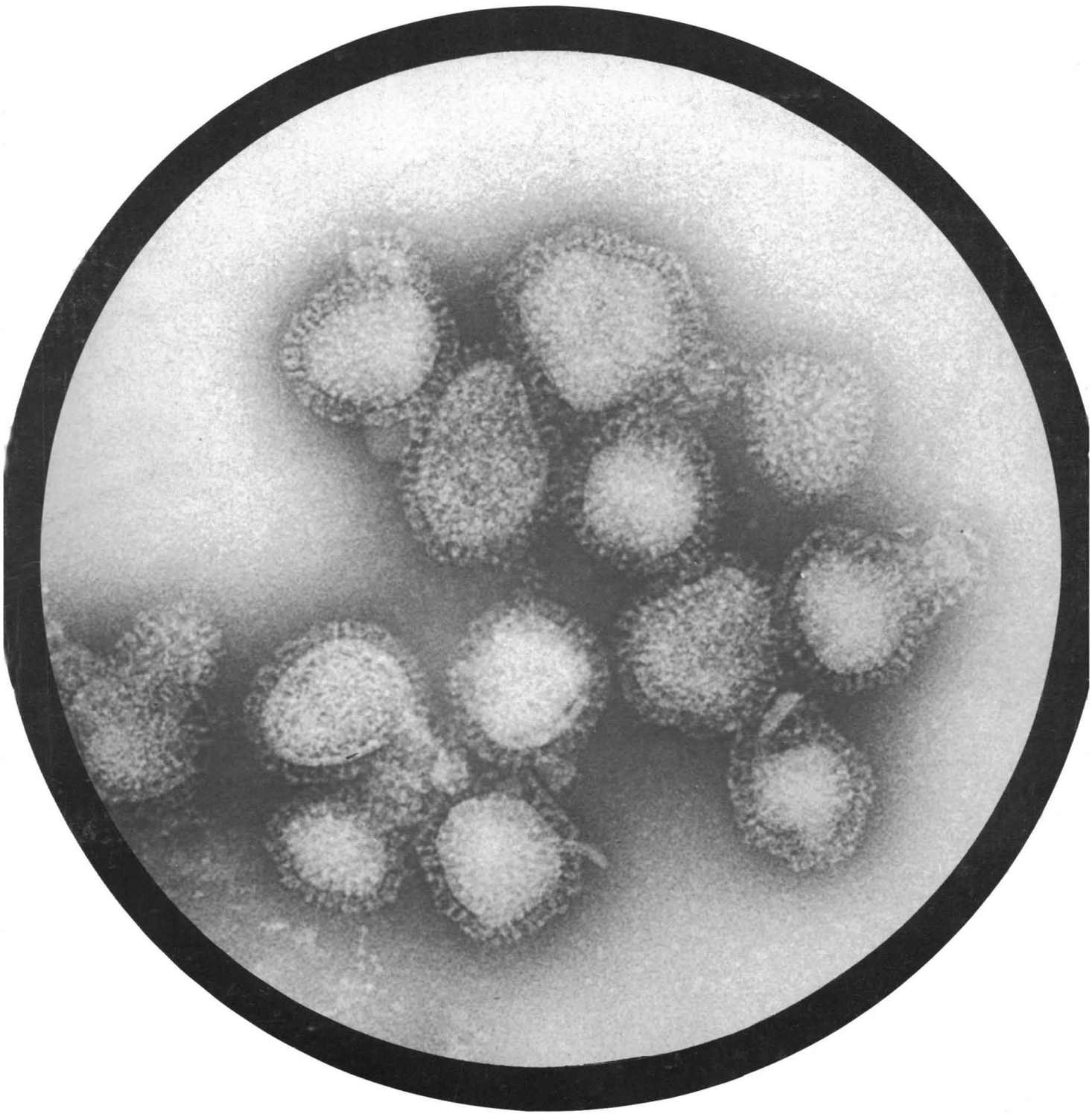
SCIENCE

24 January 1969
Vol. 163, No. 3865

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



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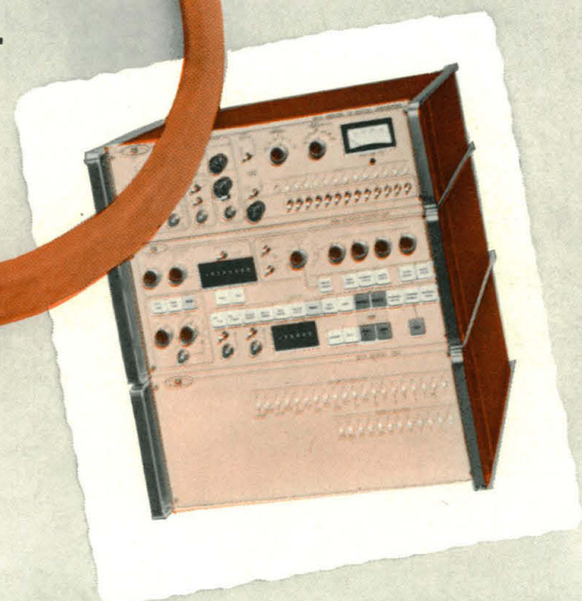

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Write for Bulletin 59A

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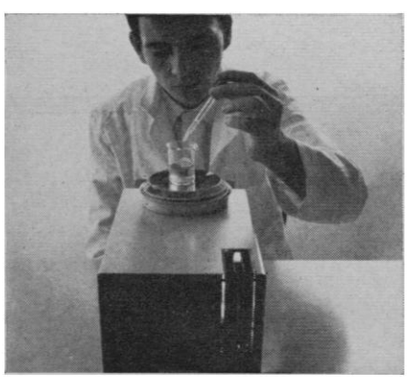
WEIGHT WATCHERS:

These Mettler balances can help reduce your weighing problems

If you have weight problems, chances are they can be solved with one of these three Mettler balances. Two are top-loaders, one an analytical. Collectively, they solve virtually any weighing problem in the laboratory. Individually, they perform their special jobs with unique speed, ease and precision.

Weight Watching Has Never Been Easier

The Mettler P1200, a well established and versatile top-loading balance, now has digital readout. This feature permits even relatively unskilled operators to obtain accurate results without misinterpretation or reading errors.



The P1200 will tackle weighings to 1200 grams (plus 100-gram tare), and give you a precision of ±5 mg. That's better than one part in 250,000. But despite its capabilities for handling the bigger weighing jobs, the P1200 will also complete a weighing in just three seconds. It will also checkweigh to plus or minus values as fast as you can place an object on the scale, and without referring to scale readout. Powdery, granular or liquid substances can be filled rapidly by the use of a filling guide which shows the approximate weight on the pan throughout the entire weighing operation. This eliminates time-consuming interruptions for reading the balance.

Remove Grams — Positively

The P160, another top-loader, weighs unknowns to 160 grams with a precision of ±1 mg. In addition to having all the features of the P1200, it is ideally suited for weight loss studies. It has a reverse scale which gives a positive reading as weight decreases in drying, evaporation and residue determination studies. This feature eliminates time-consuming calculations and the possibility of arithmetical errors. It also simplifies gravimetric titrations (for more information on the advantages of gravimetric titrimetry, write for Bulletin M-1014A).

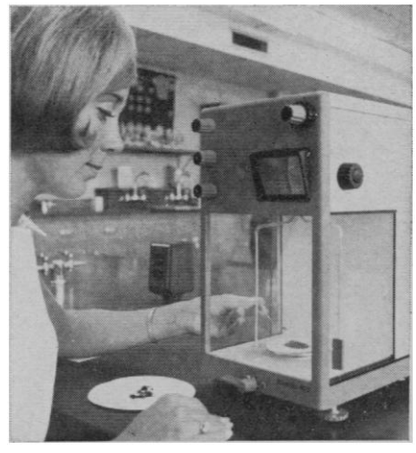
A Well-Balanced Balance

Slight changes in the balance level of the P1200 and the P160 (as in all Mettler top-loaders) are automatically compensated for by a zero point restoration feature. We call it Mettler Levelmatic. If your balance is out of plumb beyond its compensation range, you won't be able to make a weight reading because the readout is automatically obscured. Because Levelmatic automatically compensates for most shifts in zero position, it is rarely necessary to re-zero the balance before weighing.

Have Your Cake and Eat It

If you need an analytical balance to watch your weight, consider the Mettler H20 . . . it's really two balances in one. It gives you the 160.1-gram capacity of a macro-analytical balance, and the ±0.01 mg precision of a semi-micro instrument. The H20 readout, like the P1200 and P160, is digital. It also has a high-speed filling guide, and an optional accessory will let you weigh objects below the balance; for example, to make specific gravity measurements by weighing objects submerged in liquids.

Because of the unrestricted optical taring feature of the H20, you can tare off the weight of your container in seconds, and begin weighing-in with readout at zero. You can't make a weighing mistake. If you're adding several components, you can dial back to zero for each one.



Some Food For Thought

In case you have a weighing requirement that can't be solved by one of these three balances, Mettler has 35 more models ranging from top-loaders that weigh to 13 kilos all the way through analyticals to ultra micro instruments with precision of ±0.1 μg. We'll bet a gram-cracker that one of these will fill the bill. To arrange for a free demonstration or trial, or for further particulars, write to Mettler Instrument Corporation, 20 Nassau Street, Princeton, New Jersey 08540.

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24 January 1969
Vol. 163, No. 3865

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COVER

Influenza virus (A_2, Hong Kong). Recently a symposium was held to discuss new approaches to the study and control of influenza viruses. Emphasis was placed on the genetic aspects of influenza with the hope that new information might be gained for the effective control of the influenza virion as a disease-producing entity and for future direction of influenza research (negative contrast electron micrograph, about × 330,000). See page 409. [Frederick A. Murphy, National Communicable Disease Center, Atlanta, Georgia]

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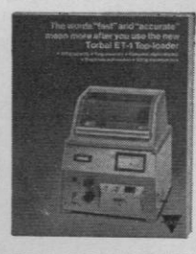

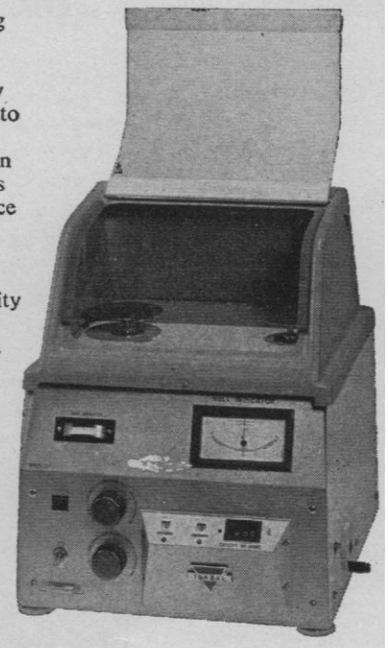

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know of the peculiar difficulties of disproving an erroneous first impression.

The propriety of government control over drug manufacturers is widely debated in such journals as *Clinical Pharmacology and Therapeutics*. Reports of government action on behalf of the community when these controls are not observed by manufacturers are common. It would be useful, and fair, if scientists in society were allowed to judge the information that causes such action before conceding any restrictions on experimental technique. There must be better ways of combating carelessness or deception without tampering with the need to get the answer right.

A. S. E. FOWLE

29 Manor Way, Beckenham, Kent, England

Drosophila: Tender Loving Care

Sonneborn could have found no more apt appellation for H. J. Muller than "Crusader for human betterment" (15 Nov., p. 772). I knew Muller well. As his student assistant at the University of Texas, he and I, together with our wives, spent much time cycling in and around Austin.

Muller was an intense, hardworking scientist who had little time for social frivolities. In addition he was quite shy and sensitive, although he easily lost himself in his scientific pursuits. One of my jobs was the care and feeding of *Drosophila*. This may sound simple but Muller was exacting in his requirements. I remember one Christmas vacation period in Austin when the weather turned quite cool, so that I was afraid the *Drosophila* might suffer in the unheated university building. I carried the tubes housing them home in my inner pocket, and since my meager quarters were not too thoroughly heated at all times, I took them to bed with me. I was very proud of their survival, and when I told Muller of this at the famous Dartmouth conference on "Great issues of conscience in modern medicine" some years ago, he conscientiously asked me, "Do I still owe you something for this?"

Muller contributed a great deal to the development of my career in medicine. I am one of many who have owed much to this man, rather small physically, but a giant in every other respect.

RAYMOND WING

Fairview Avenue and 21st Street, Easton, Pennsylvania 18042

If Not Grades, What Criteria?

Schagrin's letter (15 Nov.), proposing a system in which grades would be used internally at the college but not transmitted to graduate schools, prospective employers, and others, and would be replaced by "letters of recommendation or perhaps evaluation forms," seems at least a trifle naïve. No sensible person attributes more than modest importance to grades, but they do have value, particularly in some fields of study, in giving some indication of mastery of the subject matter—a point of some interest to institutions with which the student might like to become associated. It is obvious that if grades, as now constituted, are not made available, the letter of recommendation will perform exactly the same function under another name.

Schagrin's solution is reminiscent of the Midwestern legislator who observed that railway accidents often involved the last car on the train, and introduced a bill requiring the omission of the last car.

R. L. HALL
McCormick & Company, Inc.,
11350 McCormick Road,
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Schagrin's proposed solution to the difficulties and dilemmas of grading interest me greatly and should interest many others as well. I would especially like to know about the other criteria for selection (besides grades) that he is suggesting for institutions, such as business, government, and the military, to use which have *demonstrably* higher correlations than grades with subsequent performance. On what basis, if not on the basis of performance in college, is he suggesting that letters of recommendation be written, and on what basis would evaluation forms be executed if not on the basis of performance in college? On what basis are grades assigned if not on the basis of performance in college? If grades cannot be trusted to be anything more than "tokens to purchase favors for graduates," how can letters of recommendation and the ratings that appear on evaluation forms be trusted to do more?

Is Schagrin suggesting (perish the thought!) that scores on standardized tests be used as a substitute for grades for evaluating students' performance?

WILLIAM H. ANGOFF
Educational Testing Service,
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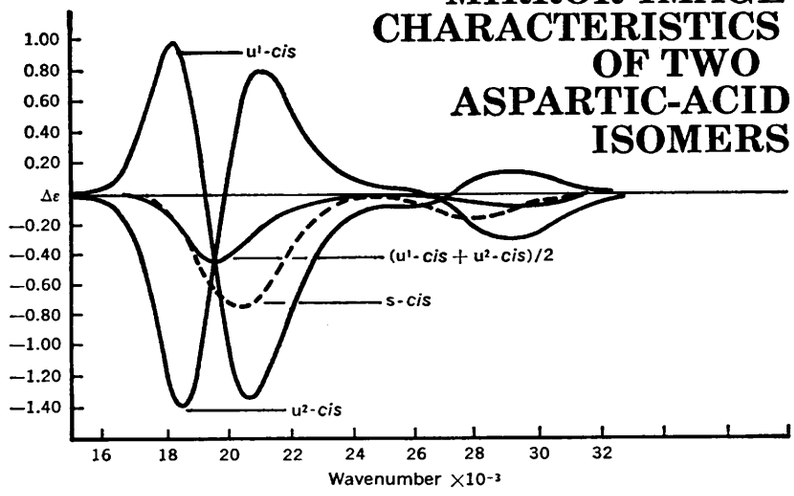
CHEMICAL PROFILES ... drawn by Durrum

PROVING THE MIRROR-IMAGE CHARACTERISTICS OF TWO ASPARTIC-ACID ISOMERS

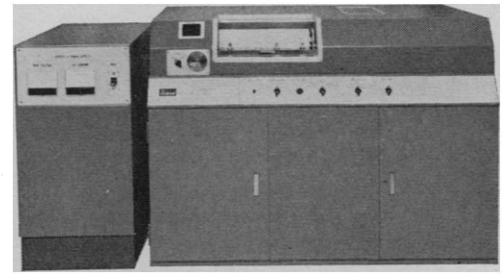


Aspartic acid, with its three donor sites, can form a variety of hard-to-identify chelate isomers. The circular-dichroism profiles drawn here, plotted from data gathered by a Durrum-Jasco CD recorder, are typical of the molecular detective work* that can be achieved with this versatile instrument.

The steric requirements of aspartic acid indicate that in a cobalt-diethylenetriamine complex, three isomers will predominate: one s-*cis* (symmetrical), shown as a dashed-line profile in the drawing above, and two u-*cis* (unsymmetrical) isomers, shown in color. The latter are essentially mirror images of each other, and the Durrum-Jasco instrument provides a way to identify one from the other.

The configurational contributions to the CD traces of the two mirror-image isomers should, in theory, cancel out, leaving an "average" trace that approximates that of the s-*cis* isomer where there are no configurational contributions. As seen here, a very close correlation is achieved, proving that the two u-*cis* isomers are indeed pseudo-mirror images and providing clues as to their specific forms.

The Durrum-Jasco CD recorder is a powerful analytical tool, used throughout the world to classify and identify complex organic and biochemical compounds. In addition to detailing the conformation and configuration of such substances as steroids, alkaloids, proteins, nucleic acids and synthetic polymers, the instrument can serve to measure their concentrations, kinetic properties, and stereochemical characteristics. Durrum-Jasco CD prices start at $29,600.



*AS REPORTED BY J. IVAN LEGG AND DEAN W. COOKE IN THE DECEMBER 20, 1967 ISSUE OF JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.

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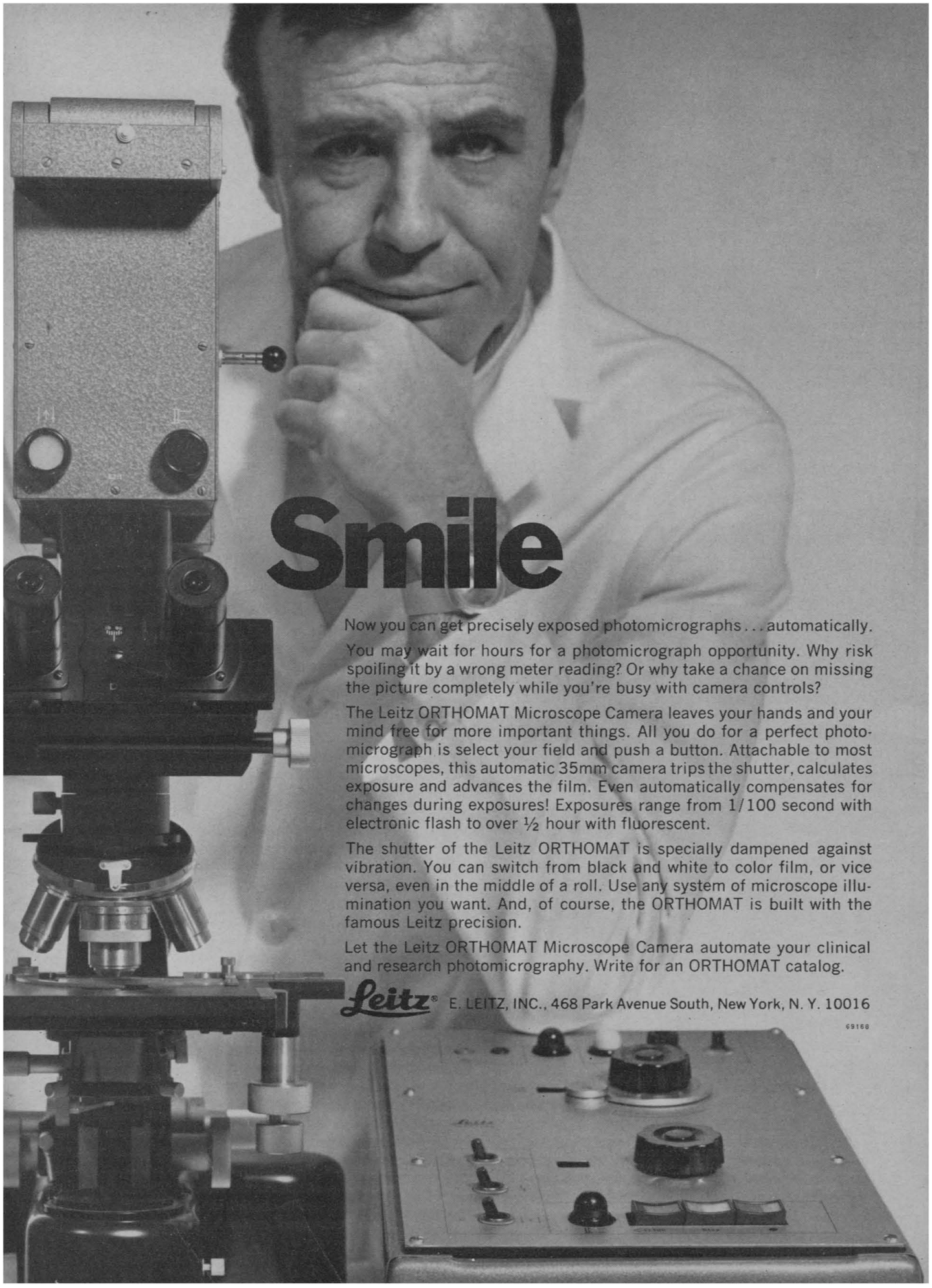
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On-again, Off-again Funding of Academic Science

Professors on campuses throughout the country are expressing justifiable concern over serious and severe limitations on expenditures of "their" grant funds from federal sources. Local university officials and agency program officers are being unjustly criticized for taking actions that were forced on them by the Bureau of the Budget (or, if you prefer, by the President)—whose actions, in turn, resulted from the congressional mandate to the Executive Branch to reduce fiscal year 1969 expenditures by $6 billion.

No amount of fault-finding or blame-placing will cure the present circumstance, but it would be useful to consider the kinds of arguments and pleas one might present to the key decision-makers of the federal establishment to insure against continued or repeated slashes of funds for academic science. The national leadership can and must be convinced that on-again, off-again funding of scientific activities in our colleges and universities is a bad policy—one that is both expensive and dangerous.

Those responsible for making appropriations decisions probably will never again allow large annual increments of federal support comparable to those that sparked and fueled the growth of scientific activities on U.S. campuses in the late 1950's. But it is relatively easy to show that a series of feast-famine cycles in the support of research and education in our colleges and universities can only lead to enormously costly discontinuities and lost opportunities. A determined effort to demonstrate this is possible and timely; *Science* and other journals have already called attention to some of the more unfortunate cases of difficulties now being faced by many universities.

The relationship between the federal government and our institutions of higher education has been far more successful and mutually rewarding than was predicted by most of the backers of such innovations as the National Science Foundation. The early worry concerning the possibility that unhealthy degrees of control or influence might accompany federal financial aid has, happily, proved to be largely unjustified. But the question of continuity, with reasonable levels of growth, has come up repeatedly—and currently looms as a major issue.

The funds made available by federal agencies to colleges and universities for strengthening their research and educational programs have without question strengthened U.S. science and technology; but they have also created a condition of dependence. The notion that federal funds can be held back or withdrawn—temporarily or permanently—without damaging the research and educational programs of the universities is dangerously in error. More important, all such discontinuities in funding will damage the national research and development effort, both in the immediate future and in the longer period affected by the lessened production of Ph.D.'s in science.

Congressional leaders (and others) have long decried the absence of clear-cut and unambiguous policies to guide national programs for the support of science. Perhaps the search for such policies has become too complicated. A guide to action that would seem, on the evidence, to be axiomatic, yet one which neither the Congress nor the Executive Branch has fully embraced, is this: avoid discontinuities in the federal support of academic science.—BOWEN C. DEES, *University of Arizona*

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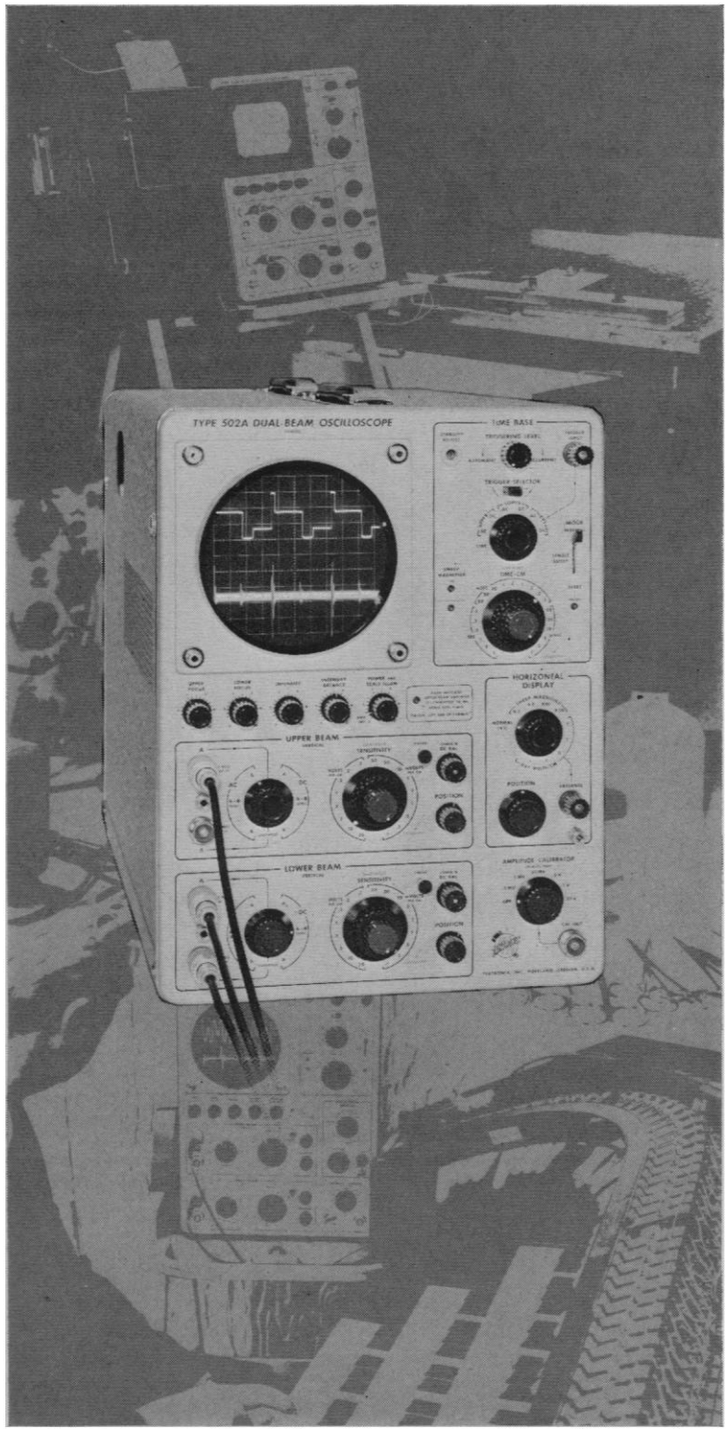

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resolved by polyacrylamide gel electrophoresis. These segments ranged in size from 2.5×10^5 to 7×10^5 daltons which would suggest that they might represent monocistronic sequences of polynucleotides. Evidence was also presented (Pons) that the replicative form (RF) of influenza RNA obtained from virus-infected cells can be resolved as five components resistant to ribonuclease. These observations evoked discussion as to the actual physical state of the RNA genome within intact virions versus its intracellular form. The suggestion (Braun) that the RNA may exist in influenza particles as a single molecule but may be replicated as separate fragments appears worthy of consideration. Pons ended his discussion of physicochemical studies with recent data concerning the molecular basis for the classical "Von Magnus phenomenon"; that is, the multiplicity-dependent production of incomplete, noninfectious influenza virus. Analyses of radiolabeled virus by gel electrophoresis showed that the incomplete form of virus contained the same protein components as fully infectious virus, but that it lacked one of the five RNA components. It will be of obvious interest to determine what genetic function or functions this missing RNA segment can perform in intact genomes.

Frank Fenner has long advocated the use of conditional lethal mutants for circumventing the technical problems that have hampered genetic studies of animal viruses. One could scarcely doubt the usefulness of this approach when considering the work discussed by Fenner on temperature-sensitive (*ts*) mutants of influenza virus, strain WSN. These data, many derived from a recent doctoral dissertation (J. Mackensie), showed that a genetic map can be constructed with influenza *ts* mutants providing that conditions for recombination are highly standardized including treatment of cells with *Vibrio cholerae* neuraminidase. Sixteen *ts* mutants of WSN virus were first ordered along a linear map that showed reasonable additivity and a maximum recombination frequency of 12 percent. However, to resolve the discrepency of lower-than-expected recombination between the terminal mutants a circular map was constructed which Fenner stressed as being quite tentative. For unexplained reasons attempts were not successful to obtain complementation between these *ts* mutants which differed from one another for various defects. Hirst discussed recent recombination studies

with similar *ts* mutants of WSN originally isolated by Simpson and Hirst and he was able to group nine nonreverting mutants within a linear map giving a maximum distance of 13 percent. Except for the suggested circular arrangement of the genetic map obtained in Fenner's laboratory it was obvious that fairly good agreement existed between these two independent sets of data.

The writer (Simpson) opened a discussion on heterozygosis with a presentation of recent results suggesting that, with some crosses between influenza (WSN) *ts* mutants, some clones presumptively classified as ts^+ or "wild-type" recombinants are probably segregating heterozygotes. It was suggested (Zinder) that most of the influenza "recombinants" obtained from crosses with *ts* mutants might be heterozygotes rather than true recombinants, similar to the events detected in crosses involving amber mutants of bacteriophages (fl). Some participants pointed out that good evidence for the occurrence of true recombinants of the influenza virus exists. However, since the very high recombination frequencies (10 to 13 percent) of influenza *ts* mutants remain unexplained (considering genome size), it is not at all inconceivable that either genetic or replicative heterozygotes could account for this anomaly by exaggerating and masking true recombination frequencies. Evidence was also presented (Simpson) that stocks of the influenza *ts* mutants contain a large proportion of virus that is noninfectious but genetically competent in recombination.

The genetics of paramyxoviruses was discussed by Simon who presented data from a dissertation (J. Dahlberg) on *ts* mutants of Newcastle disease virus (NDV). These workers performed complementation tests with 48 *ts* mutants that fell into eight or nine groups although there was strong clustering within a single group. While segregation analyses or other tests for heterozygosis were not carried out, it was concluded that recombination did not occur ($<5 \times 10^{-5}$) with these mutants and that all "ts^+" clones were actually complementing heterozygotes. Simon presented evidence that populations of NDV are heterogeneous with regard to their ploidy, many particles incorporating more than one genome. The occurrence of ploidy and heterozygotes among myxoviruses (influenza) and paramyxoviruses (NDV) has long been recognized but it is apparent that their full significance in genetic interactions is yet to be evaluated.

Pereira closed the discussion on genetic recombination with a review of his work on interaction of human and avian strains of influenza A virus. Using the technique of cross reactivation, it was shown that reactivation of fowl plague virus with different human strains of influenza resulted in transfer of the genetic determinants for neuraminidase protein of the helper virus (noninactivated human serotypes). The polygenic nature of these determinants was suggested. The final discussion topic of the genetics session involved the recent work of Chanock and associates concerning progress in the development of vaccine strains employing attenuated *ts* mutants of various respiratory agents including respiratory syncitial virus (RS), rhinoviruses, and even *Mycoplasma pneumoniae*. The desirability of isolating such mutants with presumed affinity for localization in the upper respiratory tract, where they should be capable of stimulating local production of IgA-type antibodies, was suggested by the finding that circulating antibodies actually exert an adverse effect in the case of infections evoked by RS virus. The successful isolation of several *ts* mutants of these respiratory agents was described (Chanock, Perkins, Steinberg). One now awaits an experimental confirmation that such mutants will be as useful as one might anticipate. Appearance of virulent revertants may be precluded by selection of appropriate mutants under conditions where multiple mutations are almost certain to have occurred.

The session on the biosynthesis of influenza virus and its components was disappointing in the sense that no new data became available shedding light on some of the enigmas surrounding the replication of these viruses, such as the nature of the actinomycin-sensitive, host-controlled functions. Pons reviewed his earlier work showing that actinomycin D blocks formation of the influenza replicative form of RNA. It was suggested (Braun) that some insight into this problem might be gained if the influence of agents stimulating nucleic acid synthesis (for example, by oligonucleotides) were investigated. Zinder suggested that a more critical examination of the effect of protein inhibitors, added late in the infection cycle, on viral RNA synthesis might be warranted. Interesting new findings concerning the surface structural proteins of influenza virions from studies of

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