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14 December 2001
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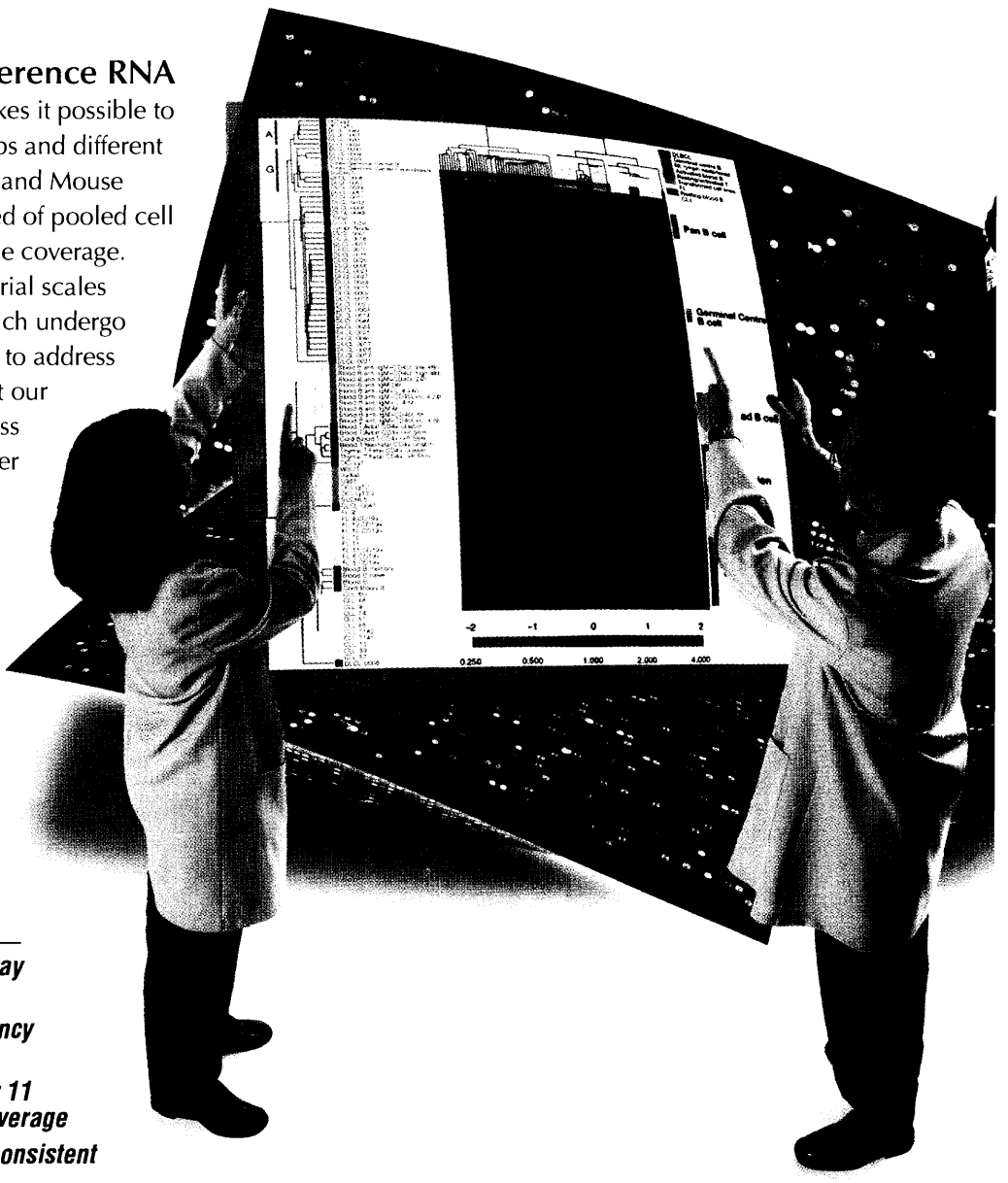

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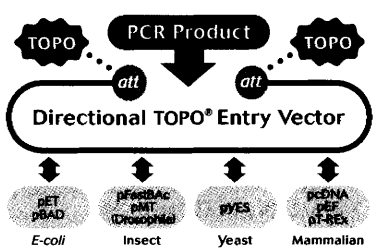

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NEWS

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Genetics in action

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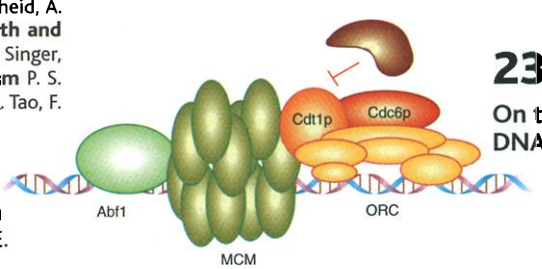

2301
On the origins of DNA replication

2293
Is this the model for science?

RESEARCH

RESEARCH ARTICLES

REPORTS

COVER 2317

A transgenic corn plant emerging from undifferentiated corn tissue (callus). *Agrobacterium tumefaciens*, a bacterium that naturally transfers DNA to plants, was used to introduce a gene conferring herbicide tolerance into the plant. The genome sequence of *A. tumefaciens* C58 is reported by Goodner *et al.* and Wood *et al.* in this issue. [Photo: Santiago Navarro and Mike Mann, Monsanto]

2351

Plants' evolutionary roots

New on *Science* Express Gut cell transformation

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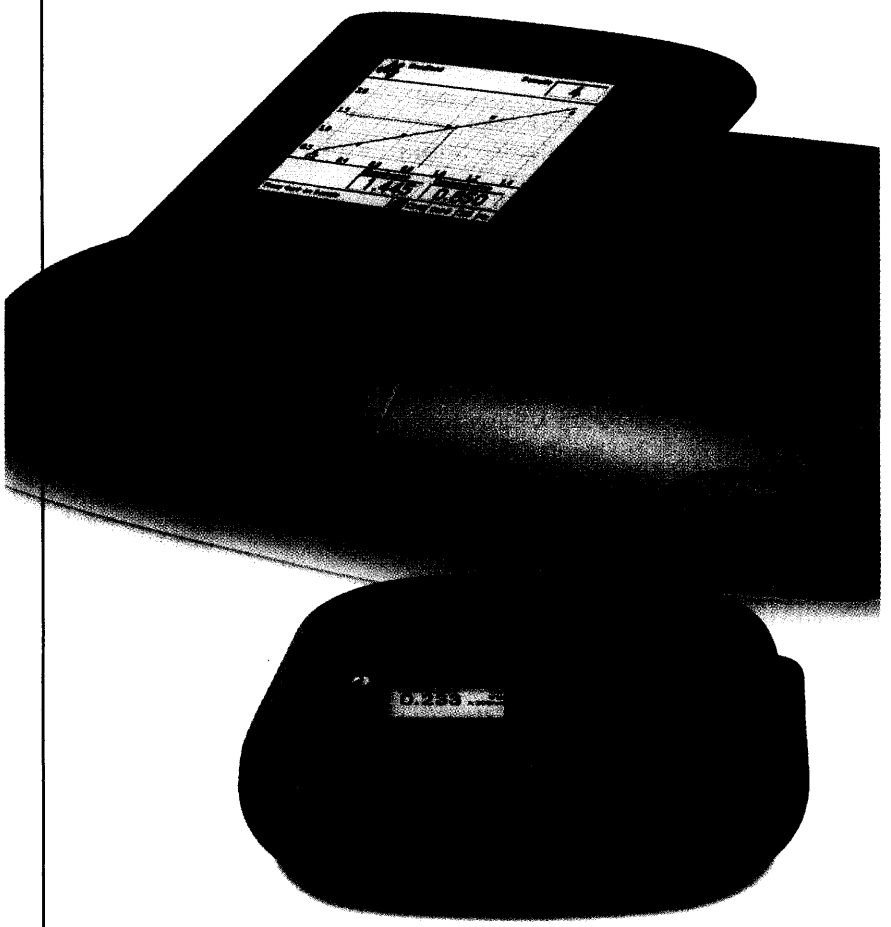

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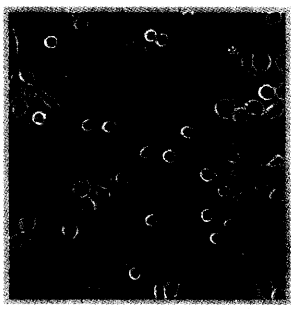
Electrically Driven Single-Photon Source Z. Yuan *et al.*

An electrically driven single-photon source is demonstrated using a quantum dot embedded in diode structure.

A Combined Experimental and Computational Strategy to Define Protein Interaction Networks for Peptide Recognition Modules A. H. Y. Tong *et al.*

Combined results of experimental and computational screens allow for accurate prediction of precise modes of interaction between protein partners later confirmed to interact in vivo.



SHP-2 Tyrosine Phosphatase As an Intracellular Target of *Helicobacter pylori* CagA Protein H. Higashi *et al.*

2269

The mechanism by which a bacterial protein may induce host cell transformation is delineated.

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career resources for scientists

Singapore: Environmental Science and Engineering—An Outlook on R&D Y. Thanabalasingam

What scientists and engineers in resource-scarce Singapore are doing to improve technologies for water and wastewater treatment, waste minimization, and air quality.

Canada: Financial Planning for Scientists—Stock Options C. Boulakia

Read about how options work and how much they might enter into a financial planning strategy in times of boom or bust.

US: Return of the Natives C. Farrar

A New York biologist finds his niche in the city—and helps other native species rediscover theirs.

Europe: French Ph.D.'s Need Luck As Well As Talent F. Voisin-Demery

In the latest installment of the Eurodoc Exchange, we hear that the major problems faced by French Ph.D.'s include a lack of funding and an absence of postdoc positions.

UK: Sowing the Seeds of Change H. Marshall

The latest Athena dissemination conference heard the results of five projects aimed at tackling the barriers to women's career progression in higher education.

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Classifying Longevity Genes R. A. Miller

Six categories of genes that affect life-span.

Genes/Interventions Database

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signal transduction knowledge environment

Review: Plant Receptor-Like Kinase Gene Family—Diversity, Function, and Signaling. S.-H. Shiu and A. B. Bleecker

Plants encode a plethora of transmembrane-spanning protein serine-threonine kinases important for growth, development, and defense. Some of their signaling secrets are revealed.

Perspective: Meeting Report—Signaling Schemes for TGF-β A. B. Roberts and R. Derynck

Progress in TGF-β signaling, from a FASEB Research Conference.

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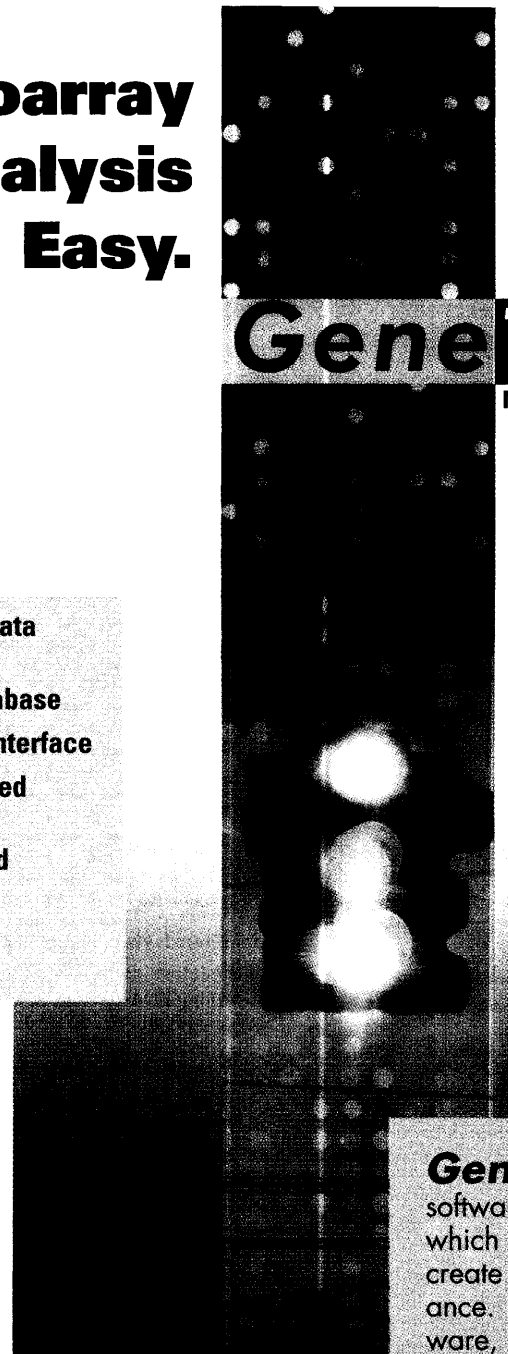

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THIS WEEK IN Science

edited by Phil Szuromi

Seismic Hazard in Northern India

The Himalayan Frontal Thrust fault (HFT) in northern India, an active structural boundary related to the collision of India with Eurasia, has produced four major earthquakes since 1897. Kumar *et al.* (p. 2328) dug trenches along a tear fault across the HFT, the Black Mango fault, to estimate the amount of deformation that occurred before 1897. They found evidence for three large earthquakes in the previous two millenia with estimated maximum uplifts of 2 to 6 meters. The results are consistent with rates of fault slip of 10 millimeters per year and crustal shortening of about 8 millimeters per year on the HFT. These paleoseismic data reinforce the severity of seismic hazards in northern India.

2368 Sickle Cell Disease and Gene Therapy

A gene therapy protocol for sickle cell disease has been developed by Pawliuk *et al.* (p. 2368; see the news story by Marshall) and tested in two mouse models. A lentiviral vector containing an anti-sickling variant of the globin gene was designed to promote successful transfer to hematopoietic stem cells and high expression in red blood cells. The transgene was expressed in >95% in red cells of normal mice 5 months after transfer and continued to be expressed 3 months after a secondary transfer. For the two mouse models, the variant protein had normal oxygen retention and prevented the manifestations of sickle cell disease (abnormal red blood cells as well as urine concentration).

CREDIT: PAWLIUK *ET AL.*

Squeezing Superconductivity

The phase diagram of metallic superconductors is generally very simple. In a sufficiently low magnetic field, there are some temperatures below which the metal starts to superconduct. What happens to superconductors as their sizes are reduced below the coherence length of the Cooper pairs that carry the supercurrent? Liu *et al.* (p. 2332) now confirm theoretical work which predicts that under certain conditions, superconductivity in systems of restricted geometry is destroyed, even at the lowest temperatures. They reveal a phase diagram quite different from the conventional one in which superconducting regions are separated by nonsuperconducting regions.

Basal Melting

Great continental ice sheets like those now found in Greenland and Antarctica contain well-defined regions where streams of fast-moving ice flow through the surrounding, more stationary areas. Fahnestock *et al.* (p. 2338; see the Perspective by Hulbe) used aircraft-borne ice-penetrating radar to determine basal melt rates under the Greenland Ice Sheet. They identified a large area of elevated heat flow located at the origins of rapid ice flow in the ice stream that flows north off of the summit dome. Magnetic anomalies and topography suggest a volcanic origin for this heat source.

Rethinking Glassy Water

A liquid converts to an amorphous state at the glass transition temperature T_g. Unlike a thermodynamic phase transition, T_g is determined by kinetics, and experimental values can vary with the cooling rate. The T_g for water has been particularly difficult to resolve. Two stable amorphous states of water have been identified that do not interconvert below 150 K, but previous experiments have given a best estimate for the T_g for water of 136 K. Velikov *et al.* (p. 2335; see the Perspective by Klug) have now compared water to other glass-forming materials, based on a common behavior of the excess heat capacity (a measure of the heat liberated at melting) plotted against temperature divided by T_g. Their analysis suggests that the T_g for water should be closer to 165 to 170 K.

Profile of a Genetic Engineer

The causative agent of crown gall disease in plants, *Agrobacterium tumefaciens*, came into the limelight when biotechnologists realized its utility for transferring foreign DNA segments into plant genomes. Wood *et al.* (p. 2317) and Goodner *et al.* (p. 2323), have now sequenced the genome of *A. tumefaciens* (see the news story by Pennisi). Unusual for prokaryote genomes, this genome includes both a linear chromosome and a circular chromosome. Various analyses from the two research groups elucidate the chromosomal structures, DNA replication origins, diversity of gene families, and the organization of metabolically related genes.

Seeing Phylogenetics Through the Trees

Bayesian phylogenetic techniques (see the review by Huelsenbeck *et al.*, p. 2310), in which statistical measures are used to assess the likelihood of the numerous complex trees that can be constructed, are providing new insights into old problems. The characteristics of the common ancestor of the land plants and charophycean algae have remained enigmatic since Darwin's day. Karol *et al.* (p. 2351) present a multigene Bayesian phylogenetic analysis of the plant kingdom that confirms the charophycean algae to be the sister taxon to land plants but also substantially resolves branching order throughout the charophycean algae. Murphy *et al.* (p. 2348; see the news story by Pennisi) apply Bayesian techniques to the enigma of the early radiation of placental mammals 100 million years ago. They resolve all but a few nodes on the mammalian phylogenetic tree and provide robust evidence that the placental mammals had their most recent common ancestor in southern-hemisphere Gondwana.

A Closer Look at DNA Replication

Replication of genomic DNA, a highly regulated process that occurs just before a cell divides, is initiated from DNA sequences

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CONTINUED ON PAGE 2247

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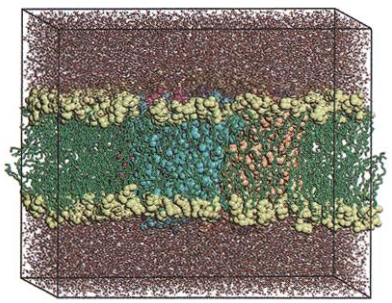
called replication origins. Identifying these origins through their sequence characteristics alone has posed a challenge because not all of the matching sequences function as origins. Thus, to map all of the origins in the yeast genome, Wyrick *et al.* (p. 2357; see the Perspective by Stillman) identify every location bound by proteins of the origin replication complex (ORC), as well as by so-called minichromosome maintenance proteins that are also required for replication. Origins are found away from transcribed regions and cluster at repetitive sequences at telomeres, where they may also be involved with setting up chromatin domains, as well as at transposable elements, which pepper the genome. The authors find evidence that the processes of replication and transcription interfere with one another. Although much can be learned from such studies of populations of DNA molecules in cells, the details of how replication occurs at specific locations on individual DNA strands is also critical. Norio and Schildkraut (p. 2361) have now developed a methodology to follow the replication of single DNA molecules from the Epstein-Barr virus. Replication is initiated in specific zones rather than at predictable individual sites, and pausing plays a significant role in the pattern of duplication. Termination of replication, on the other hand, can occur anywhere.



CREDIT: DE GROOT AND GRUBMÜLLER

Modeling Molecular Filtration

Proteins in the aquaglyceroporin family passively conduct small, non-ionic molecules (water and glycerol) across biological membranes. How they do this at high rates (10^9 molecules per second) with high specificity (water instead of protons and glycerol instead of water) is a mystery. Now, de Groot and Grubmüller (p. 2353; see the Perspective by Berendsen) present real-time molecular dynamics analysis of permeation events through the water transporter AQP1 and the glycerol transporter GlpF. These simulations support the proposal that the conserved asparagine-proline-alanine motif functions primarily as a size filter and suggest that a newly identified region, called ar/R for its aromatic and arginine elements, serves as a barrier to proton transport.

Bacterial Voltage-Gated Sodium Channels

Voltage-gated sodium (Na) channels and related potassium and calcium (Ca) channels have numerous important physiological roles in nerves, muscle, and other tissues, and are also targets for clinically important drugs. To understand the structural basis of ion selectivity and voltage-regulated gating (opening and closing) of these channels, it would be helpful to be able to study such channels from prokaryotes. Ren *et al.* (p. 2372; see the Perspective by Catterall) have now expressed a voltage-sensitive, ion-selective channel from *Bacillus halodurans* in mammalian cells (in which the channel's properties can be analyzed). Although the primary sequence of the new channel that they describe looks more like that of a Ca channel, the new channel (named NaChBac) is actually selective for Na^+ ions. Furthermore, whereas known Na and Ca channel proteins have four similar domains in which the polypeptide traverses the membrane six times, the new channel has only one such domain. The discovery of NaChBac promises to enable detailed structural and functional analysis of voltage-dependent gating mechanisms.

X Function

Hepatitis B virus (HBV) infects 300 million people worldwide and causes liver disease and cancer. The X-protein of HBV is essential for viral infection and has been implicated in carcinogenesis, but its exact role has been enigmatic. It is known to infiltrate cell signaling pathways and activate modest transcription from various promoters, as well as strongly activate viral replication in certain cell lines. The X-protein activates Src kinase without interacting directly with Src. Bouchard *et al.* (p. 2376; see the Perspective by Ganem) have now discovered that this activation is mediated by the activation of another kinase called Pyk. The activation of Pyk is caused by a release of calcium from intracellular stores (most likely the mitochondrion) triggered by the X-protein.

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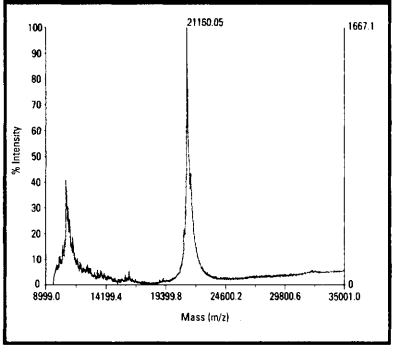

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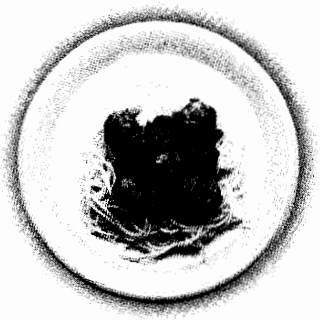

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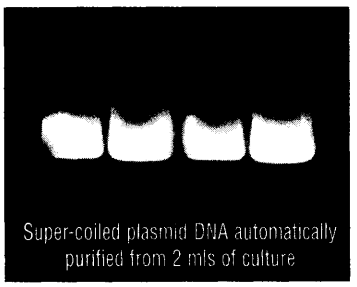

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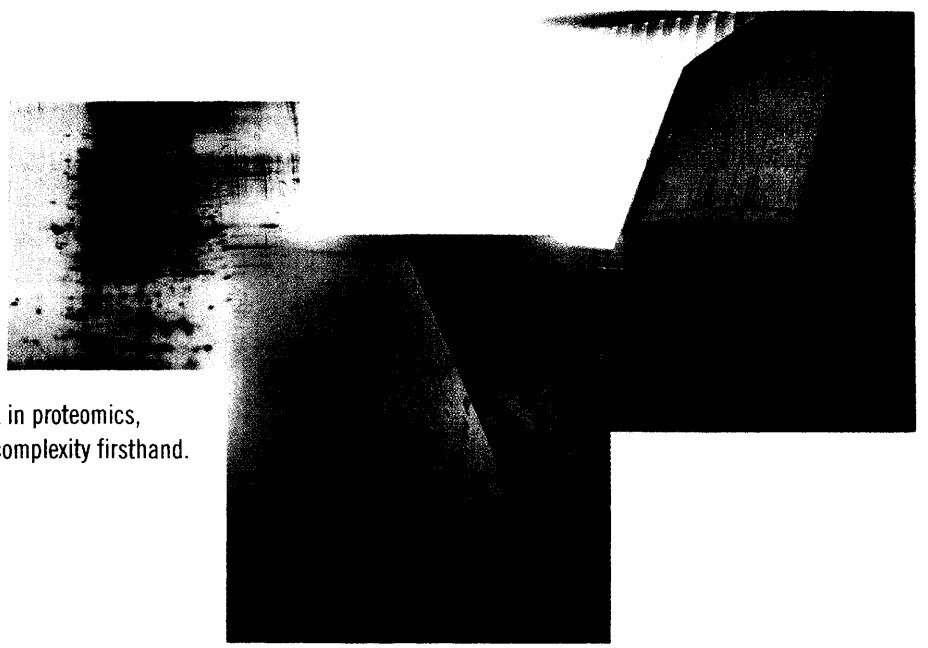

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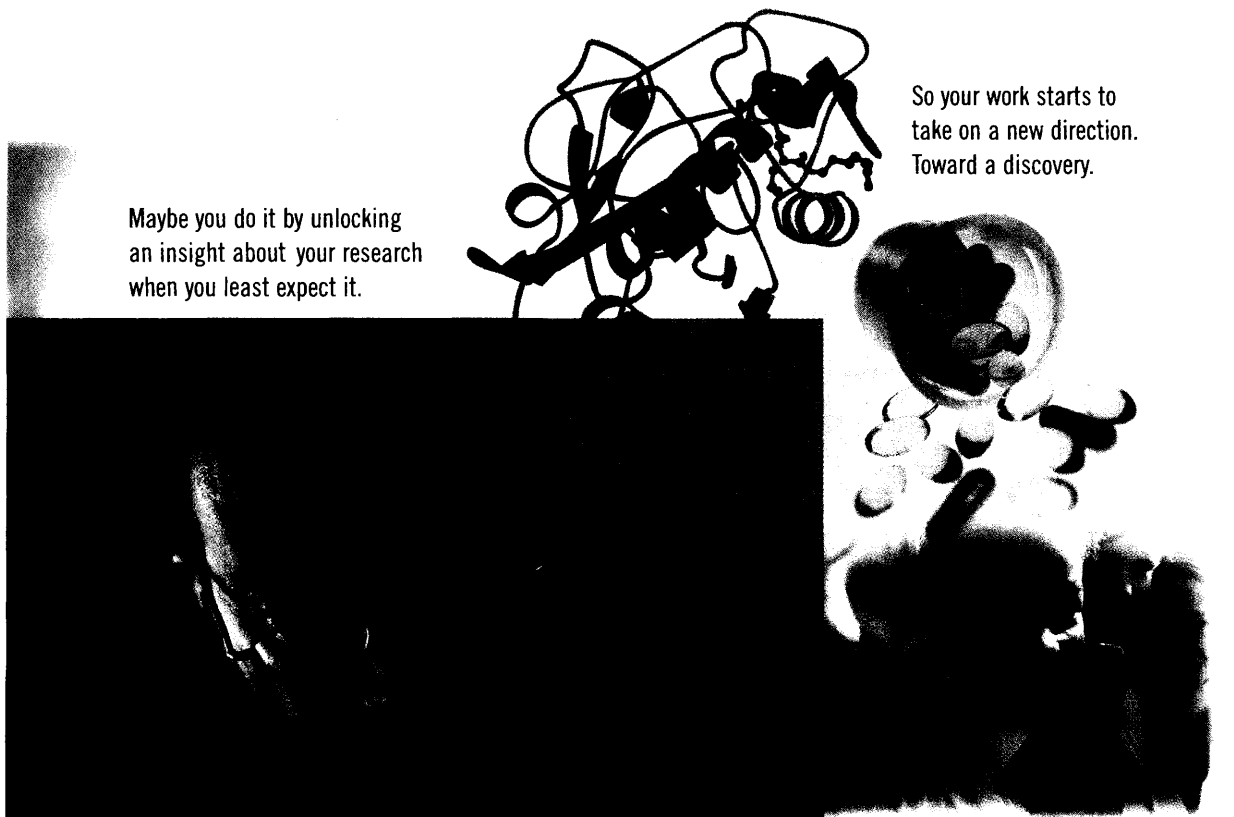

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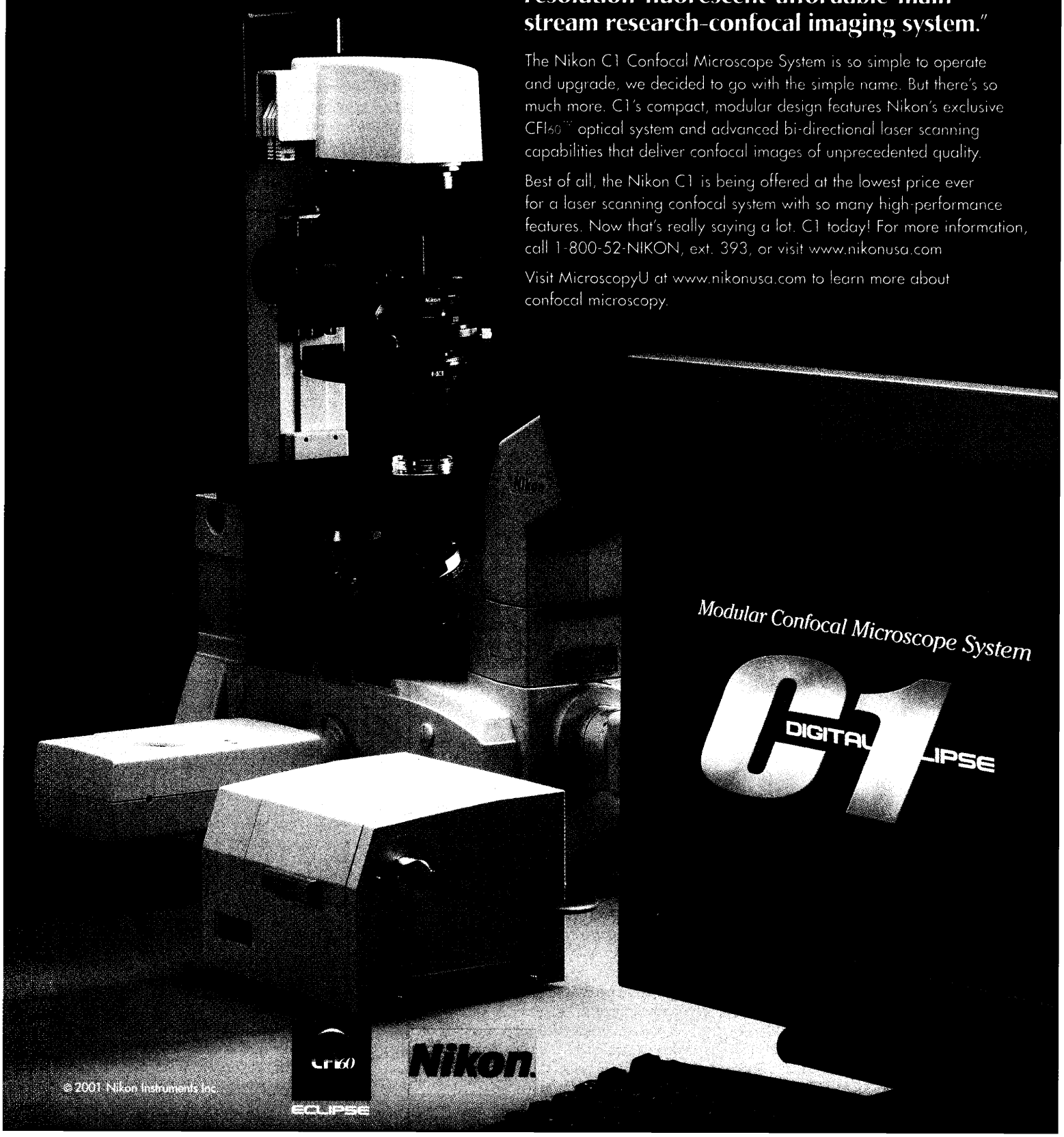

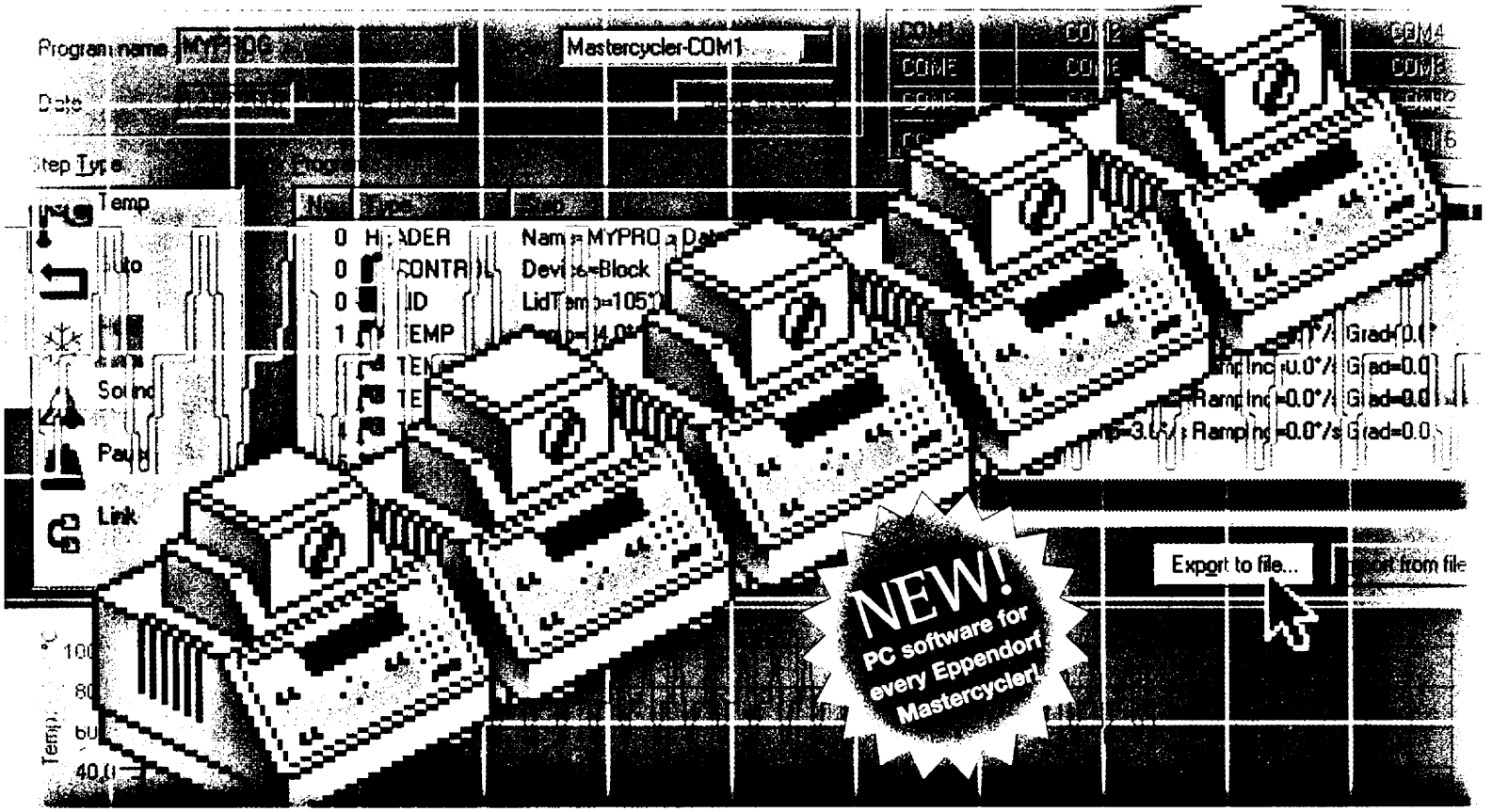

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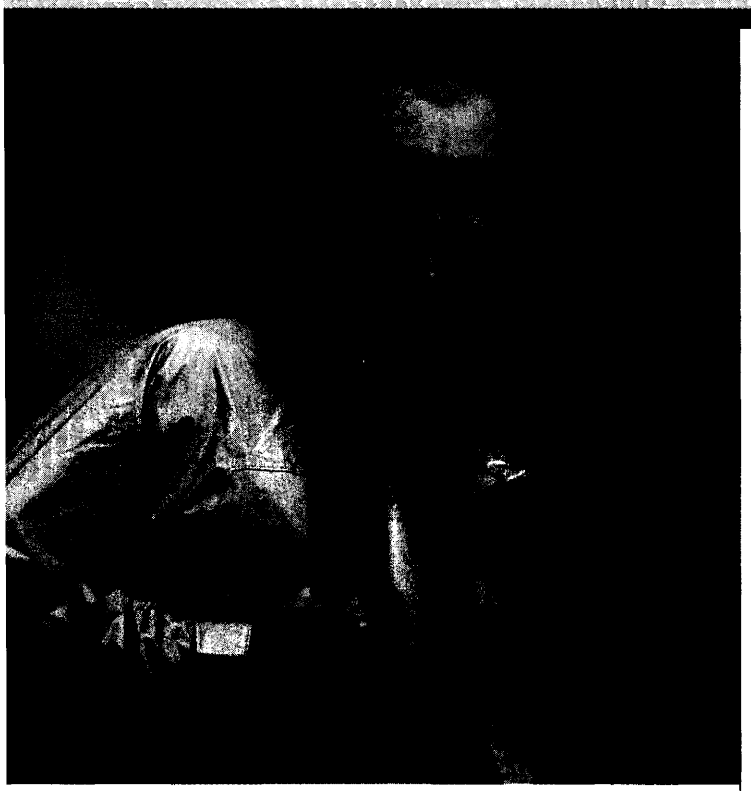

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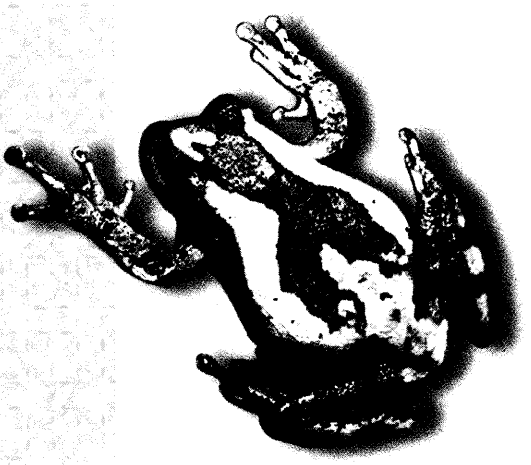

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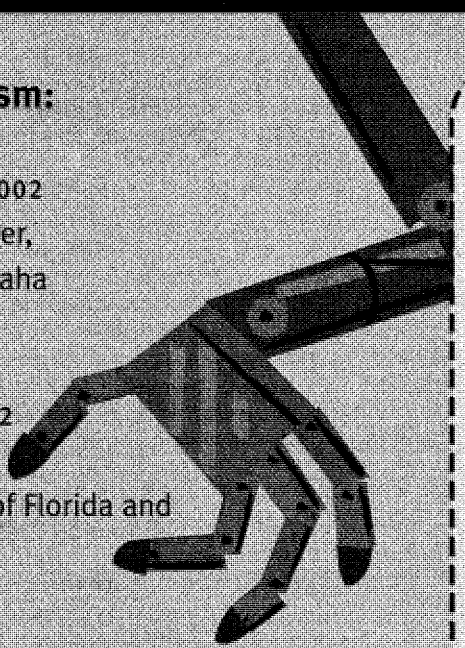

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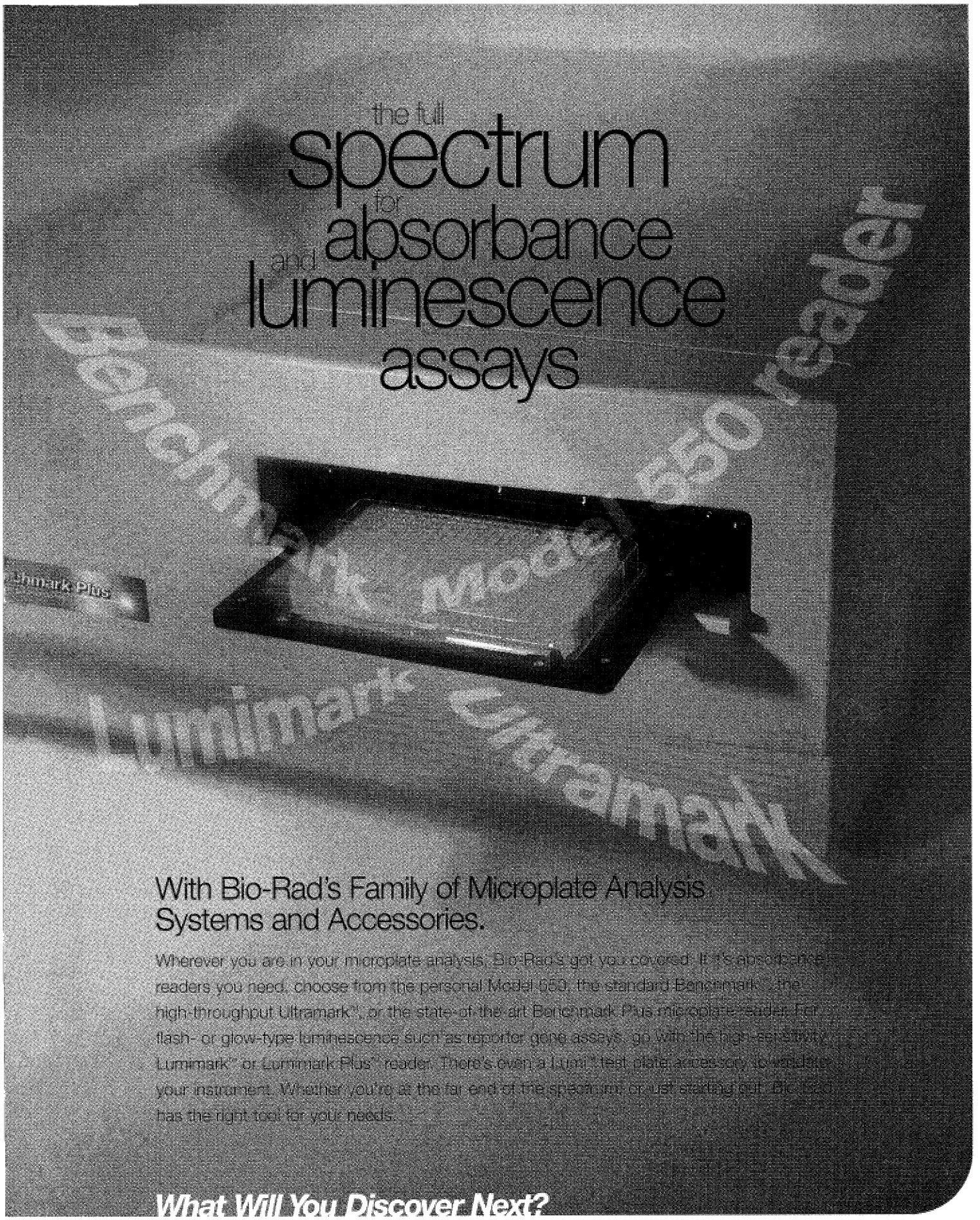

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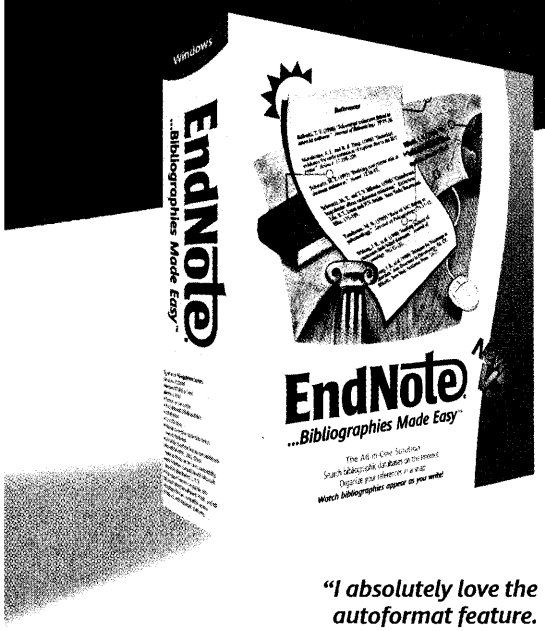

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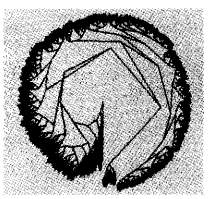

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