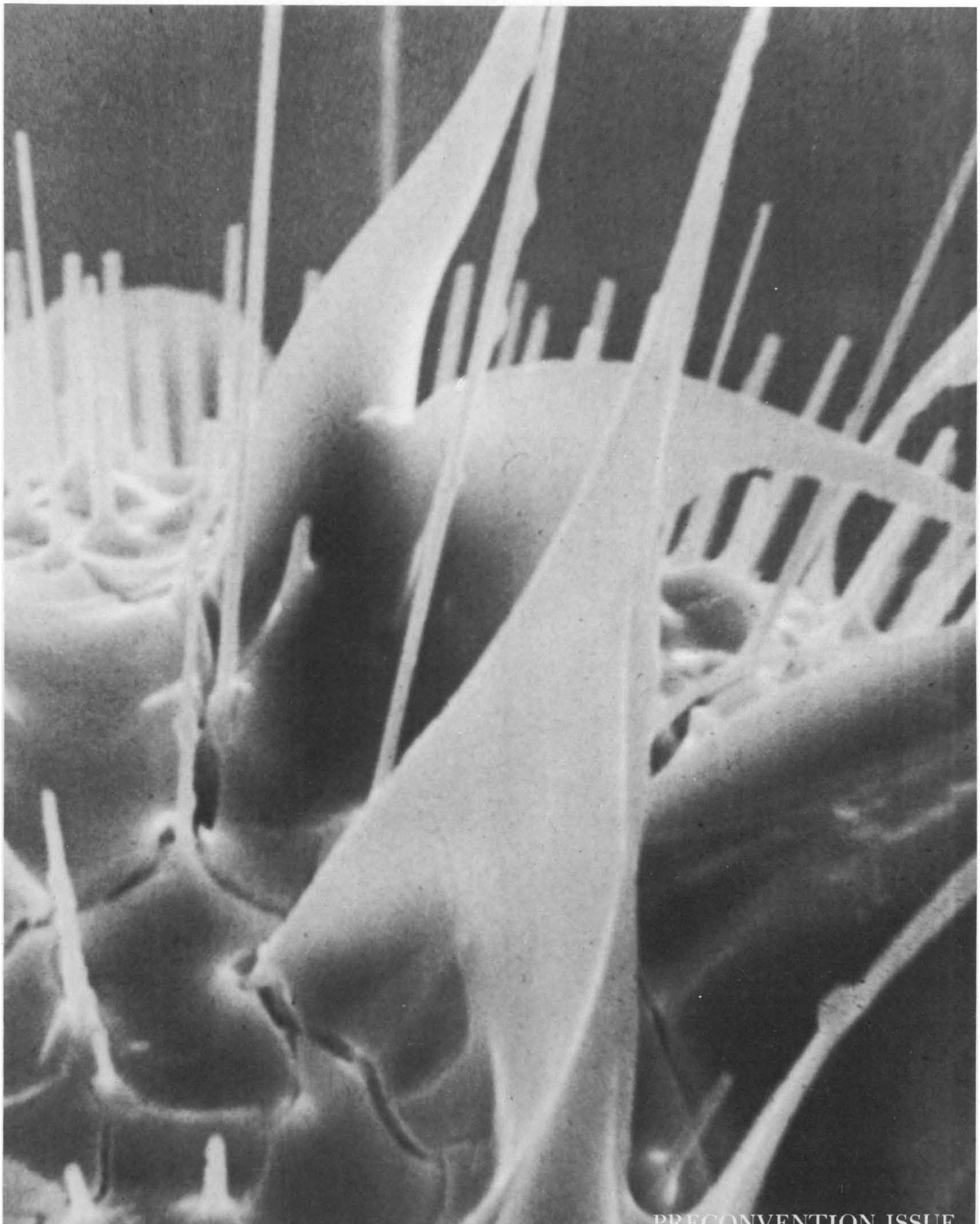
SCIENCE

8 December 1967
Vol. 158, No. 3806

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



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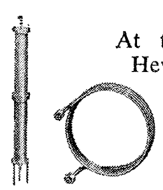
COVER

Globigerina bulloides (d'Orbigny), Recent, from 200-meter depth on the Scotian Shelf. Details of spinal development on the ultimate chamber adjoining the apertural opening of the shell (× 3500). The new scanning electron microscope ranges in magnification from × 50 to greater than × 100,000. See page 1318. [G. A. Bartlett, Bedford Institute of Oceanography]

A close look at the pill and other molecules ...with effective instruments

The Art of Making Fine Chemicals



At the 1965 Pittsburgh Conference, Hewlett-Packard introduced to the chemical industry a large-scale preparative gas chromatograph. Where prep GC had previously been limited to producing, at best, a few *milliliters* of high-purity chemicals during a long day's operation, this new H-P instrument easily separated a *liter* of equally pure materials in a few hours.

As is often the case with technological advancements that suggest a commercial value, incredulity ensued—partly because claims about the instrument were misunderstood, partly because the largest element of the scientific community is from Missouri. Large-scale prep GC became one of 1965's chemical controversies. Yet today, a scant 3 years later, H-P's large-scale prep GC is a fixture in scores of chemical companies around the world, on the basis of its *demonstrated* rather than claimed capabilities.

The characteristic elements of the H-P instrument are the 4-inch diameter column whose relative capacity ratio is more than 100 times greater than conventional prep columns; and the flow homogenizer, an ingenious piece of hardware that removed the last barrier to the use of such large columns, i.e., non-uniform carrier gas flow leading to loss of resolution. Because of these two elements, the instrument has a gargantuan appetite for performing high-purity separations. For example, it separated a gallon of rectified turpentine (that's almost 4 liters) into 1733 milliliters of α-pinene, 701 milliliters of β-pinene, both with a purity of over 98%; instrument running time was 30 hours. In a 7-hour run, the instrument separated 970 milliliters of C_8, C_9 and C_{10} methyl esters, collecting 906 milliliters in the following purities: C_8 and C_{10}, 99.8%; C_9, 99.2%. The same work would have taken 6 months on a conventional prep GC.

Based on these and many similar separations, the importance to the chemist of the H-P prep GC is easily described: it produces high-purity chemicals so fast, so conveniently, and so economically that every chemist who needs them—analytical, organic, biomedical—can now prepare his own, whether he needs a microliter or several liters of a pure substance . . . for use in reaction studies, for analysis, or even for commercial purposes. Of course if all three types of chemists work in the same lab, the H-P prep GC also creates a new problem: who gets to use it first. For help in solving most prep GC problems except this one, write for Data Sheet 775/6.

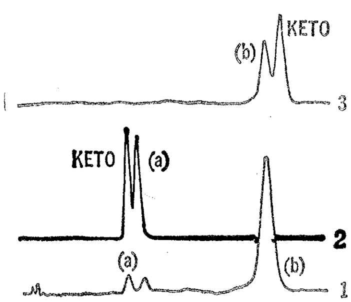
Pandora's Pill Box

Although five to seven million American women have already consumed more than four billion oral contraceptives, there is still much uncertainty concerning their long-term effect on the human body.

The issues are scientific and the questions involve chemistry, biochemistry and physiology . . . endocrinology, pharmacology, and gynecology. The answers are in widespread research in every scientific discipline concerned.

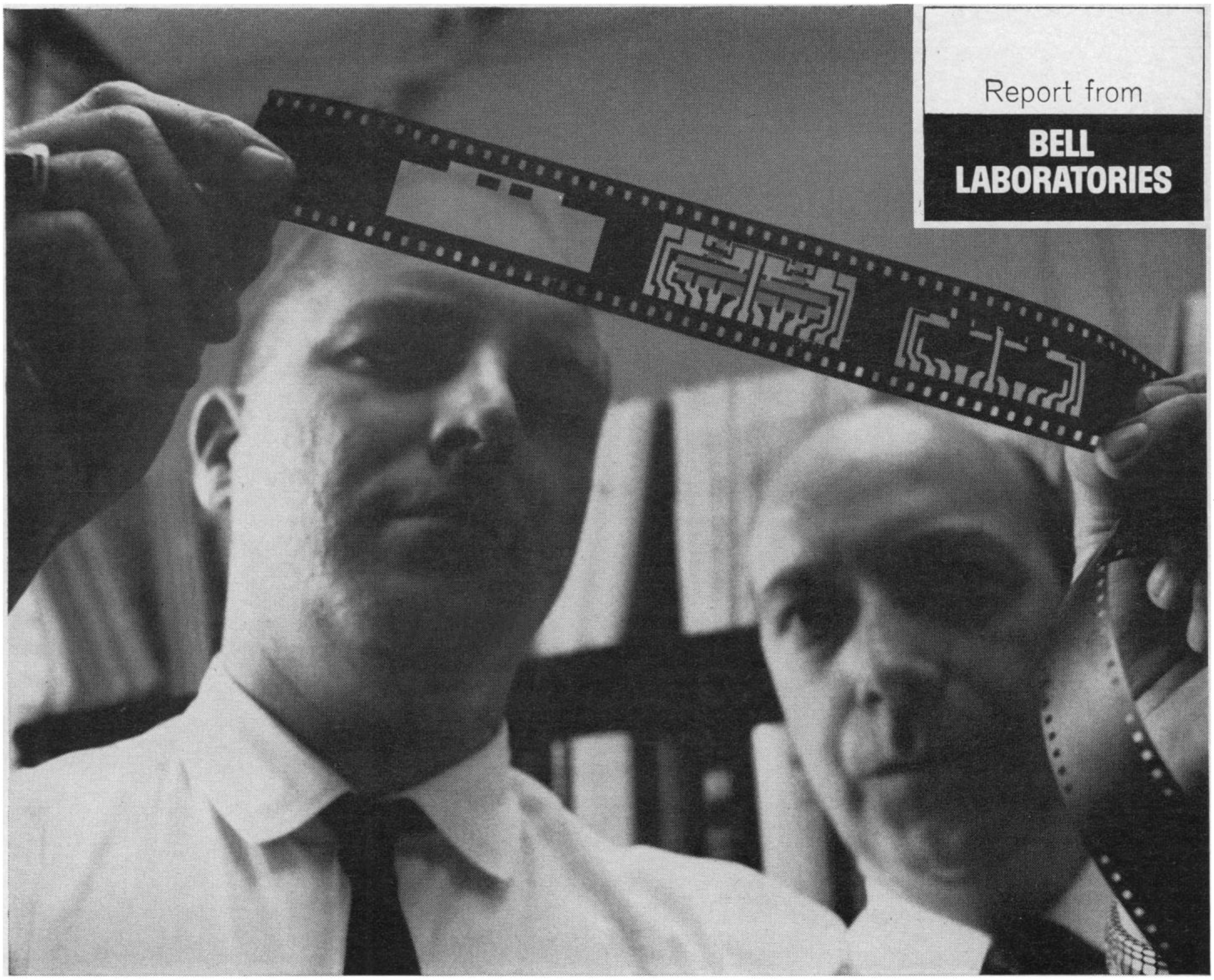
It is in the chemical and biochemical disciplines that Hewlett-Packard assumes its concern with the massive anti-fertility drug research program, specifically, through its Gas Chromatography Applications Laboratory, in Avondale, Pa. Thus far, Avondale's involvement has centered around two of the most widely used synthetic hormones: *Norethindrone* and *Mestranol*. Both are labile steroids, subject to thermal degradation. When these steroids break down—whether during manufacture, in the human environment, or during analysis—they form a keto analog so similar in chemical structure to the original molecule that it is extremely difficult to differentiate one from the other. The rub is that the scientist *must* be able to tell them apart since the steroid is an effective anti-fertility agent while the keto analog is not.

Thus there can be no confidence in any chemical analysis of the pill unless it is first demonstrated that the analytical procedure can separate the steroid from its keto analog . . . and that it can preserve the chemical integrity of the two types of molecules during the analysis.



As far back as 1964, our application chemists proved that the Model 402 High-Efficiency Gas Chromatograph has both capabilities. The proof is presented here in the form of three chromatograms. The first, an analysis of a sample containing the two steroids, shows the presence of *Norethindrone* (b) and *Mestranol* (a), and the absence of their keto analogs: this is proof that the 402 respects the chemical integrity of the steroids. If the Model 402 were causing degradation of the steroids, the chromatogram would show the presence of at least some quantity of the keto analogs. The second chromatogram shows the presence of both the steroid *Mestranol* and its keto analog, thus demonstrating the 402's ability to separate one from the other when the two coexist in a sample. The same is true of the third chromatogram, this time with respect to *Norethindrone*.

Lest it become obscure at this point, the noteworthiness of these analyses is twofold: they demonstrate the 402's ability to detect the labile steroids used in anti-fertility drugs without causing degradation during the analytical procedure; and its ability to separate compound pairs of such steroids one from the other and from their keto analogs. Extrapolating from these points, the 402 can be seen as a fast means for quality control in anti-fertility drug preparation, as the basis for investigation of its clinical progress and beyond that as a possible means for *in vivo* patient monitoring. A report of the anti-fertility drug analysis as it was originally presented in *Facts & Methods*, Vol. 5 No. 3, is available on request.

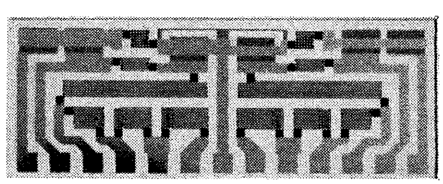


Thin films: faster by computer

Arthur G. Gross and Harry M. Kalish of Bell Telephone Laboratories have developed a computer program whose end product is a set of correctly sized photographic "masks" for making prototype thin-film networks. The masks control the deposition and shapes of various widths and thicknesses of conductive, resistive, and dielectric materials that make up such circuits. (These frequently begin as tantalum, deposited onto a glass or ceramic substrate and chemically treated to produce desired electrical properties.)

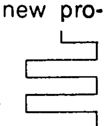
Controlled by the new program, a computer feeds a precision microfilm plotter which prints the masks on 35mm film (photo above).

With this system, a prototype can be ready in a day, as against the weeks that may be involved in making high-precision masks for volume circuit production. Usually, for example, a draftsman must make rough sketches and prepare a list of numbers (coordinate points) accurately describing the geometry of the final circuit. Then the actual shapes—greatly enlarged—are cut into plastic sheets on a "coordinatograph." Later, the plastic patterns are photographically reduced to circuit-sized masks, perhaps ½ by 1 inch.



An experimental thin-film filter network —in actual size—made from 35mm film masks. In the top photo, A. G. Gross (left) and H. M. Kalish hold three of the masks used. Each mask controls the formation of a layer of conductive, resistive, or dielectric material. The circuit is built up of a number of such layers.

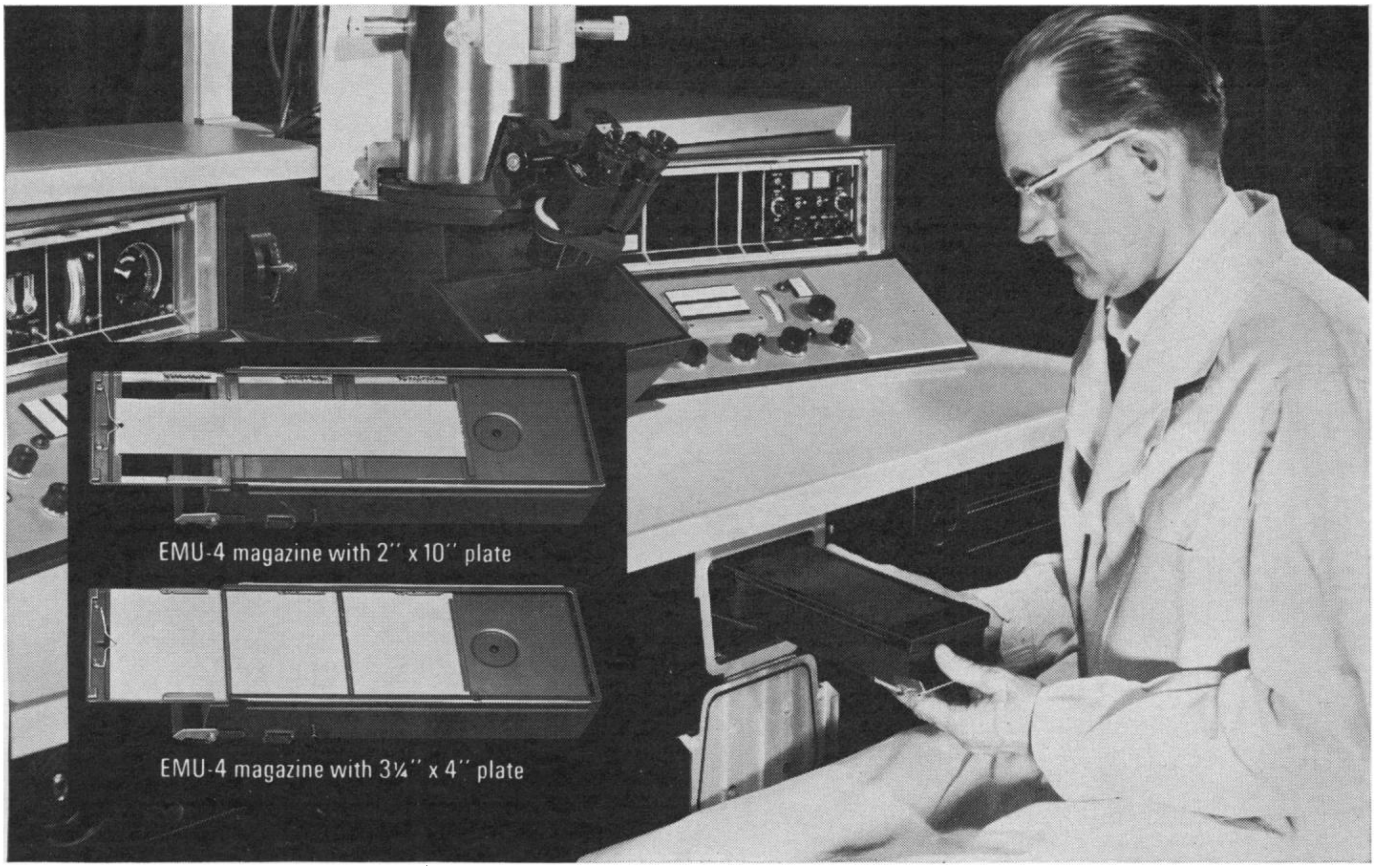
In addition to reducing time and handling, Bell Laboratories' new program relieves the engineer of another tedious job: designing the meandering lines that constitute resistors in these circuits. And the computer resistors are "optimized" . . . fitted into the smallest possible area.



To give the engineer freedom to use irregular plane shapes, the program includes a subroutine which closely approximates geometric figures used in making thin-film circuits.

Bell Telephone Laboratories
Research and Development Unit of the Bell System

EMU-4...The "New Look" in Electron Microscopes



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Which plate size is best for electron micrographs?

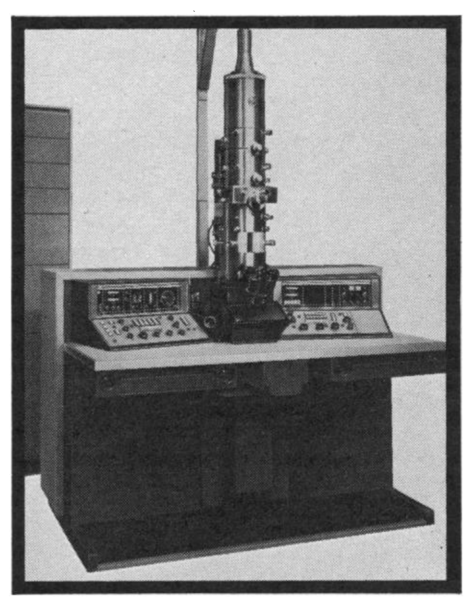
The best plate size is a *standard* size, for only a standard size gives you a selection of emulsion characteristics, is easily and quickly available in local supply and demands no premium in price.

The EMU-4 plate cassette—there are six in a magazine load—is designed with those thoughts in mind: They accommodate—interchangeably—the standard 2" x 10" spectroscopy plate or the standard 3¼" x 4" projector-slide plate or cut film in 4" x 10" pieces (which is precisely one-half of a standard 8" x 10" piece of sheet film).

Since they are universally available, these plates are competitively priced, offer wide choices of emulsion types and are usually stocked at local supply houses.

Using standard-size photo materials is but one of the many features of the new EMU-4. Among the others are: transistorized, modularized electronics; an almost-impossible-to-contaminate objective aperture; a truly universal specimen chamber; a quick-change specimen airlock and many others.

For additional information, write RCA Scientific Instruments, Bldg. 15-5, Camden, N. J. 08102. In Canada: RCA Victor Co., Ltd., Montreal. Overseas: RCA International Division, Clark, N. J. 07767.



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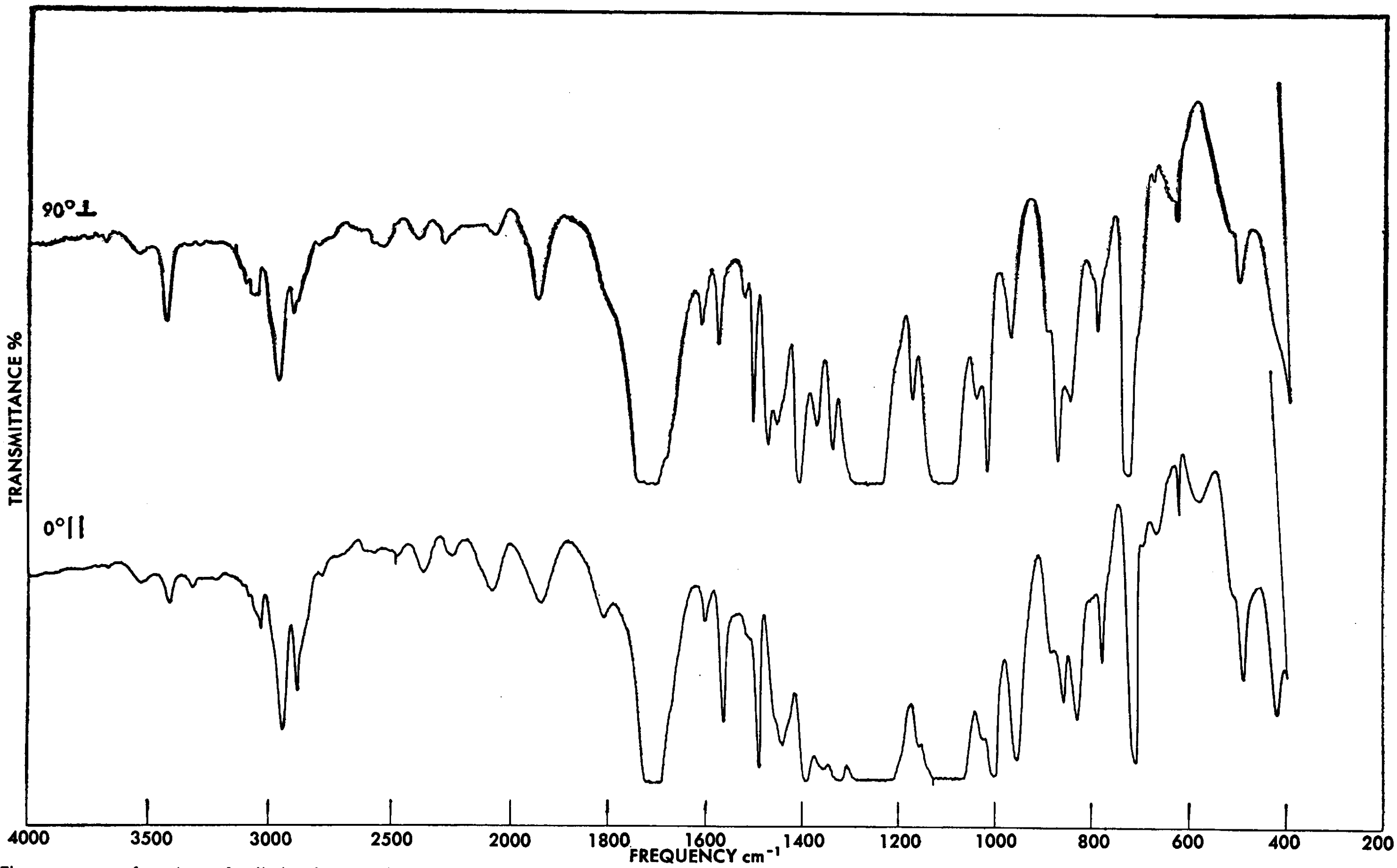

These spectra, of a piece of rolled polyester film only 1.5 mm square, were taken with the aid of two P-E accessories: a wire-grid polarizer and a 1 X 4 refracting beam condenser (see illustration). They show how polarized radiation can be used to obtain fundamental information on even the smallest polymer samples. From the dichroic behavior of two absorption bands, it can be seen that the polymer chains are preferentially aligned parallel to the machine, or rolling direction. Here's how: the two spectra were taken with the wire grid polarizer at orientations 90° apart. The relative intensities of the C=O band at 1725 cm^{-1} and the aromatic carbon-hydrogen bending vibration at 1500 cm^{-1} can be used to determine the relative orientations of the transition moments associated with these vibrations. The 1725 cm^{-1} band has its maximum intensity when the polarizer is oriented to transmit radiation perpendicular to the machine direction of the film: i.e., the band exhibits perpendicular dichroism. On the other hand, the 1500 cm^{-1} band shows parallel dichroism. The Model 621 makes this kind of analysis easy to do.

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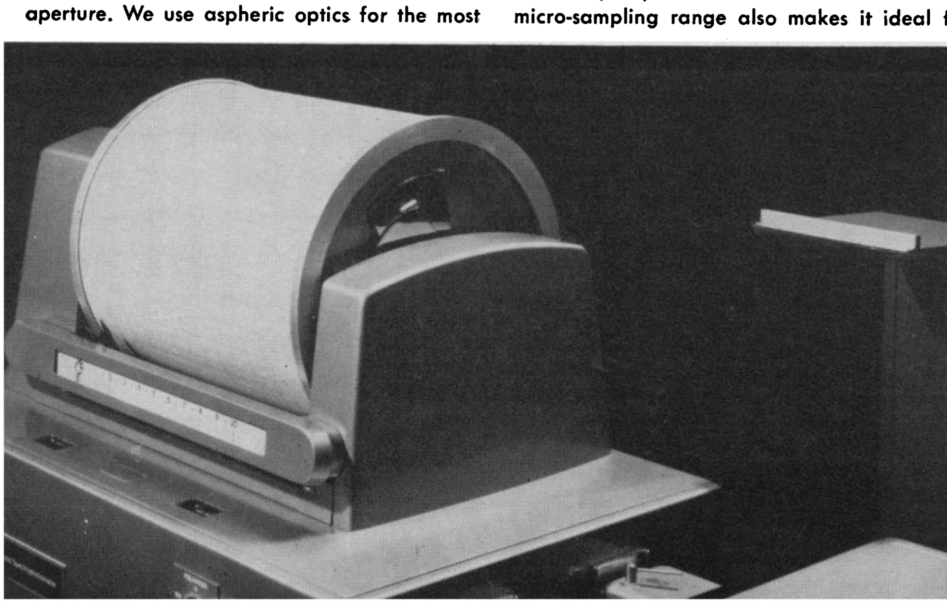

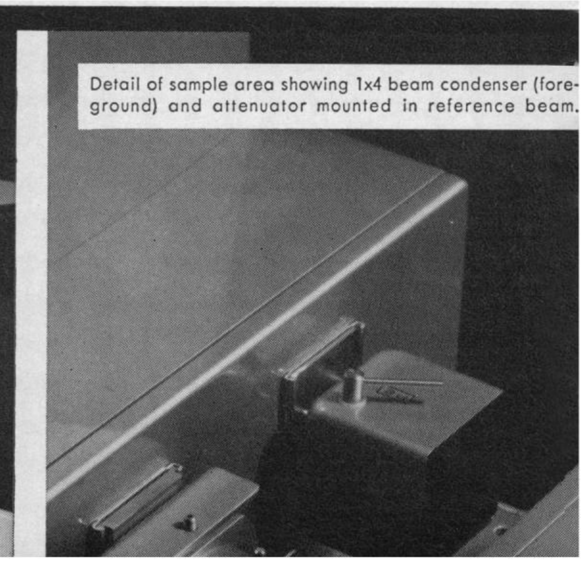

Detail of sample area showing 1x4 beam condenser (foreground) and attenuator mounted in reference beam.

A Revolt against Time and Effort Reports

I believe the following considerations should be brought to the attention of the academic scientific community. They concern time and effort reports required in connection with government research grants. In October 1966, the Association of Graduate Deans passed the following resolution:

> Be it resolved that the Association of Graduate Schools instruct its President to call upon the Association of American Universities to join in addressing to the President of the United States our respectful requests: 1. that the present requirement for reporting of effort by individual members of the professional staff be suspended immediately because it admits no meaningful compliance.

This resolution is reproduced on page 126 of the *Journal of the Proceedings* of the AGS, 1966, with further explanations as follows:

> The earlier motion on individual effort-reporting had proposed involving CGS in the attempt to get a revision, and had not proposed immediate suspension of the present requirement while negotiations were being undertaken. Dean Halford feared that if negotiations alone were proposed the results would be delayed two to four years, and that AGS had the most at stake in this area whereas most of the institutions in CGS were not deeply involved in this problem. Furthermore, as the presidents of AAU had expressed interest in working with the AGS in implementing specific recommendations of the Policies Committee report, and since there are on many campuses separate officers other than the graduate deans who serve as research coordinators, the group decided to address the AAU presidents in these matters. Dean Halford announced that in the event that this invitation to the presidents is not acted upon by them, the dean would be informed by mail as to some alternate course of action.

[*After adjournment of the AGS meeting, President McCarthy transmitted this resolution to President Grayson Kirk and President Nathan Pusey, President and Secretary of AAU respectively. On December 2, 1966 he was informed that President Kirk had appointed a committee to consider the issues raised in this resolution. Its members were Herbert E. Longenecker of Tulane as chairman; President Fred H. Harrington, Wisconsin; President James A. Perkins, Cornell; Dean Ralph S. Halford, Columbia; and Dean Joseph L. McCarthy, University of Washington.* —ED.]

I am informed that the committee appointed by the presidents has never met. But, in any case, what did the presidents expect after the problem had been considered by a body like the Association of Deans? As I have emphasized repeatedly, the threat to unfettered academic support does not only arise from certain pressures in the government, but from inadequate representation of academic interests by some university administrators (Letters, 17 Feb.). I regard the inaction of the presidents, members of the AAU, as a failure in the exercise of academic responsibilities.

By their inaction, the presidents will lose the confidence of the professors, and they have allowed a bad situation to deteriorate still further. The professors will lose confidence in normal channels of administration, and seek other channels for redress. As an example, the Council of the American Mathematical Society on 29 August passed the following resolution:

> The Council of the American Mathematical Society urges responsible university officers to take immediate action to have time and effort reports and similar documents pertaining to faculty members' time eliminated, because it considers that such documents are incompatible with academic life and work. The council reiterates the traditional view that teaching and research are inseparable and that accounting procedures in universities must take account of their unitary character.

Simultaneously, the Council instructed the president of the AMS to appoint a committee "to work toward mutually acceptable modifications with appropriate Government administrators." This committee has been appointed (G. W. Mackey, Harvard; R. S. Palais, Brandeis; Alex Rosenberg, Cornell).

Under the circumstances, I don't see how deans with any self-respect can continue to pass on for signing to their faculties the time and effort reports. And furthermore, I don't see how the professors can agree to sign them.

As for the larger picture, the universities are becoming more and more dependent financially on the government. At a time when policies governing the universities are being determined for the foreseeable future, it is extraordinarily important that our administrators should insure, in their dealings with the government, that traditional academic values and standards are upheld. Ultimately, it is also the responsibility of the professors to refuse to submit to requirements which destroy these standards.

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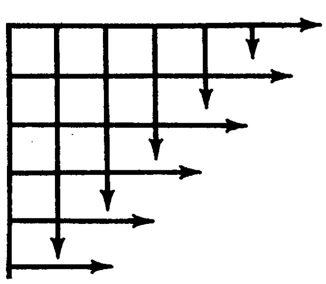

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SCIENCE

Selective Service Solution

At the end of the current academic year the pool of men eligible for Selective Service induction will suddenly be swelled by the addition of 1968 college graduates, men who receive graduate degrees in June, and those who complete their first year of graduate work. Under existing regulations the oldest men in this pool must be inducted first. The result will be that the Army will receive very few inductees in the preferred 19-to-20 age range and will find from 50 to 75 percent of draft calls being filled by men with college degrees or with a year or more of graduate work—a prospect that pleases neither the Army, the employers of engineers and other professional manpower, nor persons interested in the continuity of graduate education.

The present regulations must be changed. The changes should be announced soon and should be designed to retain flexibility in the size of draft calls; provide the Army with a better age mix of inductees; and reduce the uncertainty concerning induction that now makes it difficult for young men (and also for others, such as graduate school faculties) to plan with reasonable confidence for a year or more ahead.

There is substantial but by no means unanimous support for the proposition that, when not all young men are required to enter military service, those who are required to do so should be selected by some random method. The President proposed this idea to Congress, but did not spell out the details. Lacking a specific plan, Congress refused to approve, but invited the President to submit new legislation later. It now seems unlikely that new legislation will be adopted in time to be of much help in 1968; there are too many other items on the congressional docket. Legislation, however, is not necessary; the Executive already has the authority necessary to accomplish most of what is needed.

One kind of "lottery" could be used without new legislation. The existing law would permit reversing the present oldest-first method of selection by designating a specific age group—probably the 19-year-olds—as the "prime age group" for induction. Older men who have been deferred—for example, men allowed to enter graduate school this past fall—would be treated when their deferment ended as if they were just reaching age 19. The prime age group would therefore include men who who were actually 19 and older men being treated as if they were 19. Selection would still have to be on an oldest-first basis, but the "oldest," under these circumstances, would be those born in the earliest months of the year. Thus the "lottery" of birth dates 19 or more years ago would now be used to determine order of induction.

This system would call a large number of college graduates and graduate students into military duty next year, but would leave a larger number free to continue graduate work or to enter essential occupations. It would provide the Army with a better age mix in 1968 than existing regulations would, and a still better mix in following years. And it would give all of the young men involved a better opportunity to plan realistically, for each could estimate with some degree of assurance whether and when he was likely to be called for induction.

These arrangements would not solve all of the problems; for example, there are still uncertainties as to which graduate students should be deferred. The arrangements may not be permanent in all details; for example, we are unlikely to continue to penalize those with January birthdays year after year. But the proposed regulations would allow orderly planning for the year ahead. They can be introduced quickly and without new legislation. They offer the best immediate solution of an urgent problem.—DAEL WOLFLE

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