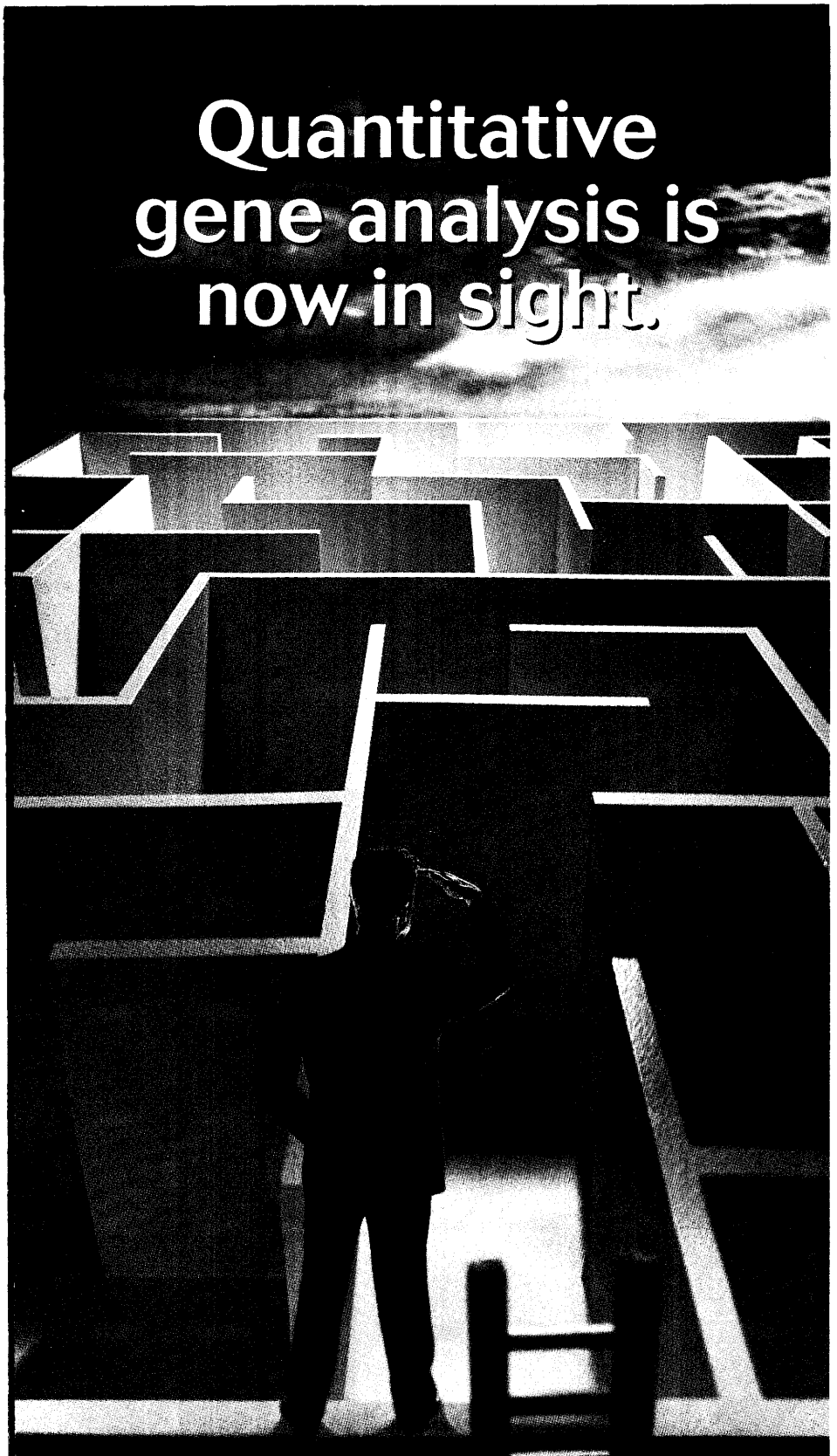
22 June 2001

Science

Vol. 292 No. 5525
Pages 2205–2384 $9

Plant Pathology

American Association for the Advancement of Science



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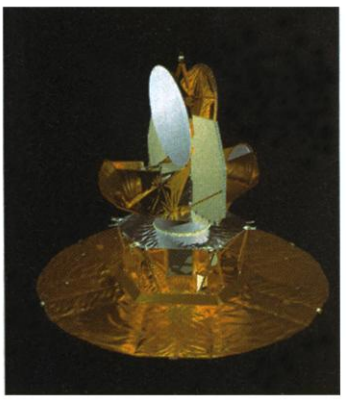

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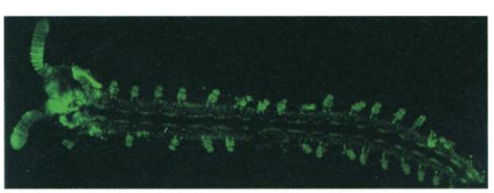
Cosmic background in the forefront

NEWS

2261
The fate of carbon

SCIENCE'S COMPASS



2256
Evo-devo duo

RESEARCH

RESEARCH ARTICLE

REPORTS

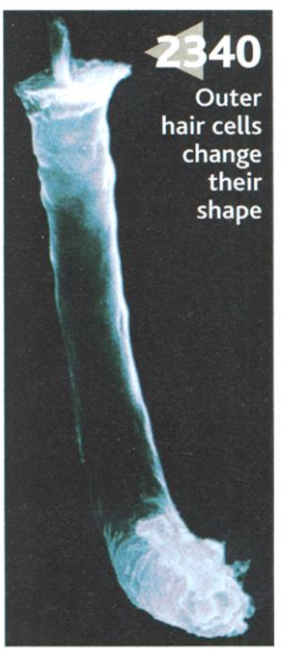
PLANT PATHOLOGY

NEWS

REVIEWS

COVER 2269

In *Through the Looking-Glass and What Alice Found There*, the Red Queen complained that in Wonderland "it takes all the running you can do, to keep in the same place." She has thus become the namesake of coevolutionary arms races in which plants continually adapt to retain resistance against their ever-evolving pathogens. The intricacies of the interactions between plants and their pathogens are explored in a special section beginning on page 2269. [David Galchutt]



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Resource Needs for HIV/AIDS B. Schwartländer *et al.*

Schwartländer *et al.* provide estimates for the costs of preventing and combating HIV/AIDS internationally.

Coupled Transcription and Translation Within Nuclei of Mammalian Cells F. J. Iborra, D. A Jackson, P. R. Cook

Evidence that translation of RNA into protein can occur in the nucleus puts a firm dent in the dogma that translation occurs exclusively in the cytoplasm of eukaryotic cells.

Haplotype Diversity and Linkage Disequilibrium at the *G6PD* Locus: Implications for the Origins of Malarial Resistance S. A. Tishkoff *et al.*

Glucose-6-phosphate dehydrogenase deficiencies are common because they confer some resistance to malaria and appear to have evolved recently, within the past 1600 to 12,000 years.

Clinical Resistance to STI-571 Cancer Therapy Caused by *BCR-ABL* Gene Mutation or Amplification M. E. Gorre *et al.*

2231 Advanced-stage leukemia patients who relapse after treatment with the potent new drug STI-571 do so because their tumor cells reactivate the same Bcr-Abl signaling pathway that originally made the cells tumorigenic.

TECHNICAL COMMENTS

White Dwarfs and Dark Matter

Oppenheimer *et al.* (Research Articles, 27 Apr. 2001, p. 698) observed a population of faint, cool white dwarfs—the kinematics of which were consistent with membership in the galactic halo—and suggested that the population accounts for 2% of the halo's "dark matter." Gibson and Flynn present calculations to argue that the objects found by Oppenheimer *et al.* actually "have a local density that is a factor of 2 to 4 less than their claimed detection of 2%." Separately, Graff compares the group's findings with those of the Luyten Half Second (LHS) survey and concludes that, far from discovering a new population of halo dark matter, Oppenheimer *et al.* have "only rediscovered the white dwarfs of the [galactic] disk." Oppenheimer *et al.* respond that the Gibson and Flynn analysis rests on invalid assumptions and presupposes accuracies not permitted by the actual data. Graff's arguments "likewise do not withstand close scrutiny," they assert, in part because "our survey and the LHS are not directly comparable."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/2211a.

science's stke www.stke.org

Review: Cycling of Synaptic Vesicles—How Far? How Fast! T. Galli and V. Haucke

An overview, with animations, of the mechanisms by which synaptic vesicle recycling may occur.

Perspective: TGF-β Flips the Myc Switch A. Orian and R. N. Eisenman

Exquisite control of the cell cycle by TGF-β.

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US: Tenure—Under Fire, but Hunkered Down J. Austin

University administrators and others attack, but so far tenure's battle-lines are holding.

UK: The French-Speaking Biologists Network F. Boudsocq

French postdocs in the United States have set up a worldwide organization to help them keep in touch with research in France.

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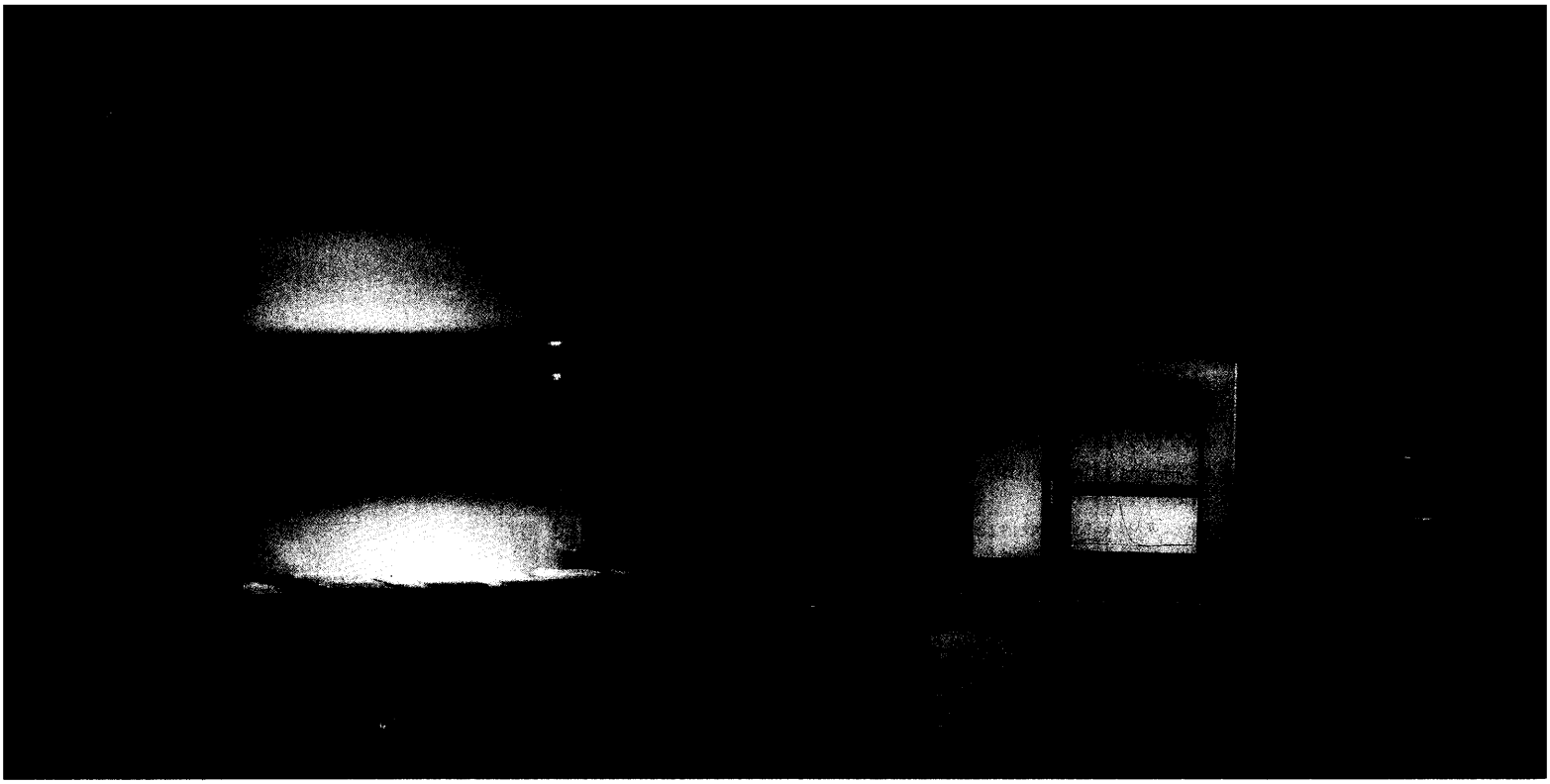

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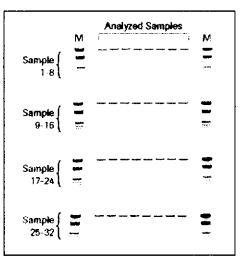

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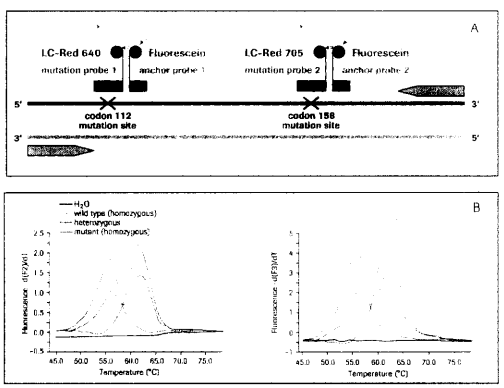

Dual-color genotyping using the LightCycler Instrument. ***A.*** *Schematic of the PCR.* ***B.*** *Melting curve analysis was performed on different genotypes at codons 112 and 158 of the Apo E sequence (in channels 2 and 3) to discriminate wild type, heterozygous, and mutant genotypes.*

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THIS WEEK IN Science

edited by Gilbert Chin

Lining Up Liquid Crystals

For most liquid crystal (LC) devices, the substrate for the device needs to be treated to induce a particular alignment of the LC at the surface. The standard procedure is to rub the surface, producing an alignment parallel to the rubbing direction. Stöhr *et al.* (p. 2299) use near-edge x-ray absorption fine structure (NEXAFS) spectroscopy to correlate the orientation bond order at the surface with various treatment methods. They find that any method that induces order at a carbonaceous surface can be used to generate a substrate, and that ion-beam irradiation of diamond-like carbon films can be used to replace rubbing and thus form the basis for the next generation of LC devices.

2310 Stomatal Matters

Global temperatures and the concentration of atmospheric CO_2 are remarkably well correlated over the past 400,000 years, and there is reason to expect that they also were correlated further back in time. However, proxy measurements of CO_2 for some warm intervals during the past 60 million years are grossly inconsistent, ranging from 300 parts per million (ppm) to more than 3000 ppm. Royer *et al.* (p. 2310) address this disagreement by estimating the concentration of atmospheric CO_2 with measurements of the stomatal density (a function of ambient CO_2 levels) of fossil leaves from warm intervals during the Miocene and the Paleocene/Eocene boundary. They find that CO_2 concentrations during these periods remained relatively low, mostly between 300 and 450 ppm, and that the amount of warming expected from the corresponding CO_2 forcing is much less than that which has been estimated from a variety of paleotemperature proxies. These results imply that factors other than CO_2 are needed to explain these intervals of global warmth.

Precise and Reliable Brain Trains

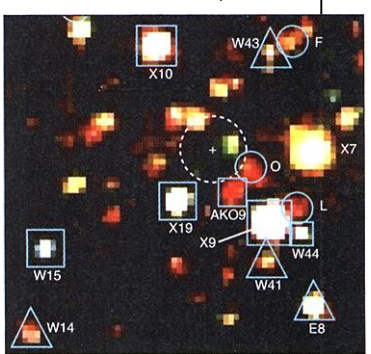
The precision of action potential timing has become a central issue for the understanding of interneuron function in the cortex. Using paired recordings in brain slices, Galarreta and Hestrin (p. 2295; see the news story by Helmuth) studied the reliability of precise spike transmission between pyramidal cells and fast-spiking interneurons, a subset of cortical inhibitory cells. Neuronal firing at this connection occurred during a limited time window that lasted for about 1 millisecond and corresponded closely to the rising phase of the excitatory postynaptic event. This precise transmission may constitute an essential mechanism that enables the synchronous firing of fast-spiking GABAergic networks.

Acoustic Oscillations in Accord

A standard model of the evolution of the universe assumes that an initial inflationary phase was followed by a Hot Big Bang. This process created a universe full of ionized plasma during its first 100,000 years, and the competing interactions between photon pressure and gravitational pressure in higher density clumps created acoustic oscillations in the plasma. These acoustic oscillations left features in the cosmic microwave background (CMB), which represents a radio-wavelength remnant of the early universe, that were recently measured. Miller *et al.* (p. 2302) have analyzed the acoustic oscillations imprinted on the matter-density distribution of clusters of galaxies and individual galaxies formed in the recent universe and found that the oscillations are consistent with the CMB results. Thus, oscillations recorded in young galaxies match with oscillations recorded in the very old plasma and provide further support for the Inflationary Hot Big Bang model of formation of the universe.

A Bit Too Quiet in Old Star Clusters

Globular clusters are spheroidal structures found in the halos of galaxies that formed early in the universe (about 12 to 14 billion years ago) before galactic disks formed. Grindlay *et al.* (p. 2290; see the 18 May news story by Watson) studied the stellar population in 47Tuc, a globular cluster in the Milky Way Galaxy using the Chandra X-ray Observatory. They found that about 50 to 55% of the x-ray sources are millisecond pulsars (MSPs), 30% are accreting white dwarfs, 15% are binaries in flare outburst, and a few are quiescent, low-mass x-ray binaries. MSPs may be spun up by accretion onto the neutron star in quiescent x-ray binaries, but the number of quiescent binaries in 47Tuc is too small to explain the number of MSPs, so alternative modes of formation may be needed to explain the population of MSPs in 47Tuc. These and other findings for 47Tuc suggest the need for revisions to models of early stellar evolution.



CREDIT: GRINDLAY *ET AL.*

African Rains

The tropics are thought to be an important source of global climate variability, as well as an area whose response to climate change must be understood better in order to anticipate possible impacts of global warming (see the Perspective by Gasse). However, high resolution records of continental temperature and precipitation of this area are relatively scarce. Barker *et al.* (p. 2307) report results from oxygen isotopic analyses of silica from diatoms that lived in alpine lakes on Mt. Kenya and conclude that the changes in the amounts of rainfall and evaporation, rather than variations in temperature, were responsible for the important isotopic shifts that occurred there during the Holocene.

Redox Control of Growth

Prokaryotes sense change in environmental oxygen through a two-component signal transduction system and adjust their metabolism accordingly. Surprisingly, oxygen is not the molecular signal that regulates this process, which involves a membrane-as-

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CONTINUED ON PAGE 2215

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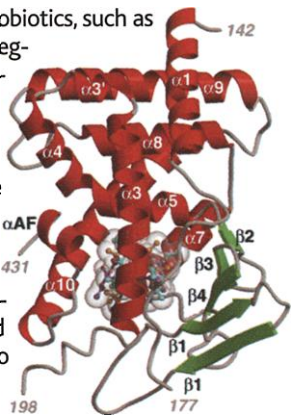
sociated sensor kinase and a response regulator that modulates gene expression. Georgellis *et al.* (p. 2314) have determined that the redox state of membrane-bound quinones regulates the ArcB sensor kinase of the bacterium *Escherichia coli*; quinones are carriers in electron transport chains that are linked to metabolic reactions.

Whither CO_2?

Calculation of the amount of carbon dioxide fixed by photosynthesis is crucial to predicting the course of future climate change (see the Perspective by Wofsy). The size of the U.S. terrestrial carbon sink has been a subject of much debate. Pacala *et al.* (p. 2316) provide a comprehensive analysis comparing estimates derived from forest inventories with those from atmospheric models of carbon dioxide concentration. Although the estimates of the sink vary by a factor of nearly two (from 0.3 to 0.6 petagrams of carbon per year), the range of estimates from both methods is similar. Fang *et al.* (p. 2320) report changes in the storage of living forest biomass carbon over the past half century in China, using data from the continuous national forest inventory. Their results suggest that reforestation in China may be contributing to global terrestrial carbon sinks.

Collateral Damage

Potentially dangerous drug-drug interactions can occur when xenobiotics, such as the St. John's wort ingredient hyperforin, activate the nuclear pregnane X receptor (PXR) because this receptor is a transcription factor that stimulates expression of cytochrome P450, an enzyme that metabolizes many small molecules, such as the immunosuppressive drug cyclosporin. Watkins *et al.* (p. 2329) have determined the crystal structures of the ligand-binding domain of the human PXR alone and in complex with the cholesterol-lowering drug SR12813. Although the PXR is known to bind a variety of compounds, several polar residues within a mostly hydrophobic cavity were shown to specify a directed promiscuity and to mediate binding of SR12813 in three distinct orientations; targeted mutagenesis of these residues served to graft sensitivity to SR12813 onto the formerly inert mouse PXR.



CREDIT: WATKINS *ET AL.*

Make or Break

Large bacterial viruses (phage) break out of their host cells by making a hole in the host's cell membrane, which allows the release of a virus-produced enzyme that degrades the cell wall (see the Perspective by Hatfull). The small, single-stranded counterparts of these phages have a different strategy for attacking the cell wall and produce proteins that inhibit various steps in bacterial cell-wall synthesis. Bernhardt *et al.* (p. 2326) show that the protein A_2, from the group III ssRNA phage Qβ, blocks the first enzyme in cell wall synthesis, and, as a result, 20 minutes later the cell walls of the growing bacteria begin to disintegrate.

Executive Recruiters

Transcription activators can recruit the histone acetyltransferases (HAT) complexes SAGA and NuA4 to stimulate transcription from chromatin-assembled DNA templates, but the mechanism for targeting these complexes to promoters is unclear. Brown *et al.* (p. 2333) now demonstrate that acidic activators interact with Tra1p, a subunit that is found in both of these complexes; hence, Tra1p is likely to be an essential component involved in the recruitment of HAT to promoters for the modification of histones.

Ionic Mechanism of Hearing

The outer hair cells of the mammalian cochlea are specialized cells and function early on in the hearing process. Recently, prestin, the motor protein responsible for the electromotility of outer hair cells, has been identified and cloned. Oliver *et al.* (p. 2340) found that the unusual voltage sensitivity of this protein is not intrinsic but depends on the presence of intracellular anions, such as bicarbonate and chloride, which behave like extrinsic voltage sensors. In binding to the motor protein, they trigger the structural rearrangements in the molecule that underlie outer hair cell electromotility.

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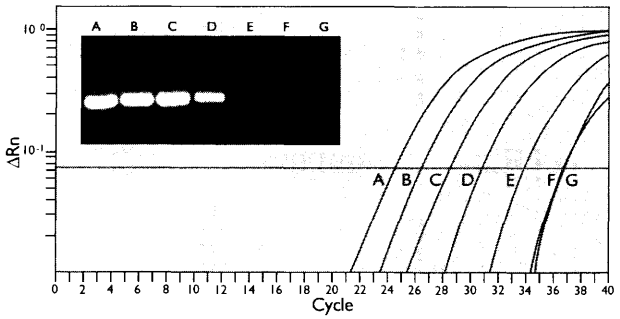
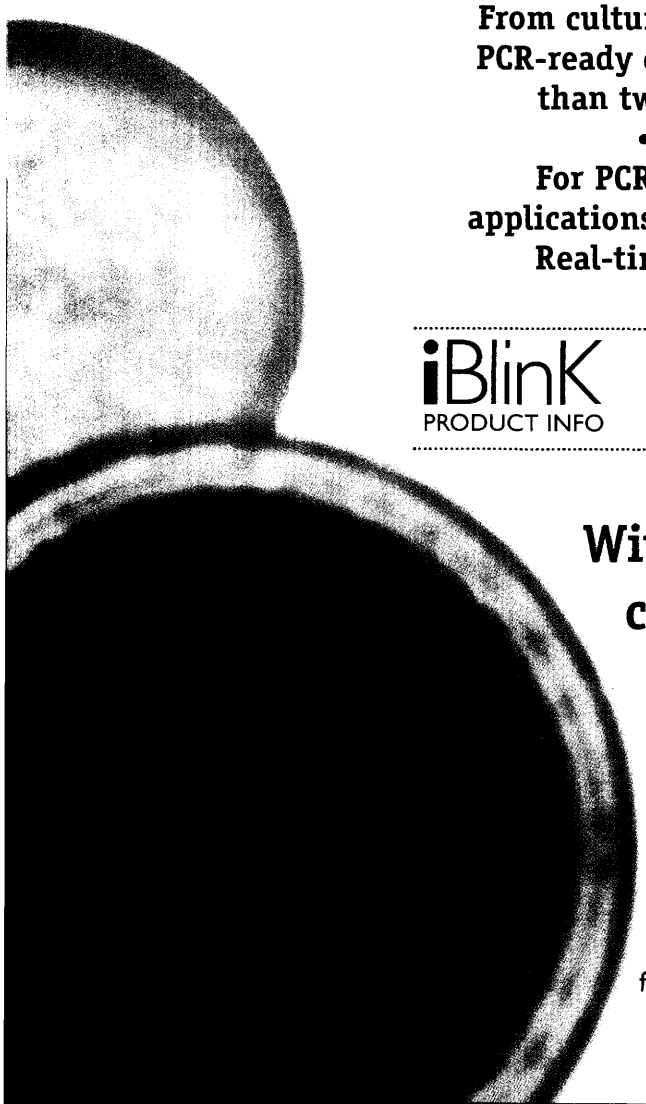


Amplification Plot, Real-time GAPDH PCR
Lane A) 500 cell equivalents B) 200 cell eq C) 50 cell eq D) 10 cell eq E) 1 cell eq F) no-RT control from 500 cell eq G) no-template control

Inset: Gel-based GAPDH PCR, 35 cycles
Lane A) 250 cell equivalents B) 125 cell eq C) 62 cell eq D) 31 cell eq E)16 cell eq F) no-RT control from 250 cell eq G) no-template control



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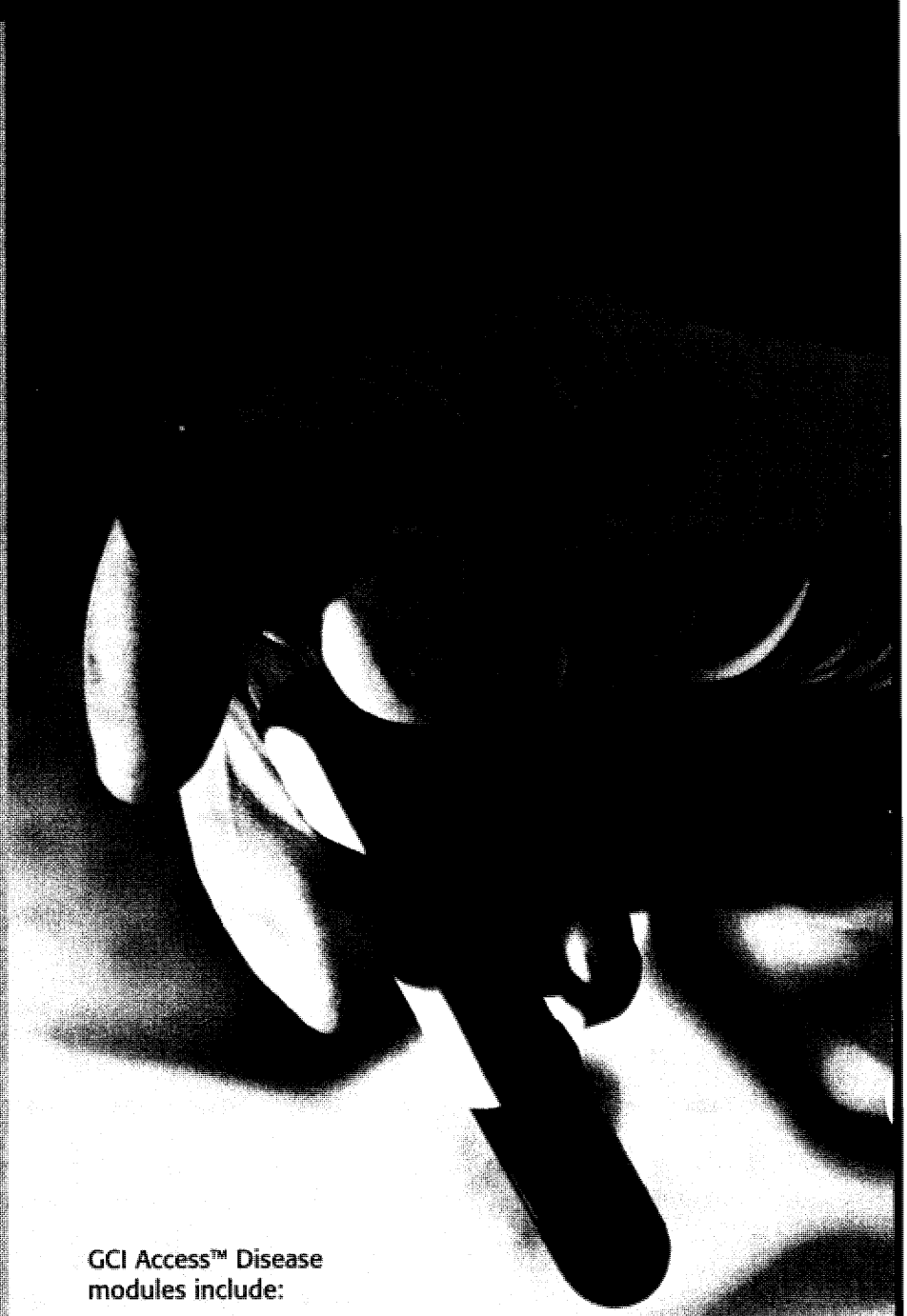

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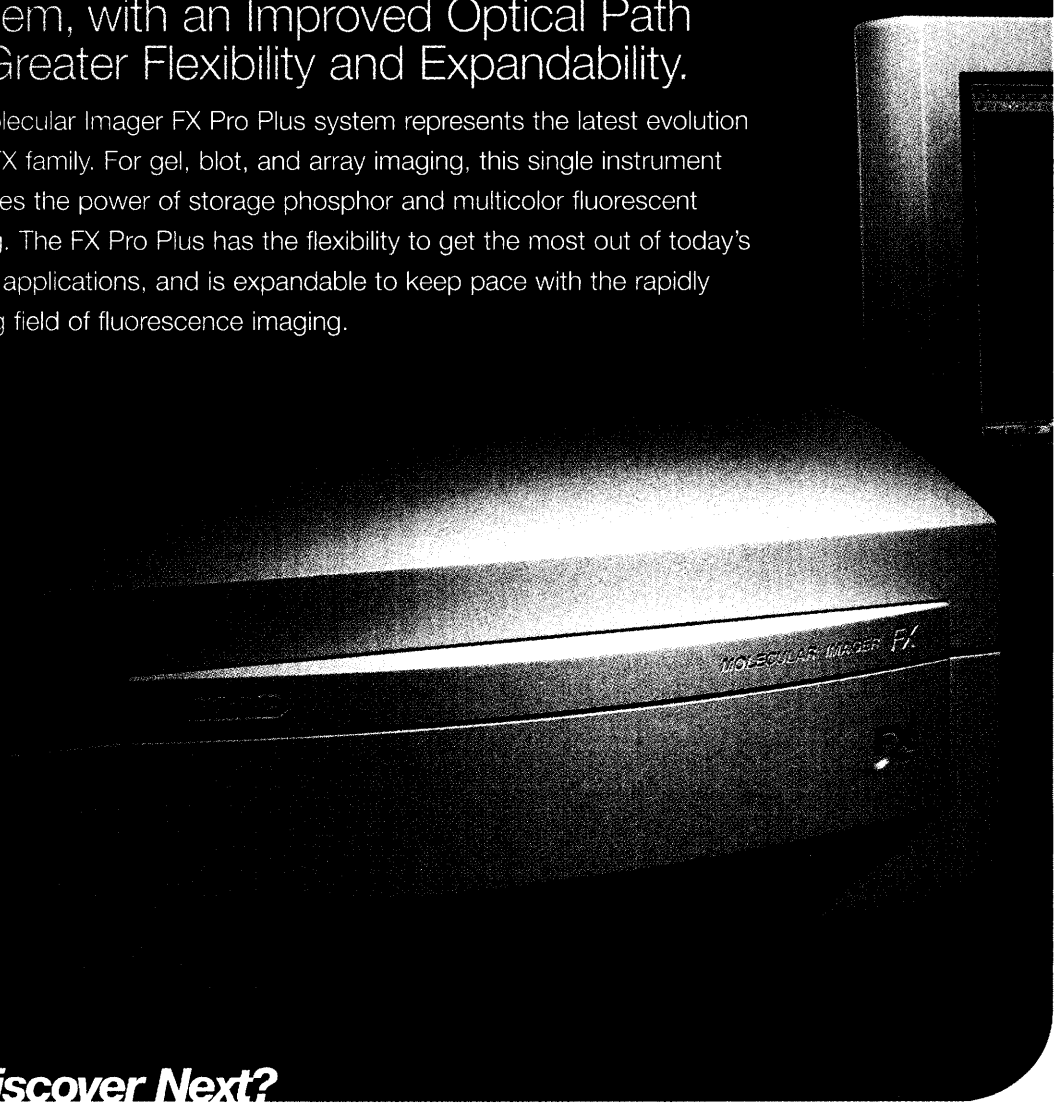

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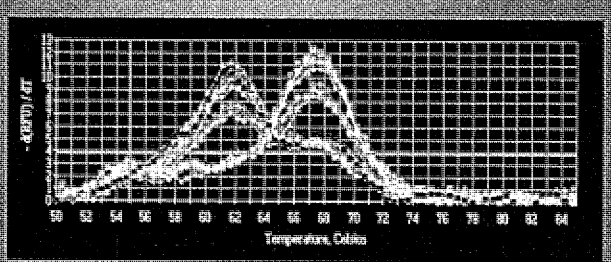

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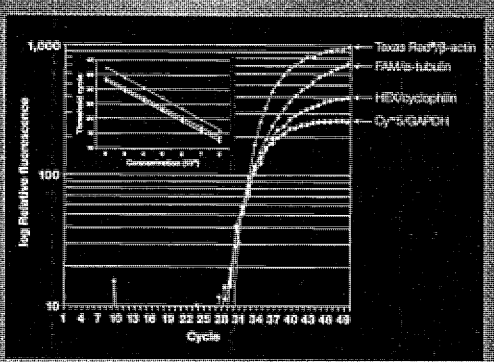

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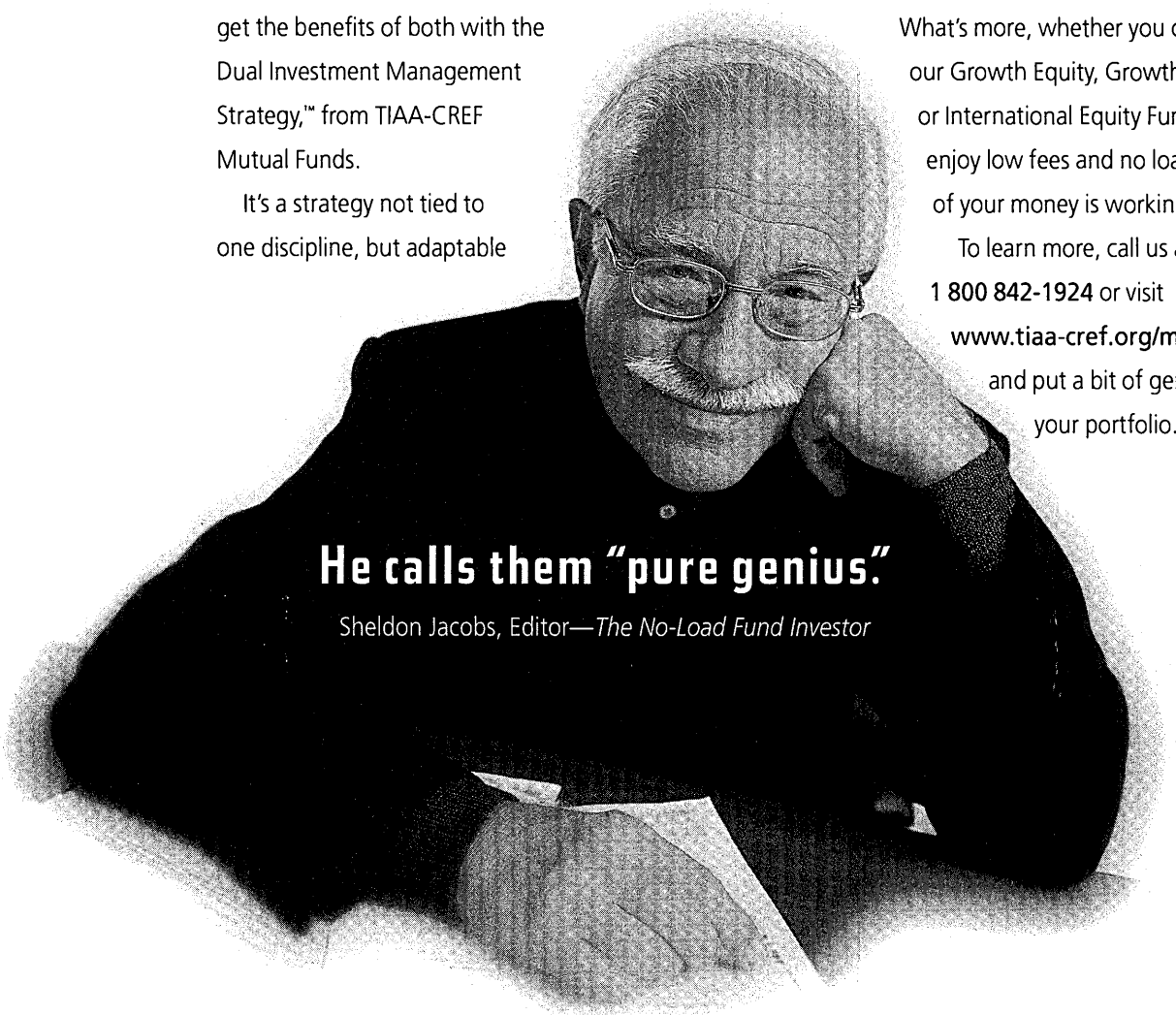

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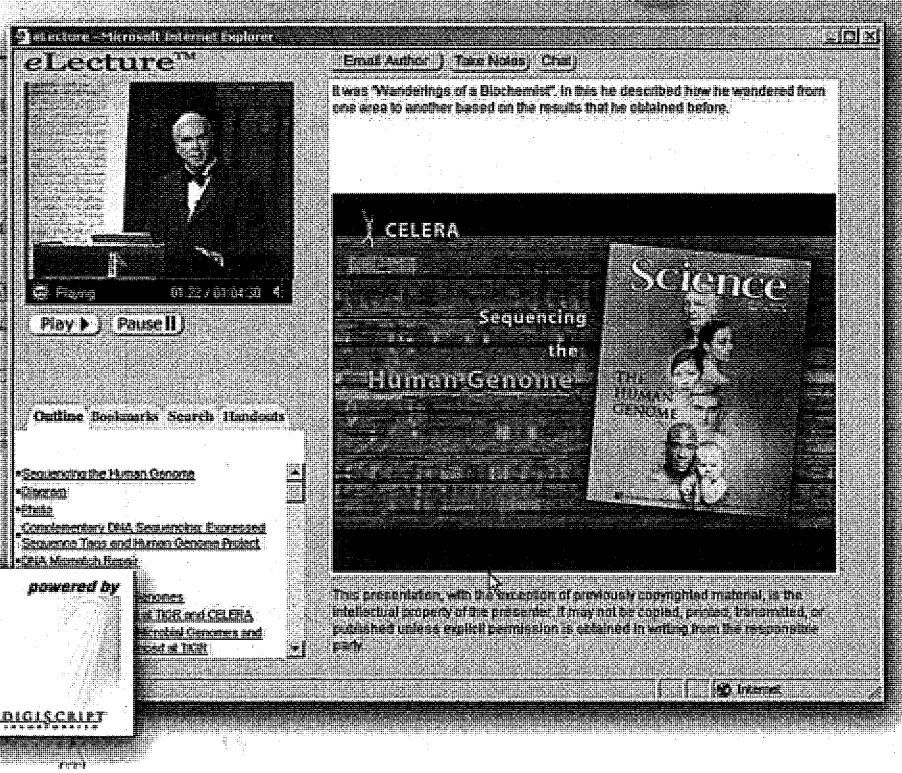

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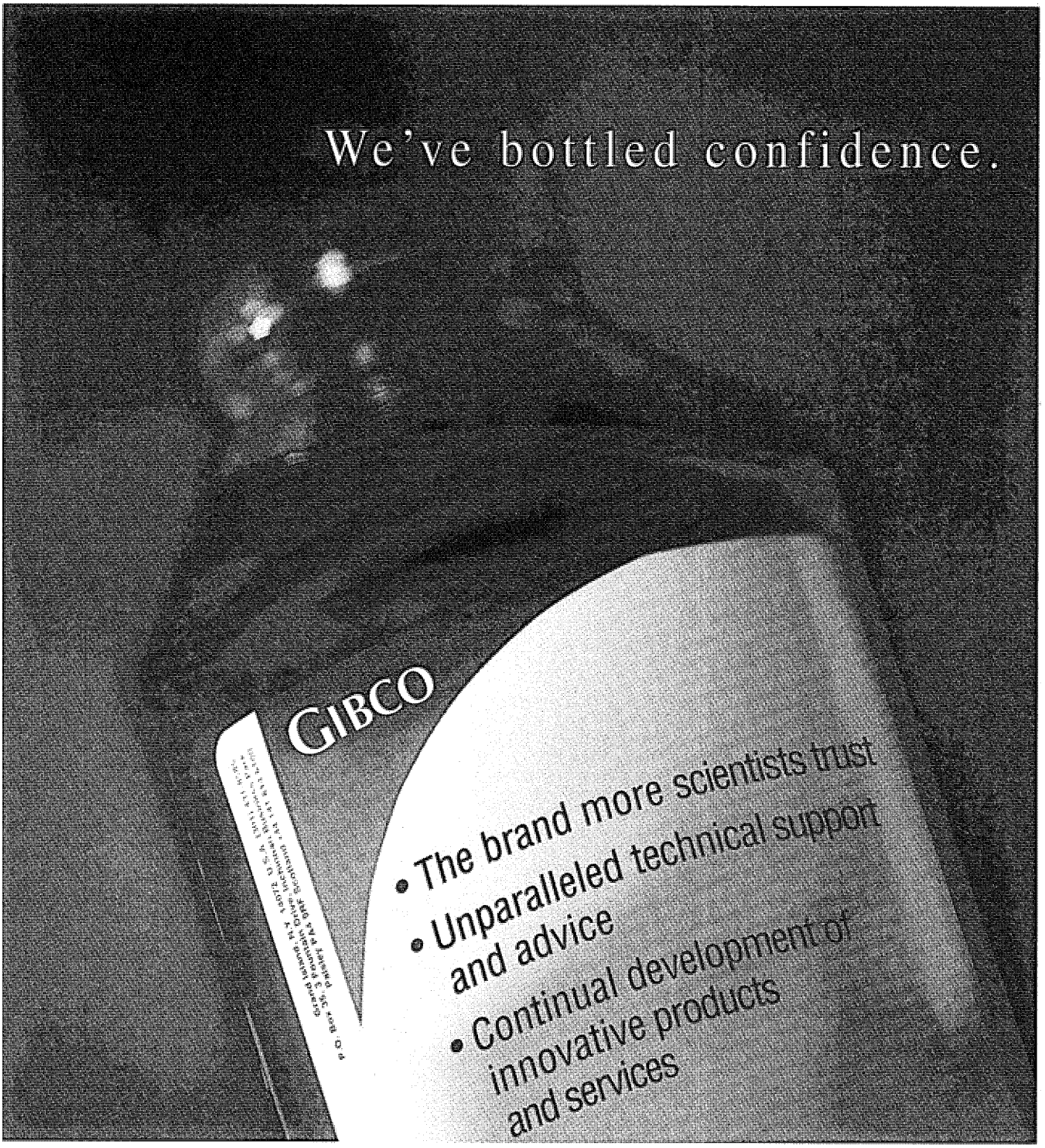

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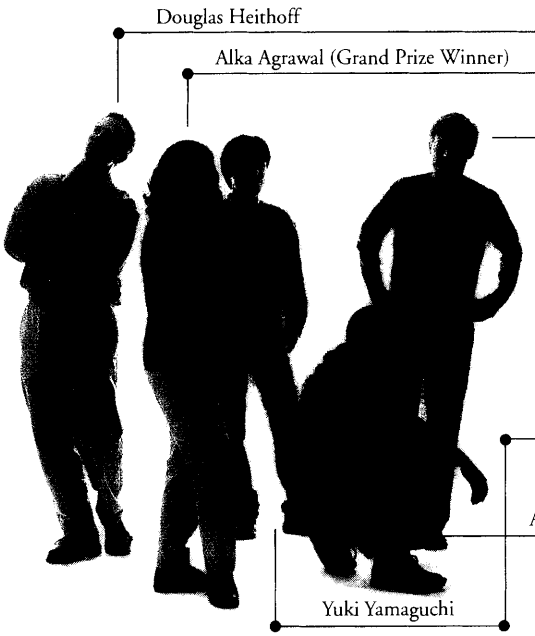

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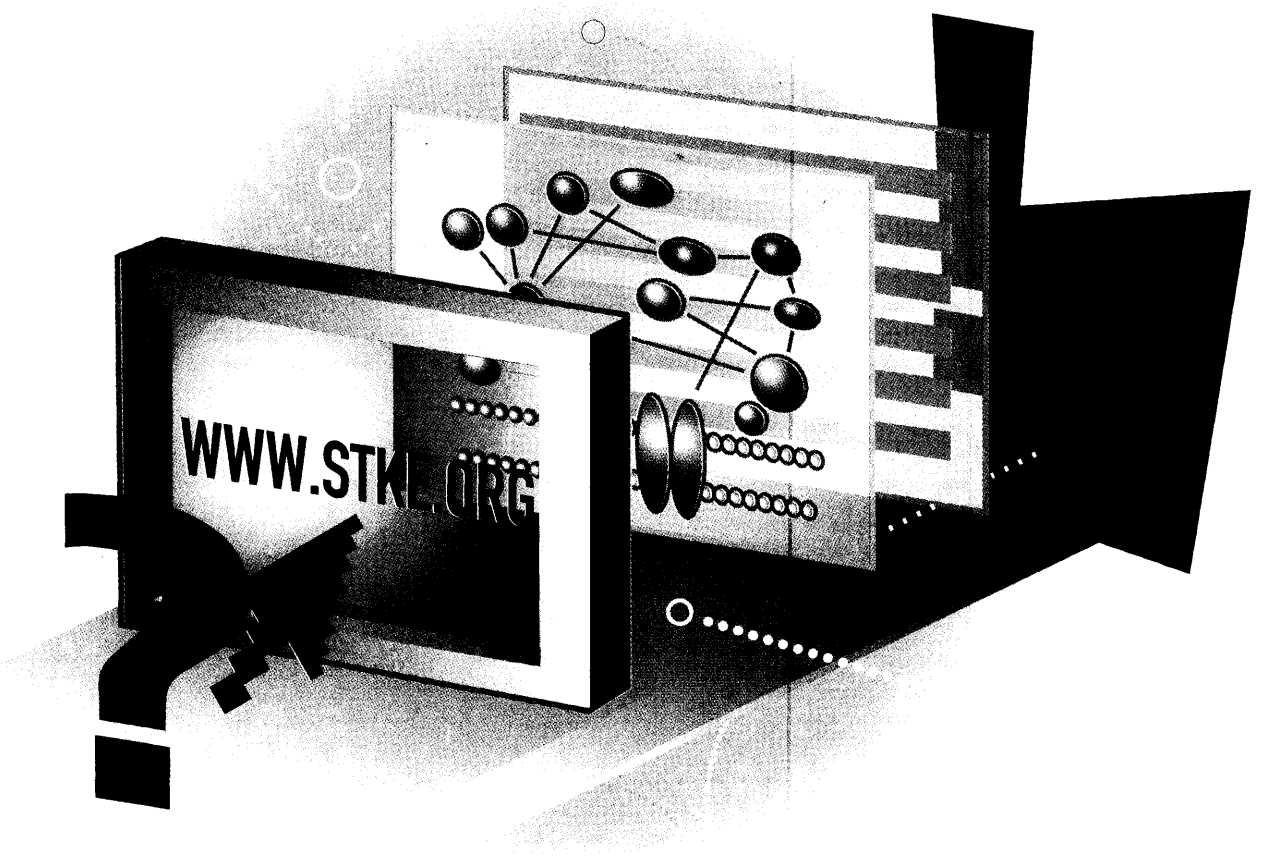

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