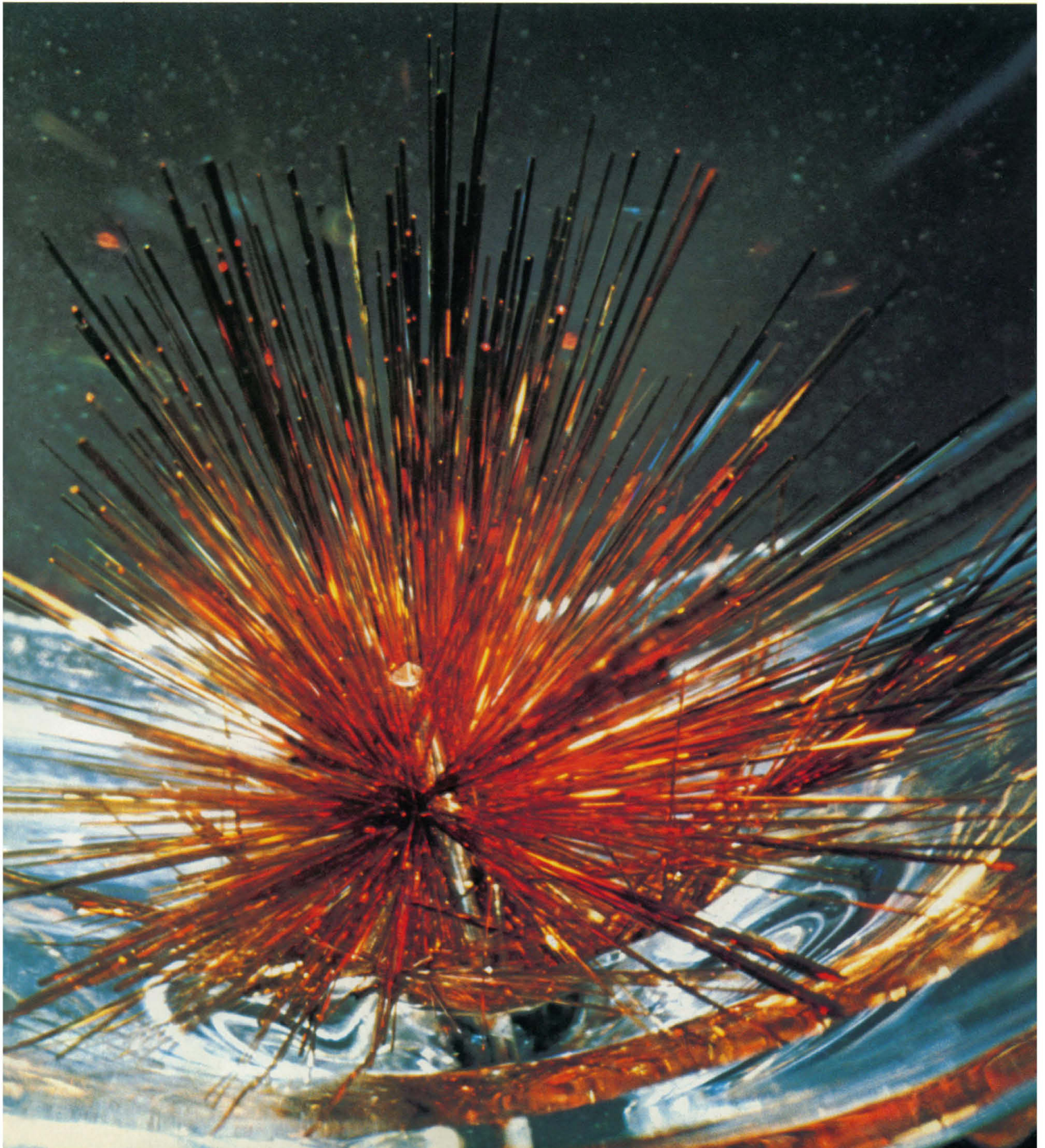
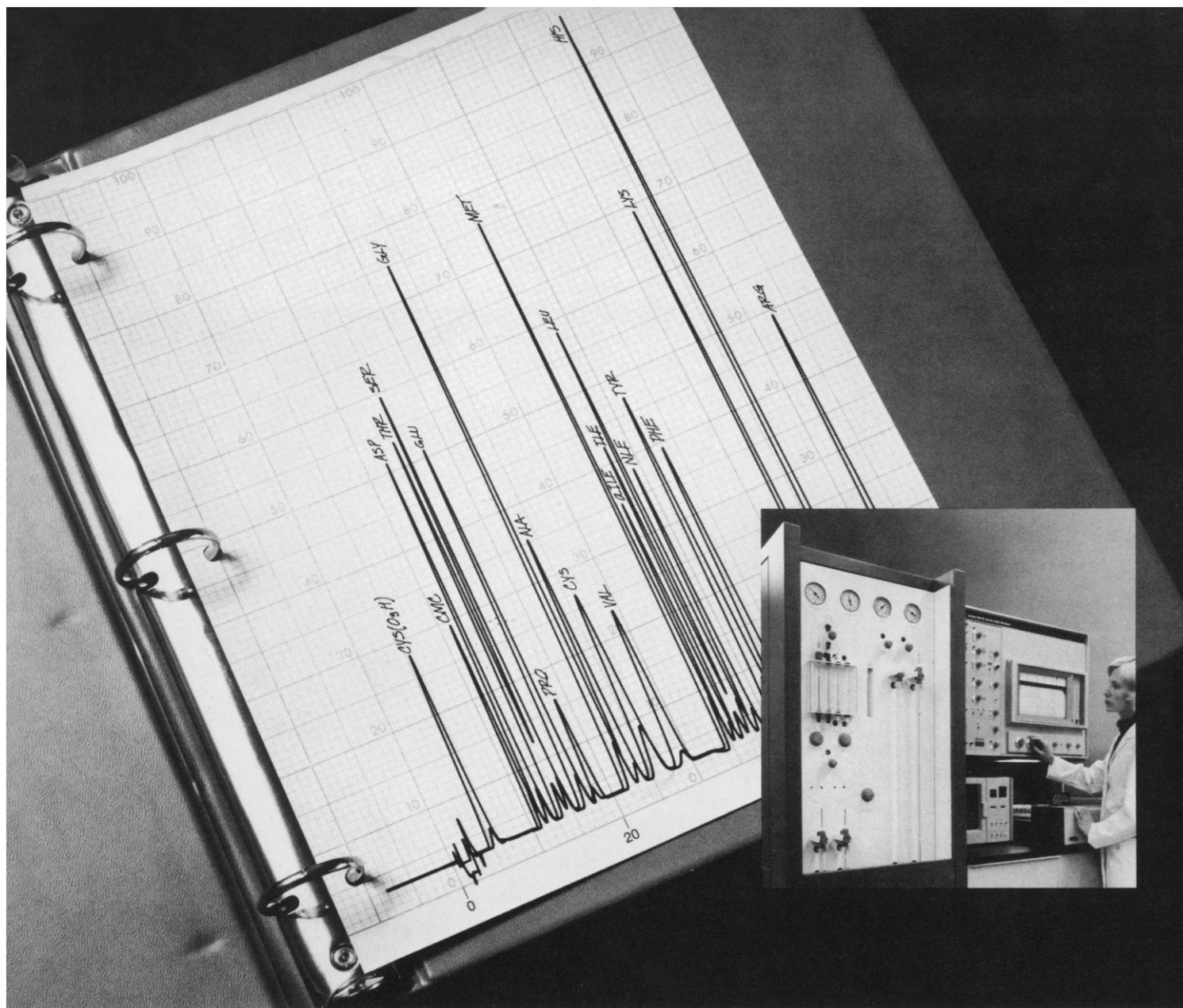


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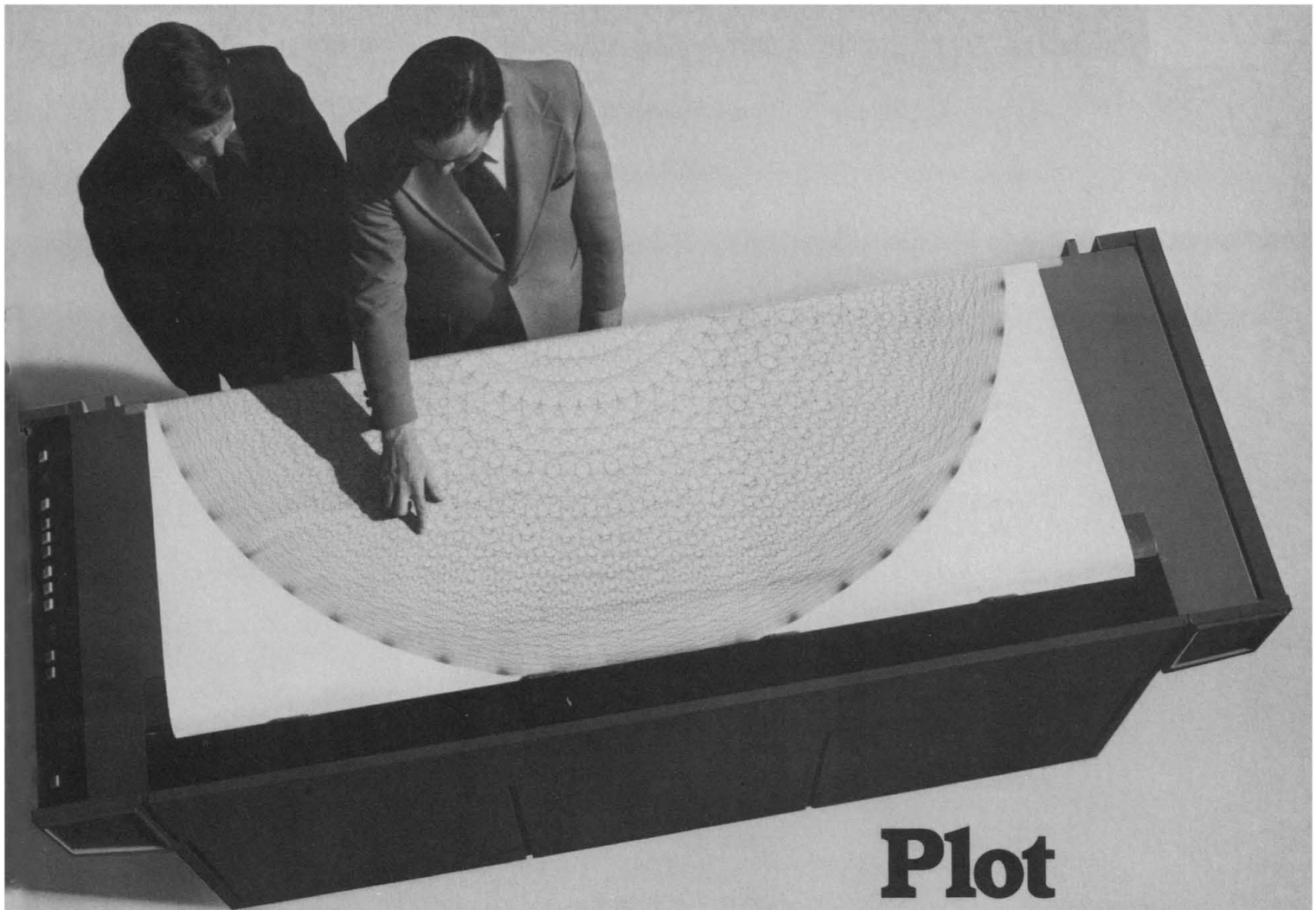
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LETTERS	Mutagens and Carcinogens: <i>B. N. Ames, J. McCann, C. Sawyer</i> ; Sergei Kovalev: A Colleague in Trouble: <i>T. Eisner</i> and <i>E. O. Wilson</i> ; Radioactive Waste Disposal: <i>K. B. Krauskopf</i>	132
EDITORIAL	The University Tenure "Problem": <i>H. Shull</i>	137
ARTICLES	Insect Pheromone Synthesis: New Methodology: <i>J. A. Katzenellenbogen</i>	139
	Land Degradation: Effects on Food and Energy Resources: <i>D. Pimentel</i> et al.	149
	Autoregulation and Function of a Repressor in Bacteriophage Lambda: <i>M. Ptashne</i> et al.	156
NEWS AND COMMENT	Animal Rights: NIH Cat Sex Study Brings Grief to New York Museum	162
	Thermonuclear Fusion: U.S. Puts Wraps on Latest Soviet Work	166
	Science Court: High Officials Back Test of Controversial Concept	167
RESEARCH NEWS	The Ozone Layer: The Threat from Aerosol Cans Is Real	170
	Coal Research (IV): Direct Combustion Lags Its Potential	172
BOOK REVIEWS	A World Destroyed, reviewed by <i>D. C. Watt</i> ; The Helium Liquids, <i>R. J. Donnelly</i> ; Intercellular Communication in Plants, <i>S. Aronoff</i> ; Thyroid Hormones, <i>A. Gorbman</i> ; Hormones, Behavior, and Psychopathology, <i>J. P. Tupin</i> ; Books Received; Book Order Service.	174
REPORTS	Man-Made Radionuclides and Sedimentation in the Hudson River Estuary: <i>H. J. Simpson</i> et al.	179
	Histologic Structures Preserved for 21,300 Years: <i>M. R. Zimmerman</i> and <i>R. H. Tedford</i>	183

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Bat Mortality: Pesticide Poisoning and Migratory Stress: <i>K. N. Geluso, J. S. Altenbach, D. E. Wilson</i>	184
Formation and Transport of Secondary Air Pollutants: Ozone and Aerosols in the St. Louis Urban Plume: <i>W. H. White et al.</i>	187
Electrochemical Growth of Highly Conducting Inorganic Complexes: <i>J. S. Miller</i>	189
Volcanic Ash: Terrestrial versus Extraterrestrial: <i>J. A. O'Keefe</i>	190
Muscle Crossbridges: Absence of Direct Effect of Calcium on Movement Away from the Thick Filaments: <i>R. A. Mendelson and P. Cheung</i>	190
Structural Basis for ON- and OFF-Center Responses in Retinal Ganglion Cells: <i>E. V. Famiglietti, Jr., and H. Kolb</i>	193
Cytochrome P-450 and Drug Metabolism in <i>Trypanosoma cruzi</i> : Effects of Phenobarbital: <i>M. Agosin et al.</i>	195
Progesterone Binding to Hen Oviduct Genome: Specific versus Nonspecific Binding: <i>T. C. Spelsberg, G. M. Pikler, R. A. Webster</i>	197
Hyaluronidase-Induced Reductions in Myocardial Infarct Size: <i>D. Maclean et al.</i>	199
Nuclear Inclusions in Paget's Disease of Bone: <i>B. G. Mills and F. R. Singer</i>	201
Thyroid Hormones: Effect of Physiological Concentrations on Cultured Cardiac Cells: <i>J. S. Tsai and A. Chen</i>	202
Trypanosomiasis: An Approach to Chemotherapy by the Inhibition of Carbohydrate Catabolism: <i>A. B. Clarkson, Jr., and F. H. Brohn</i>	204
Depletion of Brain Catecholamines: Failure of Ocular Dominance Shift After Monocular Occlusion in Kittens: <i>T. Kasamatsu and J. D. Pettigrew</i>	206
Responses of Infants to Visually Presented Objects: <i>P. C. Dodwell, D. Muir, D. DiFranco</i>	209
Sexual Dimorphism in Vocal Control Areas of the Songbird Brain: <i>F. Nottebohm and A. P. Arnold</i>	211
<i>Technical Comments</i> : Relaxation Time versus Water Content: Linear or Nonlinear?: <i>K. R. Brownstein and C. E. Tarr; P. T. Beall, C. F. Hazlewood, P. N. Rao; Serotonin Depression: D. F. Kripke</i>	213
PRODUCTS AND MATERIALS Radiation Dosimeter; Amino Acid Analyzer; Colony Counter; Professional Calculator; Noncontact Thermometer; Literature	216

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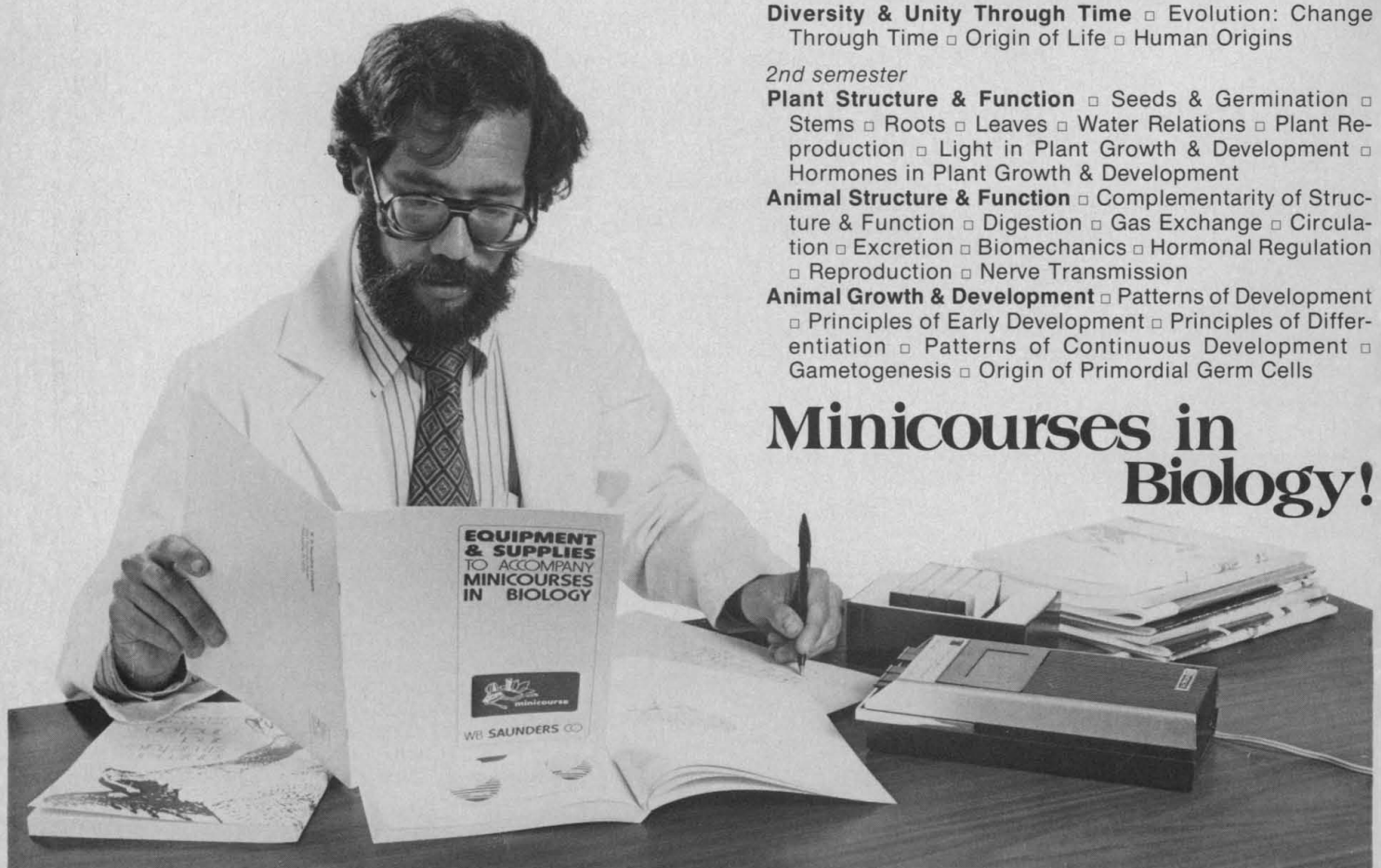
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2nd semester

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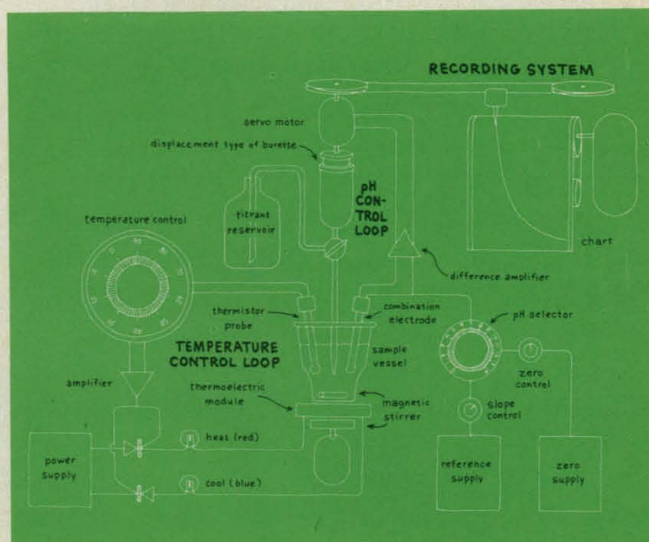
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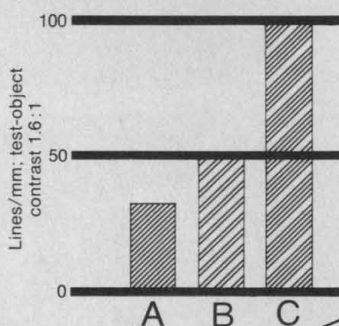
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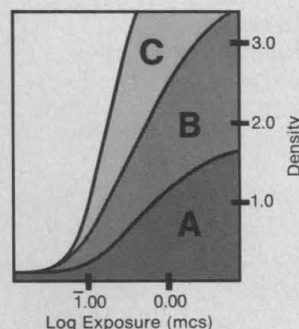
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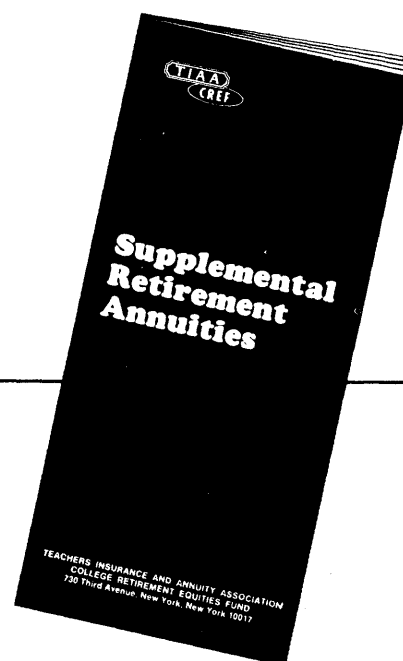
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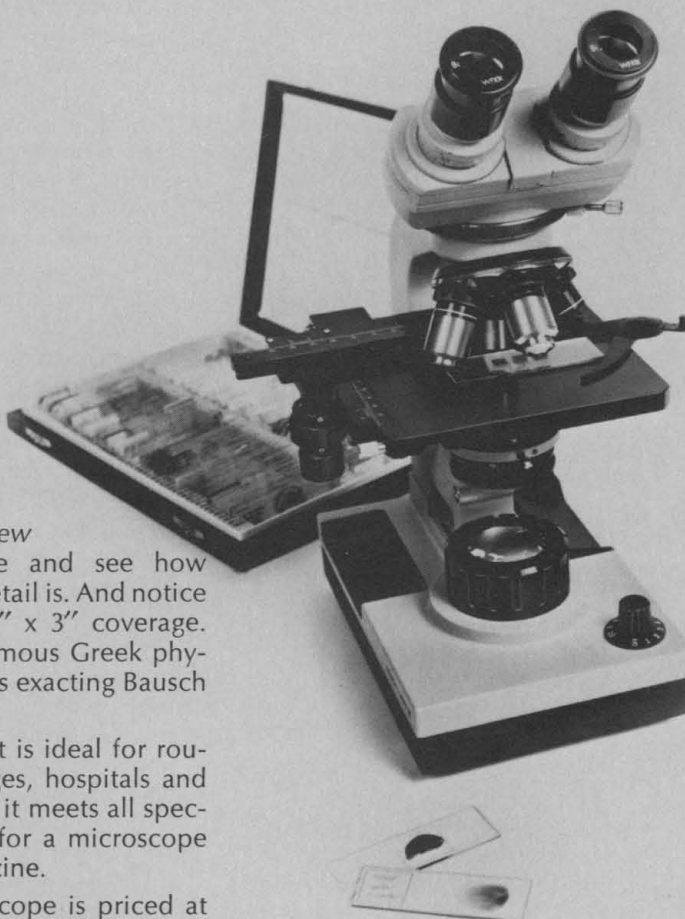
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LETTERS

Mutagens and Carcinogens

Andrew Sivak (Letters, 23 July, p. 272) makes three criticisms about mutagenicity testing as an indication of potential carcinogenicity, and in particular about our test system of *Salmonella* bacteria and liver enzymes (1, 2). We think he does not analyze any of the points clearly.

1) Sivak says that when we discuss our test results, which show an excellent correlation with animal carcinogenicity data, it is not clear whether we mean a qualitative or a quantitative correlation. Our articles are very clear; the correlation we discuss is qualitative (90 percent of 175 carcinogens are mutagenic in the test) and not related to potency. In our discussion of our data (2) (which Sivak does not quote), we point out (2, p. 951) some of the hazards of attempting to equate mutagenic potency with carcinogenic potency, and we discuss this subject briefly.

Sivak quotes some data for carcinogenic potency in an attempt to show that it does not correlate with mutagenic potency and states (without any qualifiers) that there is a "lack of correlation between microbial mutagenicity and rodent carcinogenicity results." His analysis is invalid for several reasons. (i) He gives a table of raw data on subcutaneous injections of chemicals in mice but does not say how to calculate the potency of a carcinogen from such data. Calculating the potency of a carcinogen is complicated even with the best of data, and data on subcutaneous injections (with tumors at the injection site and uncertainties as to the active dose) are inappropriate in any case. Such studies are not designed for that purpose (and are not particularly relevant to human exposure). (ii) Sivak also uses the Iball index of carcinogenic potency for polycyclic hydrocarbons, which is primarily of historical interest as an oversimplified view of what is now known to be a much more complex phenomenon. The Iball index makes no provision for dose and does not take into account the higher power relationship of the number of tumors with elapsed time (3). (iii) Sivak does not discuss the range of values necessary for a correlation. Carcinogenic potency (and mutagenic potency) varies over about a millionfold range (from an extremely weak substance such as chloroform to an extremely potent carcinogen such as aflatoxin B1). If, in addition to detecting 90 percent of carcinogens in a rapid and inexpensive test, one could also obtain mutagenic potency data that would en-

able one to predict the approximate potency of a carcinogen with some degree of probability, this would be extremely useful. One would like to be able to do this in drug development and in evaluation of the hazard of complex mixtures (such as water effluents, air pollution samples, and so forth), in which animal cancer tests are impractical. It is clear that by using a simplified system such as a rat liver homogenate and bacteria, one would *not* expect to be able to precisely predict carcinogenic potency in a rat (or a human). If one could predict it with a high probability within \pm an order of magnitude this would be extremely useful, considering the range of carcinogenic potency. We believe the test may well be able to do this. Sivak chooses his carcinogenic potency examples from a much too narrow range where one could not see any correlation that existed.

Russell and Meselson (4) at Harvard are actively pursuing the area of the degree of quantitative correlation between a chemical's carcinogenic potency in animals and mutagenic potency in the *Salmonella* test, and following their lead we are doing the same. There are some animal carcinogenicity data from feeding experiments of appropriate quality for calculating carcinogenic potency and also some data on humans that meet the requirements.

2) Sivak says that we selected our strains to detect carcinogens and therefore the fact that they detect carcinogens is "self-fulfilling and not a true test." We selected our strains primarily on the basis of maximizing the detection of known mutagens (we did not think about carcinogenicity until much later), and fewer than 10 percent of the 175 carcinogens we actually tested in the validation of the method were used in the development of the strains. [In addition, the test has been independently validated (90 percent correlation) in a blind study of 120 chemicals (5).] Very few chemicals in general are mutagens or carcinogens, and the finding that more than 90 percent of carcinogens tested have been detected as mutagens (and that almost every mutagen that has been given an adequate cancer test is a carcinogen) may actually mean something. The chemicals known to be carcinogenic in humans represent an unselected sample, and the test detects almost all of them as mutagens (2).

3) Sivak questions the "equivalency" (we would not use that word) of mutation in bacterial DNA with "the multistep, multifactorial process of carcinogenesis in eukaryotic organisms." We have briefly discussed the idea of DNA damage (somatic mutation) as the initiator of most chemical and radiation carcinogen-

esis (2, 6). This is a coherent theory that is supported by a wide variety of evidence. Sivak does not add any new arguments against it. We would welcome the presentation of a more specific alternative theory.

BRUCE N. AMES

JOYCE MCCANN

C. SAWYER

Department of Biochemistry,
University of California, Berkeley 94720

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Sergei Kovalev: A Colleague in Trouble

Scientists in the United States are often unaware of real threats to their profession—the pursuit of truth—except for incidentals, such as the exigencies of budgets or the snarls of red tape. For some of our colleagues in the Soviet Union, merely raising what their political bosses deem the wrong questions can ruin their careers and threaten their very lives.

We are reminded of this most forcefully by the fate of the biologist Sergei Adamovich Kovalev, as described in an urgent message from academician Andrei Sakharov. If Kovalev had taken a narrow view of his profession, he might still be doing research in cellular physiology at his alma mater, Moscow State University. Instead, he is suffering from serious, untreated illnesses at "corrective labor colony number 36" near Perm.

Kovalev's "crimes," according to the laundry-list indictment on which he was tried last December, consist of embarrassing inquiries made on behalf of political dissidents in the Soviet Union. He has wanted to know, for example, why the cybernetician Leonid Plyushch was punished for his political heresies by 30 months in a psychiatric prison at Dnepropetrovsk amid violent criminals; why Alexander Solzhenitsyn was hounded from his homeland; why thousands of political and religious dissidents are being brutalized in camps and psychoprisons for attempting to exercise the rights guaranteed in the Soviet constitution.



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When Kovalev was denied a defense counsel of his choice, he tried to defend himself against the charge of "anti-Soviet agitation and propaganda." The judge struck all his motions and would not permit the calling of witnesses who could have testified to the truth of the alleged "slander" by the accused. Kovalev declared a hunger strike and left the courtroom, certain of the preordained verdict—guilty—and the sentence—a maximum 7 years in a "strict regime" camp for "especially dangerous state criminals," followed by three years of internal exile.

He was not present to hear the prosecutor's revealing final words: "The Soviet authorities don't care about a man's opinions if only he keeps them to himself and does not engage in criminal activity. In Kovalev's thoughts on liberty as expressed in the documents he signed, one thing is clear—he is trying to portray liberty as something independent from society. We know that liberty is the product of the historical development of society and that each society has its own particular character. . . . Our state forbids actions which are foreign to its nature."

Sakharov, who had himself been barred from testifying for Kovalev, was aghast at such a "blatantly unlawful" trial. He called the defendant "my close friend, a man of great spiritual beauty and force, of limitless altruism, dedicated to the defense of human rights and the struggle for publicity against illegality."

Cornell University's Section of Neurobiology and Behavior recently offered Kovalev an appointment as visiting scholar, citing the more than 60 publications that demonstrate Kovalev's competence as a researcher. Cornell would give Kovalev a chance to resume his scientific work. If the promises of the Soviets and 34 other nations at Helsinki in August 1975 carry any weight, then Kovalev's path would be cleared by the official blessings given scientific exchanges (1).

The latest word from Sakharov is that time is running out. He sees Kovalev's survival as dependent on an operation that only the Leningrad central prison hospital is equipped to perform. He asks Kovalev's American colleagues to appeal to Soviet authorities to grant this request, adding their voices to the unanswered pleas of Mrs. Kovalev, Lusya Boitsova.

Because of the international nature of science, its practitioners have a more direct concern—and responsibility—for the human rights of colleagues in other

countries. Those who wish to respond on behalf of Sergei Kovalev can send a letter, telegram, letter, or card to the Medical Administration of the Soviet Ministry of Internal Affairs, Moscow, Petrovka 25a, Medupravleniya, MVD SSSR.

THOMAS EISNER

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Notes

1. A. resolution has been introduced in the House of Representatives by Matthew F. McHugh (D-N.Y.) expressing the sense of Congress that the President should urge the Soviet Union to allow Kovalev to accept the invitation of Cornell University to be a visiting scholar, in keeping with the Helsinki accord.

Radioactive Waste Disposal

A panel established by the Committee on Radioactive Waste Management of the National Research Council has been assigned the task of evaluating waste practices at the Hanford Reservation in Washington State. Such practices include the partial solidification by evaporation of huge quantities of high-level radioactive liquid waste remaining from plutonium production, the separation of radioactive nuclides from the liquid wastes, the discharge of low-level radioactive liquid waste to the ground, the trapping of gaseous and particulate waste, and the recovery for safer storage of soil into which waste containing actinide elements has previously been discharged.

The panel is seeking information from all possible sources to guide its study. In particular, reports on recent work dealing with ideas or technological innovations that might be applicable to Hanford practices would be helpful. Many reports of this sort have been published and are readily available, but some may exist in unpublished form. The panel would appreciate knowing about unpublished work, and reports describing it can be sent to Dr. John Pomeroy, Executive Secretary, Committee on Radioactive Waste Management, National Academy of Sciences-National Research Council, 2101 Constitution Avenue, NW, Washington, D.C. 20418.

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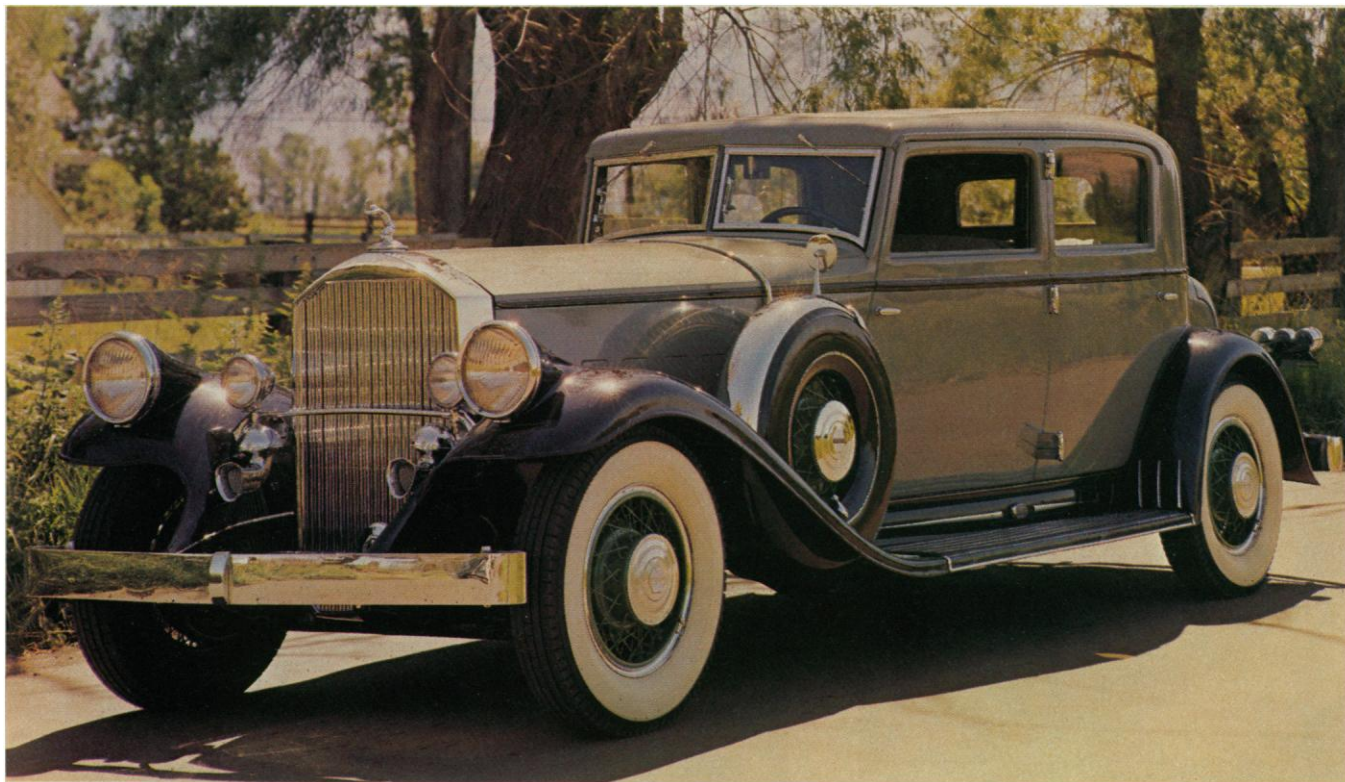


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The University Tenure "Problem"

Many of our major universities have relatively high ratios of tenured to nontenured faculty members. In many cases, more than half the faculty is tenured; more commonly, three-quarters or more may be tenured; and in a few exceptional situations, all faculty members are tenured. I believe that such high ratios are not desirable for our large research universities, but I would argue that the problem is not as serious as many think. A decade ago, when there was little concern about the tenure ratio, it was becoming a serious problem. Today it attracts much more attention, but I believe there is less to be concerned about. Given reasonable decisions on the part of university administrators, the problem may even disappear within the next decade.

First, we have passed through most of the years of few or even no retirements. In the period 1935 to 1945 few faculty members were hired, which accounts for the low retirement rate in the recent past.

Second, considerable attention is being paid to facilitating early retirement. Some universities have lowered the mandatory retirement age, a step they may come to regret in the not too distant future. Voluntary early retirement is likely to increase in popularity, partly because of the introduction in the early postwar years of more generous retirement plans, coupled with the initiation of the College Retirement Equities Fund as an auxiliary retirement annuity. If the economy continues to improve, and if the stock market advances sharply over the next decade, as many believe it will, older faculty members will find it increasingly attractive to retire early.

Third, undergraduate enrollments have increased and will probably remain high throughout much of the next decade. As a result, new positions are being created and replacements for retiring faculty members are being authorized to meet teaching needs. Even now, hiring in the research universities is about commensurate with that expected on the average for an even faculty age distribution.

Fourth, the large number of faculty members employed between about 1955 and 1968 will soon reach retirement age, and retirements should peak between 1985 and 1990. This period will provide an opportunity to decrease the ratio of tenured to nontenured faculty members to a more reasonable steady-state level.

This positive prognosis depends, however, on certain courses of action. It is still important that the tenure decision be made very selectively, with an eye toward the obligations of the institution to its future students. If a particular tenure decision is a debatable one, it should be negative.

It is important to adjust the lopsided age distribution of our faculties by filling almost all positions at the beginning level. Tight budgets are forcing us in this direction, but we should do so even if funds are plentiful.

Finally, we must continue high utilization of innovative young faculty members in the combined research-graduate education role. The creation of this opportunity for the young is, I believe, the outstanding educational accomplishment of the United States in this era. When a steady-state age distribution is reached there will be fewer young people on our faculties. We must strive to protect their interests, conserve their time, and discourage diversionary assignments. More of the routine teaching should be shouldered by older faculty members, preferably voluntarily, but if not, by assignment.

If we work systematically to protect what is genuinely vital for the future, the university tenure "problem" will disappear quietly from the scene.

—HARRISON SHULL, *Chemistry Department, Indiana University, Bloomington 47401*

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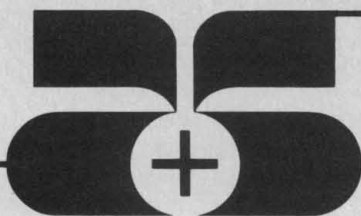
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BioTran II (Fig. 1) will detect and count colonies, plaques, and particles as small as 2 millimeters in diameter. It uses a multiple illumination system to count colonies on light and dark agars, whether the agar is opaque or translucent and whether the colonies are growing in or on the agar. User selects reflected or transmitted light and light- or dark-field

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Professional Calculator

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Literature

Electronic Components describes a complete line of these devices. A new impedance bridge is featured. James Millen Manufacturing. Circle 703.

Organic Chemicals includes 450 new additions to an already extensive line. Mallinckrodt, Science Products Division. Circle 704.

Ultrafiltration Membrane-Equipment Selection Guide includes latest data on membrane and hollow fiber solute rejection, flow-rates, environmental resistance. Amicon. Circle 711.

Laboratory Computer Systems is devoted to systems based on two new central processing units. Digital Equipment. Circle 712.

Chromatographic Apparatus describes sample preparation, columns, chromatographs, and accessories. Kontes. Circle 713.

Instruments for Neurophysiological Research features stimulators, probe-electrometers, amplifiers, stimulus isolators, iontophoresis programmers, and many others. W-P Instruments. Circle 714.

Automated Data Retrieval Systems controls laboratory apparatus and analyzes the information obtained. Etec. Circle 715.

Clinical Standard Microscope Catalog describes instruments for hematology, cytology, microbiology, pathology, urology, and other clinical applications. Carl Zeiss. Circle 716.

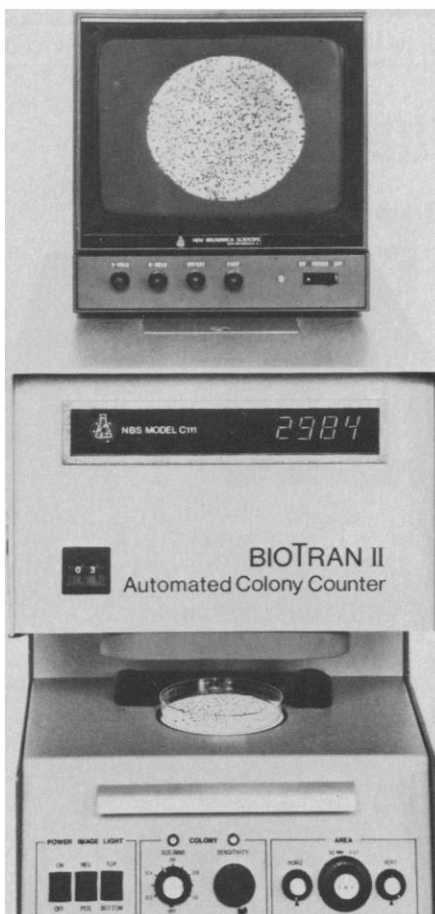


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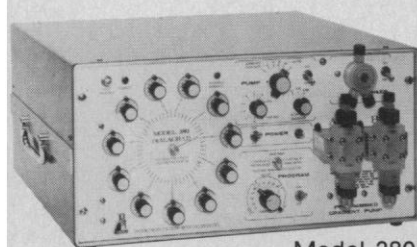
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RESEARCH NEWS

(Continued from page 173)

er and the regulator of scrubbers, a conflict that has severely hampered the agency's research staff. Hollinden believes that "there is an important role for ERDA, not EPA, in sponsoring further federal research on regenerable scrubbers."

At present, however, ERDA does not support scrubber R & D. Instead, its main emphasis in the area of direct combustion of coal is on fluidized bed boilers—the main alternative to scrubbers, but a technology that is not as close to commercial use. Fluidized bed boilers—a name that derives from the flow of air up through the boiler at a rate sufficient to suspend and "fluidize" a bed of particles, normally coal and limestone—offer a number of potential advantages, in particular that they might eventually be cheaper, more efficient, and more versatile than the combination of conventional boiler and scrubber.

Conventional boilers, for example, are designed for particular coals, but fluidized bed boilers can be designed relatively independent of the type of coal or other fuel they are to burn, because they operate at temperatures below the melting point of coal ash. Temperature is controlled by a series of tubes within the bed through which water is pumped to remove heat and generate steam. These tubes, which are in direct contact with the solid particles of the bed, permit a rate of heat transfer several times that of a conventional boiler. As a result, fluidized beds are expected to be more compact, of standardized designs, and possibly able to be fabricated in the shop rather than in the field.

Sulfur dioxide evolved during combustion is absorbed within the bed by limestone particles and removed as calcium sulfate in the form of a dry solid. Although the process consumes as much limestone as a scrubber, the waste material is more easily disposed of than sludge, and there have been preliminary experiments with regenerable absorbents such as magnesium oxide. However, fluidized beds do not appear capable of removing more than about 90 percent of the sulfur in coal (scrubbers do not seem to be similarly limited), and their ability to control emission of small particulates is still uncertain.

The advantages of fluidized bed boilers for power generation are still to be demonstrated, however. Initial development of the technology with small units in the United States and in Great Britain nearly came to a standstill in the late 1960's when the Office of Coal Research (OCR), the main supporter of the

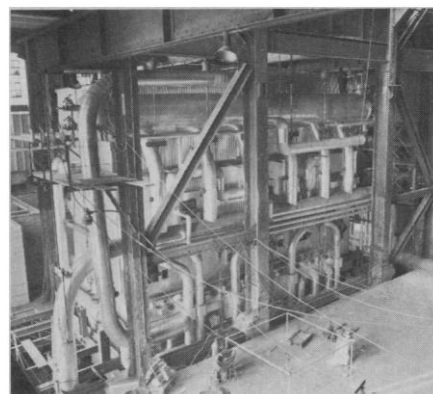


Fig. 2. One cell of a fluidized bed boiler at Rivesville, West Virginia. The experimental unit is the largest yet built and is now beginning shakedown operations. [Source: Pope, Evans, and Robbins, Inc.]

concept, ran out of money. The project was kept alive for some years with support from EPA, but larger units were not begun until 1973, when OCR (now ERDA) contracted for a 30-megawatt plant to be built in Rivesville, West Virginia, by Pope, Evans, and Robbins, Inc. That facility (Fig. 2) has only recently been completed and is beginning test operations this month.

The Rivesville plant represents a substantial jump in size from the original pilot plans—too large, in the opinion of some engineers, who believe that experience with intermediate-size units would have been desirable. Indeed, EPRI has contracted with Babcock and Wilcox, a major boiler manufacturer, to build an intermediate-size boiler. The Rivesville plant is also of a novel, modular design, consisting of three identical combustion cells and a fourth cell to burn fine coal particles that escape from the other three. According to John Mesko of Pope, Evans, and Robbins, the modular design makes it easier to control the steam output of the boiler over a wide range, and also facilitates rapid construction. He is optimistic that the boiler will operate successfully. Other observers are hopeful, but less certain. Shelton Ehrlich of EPRI, who earlier helped to develop the fluidized bed concept for Pope, Evans, and Robbins, says that it "represents something of a gamble." Bruce Henschel of the EPA's Research Triangle Park laboratory in North Carolina describes it as a "very visible project whose failure would have a dampening effect" on the utility industry's confidence in the technology.

If the Rivesville unit does work well, the technology may find rapid commercial use. Foster-Wheeler, a boiler manufacturer that is supplying part of the Rivesville plant, has announced plans to offer warranties on units of comparable size, which are suitable for

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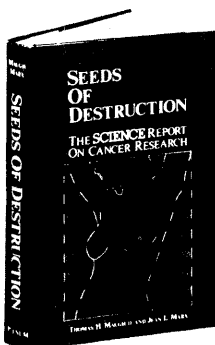
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steam and on-site power generation for industry, as soon as 6 months of successful operation have been completed. ERDA is considering a larger demonstration unit, probably 200 megawatts, for power industry use. TVA recently announced plans to develop and build a 200-megawatt unit, with or without ERDA's help. Development of fluidized bed technology has also been proceeding rapidly in Europe in recent years. A 25-megawatt unit based on Norwegian designs is now under construction in Enköping, Sweden, to supply hot water for that city's district heating system.

Most likely, both fluidized beds and scrubbers will be needed in the 1980's and succeeding decades. But beyond their present problems, these technologies may face new obstacles: evolving environmental standards that would require the control of additional pollutants could alter their relative economic attractiveness, and new information about the atmospheric chemistry and health effects of sulfur compounds and other pollutants, now poorly understood, might obviate the need for or considerably modify the application of these devices.

Oxides of nitrogen, for example, are not now controlled at all, and their output is growing exponentially. Were standards to be imposed, they could be readily met with fluidized bed boilers because of the low temperatures at which they operate but would require additional scrubbing equipment on conventional boilers. For sulfur emissions, there is now substantial evidence that suggests the health hazard is due to sulfuric acid and sulfate particulates, not the sulfur dioxide that has been the main target of the sulfur control effort. But the origins of the acid rainfall that occurs in the northeastern United States and the high sulfate particulate concentrations found in many cities are not agreed on. If they are somehow formed from the sulfur dioxide released at power plants, still tighter sulfur controls might be needed; if, on the other hand, they have a different origin altogether, sulfur dioxide controls might conceivably be relaxed enough that cleaning coal before it is burned would suffice. The existing information appears to be inadequate to resolve the issue.

Despite the uncertainties, both scrubbers and fluidized bed boilers should benefit from additional R & D, and both deserve to be considered together as the most promising candidates for increasing the contribution of coal to the U.S. energy supply, at least until synthetic fuels are more economically viable.

—ALLEN L. HAMMOND

SCIENCE, VOL. 194

BOOKS RECEIVED

(Continued from page 178)

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Science and Absolute Values. Proceedings of a conference, London, Nov. 1974. International Cultural Foundation, Tarrytown, N.Y., 1975. Two volumes. xxxii + pp. 1-710 and xvi + pp. 711-1454. Cloth, \$39.95; paper, \$14.95.

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ues. Don Koberg and Jim Bagnall. Kaufmann, Los Altos, Calif., 1976. 240 pp., illus. Paper, \$6.95.

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The World of Rocks and Minerals. Anita Mason. Photographs by Eric Storey. Larouse, New York, 1976. xviii, 108 pp. Cloth, \$8.95; paper, \$4.95.

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