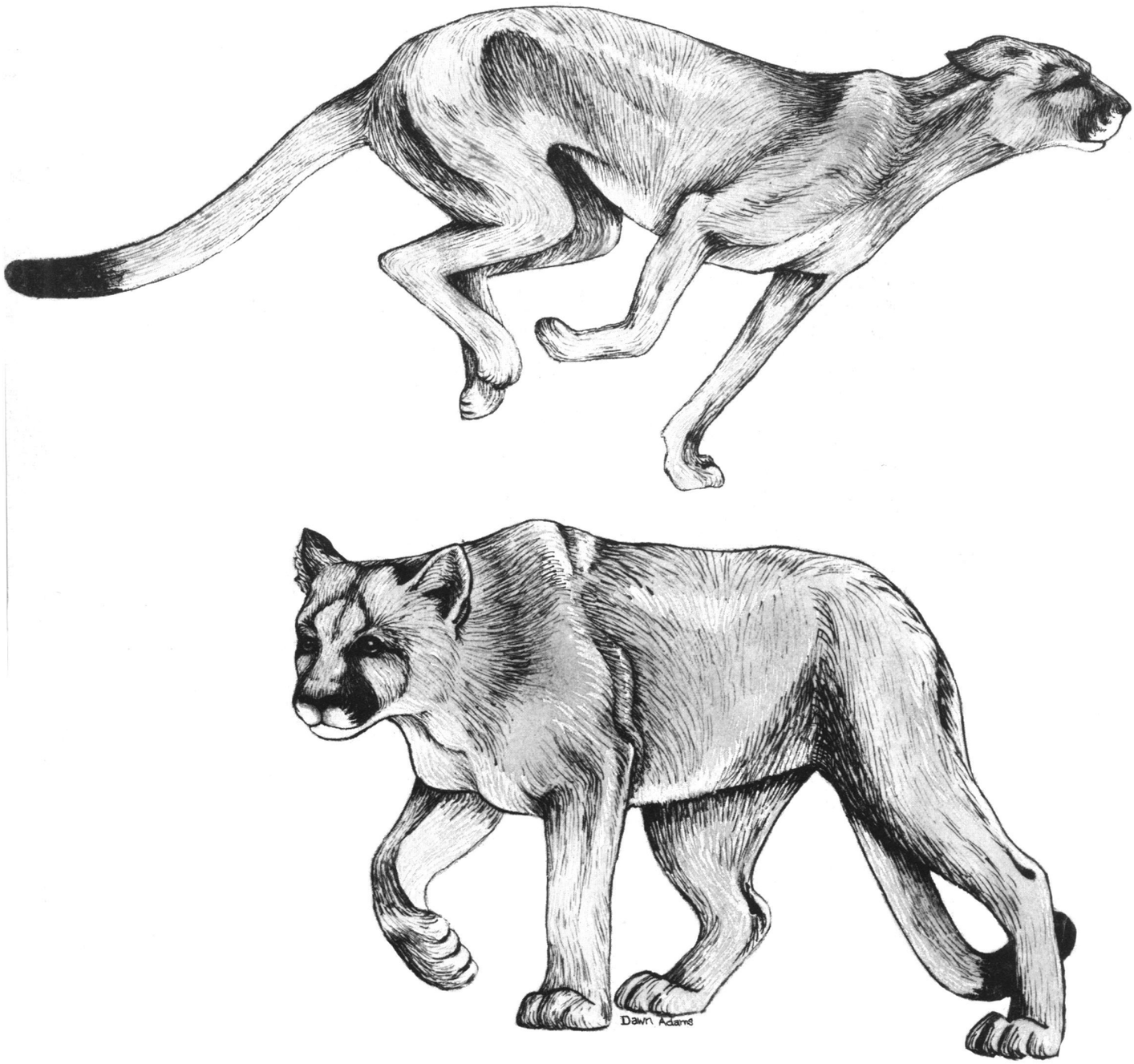
SCIENCE

11 March 1977

Volume 195, No. 4282

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



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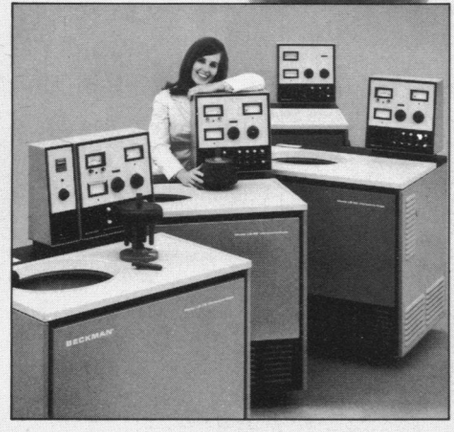

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COVER

Two species of North American cats. (Top) Restoration of extinct, cheetah-like cat (*Felis trumani*), late Pleistocene, North America; (bottom) living mountain lion (*Felis concolor*), late Pleistocene and recent of North and South America. See page 981. [Drawings by D. Adams]

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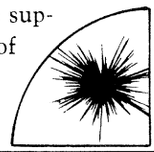

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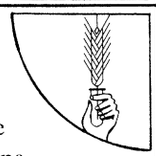
FOOD: Politics, Economics, Nutrition, and Research



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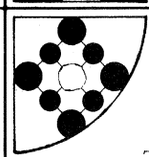

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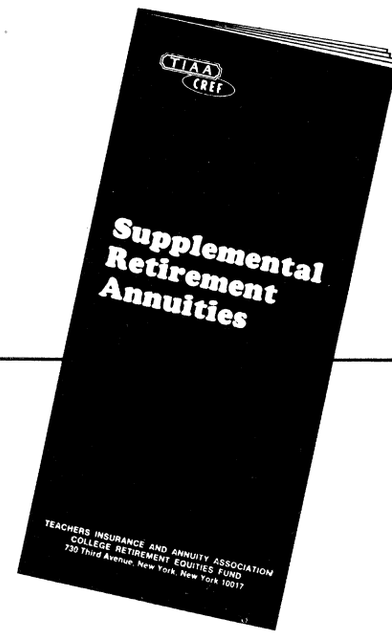

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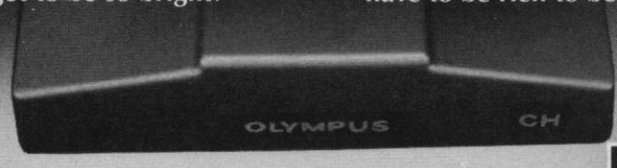

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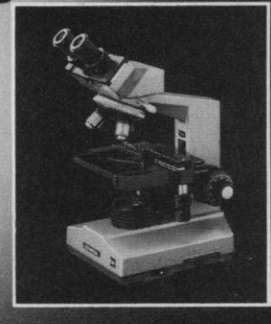

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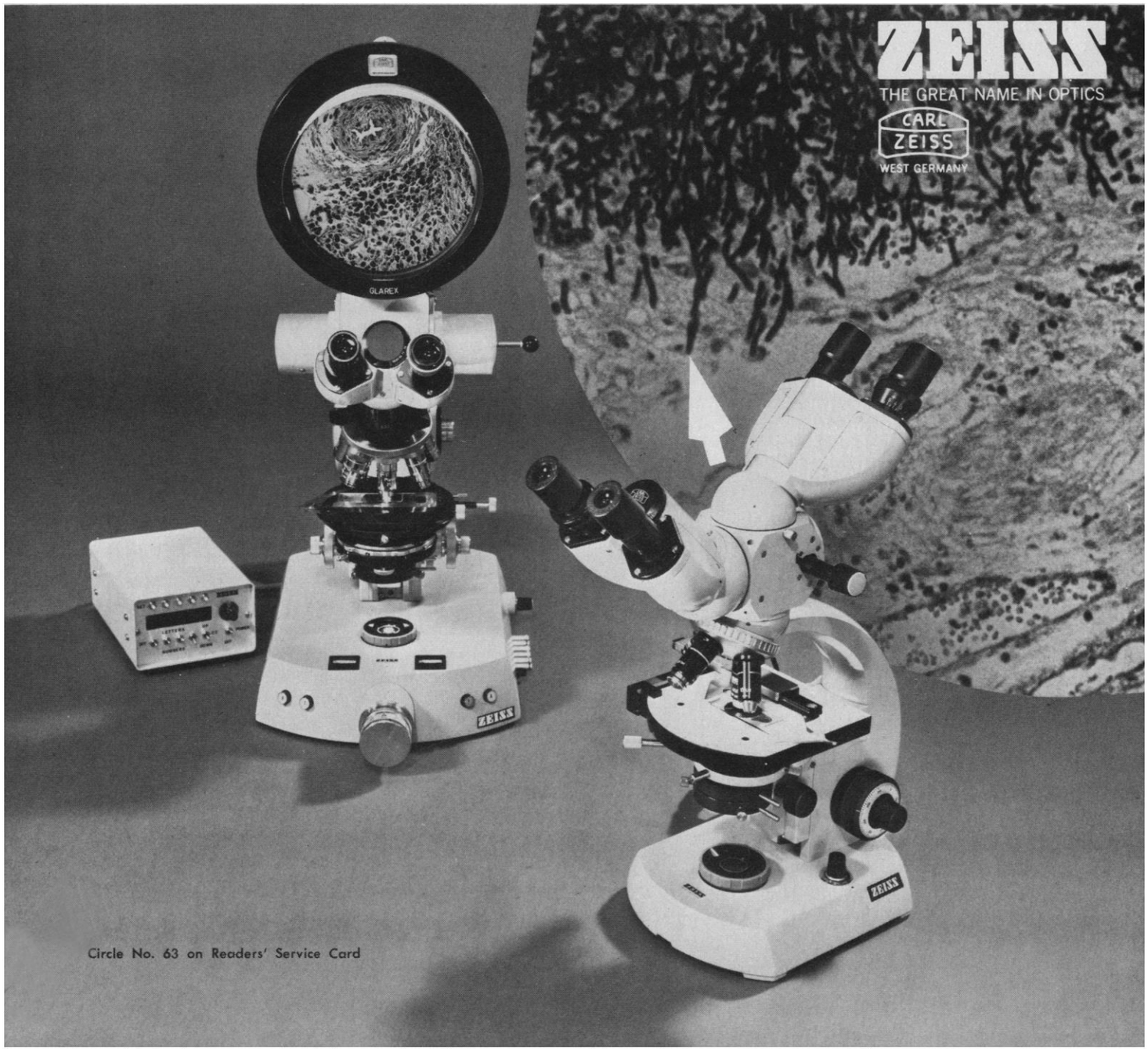

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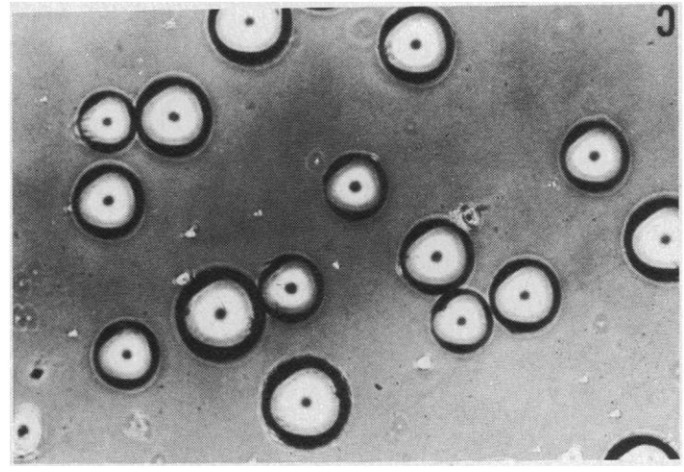
For tissue culture, cell studies...



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1977, 288 pp., $16.50/£11.70 ISBN: 0-12-004701-2; also available in Library Edition with Microfiche, $21.50/£15.25 ISBN: 0-12-004770-5; Microfiche only, $11.50/£8.15 ISBN: 0-12-004771-3

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1976, 284 pp., $23.50/£16.70 ISBN: 0-12-163950-9

5. Thermal Uses and Properties of Carbohydrates and Lignins

Edited by FRED SHAFIZADEH, KYOSTI V. SARKANEN, and DAVID A. TILLMAN

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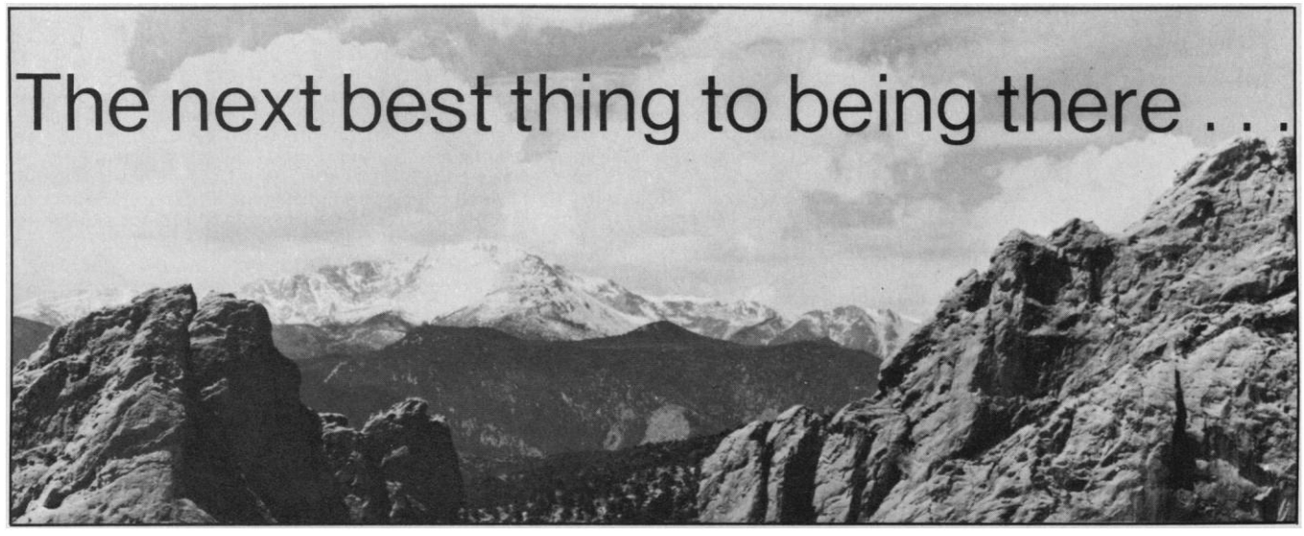

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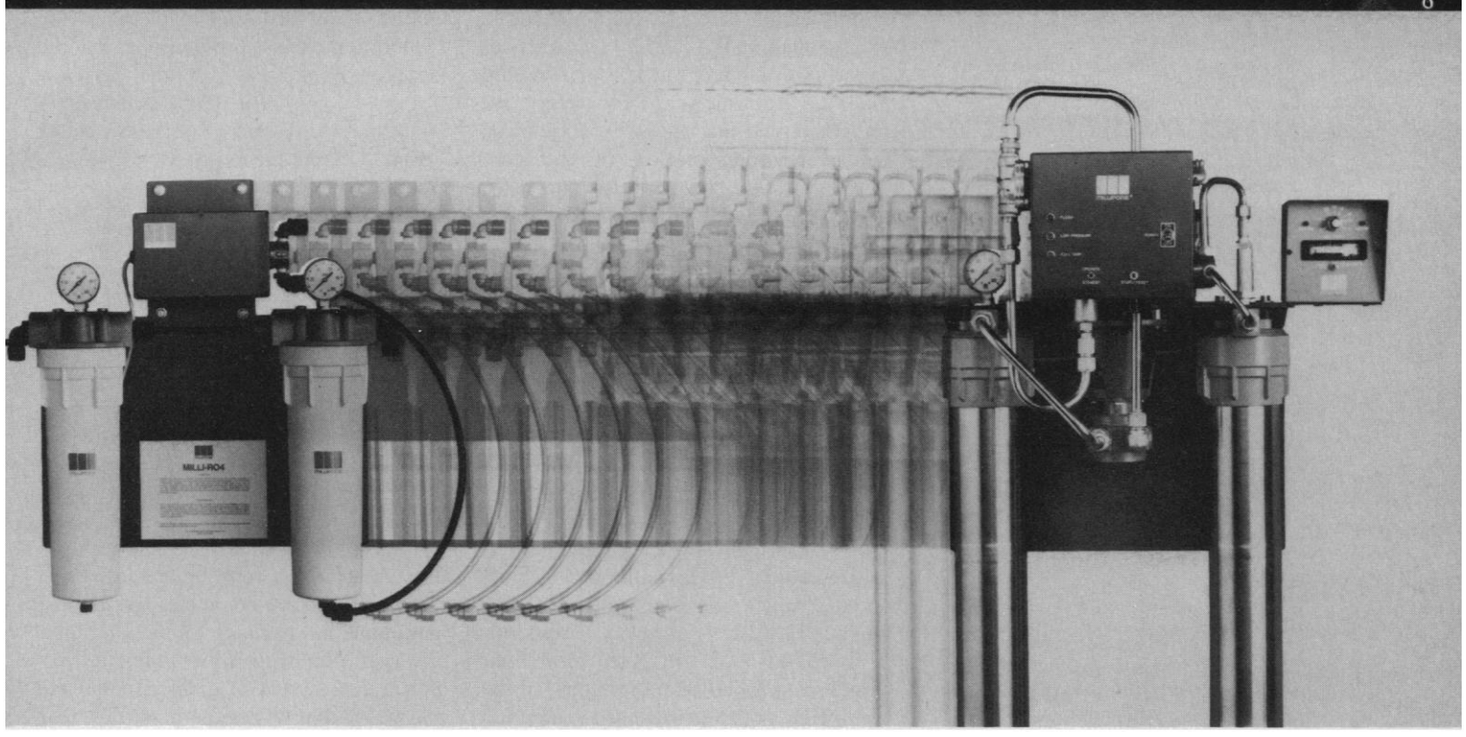

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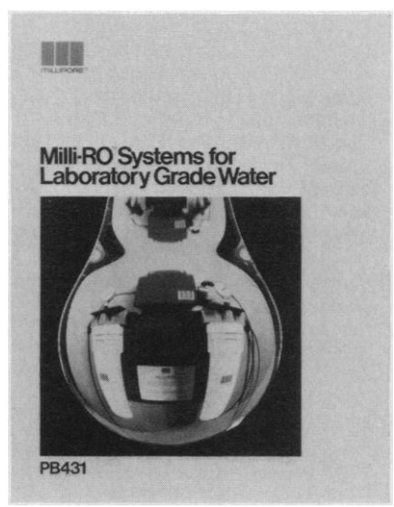

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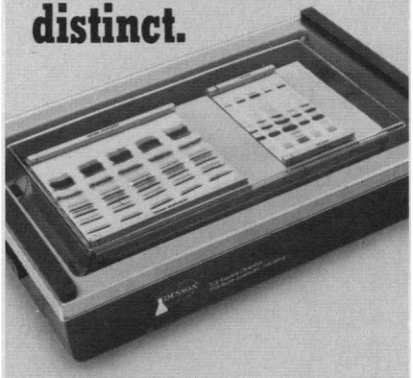

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LETTERS

The *Argo Merchant* Oil Spill

It is unfortunate that Philip H. Abelson's message "Journalists might have provided a better perspective on the event" in his editorial "Oil spills" (14 Jan., p. 137) also applies to several paragraphs of the editorial. As contributors to the National Academy of Sciences report *Petroleum in the Marine Environment* (*1*), to which Abelson refers, we are concerned that his editorial gives an incorrect representation of the conclusions of that report. For example, he compares the estimated annual biosynthetic production of hydrocarbons with annual inputs of petroleum hydrocarbons. However, he fails to point out that there are important compositional differences between petroleum hydrocarbons and biosynthesized hydrocarbons: many of the toxic components of petroleum are not biosynthesized to an appreciable extent, if at all.

When describing processes dissipating oil, Abelson states that substances with a molecular weight less than 300 are "volatilized quickly." How quickly? We analyzed samples of surface oil on 27 December 1976 (R.V. *Oceanus* Cruise 20), 7 miles east of the *Argo Merchant* wreck, and found that 18 percent of the wet weight of the tar was the "aromatic" fraction. Major components of this fraction were C_1 and C_2 alkylated naphthalenes with molecular weights of 142 and 156, respectively. These compounds have been shown to be toxic to some marine organisms and to cause shifts in the species composition of phytoplankton at concentrations of 100 parts per billion in controlled experimental ecosystems. Whether they did in the case of the *Argo Merchant* spill is at present unknown and may never be known.

Abelson discusses mechanisms by which tar balls are removed from surface waters—including sinking as a result of increasing density by various means and because of incorporation into zooplankton fecal pellets. That discussion has a disturbing ring of the "out of sight, out of mind" philosophy regarding pollution. Although sunken tar is out of sight it is not mysteriously lost from the ecosystem. Some may be deposited to sediments, where it may be eaten by benthic animals and introduced into the food web. In the George's Bank area the sediments, as a whole, are an integral part of the benthic ecosystem supporting one of the world's richest fisheries. There is adequate evidence to demonstrate a need for concern should toxic components of the oil become incorporated into the benthic ecosystem. Whether there are short-term (months) and long-term (years) effects on the fisheries can only be documented by adequate study of the area surrounding the *Argo Merchant* spill. This area should be studied to provide a better data base for evaluating and predicting the environmental impact of future spills and the chronic discharge of oil resulting from petroleum exploration and production in the George's Bank area.

JOHN W. FARRINGTON
HOWARD L. SANDERS
JOHN M. TEAL, J. FREDERICK GRASSLE
Woods Hole Oceanographic Institution, Woods Hole, Massachusetts 02543

References

1. Ocean Affairs Board, *Petroleum in the Marine Environment* (National Academy of Sciences, Washington, D.C., 1975).

Interference with Radio Astronomy

The plight of optical astronomers who have been forced by city lights to retreat to remote, uninhabited areas is well understood. Until recently it appeared that radio astronomers could also avoid most man-made interference by locating their observatories away from populated regions. The advent of artificial satellites has meant that no region on earth is free from transmissions in the very high frequency, ultrahigh frequency, and microwave bands which, a few years ago, were almost entirely devoid of interfering signals at sites that had been carefully chosen for radio astronomical observatories.

Recognizing the importance of radio astronomy, the International Telecommunications Union (ITU) has allocated specific bands for radio astronomy. In addition, because of the detrimental effect of space transmissions, radio astronomers are continuing their efforts to have bands adjacent to the radio astronomy bands allocated to terrestrial services only. The 1400- to 1427-Mhz band at the hydrogen line which has been allocated exclusively to radio astronomy is of course of particular importance. The anticipated value of this allocation has been increased by the absence of assignments in adjacent bands to services using transmitters in space.

We must report a case of nonconformance with this international allocation. At our observatory near Penticton, British Columbia, Canada, a spectroscopic rotation synthesis telescope has been operating successfully for several years, mapping supernova remnants, external galaxies, x-ray sources, and other

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astronomical objects using the protected band 1400 to 1427 Mhz. In May 1976, we began receiving strong interfering signals every day. Their characteristics clearly indicated that they originated in an orbiting satellite in contravention of the ITU Table of Radio Allocations (*1*). The transmissions occur simultaneously at three frequencies, which peak at 1427.23, 1427.43, and 1427.63 Mhz. The signals are so powerful that they are received in the sidelobes of our antennas regardless of where the antennas are pointing.

We wish to draw to the attention of our colleagues at observatories in other countries the existence of these interfering signals and warn them of possible deleterious effects on observations. We have been unable to ascertain officially the national administration responsible for these internationally nonconforming transmissions, but we appeal to all our colleagues to urge their own authorities to restrict space transmissions to frequencies sanctioned by the International Table of Allocations.

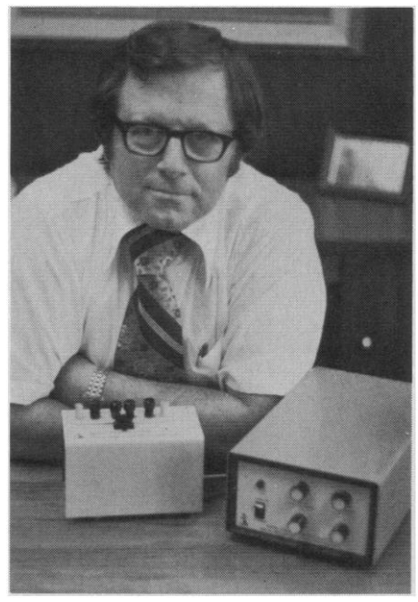
EDWARD ARGYLE
CARMAN H. COSTAIN
PETER E. DEWDNEY, JOHN A. GALT
THOMAS LANDECKER, ROBERT ROGER
Dominion Radio Astrophysical Observatory, Herzberg Institute of Astrophysics, Penticton, British Columbia, Canada V2A 6K3

References and Notes

1. *Radio Regulations Resolutions and Recommendations* (General Secretariat of the International Telecommunications Union, Geneva, 1976). Article 3, Section 1, reads: "The Members and Associate Members of the Union agree that in assigning frequencies to stations which are capable of causing harmful interference to the services rendered by the stations *of another country*, such assignments are to be made in accordance with the Table of Frequency Allocations and other provisions of the Regulations" (emphasis added).

A Coming Battle?

Anyone who would like a preview of the coming battle between the old guard of scientists who identify with Big Science agencies (AEC, ERDA, NRC, NASA, NAS, and so forth) and the new breed of scientists who identify with the public that feels threatened by the technology of Big Science can read all about it for the price of postage ($0.50 in the United States). The *Proceedings of a Congressional Seminar on Low-Level Ionizing Radiation* has just been published. This seminar has many of the features of an adversary science hearing. For instance, there were accusations that radiation in the vicinity of 1 rad is a serious hazard, a total denial of this accusation, cross-examination of sorts, a transcript of testimony, and a public au-



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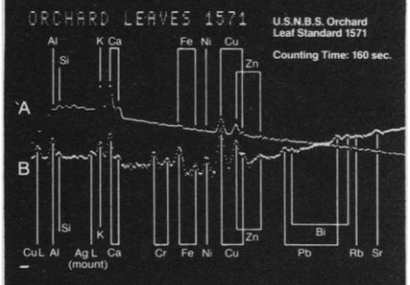

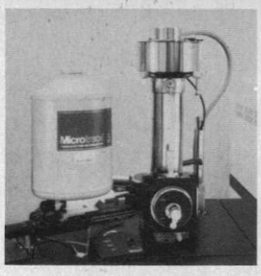

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dience. In this open public hearing, the tactics of infighting that are so effective in closed professional groups did not work very well. The old guard came off rather badly.

This was also a clash between scientists who had found evidence of serious hazards in their studies of humans exposed to nuclear or diagnostic radiation and scientists who denied these hazards on the basis of traditional theoretical calculations, animal studies, and the usual "put-downs" of human data. However, at this meeting the scientists who deal directly with human data and human problems were in no mood to give physical scientists pride of place. They argued that in public health issues it was human data that mattered. The concerned citizens in the audience clearly accepted this argument and rejected the claim of the old guard that it spoke "in the name of science." This seminar may well be the beginning of an increasingly bitter schism in the sciences.

In the past, the old guard has controlled the organizational machinery of science. They have often used this clout to block publication, honors, grants, and other benefits for public-interest scientists who have spoken out against radiation or other technologies pushed by Big Science. The struggle is no longer so one-sided because the public is fed up with being the guinea pigs for Big Science technologies. The scientists who have long opposed the abuses of technology are beginning to get the political clout to retaliate in kind. An all-out battle between the old guard and the new breed could bring back the good old days of the 1930's, when there was very little federal support for any science.

None of the house organs of Big Science have reported this important seminar, but any reader who would like to read the handwriting on the wall can get a transcript by writing to the House Environmental Study Conference, House Annex Building No. 2, Washington, D.C., Attention: Sarah Glazer. The moral is clear: If science does not support the public, the public will not support science.

IRWIN D. J. BROSS
109 Maynard Drive, Eggertsville, New York 14226

Mass Vaccination: Probability of Three Sudden Deaths

Recent events dramatize how hard it is to gauge the risks and benefits of a large-scale vaccination program for a disease which may or may not become epidemic. Evidence of increased risk to Guillain-Barré syndrome has curbed the swine flu vaccination program. I shall focus on the other major event which discouraged early public acceptance of the program, namely, the three sudden deaths following swine flu inoculations in Pittsburgh.

Philip M. Boffey's article (News and Comment, 5 Nov. 1976, p. 590) gives many interesting medical details pertinent to deciding whether the three deaths following swine flu vaccination in Pittsburgh were coincidental. Probabilistic arguments show that, although the chances of three or more deaths in any one clinic on a single day are minute, the chance that some clinic would experience three or more deaths on some day during the first week of the inoculation program is appreciable and could easily be as high as 10 percent, even if the vaccine is perfectly safe. This line of reasoning is pertinent, since if any clinic experienced three or more deaths on some day early in the vaccination program, it is likely that this event would come to public attention and adversely affect public acceptance of the program.

Suppose n_{ij} patients with the average death rate α_{ij} visit clinic i on day j of the program. Then the expected number of deaths for that clinic and day is $\lambda_{ij} = n_{ij}\alpha_{ij}$, and the probability of two or fewer deaths, p_{ij}, is, from the Poisson probability law

$$p_{ij} = (1 + \lambda_{ij} + \lambda^2{}_{ij}/2)\exp(-\lambda_{ij})$$

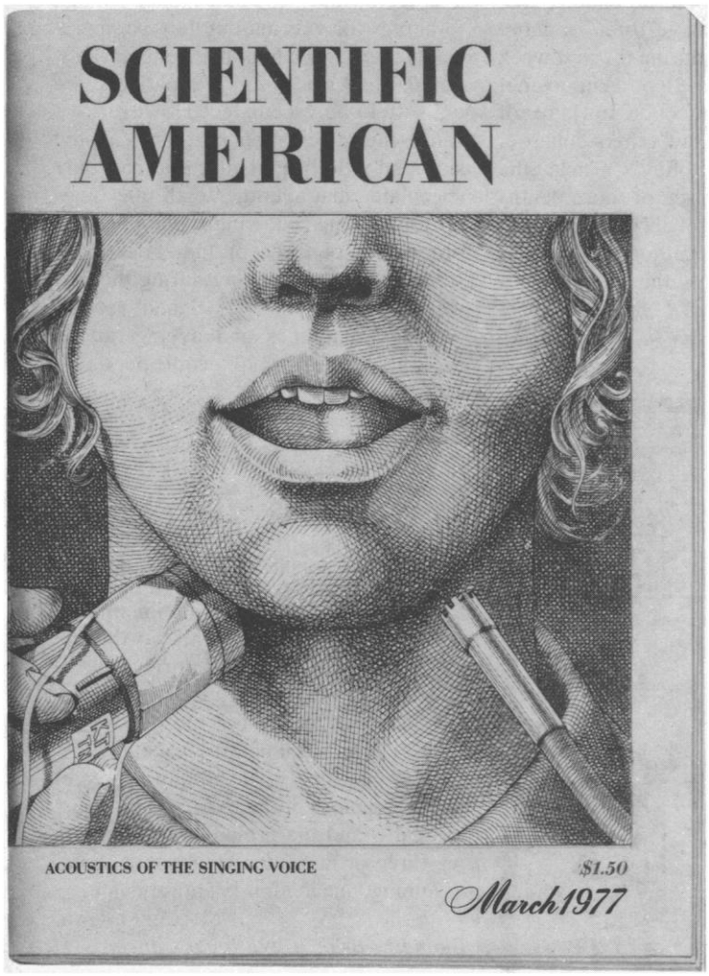
assuming that each individual has a small, statistically independent chance of dying each day. The probability that all clinics experience two or fewer deaths on all seven days of the initial week of inoculations is the product

$$\prod_{j=1}^{7} \prod_{i=1}^{m} p_{ij}$$

where m is the total numbers of clinics, and the probability that some clinic experiences three or more deaths on some day during this week is 1 minus this product.

To use these formulas we must know the numbers of people who visit each clinic each day and their average death rate. Suppose $m = 100$ clinics each care for $n_{ij} = 1000$ people each day, and that the average death rate is $\alpha_{ij} = 10$ deaths per 100,000 patients per day. This is approximately the death rate for all U.S. people aged 65 to 75 (*1*). The probability of fewer than three deaths in one such clinic is

$$(1 + 0.1 + 0.005)\exp(-0.1) = 0.99985 = p_{ij}$$



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and the probability of three or more deaths in one such clinic on a given day is only $1 - p_{ij} = 0.00015$. However, the probability of three or more deaths on some day in some clinic during the first week is

$$1 - \prod_{j=1}^{7} \prod_{i=1}^{100} p_{ij} =$$

$$1 - (0.99985)^{700} = 0.103$$

Thus, the chance of three or more deaths in a single clinic on a single day are remote (about 1 in 10,000). Therefore, each such episode should be carefully investigated to rule out avoidable accidents. On the other hand, these calculations show that the probability that some clinic would have three or more deaths on some day during the first week could easily approach 10 percent, even if vaccination has no effect on mortality. If some of the victims saw others collapse, as is suggested in Boffey's article, the chances of having three or more deaths in some clinic are probably enhanced.

Of course the preceding calculations are hypothetical, as the numbers of patients seen at each clinic and corresponding average death rates were not used. The main uncertainty in estimating average death rates is that those who go to clinics for vaccination may be appreciably healthier than the general U.S. population, since very ill patients are unlikely to be vaccinated. However, because the vaccination program enlisted sick and elderly patients, one can only speculate what average death rate is appropriate. The following table gives the probability of three or more deaths in some clinic on some day during the first week assuming $n_{ij} = 1000$ and various numbers of clinics and average death rates, α_{ij} (deaths per 10^5 people per day).

		Clinics (m)		
		50	100	300
α_{ij}	15	.16	.30	.65
	10	.05	.10	.28
	5	.01	.01	.04
	2	.00	.00	.00

Clearly the death rate is a dominant variable. For this reason it seems worthwhile to conduct special studies during several vaccination programs to determine age-specific death rates for those who actually come to clinics for vaccinations. In this way one could obtain more reliable estimates of the expected numbers of deaths and the probability of observing three or more deaths in some clinic, assuming vaccination is entirely safe.

MITCHELL GAIL
Biometry Branch, National Cancer Institute, Bethesda, Maryland 20014

References

1. *U.S. Life Tables: 1969–71* [Department of Health, Education, and Welfare Publ. No. (HRA) 75–1150, National Center for Health Statistics, Rockville, Md., 1975)], vol. 1, No. 1, p. 7.

Alleviating Confusion

In the recent Research News article "Sexual dimorphism and mating systems: How did they evolve?" (28 Jan., p. 382), some work on sexual dimorphism in bats is described. This research is wrongly credited to Philip Meyers at the University of Michigan; his interest in sexual dimorphism is limited to *Homo sapiens*. The person to whom credit belongs is Philip Myers of the University of Michigan. We hope this letter alleviates confusion.

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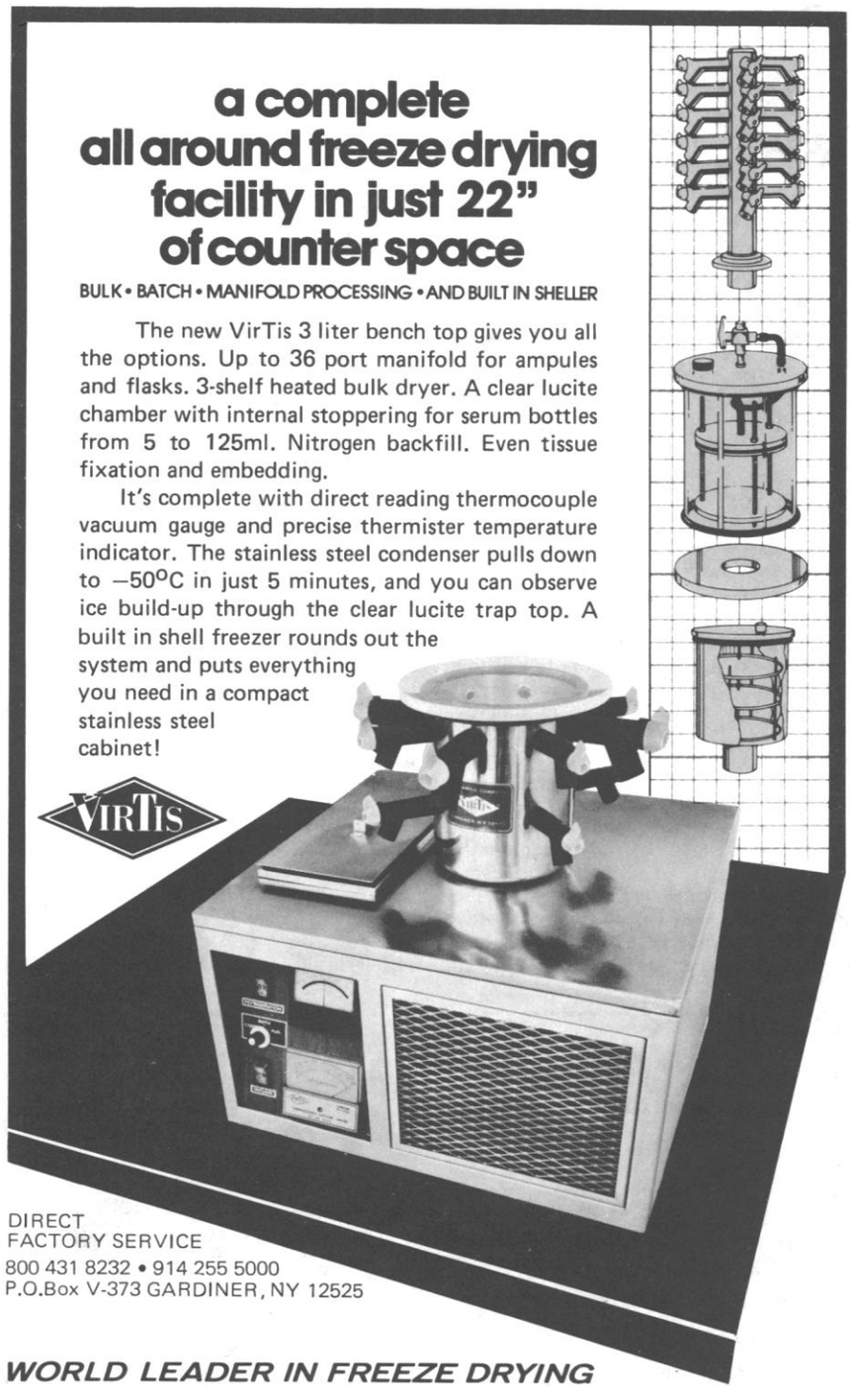
PHILIP MYERS
Museum of Zoology, University of Michigan



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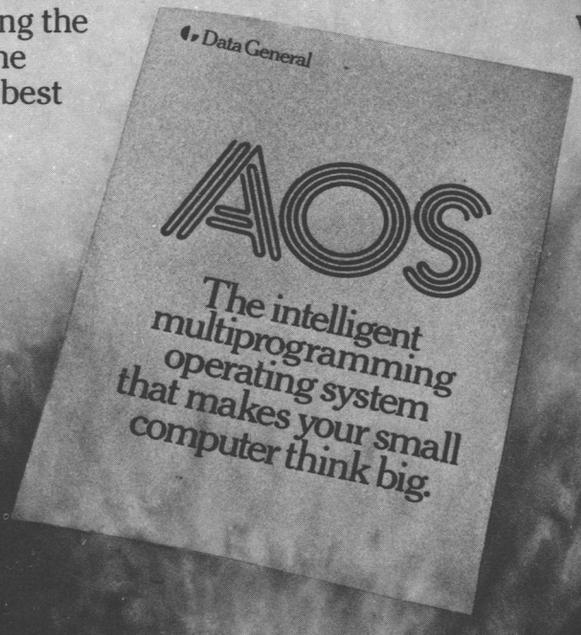

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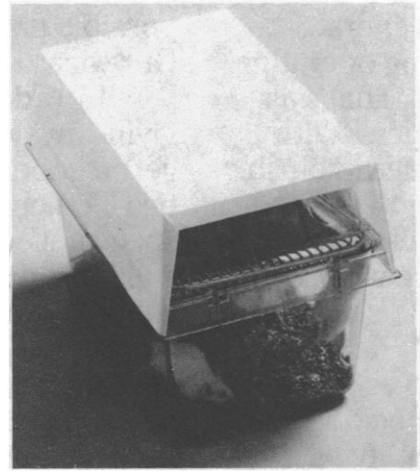

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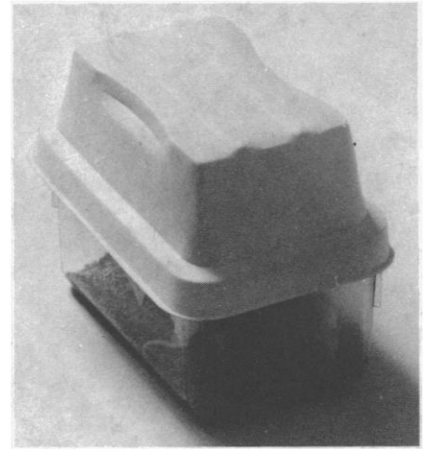

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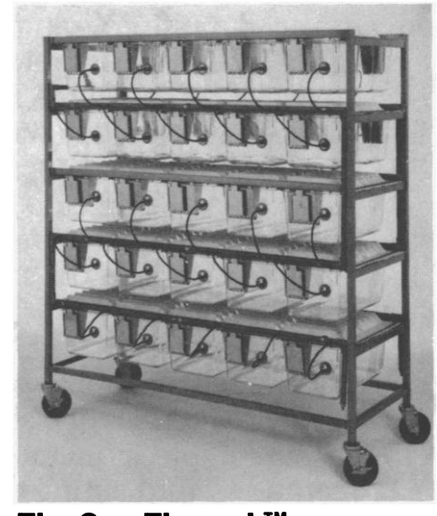

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Science: Too Much Accountability

The National Science Board last year reported that the support of basic research in constant dollars declined by 13 percent between 1968 and 1974 and that the expenditure per active scientist was down a sharp 30 percent over the same period.

The dwindling support of research, however, is compounded by an even more serious problem—the increasing control of research by legislation and regulation. No scientist questions a reasonable need to define goals and to account for the expenditure of public funds. But it seems legitimate to ask whether science today is not suffering from unreasonable and unproductive strictures that affect both the quality and the quantity of research.

Legislative constraints include the unprecedented move last April by the House of Representatives in voting to shut off funds for a National Science Foundation grant proposal. This action was led by a powerful congressman who believed that the proposal was scientifically unsound and morally unacceptable. Yet this research proposal had been judged meritorious by scientific peers after considerable study, had been endorsed by a top-ranking government advisory committee, and had been subjected to searching inquiries by senior government officials.

At the grass-roots level, it is the regulations that directly affect the pursuit of research. The actual conduct of a research program has become so engulfed by rules and regulations that research costs have escalated at a frightening rate. More subtly, however, the real damage is being done to research priorities and to the creative risk-taking of the investigators. Scientists are tending to select areas of research where money is available, such as cancer or energy research. The most productive and creative workers are stimulated to follow promising leads in directions unrelated to the subjects of their grants. The freedom to pursue these leads lies at the very core of the research process, and is the main source of its conspicuous success. Yet new and rigid rules have all but eliminated this essential flexibility and opportunity for serendipity on which original discovery depends.

Scientists, of course, are not innocent bystanders in the evolution of this problem. They have contributed their share to the creation of a plethora of new regulations. Unfortunately, new and tighter regulations imposed on top of old ones have been amply demonstrated to be an ineffective management tool to improve accountability and performance. Indeed, in each category of funding there exists the potential for abuses, but more regulations generate more abuses. A common example is the rush to buy a piece of equipment before the expiration date of a grant because it has not been possible to transfer funds into a critically needed salary category.

The solution to this problem is first to convince legislators, managers, and regulators that it exists, and that it is an important factor inhibiting the proper utilization of national resources. Scientific research must be recognized for what it is, a social rather than a business activity, even though it generates the same outward patterns of growth. Informal cooperation first becomes organized, then the organization eventually becomes laden down by a bureaucracy in which originality of thought at the expense of routine business efficiency is discouraged. A working consensus between the research scientist and his legislative and regulatory counterparts can only be achieved by a dialogue that includes a rational analysis of alternatives. With the installation of a new national administration, a fresh opportunity exists for the scientific community to initiate this dialogue with government for the benefit of all concerned.

The alternative should be obvious. It is not much of an exaggeration to suggest that had the present bureaucratic structure been in operation when poliomyelitis research was in its heyday, we might today have a compact, efficient, computer-operated, portable iron lung rather than two vaccines.—

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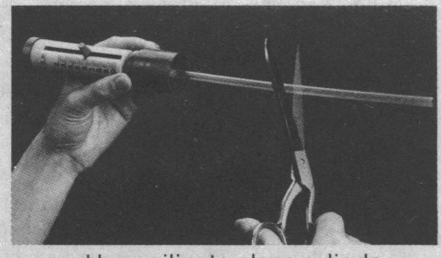

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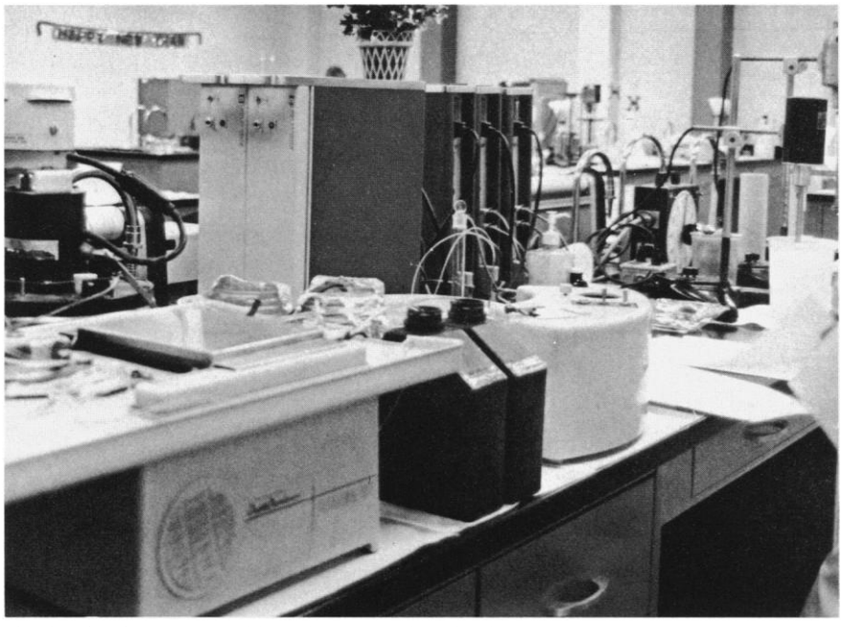
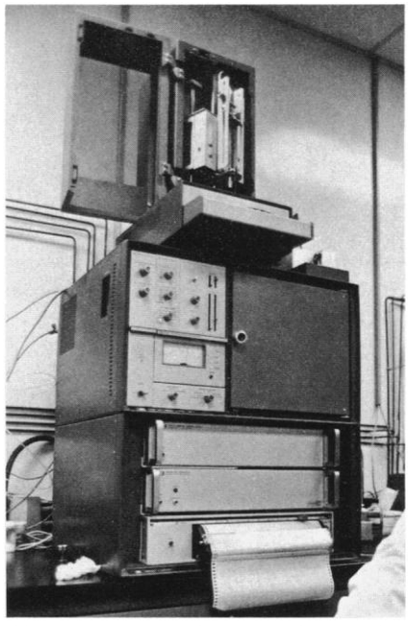
Lab Automation in Pharmaceutical Manufacturing—Whitehall Laboratories



Analog Modules connect five Technicon AutoAnalyzers to the 3354 Lab Automation System.



Chromatograph with automatic sampler provides high capacity analytical system.

Manufacturers of prescription and non-prescription drugs have exceptionally difficult analytical problems to solve. Because their products are used either in or on the human body quality control throughout the manufacturing process must be very stringent, and the number of samples passing through the control laboratories is high. The combination of sample volume and the need for careful record keeping and thorough procedure validation places a heavy data reduction load on the laboratory staff.

Whitehall Laboratories, a division of the American Home Products Corporation and a major manufacturer of non-prescription drugs (Dristan, Anacin, Primatene, etc.), installed Hewlett-Packard 3352 Lab Data Systems at both the Hammonton, New Jersey, and Elkhart, Indiana, locations. In mid-1976 the Elkhart installation was expanded to a disc-based 3354 Lab Automation System.

A very active LAB BASIC program development project is carried out at the Elkhart location, under the direction of Charles Meyer, Quality Control Manager, and Dr. John Murphy, Chief Chemist. According to Dr. Murphy, "The 3354 has become essential to us and we're finding more uses every day. We even use it to print product release sticker labels. Most of the present programming effort is in statistical routines we need for process control. The multiple terminal direct access design is a great help because I can work on a new program as though this was my own individual computer, and yet it's handling about 15 laboratory instruments at the same time."

Dr. Robert Blank, assistant vice president of Whitehall and director of research and development at Hammonton, says, "We're pleased with the system and plan to go to the 3354 this year. It isn't just the volume of laboratory work; I want to get all of the method verification work and some long term stability studies on the system too. Right now we have the computer filled with programs for our Technicon AutoAnalyzers but the disc will remove that limitation and the

Continued on following page

Continued from preceding page

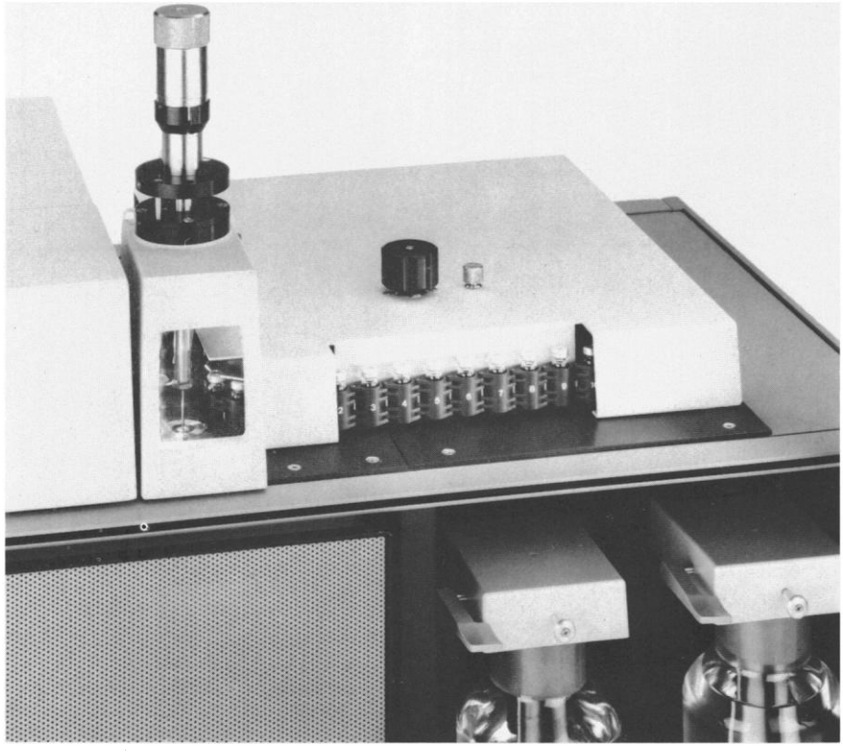
people at Elkhart will help us with the special programming we'll need."

Gerry Bryan is Quality Assurance Supervisor at Hammonton and head of the AutoAnalyzer laboratory. He says, "We used to spend a lot of time measuring charts and calculating answers. Now we can spend much more time on sample preparation and setting up the analyzers. Some of them are running 18 or 20 samples an hour, 16 hours a day, and I don't think we could keep up with hand calculations. We use LAB BASIC programs developed at Elkhart for all the AutoAnalyzers now."

Dr. Atul Shah is section head for analytical research and development at Hammonton. Dr. Shah says, "I like the immediate availability of reports. We can detect a suspicious result at once and run the sample again to check it. But I am definitely looking forward to the larger system for our validation studies. We have to do this on every procedure we use and they are very time consuming."

This is one user's experience using Hewlett-Packard 3350 Series Systems in drug manufacture. We maintain program libraries that extend system utility including statistics, RIA (radioimmunoassay) and AutoAnalyzer programs. Further information can be obtained by checking Data Systems on the Reply Card.

An Automatic LC Sampler With No Sample Waste



Many biochemistry studies require the analysis of large numbers of samples by liquid chromatography. Automatic sampling and injection would seem to be a necessity, except that existing automatic samplers for LC consume a considerable volume of a scarce sample just to flush and fill the lines, loops and other parts of the injector mechanism. The new sampler shown here will automatically inject up to 60 samples with up to 9 replicates if desired and consume only the amount of sample it actually injects.

The new LC sampler for use with HP Models 1082A and 1084A Liquid Chromatographs is similar to the Variable Volume Injector used on those instruments but with an added sample handling assembly. The samples in capped vials are loaded into a 60 position link belt. Injection volume (10 to 200 microliters) is set with the micrometer head. Runs per sample and the number of the last sample are entered on the chromatograph keyboard. From this point on the system operates unattended, producing chromatograms and analytical reports, each with a printed sample bottle number, until all analyses are completed. All of the sample withdrawn from the vial is actually injected; none of it is wasted in flushing.

The sample handling capability is easily added to existing Variable Volume Injectors to convert them to completely automatic LC samplers. For further information please check LC Sampler on the Reply Card.

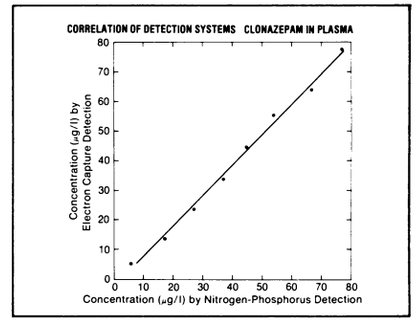
Analysis of 1,4-Benzodiazepines With a Nitrogen-Phosphorus Detector

Sensitive analytical procedures have been reported for the analysis of benzodiazepines using an electron capture (EC) detector. In most cases these same methods may be used with a nitrogen-phosphorus (N-P) detector.

Ultimate sensitivity (minimum detectable level) is somewhat better with the EC detector, but at therapeutic levels the results with the two detection systems are comparable. The figure is a comparison of N-P and EC results using plasma samples spiked with clonazepam (5 to 75 μg/l). The correlation coefficient is 0.996.

The N-P detector has a clear advantage over the EC detector when dealing with 7-nitrobenzodiazepines. The 7-nitro group often metabolizes to 7-amino, and these metabolites respond poorly to EC detection. The N-P detector has comparable response to the nitro and amino structures so that the 7-amino metabolites, many not previously reported, may be analyzed with sensitivity similar to the parent compounds.

We have just published an Application Note describing this and other biomedical uses of the N-P detector. Check Nitrogen-Phosphorus Detector on the Reply Card for your copy.

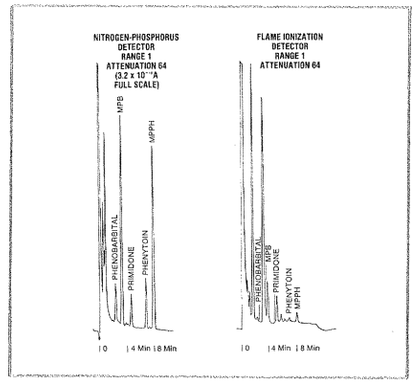


Nitrogen-phosphorus and electron capture results are essentially equivalent in the therapeutic range.

A Rapid Analytical Procedure for Antiepileptic Drugs

Analysis of drugs in serum and other body fluids often requires elaborate and lengthy sample workup to eliminate interferences due to normal (non-drug) sample constituents. Such procedures are undesirable both from the time required to process the sample and the additional opportunities for inaccuracy introduced by each processing step. Use of a selective GC detector which is insensitive to the interfering materials can greatly simplify the workup required.

In the analysis of phenobarbital, primidone and phenytoin in plasma, using a nitrogen-phosphorus (N-P) detector rather than a flame ionization detector permits reduction of the analysis time from about 2 hours to approximately 20 minutes, including the 10 minute chromatographic run. Three extractions, one centrifugation and one evaporation step can be eliminated. In addition, because of the enhanced sensitivity of the N-P detector to nitrogen-containing compounds the sample size requirement is reduced from 1 ml to 50 μl of serum, a great advantage in pediatric situations.



Nitrogen-phosphorus detector suppresses interfering compounds while giving enhanced response to antiepileptic drugs.

The figures illustrate the sensitivity enhancement of the N-P detector toward the compounds of interest and the simultaneous suppression of interfering non-nitrogen compounds. For additional information on the uses of this detector in therapeutic monitoring, including details of the short workup procedure, please check Nitrogen-Phosphorus Detector on the Reply Card.

See Us in Chicago...

Hewlett-Packard will have a major exhibit at the FASEB meeting in Chicago's McCormick Place, beginning on April 4. Gas and liquid chromatographs (including the new LC sampler), GC/mass spectrometers, lab automation systems and laboratory recorders will be on display. Factory representatives will be on hand to answer any questions. Please come see us.

Analysis of β-Hydroxy Myristic Acid Using Selected Ion Monitoring GC/MS

There is considerable interest in blood levels of β-hydroxy myristic acid as it relates to gram negative septicemia. Apparently a low level of the compound occurs normally in blood, but becomes elevated with the onset of this disease. Thus, the analysis of blood levels is a possible diagnostic technique. The work outlined here was done using GC/MS on standard samples in an effort to establish feasibility of quantitatively measuring the acid at low picogram levels.

GC/MS is a sensitive and selective technique that can be used to both detect and quantitate low levels of biologically important compounds. Selected Ion Monitoring (SIM) has now become an important aspect of GC/MS. SIM involves rapid, sequential monitoring of one or more ions rather than scanning over a continuous mass range. The spectrometer usually dwells on each ion monitored for about 50 to 500 milliseconds.

The acid was derivatized to produce the trimethylsilyl ether of β-hydroxy methyl myristate, and the trideutero analog was used as the internal standard. As is characteristic of TMS ethers, these compounds readily lose a methyl group attached to the silicon atom upon ionization in the mass spectrometer. This gives rise to ions at m/e 315 and 318 that can be used in the SIM experiments.

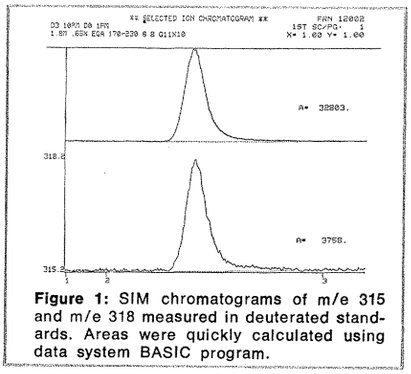


Figure 1: SIM chromatograms of m/e 315 and m/e 318 measured in deuterated standards. Areas were quickly calculated using data system BASIC program.

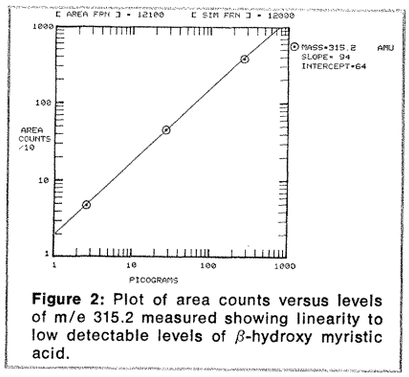


Figure 2: Plot of area counts versus levels of m/e 315.2 measured showing linearity to low detectable levels of β-hydroxy myristic acid.

An HP 5981A GC/MS with data system was appropriately calibrated to insure that the signal intensity measurements were taken at the apex of each mass peak. Three different levels of the compound were run, each with the same amount of trideuterated internal standard (D3) added (D0 refers to the "unknown"). An example of one of these analyses is shown in Figure 1.

Using the data system, the background was quickly removed, m/e 315.2 renormalized, the baseline drawn with the CRT cursors, and the areas calculated.

The results of these several levels, appropriately corrected for solvent and reagent blanks, are shown in the data-system-generated calibration curve (Figure 2). It can be seen that there is satisfactory linearity down to the minimum detectable level of 3 picograms of β-hydroxy myristic acid.

Applications information about the advantages of using GC/MS for detecting *and* quantitating biological compounds is yours for the asking. Simply check GC/Mass Spectrometer on the Reply Card.

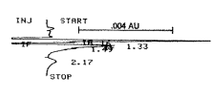
Liquid Chromatography for Simple and Rapid Theophylline Assay

Theophylline is widely used as a bronchodilator in the treatment of asthma, with the desired plasma concentration in the 10 to 20 mg per liter range. Serum and plasma theophylline levels have been measured by gas and liquid chromatography and by spectrophotometric methods. We believe that liquid chromatography is the method of choice since it requires no derivatization (as does gas chromatography) and easily discriminates between theopyhlline and caffeine, theobromine and other xanthine compounds which may be present.

The analyses shown here were performed by reversed phase liquid chromatography with a 90:10 buffered (pH 4) aqueous/acetonitrile mobile phase. The relatively high flow rate of 4 ml per minute produced a complete analysis, including caffeine, in less than five minutes. Recycling of the mobile phase appears to be practical, eliminating solvent cost as a practical deterrent.

The fixed wavelength 254 nm UV detector of the HP 1084A liquid chromatograph yielded adequate sensitivity at the 1 mg per liter level with very low baseline noise (Figure 1). Use of a variable wavelength detector at λ_{max} was considered unnecessary since any increased response would be accompanied by a considerably higher noise level.

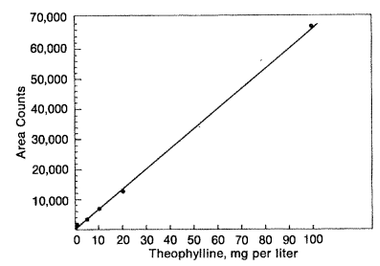
Figure 1:



Peak at 2.17 minutes is theophylline at 1 mg per liter. Sensitivity is .004 AU per 5 cm.

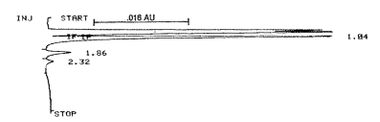
A calibration curve was constructed using synthetic (non-plasma) mixtures. Linearity is satisfactory over the entire calibration range of 1 to 100 mg per liter (Figure 2).

Figure 2:



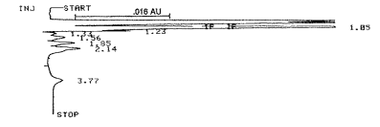
Plasma samples were treated with trichloracetic acid to precipitate protein and 20 μl of the supernatant injected. This method is preferred over direct injection of untreated plasma or serum since little time is required and deterioration of the column is avoided. A typical plasma blank and plasma spiked with theophylline, theobromine and caffeine are shown in Figures 3 and 4. Note the small peak at 2.32 minutes in the blank; this appears as an unresolved shoulder on the theophylline peak and must be taken into consideration.

Figure 3:



Plasma blank shows interfering peak at 2.32 minutes. Sensitivity .016 AU per 5 cm.

Figure 4:



Plasma spiked with theophylline, theobromine and caffeine at .016 AU per 5 cm.

There is adequate resolution between the theophylline and caffeine peaks for insertion of an internal standard (usually β-hydroxypropyl theophylline) if this is desired. In the present study an internal standard was not used since the Variable Volume Injector of the 1084A Liquid Chromatograph gives highly reproducible injection sizes. Precision checks on plasmas spiked with theophylline, theobromine and caffeine yielded coefficients of variation of 0.57% and 0.12% at the 8 and 21 mg per liter levels respectively.

For more detail and a discussion of several variations of this procedure please check Theophylline Assay on the Reply Card.

New GC/MS Bibliography Lists Recent Studies Covering Variety of GC/MS Applications

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3 August. Toxicology of novel nutrient sources (S. Miller, chairman): S. Miller, "Technological schizophrenia: problems of evaluating novel nutrient sources"; (speaker to be announced), "Special problems of protein"; H. Dymsza, "Special problems of energy"; J. Vanderveen, "Paradox of regulation: nutrient or additive." Toxicology round table: Subject to be announced (A. Forbes, chairman). Environmentally induced peripheral neuropathies (C. J. Terhaar, chairman): P. Spencer, "Current approaches to toxic neuropathies."

4 August. Nutrition as a modifier of the toxic response (P. Newberne, chairman): T. C. Campbell, "Nutrition and the metabolism of xenobiotic compounds"; A. Alvares, "Interaction between nutritional factors and drug biotransformation in man." Toxicology round table: (The influence of dietary factors in the design of safety evaluation studies) (D. Hood, chairwoman). Fat, fact, fancy, folklore (M. Gallo, chairman): T. King, "Folklore toxicology"; P. Newberne, "Toxicological significance of overfeeding."

5 August. Newer aspects of benzene toxicology (R. Weir, chairman): B. Goldstein, "Inhalation toxicity of benzene"; R. Snyder, "Benzene metabolism and benzene-induced bone marrow disease."

Transport Phenomena in Lipid Bilayer and Biological Membranes

Tilton School

Stuart McLaughlin, chairman; Paul Mueller, vice chairman.

22 August. Channels in biological membranes (C. Stevens, chairman): E. Neher, F. Conti, C. Armstrong, F. Sigworth. Channels in artificial bilayer membranes (G. Ehrenstein, chairman): S. Hladky, R. Latorre.

23 August. Ion movements through bilayer membranes (D. Tosteson, chairman): P. Lauger, S. Feldberg, F. Cohen, R. Benz, and H. Ginzburg. Poster sessions.

24 August. Epithelia (J. Diamond, chairman): B. Rose and W. Loewenstein, C. Clausen, J. White. Energy coupling mechanisms (H. Morowitz, chairman): H. Kaback, P. Dutton, and J. Nagle.

25 August. Reconstitution I (L. Hokin, chairman): D. Oxender, P. Hinkle, M. Colombini. Molecular motions in membranes (T. Thompson, chairman): W. Webb and I. Smith.

26 August. Reconstitution II (P. Mueller, chairman): E. Racker, M. Raftery, M. Montal.

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Research & Development in the Federal Budget

June 15-16, 1977

The second annual AAAS report on research and development in the federal budget, to be completed in May 1977, will be the subject of an

AAAS
Science & Public Policy
Colloquium
Washington, D.C.
June 15 and 16, 1977

The R&D budget analysis project, sponsored by the AAAS Committee on Science & Public Policy and initiated on a trial basis in 1976, resulted in Willis H. Shapley's well-received book *Research and Development in the Federal Budget: FY 1977*, and a lively colloquium attended by nearly 200 AAAS members and government officials.* The June 15-16, 1977, colloquium will again offer a forum for constructive discussion with officials of the Executive and Legislative branches and an opportunity to examine the complex relationship of R&D to the federal budgeting process. Willis H. Shapley will again be responsible for preparing the R&D report, which will be available in book form at the June 1977 colloquium.

Specific topics this year will include the impact of the "transition" on R&D decisions, future trends in R&D budgeting, and problems of criteria for federal budget decisions. For information and reservations, please write to

Ms. Catherine Lighthizer
AAAS Division of Public Sector Programs
1776 Massachusetts Ave., N.W.
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**Research and Development in the Federal Budget: FY 1977* ($5.50) and the 1976 *Colloquium Proceedings* ($10.00) may be purchased from AAAS.

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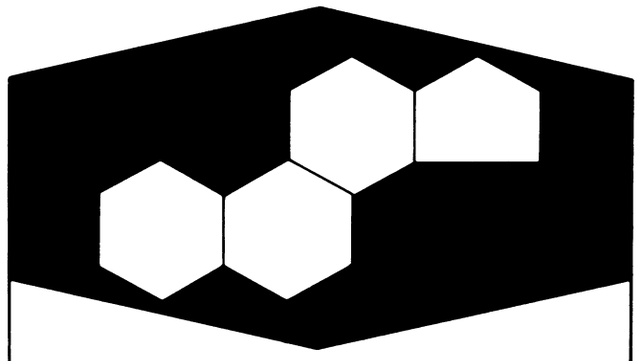

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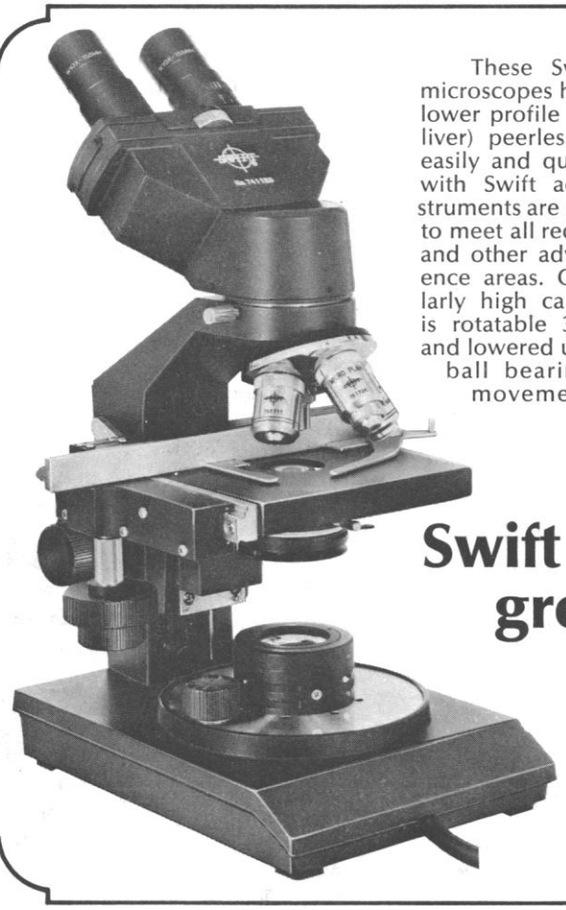

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Literature

Monitoring Guide for Airborne Contaminants lists recommended sampling procedures for over 140 hazardous substances. National Environmental Instruments. Circle 726.

Immunobeads are micron-sized, hydrophilic particles with covalently bonded antibodies for immunoassay. They are the subject of a product bulletin also devoted to the reagents marketed with them. Bio-Rad Laboratories. Circle 730.

Gas Chromatograph describes the GC 3B instrument and includes design specifications and applications. Shimadzu Scientific Instruments. Circle 671.

Infrared Spectra of Organosilicon Compounds includes 35-millimeter slides, an audio cassette, a script, and a booklet of problem spectra. Science Media. Circle 672.

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Stopped-Flow Fluorescence and Light Scattering describes a fluorescence accessory for study of fast chemical reactions. Durrum Instrument. Circle 674.

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Mining Maps that feature mining districts and mineral deposits in Colorado and Wyoming are included in a brochure for mineral exploration. Mineral Research. Circle 676.

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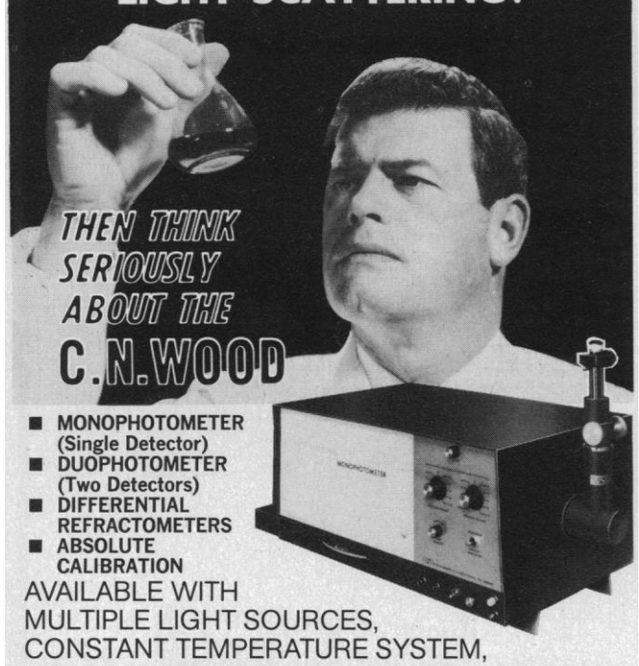

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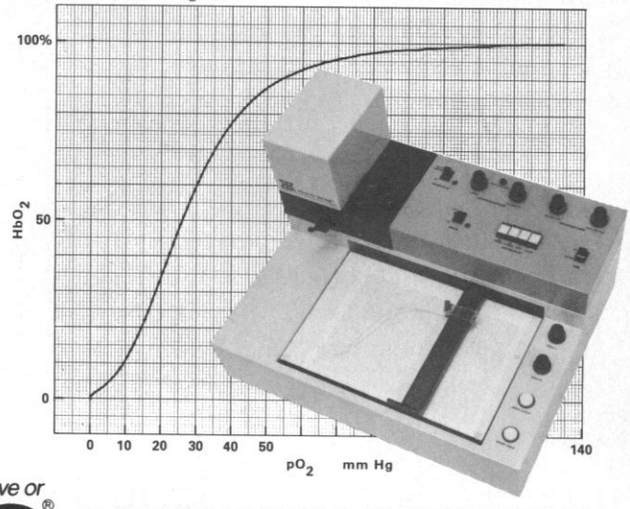

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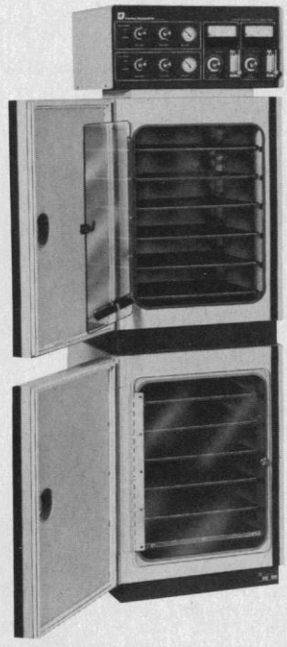

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Ecology and Management of Animal Resources. J. Roger Bider, Eric Thompson, and R. W. Stewart. Les Presses de l'Université de Montréal, Montreal, 1976. xxii, 248 pp., illus. Paper, $12. Ecologie de la Zone de l'Aéroport International de Montréal.

The Eggs and Planktonic Stages of British Marine Fishes. F. S. Russell. Academic Press, New York, 1976. xvi, 524 pp., illus. $49.75.

Elementary Particle Physics. E. Paul, H. Rollnik, and P. Stichel. Springer-Verlag, New York, 1976. vi, 148 pp., illus. $26.30. Springer Tracts in Modern Physics 79. *To order this book circle No. 351 on Readers' Service Card.*

The Endocrine Function of the Human Ovary. Papers from a meeting, Florence, Italy. V. H. T. James, M. Serio, and G. Giusti, Eds. Academic Press, New York, 1976. x, 520 pp., illus. $25.25.

Engineering Geological Maps. A Guide to Their Preparation. Unesco Press, Paris, 1976 (U.S. distributor, Unipub, New York). 80 pp., illus. Paper, $12.55. Earth Sciences, 15.

Epileptic Seizures—Behaviour—Pain. Proceedings of a symposium, St. Moritz, Jan. 1975. W. Birkmayer, Ed. University Park Press, Baltimore, 1976. 372 pp., illus. $29.50.

Fluorescent Protein Tracing. R. C. Nairn. Livingstone (Longman), New York, ed. 4, 1976. xviii, 648 pp. + plates. $45.

Fossils and Progress. Paleontology and the Idea of Progressive Evolution in the Nineteenth Century. Peter J. Bowler. Science History Publications (Neale Watson), New York, 1976. viii, 192 pp., illus. $9.95.

Fred Bear's Field Notes. Fred Bear. Doubleday, Garden City, N.Y., 1976. xii, 288 pp., illus. $8.95.

The Geology of Bates County, Missouri. Richard J. Gentile. Missouri Department of Natural Resources Geological Survey, Rolla, 1976. iv, 90 pp., illus. + loose map. Paper, $2. Report of Investigations, No. 59.

Geometric Algebra over Local Rings. Bernard R. McDonald. Dekker, New York, 1976. xiv, 422 pp., illus. $29.50. Monographs and Textbooks in Pure and Applied Mathematics, 36.

Guide Dogs for the Blind. Their Selection, Development, and Training. Clarence J. Pfaffenberger, John Paul Scott, John L. Fuller, Benson E. Ginsburg, and Sherman W. Bielfelt. Elsevier, New York, 1976. xii, 226 pp., illus. $24.75. Developments in Animal and Veterinary Sciences, 1.

Handbook of Biochemistry and Molecular Biology. Proteins. Gerald D. Fasman, Ed. CRC Press, Cleveland, ed. 3, 1976. Three volumes, illus. Vol. 1. xiv, 428 pp. $49.95. Vol. 2. xvi, 790 pp. $61.95. Vol. 3. xviii, 634 pp. $56.95.

High Resolution NMR Spectroscopy in Solids. M. Mehring. Springer-Verlag, New York, 1976. xii, 248 pp., illus. $27.90. NMR Basic Principles and Progress, 11. *To order this book circle No. 352 on Readers' Service Card.*

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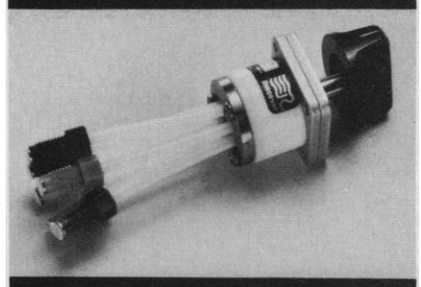

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Music in Developmental Therapy. A Curriculum Guide. Jennie Purvis and Shelley Samet, Eds. University Park Press, Baltimore, 1976. x, 254 pp. Spiral bound, $9.75.

Niels Bohr Collected Works. L. Rosenfeld, Ed. Vol. 3, The Correspondence Principle (1918–1923). J. Rud Nielsen, Ed. North-Holland, Amsterdam, 1976 (U.S. distributor, Elsevier, New York). xii, 702 pp. $105.95.

Nitrogen, Phosphorus and Sulphur—Global Cycles. B. H. Svensson and S. Söderlund, Eds. Swedish Natural Science Research Council, Stockholm, 1976. 192 pp., illus. Paper, Sw.Cr. 40. Ecological Bulletins, No. 22. SCOPE Report 7.

Non-Vocal Communication Techniques and Aids for the Severely Physically Handicapped. Papers from a workshop, 1975. Gregg C. Vanderheiden and Kate Grilley, Eds. University Park Press, Baltimore, 1976. xvi, 228 pp., illus. Paper, $12.50.

Nuclear Analytical Chemistry V. Tables, Nomograms and Schemes. J. Tölgyessy, Š. Varga, P. Dillinger, and M. Kyrš in collaboration with J. Rais, C. Konečný, and L. Kokta. University Park Press, Baltimore, and VEDA, Bratislava, Czechoslovakia, 1976. 494 pp. $29.50.

Primate Models of Human Neurogenic Disorders. V. G. Startsev. Translated from the Russian edition (Moscow, 1971) by Marienne Schweinler and Vadim Pahn. Douglas M. Bowden, Transl. Ed. Erlbaum, Hillsdale, N.J., 1976 (distributor, Halsted [Wiley], New York). x, 198 pp., illus. $19.95. *To order this book circle No. 360 on Readers' Service Card.*

Proceedings of the Sixteenth International Machine Tool Design and Research Conference. Manchester, England, Sept. 1975. F. Koenigsberger and S. A. Tobias, Eds. Macmillan, London, 1976 (U.S. distributor, Halsted [Wiley], New York). viii, 598 pp., illus. $87.50. *To order this book circle No. 354 on Readers' Service Card.*

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Progress in Neurobiology. Vol. 6. G. A. Kerkut and J. W. Phillis, Eds. Pergamon, New York, 1976. viii, 382 pp., illus. $50.

Protein Crystallography. T. L. Blundell and L. N. Johnson. Academic Press, New York, 1976. xvi, 568 pp., illus. $43. Molecular Biology.

Radiologic Examinations in Orthopaedics. Methods and Techniques. E. Hafner and H. Ch. Meuli. University Park Press, Baltimore, 1976. 200 pp., illus. $39.50.

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