ligand-binding site interaction.

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