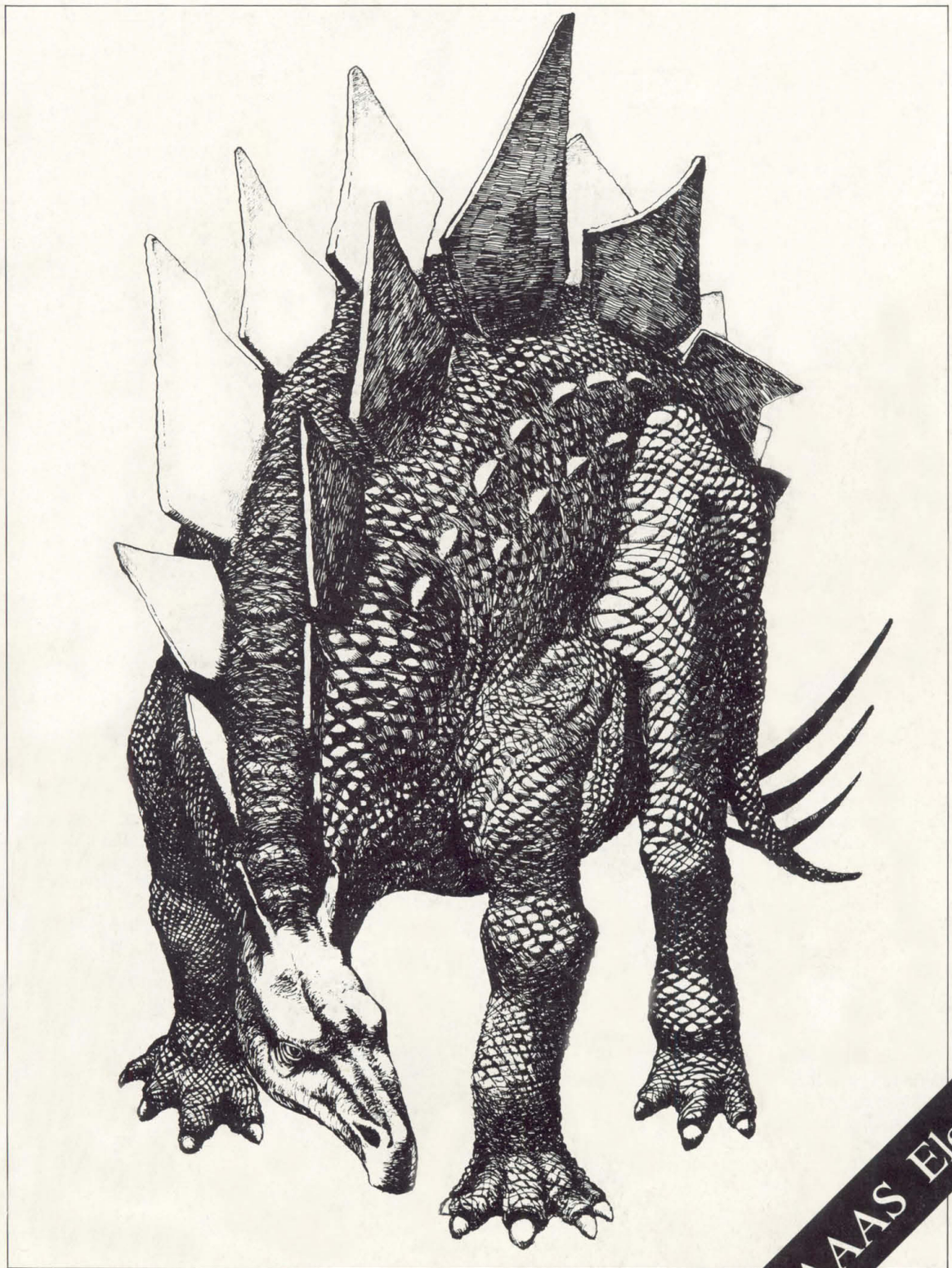
SCIENCE

11 June 1976

Volume 192, No. 4244

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



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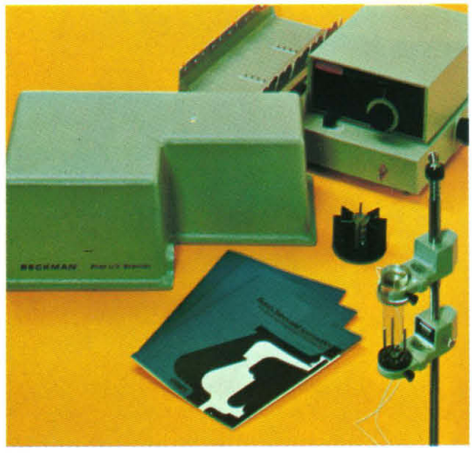

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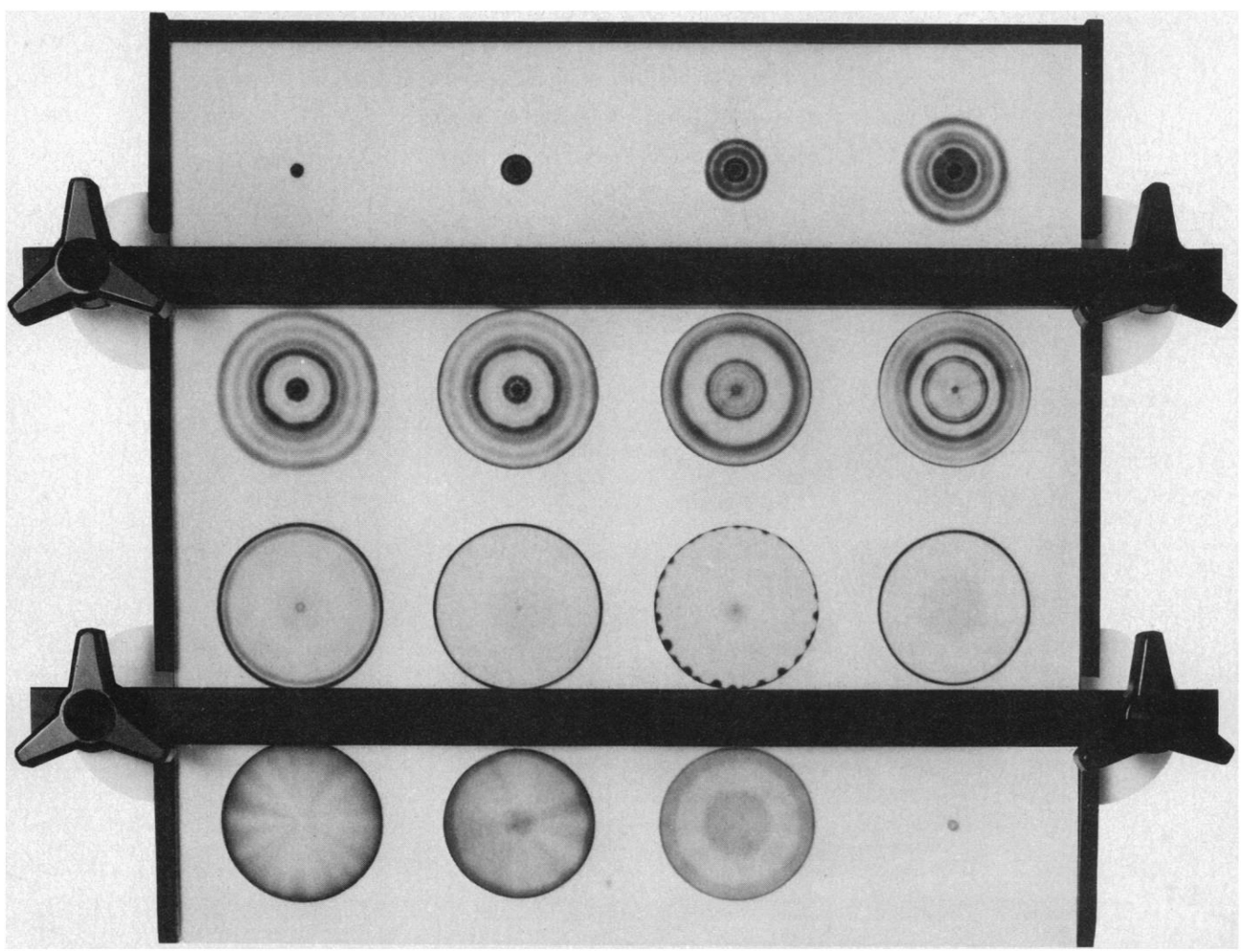

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11 June 1976

Volume 192, No. 4244

SCIENCE

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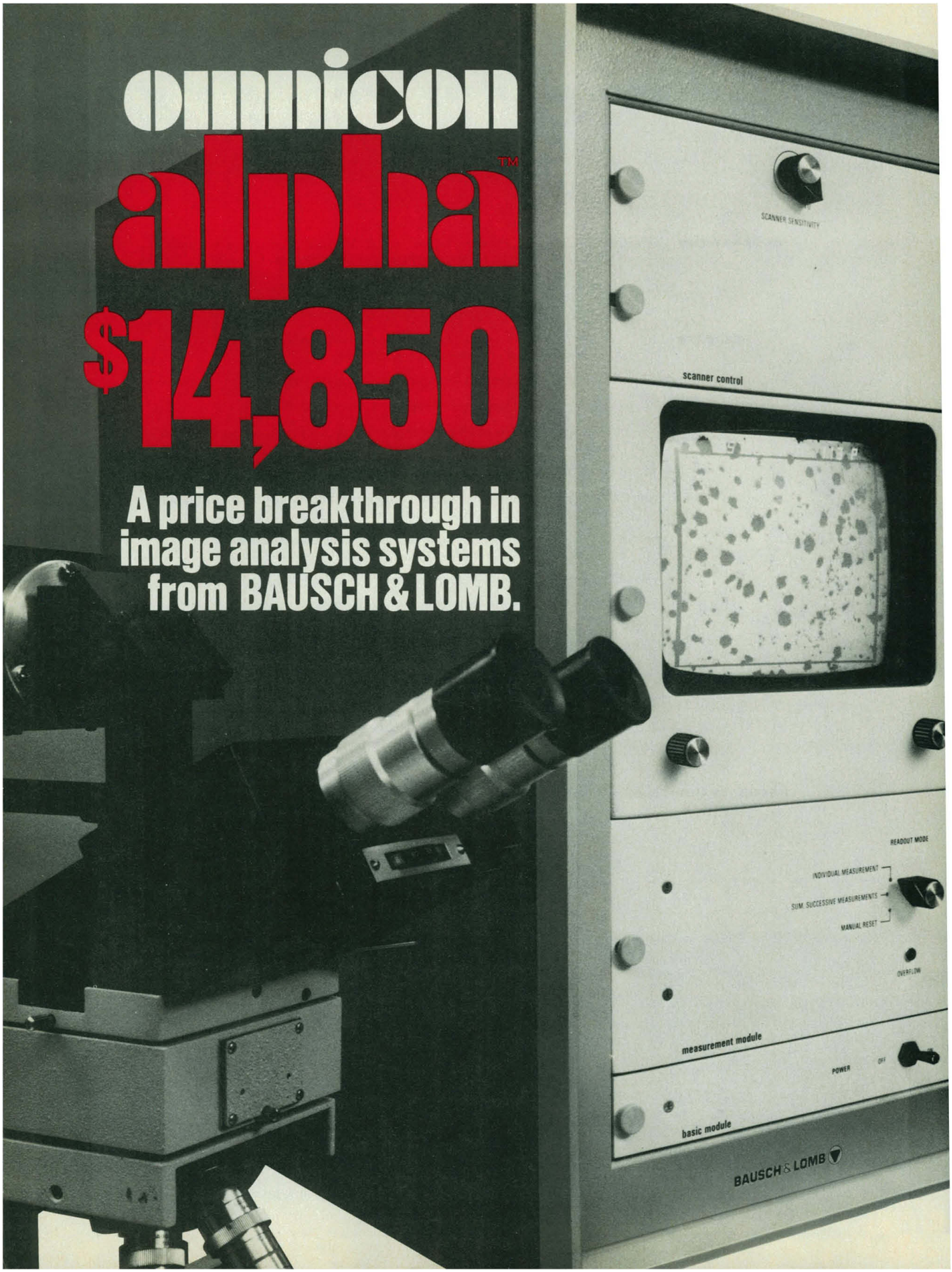
COVER

While previously believed to be "armor" and/or structures for "displays," it now appears that the plates along the arched back of the dinosaur *Stegosaurus* served an important thermoregulatory function as forced convection heat-loss fins. Such fins are not unlike fins used in compact engineering heat exchangers. See page 1123. [From an original etching © by Daniel Rosner, Yale University, 1976]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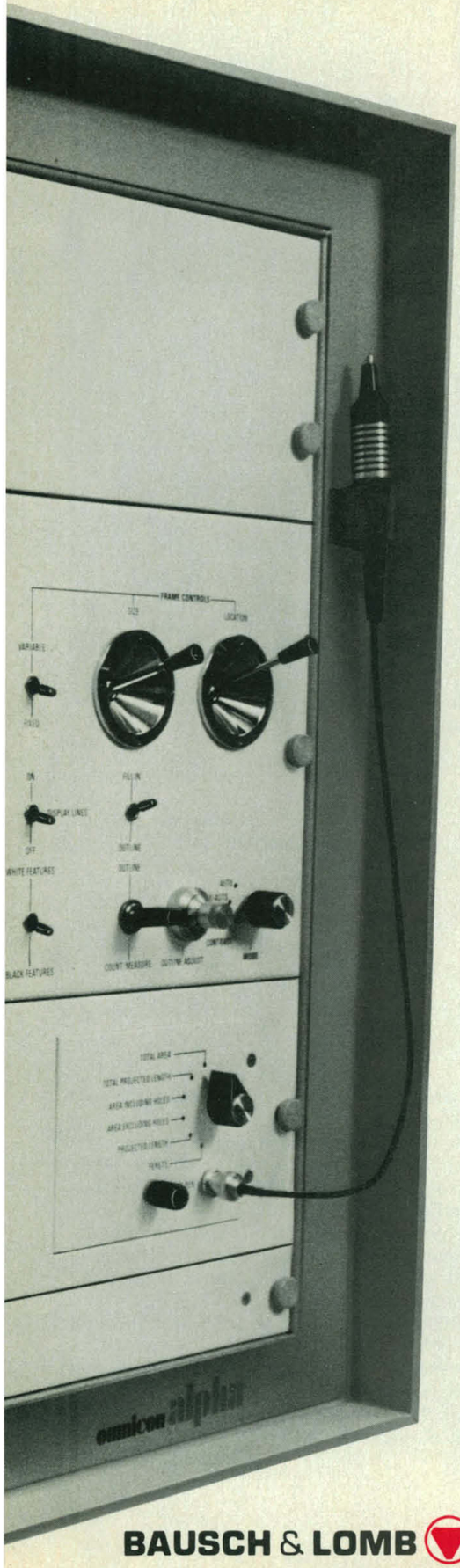

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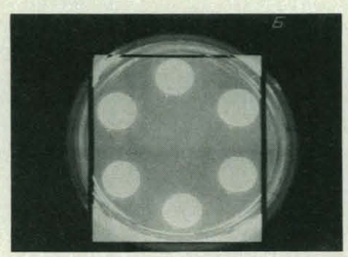

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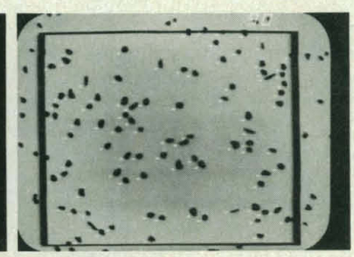

A count in one field of view of particles from a sieve sample.

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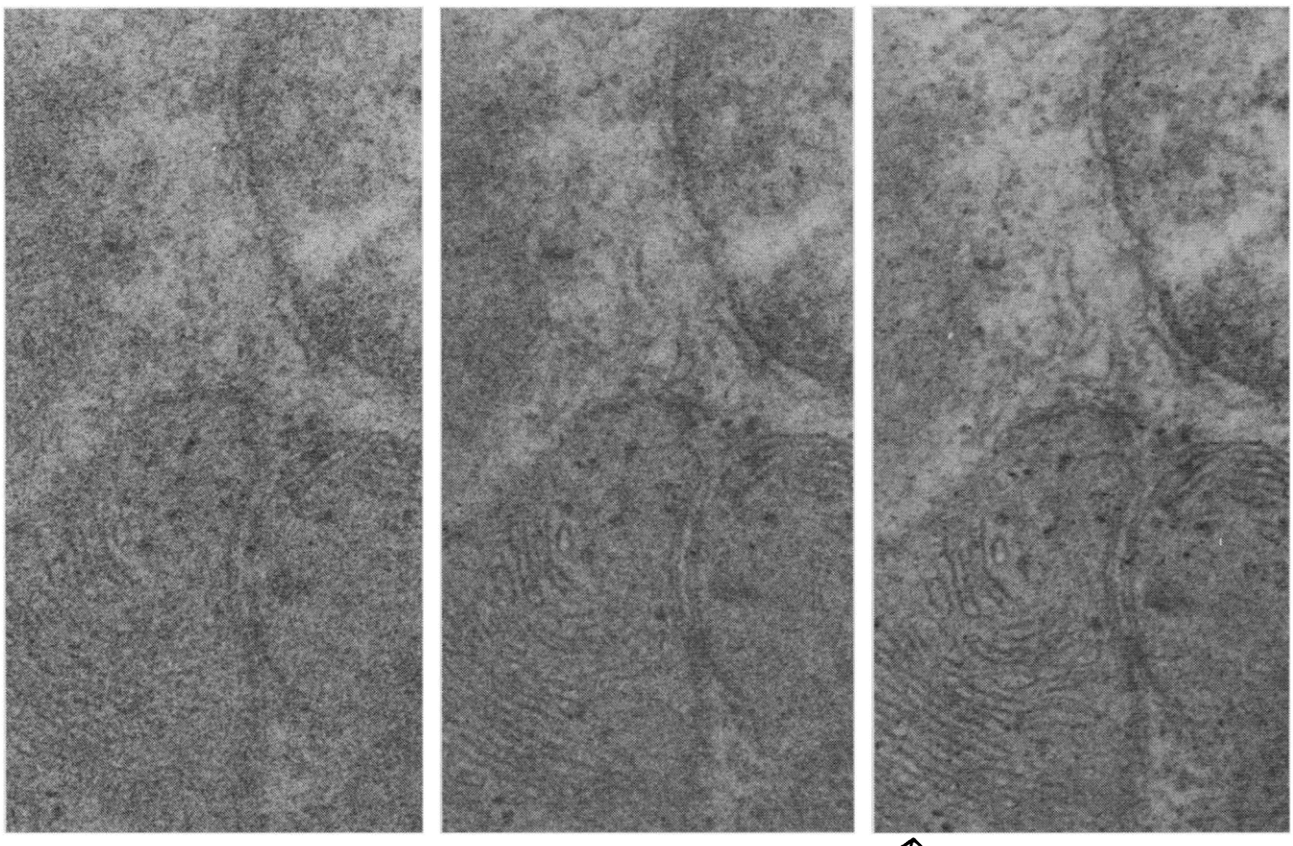

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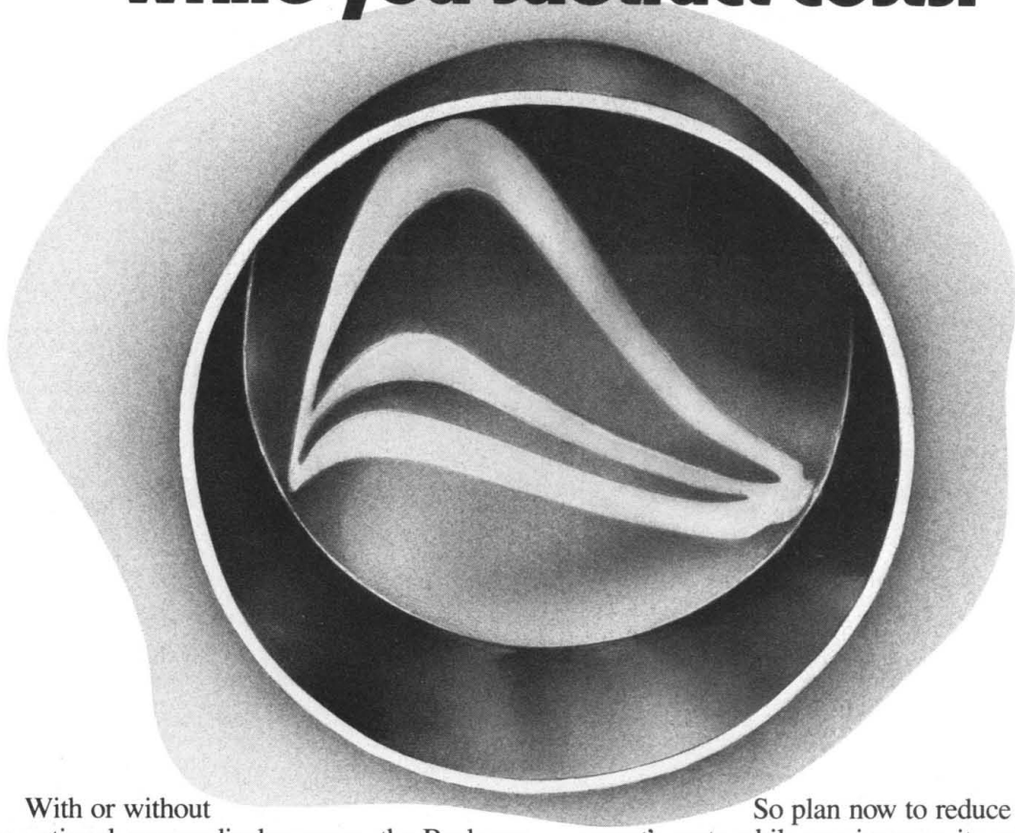

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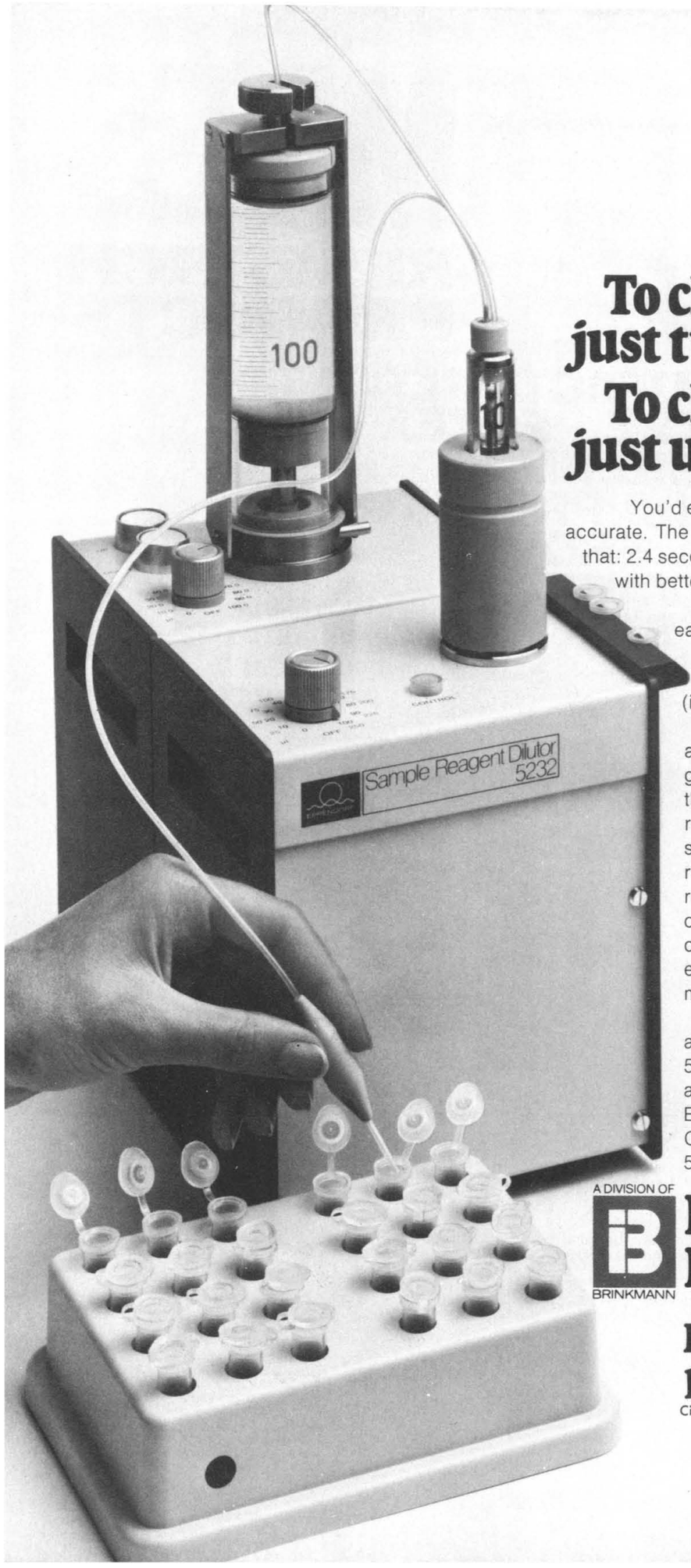

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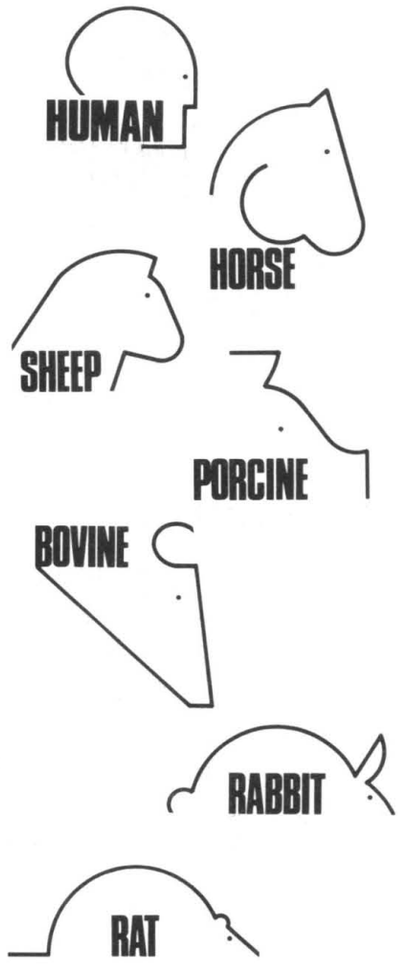

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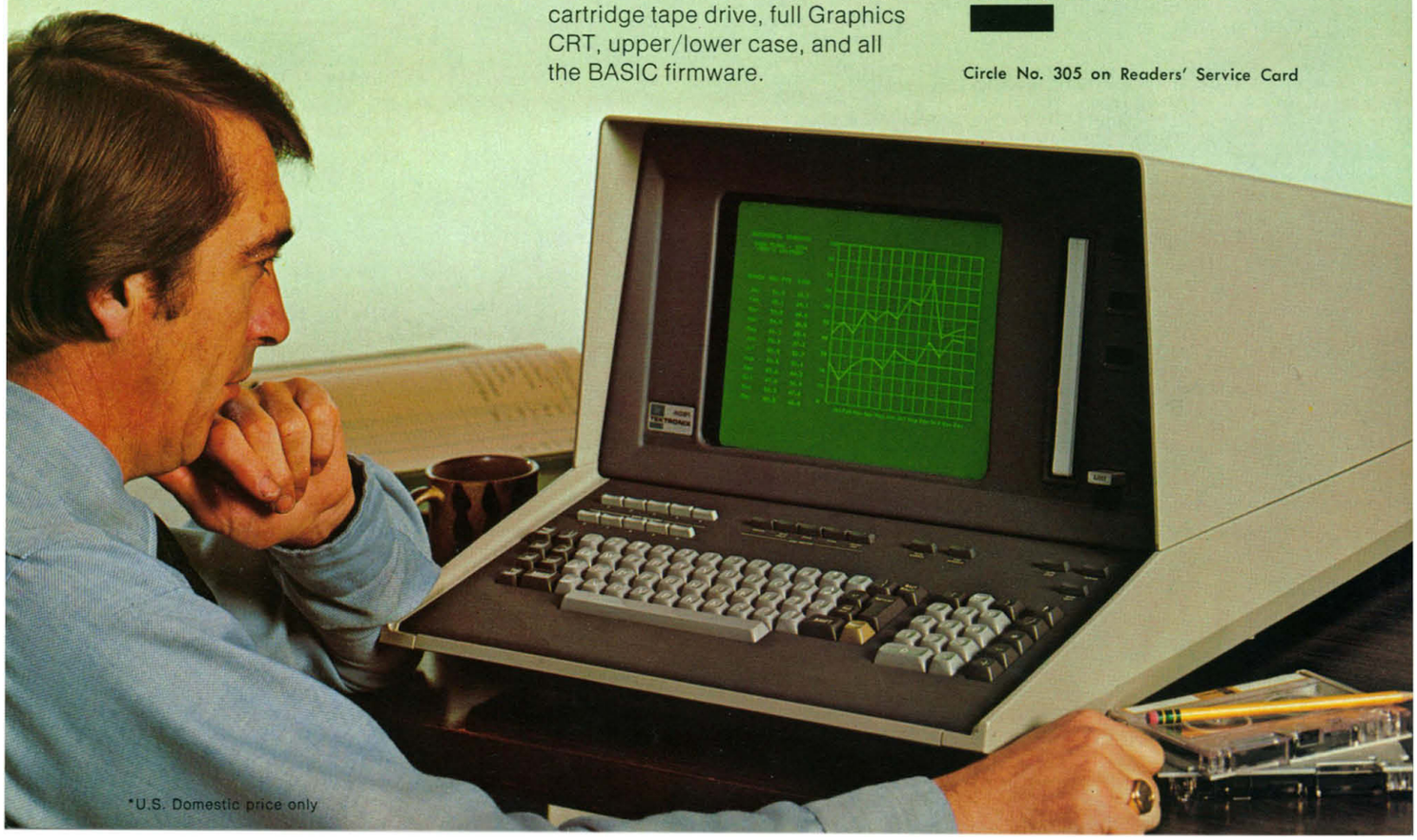

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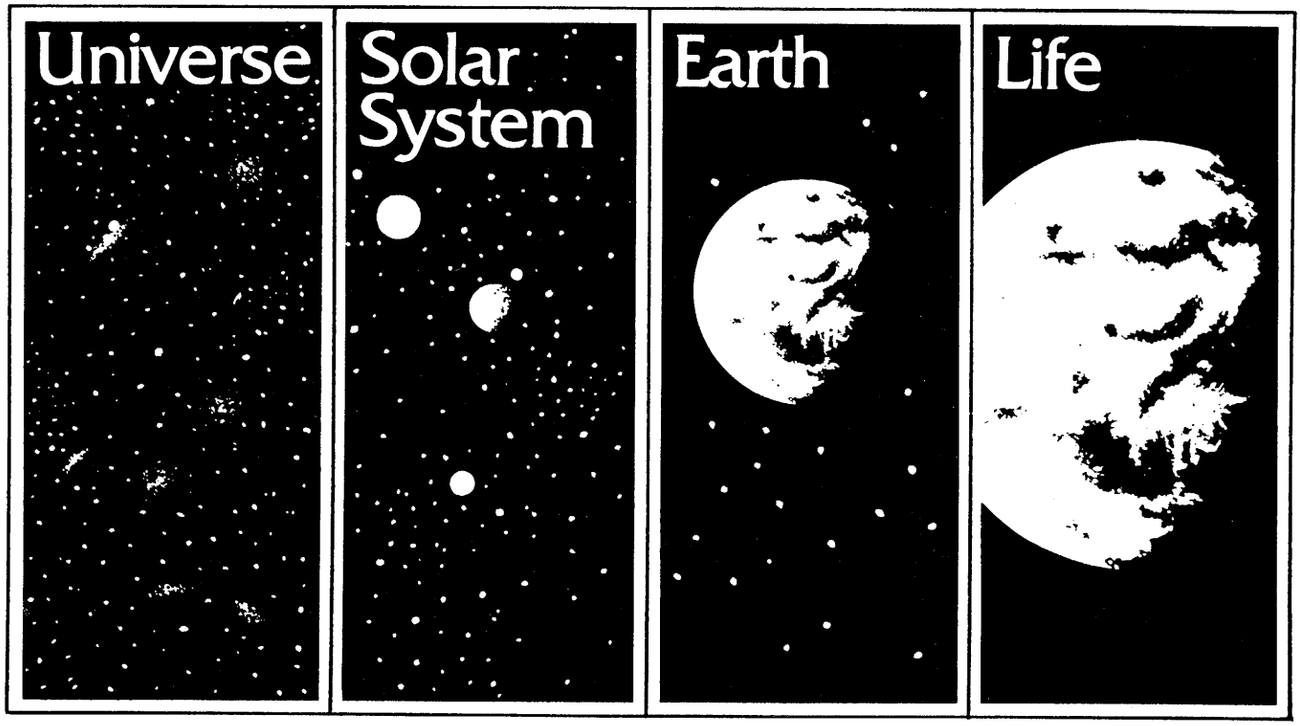

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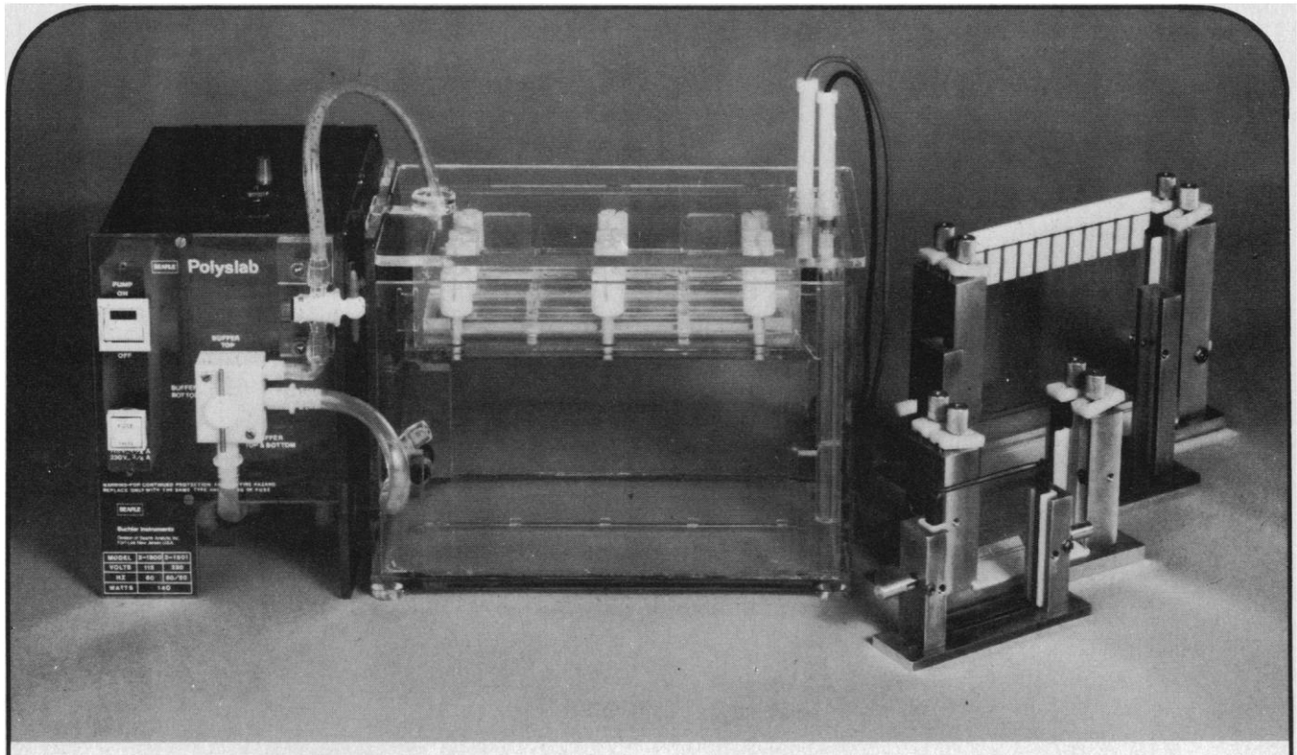

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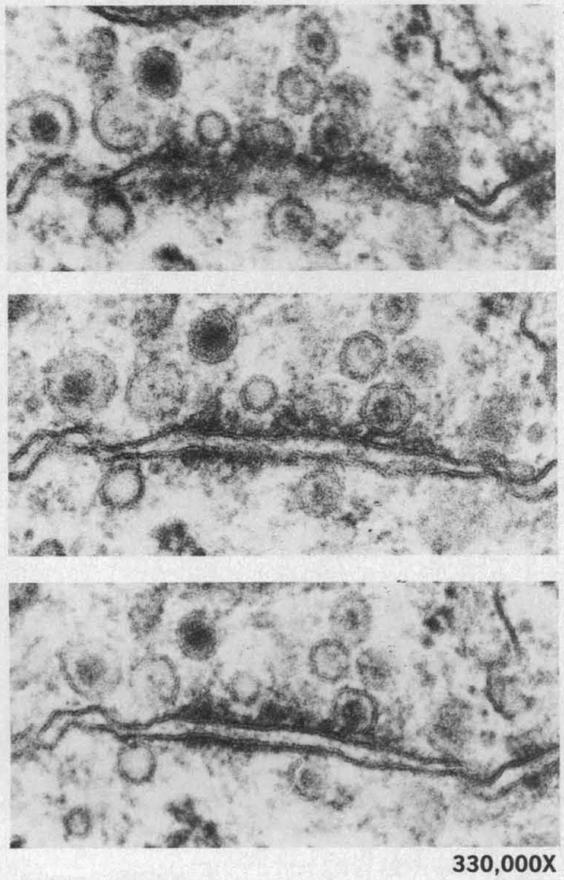

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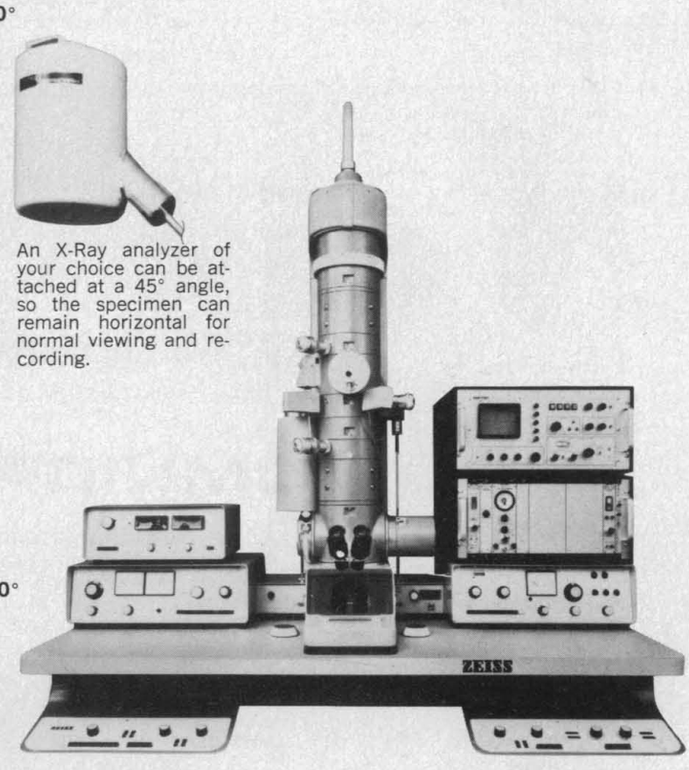

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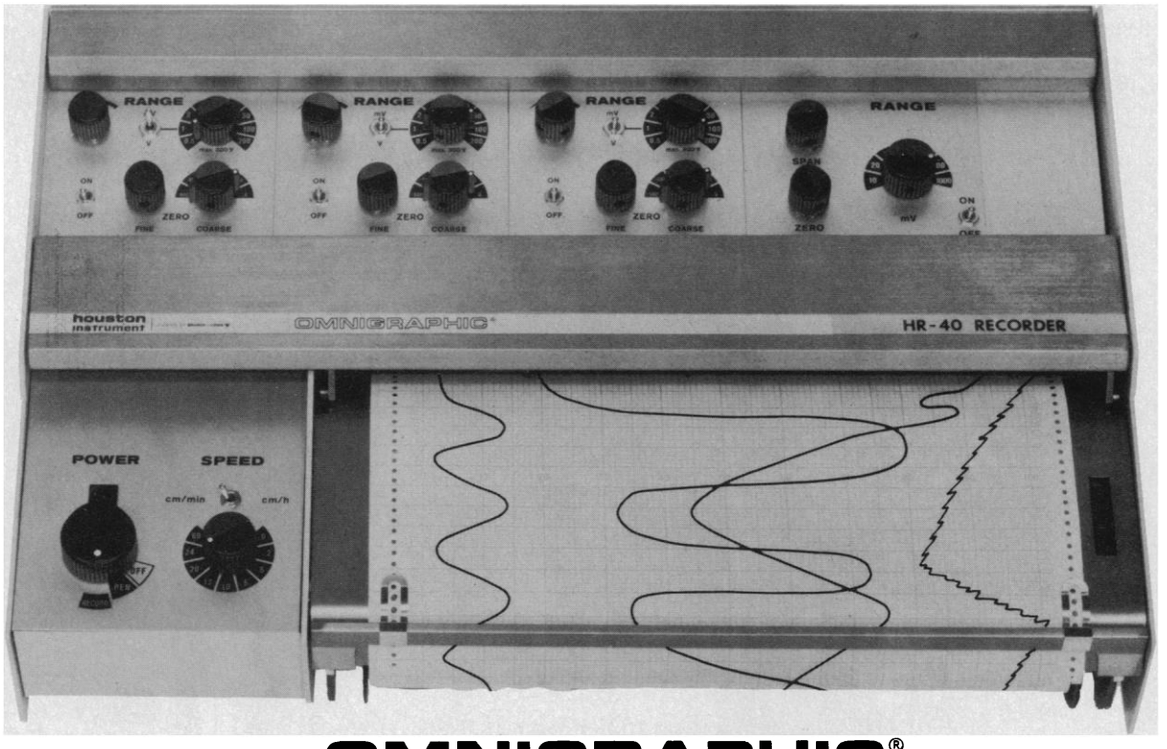

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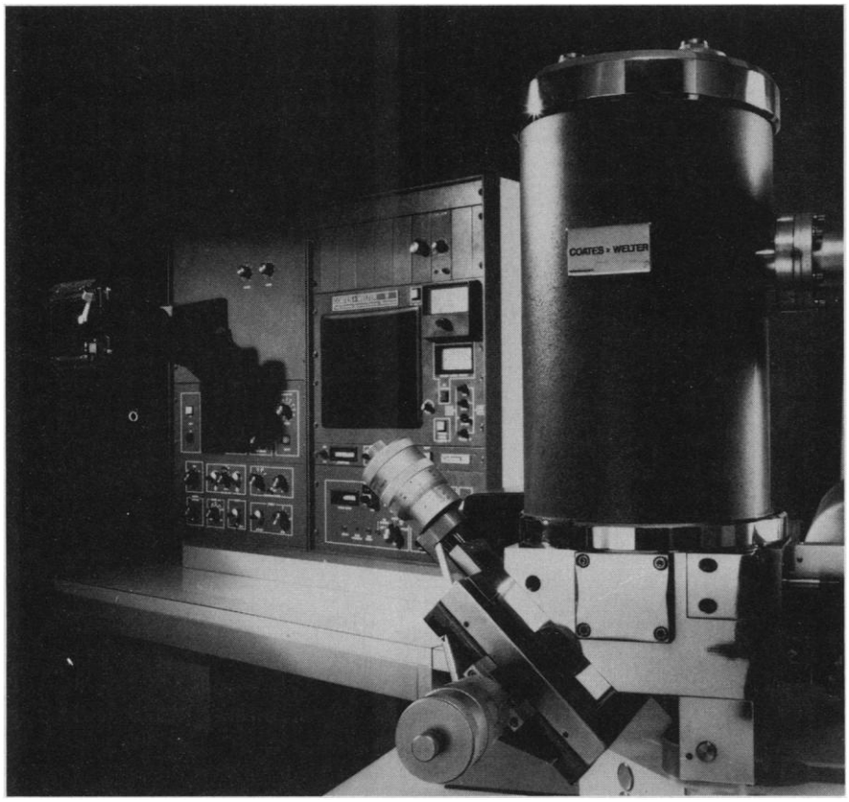

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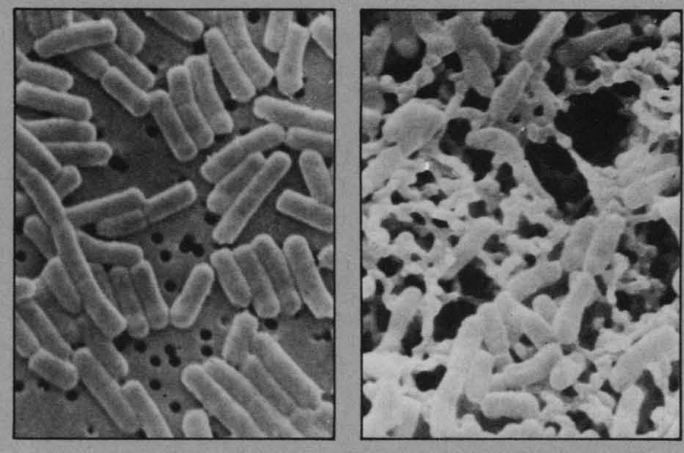

Scanning electron micrographs of *Bacillus subtilis,* 5000X, on 0.4 μm pore size polycarbonate membrane on the left and a standard 0.45 μm pore size cellulosic membrane on the right.

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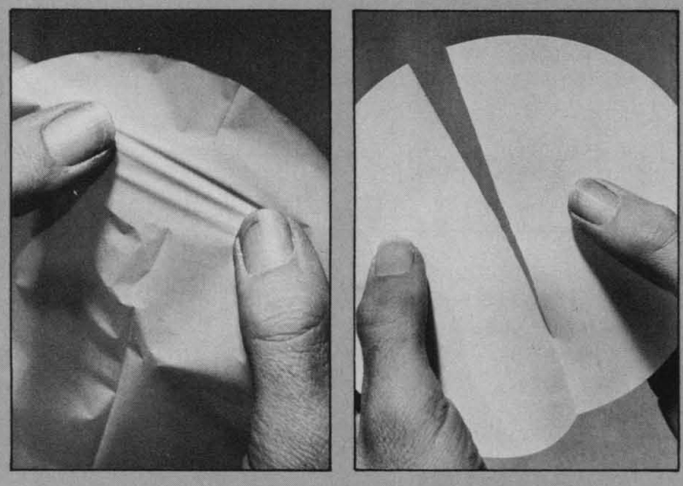

Uni-Pore membranes can be bent and folded without damage as shown in photo on the left. Cellulosic membranes crack and break under the same treatment as shown in photo on the right.

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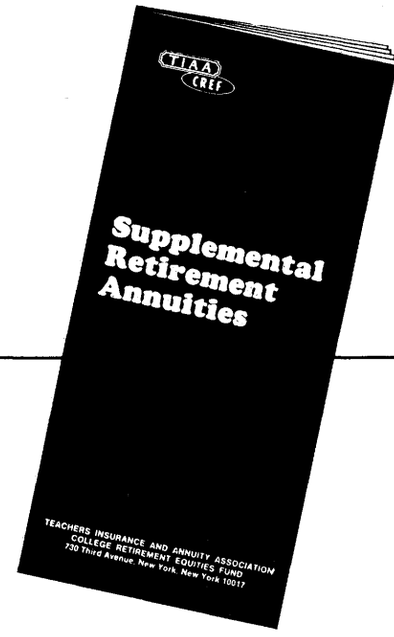

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LETTERS

Details of the DeFunis Case

John Walsh, in his article "Universities and the law: Legislation, regulation, litigation" (News and Comment, 23 Apr., p. 354), refers to the University of Washington and says that "with about 15,000 students, it is the second largest employer in Seattle." The reference should have been to 15,000 employees, not students, since more than 35,000 students are currently registered at the University of Washington.

In his discussion of the DeFunis case, Walsh omits a stage of the proceedings which is quite important. While DeFunis won his case in a lower court, the University appealed it to the Supreme Court of the State of Washington, which reversed the lower court's decision and upheld the position of the University of Washington. Thereafter DeFunis appealed to the Supreme Court of the United States, where the case was ultimately declared moot. Because the University had complied with the lower court's order requiring DeFunis's admission, and Justice Douglas had stayed any change of that order pending DeFunis's appeal to the U.S. Supreme Court, DeFunis was able to remain in school during the entire pendency of the litigation.

Otherwise, Walsh's article performs a useful service in describing the increasingly heavy involvement of courts and lawyers in the affairs of higher education.

JAMES B. WILSON
University of Washington Division, Office of the Attorney General, State of Washington, Seattle 98195

Energy in the Soviet Union

Philip H. Abelson's editorial "Energy diplomacy" (30 Apr., p. 429) is one of the most significant he has written. However, in comparing U.S. and Soviet resources, he mentions only oil and natural gas. The unfortunate aspect of the problem is that the Soviets are leading the Americans in almost every aspect of the energy problem.

The Soviet Union has five huge river systems and a considerable part of the Amur system, which they share with the People's Republic of China. Although the Dnieper River system has been fully developed to take advantage of its hydroelectric capabilities and the Volga is rapidly being developed (*1*), the rivers of Siberia are only in the early stages of development. Full development of the hydroelectric potential of all these river systems could provide the complete electrical needs (residential, commercial, and industrial) for between 70 million and 100 million people. One source estimates that the Soviets may possess as much as 12 percent of the world's potential hydroelectric power (*2*).

In the nuclear energy field the Soviets now have a prototype breeder reactor in operation (*3*), whereas the United States won't have its prototype in operation until some time in the 1980's. One of the world's largest research programs on nuclear fusion has been in existence in the Soviet Union for many years, including research on both magnetically confined plasmas (*4*) and laser fusion (*5*). The concept of the Tokamak, now used in both the U.S. and Soviet research programs, originated in the Soviet Union.

The Soviet Union also has one of the two existing electric generating stations using tidal power (*6*) and, even though small, it is one more tidal energy plant than the United States possesses. The Soviets also have significant research and development programs in other energy areas, such as MHD (magnetohydrodynamics) (*7*) and geothermal (*8*). About the only area in which the United States appears to have a significant lead over the Soviets is in solar energy, but we are only beginning to emphasize this source.

While we grow more and more dependent on foreign oil as our primary source of energy, the Soviets continue to develop and amass domestic energy resources. These two distinctly different courses of action could easily create a significant energy imbalance in the not-too-distant future. All the talk about the relative strengths of the two countries would then become nothing more than hollow rhetoric.

C. SHARP COOK
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Solar Energy Development

Christian B. Anfinsen's comment (Letters, 16 Apr., p. 202) that a major solar energy effort might unburden us of dependency on nuclear power is appropriate. Analyses in the Project Independence task force report on solar energy (*1*)—to which more than 100 professionals from government, industry, and academia contributed—suggest that by the end of the century the nation could be obtaining about four times as much total energy, and about twice as much electricity, from the sun (*1*, p. I-7) as is expected from nuclear fission (*2*, pp. V-5, VI-2, and VIII-6). Each of four individual solar technologies has the potential to deliver more power sooner than, and at least as cheaply as, the liquid metal fast breeder reactor (LMFBR).

Incomprehensibly, the Administration is deliberately moving slowly in developing this potential. The definition report of the National Solar Energy Research, Development, and Demonstration Program issued by ERDA (Energy Research and Development Administration) projects outputs of solar electricity that are 22 to 27 times less in 1985 and 5 to 13 times less in the year 2000 (*3*, pp. I-4, V-5, and V-6) than those projected in the Project Independence report. In contrast to the heavy documentation of the latter, the ERDA report gives no details about the derivation of its estimates. Of the goal set for solar energy production, it acknowledges that "Significantly higher levels are possible . . . ," and describes the goal as ". . . *a modest and highly attainable impact for solar energy in deference to conventional fossil fuel and nuclear sources* [italics mine]" (*3*, p. V-6).

The final environmental statement on the LMFBR (*4*) recently released by ERDA treats the solar alternatives superficially and, like the definition report, makes no reference to the Project Independence report, which is still the most comprehensive analysis of the solar energy potential.

Although more than 60 percent of the mail sent to ERDA is said to be concerned with solar energy (*5*), as of 20 February, only 72 of ERDA's 8000-odd employees were assigned to the Division of Solar Energy. Even its Office of Public Affairs, with 92 employees, had more.

ERDA recently created a new administrative division for the LMFBR, while its Division of Solar Energy continues to be responsible for varied technologies, some of which have no more in common with each other than with hydropower or coal, which are also forms of "solar" energy.

Nuclear advocates say that solar power is too costly. But they do not acknowledge that government promotion and subsidy give nuclear power an artificial competitive advantage. Certainly, the characterization by Zebroski and Minnick (Letters, 26 Mar., p. 1214) of nuclear power as "highly attractive as a source of long-term, low-cost power" should not go unchallenged. The cumulative direct cost to the federal government of supporting nuclear power through the end of 1975 was about $8.15 billion (1975 dollars). This is equivalent to 15.9 mills for every kilowatt-hour of commercial nuclear power ever generated in the nation. It is equivalent to about 85 percent of the total capital that industry had invested in all commercial nuclear plants operating at the end of 1975 (*6*). During 1975, the federal government spent about 10 percent more supporting fission power than the nuclear industry spent to generate power (if we assume a high estimate of 5 mills per kilowatt-hour as the industry's production cost) (*6*, p. XV). During the coming fiscal year, the federal cost of nuclear power is due to increase 35 percent, but the nation's licensed nuclear capacity will increase during 1976 by only 13 percent. The budget of the Nuclear Regulatory Commission alone averages well over $6 million for each 1000 megawatts of nuclear capacity (the size of a large reactor) licensed at the end of 1975. Indirect federal costs, state government costs, and other externalities have not been estimated.

Moreover, costs of nuclear power to taxpayers are due to sharply increase. The cumulative federal cost of the LMFBR program, "[u]ntil the time that the option is made available to utilities to buy a commercially viable breeder" (*7*), is now expected to be $12.88 billion (1975 dollars). Before the prototype commercial large breeder is completed, the cumulative federal cost of civilian fission power could easily exceed $25 billion (1976 dollars). This does not include the expenditures made through the Tennessee Valley Authority, the world's largest purchaser of nuclear reactors; it plans to spend $9.4 billion to increase its nuclear generating capacity by 1984.

Moreover, it is not a foregone conclusion either that it will be possible to overcome the technical obstacles to building a commercial LMFBR or that it will be possible to make it economical (*4*). ERDA's National Plan says, "Because the technical risks are too great and the financial pay-offs so far in the future, ERDA will develop the fuels, materials, and components technology to support the construction and operation of large-scale LMFBR's by industry" (*2*, vol. 2, p. 89). Nuclear proponents Hans Bethe and Alvin Weinberg have said, respectively, "Nobody can predict the price of a fast breeder" (*8*), and "Whether LMFBR's can be the basis for a truly commercial industry still remains to be seen" (*4*, vol. 1, p. 1-C-8).

Federal budgets, both present and recommended, for all solar technologies combined are less than one-tenth those related to civilian fission power, and the budget for the LMFBR alone is almost five times as great. The proposed fiscal year 1977 budget for ERDA's commercial radioactive waste program amounts to more than half the projected outlay for solar energy. Although improved energy storage is essential for optimal solar technology implementation, less than 1.5 percent as much is budgeted for this as is budgeted in support of nuclear fission power. (Only $2 million is allotted for improving the storage of hydrogen, one of the most likely fuels of the future.) ERDA's senior solar energy administrator recently resigned, protesting the low priority given to harvesting the sun.

In 1952, noting the danger of becoming dependent on Middle Eastern oil (*9*, vol. 3, p. 9), President Truman's Materials Policy Commission said, "We must look to solar energy . . . it is time for aggressive research in the whole field of solar energy—an effort in which the United States could make an immense contribution to the welfare of the free world" (*9*, vol. 4, p. 213). That advice was not followed. Nuclear fission, in 1975, after a quarter of a century of federal promotion and support, provided barely more than half as much electricity as that provided by hydropower—1 percent of the energy used for the nation's work. One solar technology alone—wind generators equipped with 6 days' storage capacity—might deliver this much power as cheaply by 1985 (*1*, pp. I-B-10 and I-7).

Can we afford to continue marking time on implementing the solar technologies and betting so heavily on an exotic unknown such as nuclear fission power?

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Breast Cancer and Chemotherapy

In her article of 12 March (News and Comment, p. 1029), Barbara J. Culliton discusses a study by Bonadonna *et al.* (*1*), in which chemotherapy was used as an adjuvant to radical mastectomy, and criticizes as "greatly exaggerated" my characterization of the study as a work of "monumental importance" (*2*).

Appearance of clinically manifest breast cancer after the initial resection predictably leads to death despite temporary remission. Axillary node metastases at the time of mastectomy are sentinel lesions indicative of a high probability of micrometastases in other body sites. Without chemotherapy, only 23.9 percent of 163 women with one or more positive axillary nodes and 13.8 percent of 87 women with four or more positive nodes at the time of surgery were alive 10 years later (*3*).

Modeling from combination chemotherapy of acute leukemia, Cooper (*4*) described a chemotherapeutic program for metastatic breast cancer using five drugs—vincristine (V), prednisone (P), cyclophosphamide (C), methotrexate (M), and 5-fluorouracil (F). In terms of remission induction, this regimen was superior to any single drug therapy previously employed; nonetheless, half the patients in a group treated with the five-drug therapy were dead in 1 year and 75 percent in 2 years (*5*). Others studied components of Cooper's five-drug regimen by omitting one or two drugs. A three-drug combination (CMF) was found more effective than a single oral drug, L-phenylalanine mustard (L-PAM), in suppressing metastatic breast cancer (*6*). Both treatments were then tested immediately after surgery in women who had axillary node metastases. The L-PAM study, conducted in the United States, was published (*7*) as a report of early findings at a time when significant delay in appearance of recrudescent cancer ($P = 0.2$) was seen only in premenopausal women.

Bonadonna *et al.* (*1*) reported a controlled, randomized trial in 386 women in which 12 monthly courses of CMF were administered to one group after surgery; a control group received no postoperative treatment. After 27 months, there were 11 relapses in 207 patients (5.3 percent) in the CMF group and 43 in 179 patients (24.0 percent) in the control group ($P = < .000001$). Furthermore, CMF was significantly superior for patients in *every* subset of the study classified by age, ovarian function, number of nodes involved, and extent of mastectomy. This was also true for the 90 percent of patients with the commonest pathologic type of tumor and the 89 percent whose tumors were more than 2 centimeters in diameter. Bonadonna *et al.* presented their relapse data in the form of life-table plots, the most effective way to describe the events that occurred. These events, in turn, give the best indication of how the entire group, of which the early members are a subset, will behave. Treatment failure distributions after 27 months were projected to be 10 percent for the CMF group and 43 percent for the control group ($P = .00002$). No patient treated with the full CMF regimen had relapsed after the drug therapy was ended. For the subset of 122 patients with the worst prognosis—those with four or more metastatic nodes—the projected treatment failures by life-table plot are 19 percent for the CMF group and 76 percent for the control group ($P = .001$). All relapsed patients are expected to die. Like many experimental neoplasms, disseminated human cancer can in some instances be cured by drugs when micrometastatic, but rarely when clinically evident. This principle, adopted from experience with experimental and clinical acute leukemia, has also been demonstrated in Wilm's tumor, osteogenic sarcoma, embryonal rhabdomyosarcoma, Ewing's tumor, and Hodgkin's disease. The Italian data and the experience with micrometastatic cancer as a biologic phenomenon rather than a unique characteristic of breast cancer support the proposition that some patients in the CMF treatment group have been cured. Mortality data after 32 months show a difference: 11 of 179 patients in the control group have died, compared with only 4 of the 207 patients treated with CMF ($P = .03$) (*8*).

Culliton and Costanza (*9*) assert that postoperative chemotherapy is still an experimental method not to be undertaken outside the research setting because of unknown late effects. The drugs have been in use singly for 18 years or more, and in combination for half that time. The risks are reasonably well un-

derstood. The late effects of the disease are also well known and are worse. At current rates some 89,000 women will develop breast cancer this year in the United States alone. It is expected that, of these, 47 percent will have axillary metastases (*10*). These 42,000 women in 1 year cannot all go to the approximately 200 university hospitals and research institutions in the country. As many as can should, so the absolute therapy may some day be found. But emotional, economic, and logistic considerations preclude this option for the majority. What use biostatisticians if an important, beneficial finding that could have occurred by chance only twice in 100,000 times (or once in a million) is denied to the women in Anyplace, U.S.A.? If there were delay for years of follow-up studies before adopting the therapy, 10,000 women every 4 months would be consigned to a course of inaction that leads to an early death from metastatic cancer. Women in these numbers could not conceivably succumb from adverse effects of the treatment. There were no drug deaths among Bonadonna's patients. Who makes the lag in translating research success into clinical practice?

I advocated and advocate research, but wrote (*2*) that its impossibility for most patients should not impede adoption of this treatment by *qualified* physicians. This adjective appears to have gone unappreciated; 727 certified internists have already been further certified by the American Board of Internal Medicine in the subspecialty of medical oncology (*11*). Hundreds of other physicians are experienced in the use of these drugs in patients with advanced, clinically manifest breast cancer, where the chance for cure approaches zero.

Bonadonna's study has demonstrated the effectiveness of CMF in controlling local recurrence of metastases on the chest wall (there have been three recurrences in the CMF group of 207 patients and 11 in the control group of 179 patients) and in bringing about improved remission and survival rates after 27 months. One might hope the use of adjuvant postoperative radiotherapy for breast cancer—long-entrenched and widely used, but with no evidence of survival benefits (*12*)—would cease and give way to chemotherapy (*13*). Cullitton expresses apprehension about sterility from chemotherapy for breast cancer, a virtual nonissue. Dead women tell no tales, nursery or otherwise. Furthermore, less than 20 percent of women with breast cancer are under age 45 (*10*).

After developing his regimen, Cooper treated in adjuvant fashion 100 women with breast cancer with four or more metastatic axillary lymph nodes. Of these, 73 were treated with VPCMF for the 9 months immediately after radical mastectomy. By life-table plot, 70 percent of them are alive without evidence of disease after 8 years, a phenomenon strikingly different from Bonadonna's control patients but not dissimilar, during the initial portion of the curve, from his CMF patients (*14*). These data should also be compared to historical precedents: of 14,294 women with one or more positive nodes, 58 percent were dead in 8 years (*10*); of 88 women with four or more positive nodes, 81 percent were dead in 8 years (*3*).

A delicate balance exists between making available today's research achievements in the practice of medicine and the conduct of ongoing clinical research to attain the ultimate objective. The ethics of the clinical investigator of breast cancer are concerned not only with today's victims; he must serve as steward for future millions the world over who will die of breast cancer each decade until prevention or cure becomes a reality for all. Salvage of the breast should remain a secondary goal until salvage of the patient is firmly assured. The appearance of these chemotherapeutic data (*1, 7, 14*), however, which prove the feasibility of an approach to the real problem of breast cancer, micrometastatic disease, is of more significance for today's patient than any other therapeutic advance in breast cancer since the modern era of breast cancer surgery began before the turn of the century.

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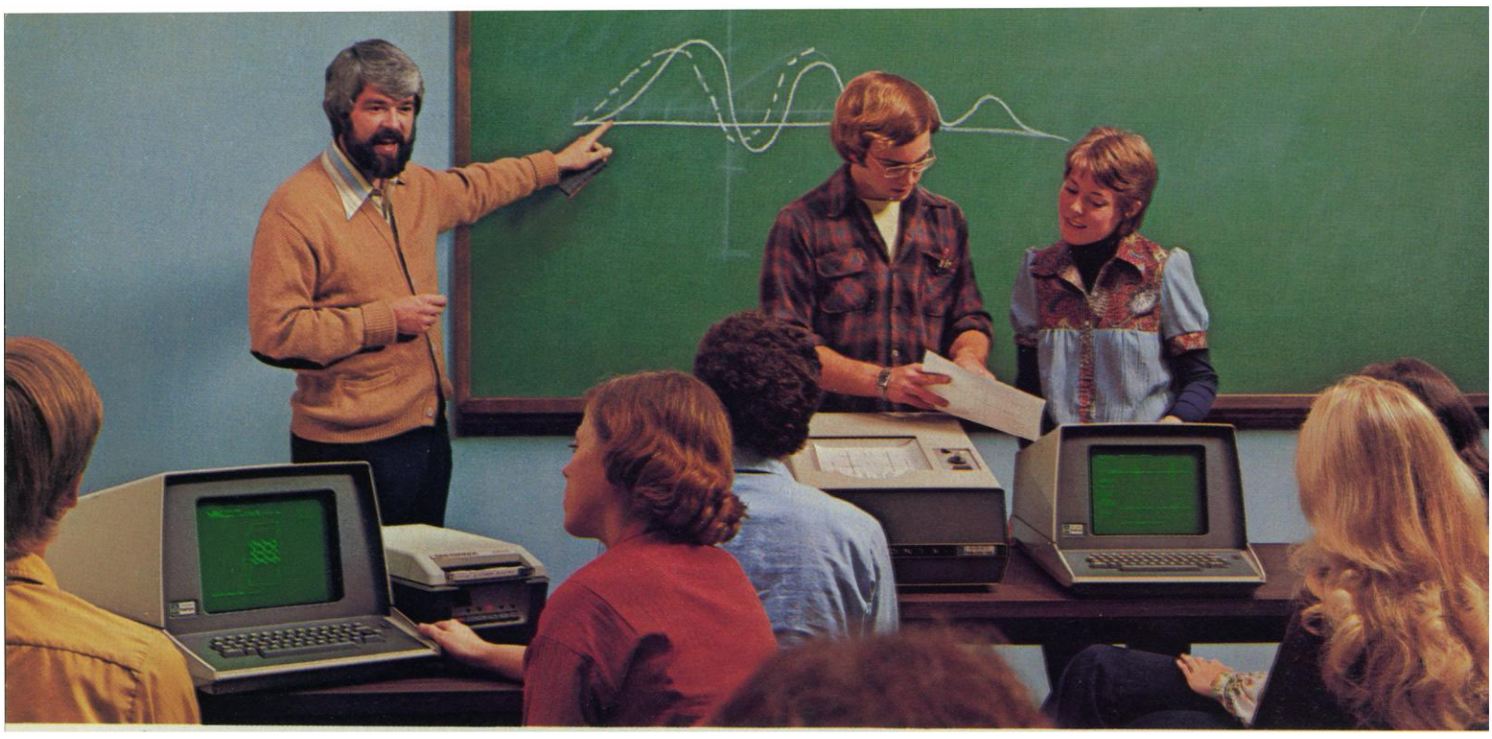

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SCIENCE

Turning Out the Vote

This annual election issue of *Science* serves as a reminder of how much the AAAS has changed since the new constitution and bylaws were enacted in 1973. The reforms made then were intended to return the power of election to the members, so that the many rather than the few would determine the quality of the Association's leadership. The choice of a president, a board of directors, a council, the committee on nominations, section chairpersons, the nominating committees of the electorates, and the members-at-large of 21 section committees now rests with the members. It is a formidable and expensive process. All of the candidates, it is worth noting, are volunteers, not in the sense of itching for office but in terms of giving their time and efforts generously to the advancement of science.

Last year some 29,000 members—about 24 percent of the eligible voters—cast their ballots for the election of a president of the AAAS. It turned out to be a close contest between two impressive candidates. We think that if the new constitution is going to work as it was meant to, the major offices should at the very least reflect the voting preferences of a majority of the members rather than a minority, however conscientious that minority may be.

Voter apathy is a troubling phenomenon in any electoral situation, including ours. The AAAS is sometimes alluded to as the "lower house" of American science, suggesting a populist alternative to those venerable institutions whose members are knighted and lead a more elegant existence. We, in our humbler way, represent a potential of diverse opinion and energies that has merits of its own. But if we are democratic in our character, we ought to exercise the privileges that go with democracy. Turning out the vote is a good sign that we are alive and well, and that the lower house is in purposeful session.

The prospects for science and technology at the present time are not as clear as they should be. Perhaps one of the reasons is that the so-called scientific community does not act as a community but is seen as a feudal system without a unifying agenda. In such a state it is slow in its reactions and divided in its objectives. The AAAS, as a kind of loose holding company connecting nearly 300 affiliated societies, is certainly not the appointed representative of science in its relations with government, the media, and the public. But it can and should have a voice that is heard and respected for the company it keeps. That voice could come through loud and clear, to a greater extent than it now does, if its members voted with authority. Counting heads is one measure of the significance of the AAAS, but counting votes is better.

This issue of *Science* contains the information about nominees for elective office; those elected will assume their responsibilities in 1977. Ballots will be mailed around 1 September, but biographical data will not accompany them. This issue of *Science*, therefore, should be retained and consulted when the ballots arrive. It would help if members would read the biographical information and the short statements of the nominees *now* and note the candidates they prefer so that in September the ordeal of marking the ballots will be less trying.

There is much talk of accountability, and the lack of it, where public service is concerned. In practice, those in office respond to the concern or the disinterest, as the case may be, of the electorate. This may not guarantee accountability, but it probably brings us about as close to it as we are likely to get, either in national affairs or in the AAAS. The cheerful exhortation to vote "early and often" may not fit the case, but a large and lively vote will say a good deal about the vital signs of the AAAS.—WILLIAM D. CAREY

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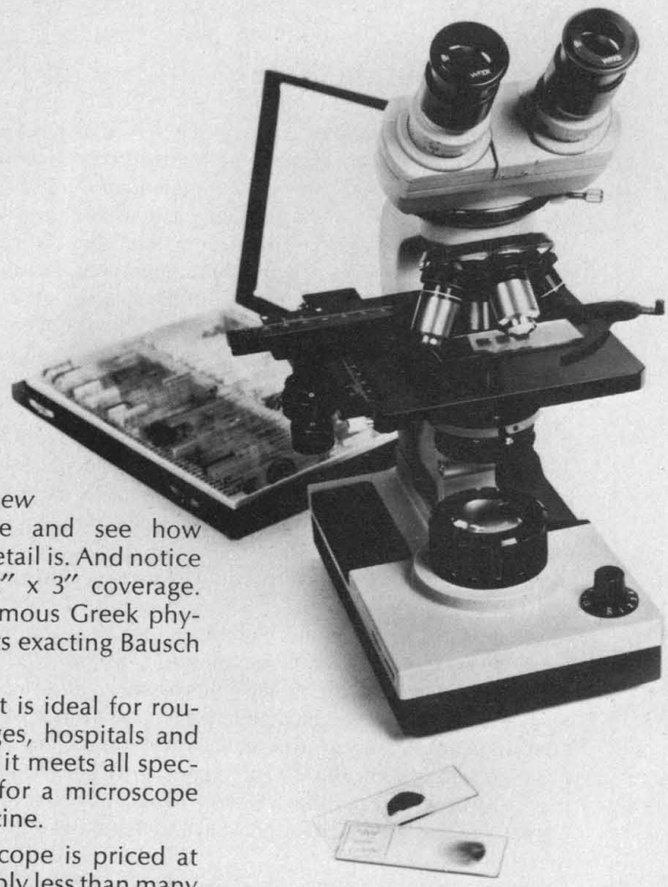

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Gradient Elution Accessory

This device is comprised of two elements, the SSV-6 automatic stream selection valve and the DP-410 programmer. It allows up to six solvent changes and is designed for situations in which isocratic elution will not yield the desired separation. The programmer activates the valve to any of six positions at any of ten intervals. The accessory also performs temperature programming, column switching, and operation of fraction collectors. Glenco Scientific. Circle 706.

Marine Aquarium

The Marine Lab offers temperature control from 3°C to near ambient, automatic filtration and aeration, and complete life-support system. Two models are available—70- and 125-gallon capacities. Filtration system consists of prefilter, calcareous-substrate biological filter, high-volume air lifts, protein-separation filter, and activated carbon filter. Each aquarium is provided with a hydrometer, thermometer, synthetic sea salts, activated carbon, calcareous substrate, and polyester filter pads. Lab-Line Instruments. Circle 711.

Iodine-125 Counter

MiniAssay 6-20 consists of a high-voltage supply and discriminator scaler with crystal control timer in a single unit. This device can be connected to a well counter and will operate with most types of scintillation detectors that have a single input for the high-voltage supply. Counting intervals may be selected from among eight settings from 1 to 1000 seconds and a ninth unlimited setting. The timer is accurate to better than 0.01 percent. The unit is suitable for teaching or for radioimmunoassay. Research Products International. Circle 712.

Submersible Combination *p*H Electrode

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Infrared Detectors in Gas Chromatography is a wall chart listing spectral properties of commonly used solvents. Wilks Scientific. Circle 715.

Graphic Chart Papers features a line of recorder charts and graph papers and includes information on the use of charts and graphs. Codex Book. Circle 716.

Resin Report is a newsletter. The April 1976 issue features an article on making a Stein-Moore single-column amino acid analyzer. Durrum Chemical. Circle 717.

Nalgene Labware describes a complete line of plastic laboratory apparatus including a dozen new products. Nalge. Circle 720.

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—RICHARD G. SOMMER

RESEARCH NEWS

(Continued from page 1091)

involved because of their genetic association with immune response genes. The genes for histocompatibility antigens and those controlling immune responses to a number of antigens are closely linked on the same chromosome. Faulty control of immune responses has been strongly implicated in the etiology of lupus. Thus, association of the disease with a particular histocompatibility antigen might actually reflect linkage with an immune response gene whose expression produces the faulty immune responses of SLE.

Some investigators, such as Lawrence Shulman of Johns Hopkins University Medical School, have found associations between SLE in humans and particular histocompatibility antigens. Not all of them have implicated the same antigens, however. In the Johns Hopkins study, two of the antigens, HL-A1 and HL-A8, were found more frequently in lupus patients than in controls. Approximately 20 percent of the patients had at least one of the antigens, with 12 percent having both. The comparable figures for the controls were less than 10 percent and 5 percent, respectively. Shulman says that association of these antigens with severe disease involving the kidney and brain is even greater.

To say that the etiology of SLE is complex is an understatement. Genetic susceptibility, viruses, and a defective immune system all appear to be involved. Since some type C viruses have been implicated in the development of cancers in addition to that of autoimmunity, Lerner and other investigators have hypothesized that autoimmunity may be the price of protection against virus-induced tumors. In other words, when the virus stimulates the immune system sufficiently to prevent tumor growth, autoimmunity results, either as a result of immune complex formation or by attack of the immune system on cells bearing viral antigens, or both. On the other hand, when the response of the immune system is weak, tumor growth can occur.

But SLE, although more common than once thought, is still a relatively rare disease in humans, if not in NZB mice. This implies that additional factors, possibly genetically determined and possibly involving abnormal immune responses, must also be considered. Some investigators even think that when the mystery of SLE is completely unraveled, the condition will turn out to be a complex of diseases with somewhat different etiologies.—JEAN L. MARX

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(Continued from page 1122)

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