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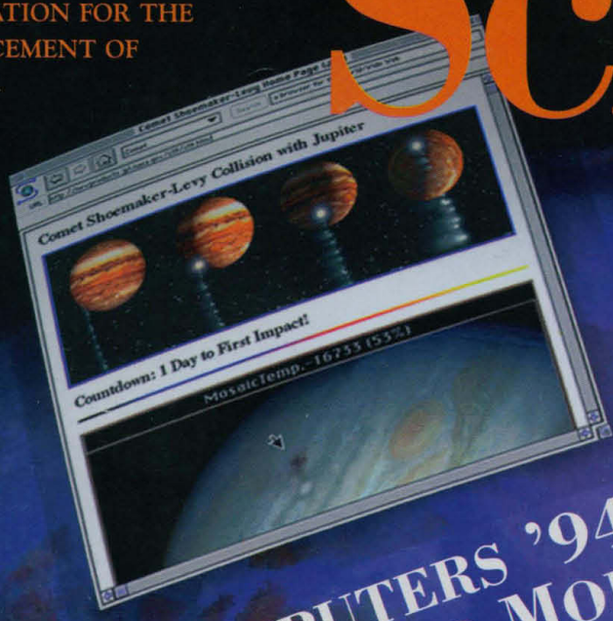
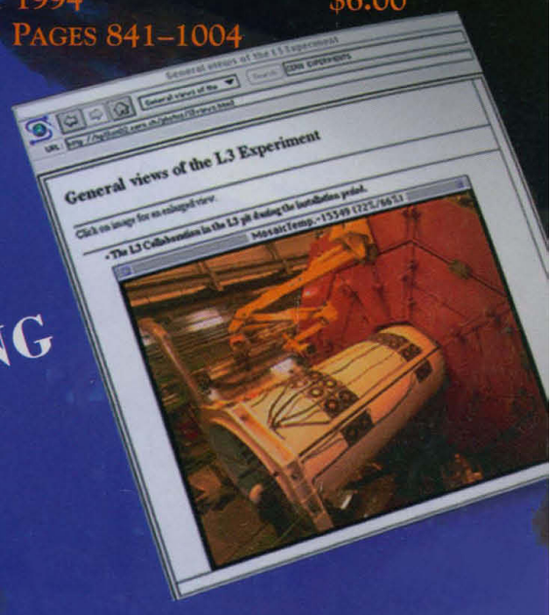
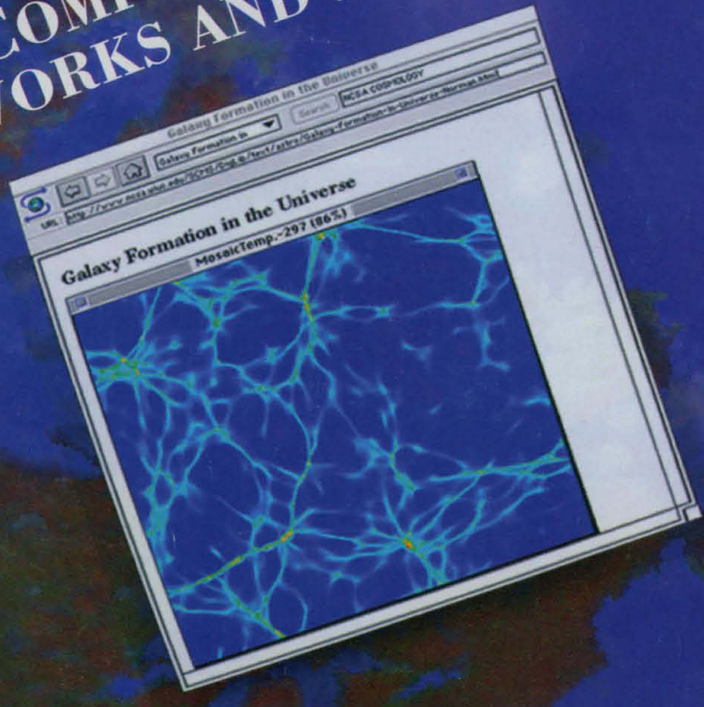
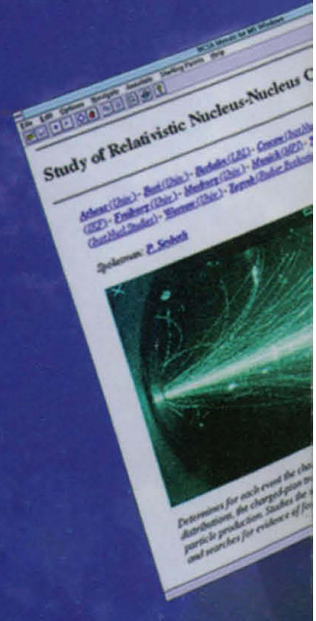
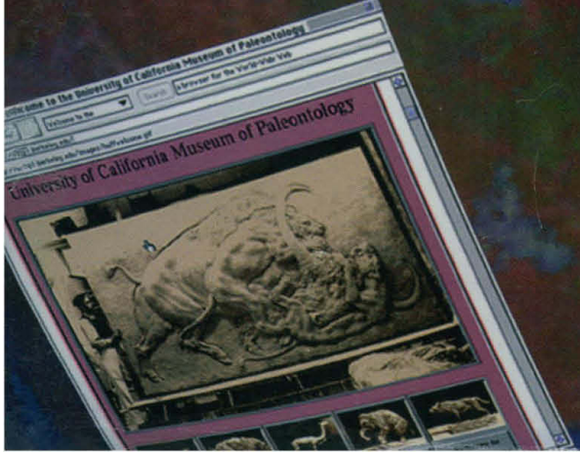


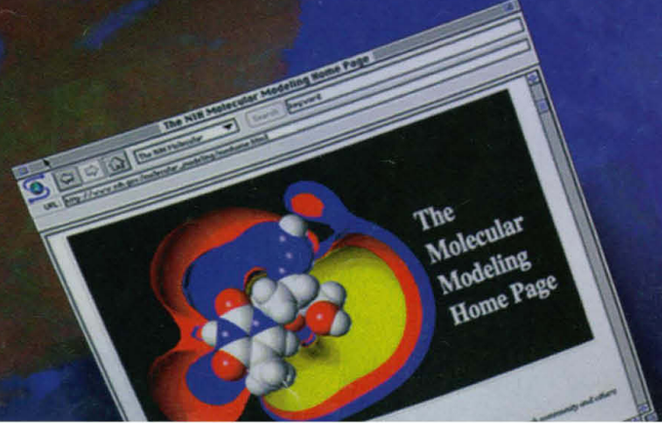


COMPUTERS '94
NETWORKS AND MODELING









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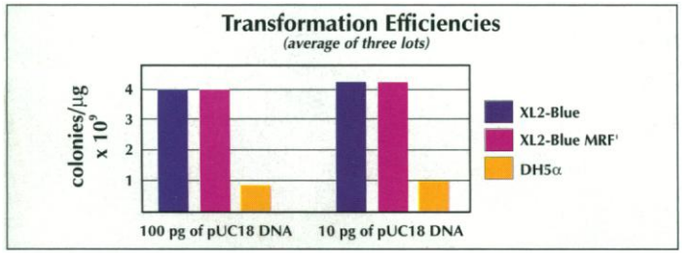

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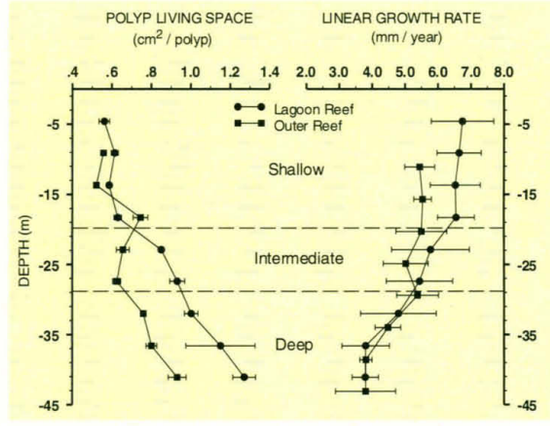

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Fluffy, meaningless business graph

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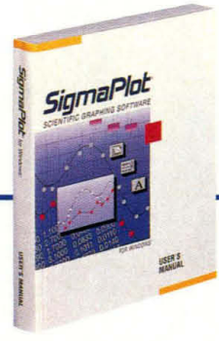

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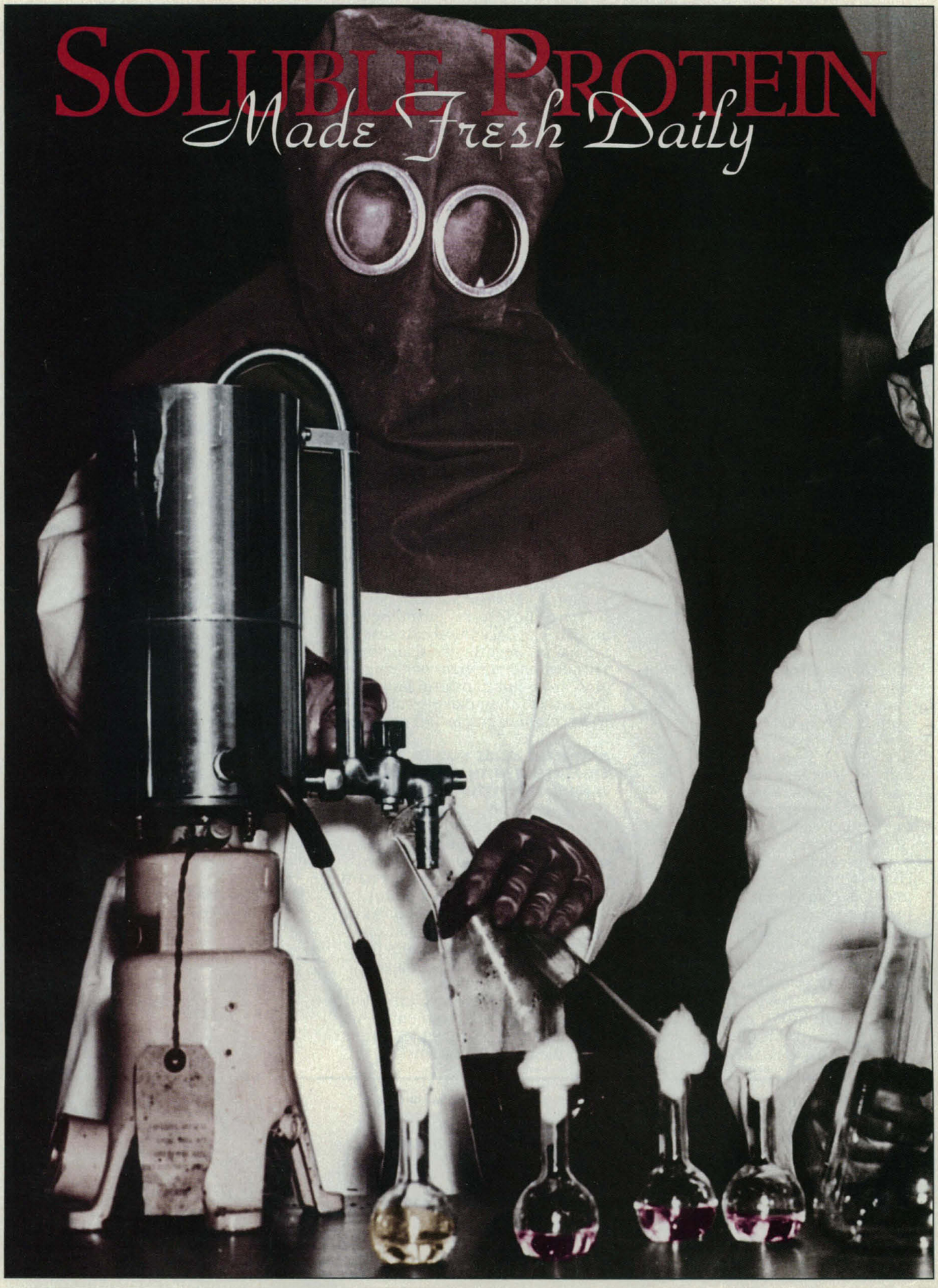

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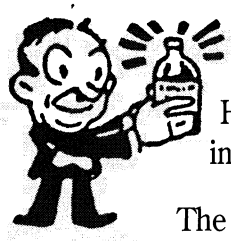

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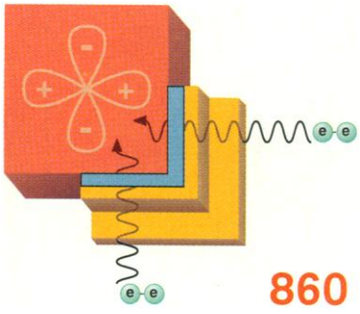

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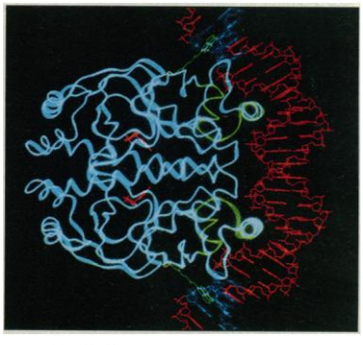

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COVER

Composite of computer screens above a globe roughly corresponding to the location of the data. The screens were created with Mosaic software developed at the National Center for Supercomputing Applications (NCSA) for browsing the World Wide Web. This Internet technology enables scientists to make their information rapidly available to the global community. These and other issues are discussed in this special issue on computing. See the Editorial on page 851 and the News Reports, Perspectives, and Articles beginning on page 879. [Image: I Kallick and B. Schatz at NCSA, using public domain sources on the Internet]

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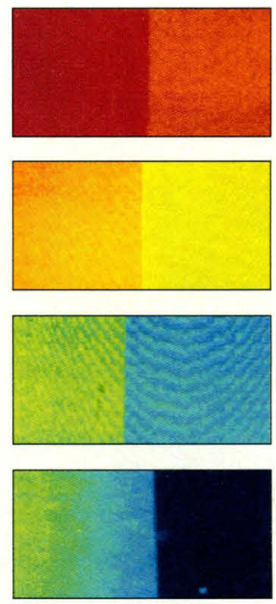

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A picture of order

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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Off and on binding

Measuring the binding kinetics of critical molecular interactions in T cell activation, such as the binding of T cell receptors (TCRs) to major histocompatibility complex (MHC) molecules that present peptide antigens, can be complicated by interactions between other molecules. Corr *et al.* (p. 946) determined the rates of association and dissociation for complexes of soluble analogs of MHC class I molecules bearing synthetic peptide antigens to purified TCRs that were immobilized of the surface of a biosensor. Dissociation is rapid (a half-time of about 27 seconds), which suggests that multivalent binding may be necessary to initiate a TCR signal.

■

The ravages of time

The surface of Venus has both impact craters and volcanoes, and because younger volcanic surfaces will have suffered fewer impacts than older ones, it is possible to deduce the history of volcanic activity from the statistics of cratering on lava flows and coronae. Radar mapping by the Magellan spacecraft produced a detailed catalog of Venus's surface features, from which Namiki and Solomon (p. 929) deduce that neither of two extreme models—single-age and steady-state volcanism—are correct. Large volcanoes show activity throughout the past 500 million years, during which time 20% of Venus has been resurfaced.

Thinking about moving?

The human cerebellum, a portion of the brain, is located dorsally, underneath the large cerebral hemispheres and nestled against the brainstem, with many parallel striations running horizontally on its surface. Classically, its function is thought to be the coordination of movement and maintenance of posture, but Kim *et al.* (p. 949) provide support for a more recent and controversial proposal that the cerebellum contributes to cognitive processing. They used magnetic resonance imaging to demonstrate the activation of a part of the cerebellum, the dentate nucleus, during attempts to solve a pegboard puzzle. The dentate serves as one of the three major output centers of the cerebellum and projects to the cerebral cortex by means of the thalamus.

Nothing like the sun

Most stars emit only weakly at radio wavelengths: the sun, although it has measurable microwave emission, would be undetectable at typical interstellar distances. Güdel *et al.* (p. 933) report the detection of four apparently solar type stars with strong microwave emission, as much as 3000 times more intense than that of the sun. Two of the four are young and rapidly rotating, so that their radio emission may be due to coronal activity induced by a strong dynamo, but the third is very similar to the sun and the fourth appears to be considerably older. In the last case especially, the source of radio emission remains mysterious.

■

Old boulders

A key to dating glacial advances in many areas is accurate dating of moraines. One potentially powerful means of dating is analysis of cosmogenic nuclides incorporated in boulders exposed on moraine surfaces. Hallet and Putkonen (p. 937) show how the post-deposition geomorphic evolution of the moraine, including degradation of boulders and exposure of new boulders, affects the apparent age that is determined. They apply their analysis to a key sequence of moraines along the Sierra Nevada in California that record five major glacial advances.

■

Tiny bright lights

Light-emitting diodes are sources of monochromatic light that are finding increasing use in solid-state lasers and in communications. Schubert *et al.* (p. 943) studied the photoemission of such a device fabricated between two partially reflective parallel surfaces—a Fabry-Perot cavity. In this device, the intercavity spacing is of the order of the optical wavelength, so the energy of the photons that propagate along the cavity is quantized and the emission properties are strongly modified compared to a classical optics cavity. One advantage is that the emission efficiencies are greatly improved.

■

Making the cut

Manipulations of DNA at the chromosome level would be facilitated by a cleaving agent that could recognize sites longer than the 8–base pair (bp) limit of restriction endonucleases and thus produce fewer cuts and longer pieces. Pendergrast *et al.* (p. 959) targeted a nonspecific DNA cutting agent, copper:*o*-phenanthroline, by attaching it to the catabolite gene activator protein (CAP). Because CAP bends DNA only when it binds to a specific 22-bp binding site, cutting is highly selective for that site.

■

Use it and lose it

Most organisms follow the rule of DNA "constancy"—every cell contains at least one copy of the entire genome. Many nematode species, such as *Ascaris lumbricoides* break this rule. Somatic (non-germline) cells discard much of their DNA through a process called chromatin diminution. Etter *et al.* (p. 954) show that this nematode carries genes for two different isoforms of a small ribosomal protein, S19. The gene for the isoform that is more highly expressed in germline cells is eliminated during chromatin diminution, so somatic cells express just one form. This process represents a "throw-away" approach to gene regulation.

■

Take two

The usefulness of aspirin as an anti-inflammatory drug has been attributed to its ability to inhibit prostaglandin production. Kopp and Ghosh (p. 956) link aspirin to another pathway. They demonstrate that sodium salicylate and aspirin inhibit the activation of NF-κB, an inducible transcription factor that regulates the transcription of many genes involved in the inflammatory response. Aspirin may inhibit NF-κB by interfering with the pathway that leads to the phosphorylation and degradation of IκB, the inhibitor of NF-κB.

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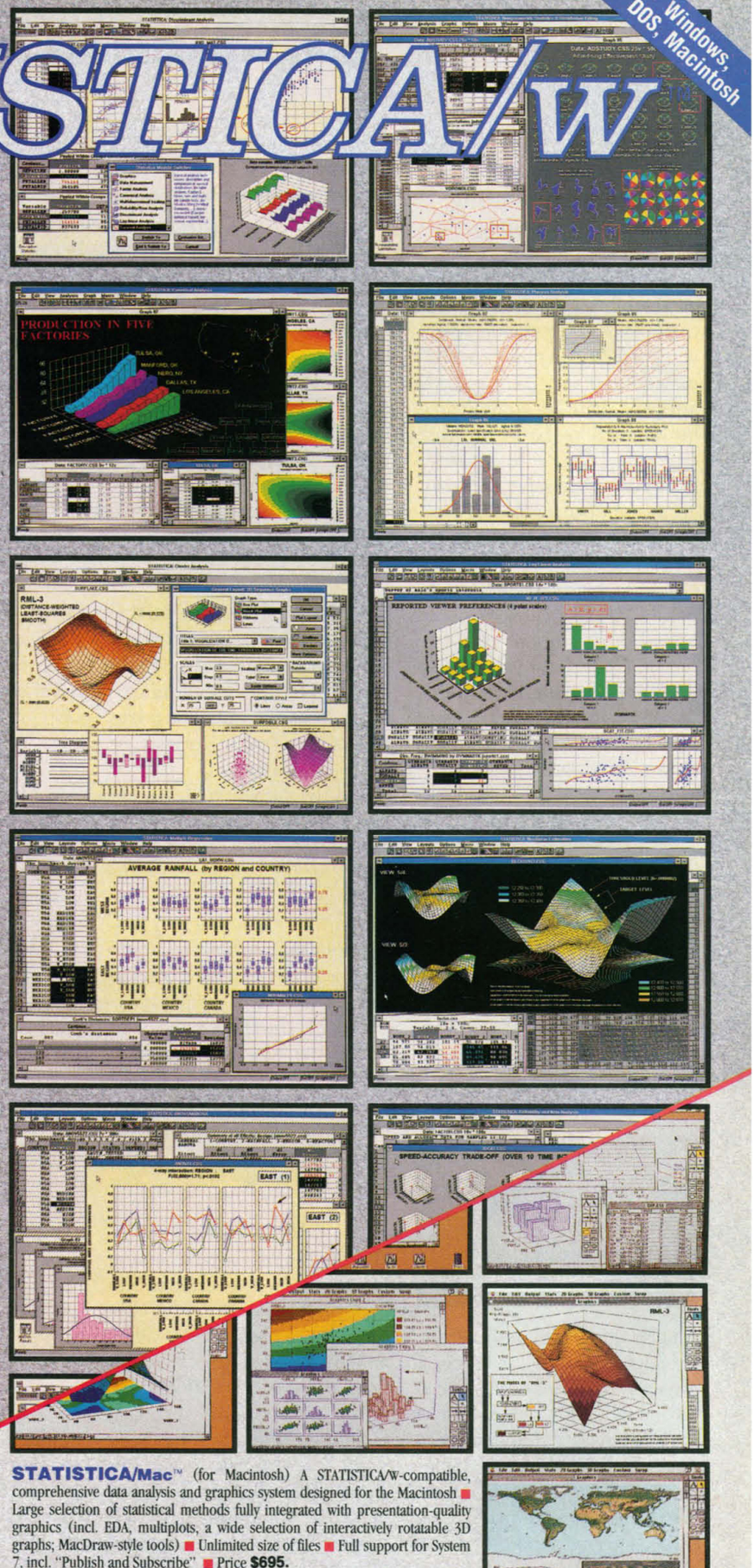

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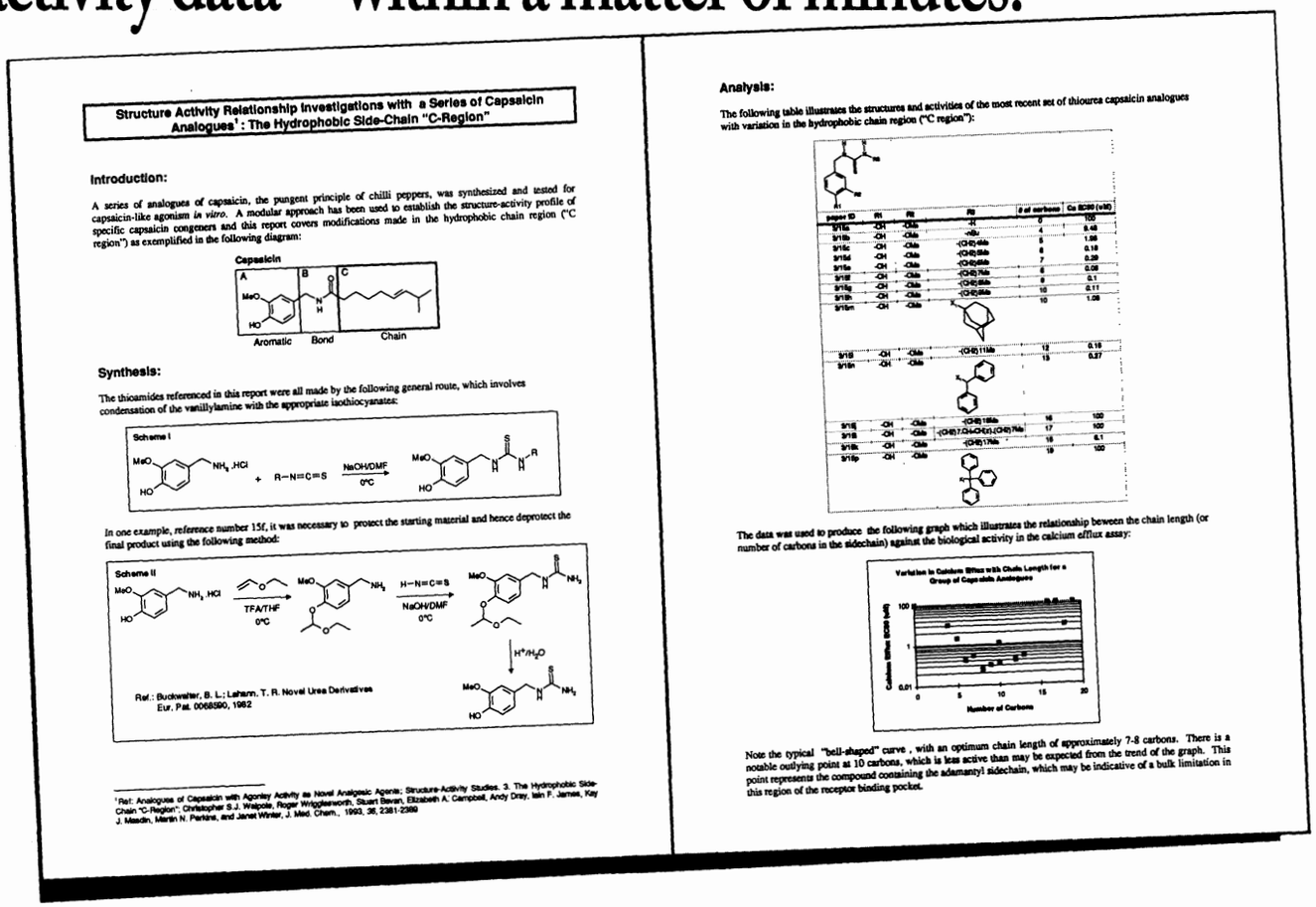

Structure Activity Relationship Investigations with a Series of Capsaicin Analogues[1]: The Hydrophobic Side-Chain "C-Region"

Introduction:

A series of analogues of capsaicin, the pungent principle of chilli peppers, was synthesized and tested for capsaicin-like agonism *in vitro*. A modular approach has been used to establish the structure-activity profile of specific capsaicin congeners and this report covers modifications made in the hydrophobic chain region ("C region") as exemplified in the following diagram:

Capsaicin

Aromatic Bond Chain

Synthesis:

The thioamides referenced in this report were all made by the following general route, which involves condensation of the vanillylamine with the appropriate isothiocyanates:

Scheme I

In one example, reference number 15f, it was necessary to protect the starting material and hence deprotect the final product using the following method:

Scheme II

Ref.: Buckwalter, B. L.; Lehann, T. R. Novel Urea Derivatives Eur. Pat. 0068590, 1982

[1] Ref: Analogues of Capsaicin with Agonist Activity as Novel Analgesic Agents; Structure-Activity Studies. 3. The Hydrophobic Side-Chain "C-Region"; Christopher S.J. Walpole, Roger Wrigglesworth, Stuart Bevan, Elizabeth A. Campbell, Andy Dray, Iain F. James, Kay J. Masdin, Martin N. Perkins, and Janet Winter, J. Med. Chem., 1993, 36, 2381-2389

Analysis:

The following table illustrates the structures and activities of the most recent set of thiourea capsaicin analogues with variation in the hydrophobic chain region ("C region"):

The data was used to produce the following graph which illustrates the relationship between the chain length (or number of carbons in the sidechain) against the biological activity in the calcium efflux assay:

Variation in Calcium Efflux with Chain Length for a Group of Capsaicin Analogues

Number of Carbons

Note the typical "bell-shaped" curve, with an optimum chain length of approximately 7-8 carbons. There is a notable outlying point at 10 carbons, which is less active than may be expected from the trend of the graph. This point represents the compound containing the adamantyl sidechain, which may be indicative of a bulk limitation in this region of the receptor binding pocket.

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GRAINCOLLECTION
HUMANS' NATURAL ECOLOGICAL NICHE

SERGIO TREVIÑO
Translated by:
Rebeca San Martín-Feeney

The logically harmonious thesis contained in this work will revolutionize our current way of thinking about human origins and behavior.

Ernst Mayr, Professor of Zoology, Emeritus, at Harvard University, considered by many to be the greatest evolutionist of the century, has written to the author:

> "...I am rather inclined to accept your thesis of the role of graincollecting in the history of mankind, persuaded by your arguments and those of others.
> Thank you very much for your interesting and closely argued book!"

How did bipedalism, the loss of body hair, and tool use originate? After more than 130 years of scientific research, the origin of these basic human characteristics is still unknown. Bipedalism, the loss of body hair, and tool use originated 14 million years ago, when our very distant ancestors, *Ramapithecus,* turned graincollectors. Erroneously, we still equate biological evolution with "progress", and therefore, believe humans descend from knuckle-walking, hairy, unskilled tool users who resembled the living great apes, when, in fact these apes descend from bipedal, naked, skilled tool users, who resemble modern man.

The large intestine, humans' largest internal organ, is presently used only to absorb water and electrolytes, although its sacculated nature indicates an evolutionary adaptation to digest cellulose. This intestine's movements are so slow that the first radiologist to observe it said it presented a picture of still life. Much of this inactivity can be attributed to mankind's omnivorous diet. Nonetheless, it follows that, when following an **exclusively** granivorous, cellulose-digesting diet, our large intestine proves to be much more useful and efficient, since our ancestors up to 50 thousand years ago **always** used it to digest cellulose fiber. We are presently neglecting a very useful capability that our ancestors adaptively acquired. Humans, as **all** other primates, were meant to be vegetarian cellulose-digesters and have slim bodies. The size of the human mouth is small for almost any type of omnivorous feeding, making this feature, as well as our powerful teeth, characteristic more of seed-eaters than of carnivorous or omnivorous mammals.

It is inconceivable to think that hominids and their protohominid ancestors lived in the savannas for millions of years and never developed the practice of feeding from gramineous seeds until the discovery of agriculture, or until fire was used to cook food. If we take into consideration that early hominids were already **bipeds and tool users,** and **the seeds from grasses would lightly touch their hands as they walked in the long-grass grasslands,** it would be illogical to assume that, in spite of the many vicissitudes they suffered during so many million years of living in the savannas, they never tried to feed from these seeds or that they never thought of removing the seeds with their hands. The author argues that when injuring themselves by removing the seeds, they used a **natural** small stone tool to protect their hands, which achieved an unanticipated advantage: they improved their efficiency in removing and threshing seeds.

We invite you to read this book and explore in it the scientific bases of these arguments, upholding the importance of the role of graincollecting in human evolution and behavior.

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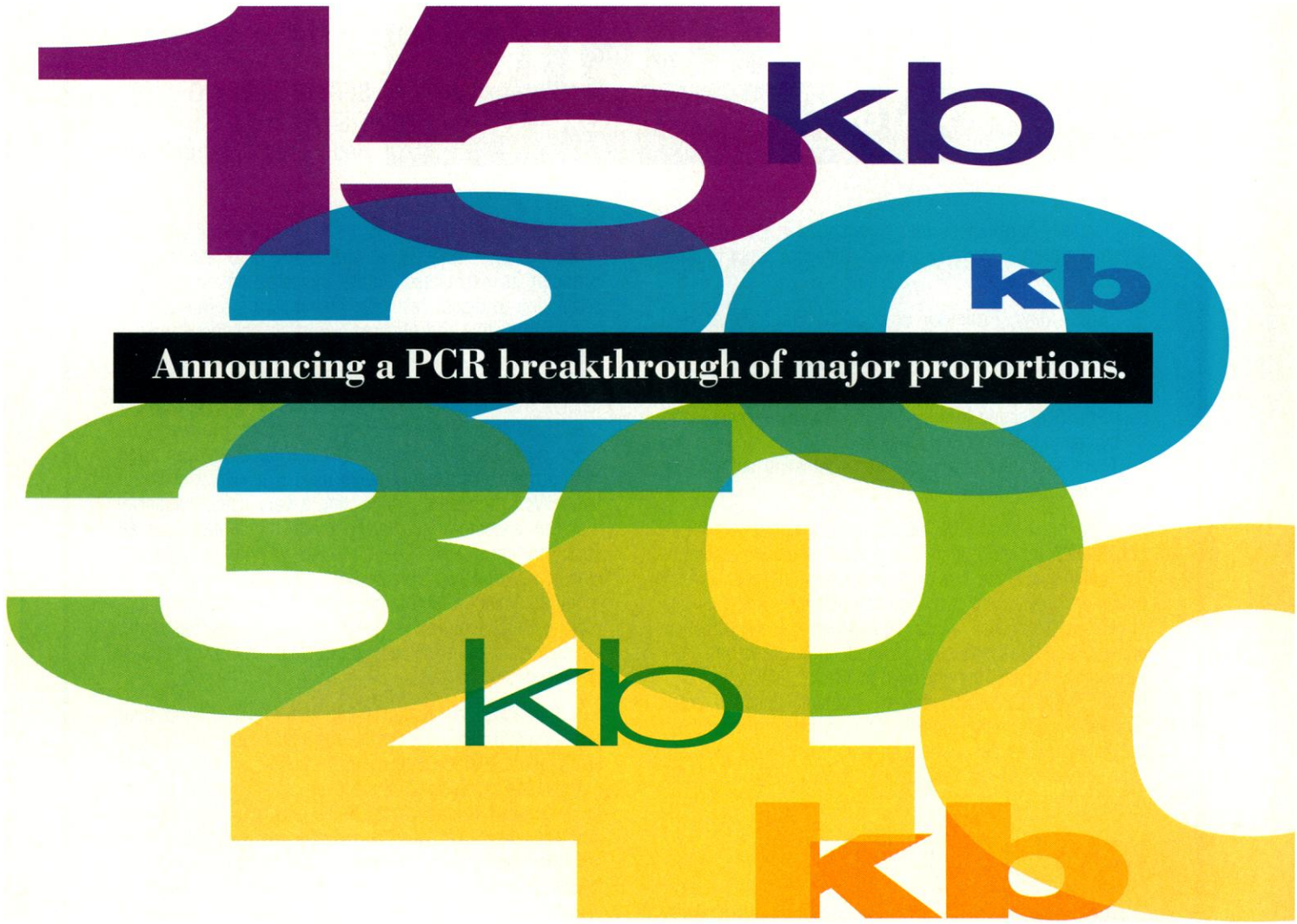

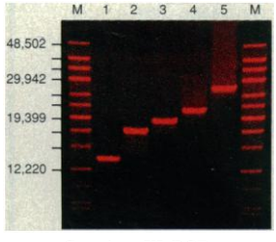

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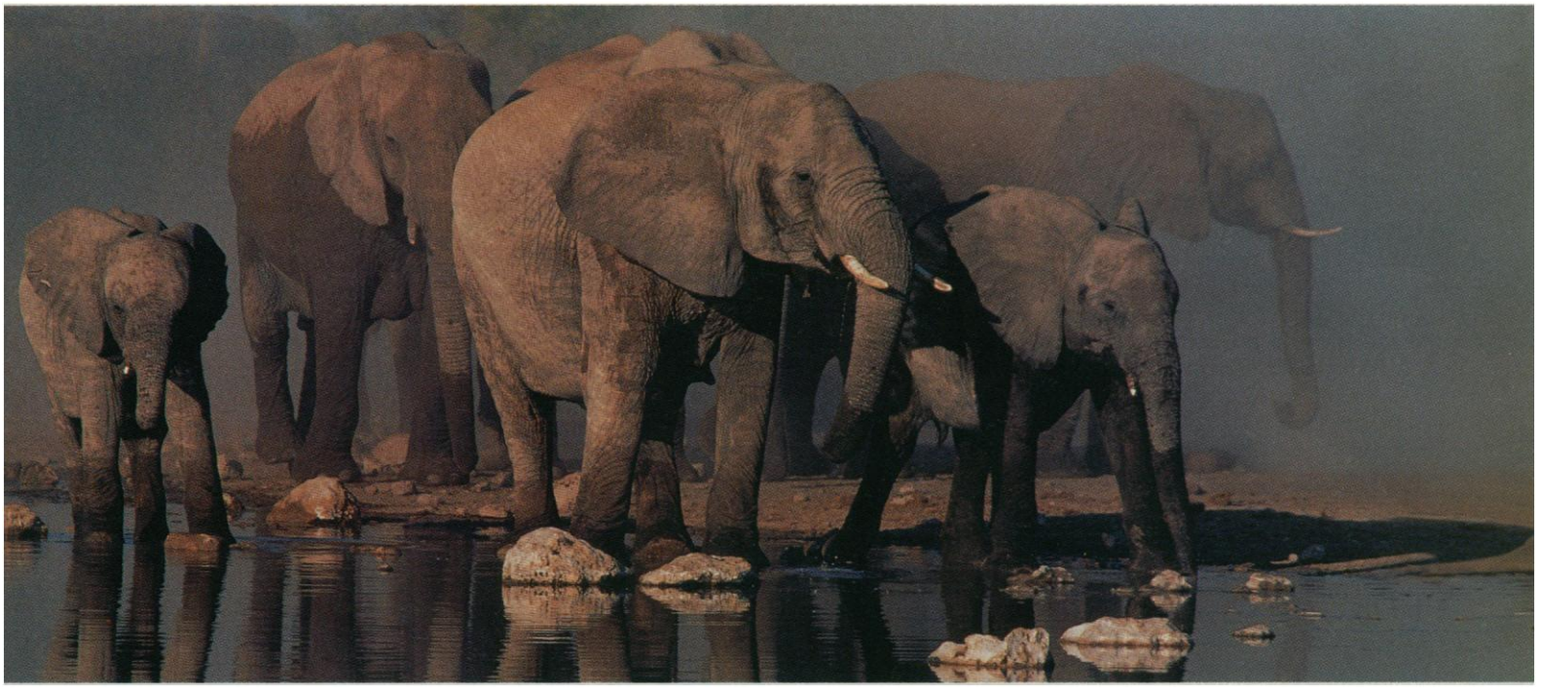

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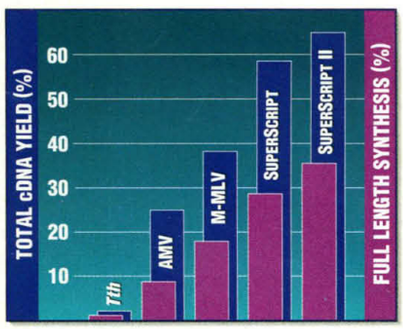

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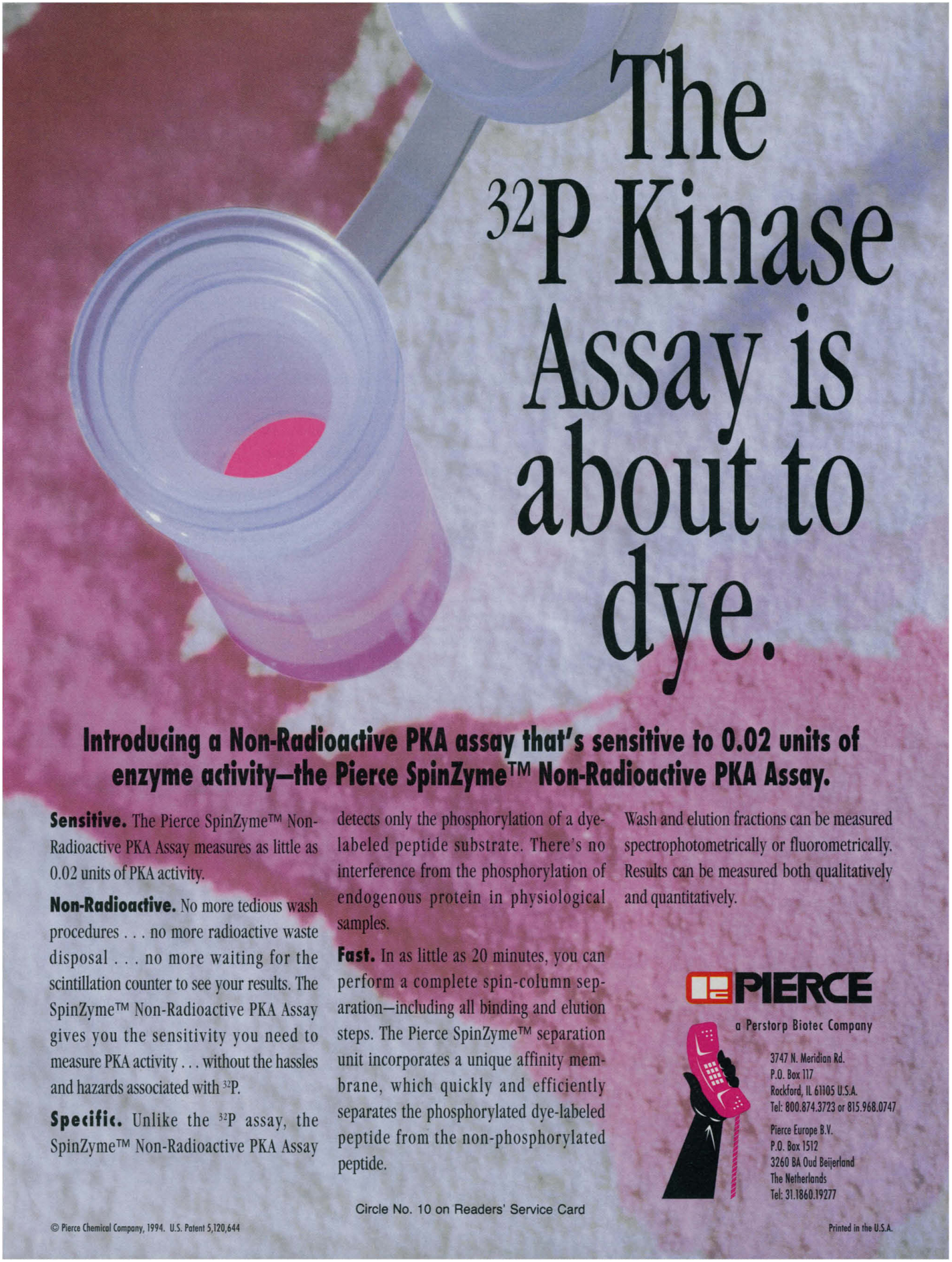

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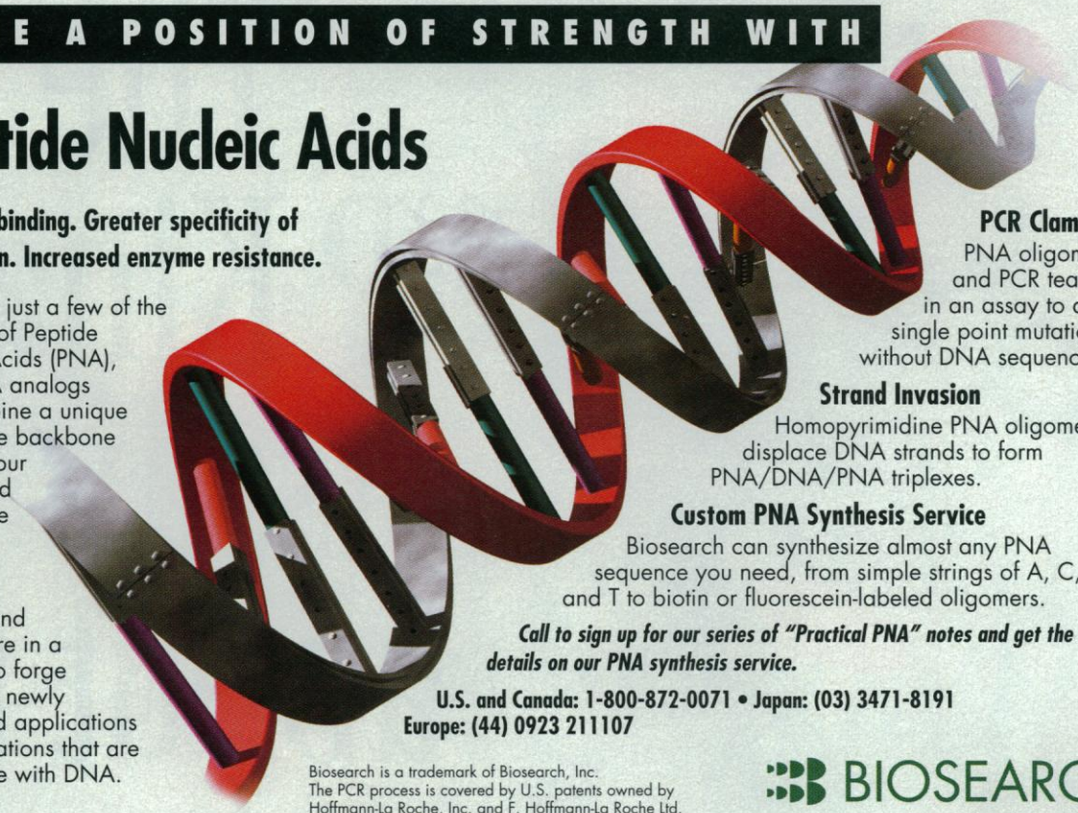

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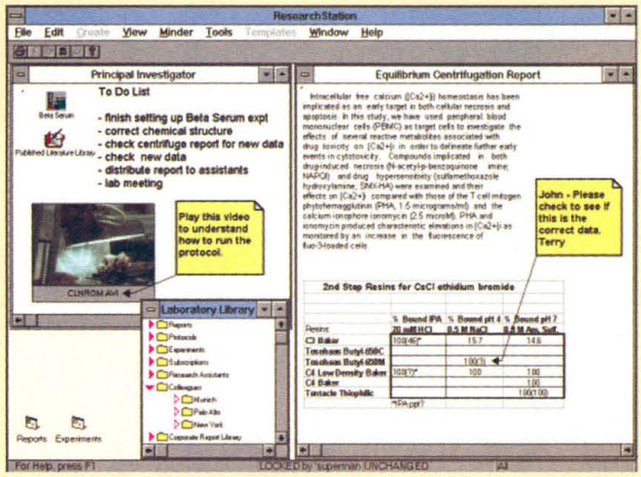

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- Control access and editing authorization (optional)
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ResearchStation is complemented by a growing line of MEGALON desktop software for scientists, including ChemStructure™ drawing and presentation software, Compounds™ chemical structure and information database, and Unistat® comprehensive statistics package. For more information, contact the MEGALON office nearest you. Via e-mail, send requests for general information to info@megalon.com, and requests for sales and distribution information to sales@megalon.com. MEGALON product demos are available via anonymous FTP from ftp.megalon.com.

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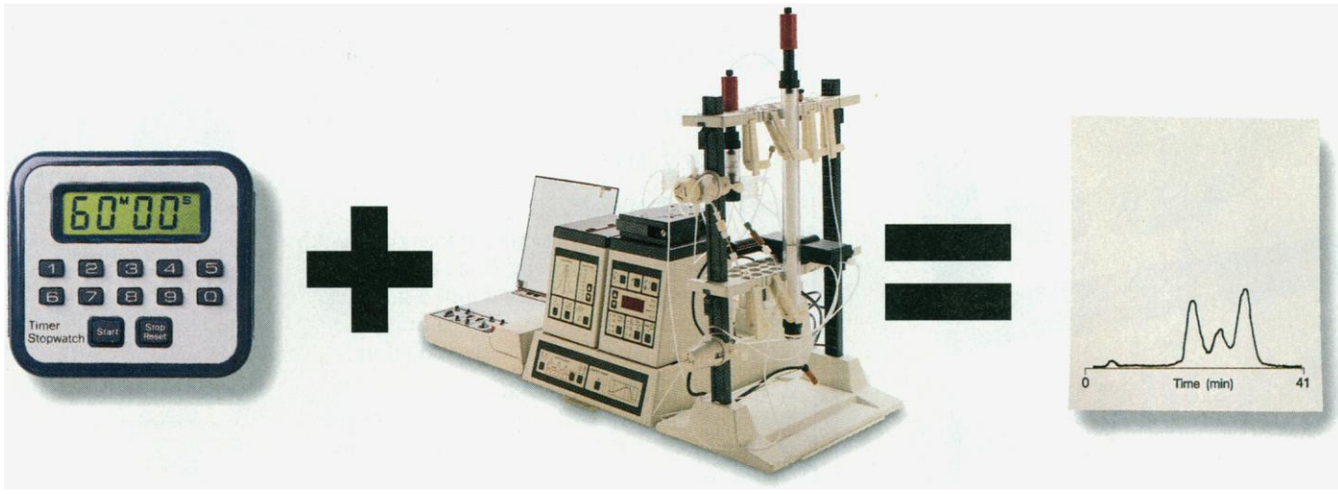

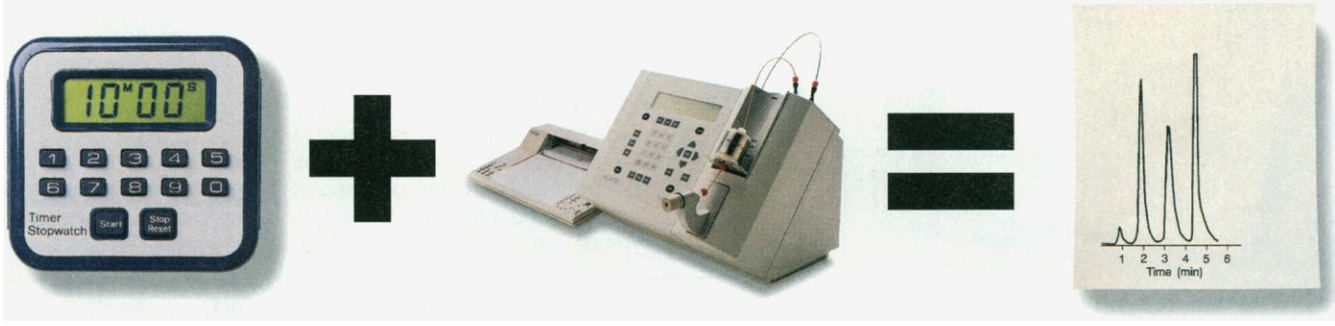

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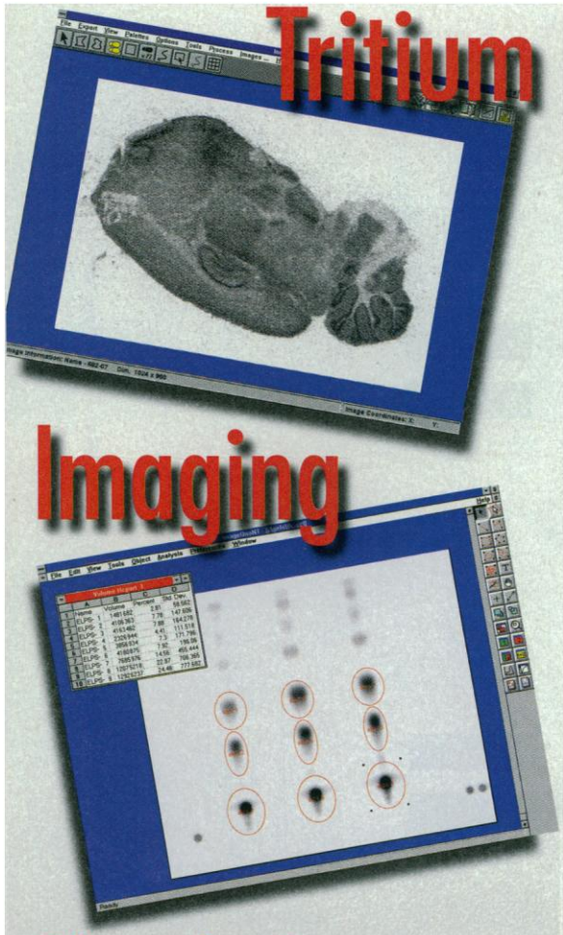

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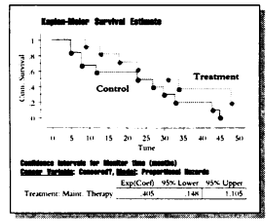

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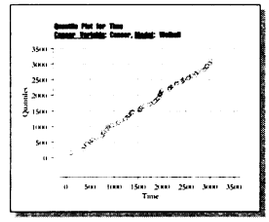

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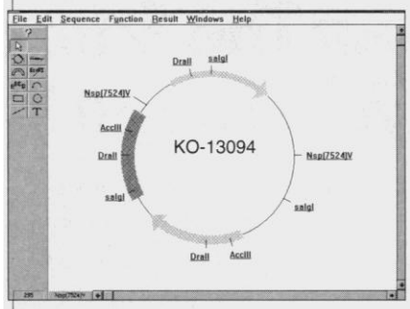

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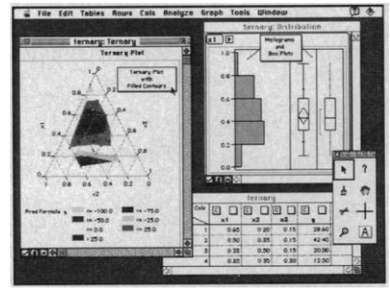

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