SCIENCE

1 October 1971

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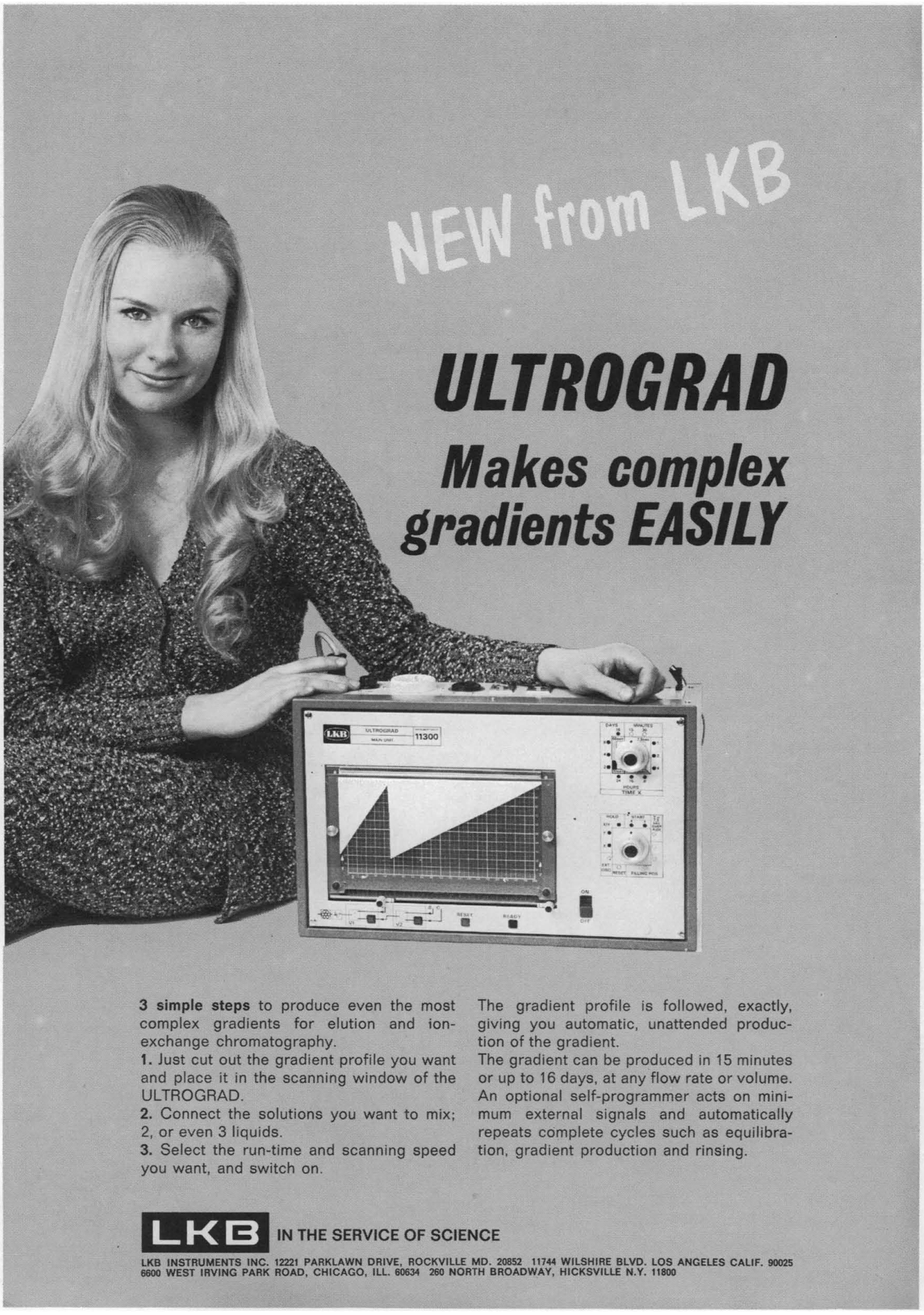
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



3 simple steps to produce even the most complex gradients for elution and ion-exchange chromatography.

1. Just cut out the gradient profile you want and place it in the scanning window of the ULTROGRAD.

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The gradient profile is followed, exactly, giving you automatic, unattended production of the gradient.

The gradient can be produced in 15 minutes or up to 16 days, at any flow rate or volume.

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We want to be useful ...and even interesting

Kodak

The protein in the products and the protons in the protein

While merely minding our own business—photo materials—we have come up with a way of analyzing a proton magnetic resonance spectrum of protein that may merit attention elsewhere. Like sausage makers, we have yet to find a good replacement in our products for protein. In our case it's the protein gelatin. We think we are beginning to understand the signals from the variously situated protons in the macromolecule. The sausage business can probably get along without our contribution, but investigators of metal-activated enzymes may be interested.

As reported earlier this year in *Science* *171*:573-4, P. I. Rose of the Kodak Research Laboratories first obtained spectra from model compounds like homopolypeptides and amino acids. This provided a glossary useful in analysis of the complicated gelatin spectrum. He then observed changes from the introduction of the paramagnetic Co^{++} ion. Aspartyls and glutamyls are the two protein building blocks that have carboxyls on their side chains. The PMR spectrum clearly shows that's where the Co^{++} gets bound.

Microfilm, the information medium that advances when expected to retreat

While our own and many other laboratories labor toward more sophisticated information storage devices than the familiar gelatin dispersions of silver halide, the photographic process continues to entrench itself all the deeper.

Wet chemistry? *What* wet chemistry? Film? *What* film? Oh, there is reputed to be film inside those cartridges, but you never touch it. Meet the newest Kodak microfilm system:

Drop in to microfilm

Drop in to process

(no external plumbing)

Drop on to retrieve

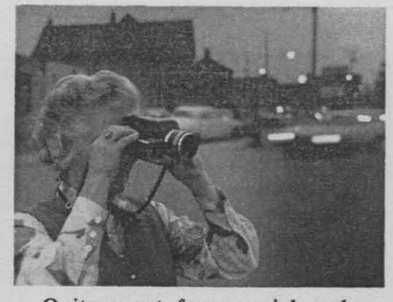
Wouldn't "Instamatic" be a good trademark to put on such equipment? Darn right.

To talk about it, look for Kodak in the Yellow Pages under "Microfilming."

The little orange light that signals a long and somewhat metaphysical message

We are pleased to announce a new generation of movie cameras intended, when loaded with the new KODAK EKTACHROME 160 Movie Film (Type A), to dispense with photographic lights when shooting at indoor social or athletic events.

To allow movie-making at the same light level as suffices for the eyes of the participants in such events, KODAK XL Movie Cameras come with $f/1.2$ EKTAR Lenses. All the light from the lens reaches the film. The shutter has a 230° opening instead of the usual 165°. Choice is provided of 18 or 9 frames/sec. Steadiness is provided by making you use your forehead for support. The same film is also OK in full sunlight when used in these cameras.



Quite apart from social gatherings, there may be applications for unobtrusive movie-making at very low light level. You point the camera at what you want to film. Perhaps an orange disk lights up above the scene in the viewfinder.

The signal light goes on somewhere between roughly 6 and 8 footcandles of illumination on the scene. Half that if you are willing to shoot at 9 frames/sec. The following message is thereby conveyed:

"What you will get if you press the button right now will look darker than what is generally expected in good pictures. On the other hand, it may be no worse than what you are seeing in the viewfinder at this moment. Indeed, if the picture you will see projected on the screen were to look brighter than what you are now seeing, it would no longer be a truthful representation, would it? Remember that the photographic process integrates light but your visual mechanism does not. Remember that on the darkest of nights still pictures can be forced by sufficient exposure to look like full daylight. In one sense, such a picture is a lie, of course; but if it happens to be a picture of your house, the house looks genuine enough.

"Now you are trying to make movies, and we are warning you that unless you can turn off this orange light by getting more illumination on this scene or by finding some brighter scene to photograph, you may not be satisfied with your results. But if you prefer subjective realism to objective delineation, you may like them very much."

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COVER

Fox squirrel (*Sciurus niger*). The bones of these squirrels are stained red by uroporphyrin I, an abnormal porphyrin which accumulates because of a partial deficiency of the enzyme uroporphyrinogen III cosynthetase. A similar enzyme deficiency occurs in the human and bovine disease, congenital erythropoietic porphyria. See page 59. [Bill Clark, University of Maryland]

Recent Advances in the Preparation of L.S.C. Samples

Radioactive Proteins

A paper on the *"Rapid and Simplified Method for Liquid Scintillation Counting of Radioactive Proteins"*[1] clearly indicates the advantages of Aquasol for determining radioactivity of proteins. Observed counts from replicate samples prepared in Aquasol are highly reproducible; in addition, the observed radioactivity with Aquasol is higher than with a toluene/Triton X-100 (2:1) scintillation solution. Liver samples prepared in Aquasol accurately indicate actual protein activity, as shown by a linear response to protein concentration, and by a decrease in radioactivity of protein following cycloheximide and dimethylnitrosamine. Aquasol has the unique property of forming gels when mixed with water. This gel will hold the protein in suspension. On the other hand, samples prepared in toluene/Triton X-100 (2:1) scintillation solution settle on the bottom of the vial where self-absorption becomes an important factor. A procedure using Aquasol with acid-precipitated proteins follows:

1. Apply hot acid-precipitated proteins to Millipore filter under vacuum
2. Wash filter cake
3. Place filter cake and filter into liquid scintillation vial with 3.5 ml water
4. Add 11.5 ml Aquasol, shake well and count

Lipid Extraction From TLC

Data from the article, *"Recovery of Lipids from Thin-Layer Chromatography for Radioassay"*[2] demonstrates that the combination of a multipurpose scintillator, Aquasol, and a suitable elution system can give complete recovery of all classes of lipids from TLC plates. Both neutral and phospho-lipids give quantitative recoveries in the indicated systems. It was ascertained that up to 300mg of silica gel could be added to Aquasol without impairment of ^{14}C counting efficiency. Specific applications follow:

Neutral Lipids

1. Develop plate in hexane:ether:acetic acid (90:10:1)
   Unsaturated Lipids — expose to iodine vapor and allow for sublimitation of iodine.
   Saturated Lipids — develop in duplicate and spray one spot with sulfuric acid.
2. Suspend silica gel in 15 ml Aquasol
3. Shake well and count

Phospholipids (except phosphatidylcholine)

1. Develop plate in chloroform:methanol:7M ammonia (230:90:15)
2. Visualize spots by exposure to iodine vapor or H_2SO_4 spray
3. Suspend silica gel in 15 ml Aquasol
4. Shake well and count

Labeled Inulin

Inulin labeled with tritium or carbon-14 is widely used for assessment of glomerular filtration rate and determination of extracellular spaces. Signficant decreases in observed radioactivity with time have, in many instances, precluded the use of liquid scintillation counting as an analytical technique. The *"Evaluation of Liquid Scintillation Systems for the Assay of Tritiated Inulin"*[3] conclude that an Aquasol/water system affords ease of sample preparation, high counting efficiency and long-term sample stability. Samples prepared by this technique remained stable over the ninety-day experimental period, maintaining a satisfactory counting efficiency of approximately 27 percent. A brief description of the sample preparation technique is as follows:

1. Place tritiated inulin aliquod in liquid scintillation counting vial
2. Adjust sample volume to 3.5 ml with water
3. Add 11.5 ml Aquasol, shake well to form stiff gel, count

Acrylamide Gels

Data from *"Acrylamide Gel Electrophoresis of Radioactive Compounds With Accompanying Low Background"*[4] describes a method for the detection of radioactive components in polyacrylamide gel disc electropherograms by automated mechanical fractionation with the use of Aquasol. Aquasol also can be successfully utilized in the conventional, non-automated acrylamide gel counting procedures with minimal background interference. Unpublished data provided by Harris-McEvoy follows:

N, N'-methylenebisacrylamide cross-linked

1. Place 20 mg wet sample into glass liquid scintillation vial
2. Cover gel with 0.1 ml 30% H_2O_2 and cap tightly
3. Incubate at 50° until digested
4. Allow to cool
5. Add 10 ml Aquasol, shake well and count

Ethylene diacrylate cross-linked

1. Place 20 mg gel samples into liquid scintillation vials
2. Add 1.5 ml 10% NH_4OH and cap tightly
3. Incubate at 50° until digested
4. Allow to cool
5. Add 10 ml Aquasol, shake well and count

Reduction of Adsorption by Phosphates and Sulfates in Glass L.S.C. Vials

Data on the *"Incorporation of High Concentrations of Phosphates and Sulfates in Samples for Liquid Scintillation Counting"*[5] reports of problems associated with solubility and adsorption on the walls of glass vials by solutions of phosphates and sulfates. For instance, the loss of counts and reduction of apparent radioactivity over a period of time can be minimized by using Aquasol as follows:

1. Add up to 2 ml sample to 15 ml Aquasol
2. If precipitation or turbidity occurs, add water in increments of 0.2 ml, with shaking, until sample clears
3. Count

30% (W/V) Sucrose Density Gradients

Thirty percent (w/v) Sucrose gradient cuts were measured by liquid scintillation counting utilizing Aquasol. The results for tritium labeled samples follow:[6]

Sample Volume	Aquasol Volume	% of Sample	^3H Efficiency	Figure of Merit†
0.5 ml	14.5 ml	3.3	29.9 ± 0.1%*	14.9
1.5 ml	13.5 ml	10.0	29.3 ± 0.4%	44.0
2.5 ml	12.5 ml	16.7	27.0 ± 0.6%	67.5
3.5 ml	11.5 ml	23.3	26.7 ± 0.1%	93.3

†Figure of Merit (efficiency) (volume added sample)

- Counting performed on Packard TriCarb Model 3320
- Absolute efficiency of TriCarb is 60% with sealed ^3H standard in toluene
- Settings: Gain — 50%, Discriminators 50-1000
- 3 samples at each point. Internal standard = 125190 DPM
- All samples clear at room temp.

*S.D. of the mean

References and Notes

1. Marvin A. Friedman, Gail Miller, Arthur McEvoy and Samuel S. Epstein, *Anal. Chem.*, Vol. 43, No. 6 (1971).
2. David Kritchevsky and Saroj Malhotra, *J. Chromatog.*, 52, 498-499 (1970).
3. Arthur McEvoy and Wayne G. Harris, *Anal. Biochem.* (in press) (1971).
4. Bohdan Bakay, *Anal. Biochem.*, 40, 429-439 (1971).
5. Unpublished data, Assay Laboratory, NEN Corp.
6. Unpublished data, Assay Laboratory, NEN Corp.

also destroy the morale of an entire department or university by cutting budgets and by not making any efforts to hold quality faculty members who have offers from other universities. Furthermore, in many fields faculty do not have grants from outside sources to protect them from the administration.

Faculty can, according to Pake, exercise control over their destinies by electing the committees which make decisions crucial to the institution. But what is to prevent the central administration from ignoring the decisions of the faculty? The fear that they might become unpopular? The faculty has not hired them, as they are usually appointed by the trustees. The trustees, then, are the ones to whom the central administration may look for their rewards.

Most disturbing to me is Pake's notion that the faculty has an obligation to watch the purse. Pake seems to imply that the faculty must supervise their own activities in the larger community, so that the fiscal situation of the university is not threatened. This means that the faculty would become lobbyists in the community. Isn't it the duty of the central administration to concern itself with funds, the state legislature, the community, and so forth? The proposal that the faculty be given their salaries in terms of units could spell disaster for the free university. It would mean that a professor would be evaluated in terms of whether he contributed to the general pie or took away from it. Professors acting as private citizens who advocated unpopular causes in the community would soon become anathemas on the campus. They would be suppressed or fired because they reduced the value of the academic share.

Pake's suggestion that a central administrator be given the power to "rearrange the academic units within which the professors serve" would also be disastrous. A central administrator would become involved in cost accounting procedures and might possibly even rearrange departments to get rid of those professors that threatened the traditional elements in the community. It is not the duty of a university to process the largest number of units for the cheapest price possible. A more viable role for the university administrator would be to explain the purpose of education (as it used to be) to the general public. The American university no longer serves

traditional intellectual functions. The trend of the American universities to become factories would be furthered by Pake's suggested reforms.

SCOTT G. MCNALL
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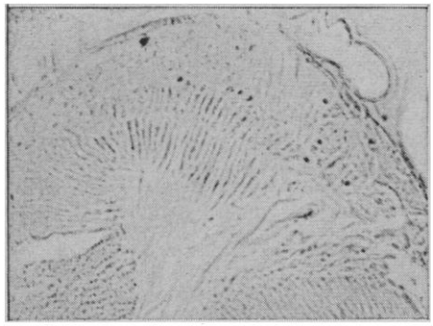
In my article, I attempted to delineate current problems and the university power structure as objectively as I could, based upon my several perspectives as student, alumnus, faculty member, administrator, and now trustee. I champion the exercise of real responsibility by the faculty: setting educational policy, providing educational opportunity for students, maintaining awareness of financial constraints, and initiating actions aimed at terminating tenure for cause, whether the cause be teaching incompetence or faculty abridgement of academic freedom. My suggested prescription for moderate increase in administration power would be unnecessary if faculty would conscientiously meet those responsibilities.

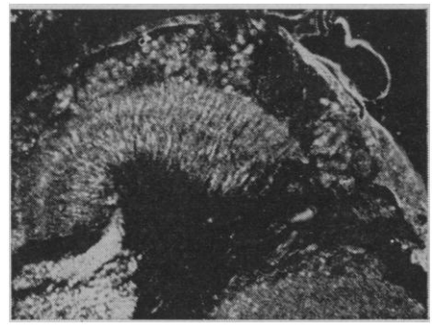
I agree with Griffin that administrators should take time to talk with faculty and students. Chancellor Eliot, with whom I served at Washington University for 7 years, did so extensively. But even a remarkable chancellor in a relatively small university of 7000 students and 1000 faculty found his energies severely taxed as he added those campus chats to his burdensome official responsibilities. On state university campuses with tens of thousands of students, such personal communication by administrators strikes me as impossible.

Most of the letters I have received seem to concede my view that the faculty holds large de facto power. But a few writers (all faculty members in state universities) agree with McNall. Possibly my picture is more applicable to strong private universities like those I know well (Carnegie-Mellon, Harvard, Stanford, and Washington), although I believe it also applies to several major state universities, for example, Berkeley. If it is true that in many state universities an impotent faculty is dominated by administrators and trustees or regents, then we must be even more concerned about the financial (and other) crises that threaten the survival of our private colleges and universities.

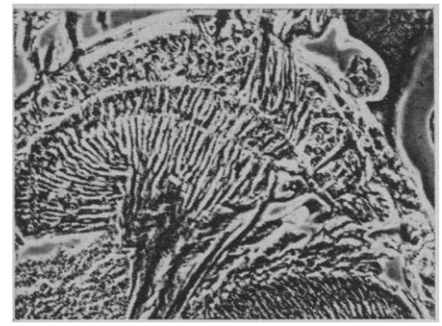
GEORGE E. PAKE
Xerox Corporation, Palo Alto Research Center, Palo Alto, California 94304



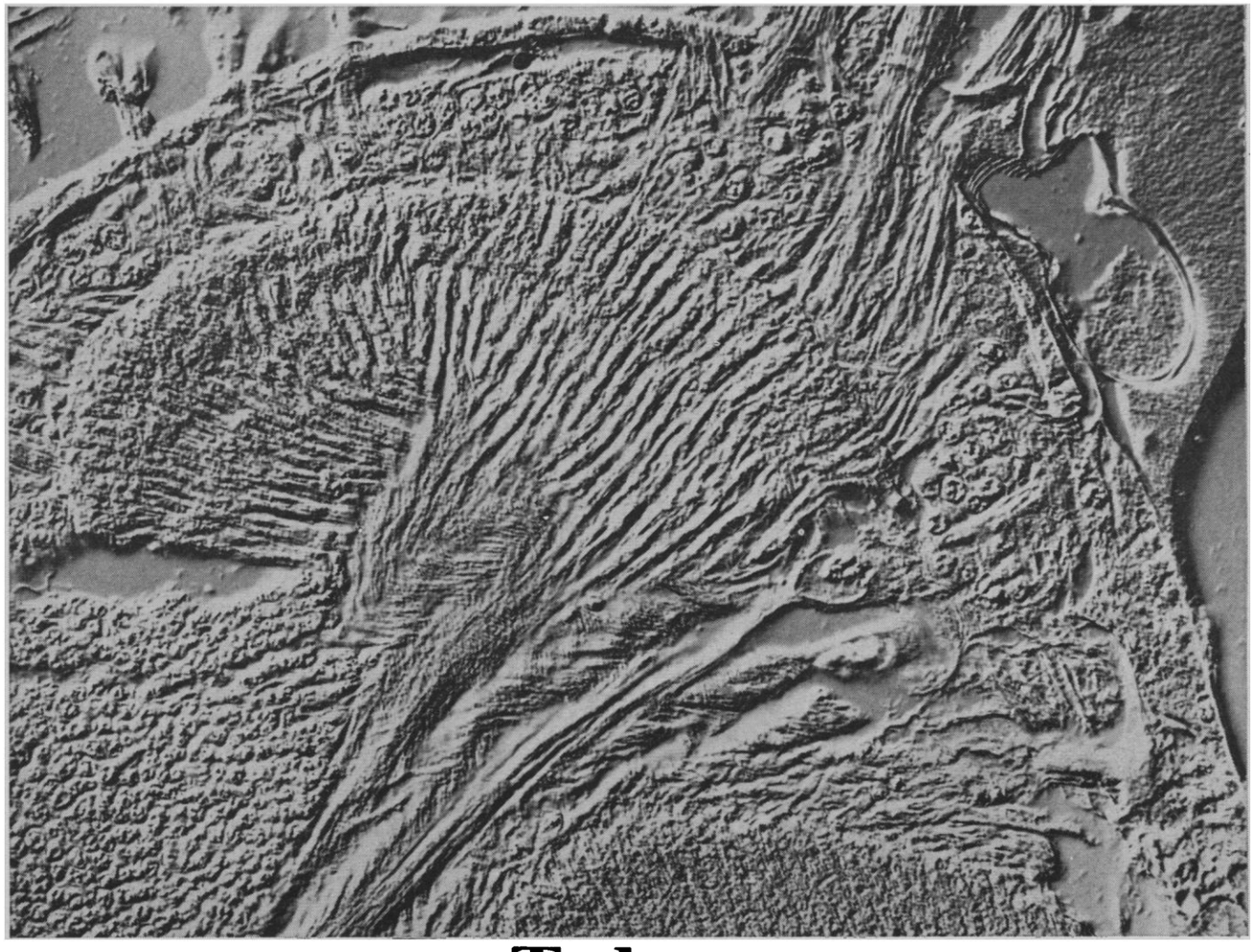
FIRST BRIGHTFIELD



THEN DARKFIELD



THEN PHASE CONTRAST



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Dictation to Science by Laymen

There is the danger that there will be overemphasis on the applied phase of science, for the public is alert to the tangible benefits to be had from it, but hardly realizes the fact that they are all dependent upon long-term advance in fundamental science. . . . As a people we are strongly philotechnical, we have always excelled in the applied, we have not turned with the same success to more philosophical matters. . . .

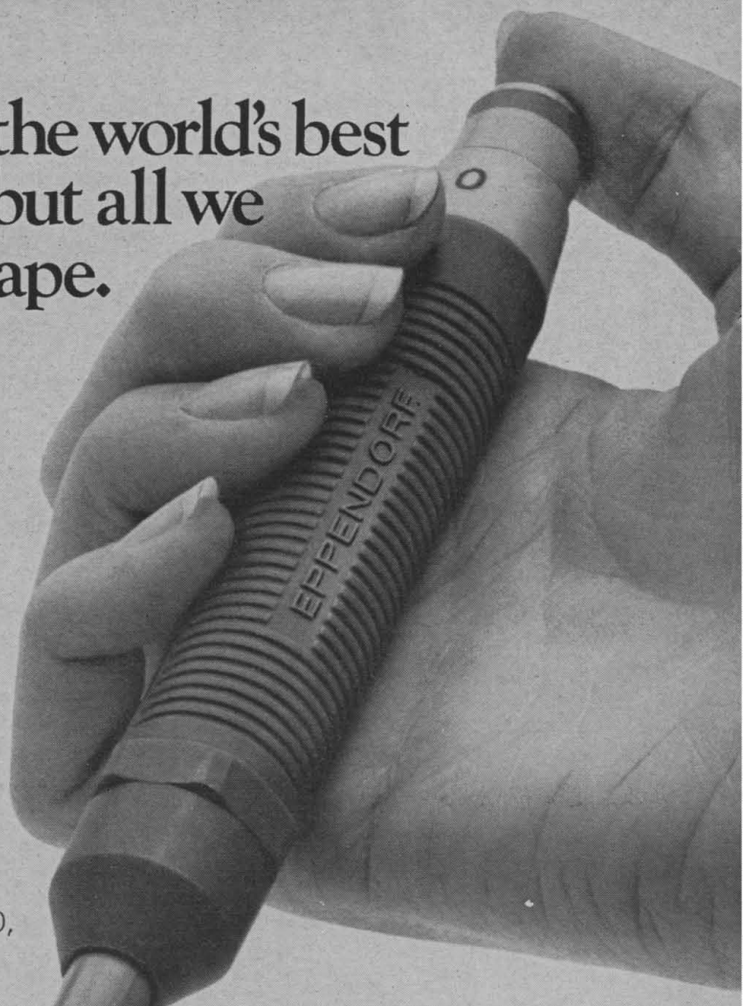
There is also a danger that control of funds may occasion injurious dictation to science by laymen. The fact that this is a somewhat subtle matter renders the danger much greater. In applying science it is often correct that a group of laymen should set the general objectives—in industrial research, for example, where men of diverse backgrounds and interest need to meet with the scientists and engineers in order to create a program that is sound from the standpoint of the industry. . . . The danger is that this lay participation will go beyond its appropriate function, enter into the methods themselves, and seek to influence the choice of the particular paths to be followed. If a scientist is really competent in his field, he knows better than anyone else how, in the exceedingly complex situation surrounding the frontier of knowledge, to single out an approach which may lead toward great attainment. Interference with him by any individual, board, or committee as he thus determines his way annoys him greatly, and should. The finding of the path is one of the finer parts of his art; in fact his rise to eminence depends very decidedly upon the wisdom with which he can thus choose.

To illustrate, there is today in this country a great urge to clear up once and for all at least the worst aspects of the great curse of cancer. Moreover, because of recent advances, new approaches of promise exist. Certainly funds poured into this field at the present time are well invested. Yet how does one proceed from here? One method favorably known to Americans because of the great advances which it has produced in applied science is to assemble a group of highly intelligent citizens, to build up great laboratories and install therein competent scientists, and to create patterns of effort paralleling those that have been successful in large industrial laboratories, with the single aim of finding a cure. But there is an alternative method, recommended by its admirable results in fundamental research. This is to select scientific men of great power—men who are thus regarded by their colleagues—and see to it that they get every bit of support which they can utilize effectively, in their own undertakings, and in accordance with their own plans. Such an effort should cover every contributory field, and hence the entire science of man's physical and chemical constitution and growth. It might be that the first method would find a solution—such things do happen. The question is essentially one of timing. If investigation of cancer has come to the stage of applied research, then the organized approach is entirely sound. If that investigation is still in the stage demanding fundamental research—and the evidence emphatically indicates that it is—then the second method is the one to follow. Through it, by and large, have come the great accomplishments in fundamental science, and it is sure to bring results in the long run, in many fields of application at once, and over a broad range. The characteristic and productive urge of Americans to move swiftly into applied research for immediate and practical results could easily lead to the ignoring of this vital fact.

—VANNEVAR BUSH, *304 Marsh Street, Belmont, Massachusetts 02178*

Excerpts from Report of the President, *Carnegie Institution of Washington Year Book No. 45*, for the year 1945–1946, pages 1–13. Issued 13 December 1946.

We tried to improve the world's best automatic micropipet, but all we could change was its shape.



We thought we could improve the revolutionary Eppendorf Micropipet, but finding what to improve on the world's best automatic micropipet wasn't easy.

For example, we tried to improve the Eppendorf's unbelievable accuracy and precision. But how do you improve on 99% sample recovery with aqueous solutions, and 97% with serum; and less than 1% standard deviation at 10 μl.?

We tried to improve handling ease. But what could be handier than push-button operation, and fabricated *disposable* polypropylene tips with exclusive non-wetting features to reduce errors?

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