18 May 1979 • Vol. 204 • No. 4394 $1.50

SCIENCE

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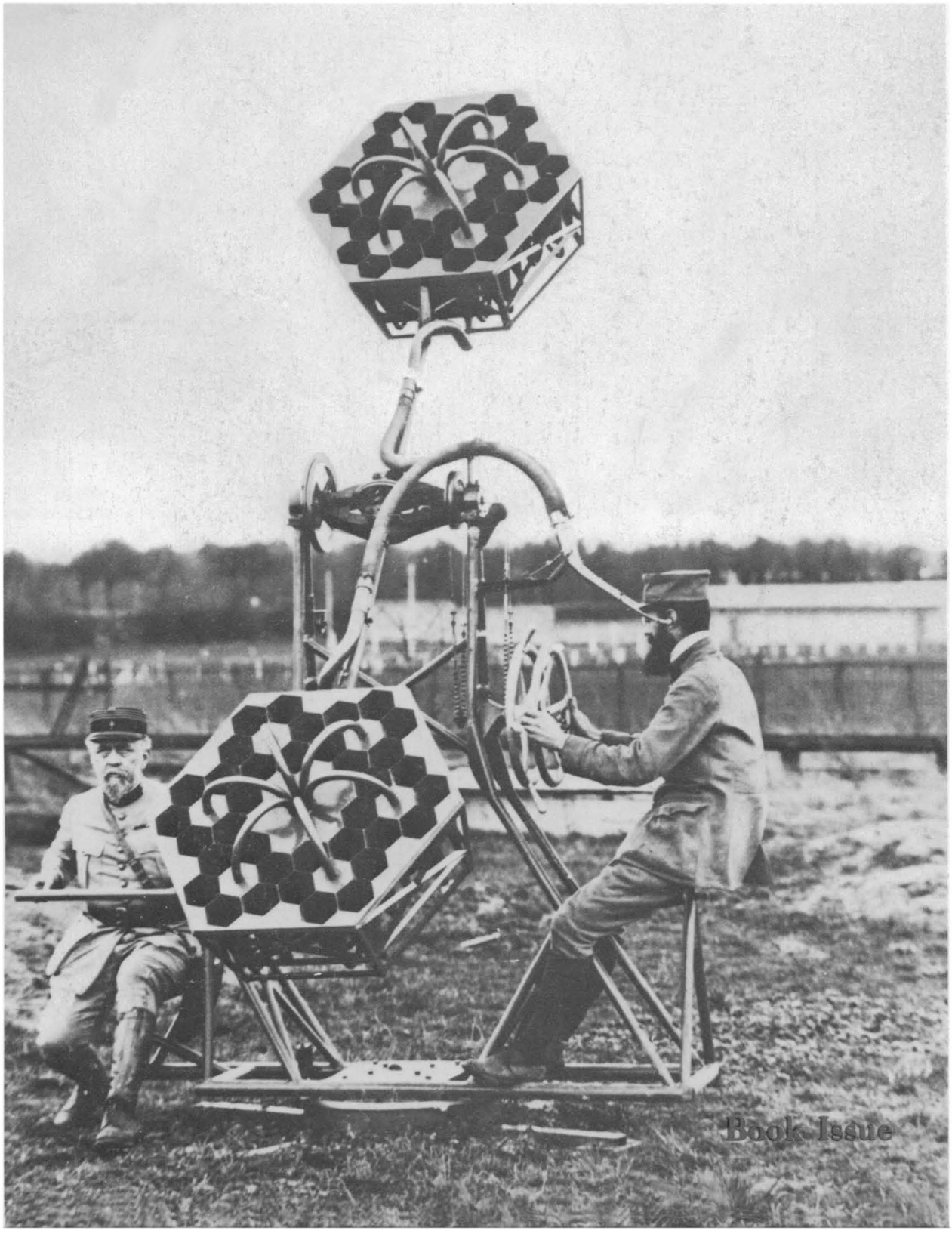

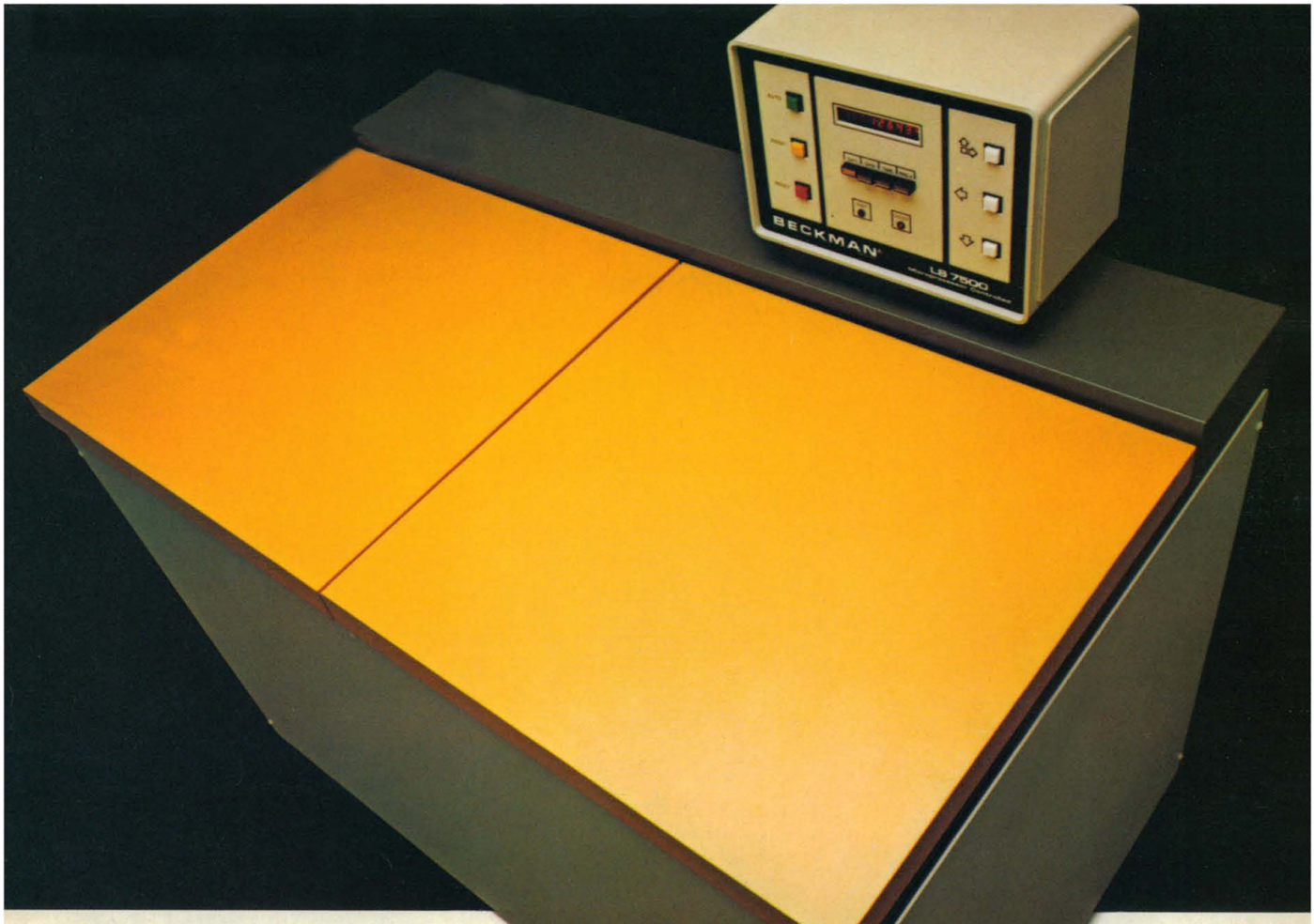

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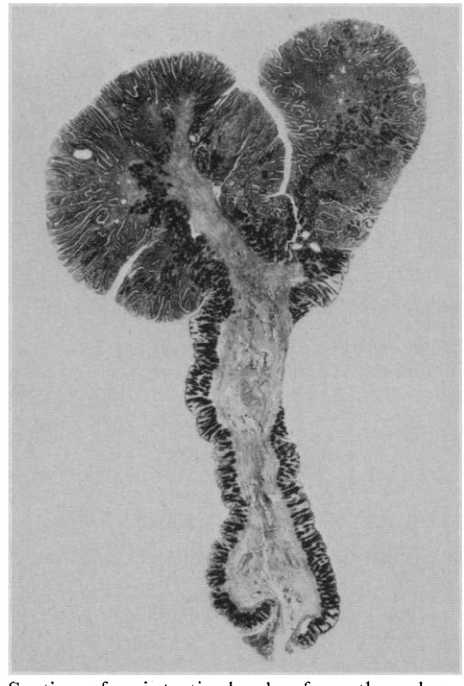

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18 May 1979

Volume 204, No. 4394

SCIENCE

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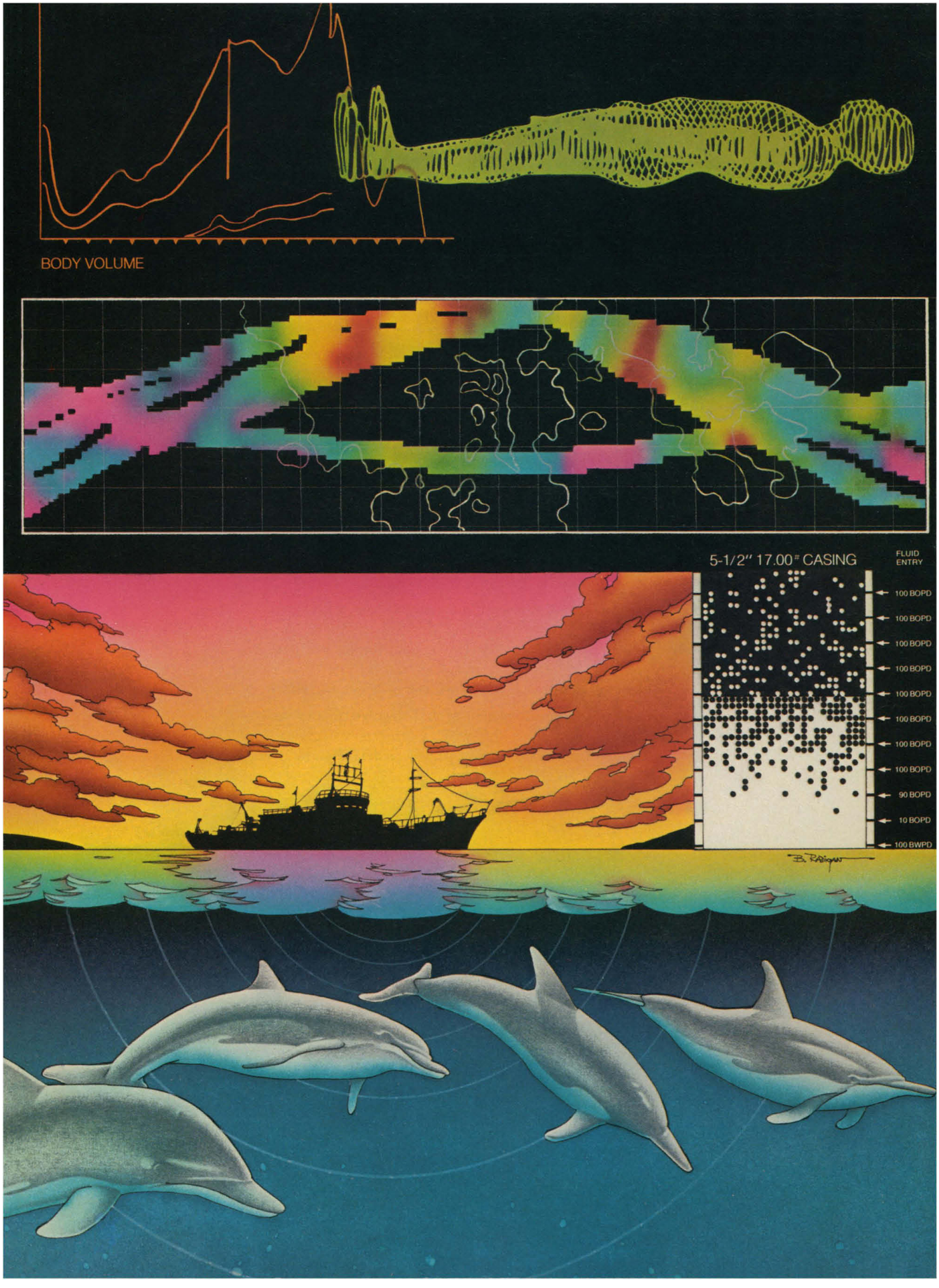
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

COVER

The physicist Jean Perrin (right) using an apparatus to detect enemy airplanes by sound during the First World War. Photograph from American Institute of Physics Niels Bohr Library, reproduced in Spencer R. Weart's *Scientists in Power*, reviewed on page 741.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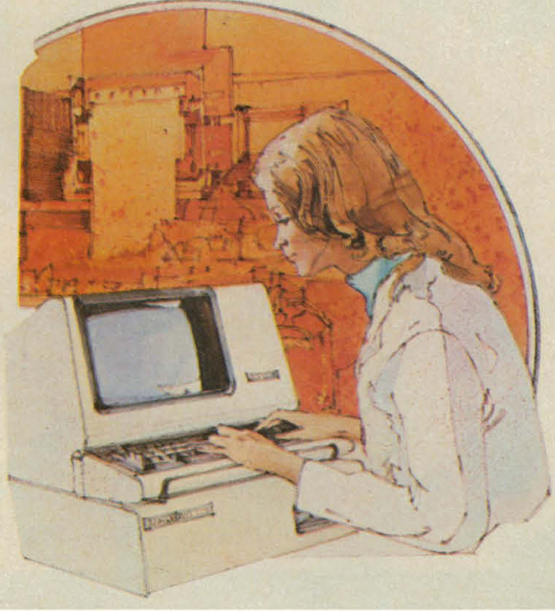

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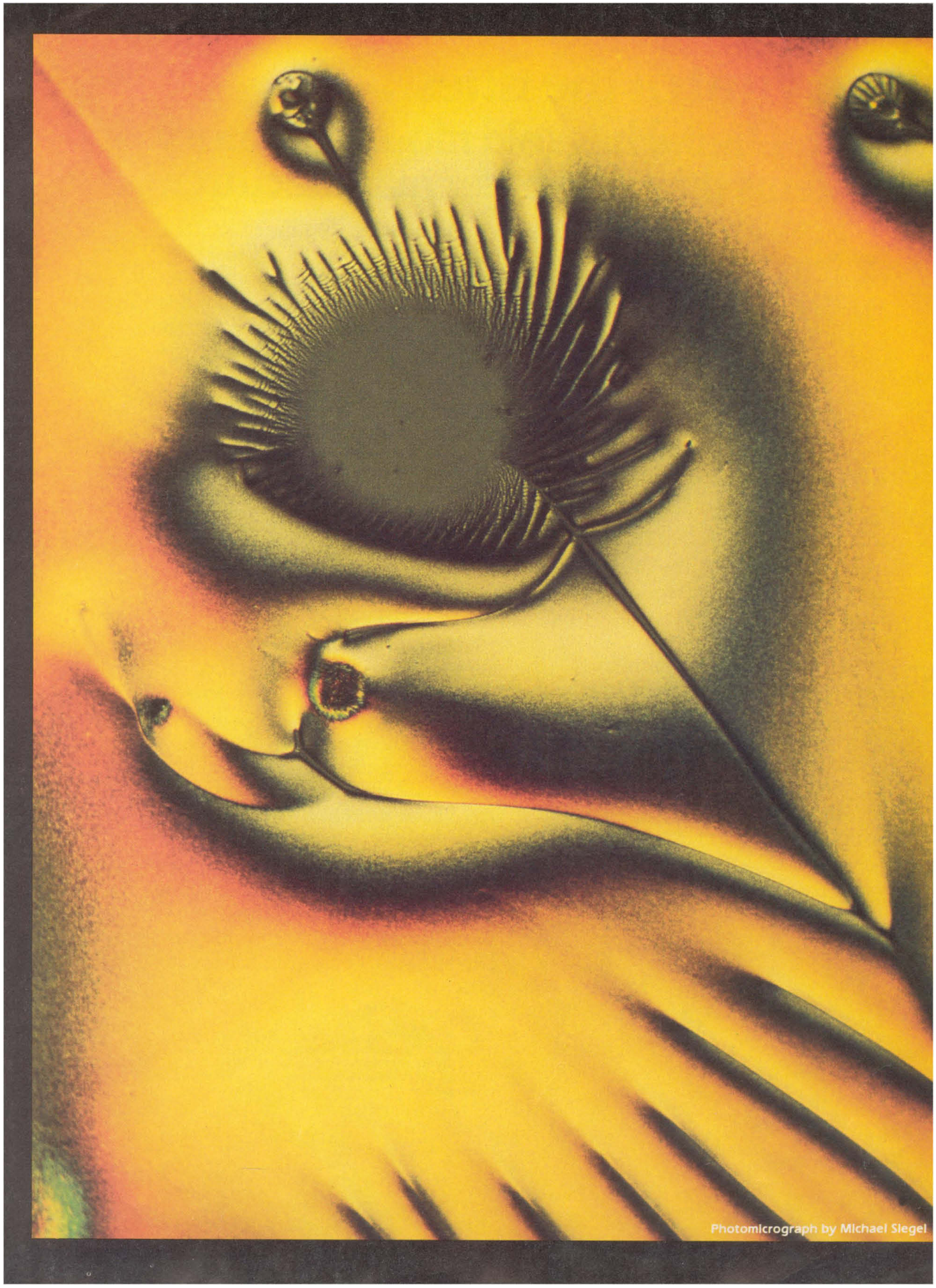
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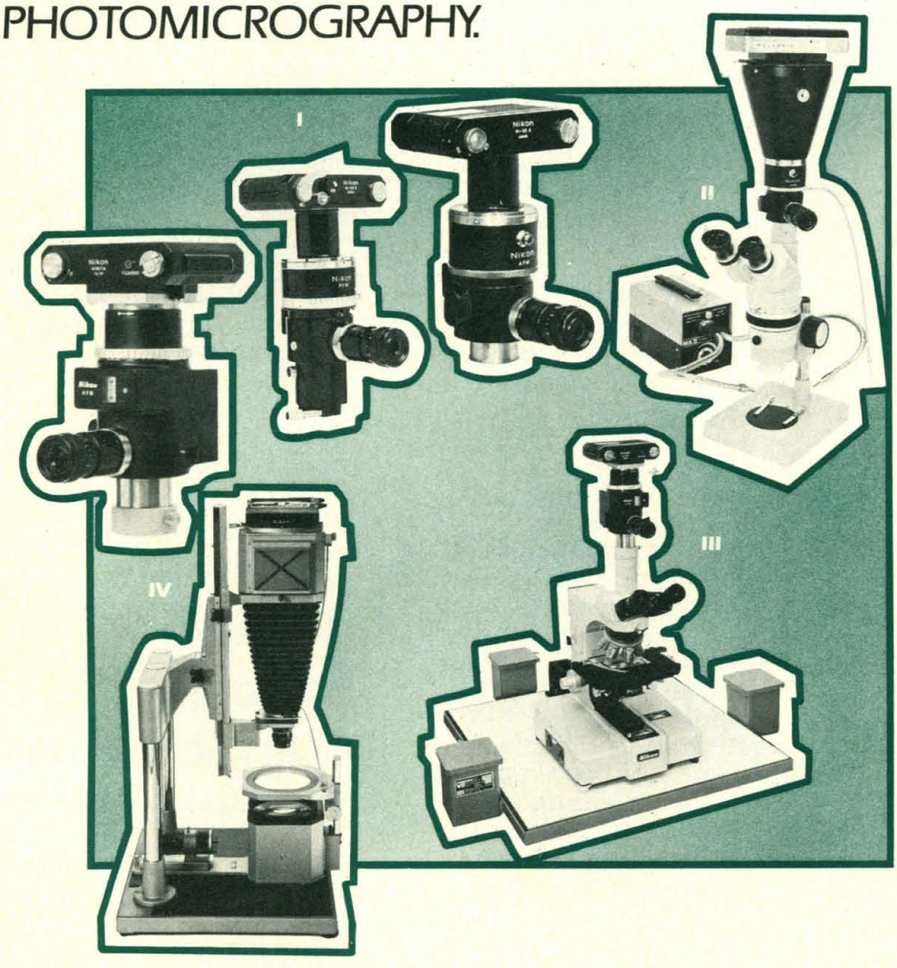

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If your research substances, start with Chemical

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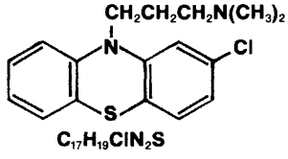
The Secret of Systematic Indexing... One Substance Gets One Name

Chemical substances present a special searching problem because one substance may go by many names. The drug Chlorpromazine is a good example. Different journal articles call it "Aminazin," "Clorpromazin," "Propaphenin," or "2-Chloro-10-(3-dimethylaminopropyl) phenothiazine." There are at least 100 designations (including trade names) for this one substance:



Do you need to look up 100 names for Chlorpromazine to avoid missing literature on this drug? Not if you use the CAS Indexes to CHEMICAL ABSTRACTS (CA).

In CA, one substance goes by one name—the CA Index Name. That's why all references to a given substance are found at one place in the CA Chemical Substance Index. Find the name and you'll find the references—it's simpler than you might think.

CA Index Names exemplify the *controlled vocabulary* used in CA indexes to assure that all substances will be referenced consistently. These names are chosen according to accepted recommendations of the International Union of Pure and Applied Chemistry (IUPAC).

By indexing the same substances always in the same way, CA avoids the confusion caused by differences in terminology used in the original literature. Moreover, most CA Index Names are precisely descriptive of a substance's molecular structure. This is an important benefit, because you can translate the name into the structure from which it was derived, and vice versa.

CA chemical substance names became more systematic with the beginning of the CA Ninth Collective Index period (1972-1976). Many nonsystematic names were cross-referred to more fully systematic names in order to improve searching of a single substance and its closely akin derivatives.

Fully systematic names permit structurally related substances to be grouped alphabetically in the CA Chemical Substance Index. This is another contribution to efficient searching, and it was impossible when many nonsystematic, common language terms were used.

To search chemical substance references in earlier CA volumes, you should use the CA Formula Index. This will connect you with the relevant literature even though a substance's CA Index Name may have changed from one Collective Period to another. You should also check the CA Index Guide covering the period of your search to find the Index Name used at that time for a given substance.

Three Steps Toward Efficient Literature Searching

A study of Chlorpromazine involves checking three CAS publications. You can find references on many chemical substances by following essentially the same steps:

concerns chemical it should Abstracts Indexes.

1. Find the CA Index Name

First, looking up Chlorpromazine in the CA INDEX GUIDE, you find the following entry:

Chlorpromazine
See *10H-Phenothiazine-10-propanamine, 2-chloro-N,N-dimethyl- [50-53-3]*

This is the fully systematic CA Index Name. It designates the unique molecular structure and eliminates the ambiguity arising from trade names and "common language" terms applied to this drug. The five-digit number in brackets is the CAS Registry Number; it has no structural significance but provides a concise identification (somewhat like a social security number) for the substance.

2. Go to the CA Indexes

Now that you have the CA Index Name, it's a simple matter to find literature references. Assuming that studies published after 1961 are of primary interest in this case, you go to the CA Seventh, Eighth, and Ninth Collective Indexes. Each covers five years (ten volumes) of CA: together, the three collectives provide access to all chemically-significant literature referenced in CA between 1962 and 1976. For more recent studies, check the semiannual CA Volume Indexes published since 1976.

No matter what term was used for this drug in the literature, any study concerning Chlorpromazine is listed under the CA Index Name:

10*H*-Phenothiazine-10-propanamine
•
•
•
——, **2-chloro-*N*,*N*-dimethyl-** *(chlorpromazine) [50-53-3]*
10*H*-Phenothiazine-10-propanamine, 2-chloro-*N*,*N*-dimethyl- *[50-53-3]*, **analysis**
detection of, by gas chromatog., 128228u
detn. of
in blood, 111152s
in blood and urine, by gas chromatog., 128222n
in blood and urine, in overdosage, 47872x
•
•
•
10*H*-Phenothiazine-10-propanamine, 2-chloro-*N*,*N*-dimethyl- *[50-53-3]*, **biological studies**
absorption of, by cassava powder, in simulated stomach conditions, 178750d
acetylcholine metab. by brain response to, 145828g
acetylcholine of brain striatum response to, dibutyryl cyclic AMP in relation to, 127222a
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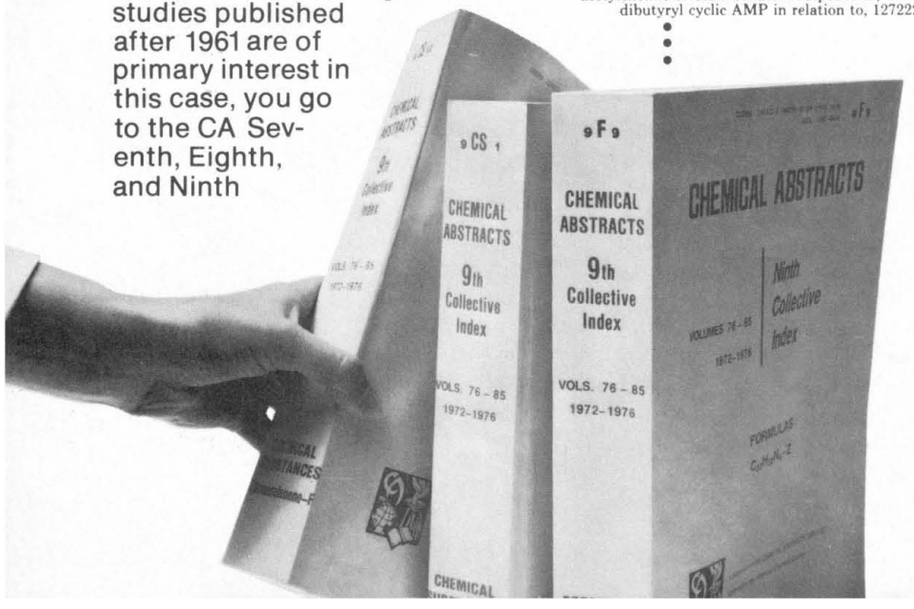

3. Read the Abstracts in CA

Having obtained the pertinent abstract numbers, you then locate and read the abstracts in CA. These provide an excellent basis for deciding which documents you need to review in their entirety. Your literature study is well underway, and you can be sure you haven't missed any important sources of information.

The Result: More Information, Your Time More Effectively Utilized

Searching scientific literature will never be easy. It takes considerable know-how on *your* part to discriminate between vitally important studies and those of marginal interest. But the job can be done more efficiently, reliably, and thoroughly with the help of abstracts and indexes from CAS.

As long as chemistry-related information continues to grow, CA and its indexes will remain an excellent beginning for your research.

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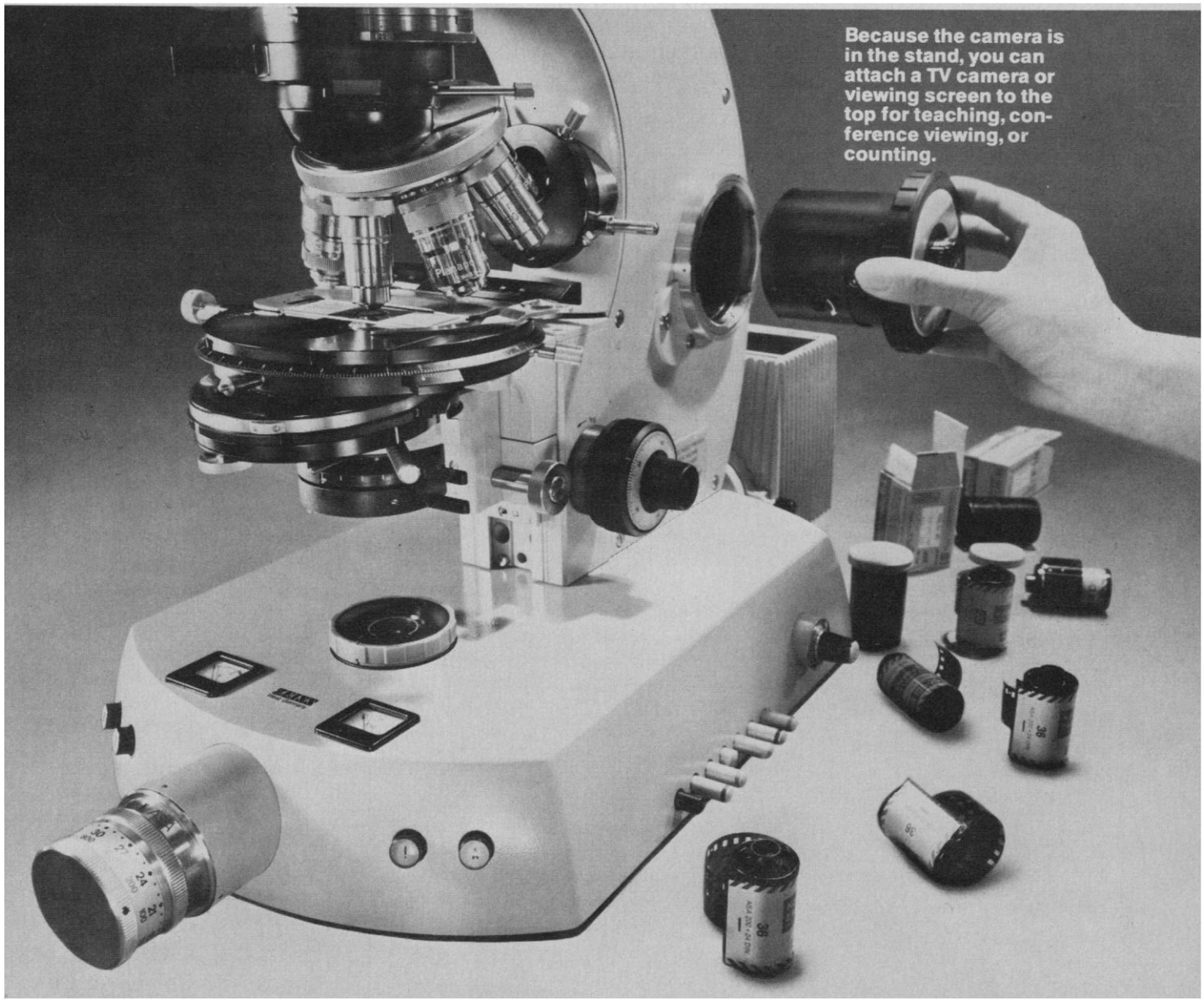

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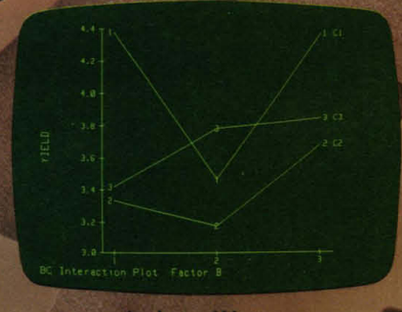

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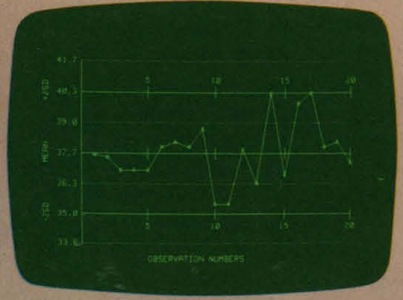
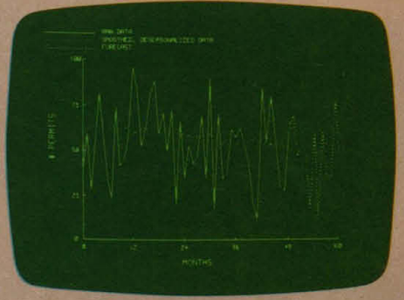


Levey-Jennings Plot



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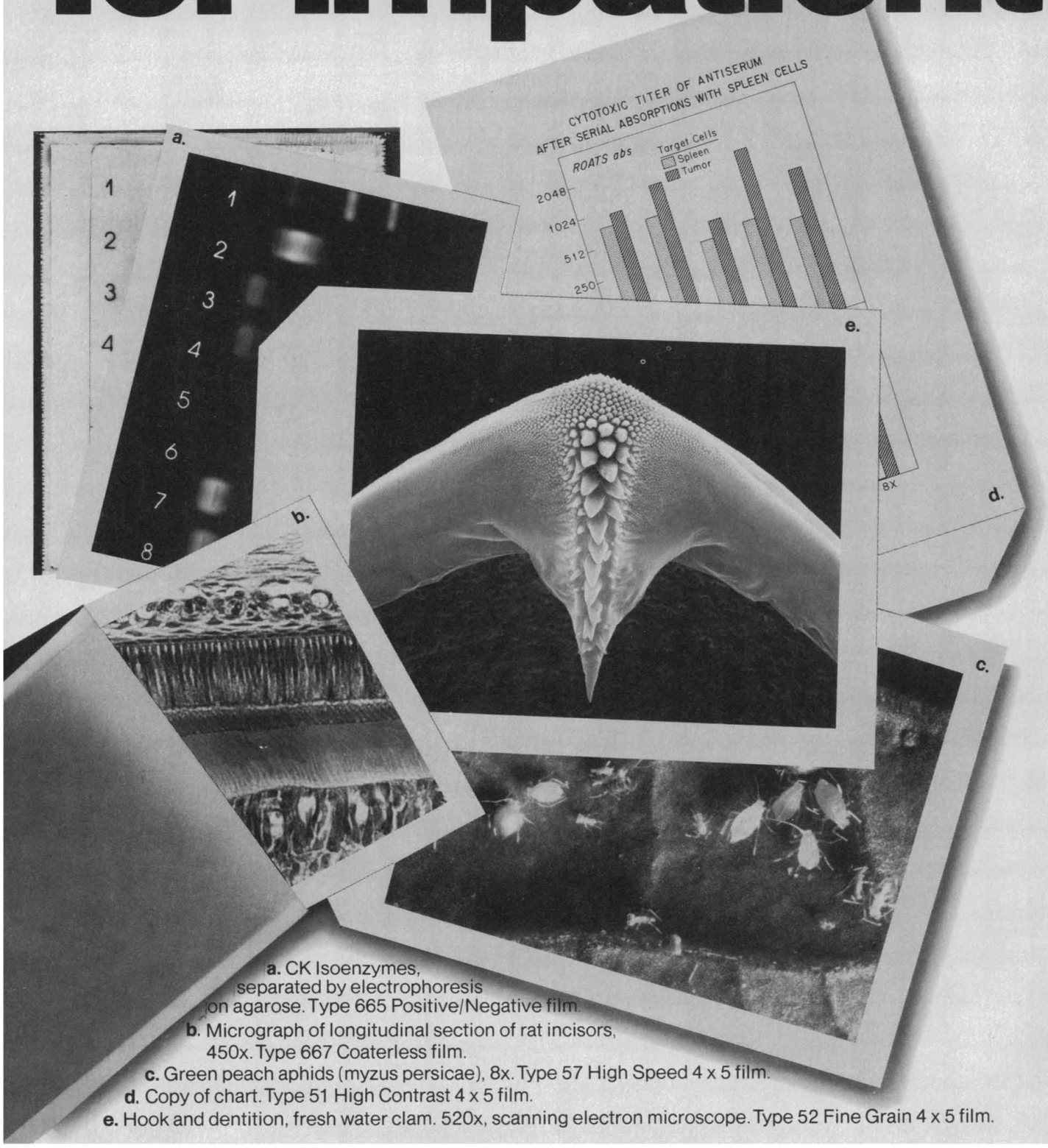

a. CK Isoenzymes, separated by electrophoresis on agarose. Type 665 Positive/Negative film.

b. Micrograph of longitudinal section of rat incisors, 450x. Type 667 Coaterless film.

c. Green peach aphids (myzus persicae), 8x. Type 57 High Speed 4 x 5 film.

d. Copy of chart. Type 51 High Contrast 4 x 5 film.

e. Hook and dentition, fresh water clam. 520x, scanning electron microscope. Type 52 Fine Grain 4 x 5 film.

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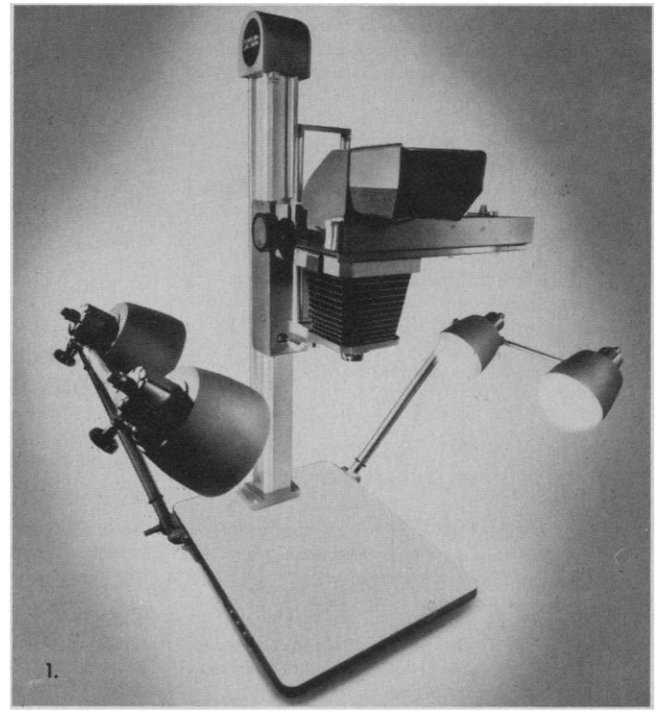
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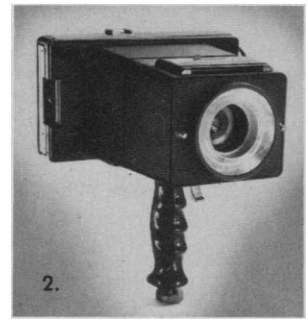
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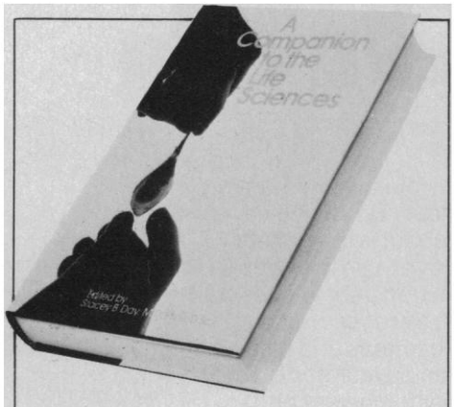

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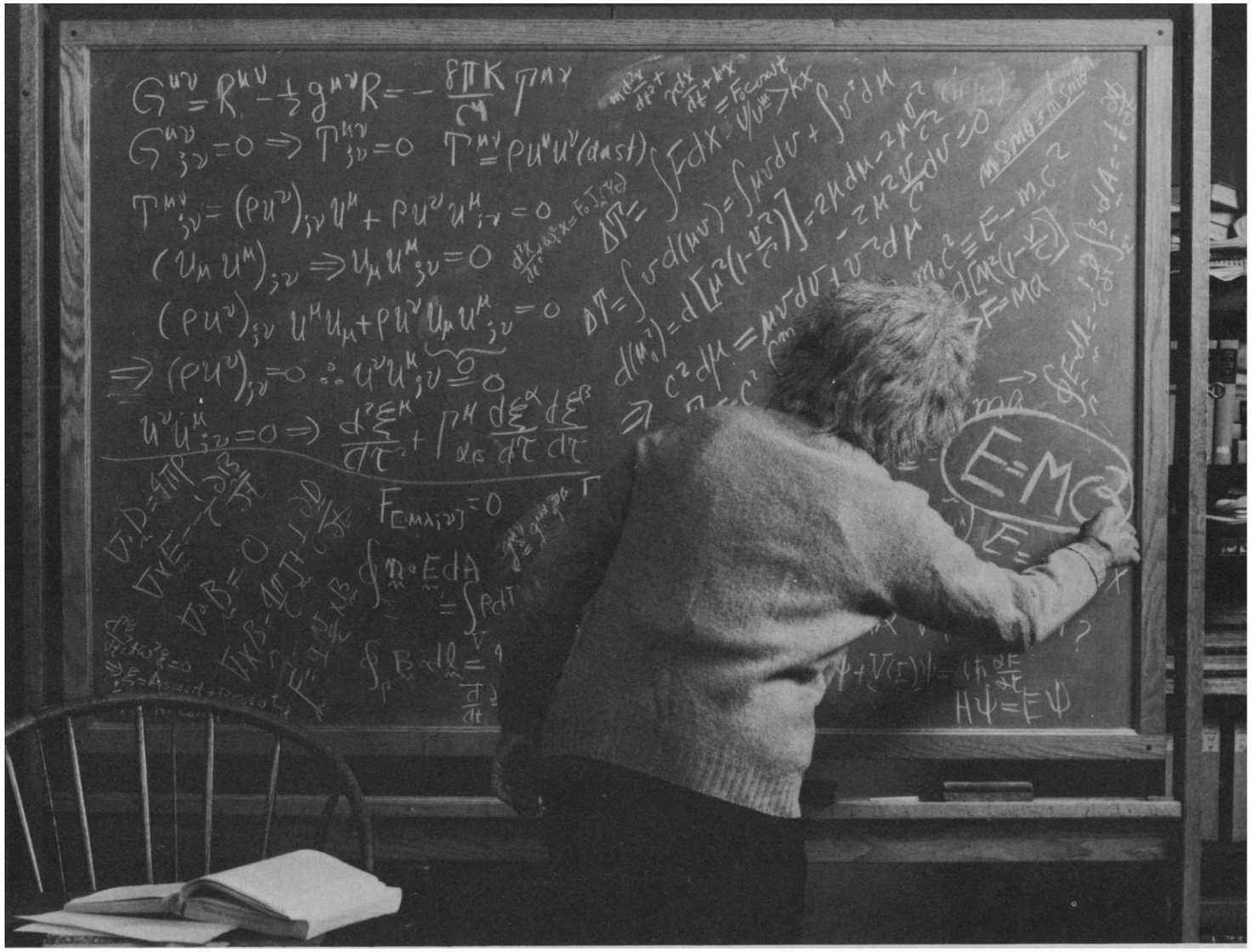

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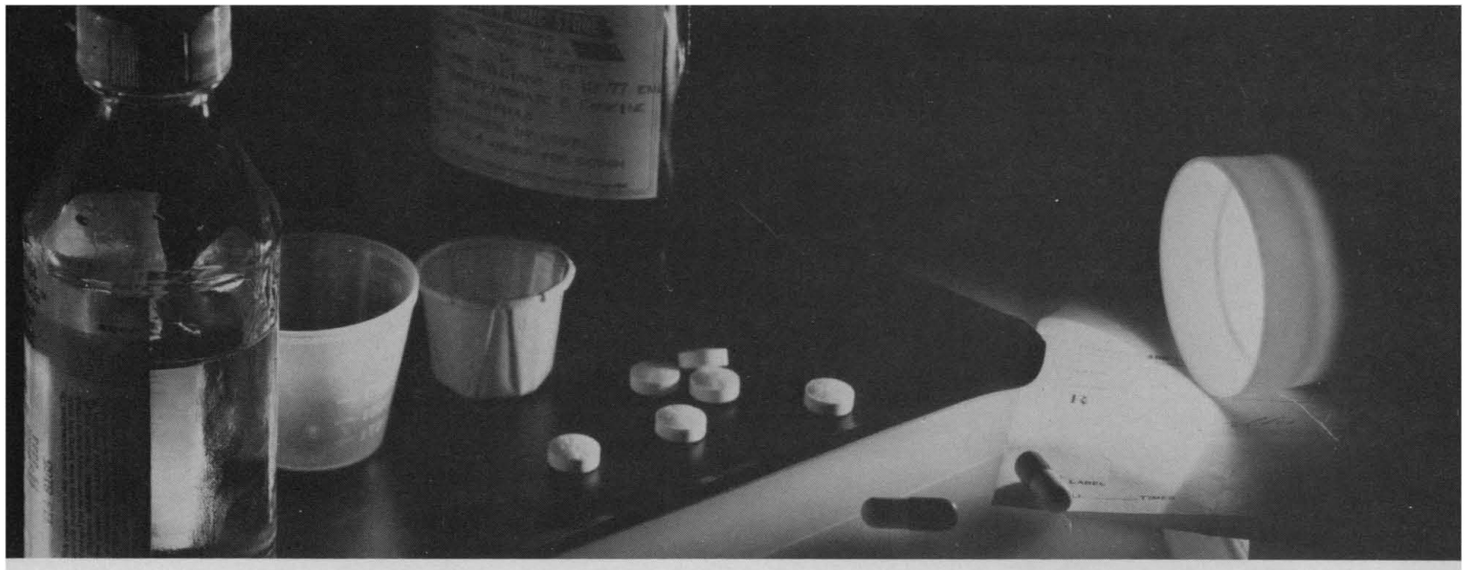

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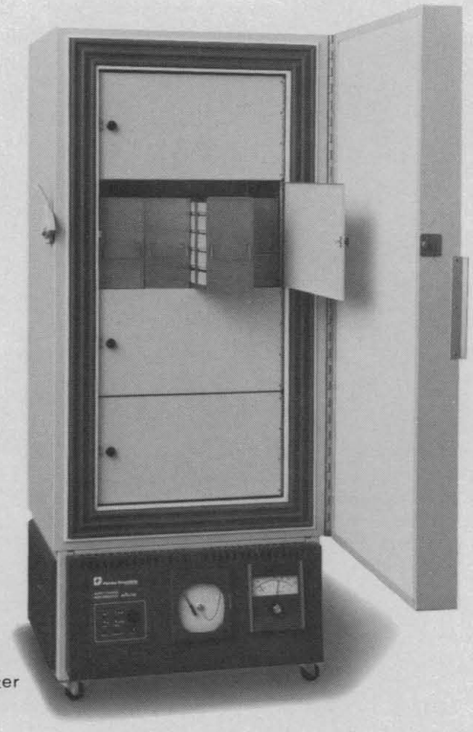

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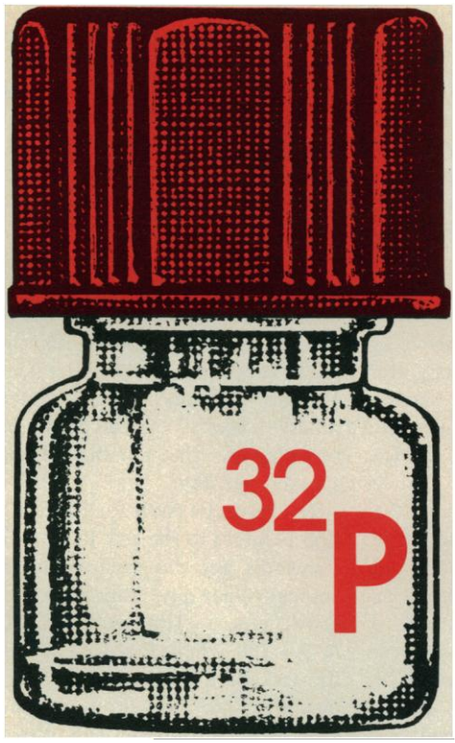

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*Method of Maxam, A.M., and Gilbert, W., *Proc. Nat'l Acad. Sci. USA, 74,* 560–564 (1977).
**Method of Rigby, P.W.J., Dieckmann, M., Rhodes, C., and Berg, P., *J. Mol. Biol., 113,* 237–251 (1977).

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LETTERS

Medical Exchanges

Secretary of Health, Education, and Welfare Joseph Califano's efforts to decrease the supply of physicians may have even further repercussions than suggested in R. Jeffrey Smith's article (News and Comment, 16 Feb., p. 630) because the asserted oversupply of physicians is being used as an argument to further discourage foreign medical study by Americans and will doubtless serve as an argument for further increasing the stringency of visa issuance to physicians from other countries. As with most efforts to artificially limit people's choice of occupation, there is a serious chance of throwing out the baby with the bath water. The baby in this case is the mass of physicians from Europe and elsewhere who are as fully qualified as American physicians who would come to the United States for residencies, research, or other training but who will be unable to do so because of visa and licensing difficulties. American medicine has benefited enormously from nonimmigrant medical exchanges; at one time it was even modish for Americans to train abroad. The vigilantes of medicine who would eliminate those underqualified physicians who hope to reap the profits of fee system medicine may also serve to isolate American medicine from the free exchanges of skills and information that have been so important to all concerned in the past. I have no doubt that medical care can only benefit from carefully scrutinizing each practitioner, but with the understanding that other countries have succeeded in producing physicians as qualified as our own.

CECIL H. FOX

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Karolinska Institutet,
Karolinska Sjukuset,
S-104 01 Stockholm, Sweden

"Low-Risk" Cigarettes: The Debate Continues

In her article of 1 September 1978 (News and Comment, p. 795), Jean L. Marx quotes briefly from our previous letter to *Science* regarding Gio B. Gori's article (17 Dec. 1976, p. 1243) on "low-risk cigarettes." A later article (*1*) builds on the erroneous statistical foundation of the first and includes a misleading table of "critical levels" for low tar and nicotine cigarettes.

Gori's fundamental conceptual error is equating a (incorrectly computed) lack of statistical significance with the absence of a substantive effect. This is stated by Gori and Lynch (*1*, p. 1256): "The inability to verify this reduced risk might lead to its being considered socially tolerable." By their analysis the risk to the smoker of "critical levels" of cigarettes may be up to 100 percent greater than the risk to the nonsmoker.

In the *Science* article the statistical methodology to which we objected is contained in reference 45. We set forth here some of the methodological errors we believe were made in the handling of Harold A. Kahn's data (*2*) relating the relative risks of cancer of the lung and bronchus to the number of cigarettes smoked per day.

1) The expression for R (Gori's equation 2) refers to the risk to a smoker of X cigarettes per day relative to the nonsmoker (0 per day), that is, R is the "relative risk." His equation 2 gives $R = 1.388$ when $X = 0$. This says that the risk of a person who smokes zero cigarettes per day (surely a nonsmoker) is 38.8 percent greater than the risk to a nonsmoker! Anyone capable of doing arithmetic should be disturbed by this result and should look with suspicion upon any conclusions drawn from an equation which yields such an answer.

2) In fitting his equation, Gori (*3*) graphs the relative risk for smokers of one to nine cigarettes per day versus ten, rather than the traditional class interval midpoint—five. He similarly graphs other points at the upper boundary of the interval of cigarette usage. That is, his graphing technique says that the average number of cigarettes consumed per day by persons who consume one to nine cigarettes per day is ten. This has the effect of greatly underestimating the risk of smoking any given number of cigarettes, that is, underestimating the slope of the dose-response curve.

3) Gori fits a quadratic equation to these data where a straight line is appropriate (that is, the quadratic coefficient in his equation is not significantly different from zero and hence should not be included). This inflates the variability of the interpolated values of the relative risk thereby increasing the estimate of number of cigarettes which may be smoked without a "significant" effect. In fact, for the properly fitted straight line and the correct "significance" computations, any number of cigarettes, however small, will yield a "significant" increase in cancer risk. The true "critical" daily number of cigarettes is zero.

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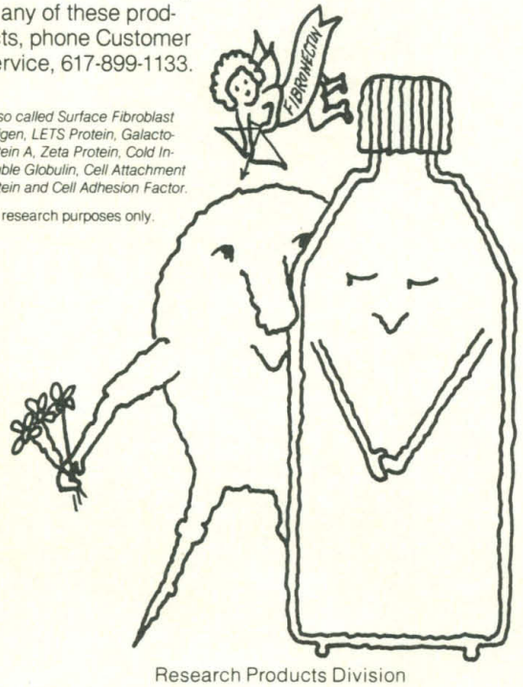

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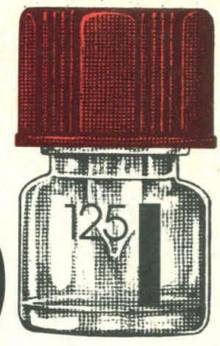

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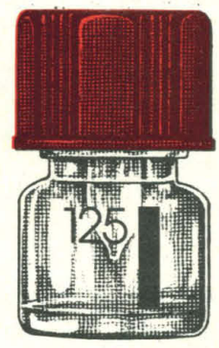

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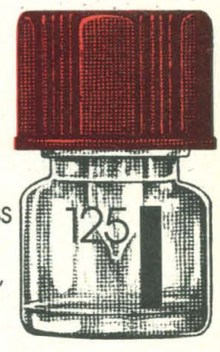

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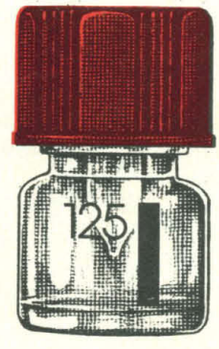

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where X is the number of cigarettes smoked per day. (When $X = 0$, $R = 1$, which is what the relative risk to a nonsmoker must be.) This yields the following interpolated increases in risk associated with various values of daily cigarette usage.

Daily cigarette usage	Increase in risk compared to that of a nonsmoker (%)
2	106
1	53
0.2	11
0.1	5

That is, smoking two cigarettes per day is associated with an estimated increase in cancer risk of 106 percent, one cigarette per day with a 53 percent increase, and so forth. Gori states in his article that for these data "the critical value lies between 1 and 2 cigarettes per day." Marx reports that "Gori says he redid the analysis in accordance with the suggestions of Gart and Schneiderman and did not find enough difference in the results to warrant changing his conclusions." We find it conceivable that someone might assert that between a 50 to 100 percent increase of cancer is "tolerable" or "acceptable," even though we think these increases are very large and not acceptable to us.

Quite apart from the subjective judgment of what is "tolerable" or "acceptable," we think it important to understand how the estimates were developed and how erroneous techniques lead to untenable conclusions.

JOHN J. GART

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MARVIN A. SCHNEIDERMAN

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References and Notes

1. G. B. Gori and C. J. Lynch, *J. Am. Med. Assoc.* **240**, 1255 (15 September 1978).
2. H. A. Kahn, in *Epidemiological Approaches to the Study of Cancer and Other Chronic Diseases*, W. Haenszel, Ed. (Monogr. No. 19, National Cancer Institute, Rockville, Md., 1966), pp.1–125.
3. Gori gives the intervals of cigarette usage as 1 to 10, 11 to 20, 20 to 39, and > 40. The original study (*2*, pp. 55–57) gives 1 to 9, 10 to 20, 21 to 39, and > 39.

Gart and Schneiderman address two separate articles, one by me published in *Science*, and the other in the *Journal of the American Medical Association* (*JAMA*) written with Cornelius J. Lynch (*1*).

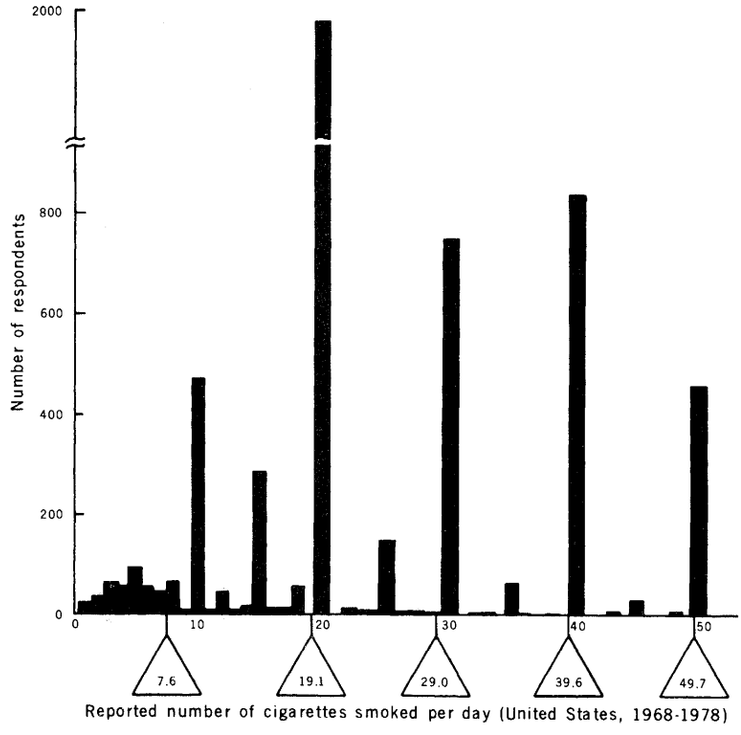
1) They object to equation 2 of the *Science* article, which applies to mortality from lung cancer. They contend that the risk to a nonsmoker is 1, whereas this equation gives a higher estimated value.

However, a risk of 1 is valid for respondents who never smoked. In surveys of U.S. populations, those who report a zero cigarette consumption at any given time include ex-smokers, pipe and cigar smokers, and occasional cigarette smokers. Epidemiological data consistently show that ex-smokers, for example, have relative risks in excess of 1 for as long as 15 years after cessation, even though they report zero cigarette use during this time.

Therefore, estimates of risk in excess of 1 are a more plausible reflection of true conditions than a statistically imposed prejudice.

Moreover, equation 2 refers to an isolated lung cancer study and is given only as a procedural example. It is worth noting that the use of only epidemiological data on lung cancer would have resulted in higher critical values than those estimated in the conclusions of the *Science* article. For those conclusions, the more conservative data referring to overall mortality were used. The estimated risks for zero cigarette consumption in the equations fitted to these studies ranged from 0.95 to 1.06. Values such as these should be viewed as underestimates of reality, because the four studies analyzed (giving over 3 million person-years of experience, almost 50,000 deaths) included a large portion of former cigarette smokers (*2*) with an ascertained residual risk of 1.4 to 1.5.

2) Gart and Schneiderman object to the choice of the upper boundary of the reported cigarette use interval, as contrasted to using a "traditional class interval midpoint." The midpoint is used when additional information is not available, a practice sometimes referred to as the "equal distribution of ignorance." For tobacco use, however, additional epidemiological information is available. In particular, mean rates of reported tobacco use do not coincide with midpoints of class intervals but usually lie between the 80th and 95th percentiles of the intervals. A review of more than 30,000 respondents of epidemiological studies sponsored by the National Cancer Institute gives a typical frequency distribution of respondents to questions about cigarette use as exemplified in the figure below and indicates that most respondents regard multiple points of five as modes rather than upper boundaries. (Interval means are displayed within the triangles.) It is also well known that respondents to cigarette use questionnaires have an understandable tendency to significantly underreport their consumption (*3*). For these reasons, the upper boundary is a more realistic statistic



than the midpoint for the purposes used. Instead of underestimating the risk, as Gart and Schneiderman contend, the use of upper boundaries gives a conservative overestimation of the risk.

3) Objection has been raised to the use of quadratic coefficients in the *Science* article's analysis, even when some of them are not significantly different from zero. It should be noted that there is no preferred statistical criterion for selecting which terms to include in a regression equation. For the equations in the *Science* article, the corrected coefficient of determination, and not significance, was the criterion used. This provides a close fit between reported and estimated data by reducing standard errors.

4) Gart and Schneiderman contend that the *JAMA* article "builds on the erroneous statistical foundation" of the *Science* article. In light of the preceding remarks, I believe that the *Science* article is not only statistically valid, but more important, is epidemiologically valid, as it addresses epidemiological realities of which Gart and Schneiderman may not be aware. The *JAMA* article uses only one statistic from the *Science* article—the average critical value of 2. By this is meant that a daily consumption of cigarettes having toxic yields equivalent to two of the average cigarettes sold in the United States during the late 1950's would not elevate the smoker's observable risk to mortality significantly above that of the average nonsmoker. Independent of the *Science* article, this critical value would be valid because the four studies upon which it is based had a 0.3 nonresponse bias that results in overestimating the risks (*2*, p. 116). This bias is larger than the difference in risk between that of nonsmokers and that of two-cigarettes-a-day smokers. Thus it alone would preclude inferring a significant difference in risk between nonsmokers and two-cigarettes-a-day smokers. Consequently, the *JAMA* article could stand on its own merits independent of the statistical foundation of the *Science* article.

I believe the *Science* and *JAMA* articles combined present a realistic procedure for gradually reducing the levels of hazard and addiction for the millions of smokers who persist in their habit despite its known health consequences. Our conclusions were, and still are, that although this would not eliminate the risk to the smoker, it has the potential of reducing the current epidemic of diseases associated with smoking to a considerably less serious public health problem.

GIO B. GORI

National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20205

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3. K. E. Warner, *J. Am. Stat. Assoc.* **73**, 314 (1978).

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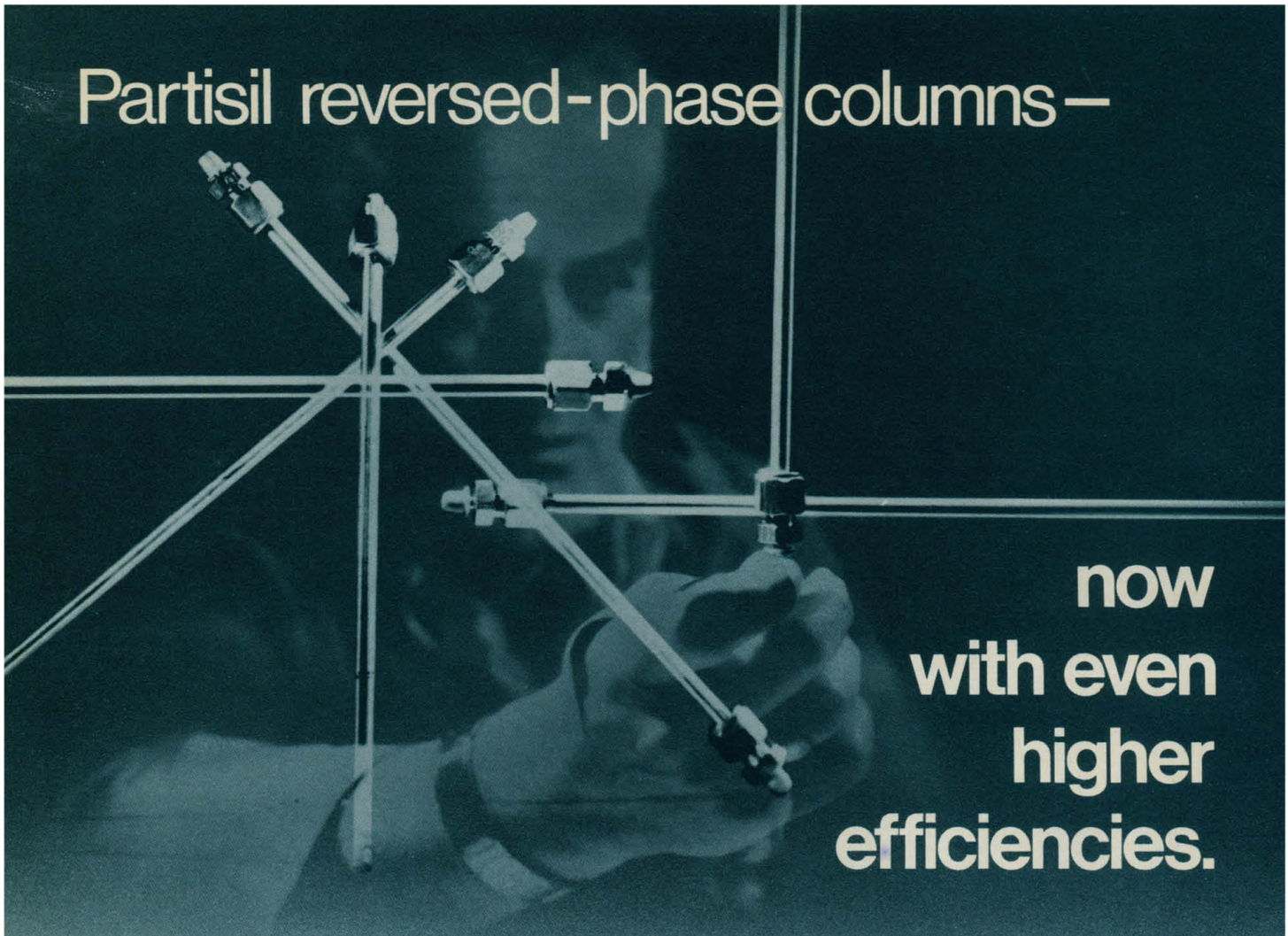

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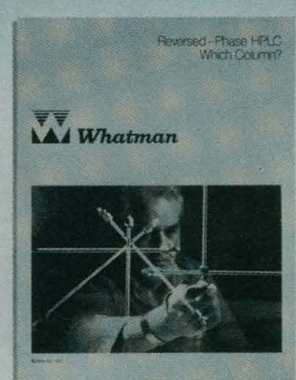

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18 May 1979, Volume 204, Number 4394 **SCIENCE**

Energy Conservation

Conservation was discussed in considerable detail in background material accompanying President Carter's energy message of 5 April. The White House release identified progress since 1973 in saving energy: (i) industrial use of energy has dropped by 6 percent although output has increased by 12 percent, (ii) energy efficiency in residential buildings has increased by 5 to 10 percent, (iii) half of U.S. homeowners have added insulation while living in the houses they now occupy, (iv) the efficiency of home appliances has increased 5 percent and the annual growth rate in home electricity use has been halved (from 6 to 3 percent), and (v) the average fuel efficiency of a new car under EPA tests will be 20 miles per gallon in the 1980 model year compared to 14.4 miles per gallon in 1974.

Many individuals have been conscientious about turning back their thermostats, getting insulation, taking public transportation, buying smaller cars, and cycling or walking to work. Most people have done about as much as they can do or are inclined to do about conservation. Despite the efforts, consumption of oil has increased steadily.

If the United States is to reduce consumption, it must take more drastic measures than have hitherto been employed. In a meeting on 1 and 2 March, the Carter Administration made a commitment to the 17-member governing board of the International Energy Agency to reduce U.S. consumption of oil up to 5 percent. Were such savings to be achieved, price increases by the oil-producing countries might be delayed. The White House enumerated measures that might lead to the promised reduction.

One of the savings proposed is to hold thermostats at no more than 65°F in nonresidential buildings during winter and no less than 80°F in summer. But in almost any building, temperatures vary widely from that at the thermostat. If the regulations are implemented, tens of millions of office workers will suffer.

Although consumption of gasoline is the largest source of demand for oil, the message touched only lightly on conservation of gasoline. The implied hope is that higher prices will discourage auto use. But as others have pointed out, gasoline costs $2.50 per gallon in some countries and consumption has not dropped. Recently, I added up the costs of owning and driving my small car. Use of it saves me considerable precious time and uncertainty. I found that fixed costs including depreciation, insurance, parking, and taxes accounted for 90 percent of the total, gasoline 10 percent. If the price of gasoline were to increase two- to fivefold I would growl, but there would be no change in my driving. At a tenfold increase, I would begin to emulate Senator Proxmire who runs to the office. The fixed costs and miles driven by individuals vary greatly, but it is likely that for the majority, the cost of gasoline is today only a minor fraction of total transportation expenses.

This nation may soon be forced to consider how to cut consumption of gasoline without causing undue hardships and even disruptions in the economy. One target should be the waste that occurs when highways are converted into miles of parking lots (often one notes that a modest decrease in traffic volume results in a greatly enhanced speed). Another target should be joyriding teenagers. Raising the age for a driver's license would also save many lives. Still another target is those heavy old autos that get about 8 miles to the gallon. Taking them off the road would also cut pollution. One move that would really bring conservation is gasoline rationing. The thought is unpleasant, but were rationing to occur there would suddenly be more car pooling, use of public transportation, walking, and more cars in better mechanical adjustment.

Greater conservation could be achieved but it would not be easy or gladly accepted. Sooner or later we may be forced to implement stringent measures, but for the present, conservation is mainly something to talk about.

—PHILIP H. ABELSON

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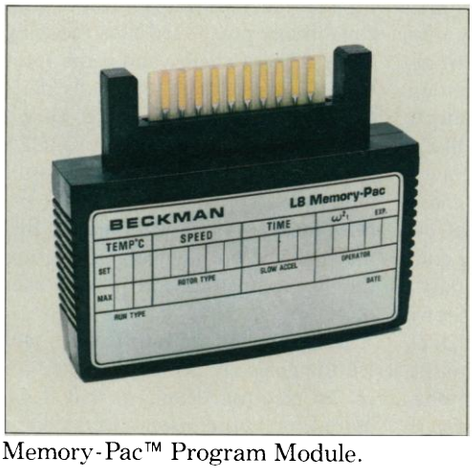

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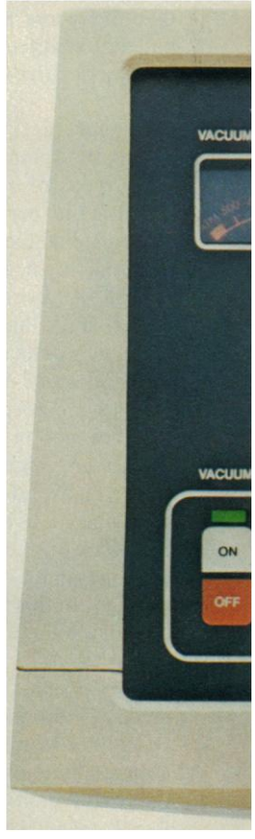

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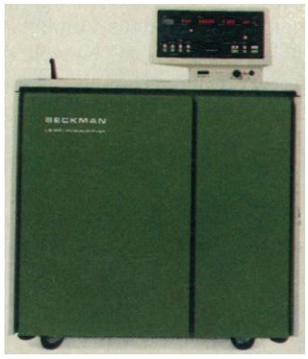

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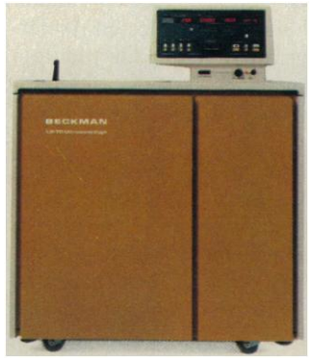

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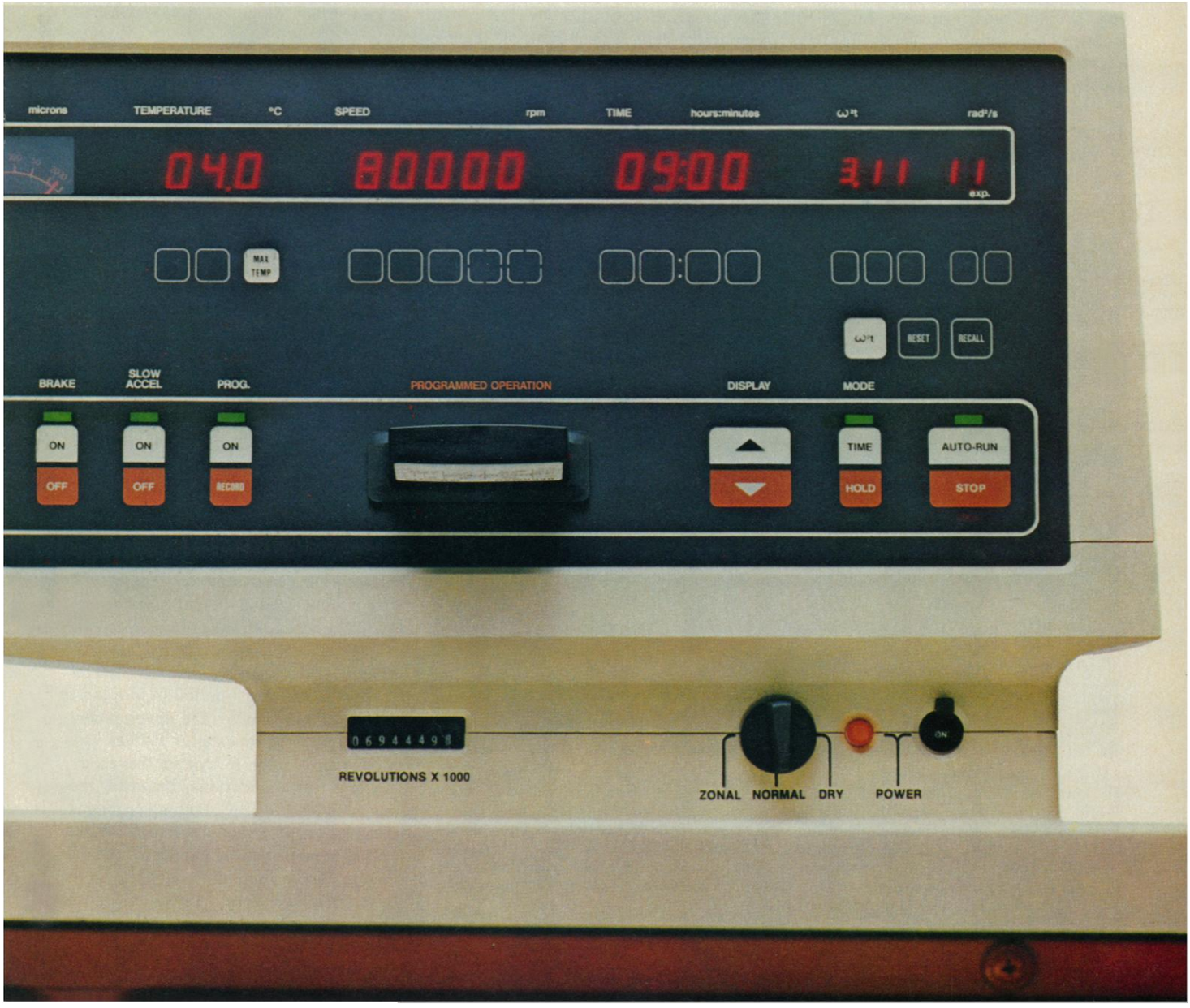

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