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  J. W. B. Hershey, Application Note DS-711. Beckman Instruments, Spinco Division, 1987.
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  D. P. Weeks et al., Anal. Biochem. 152, 376-385 (1986)
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  M. G. Peterson and J. F. B. Mercer, Eur. J. Biochem. 160, 579-585 (1986)
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  J. P. Segrest et al., Beckman TL-100 News 1:2, 1-2 (Dec. 1986)
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  T. Zysset, Ther. Drug Monit. 9, 433-438 (1987)
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  H. K. Naito, Applications Note DS-693. Beckman Instruments, Inc., Spinco Division, 1986.
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  D. L. Gard and M. W. Kirschner, J. Cell Biol. 105, 2203-2215 (1987)

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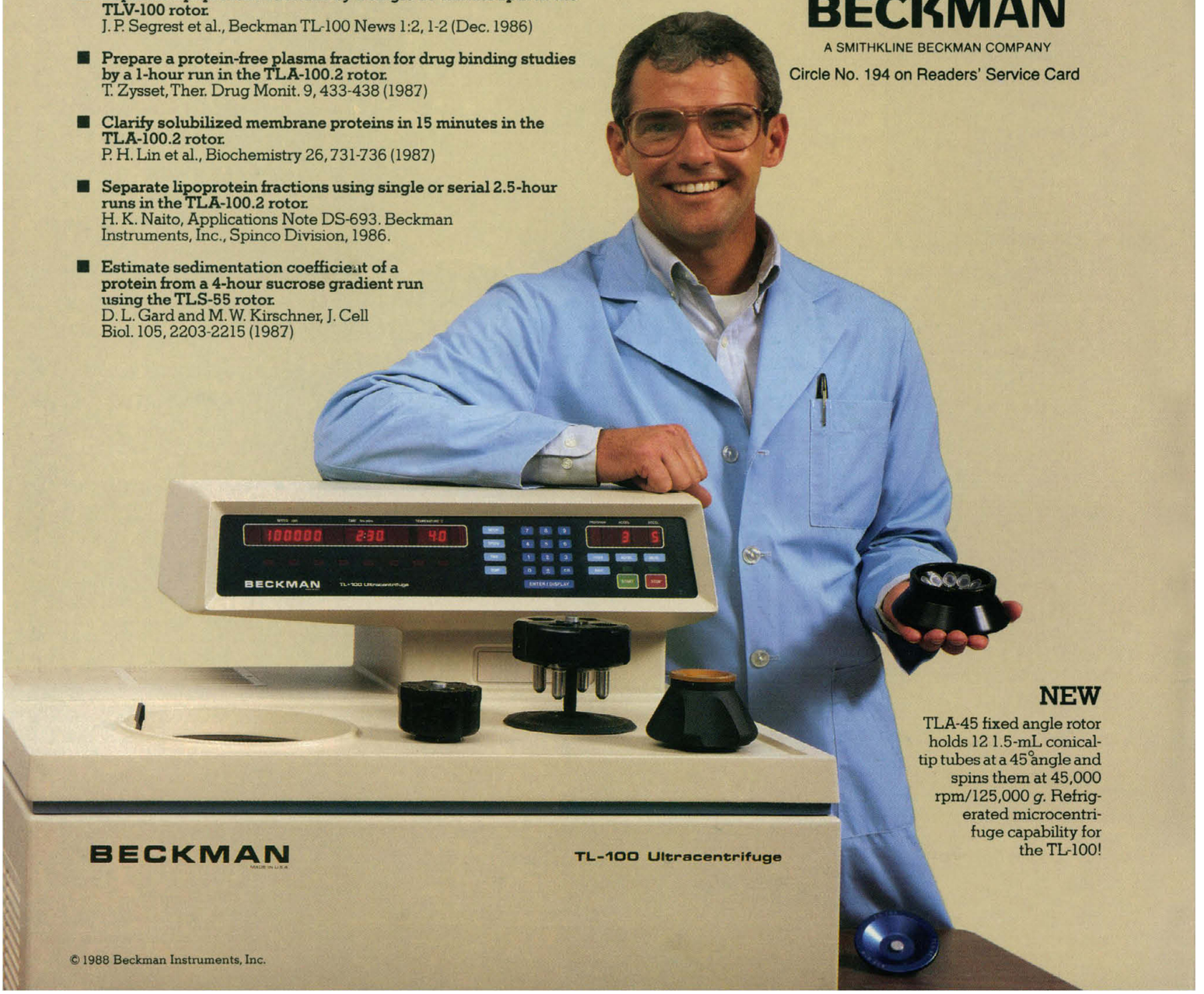

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COVER A archival Kitt Peak National Observatory 4-meter telescope color optical picture (top) and a color infrared picture (bottom) of Messier 17, a region of vigorous star formation. The infrared picture is a composite of images made through 1.2-mircrometer, 1.65-mircrometer, and 2.2-mircrometer filters, colored blue, green, and red, respectively, and represents how Messier 17 would appear if the eye responded to infrared radiation. See page 1264. [The infrared picture was made with the Kitt Peak National Observatory 2.1-meter telescope by I. Gatley, D. L. DePoy, and A. M. Fowler, National Optical Astronomy Observatories, in collaboration with Charles Lada, University of Arizona]

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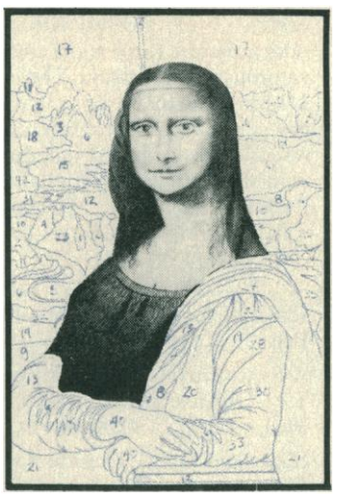

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Flawed methodology

MANY recent epidemiologic studies that claimed to establish cause-and-effect relationships between the development of a disease and prior exposure to a medical or nonmedical agent (a drug, food, or environmental substance) have been controversial, and some have been discredited. Three examples are discussed on page 1257. In a number of these studies, the methodology was faulty from the start: Feinstein points out that, in contrast to experimental studies, which begin with the formulation of a testable hypothesis, hypotheses are generated in some epidemiologic analyses only as consequences of "data dredging" during the search for statistical associations. Attention to several other "scientific principles" that, like the formulation of research hypotheses, are routine in laboratory experiments would lend strength to the validity of conclusions in epidemiologic studies of noninfectious agents. New methods, new paradigms, and new conceptual frameworks must be developed and applied to these studies so that high standards can be met here as they are in epidemiologic studies of infectious agents and in other areas of biomedical research.

Infrared astronomy

TWO-DIMENSIONAL arrays consisting of thousands of tiny infrared detectors are now in use for generating images of infrared emitters in the cosmos (page 1264). In the short time that this technology has been available, much exciting new information has been obtained about galactic centers, star formation regions (cover), colliding galaxies, planets, and other infrared emitters; single infrared detectors have been insufficient to capture the complexity of these vast regions that are partially or totally "invisible" to optical, radio, and x-ray imaging devices. Gatley *et al.* describe the new array devices and special features of infrared emissions; for example, the ability of infrared emissions to penetrate through dust of gigantic molecular clouds greatly surpasses that of optical emissions. The power of the new tools is illustrated pictorially and in comparisons with older optical images. In the near future there will be larger arrays, devices for detecting infrared emissions at longer wavelengths, and detectors deployed in space, where infrared emissions from the earth do not interfere. Gains that will be realized from opening the infrared window onto the universe are expected to be no less than astronomical.

Continental paleoclimate record

A continuous climate record from the middle to late Pleistocene (between 310,000 and 50,000 years ago) has been drawn from isotope data collected from a calcite vein in Nevada's Great Basin (page 1275). Oxygen isotopic records in calcite are related to past local surface temperatures; the ^{18}O in precipitation (which recharged ground water that deposited the calcite vein) is temperature-dependent. In general, times that had warm surface air temperatures are represented by enrichment of ^{18}O, the heavy isotope of oxygen, and relatively cold weather is represented by ^{18}O depletion. The overall shape of the Great Basin climate record is like that of marine and ice-core records, but the timing of major climate changes is offset. For example, in the Great Basin data, the last interglacial period began at least 147,000 years ago (and perhaps even earlier), whereas the marine and ice-core records place the beginning around 130,000 to 140,000 years ago. Similarly, the Great Basin data indicate that an earlier interglacial period began 272,000 years ago, about 28,000 years earlier than indicated in the marine record. Winograd *et al.* conclude that the timings of these transitions in the Great Basin data are inconsistent with predictions of the Milankovitch hypothesis that attributes ice ages and periods of deglaciation to astronomically driven changes in solar insolation. The major climate shifts in the Great Basin data apparently occurred before the putative forcing events.

Volcanism on Io

INFRARED observations made in 1986 with Earth-based telescopes indicate that volcanism on Jupiter's satellite Io may have involved the eruption of silicates (page 1280). The complex infrared signature showed greatly enhanced emissions in the 4.8-μm and 8.7-μm spectral regions, which is consistent with an eruption temperature of about 900 K. The volcanic hotspot was localized to the satellite's leading side. Conditions on Io are close to those of a vacuum, but the temperature of the eruption was significantly higher than the boiling point of sulfur in a vacuum; sulfur is thought to be a major component of Io's crust. Johnson *et al.* conclude that the 1986 eruption mobilized silicates in Io's interior, but that at different times and places both sulfur and silicate volcanism can occur.

Malaria treatment

MALARIA parasites can become resistant to the otherwise effective drug chloroquine; resistant parasites appear to actively rid themselves of chloroquine in much the same way that drugs are pumped from multidrug-resistant tumor cells. A state of resistance prevents chloroquine from killing parasites. Resistance can, however, be overcome with desipramine, a drug that is currently in use as a tricyclic antidepressant (page 1301). Bitonti *et al.* report that, when chloroquine-resistant parasites are exposed in vitro to both desipramine and chloroquine, the parasites again internalize chloroquine and become sensitive to its effects. Owl monkeys that are infected with resistant parasites develop parasitemias, but, when the monkeys are exposed to desiramine and chloroquine, parasites are rapidly cleared from their blood. Because doses of desipramine that reverse chloroquine resistance in vitro are similar to those achieved in blood during clinical treatment of depression, it is likely that desipramine may be used safely in conjunction with chloroquine for treating people with chloroquine-resistant malaria.

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2 DECEMBER 1988
VOLUME 242
NUMBER 4883

The Golden Median

We break our usual embargo policy to release prematurely a historical record purloined from a time capsule buried in the year 2050:

"No one knows the exact moment in which the glorification of mediocrity occurred in the United States. Perhaps it was the week that a number of prominent educators denounced the use of student SAT scores as a means of recruiting potential undergraduates to their institutions. Soon, the immorality of luring unsuspecting students by saying that they might be exposed to bright colleagues was recognized by all. Earlier, a number of distinguished academic institutions had abolished the grade of 'F,' saying that failing a course was too traumatic for the delicate ego of a modern college student. The giving of academic prizes and the granting of tenure were the next to go, since it had been found that the feverish rush for such honors had led to much fraud in the scientific world. 'Superior' became a pejorative word, joining the ranks of 'fascist,' 'communist,' 'liberal,' and 'conservative,' as terms to avoid at all cost. It was generally agreed that the urge to excel was a disaster for society, causing all sorts of misconduct, ulcers, unrequited love, and serious cases of terminal smugness.

"Once the true malady of society in the 1990s had been diagnosed, the beginning of a campaign to glorify the undistinguished middle was initiated. Those who had gotten to the top had clearly done so by chicanery or improper influence. Those left in the dust were either the victims of an evil system or lacked the means to procure genetic engineering on their parents. The Olympic Games, surprisingly, made the first contribution to the new movement by awarding gold medals to those who were in the middle of the pack and awarding two silver medals to those on either side of the middle person. Magazines provided the next step by canceling the appearance of beautiful women in skimpy attire on their covers, replacing them with dumpy individuals who riveted the reader's attention to the table of contents. TV anchormen were equalized when it was decreed that they must all shave their heads so that the accidental advantage of a beautiful head of hair would not be correlated with the gray matter underneath. All admission tests for college and employment, and all final examinations, were abolished because it was clear that they had been rigged against those who got low grades, whoever they might be. Chief executive officers, who had previously been chosen from those willing to sacrifice their mothers for a dollar on the bottom line, were selected from a totally different group, characterized as those who had a hand of jelly in a cotton glove.

"Once the Era of the Golden Median had been firmly established, a number of peripheral benefits ensued. Heart attacks declined appreciably as evolution selected for types who 'never do today what you can put off until tomorrow.' Fidelity became more popular because everyone tended to look and think alike, and so there was little temptation to stray. Clothing prices came down as shapeless blouses and beltless raincoats could be mass-produced at far less cost than designer garments.

"There were some disadvantages. The opprobrium cast on overachievers led to a general decline in the standard of living. However, this caused little political upheaval because the obvious fact that everyone was sinking into poverty together inspired a spirit of egalitarianism and prevented the kind of envious disruptions that had marred previous political life. Lowering the standard of living also solved the problems of the underprivileged because it was discovered that allowing the privileged to drop to the level of the underprivileged was a lot easier than making an effort to help the less advantaged move up.

"One could not expect this kind of utopian society to last too long. Mediocrity became commercialized. Cosmetics firms advertised creams that could make one look ordinary. Clothing stores had special events promoting their new lines of nondescriptwear. And unscrupulous flimflam artists sold schemes showing those at the front of the line how to move inconspicuously back to the middle. Fortunately, the internationalization of mediocrity meant that there was no urge to occupy other territories. The cancer rate dropped, since the general lack of exertion led to less inhaling of ozone. But surprisingly, people died at a younger age. No explanation of this phenomenon was found for years, until a run-of-the-mill surgeon doing a routine autopsy noted that in most of his patients all of the neurons had atrophied. It was the typical symptom of the most prevalent disease of the time: death from boredom."—DANIEL E. KOSHLAND, JR.

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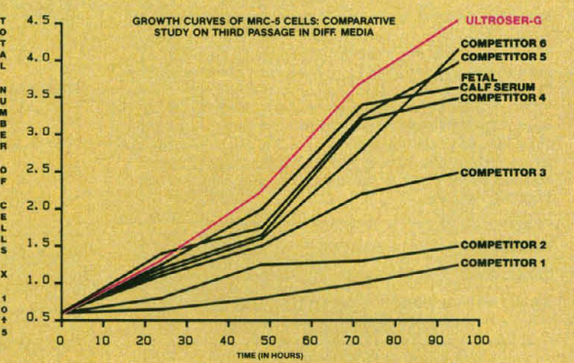

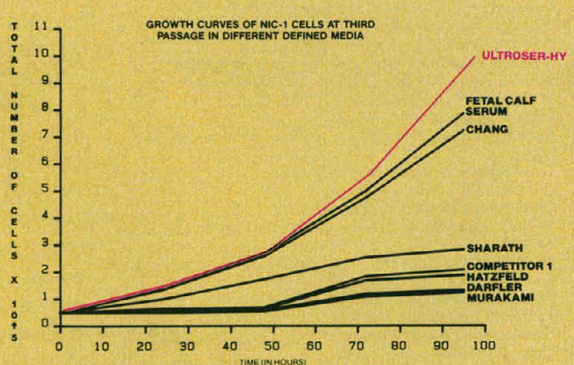

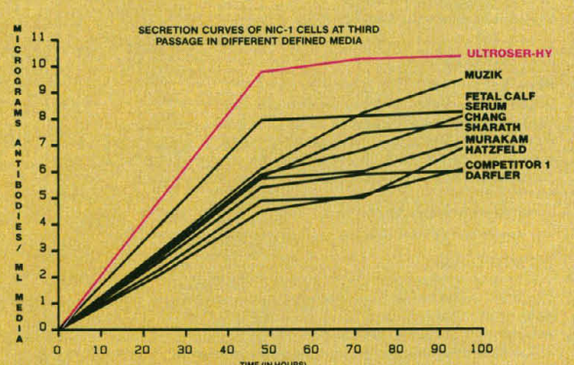

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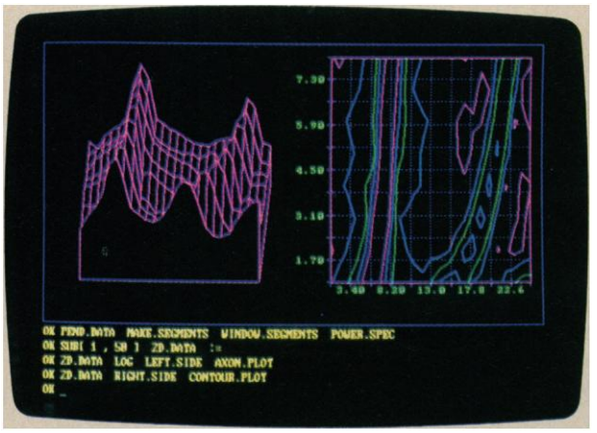

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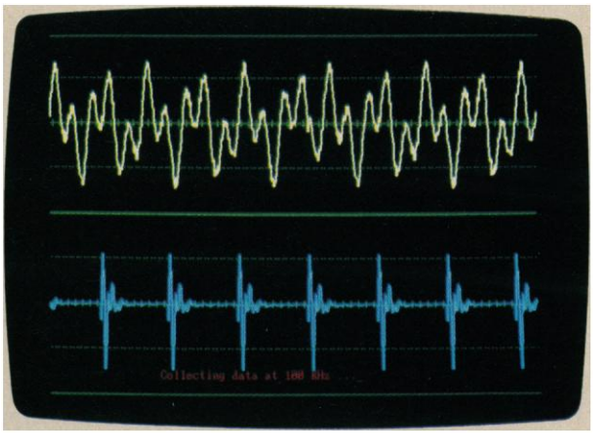

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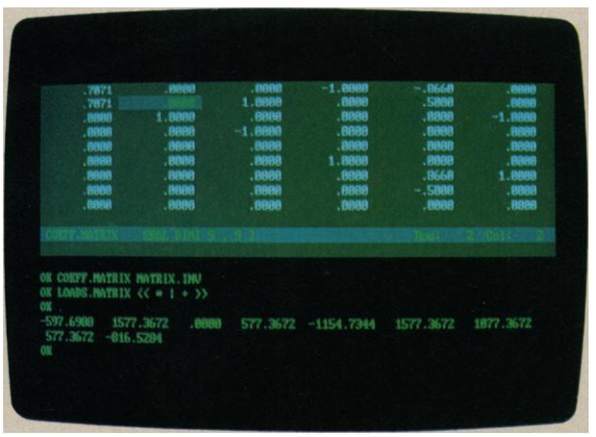

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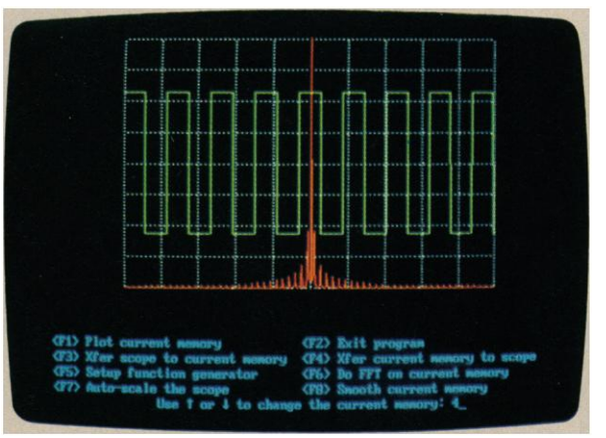

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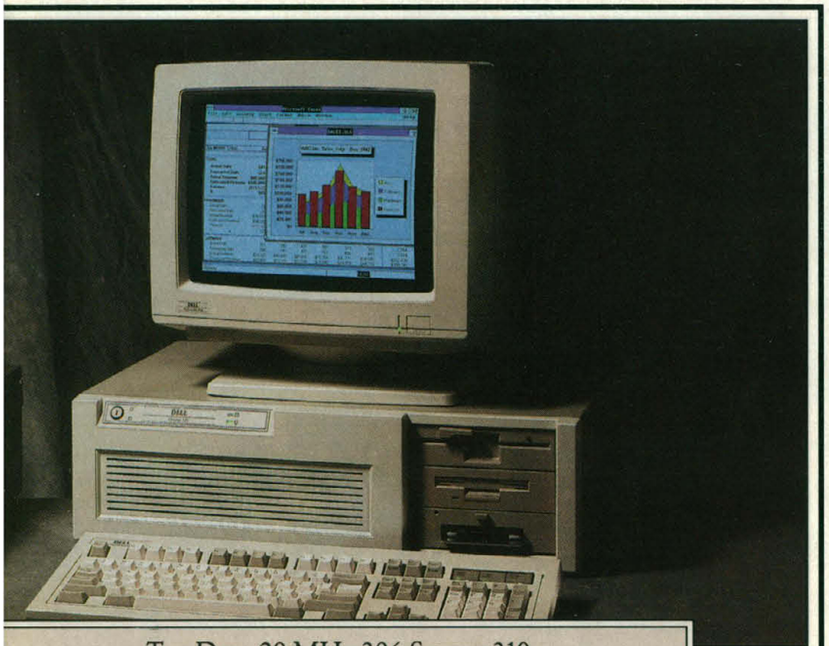

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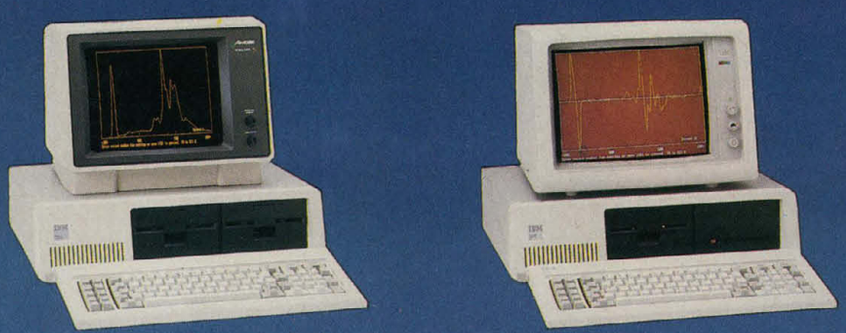

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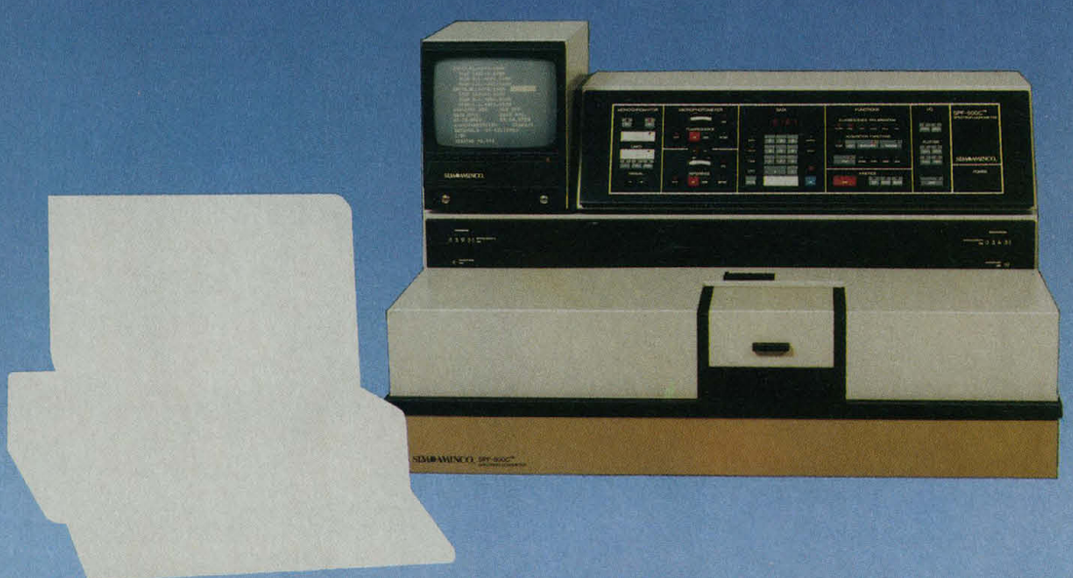

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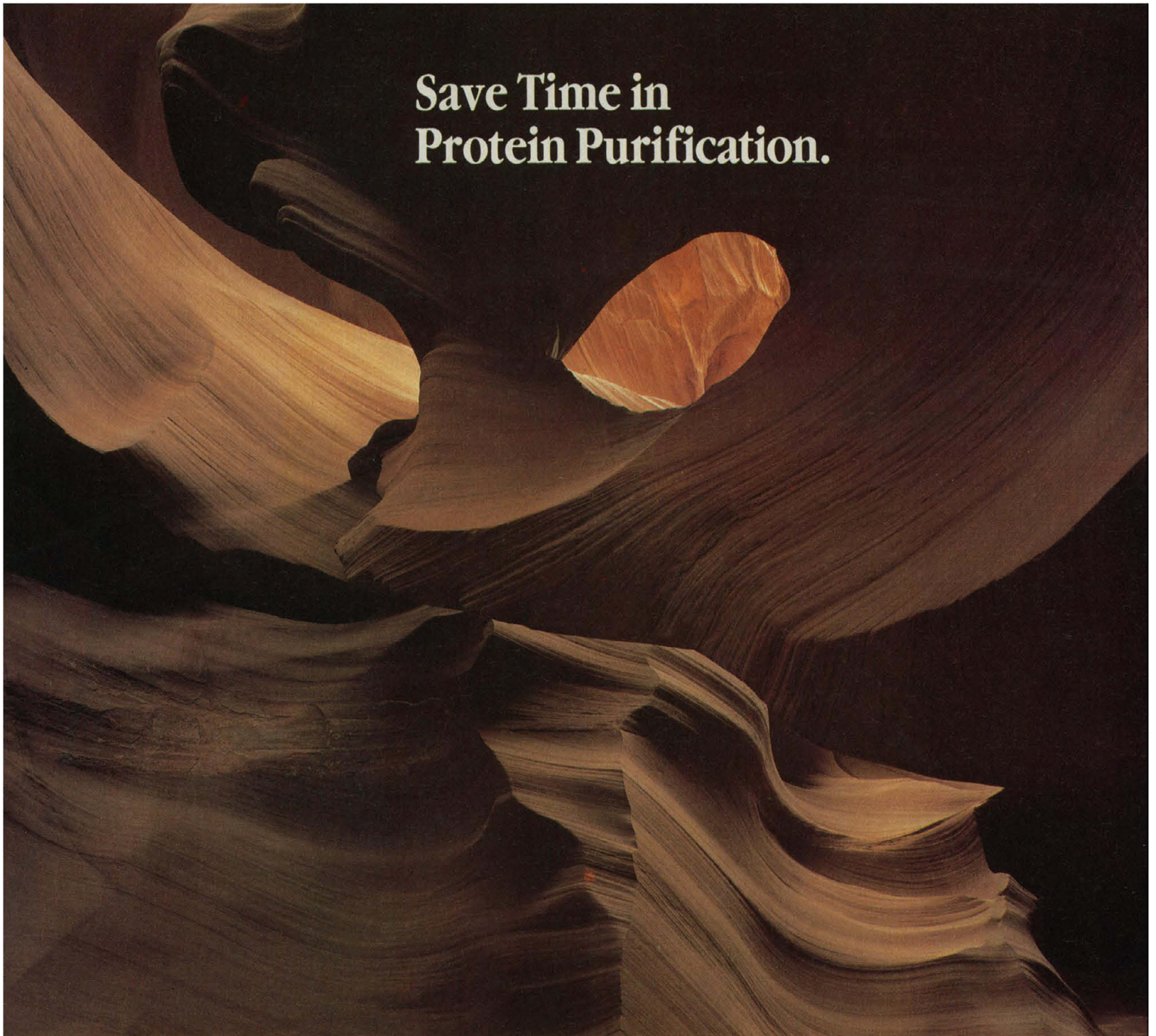

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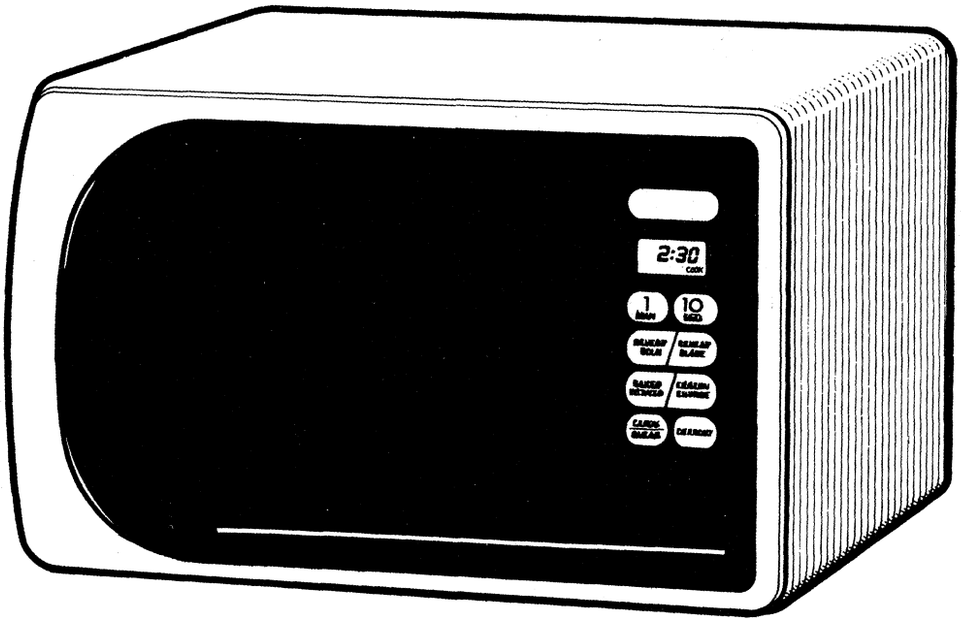

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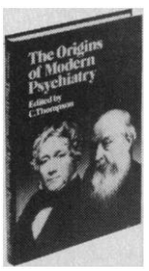

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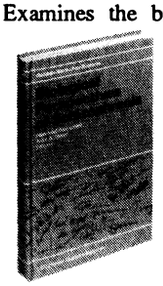

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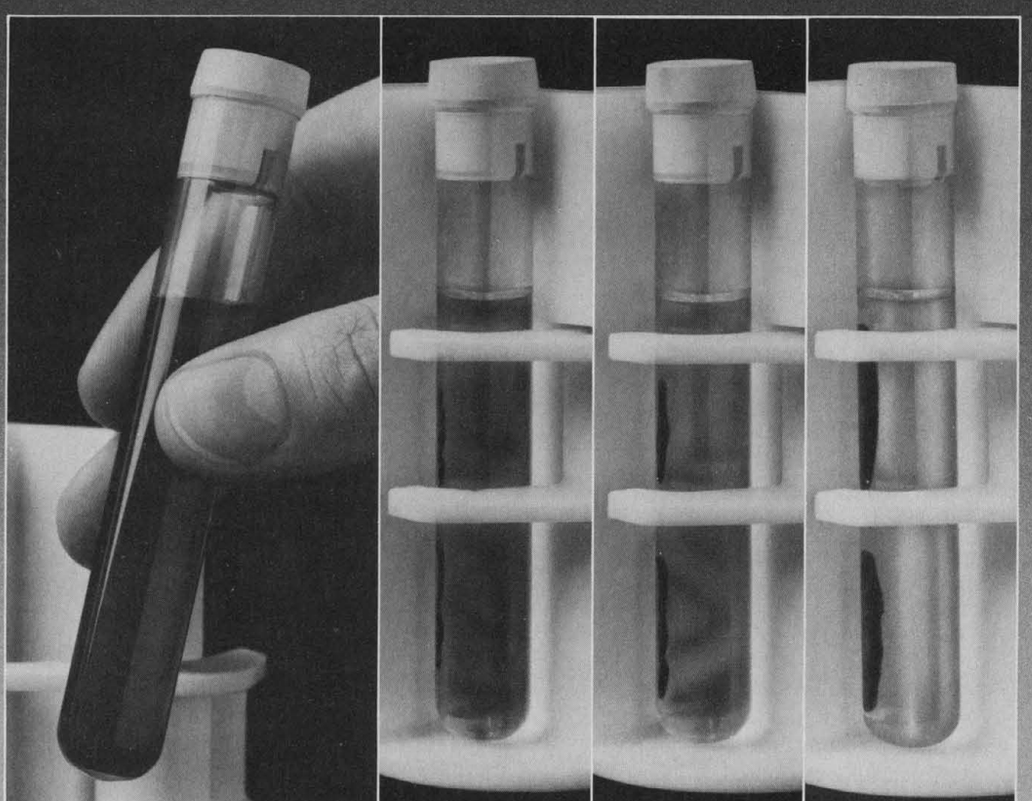

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