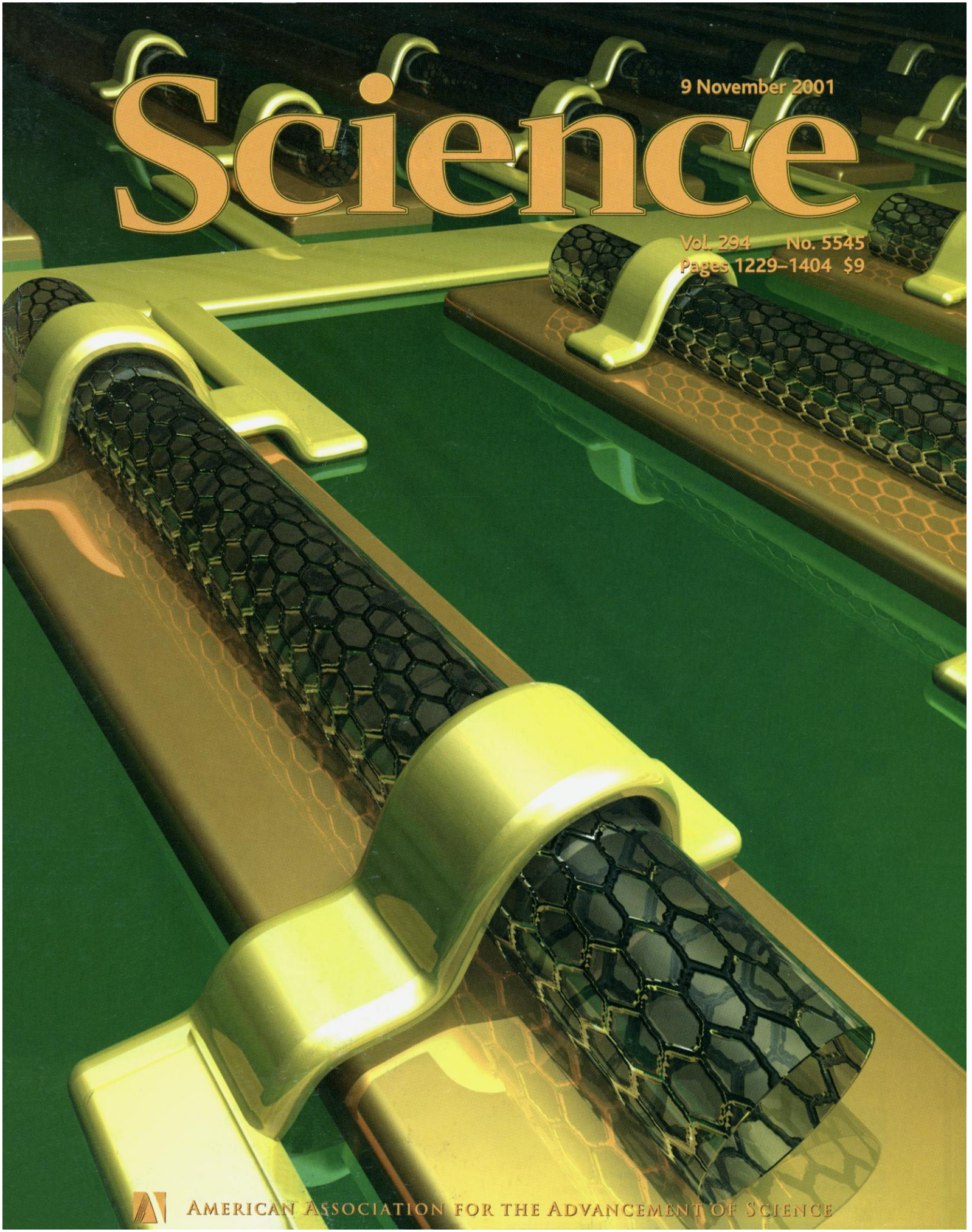
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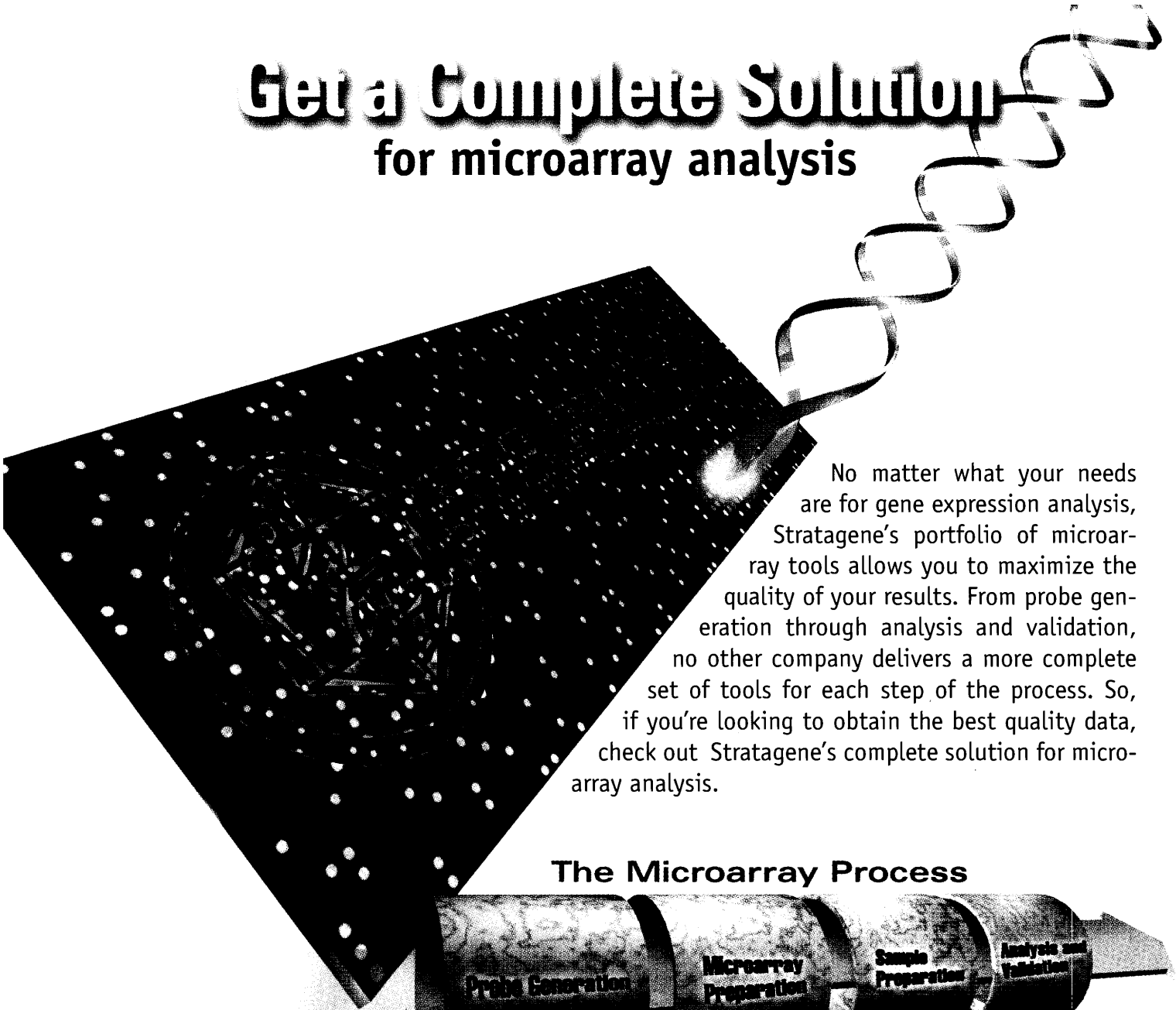

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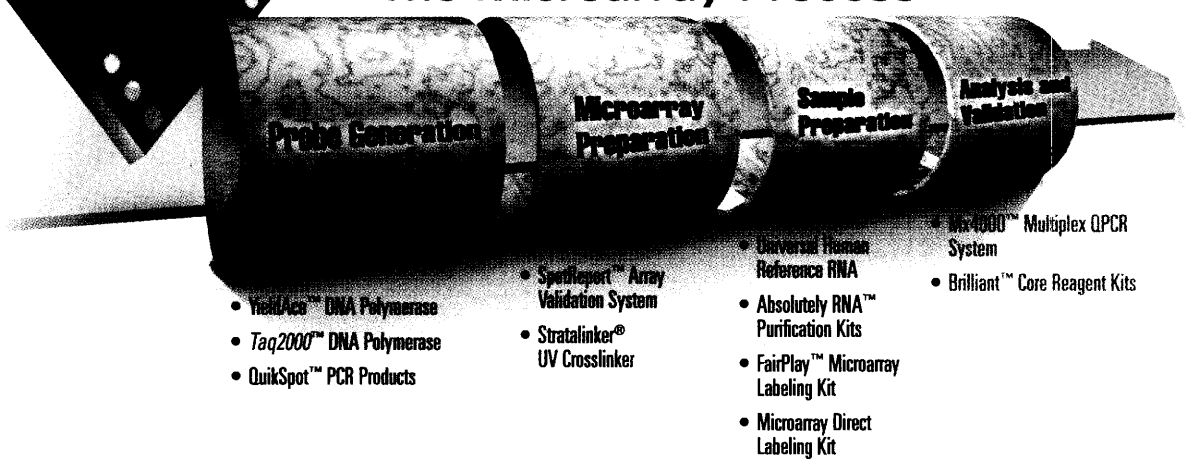

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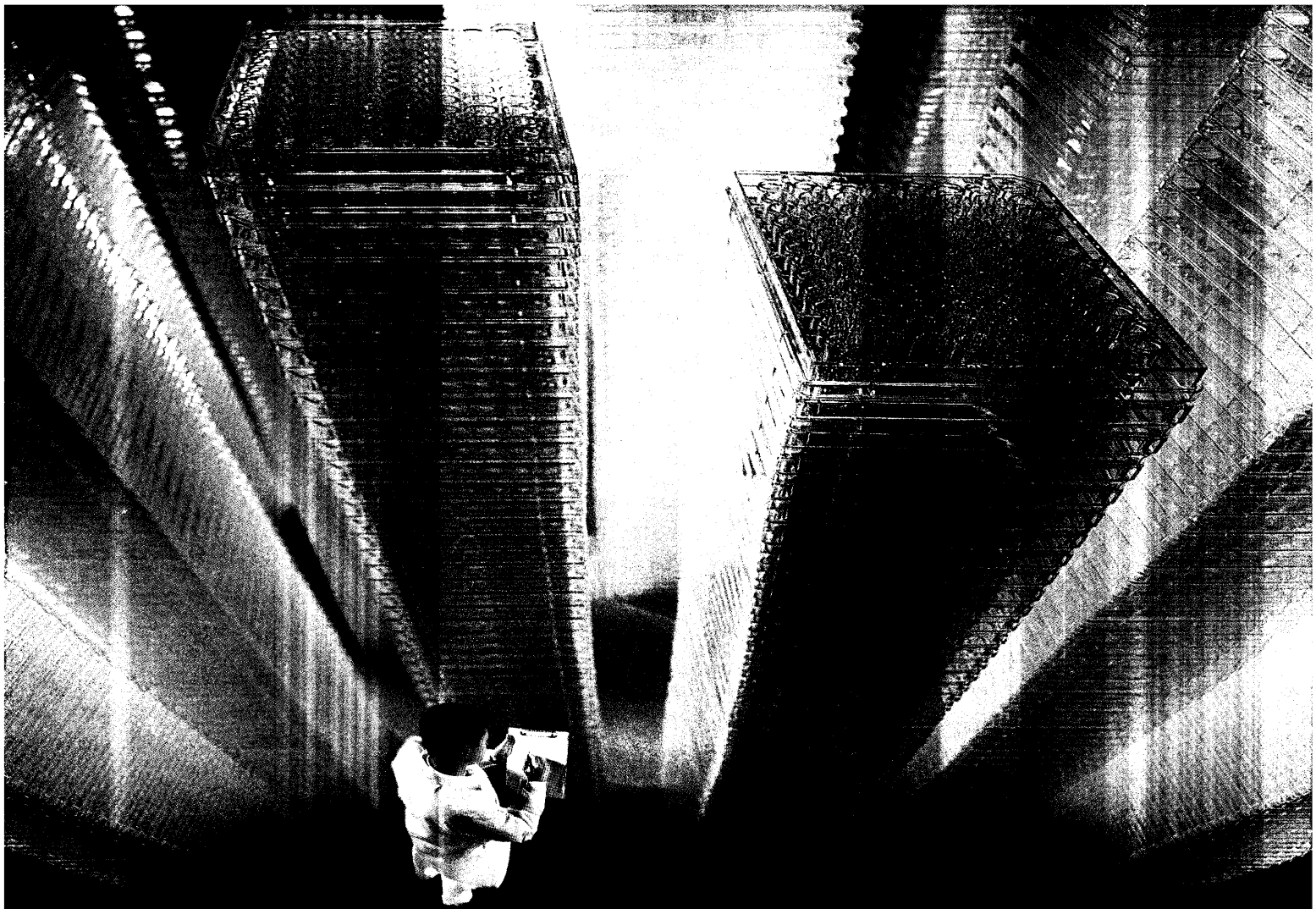

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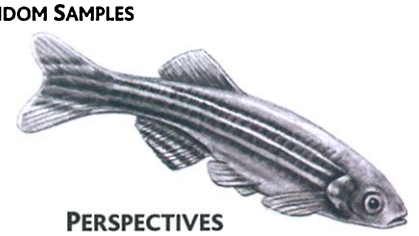

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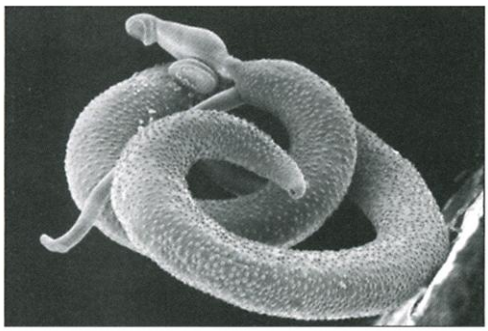

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Immune signals promote schistosome survival

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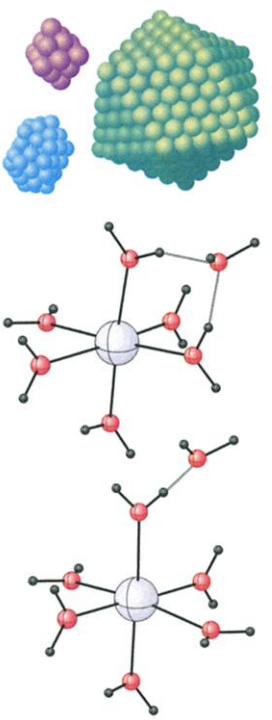
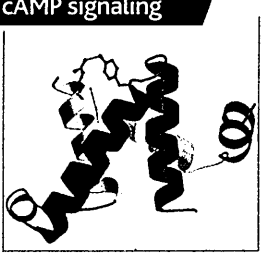
How anions get wet

COVER 1317

Carbon nanotube molecules lying on aluminum gates and coupled by gold wires. Field-effect transistors based on single nanotubes can now be assembled into the logic circuits that are the building blocks of computers. The realization of single-molecule logic circuits has been a long-standing goal within molecular electronics. [Image: TU Delft/Gripp]



New on *Science* Express Methylation switch in hormone and cAMP signaling



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CONTENT HIGHLIGHTS AS OF 9 NOVEMBER 2001

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▼ **Field-Effect Modulation of the Conductance of Single Molecules** J. H. Schön, H. Meng, Z. Bao
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1313 Decorating a monolayer of insulating molecules with a few active molecules is shown to be an effective route for obtaining a single-molecule transistor.
1317

A DNA Microarray-Based Genetic Screen for Nonhomologous End-Joining Mutants in *Saccharomyces cerevisiae* S. L. Ooi, D. D. Shoemaker, J. D. Boeke

A genome-wide genetic screen for mutants defective in end-to-end DNA joining.

A Transcriptional Switch Mediated by Cofactor Methylation W. Xu *et al.*

The methyltransferase CARM1 is a coactivator for nuclear hormones but a corepressor in the cAMP signaling pathway.

TECHNICAL COMMENTS

Drug Addiction and the Hippocampus

Vorel *et al.* (Reports, 11 May 2001, p.1175) stated that electrical stimulation of only certain hippocampal areas yielded a relapse after extinction of cocaine self-administration behavior in rats. In a comment, Berke and Eichenbaum suggest an alternative interpretation: The role of the hippocampus, they maintain, is "to provide the 'memory' of the extinction" behavior, and the electrical stimulation in the Vorel *et al.* experiments thus disrupted "the hippocampus's role in inhibiting" cocaine-seeking behavior. Vorel and Gardner respond that electrical stimulation "seems to represent activation, not inactivation, of hippocampal function," but agree that pharmacological inactivation of the hippocampus would be useful to further determine its exact role.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/294/5545/1235a

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Europe: Italy Does Not Value Its Ph.D.'s G. Germano

On the Eurodoc Exchange, Italy's doctoral students explain that the Ph.D., a relative newcomer on the Italian higher education scene, is not valued by academic or commercial employers.

Canada: The Canadian Diaspora—Mad Dogs and Englishmen D. Durocher

The author fell in love with the British way of life during his Cambridge postdoc—but after a spot of good fortune, he found himself starting up his own lab in Toronto.

US: A Spot of Bother L. Lab-Rat

Assembling a dissertation and a defense can be an unpredictable affair. Our *What's Next?* columnist finds out how completion date uncertainty can affect job search strategy.

US: Knocking on the Door of the Ivory Tower B. Gabriel

For women there are many barriers to entry into the world of academic medicine, but those barriers can be overcome.

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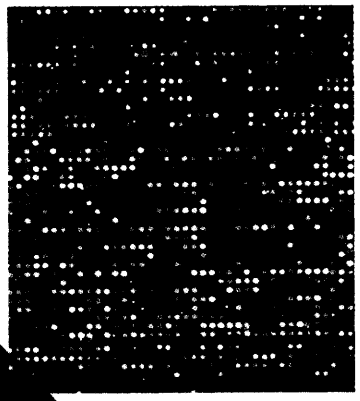

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THIS WEEK IN Science

edited by Phil Szuromi

Nanowire and Nanotube Circuitry

Nanoscale transistor elements, based either on carbon nanotubes or semiconductor nanowires, have been assembled into logic circuits (see the Perspective by Tseng and Ellenbogen). Bachtold *et al.* (p. 1317 EX ; see the cover) created local gates for carbon nanotube transitors that consist of thin aluminum wires coated with an aluminum oxide layer. With appropriate patterning, this approach allows different gates to address different transistors on the same chip. The authors demonstrate transistors with gains in excess of 10, and several circuits that can perform a range of logical operations. Huang *et al.* (p. 1313) show that crossed junctions comprising p-type Si nanowires and n-type GaN can function effectively as diodes and field-effect transistors. Using these simple building blocks, they demonstrate the ability to fabricate the OR, AND, and NOR logic gates necessary for computation.

1326 Below Thin Ice

Europa, a moon of Jupiter, has an icy shell that may cover a layer of liquid water (called Europa's ocean). There is considerable debate over the thickness of the icy shell. Turtle and Pierazzo (p. 1326; see News story by Kerr) have determined a lower limit on the thickness of the ice of at least 3 to 4 kilometers using the morphology of impact craters observed on Europa by the Galileo spacecraft and impact crater simulations using plausible rheological properties of Europan ice.

Dopamine–α-Synuclein Adducts in Parkinson's?

In Parkinson's disease, dopaminergic neurons are lost, and Lewy bodies composed of a fibrillar form of α-synuclein form. Conway *et al.* (p. 1346) looked for small molecules that could inhibit fibril formation caused by isolated α-synuclein. Nearly all of the molecules identified were catecholamines such as dopamine. The authors propose that oxidative adducts form between dopamine and α-synuclein, which lead to stabilization and accumulation of prefibrillar oligomers, or protofibrils, in affected neurons.

Profile of Metastasis

Most deaths from cancer occur when malignant cells from the primary tumor migrate to and "invade" distant healthy organs such as liver, brain, and bone. To investigate the molecular basis of this process, called metastasis, Saha *et al.* (p. 1343; see 12 October news story by Marx) used gene expression profiling methods to identify genes that were activated in highly purified liver metastases of human colorectal tumors. The *PRL-3* gene, encoding a small tyrosine phosphatase, was consistently expressed at higher levels in the metastases compared with earlier stage tumors and underwent selective amplification at the DNA level in a subset of metastases. EX

Ireland's Recent Climate

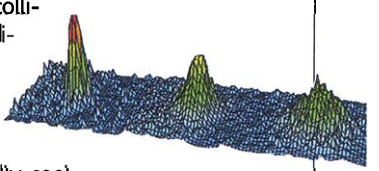
The resolution of many Northern Hemispheric records of the past 10,000 years is too low to determine whether the decade-long events seen in the highest resolution records are local or regional, or if the rapid events of the more gradual ones have had more impact on air temperatures. McDermott *et al.* (p. 1328) present a high-resolution oxygen isotope record from a stalagmite from southwest Ireland which shows that much of the higher frequency climate variability preserved in ice cores from Greenland extended to more southern latitudes. Multicentury oscillations, perhaps caused by changes in North Atlantic thermohaline circulation, appeared to have had a stronger impact on this region's climate than did the ice-rafting events that occurred with an average period of 1500 years.

Solvating Anions

Most fundamental studies of the initial stages of ion solvation have focused on cations, whose small size promotes strong interactions with solvent molecules that facilitate the formation of small clusters. The larger size of anions has made similar studies more difficult. Wang *et al.* (p. 1322; see the Perspective by Stace) now report photoemission data for the aqueous solvation of two doubly charged anions, sulfate (SO_4^{2-}) and oxalate ($C_2O_4^{2-}$), with between 4 and 40 water molecules. A gradual transition from anion features to solvent features as the number of water molecules in the cluster increases was observed, which suggests that the anion does not reside on the cluster surface but becomes solvated much like a species in bulk solution.

Adding to the Ranks of Condensates

Since the first report of the successful cooling of an ensemble of alkali atoms such that they formed a Bose-Einstein condensate (BEC), in which the atoms all have the same quantum ground state, efforts have been made to condense other atomic species. Success, however, has been restricted to an elite few elements: Rubidium, sodium, hydrogen, helium, and lithium. Modugno *et al.* (p. 1320) took an unconventional approach and used favorable collision processes to cool a mixture of rubidium and potassium (K) atoms. In this way, they overcame the limitations of direct laser cooling and were able to add K to the list of condensable species. This technique of sympathetically cooling one atomic species with another may provide a general route for expanding the list of BECs. EX



CREDIT: MODUGNO *ET AL.*

Following the Fate of Receptors

G protein–coupled receptors (GPCRs) are activated by ligand binding, but their signaling output is also regulated by receptor internalization and degradation. However, the mechanisms controlling the latter processes are incompletely understood. Shenoy *et al.* (p. 1307) report that the Mdm2 protein, better known as the ubiquitin ligase that controls the abundance of the p53 tumor-suppressor protein, associates with β-arrestin. β-arrestin appears to promote ubiquitination of the activated β_2-adrenergic receptor, and ubiquitination of the receptor and β-arrestin each seem to have separate effects on receptor internalization and proteolysis. For example, in cells lacking Mdm2, ubiquitination of

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CONTINUED ON PAGE 1239

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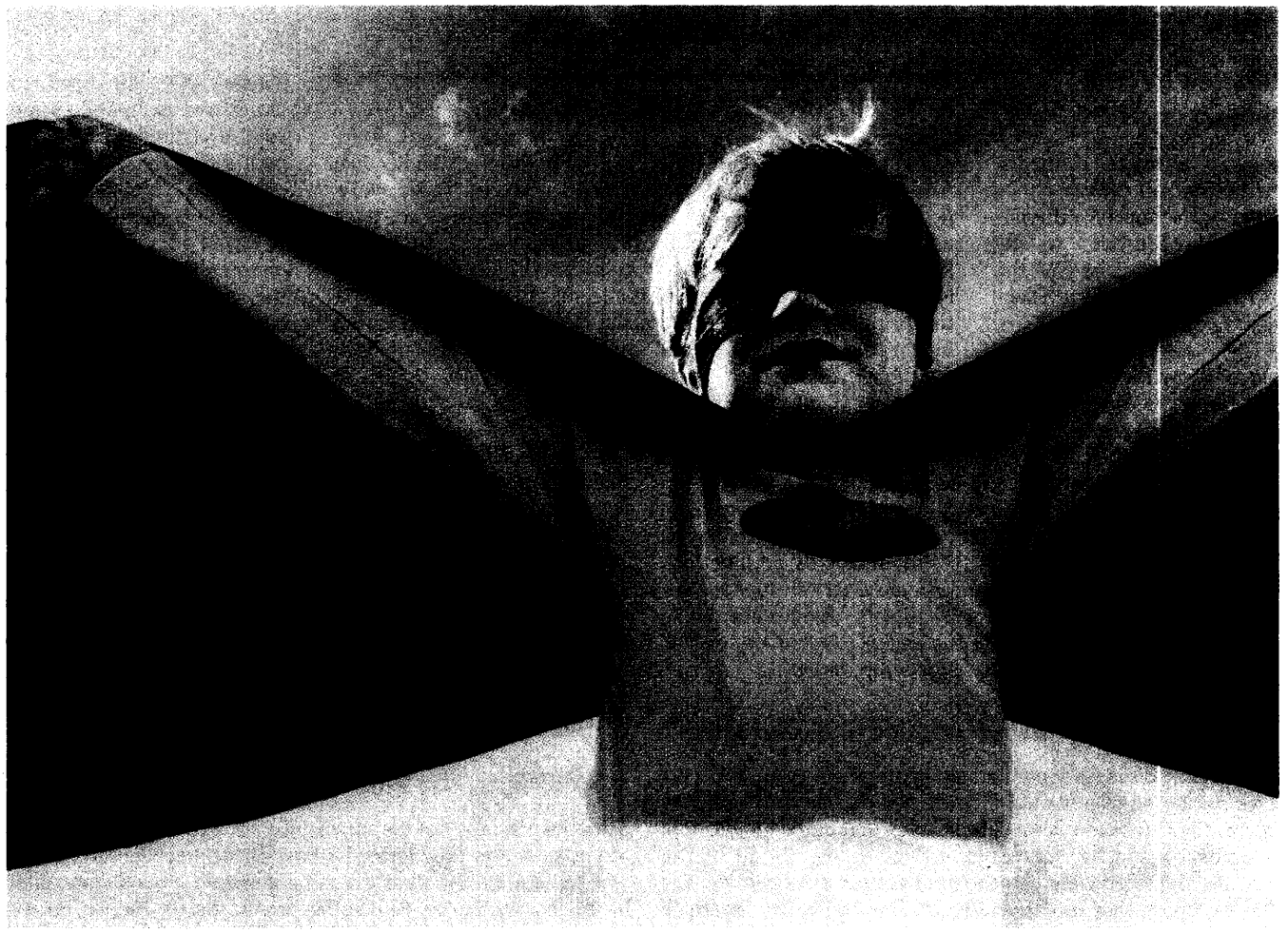

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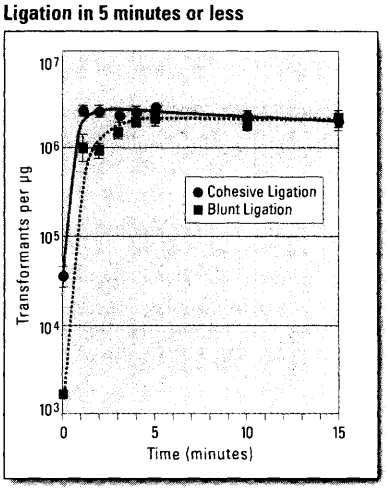

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β-arrestin (but not that of the receptor) was lost, which resulted in decreased receptor internalization but had little effect on receptor degradation.

Splitting a Template-less Polymerase

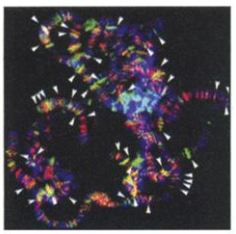
All transfer RNAs (tRNAs) have the sequence 5′-CCA-3′ at their 3′ ends that act as the site of amino acid attachment. For many tRNAs, the CCA sequence is added by the CCA-adding enzyme, an RNA polymerase that does not need a template to make these additions. Tomita and Weiner (p. 1334) have now found that the CCA-adding enzyme in the bacterium *Aquifex aeolicus* consists of two independent enzymes, one that adds CC and a second that adds A, which suggests that the enzymes evolved from a poly(A) polymerase that acquired the ability to add CC.

The Enzymology of Oxygen Sensing

When oxygen becomes limiting (hypoxia), mammalian cells respond by increasing the transcription of genes that enhance oxygen delivery or that facilitate metabolic adjustment to reduced oxygen availability. This adaptive response is mediated by hypoxia-inducible factor (HIF), a transcription factor that is stable under hypoxic conditions but is targeted for degradation in the presence of oxygen when a specific proline residue in the protein becomes hydroxylated. Bruick and McKnight (p. 1337) have identified a family of evolutionarily conserved enzymes, HIF prolyl hydroxylases, that are responsible for this posttranslational modification. Discovery of these enzymes could open up new therapeutic possibilities for the many diseases in which hypoxia plays a crucial role, such as ischemic heart disease and stroke.

Dynamic Reconstitution

Microtubules are key components of the cell's cytoskeleton. Within the cell they are constantly remodeled in a process known as "dynamic instability" whereby they grow steadily and then suddenly disassemble very rapidly. Microtubules in vitro behave in a much more predictable and stately fashion. Kinoshita *et al.* (p. 1340) now describe a system in which they have recapitulated the physiological rates of assembly and disassembly using purified components.



CREDIT: PETRUK *ET AL.*

Taming Trithorax

The *Drosophila* Trithorax class of proteins helps maintain heritable gene expression patterns and is highly conserved across species. For example, chromosomal translocations of the human Trithorax homolog are linked to infant leukemia. Petruk *et al.* (p. 1331) purified the protein and found that it forms a complex with two other factors, the coactivator and histone acetylase CBP, and Sbf1, a protein known in mammalian systems as an antiphosphatase. Histone acetylation and phosphorylation may both play a role in the action of the trithorax complex in stimulating transcriptional activity.

Delivering Cholesterol

Glial cells promote formation of synapses between neurons, and Mauch *et al.* (p. 1354; see the Perspective by Barres and Smith) now identify a glial cell factor that promotes synaptogenesis: Cholesterol in complex with apoE lipoprotein. Synapse construction requires formation of new membrane for components such as synaptic vesicles, and the extra supplies of cholesterol required to meet the demand are made up by glial cells.

Not GILT-y

When mounting an immune response, antigens must be processed for presentation within the endocytic compartments of antigen-presenting cells, but antigenic proteins frequently contain disulfide bonds that might interfere with their breakdown and presentation. Maric *et al.* (p. 1361; see the Perspective by Watts) now show that the interferon γ–inducible thiol reductase (GILT) found in late endosomes is important in the presentation of disulfide-bonded antigens. Knockout mice lacking GILT were less effective in processing and presenting disulfide-bonded antigens, including the model antigen hen egg lysozyme.

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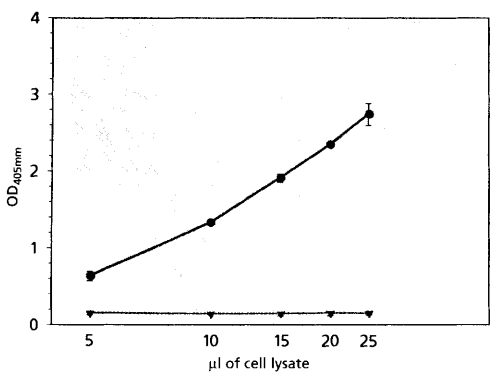
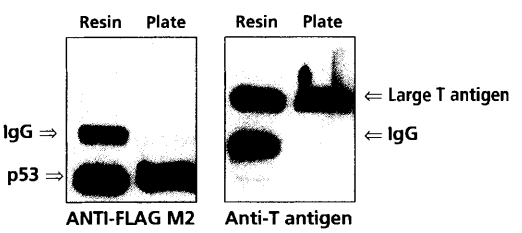


ELISA of interaction between FLAG tagged P65 and c-Myc *tagged IκBα. COS7 cells were co-transfected with pFLAG-CMV-2-p65 and p-c-Myc-CMV-2- IκBα (•) or pFLAG-CMV-2-p65 and p-c-Myc-CMV-2-Bacterial Alkaline Phosphatase (▼). Lysates were applied to an ANTI-FLAG M2 coated 96-well plate and detected with Anti-c-Myc Alkaline phosphatase and pNPP chromogenic substrate. Note that only interacting proteins p65 and IκBα were detected.*



Proteins were co-immunoprecipiated from COS-7 cell lysates expressing p53 FLAG-fusion protein and endogenous Large T antigen. Proteins were detected with either ANTI-FLAG M2 Anti-body or Anti-SV 40-T antigen. Note: IgG band is absent when using the ANTI-FLAG M2 96-Well IP System.

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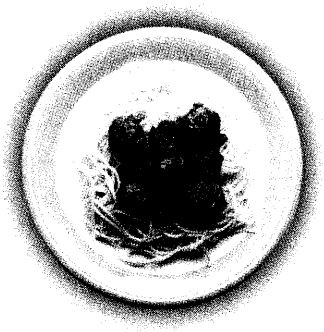

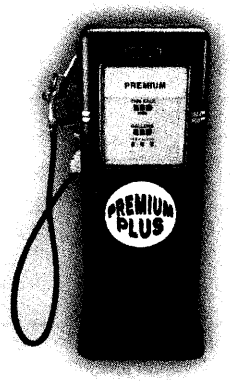

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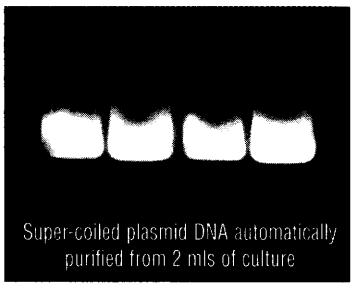

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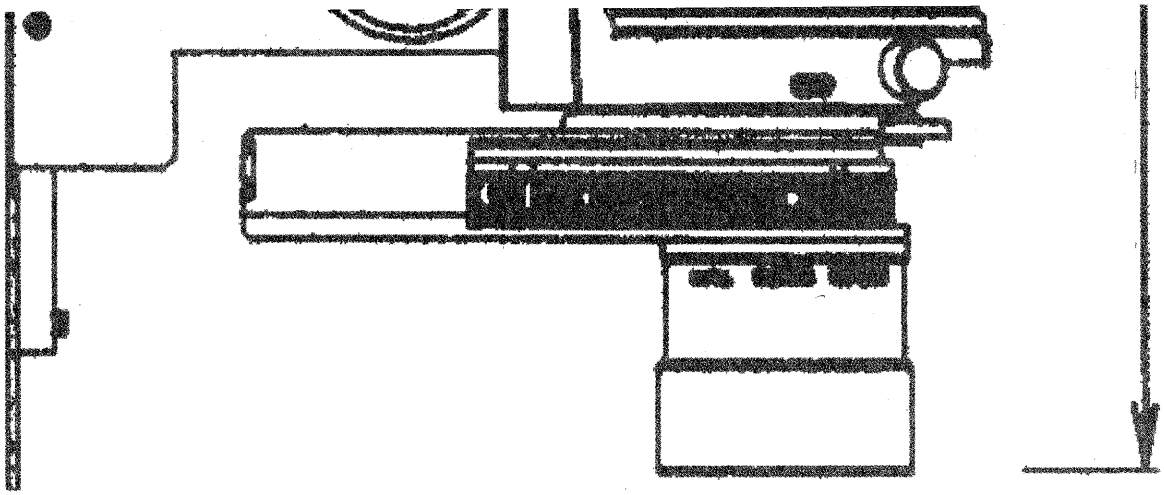

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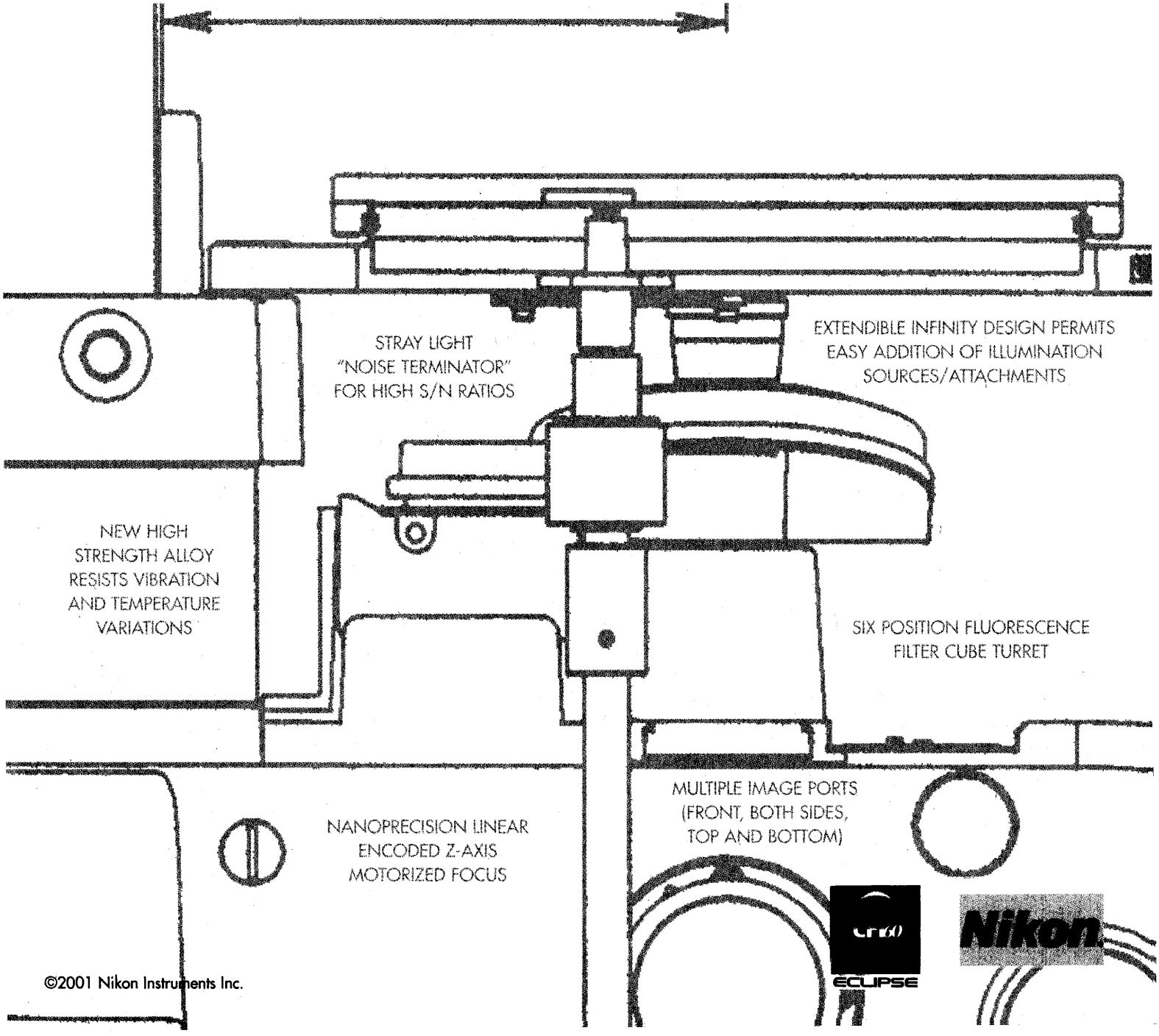

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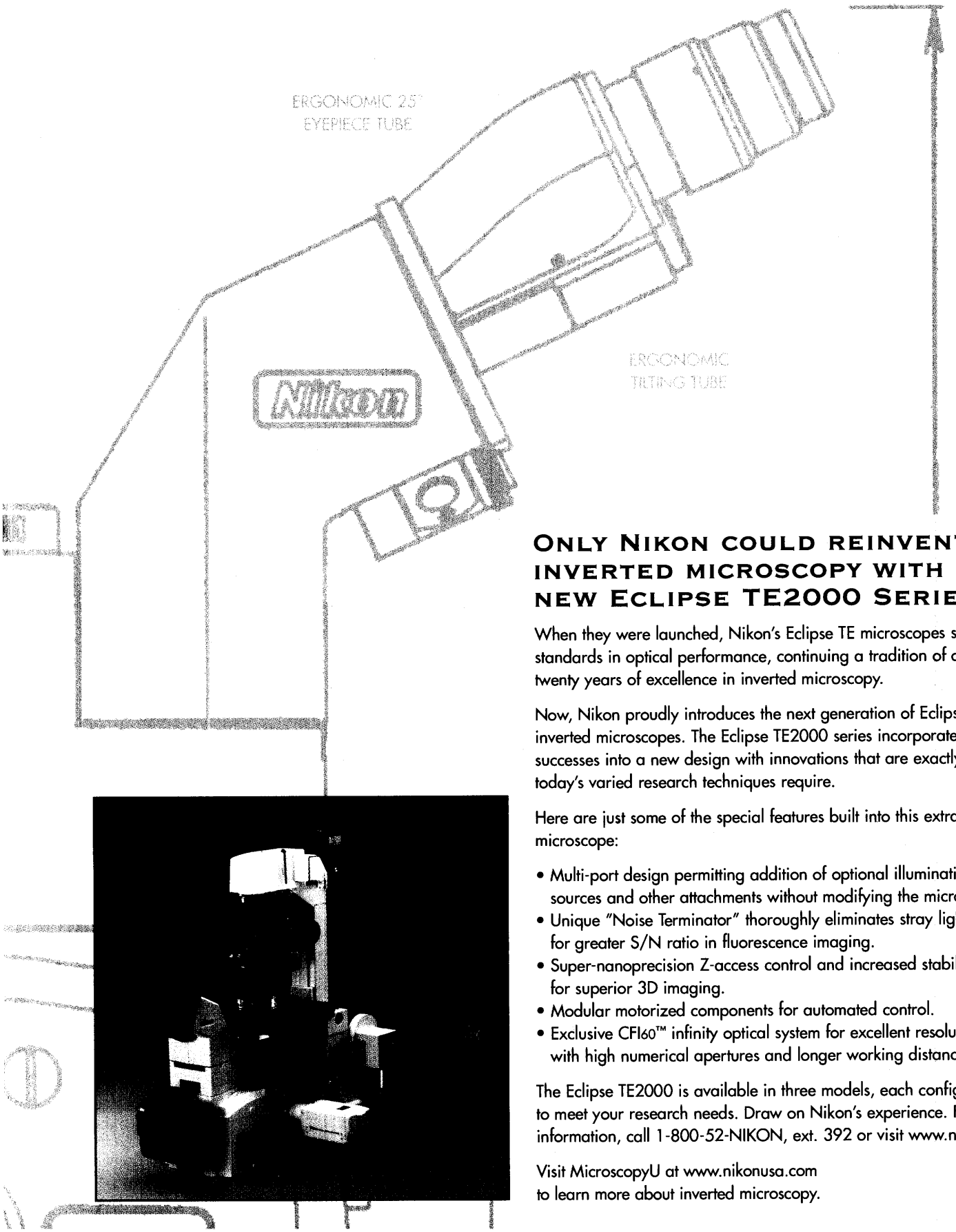

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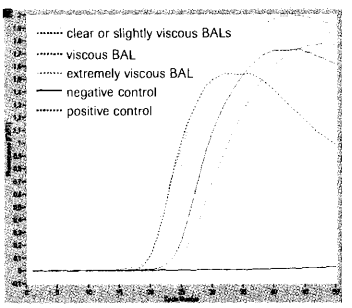

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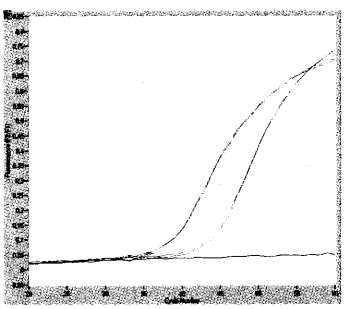

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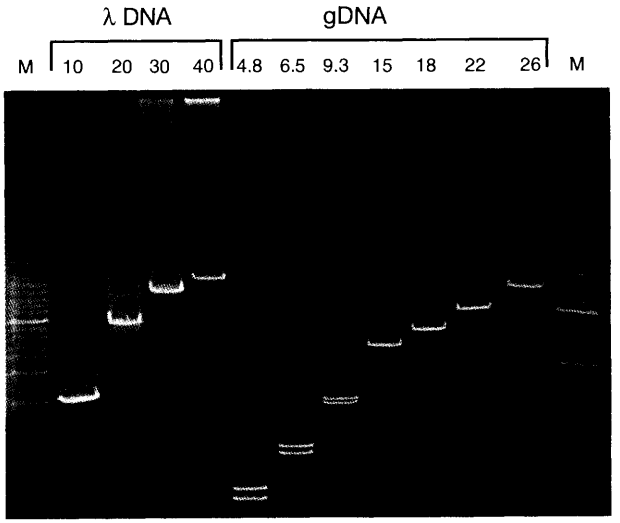

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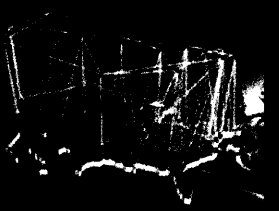

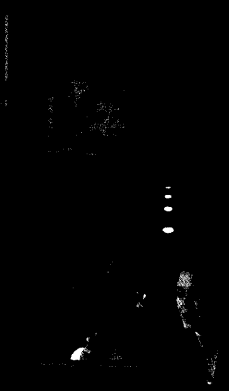

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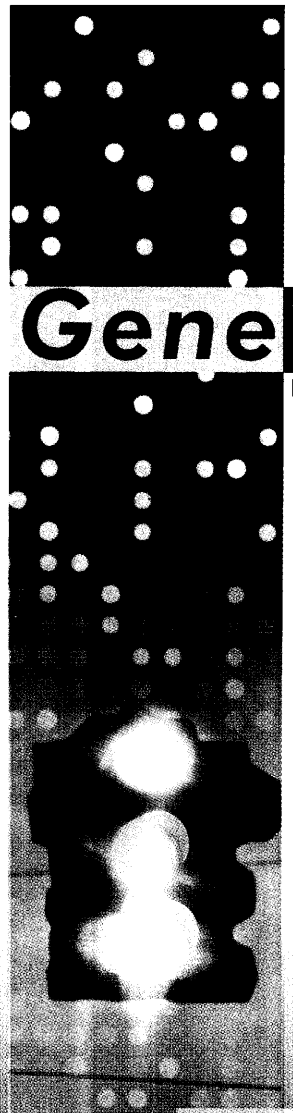
Microarray Data Analysis Made Easy.

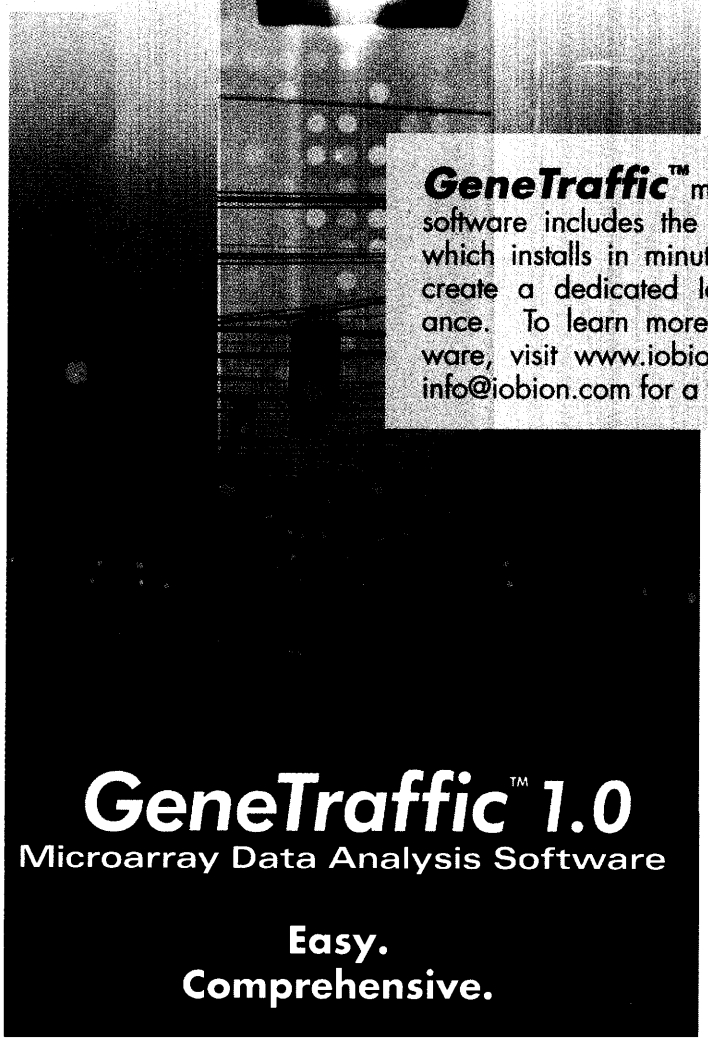


GeneTraffic™ 1.0

Microarray Data Analysis Software

- Easy-to-use microarray data analysis software
- Integrated relational database
- Intuitive graphical user interface
- Analyzes two-color spotted microarray data
- Flexible, built-in filter and normalization methods
- Web-based

GeneTraffic™ microarray data analysis software includes the Iobion system software, which installs in minutes on a Linux server to create a dedicated Iobion informatics appliance. To learn more about GeneTraffic software, visit www.iobion.com or contact us at info@iobion.com for a web demonstration.



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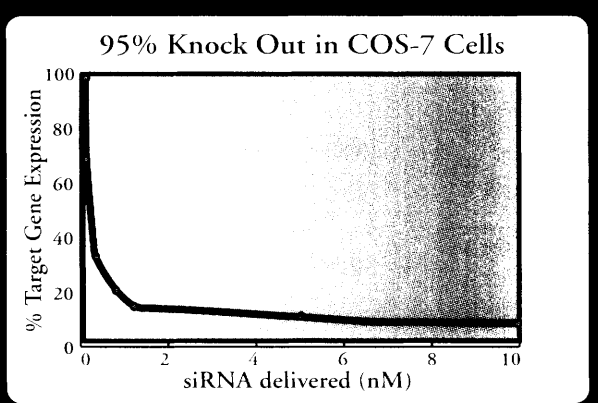

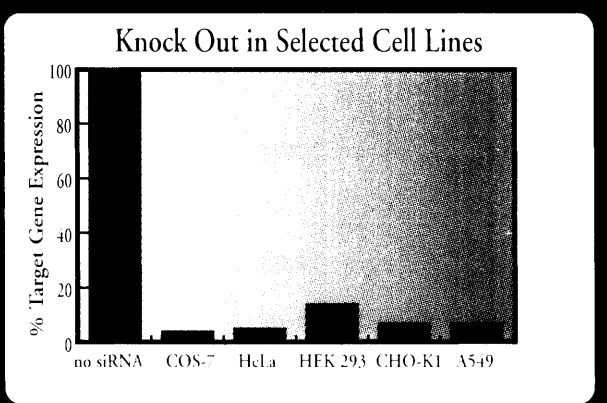

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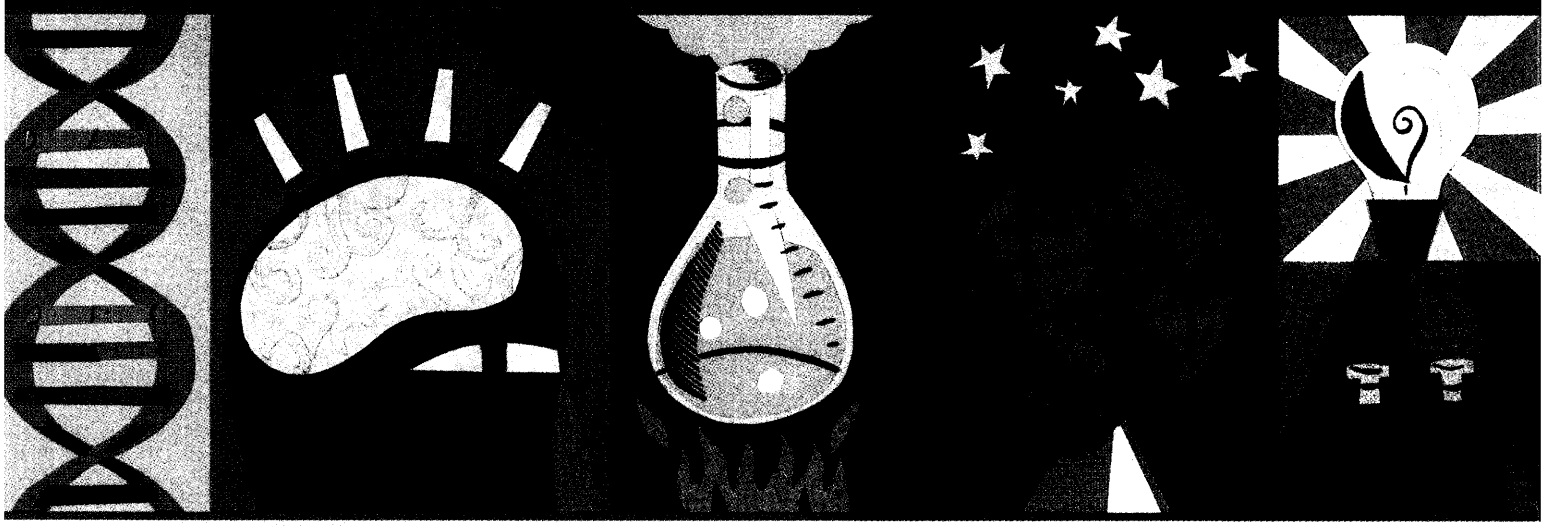

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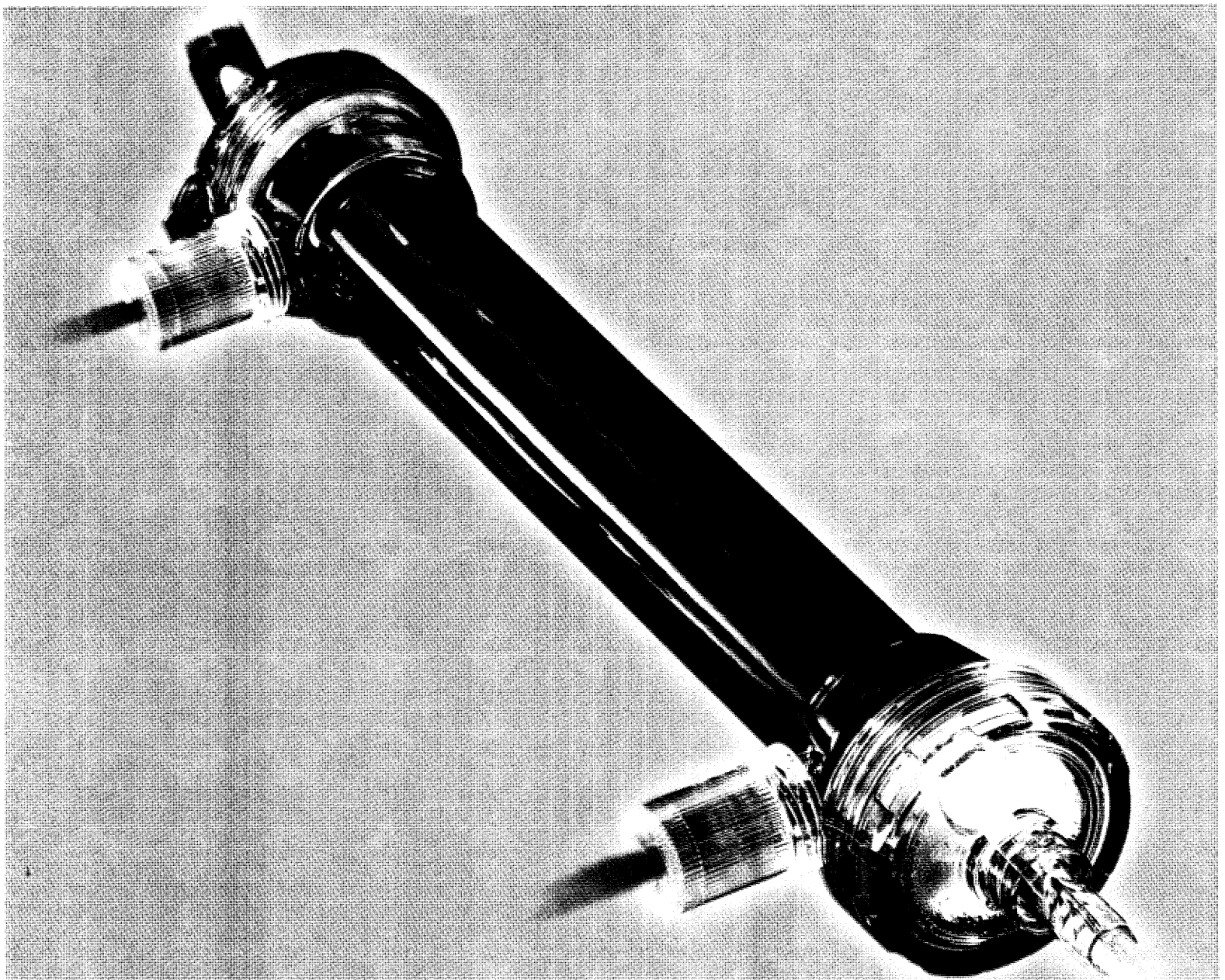

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