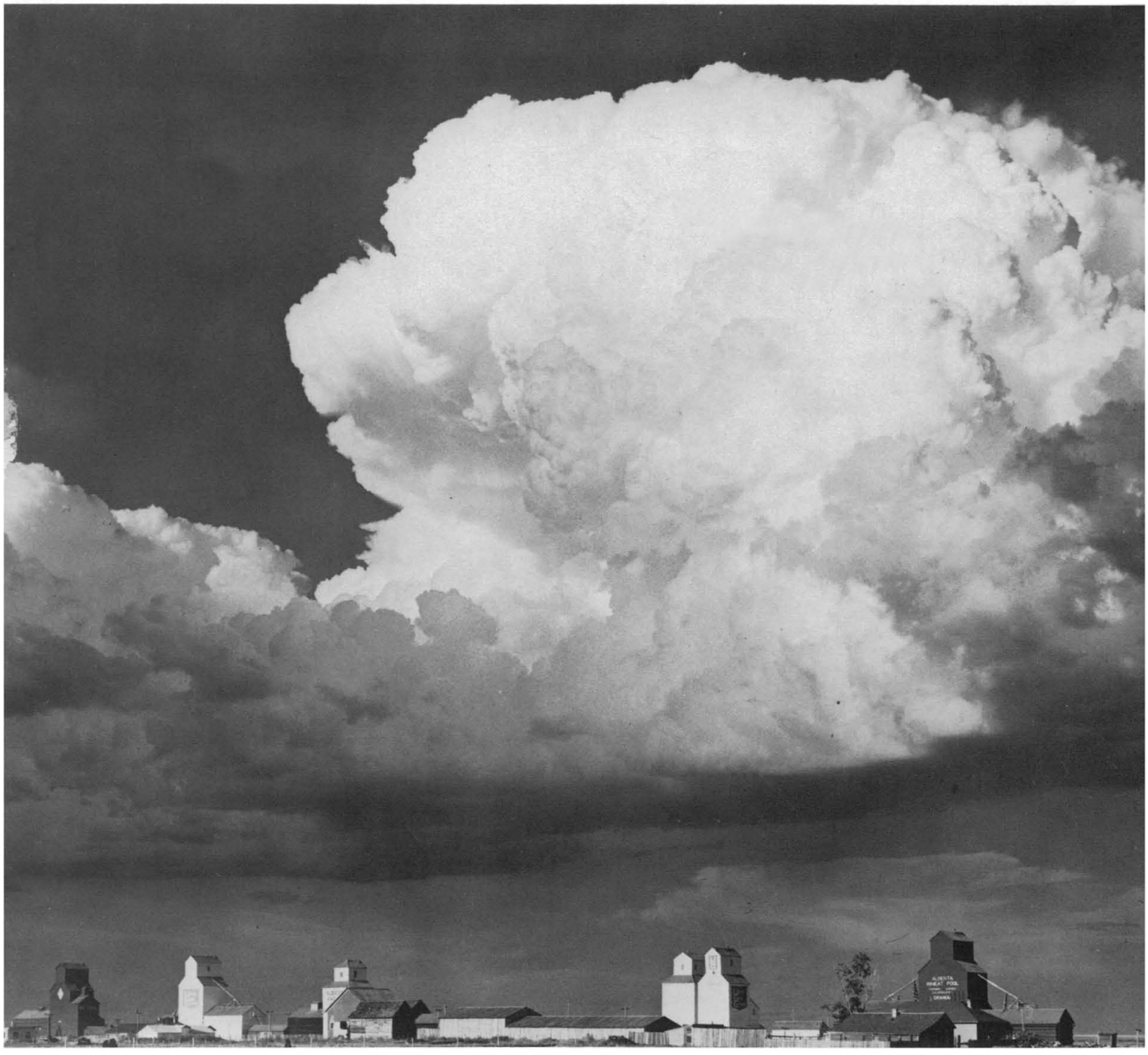
SCIENCE

14 June 1968
Vol. 160, No. 3833

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



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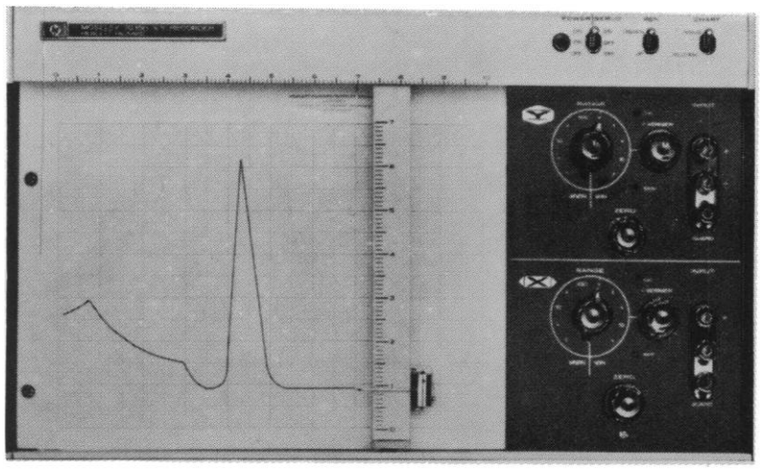

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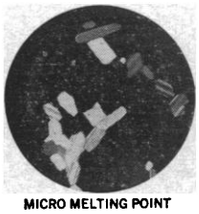
GRAPHIC RECORDERS

For automated thermal microscopy, just add the new Mettler FP-2 to your microscope

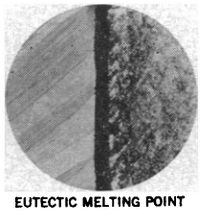
The Mettler FP-2 is an automatically controlled microfurnace and digital indicator for use with standard laboratory microscopes in thermal microscopy. By greatly increasing precision, convenience and temperature control, the system makes the time-honored technique a highly reproducible research and analytical method.

The system makes it easy to carry out studies which were considered difficult, and makes possible many studies which formerly were impossible. It enables the investigator to maintain precise control of sample temperature and to automatically record experimental data without ever looking away from the sample itself.

The instrument operates over the range of −20° to +300°C, temperatures suitable for study of fusion phenomena of virtually all organic



MICRO MELTING POINT



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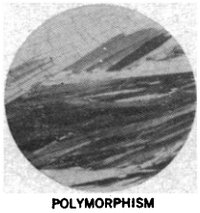
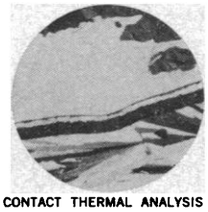


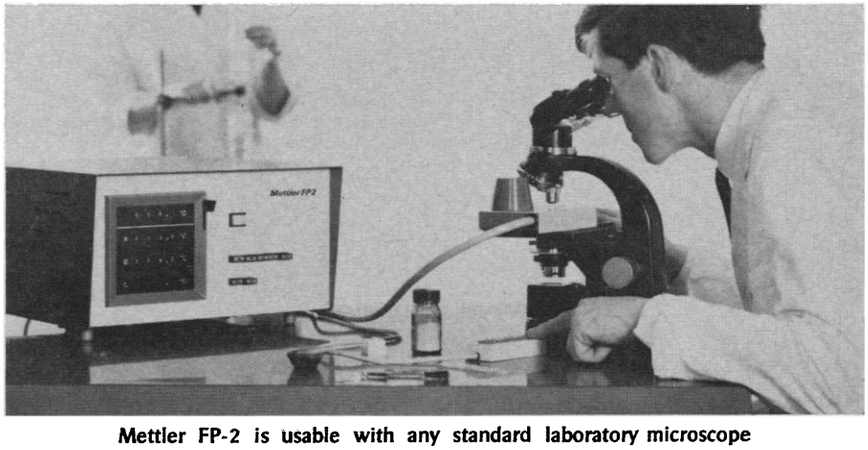
POLYMORPHISM



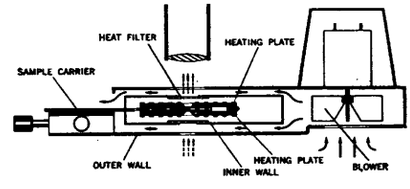
CONTACT THERMAL ANALYSIS

compounds and most inorganics. The system gives the researcher complete control over his sample temperature – increasing at a linear rate, decreasing, or holding at any single temperature. Three heating rates are provided: 10°C/minute for orientation tests, 1°C/minute for routine tests, and 0.2°C/minute for precision measurements to ±0.1°C.

The temperature control system of the Mettler FP-2 combines an electronically regulated temperature program, a platinum resistance thermometer, a low-mass sample chamber for mounting on the microscope



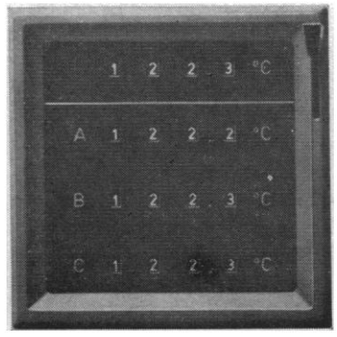
Mettler FP-2 is usable with any standard laboratory microscope



Schematic of sample chamber

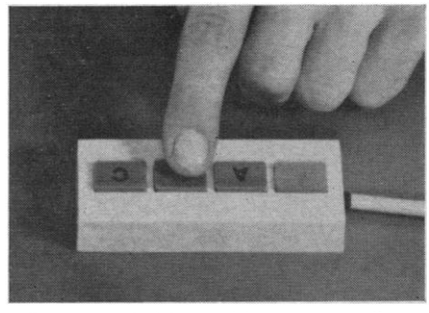
and a remote pushbutton controller for increasing, decreasing, or maintaining the sample temperature at a specific value.

The remote pushbutton controller enables the operator to record the exact temperatures at which any three thermal events occur – beginning of melt, end of melt, phase change, or any of several conditions in the crystallization process. Results are displayed automatically on the digital indicator panel.



Digital readout of analytical data

At no time during critical phase changes is the system operator required to divert his attention from the sample. He can hold the sample in isothermal condition, raise or lower the sample temperature without ever taking his eyes from the



Data recorded by pushbutton controller

microscope. In addition, the digital indicator continuously displays the sample temperature, making it unnecessary for the tedious and continuous observation of the sample during preliminary sample heating.

The Mettler FP-2 maintains control of sample temperature with precision to ±0.1°C. Its temperature program is both lag-free and surge-free, providing the strictly linear temperature advance that is essential for reproducible results.

Request your copy of the new Mettler FP-2 product bulletin and an applications booklet on thermal microscopy. Write Mettler Instrument Corporation, 20 Nassau Street, Princeton, New Jersey 08540.

Mettler®

14 June 1968
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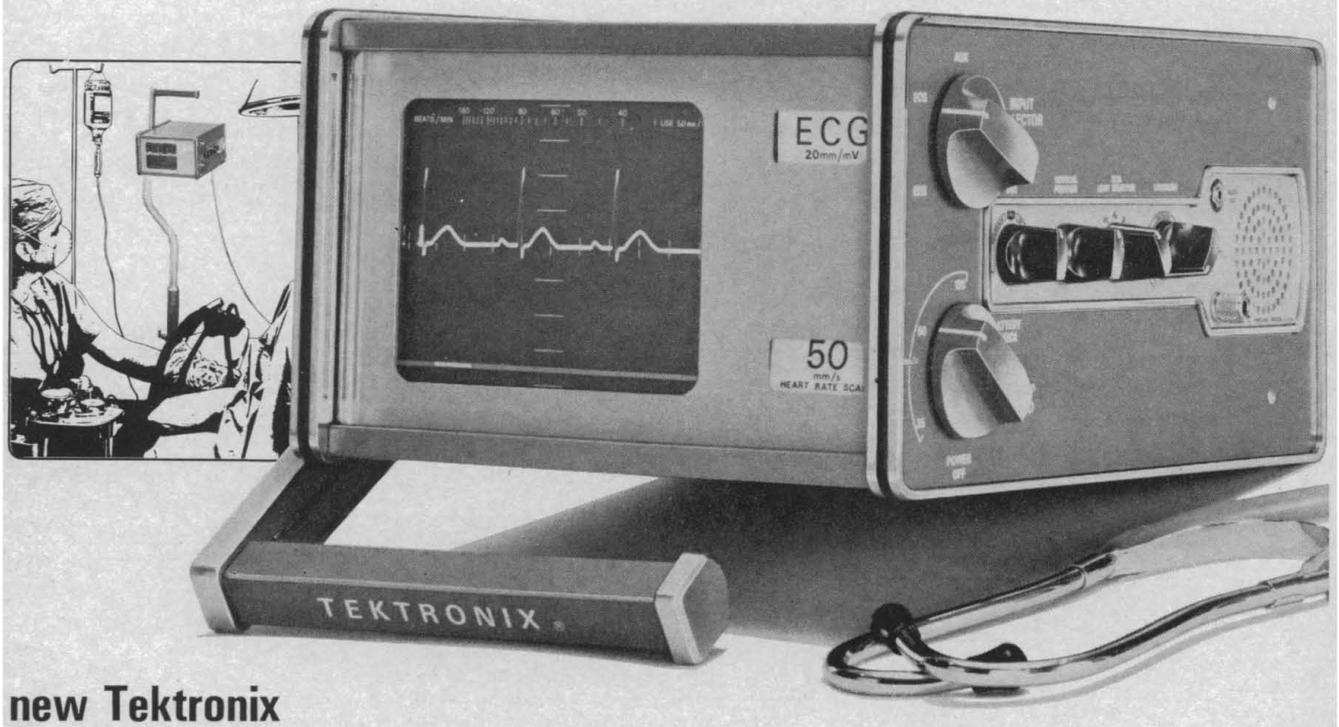
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

COVER

Grain elevators at Granum, Alberta, Canada. In 1881 the first rectangular elevator in western Canada was constructed at Gretna, Manitoba. Grain elevators had previously been round in shape. Because the rectangular shape was easier to build, this style prevailed, and soon elevators were being built in much the same fashion throughout Canada. See review of *Canada Builds*, page 1212. [National Film Board of Canada]

small...
self powered...
easy to operate...



new Tektronix Type 410 physiological monitor

- **Battery or AC powered**
- **Clear displays of ECG, EEG or related waveforms on 5-inch screen**
- **Audible heartbeat monitor with automatic alarm**
- **Direct-reading heart rate scale**

The new Type 410 Physiological Monitor is a small, self-powered, portable instrument specially designed to monitor physiological signals in the operating room. Clear displays of ECG, EEG and other related waveforms can be viewed easily on its 5-inch (8 x 10 cm) screen.

Triggered sweep in the ECG mode always positions a QRS complex at the start of each sweep. This feature permits direct reading of the patient's heart rate on a scale scribed at the top of the viewing area. Heart rate can be determined at a glance by reading the number above the peak of the second QRS complex. (Photo shows 78 beats/min.) The Type 410 provides an audible tone at each heartbeat, with an automatic alarm if the ECG signal ceases. The alarm starts within 4 seconds after loss of signal. The sound level is adjustable and an earphone jack is provided for private listening.

Six clearly-marked controls are provided for easy operation of the Type 410. The INPUT SELECTOR determines the display mode (EEG, ECG or AUX input). THE SWEEP SPEED control turns the instrument on, permits selection of 25, 50 or 100 mm/s sweeps, and also serves as a BATTERY CHECK switch. The ECG Lead Selector provides selection of I, II, III, aV_R, aV_L, aV_F, and V leads. The remaining 3 controls adjust vertical position, vertical size and sound level.

The solid-state Type 410 is 5⅜" high, 9⅛" wide and 12⅞" long, including carrying handle. It weighs 12½ pounds, including batteries. The Type 410 "warms up" and is ready for use in less than 10 seconds. It can be operated continuously from self-contained batteries for up to 12 hours, providing isolation from power-line ground which minimizes conducted (ground loop) trace interference. AC operation and battery recharging is accomplished by simply plugging the instrument into an AC outlet. A six-pin output connector permits driving of external amplifiers or recorders.

Type 410 Physiological Monitor with Accessories $825
U.S. Sales Price FOB Beaverton, Oregon

For a demonstration or a complete brochure, contact your nearby Tektronix Field Engineer or write: Tektronix, Inc., P.O. Box 500, Beaverton, Oregon 97005.

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In hope of doing each other some good

Kodak

What can you lose?

To test how much good we *can* do each other—
Yours may be one of the many, many laboratories that now do their elemental analyses by atomic absorption. The work requires standardized organic compounds of the various elements for use in nonaqueous solution, accompanied by reliable documentation. Sounds expensive, but is less so now that we have entered the picture with standards for Ag, Al, B, Ba, Ca, Cd, Co, Cr, Cu, Fe, Li, Mg, Mn, Na, Ni, P, Pb, Sr, V, and Zn.

One way to strengthen our hope of doing each other some good would be to send for the details about atomic absorption standards to Distillation Products Industries, Rochester, N.Y. 14603 (Division of Eastman Kodak Company).

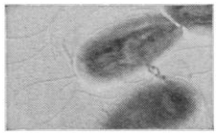
Activated sludge, a fascinating subject

We take water from Lake Ontario and put it back in the Genesee River after we are through with it. Right now we are building a $6.5 million plant further to improve the quality of the discharge. We are going to give the water back sparkling clear and fit for trout. Biggest voluntary project of private industry in support of the state's pure water program, says the Governor.

• If the factory were closed, the benefits of the light-sensitive materials made there forgotten, and the people sent far away, the quality of the water in the Genesee River would further improve. There is a better way.

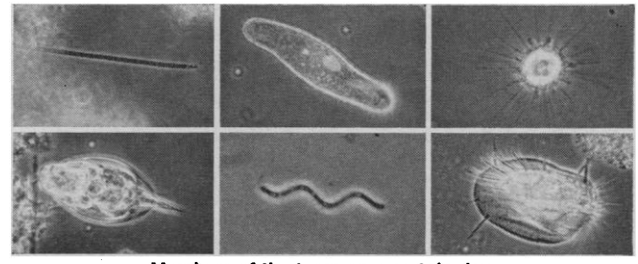
• Distillation purifies water the most. Some day nuclear energy may be cheap enough to distill half a billion gallons of water a day. But the heat evolved might change the climate. Too bold for now.

• Passing through artificial membranes also does a good job. Plant to do it might run a few hundred times the cost of any other purification plant on earth. Imprudent.



• Better at the job than any passive artificial membrane is the natural one that separates the outside world from the active and incredibly efficient and adaptable chemical plant inside a bacterium. Nobody knows how to build such a plant, nor is there any need to. Underfoot everywhere and awaiting the chance to flourish are abundant prototypes in whatever design is required to disassemble any compound presented, including phenol and other "germicides." Poison for one nurtures another.

• The public (including millions of healthy, satisfied owners of septic tanks) equates all bacteria with disease, failing to understand what a mess there would be if they were all wiped out forever.



Members of the team on a certain day

• Bacteria serve as food for organisms of more complex form, which are eaten in turn by other forms, and so up a chain. All are so small that one sees with the naked eye only brown broth, an abomination almost by definition. Yeasts and other fungal cells may also be present to compete with the bacteria for the nutrients we wish to get rid of. Except for certain bacteria at the bottom of the chain, all the organisms need oxygen. Supply that in abundance and life is lived in the tank at high pitch. Thus are wastes burned off biologically. Steps are taken to make sure the organisms remain behind when the cleansed water leaves.

• The chain of life that cleanses streams was working long before vertebrates and factories evolved. Engineers just make the process more efficient.

• Activated sludge systems like the one we are building are designed and operated by engineers who wish the biologists would get interested and clear up the mysteries of the day-to-day and hour-to-hour population changes in the tank. Predictability and clear, firm specifications are wanted.

• Biologists are well aware that many mysteries are there to be unraveled, but it's hard to establish a scientific position on a foundation of factory effluvia.

• Our management has committed us to share happily any technology we develop as the plant progresses.

Counting on the coach

Yes, it is true that in the use of super 8 movies for instruction and analysis, athletic coaches are a major influence.

No, we might not have yet marketed the new KODAK EKTAGRAPHIC MFS-8 Projector were it not for them. Coaches enjoy wide support. They will buy this projector.

It can stop by itself at any marked frames on a reel up to 400 feet long, without noticeable change in focus or brightness while a still picture, lettered question, or statement is being shown. Press a button on the remote control and movie projection resumes—6 or 18 frames/sec, forward or backward—until the next marked frame. Single-frame operation is possible so that you could in effect carry 28,800 slides in your pocket. More practical applications are conceivable.

Non-athletic education, training, and motion study endeavors can benefit as well. If you think you see how, ask Eastman Kodak Company, Motion Picture and Education Division, Rochester, N.Y. 14650, where to see a demonstration.

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1962. 322 pages, 113 illustrations. Editor: David W. Bishop.
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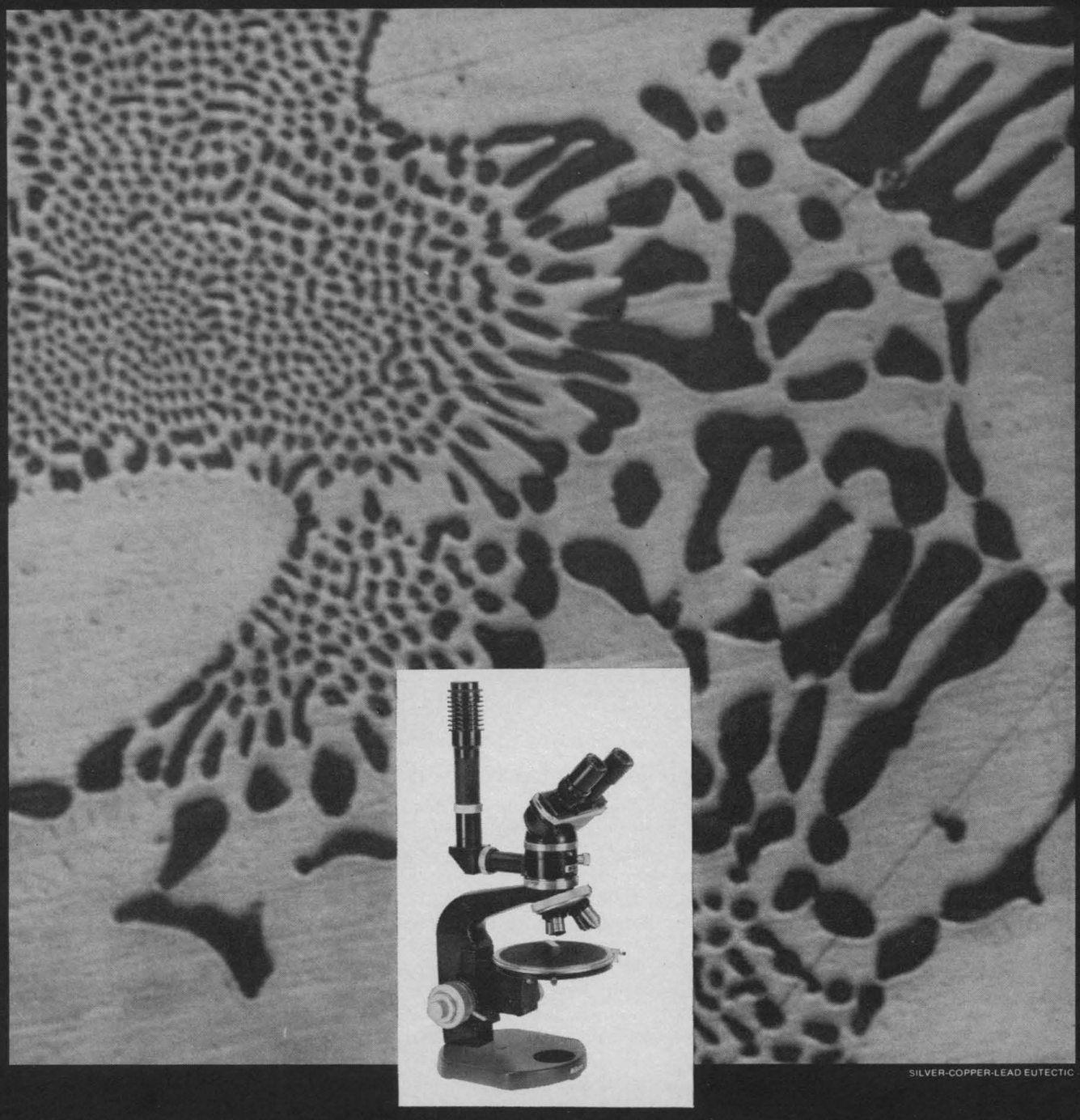

SILVER-COPPER-LEAD EUTECTIC

The surface within the surface

The smoothest surface has a subvisible structure. With conventional microscopy this structure, if not entirely invisible, still lacks definitive clarity. Differential-interference microscopy, however, translates the peaks and valleys of this micro-topography into clearly discernible differences of color and brightness.

Until now, the practical value of differential-interference observation was limited to the study of flat surfaces. The new Nikon Type R Differential-Interference Attachment extends this technique to the study of all opaque surfaces, curved as well as flat.

It permits inspection of spherical and cylindrical surfaces, such as steel balls, bearings, pistons and piston walls. It permits the observation of crystal growth on semi-conductor wafers, and reveals the otherwise imperceptible variations in IC coating. The applications are almost unlimited. Also, because the condenser of the Nikon attachment is used at full aperture, the system provides the image brightness and resolution essential for quality photo-micrography.

100

1967 I-R 100 WINNER

Selected by Industrial Research as one of the 100 most significant new technical products developed during 1967

The Nikon unit derives its unique capabilities from the use of the Savart polariscope principle: a single light ray is split by a dual quartz plate into two rays having parallel wave fronts. Interference patterns are produced by the different distances of travel created by the surface "peaks and valleys," revealing them as differences in color or brightness. These color differences can also serve as useable measurement information by referring to the standard Newton Color Scale.

So highly regarded is the contribution of the Nikon Type R Differential-Interference Attachment to the needs of modern technology, it was one of the recipients of the coveted IR-100 citation awarded to the 100 most important advances in applied research during 1967.

The Nikon Type R attachment may be used with any Nikon microscope. For complete details, write. Nikon Inc. Instrument Division, Garden City, N.Y. 11530. Subsidiary of Ehrenreich Photo-Optical Industries, Inc. (In Canada: Anglophoto Ltd. Instrument Div., Ont.)

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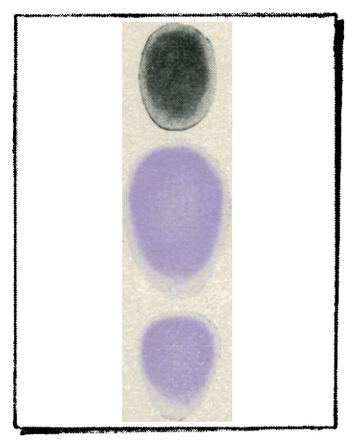

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Damage to Graduate Education

In this year of budget slashes there is growing distress over the curtailment of important research activities. The losses will be serious, but more serious will be the disruptions in graduate education.

Some research will be delayed or postponed. Some will be stopped short of completion, thus hope of socially useful or scientifically valuable returns on the money and effort already spent will be cut off. We have had big swings in federal financing before, and by now should have learned that they are wasteful. Only last year the number of new fellowship and traineeship awards from federal funds was suddenly reduced by 30 percent. In 1957, funds for the Air Force Office of Scientific Research were cut 50 percent. Some work had to be stopped in mid-course, and many people spent much time attempting to minimize the damage. One point that surely should be driven home in all official considerations of the current budget reductions is that sudden changes are costly. The same number of dollars, if spread more evenly through time, would accomplish more than can be achieved by boom-and-bust fluctuations.

Yet financial retrenchment now seems necessary. An unbalanced budget, expensive foreign commitments, and the threat of inflation require a tax increase. Congress requires an accompanying reduction in expenditures. Some of the reduction will come from funds that otherwise would be available for science and higher education. In the present situation we cannot claim that all research studies must have top priority and immediate attention. Some of the losses can be made up later, and some must be accepted as a consequence of the need to devote available funds to other purposes.

More serious and more difficult to make up later will be the losses in graduate education. More than three-fourths of the research assistants in colleges and universities are paid from federal sources; cuts in research funds will reduce the number of research assistants who can be employed. More than a third of all graduate fellowships are provided by federal agencies; fellowship funds will also be cut. (Pending reassessment of its resources and obligations, the Department of Health, Education, and Welfare has stopped making new fellowship and traineeship awards.) The discriminatory shortsightedness of current Selective Service policies adds to the difficulties. We must expect a sharp drop in the number of graduate students and, a few years hence, a decrease in the number of earned doctorates. A totally unwarranted portion of the immediate burden of the nation's problems will fall on a small group of the ablest young men and women in the country, and for years to come the nation as a whole will pay the price for letting that happen.

There will be some compensatory increase in graduate enrollment later, but experience of World Wars I and II indicates that a sharp drop in doctoral degrees is not compensated for by higher numbers later. In the most rigorous fields, in which one part or level builds most directly on preceding parts, it is very difficult for a student to return to graduate studies after a hiatus of 2 or 3 years. Physics is likely to suffer a greater relative loss than any other field.

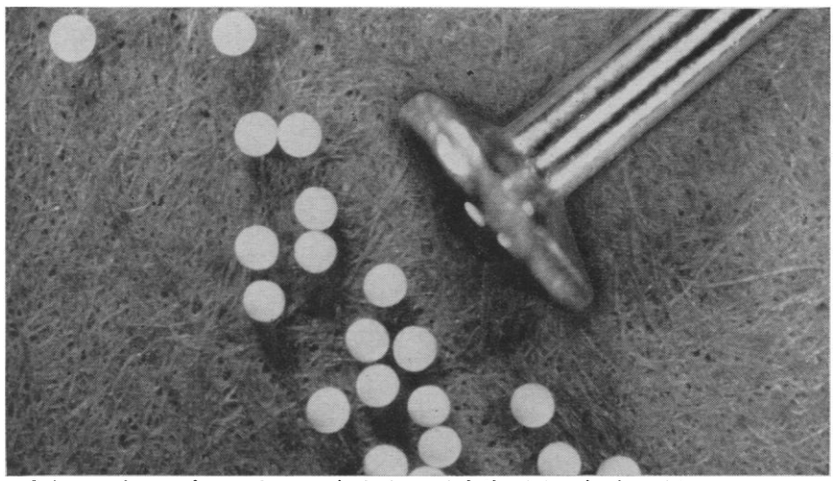
Final congressional action on most appropriations bills is still in the future, and many agency decisions on how to allocate their reduced funds are yet to be made. But it is clear that substantial reductions must be planned for. In deciding how the reduced amounts can best be used, one important criterion will be the extent to which the adverse effects on graduate education can be minimized.—MILTON HARRIS, *Chairman of the Board of Directors, American Chemical Society*, and DAEL WOLFLE

Report from

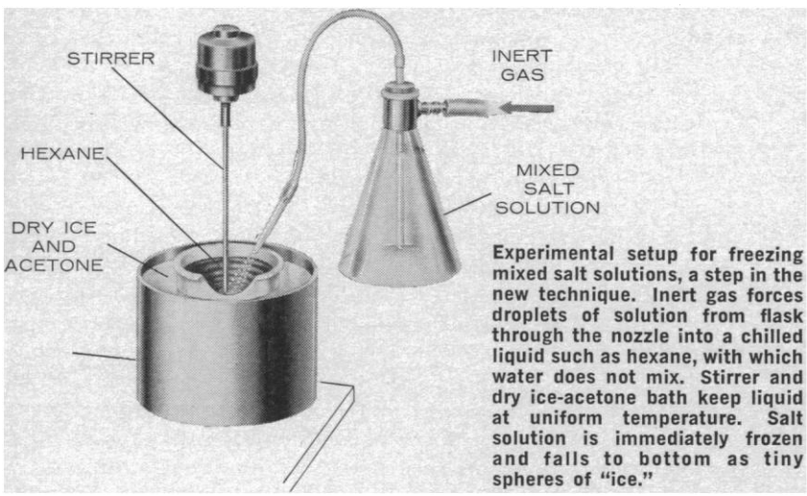
BELL LABORATORIES

Ceramics from Liquids

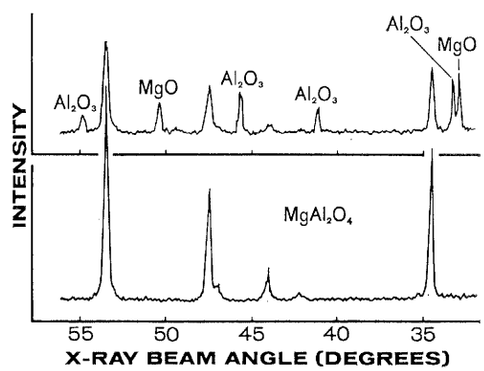
Ceramics preparation has been relatively unchanged for many years. But electrical communications are now calling for new methods; one is described below.



Spheres of ceramic powder, precisely formed, intimately mixed, and homogeneous—product of a new freeze-dry process devised at Bell Telephone Laboratories. A common pin indicates approximate size.



Experimental setup for freezing mixed salt solutions, a step in the new technique. Inert gas forces droplets of solution from flask through the nozzle into a chilled liquid such as hexane, with which water does not mix. Stirrer and dry ice-acetone bath keep liquid at uniform temperature. Salt solution is immediately frozen and falls to bottom as tiny spheres of "ice."



X-ray diffraction patterns of a magnesium aluminate, demonstrating the homogeneity possible with Bell Labs' new technique. The lower trace, from an aluminate made this new way, shows the characteristic spinel pattern of the substance. The top trace shows the pattern of an aluminate prepared by a conventional milling process; it has spikes indicating the presence of magnesium oxide and aluminum oxide phases, as well as the desired magnesium-aluminum-oxide phase.

Ceramics with precise electrical, magnetic, and chemical properties are widely used in electronics—as ferrites for computer memories, as substrates for integrated circuits, and the like. Since ceramic properties depend on microstructure, preparation must be precisely controlled. And for many purposes, current methods do not sufficiently control crystal size and composition. Grinding and precipitation from solution, for example, often introduce contamination or cause nonuniformities.

Now, scientists Frank J. Schnettler and Frank R. Monforte of Bell Laboratories have devised an improved technique, suitable for many compositions. It combines ingredients in liquid form, freezes them as tiny spheres, and converts them to oxides without changing their spherical shape. The resulting compositions are precisely controlled and uniformly mixed.

The process begins with water solutions of salts of the elements to be combined. To make a magnesium aluminate ceramic, for example, magnesium sulfate and aluminum sulfate are used. Next, as in the drawing, the solution is sprayed into a coolant and "instantaneously" frozen. Since the ratio of salts can change with temperature and with time, rapid freezing helps to maintain uniform composition. The resulting solid spheres, a fraction of a millimeter in diameter and all of identical composition, are dried at low temperature and pressure, where the water can sublime—go directly from solid to vapor.

Finally, the freeze-dried material is baked at about 1000°C to convert the salts to oxides. When this step is completed, the spheres are actually agglomerates of fine, intimately mixed or completely reacted ceramic powders. They are clean, free-flowing, and easily handled. They are easily crushed into fine powder for conventional methods of ceramic manufacture, such as extrusion or casting. Because there is no dust, toxic material can be handled safely.

If a powder is to be used directly, as in pigments or abrasives, its particle size can be controlled over a range from 100 to 5000A by varying the dilution of the original solution or the time and temperature used to convert the salts to oxides.

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possible to distinguish between movement of the indicator from one space to the other and a structural change in the mitochondria which rendered the structural protein accessible to a greater or lesser degree to the indicator.

Studies of the de-energized mitochondrial membrane were also reported by Azzone. He observed that after K^+ was added to mitochondria and then treated with Ca^{++}, the uptake of Ca^{++} and the efflux of K^+ occurred in a reaction that was abolished by uncouplers. Parallel experiments quantitated the Ca^{++} accumulation by isotopic procedures. The general conclusion was that the efflux of K^+ causes a potential across the membrane which is responsible for the uptake of Ca^{++}. In the discussion it was noted that energy-independent Ca^{++} uptake into mitochondria supplied with phosphate could be caused by the precipitation of calcium phosphate within the membrane. However, the experiments were also carried out in the absence of added phosphate. Since mitochondria contain endogenous phosphate, the question could be resolved by measuring the balance of ionic constituents, as emphasized by Edelman.

Ernster put forward a new explanation for the oxaloacetate inhibition of succinate oxidation in aged mitochondria. The evidence focused sharply on the possibility that a low concentration of free fatty acids present in the mitochondria or added to them served, in the presence of NAD or ATP, to activate electron transfer in the aged system. The remarkable feature of the experimental data was the large change of the inhibitor constant K_i for oxaloacetate before and after activation of respiration with fatty acids, ATP, and NAD. It was further pointed out that oxaloacetate had a remarkable affinity for the partly purified succinic dehydrogenase, suggesting that this bound oxaloacetate was involved in the deactivation phenomenon characteristic of the solubilized enzyme.

During the discussion, it was pointed out that a common denominator of the fatty acid activation of succinic dehydrogenase in aged mitochondria and succinate activation of the isolated succinic dehydrogenase could be a partial reduction of the succinic dehydrogenase flavoprotein prior to its reaction with succinate. This is a phenomenon related to the conditioning phenomenon of the NADH dehydrogenase of submitochondrial particles, where alteration in the availability of —SH groups

occurs after reduction with NADH. Smith reported an interesting phenomenon involved in propionate metabolism of mitochondria of sheep liver, where *dl*-carnitine showed considerable activating effects attributed generally to transport of the propionate across the mitochondrial membrane.

Papa described the pathway of α-oxoglutarate through the NAD-NADP system and glutamate dehydrogenase to form glutamate in mitochondria of rat liver. He postulated a separate compartment for the reaction of glutamate dehydrogenase and an energy requirement for the transfer of reducing equivalents to this site. The experimental results of Krebs pointed to an energy-dependent uptake of oxaloacetate. Energy supplied by Site III led to oxaloacetate uptake and NADH oxidation by the substrate. Papa showed that the rate of succinate oxidation in mitochondria of rabbit kidney is, in the presence of uncouplers, inversely correlated with the level of oxaloacetate. Hans Rasmussen showed how variable the response of the mitochondria to oxaloacetate might be. In one case, he was able to correlate an increase of succinate oxidation with an increase of intramitochondrial oxaloacetate in State 4 (mitochondria of pigeon heart supplemented with succinate).

Samuelsson described recent work on the prostaglandins and postulated interesting and fundamental interactions with the cyclic AMP and lipase.

Higgins reviewed factors contributing to the instability of enzymatic systems and emphasized, particularly, the back-activation oscillator as a representative example. He further illustrated a phenomenological comparison of oscillations in metabolites in an extract from a heart cell with analog computer solutions obtained by A. Lucas. He showed particularly how the entrainment of oscillations from the phosphofructokinase step to the 1,3-phosphoglyceric acid step could be identified in characteristic portions of the oscillation cycle. It was brought out in the discussion that manifold interactions are possible in the glycolytic sequence and the idea of a specific control site or rate-limiting step as controlling the properties of the whole sequence must be abandoned in favor of an understanding of the interaction of several controls.

Hess described a reconstruction of the oscillatory system in cell-free extracts, in which purified enzymes from hexokinase to alcohol dehydrogenase

were employed to obtain oscillations of unusual period and waveform. It was pointed out that one of the problems of employing purified enzymes for this purpose was that some of the isoenzymes might be missing, as in the case of glyceraldehyde-3-phosphate dehydrogenase.

Changeux reviewed the basis for the allosteric hypothesis and showed a molecular model of the aspartate transcarbamylase illustrating type of contact interactions between the subunits of the polymer. He then described a number of experiments on the electroplaques of the electric fish and pointed out how the allosteric hypothesis could be enlarged so as to predict some properties of the excitable membrane. There was some discussion as to whether the speed of subunit reorganization would be rapid enough for the great speed of propagated action potentials in small axons. It was also pointed out that propagation of information in a membrane system might well occur through changes in the secondary or tertiary structure affecting intermolecular contacts of protein molecules.

Cohn described in detail various types of nuclear magnetic relaxation data that could be obtained from a variety of metal-activated enzymes, such as creatine kinase and pyruvate kinase, where, in certain cases, the atomic dimensions of the metal-substrate distance for the enzyme-metal-substrate complex could be computed for the complex in solution. She further pointed to proton magnetic relaxation studies as an approach to manganese binding to the mitochondrial membrane. Enhancement of the proton relaxation rate due to manganese was observed when manganese was bound to the membrane. Other possible applications of this important method to metal-adenine nucleotide binding were pointed out.

Clark described an interesting fish poison named cunaniols (polyacetylenic alcohol) which appeared to have slow but highly significant effects upon the respiratory control of mitochondria of rat liver. Although the mitochondria provided a simple assay system for the cunaniols, the physiological target might well be in the central nervous system or in the lungs.

M. Baltscheffsky summarized her work on inorganic pyrophosphate as an energy donor, activating reversed electron transfer in chromatophores, in rat liver, and in yeast mitochondria. Particularly striking results were obtained in chromatophores from the bluegreen mutant of *Rhodospirillum rubrum*. This finding evoked discussion; a summary was made of previous, unsuccessful attempts by Lindberg to demonstrate by isotopic methods the labeling of the adenine nucleotide pool of mitochondria by labeled pyrophosphate. It is apparent that reversed electron transfer is a highly sensitive and specific reaction for energy donors and thus affords a higher ratio of signal to background than could be obtained with other techniques. The possible role of this reaction in biochemical evolution was stressed by H. Baltscheffsky.

Vernon reported on the isolation of subchloroplast and subchromatophore fractions in which the various activities of the system could be segregated to a remarkable degree. His general conclusion was that the System I particle, consisting of rods or strings, contains cytochromes *f* and b_6, while the vesicular System II particle consisting of vesicles contains a cytochrome b_{559}. Recombination of these fractions to make the complete unit of System I–System II has not yet been reported. Comparable studies of *Chromatium* chromatophores revealed P_{890} and ubiquinone in the particles with no activity in the vesicles.

Jarnefelt described preliminary attempts to find a more appropriate medium for studying the metabolism and function of slices of brain cortex, with the ultimate goal of obtaining preparations which would exhibit spontaneous activity. Tata described elegant studies on hormonally induced membrane synthesis in a variety of organs, finding a very close coincidence in the biosynthesis of the membranes of the endoplasmic reticulum and of the mitochondria. These studies suggest that the bulk of the membranes of the endoplasmic reticulum and ribosomes are turned over as a unit, and that there is a good correlation between hormonal specificity in regulating the overall biosynthetic process.

The symposium was closed with a brief summary and a vote of thanks to M. von Knorring and P. Olin of the Sigrid Juselius Foundation; to Johan Jarnefelt for organizing the meeting; and to Sir Hans Krebs for his fine contribution to various phases of the proceedings.

BRITTON CHANCE
School of Medicine,
University of Pennsylvania,
Philadelphia 19104