American Association for the Advancement of Science

SCIENCE

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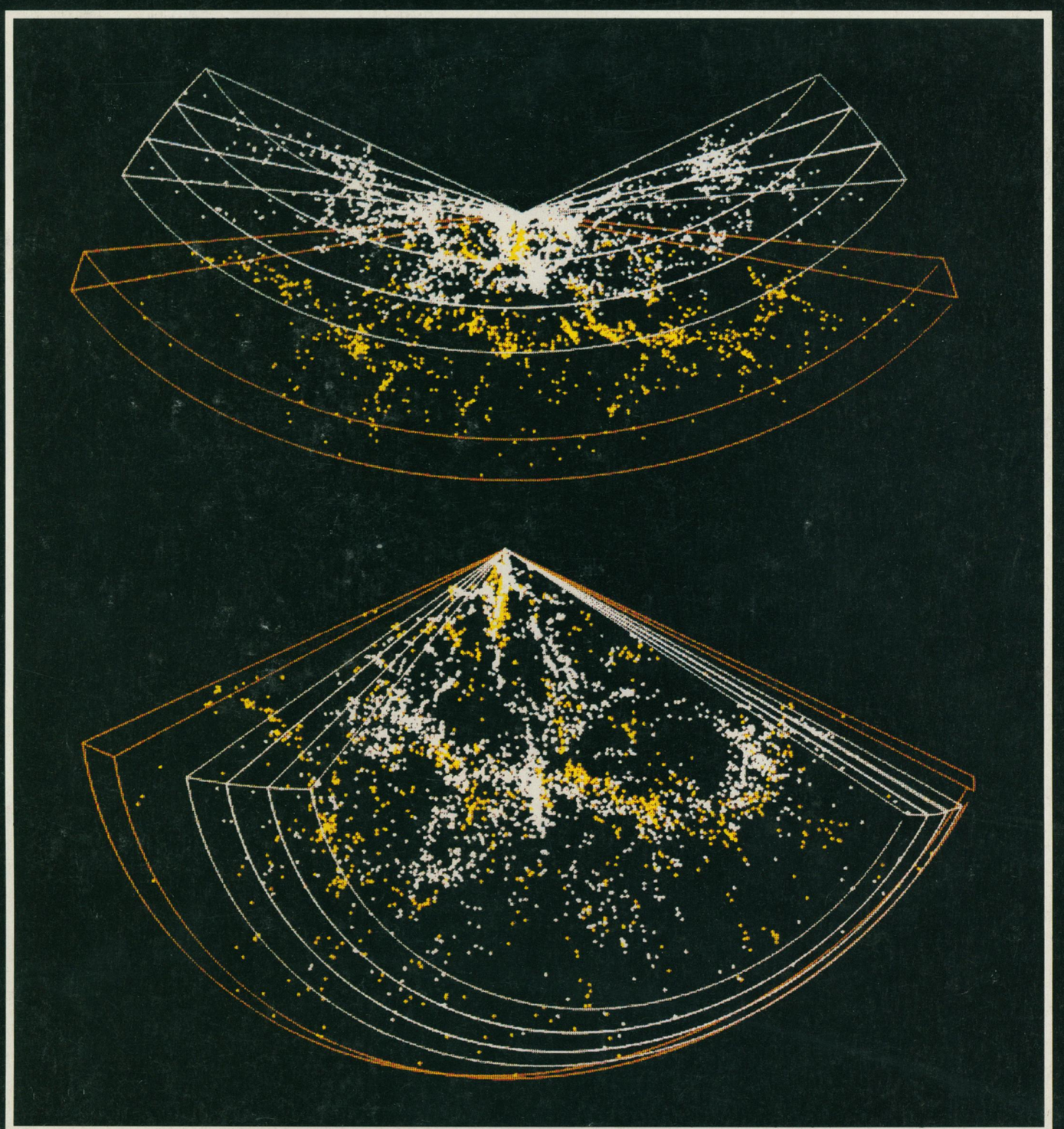

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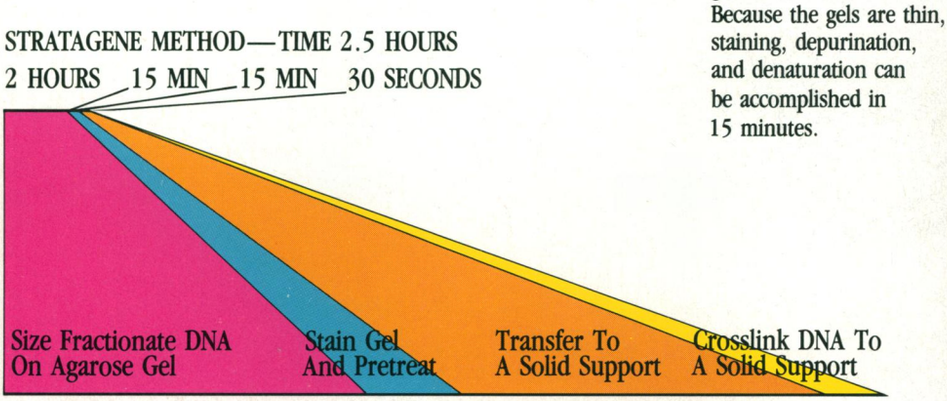


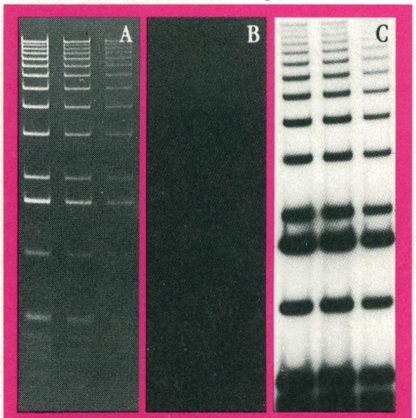
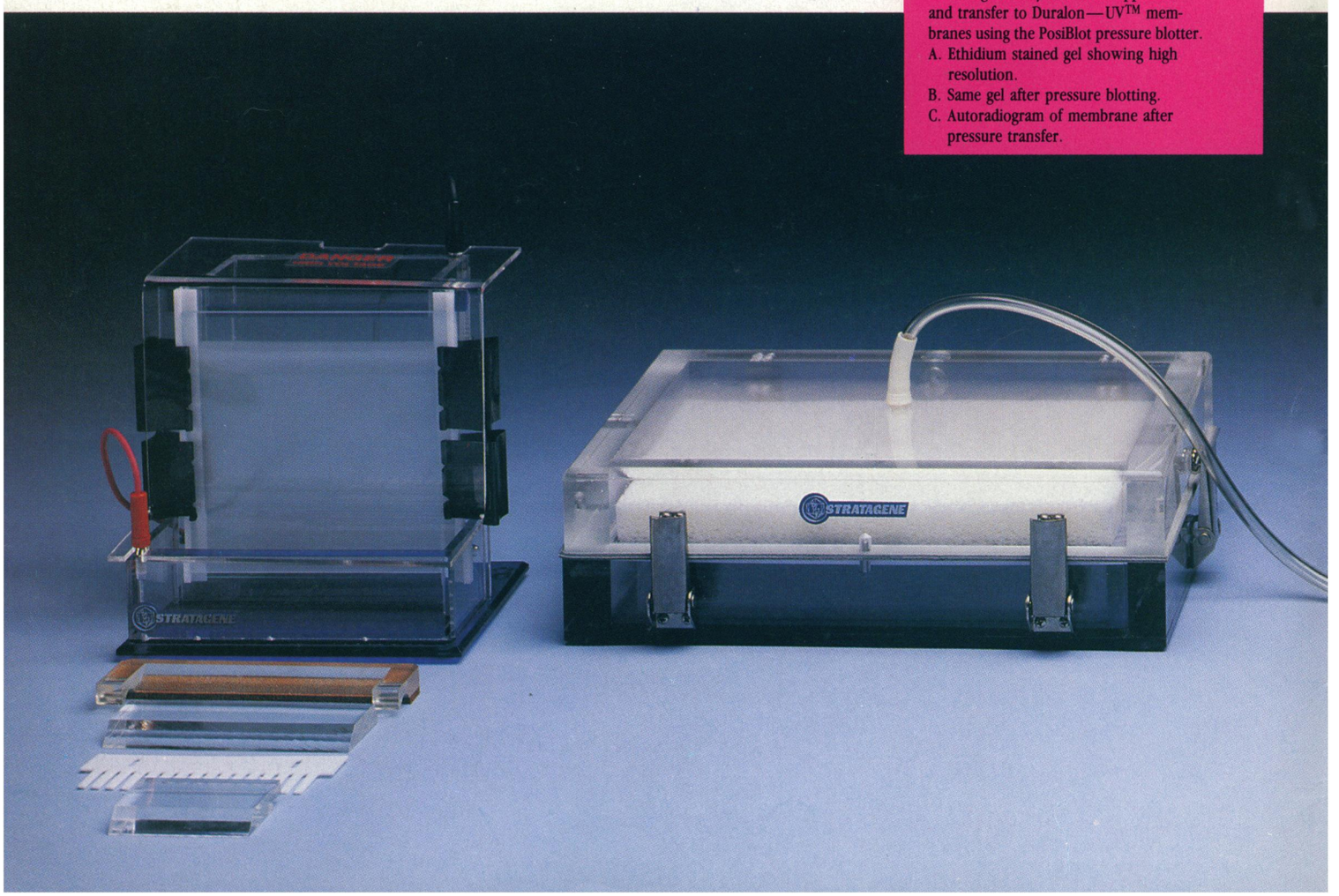


FIGURE 1:
Figure Legend: Fractionation of end labeled DNA markers on 3mm thick 0.8% agarose by the VAGE apparatus and transfer to Duralon—UV™ membranes using the PosiBlot pressure blotter.
A. Ethidium stained gel showing high resolution.
B. Same gel after pressure blotting.
C. Autoradiogram of membrane after pressure transfer.



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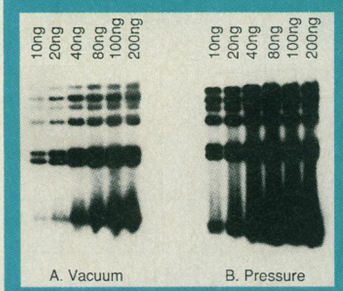

FIGURE 2:
Figure Lengend: ^{32}P end-labeled lambda Hind III markers were electrophoresed in 0.8% agarose. The DNA was then transferred to a nylon membrane with a vacuum blotter at 30mm Hg below atmospheric or with the PosiBlot pressure blotter at 100mm Hg above atmospheric. Both transfers were carried out for 15 minutes. As can be seen, pressure blotting transferred significantly more DNA in the same period of time, especially in the higher molecular weight range (largest band is 23 kilobases).

The PosiBlot™ positive pressure blotter permits the transfer of nucleic acids in 1/3 the time of vacuum blotters and 1/50 the time of capillary blotting (Figure 2). Pressure blotting does not dehydrate gels as do other methods. This allows the use of substantially higher pressure differentials, compared with vacuum blotting, without gel collapse. The PosiBlot apparatus reduces blotting time to 15 minutes.

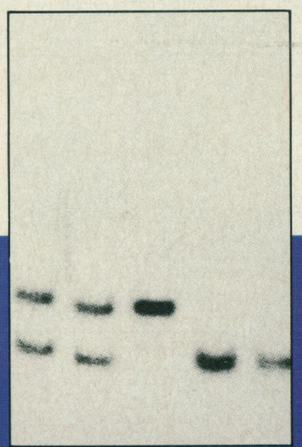

FIGURE 3:
Figure Legend: Autoradiogram showing the resolution of 2.8 and 1.3 Kb Msp I RFLP alleles revealed by a cystic fibrosis human DNA probe using the VAGE, PosiBlot and Stratalinker all in 2.5 hours.

Stratalinker™* UV Crosslinker

The Stratalinker™ UV Crosslinker fixes nucleic acids to solid supports such as nitrocellulose or nylon membranes, in less than one minute. This compares favorably to vacuum baking, which requires 2 hours. The Stratalinker actually monitors the ultra violet energy flux and deactivates the light source upon reaching the user-programmed energy level (Figure 4). Figure 3 shows an autoradiogram of a human genomic Southern blot performed using the VAGE, PosiBlot and Stratalinker all in 2.5 hours.

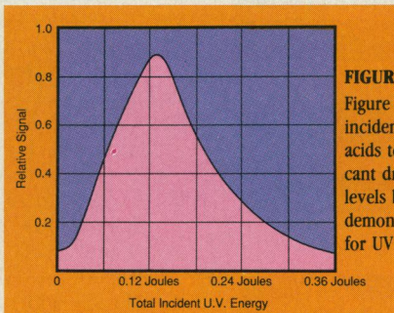

FIGURE 4:
Figure Legend: The effects of altering the incident energy for crosslinking nucleic acids to nylon membranes. The significant drop in signal intensity at energy levels below and above 0.12 Joules demonstrates the limited optimal range for UV treatment.

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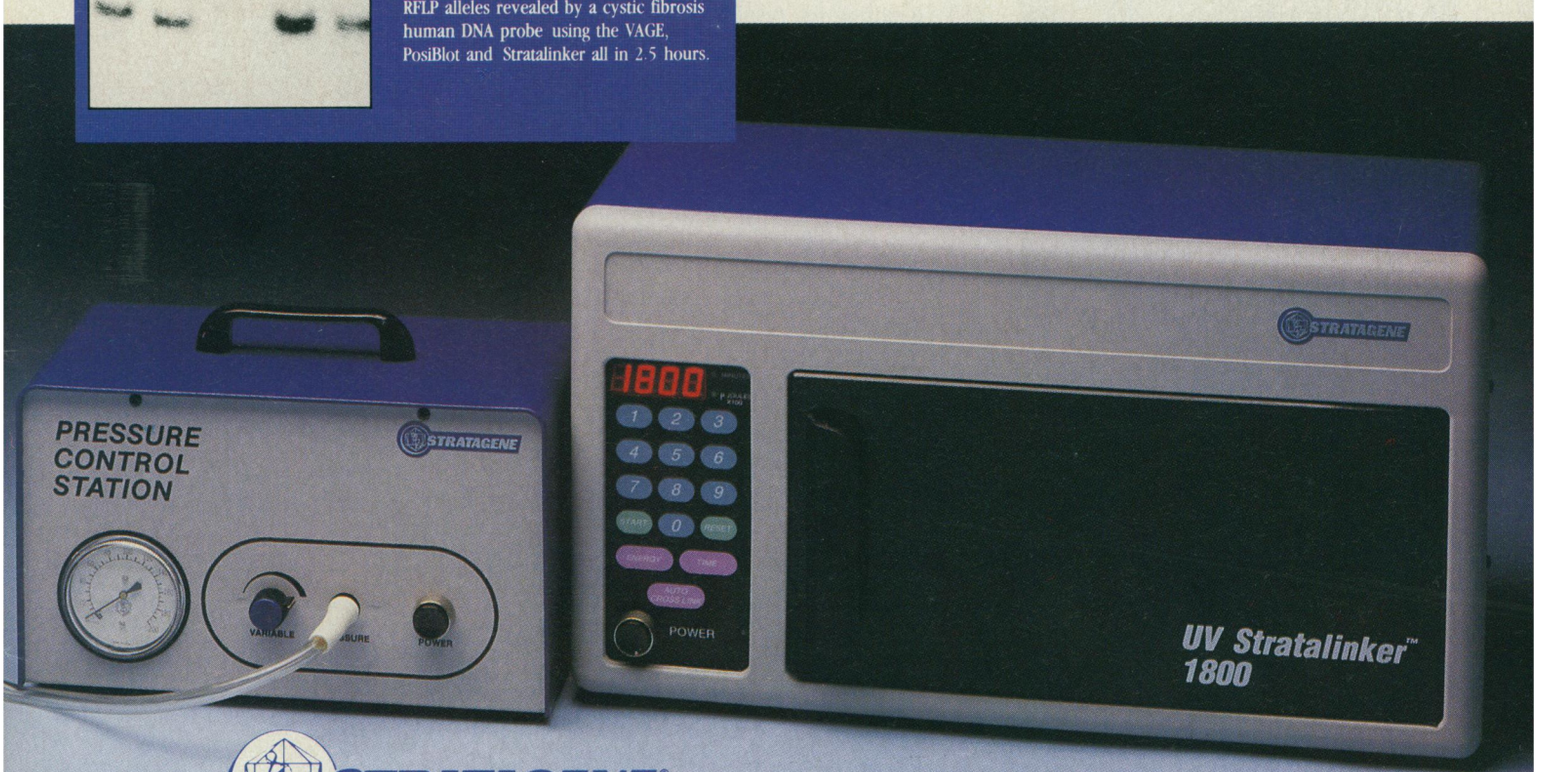

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COVER Two views of the distribution of 3962 galaxies in three-dimensional redshift space. The white points display the distribution of galaxies in the right ascension range 8^h to 17^h and declination range 26.5° to 44.5°; the orange in the declination range 8.5° to 14.5°. "The Great Wall" crosses the survey nearly parallel to the outer boundary. See pages 885 and 897. [Graphics by M. J. Geller, J. P. Huchra, E. Falco, and R. K. McMahan]

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Antibiotic history revisited

WHO first discovered a clinically useful antibiotic? If you guessed penicillin-discoverer Alexander Fleming, you share a common misconception. The correct answer, according to science historians, is Rene Dubos. Crease reports on a symposium held last month at Rockefeller University aimed at setting the record straight (page 883). Fleming was losing interest in penicillin in the early 1930s. Meanwhile, Dubos was undertaking a systematic search for soil microorganisms that could kill other bacteria; his work led to the identification of gramicidin in 1939. In addition, it prompted Florey and Chain—who along with Fleming won the Nobel prize in medicine and physiology in 1945—to reevaluate penicillin and consider its therapeutic usefulness, thereby setting the stage for one of the great medical revolutions—antibiotic therapy.

Mapping the universe

A survey of the distribution of thousands of "nearby" galaxies has revealed the largest coherent structure yet seen in the universe (page 897). Called the Great Wall, this structure, which contains more than half of the galaxies in the region, "grows" along with the survey data; that is, its full extent has not yet been uncovered. Geller and Huchra describe the Great Wall and other large-scale, thin, sheet-like structures and large voids that have been revealed in various redshift surveys (cover); their own survey has so far scanned a chunk of the visible universe comparable to the fraction of the earth covered by Rhode Island. Redshift surveys provide an approximate measure of a galaxy's distance, because, the greater the redshift (a shift in the spectrum toward longer wavelengths), the faster the galaxy is receding. After the Big Bang, matter was briefly distributed uniformly in the universe; very quickly, however, this matter began to develop "structure" and has become clustered and organized into galaxies and larger scale features. Theories of the evolution of the universe must account for this heterogeneity. Waldrop assesses how the redshift observations affect and constrain current theories of the universe's evolution (page 885).

Lipoprotein(a)

LIPOPROTEIN(A) or Lp(a) is a substance that circulates in the bloodstream; its presence in high concentrations appears to be a strong risk factor for the premature development of vascular diseases, heart attacks, and stroke. Much about the significance, evolution, production, and metabolism of this substance remains unclear, and these mysteries as well as the latest research findings are described by Utermann (page 904). Lp(a) consists of linked molecules of apolipoprotein(a) and low density lipoprotein: the former is homologous to (and perhaps competitive with) the clot-dissolving precursor plasminogen and the two are encoded in the same chromosomal region; the latter is the major transporter of cholesterol in human plasma. Lp(a) may have a particularly powerful and damaging effect in the body: it can transport cholesterol and deposit it in areas of the body where vascular injuries have recently occurred and it can interfere with the dissolution of clots in the bloodstream.

Proposed structure of bZIP proteins

LEUCINE zippers are "structural motifs" found in many proteins that bind DNA. These zippers, so named because they effectively zip up paired polypeptides into dimers, have the shape of tightly bound α-helical coiled-coils. Extending out from the zippered portion of the dimer are two identical regions rich in basic amino acids. Experiments by Agre *et al.* confirm that the basic regions are sites for DNA binding (page 922): when basic regions and leucine zippers of different proteins are mixed in a recombinant protein, the specificity of DNA binding is determined by which basic region is present in the chimera. Vinson *et al.* present a model to explain how bZIP proteins—DNA binding proteins in which the leucine zipper and the basic region are contiguous—interact with DNA (page 911). The bZIP proteins have a Y shape of which the leucine zipper is the stem and the basic regions are the arms. DNA fits between the arms with its center of symmetry positioned at the bifurcation. The arms extend along the DNA until, at some point, each arm turns sharply, securing the contact; this "scissors grip" resembles that used by wrestlers. Although the model has yet to be rigorously tested by biophysical studies, its plausibility is supported by ball-and-stick structures, computer graphic simulations, and biochemical protection and labeling experiments.

Vision chemistry

RHODOPSIN is the light-sensitive pigment found in the rods of the eye; it contains a protein, opsin, linked to a chromophore, 11-*cis*-retinal. When the chromophore is free in solution, it absorbs light maximally at 440 nanometers; when the chromophore is bound to opsin, the absorption maximum is at 500 nanometers. The difference in the absorption maxima is considered to be a consequence of one or more interactions of the chromophore with charged carboxylic acid side chains in the protein. Zhukovsky and Oprian test this hypothesis by altering five of the glutamic acid and aspartic acid residues of opsin that are thought to reside in portions of the protein within or near the surface of the membrane (page 928). Mutations in most had no effect on absorption; mutations in the glutamic acid at position 113 caused a dramatic shift in the absorption maximum. This absorption modulation, a phenomenon known as the "opsin shift," therefore appears to depend on the carboxylic acid group of this amino acid, which, though previously considered to reside near the membrane, may in fact lie within it.

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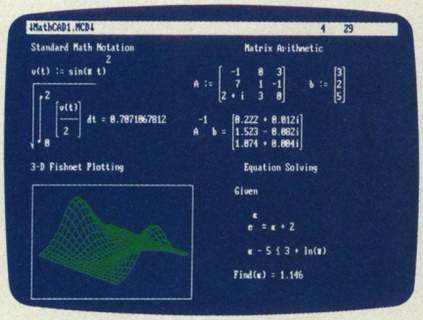

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Support for Plant Biology

Fundamental research in plant biology should have a higher priority than it presently receives. The level of support has been small in comparison with other fields. Yet few of them can potentially contribute cost effectively so much to international competitiveness, future energy supplies, human health, the environment, and intellectual excitement.

The once great U.S. superiority in global agriculture has atrophied. Technology pioneered here has been adopted elsewhere on land that is as fertile as ours but less expensive. Costs of labor in other countries are usually lower. Our one hope to compete in the long term is better use of our brains, but even there prospects are only fair. Others are active and highly competent in plant research.

Society will ultimately find it necessary to depend heavily on renewable resources for energy and chemical needs. More immediate are concerns about health effects of pesticides. At present, the major focus is on commercial chemicals. However, as Bruce Ames has pointed out, we ingest about 10,000 times more by weight of natural pesticides than synthetic ones. The natural pesticides are present in all plants and commonly make up 5 to 10% of a plant's dry weight. A sizable proportion of the plant pesticides are carcinogenic, and many others are mutagens.

Natural pesticides are part of plant defense mechanisms against insects and other herbivores. Plants have complex biochemical equipment that enables them to respond in many ways to attacks by predators or pathogens.* For example, when an insect or fungus seeks to feed on a plant, it must first penetrate the outer covering of, for example, a leaf. In the process, small molecules are released that elicit responses in the plant. One response is to induce production of proteinase inhibitors in addition to those already present. A function of these inhibitors is to block the protein-digesting enzymes of the predator and thus render the plant protein indigestible. Another defense that plants have is an enzyme capable of hydrolyzing the chitin integument of insects. Another response of the plant is to produce potent chemicals that ordinarily are not present in it. These phytoalexins are powerful antibiotics. Current research is revealing more about the mechanisms while raising further questions to be studied.

Recombinant DNA technology has opened a plethora of possibilities for improving plant defenses. Already foreign genes have been incorporated within the plant genomes that confer improved resistance to pathogens. An example is introduction of a gene coding for a viral protein. The resultant plants showed enhanced resistance to the virus in field tests.

A gene from cowpeas for a proteinase inhibitor was used to transform tobacco plants. The gene was expressed in leaves, and the plants exhibited a relatively high level of resistance to the tobacco bud worm. Ultimately it may be possible to decrease the levels of natural carcinogens in plant seeds and tubers while maintaining resistance to plant pathogens. At the same time, the role of commercial pesticides would be attenuated.

In the foregoing, discussion has been focused on only one aspect of plant biology. The powerful techniques of molecular biology and superb instrumentation make accessible many areas. However, the realities of funding sharply limit the rate of progress.

The USDA has been slow to use the expertise of the broad scientific community. At the USDA, only 6% of R&D support is distributed by competitive grants. At the National Institutes of Health 83% and at the National Science Foundation 90% of funds are furnished in such grants. NIH supplied $6.4 billion in 1988, whereas USDA provided only $40 million in competitive grants. The average annual grant size from USDA is $50,000, in contrast with $71,300 from NSF and $154,900 from NIH. USDA grants have an average duration of 2 years, those of NSF and NIH, 3 years or more.

The Board on Agriculture of the National Research Council has issued an extensive report proposing that $500 million a year in competitive grants be furnished by USDA.† Those funds would be in addition to the current budget. Given the present situation in Washington, such a large addition is unlikely. However, even modest increases would have highly beneficial effects.—PHILIP H. ABELSON

*See C. A. Ryan, *Bioessays* **10**, 20 (1989). †National Research Council, "Investing in research: A proposal to strengthen the agricultural, food, and environmental system" (National Academy Press, Washington, DC, 1989).

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The Association of African Universities (AAU) announces the publication of the 5th Edition of the ***Directory of African Universities***. Published biannually, the ***Directory*** provides 500 pages of useful information on principal officers, faculties, departments, and institutions; degrees, diplomas, and certificates awarded; admission requirements; library services; and other details about 92 African universities, including postal addresses.
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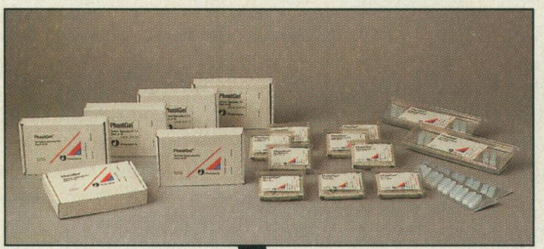
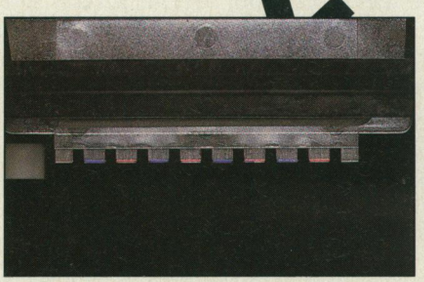
1 9:00

Choose a precast gel from an extended range of 9 different PhastGel® media. Place gel and buffer strips in the separation unit.





2 9:02

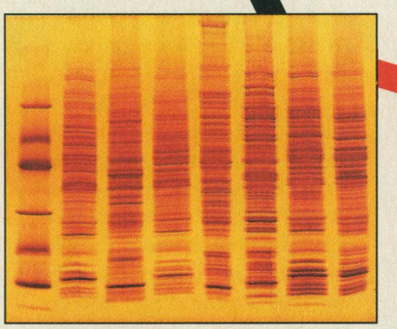
Load sample. Application is automated.

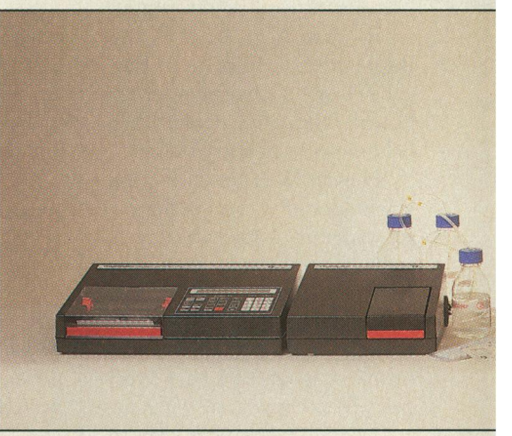
3 9:07

Program and run the method.

4 9:37

Develop the gel automatically with silver or coomassie staining kits.





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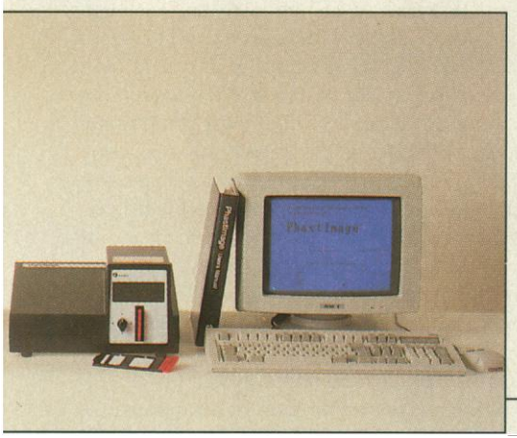
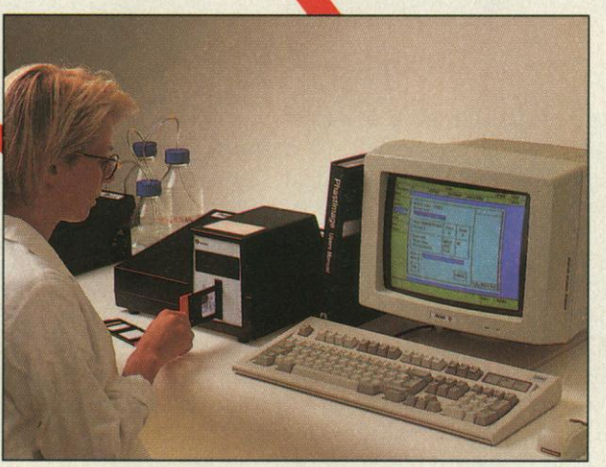
5 9:37
Transfer proteins to a membrane in 15 minutes.



6 10:07
Scan and evaluate your results.



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