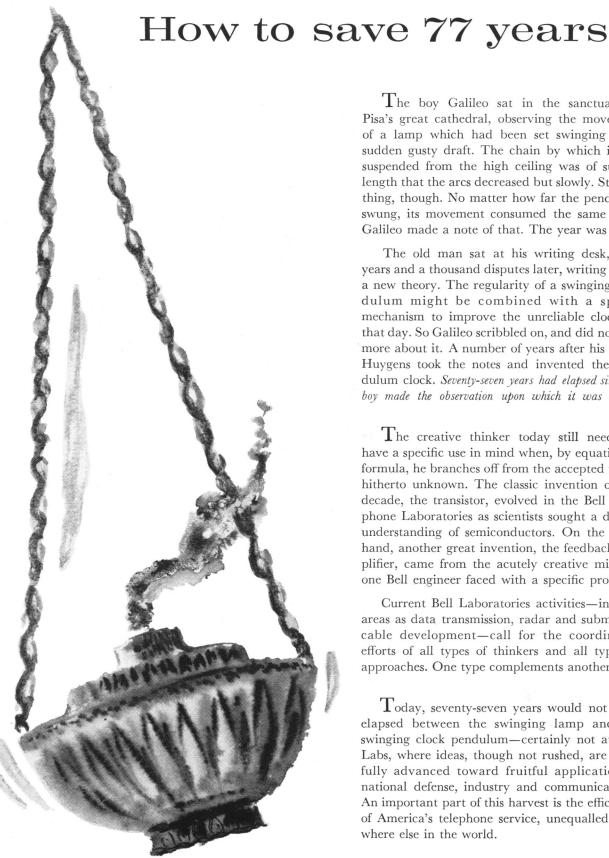
SCIENCE

9 January 1959

Volume 129, Number 3341

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The boy Galileo sat in the sanctuary of Pisa's great cathedral, observing the movement of a lamp which had been set swinging by a sudden gusty draft. The chain by which it was suspended from the high ceiling was of such a length that the arcs decreased but slowly. Strange thing, though. No matter how far the pendulum swung, its movement consumed the same time. Galileo made a note of that. The year was 1581.

The old man sat at his writing desk, sixty years and a thousand disputes later, writing down a new theory. The regularity of a swinging pendulum might be combined with a spring mechanism to improve the unreliable clocks of that day. So Galileo scribbled on, and did nothing more about it. A number of years after his death Huygens took the notes and invented the pendulum clock. Seventy-seven years had elapsed since the boy made the observation upon which it was based!

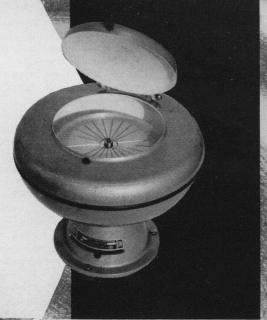
The creative thinker today still need not have a specific use in mind when, by equation or formula, he branches off from the accepted to the hitherto unknown. The classic invention of this decade, the transistor, evolved in the Bell Telephone Laboratories as scientists sought a deeper understanding of semiconductors. On the other hand, another great invention, the feedback amplifier, came from the acutely creative mind of one Bell engineer faced with a specific problem.

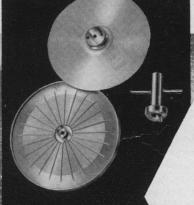
Current Bell Laboratories activities—in such areas as data transmission, radar and submarine cable development-call for the coordinated efforts of all types of thinkers and all types of approaches. One type complements another.

 ${
m Today}$, seventy-seven years would not have elapsed between the swinging lamp and the swinging clock pendulum—certainly not at Bell Labs, where ideas, though not rushed, are carefully advanced toward fruitful application in national defense, industry and communications. An important part of this harvest is the efficiency of America's telephone service, unequalled anywhere else in the world.

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ate plus graduate-or-professional type of school). In the case of technical schools, the best translation would be "institute (of technology)." On the other hand, where we speak of a "high school," Europeans usually speak of a "middle" or "secondary" type of school—never "high."

LEO PAP

State University Teachers College, New Paltz, New York

I wish to thank Leo Pap and others who have written correcting my misimpression concerning the government of Portugal.

With regard to his second point, I think it is worth while to point out that the connotation of the term *Hochschule* in German is not the literal translation to "high school." However, I assumed that most scientists realized that the use of this term in European science did imply a school of higher learning on the level of a university or college.

DAVID M. GATES
National Bureau of Standards,
Boulder, Colorado

Acetylcholine Metabolism and Behavior of Rats

Before Chow and John submitted their paper (1) for publication, they were kind enough to correspond with us at length about their findings. At that time we indicated to them our reasons for believing that their study did not afford an adequate test of our major hypothesis. In their published article no reference is made to the questions we raised, and since Chow and John interpret their data as contradictory to our major hypothesis, we would like to point out publicly why we believe that their experiment does not provide a test of our hypothesis.

In our original Science article (2) we suggested that a higher rate of cortical acetylcholine metabolism is related to a greater number of spatial responses in the Krech hypothesis apparatus. In our second Science article (3) it was made explicit that this referred only to the animal's initial problem-solving behavior. Pentobarbital sodium (which retards acetylcholine synthesis) was shown in that article to affect the animal's choices strongly if it was administered at the outset of maze experience; if it was given after four days of maze experience, the drug had little or no effect.

Chow and John gave their animals six days of maze experience. By that time the animals had adopted different response patterns. In subsequent testing Chow and John found that anticholinesterase drugs had little or no effect on the animals' choice behavior. They conclude, "The fact that such injections did not alter the hypotheses displayed by the animals in running a maze seems to indicate

that hypothesis behavior is not dependent on cortical levels of acetylcholine." Actually, our results and theirs seem to be similar where they can be compared: When animals have had prior maze experience, drugs that affect acetylcholine metabolism do not appear to affect behavior. We urged Chow and John to test the effects of injections on behavior at the *outset* of maze experience, the condition under which we did obtain drug effects. Unfortunately this has not been done, so no comparison can be made under this critical condition.

Quite aside from this major point, there are a number of additional features about the report of Chow and John that make it difficult to evaluate their results.

- 1) Their Table 1 indicates that on a random reward schedule animals of the S1 strain made predominantly spatial choices and animals of the \$3 strain made predominantly visual choices. Such a large strain difference in behaviorin the same direction but far larger than we have ever obtained—would appear to provide striking corroboration of our hypothesis, since we have shown the two strains to differ significantly in cortical cholinesterase activity. The data of the table cannot, however, be taken at face value. Correspondence revealed that over half the S1 and S3 rats were trained to give spatial or visual responses. There is no indication in the table as to which animals were trained to give specific response patterns and which adopted such response patterns spontaneously. Therefore it is impossible to evaluate the apparent strain differences, and we would prefer not to interpret these findings as supporting our hypothesis.
- 2) It has been our experience that when animals are transferred from a schedule that rewards one type of choice to a random-reward schedule, they tend to give up the previously rewarded choice rather rapidly. This did not occur in the Chow and John experiment. Their "no injection" results were obtained on the fifth and sixth days of a random-reward schedule, but many previously rewarded response patterns still persisted. This testifies to the strength of the prior training and indicates further why it would have been difficult to find a drug effect. It is not stated whether the animals were retrained between successive drug experiments (as many as five 6-day sequences were given to an animal). If response patterns persisted through such a long period, it is indeed interesting, and raises additional questions about the meaning of their data.
- 3) The legend of their table indicated that the number of times a rat was tested "varied from 4 to 30." No explanation is given as to why some rats were discarded after only four tests whereas their data up to that point were retained. Because of this feature of the experimental design, the subjects are repre-

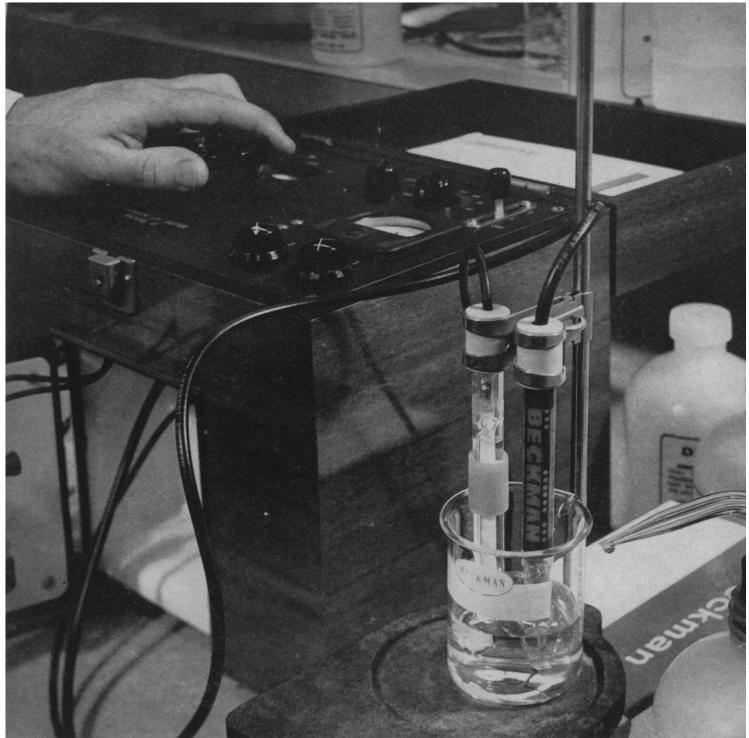


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sented very unequally in the reported data. With such a design, it is difficult to make valid comparisons among the experimental conditions.

4) Diisopropyl fluorophosphate (DFP), unlike eserine, is a persisting anticholinesterase agent; we have found the "half time" of the recovery of cholinesterase after DFP injection to be about 20 days. Therefore the animals that Chow and John tested under "saline" or "no injection" conditions during the six days after the injection of DFP would be poor controls since the effects of DFP would still be strong. There is no way of determining how many of the "control" data of Chow and John were actually obtained under the effects of DFP.

It is clear that our hypothesis relating acetylcholine metabolism and behavior has not yet been adequately confirmed (either by other workers or ourselves). On the other hand, it does not seem that the experiment of Chow and John has rendered it untenable.

MARK R. ROSENZWEIG DAVID KRECH EDWARD L. BENNETT

Department of Psychology and Radiation Laboratory, University of California, Berkeley

References

- 1. K. L. Chow and E. R. John, Science 128, 781 (1958).
- D. Krech, M. R. Rosenzweig, E. L. Bennett, B. Krueckel, *Science* 120, 994 (1954). M. R. Rosenzweig, D. Krech, E. L. Bennett, *Science* 123, 371 (1956).

The disagreement which Rosenzweig, Krech, and Bennett expressed with the conclusions stated in our recent article (1) is based primarily upon the fact that we investigated the effects of intracerebral anticholinesterases upon previously established response patterns. They stated that their major hypothesis is that the rate of cortical acetylcholine metabolism is related to the mode of response in the initial problem-solving behavior of rats in their apparatus, but not to the performance of previously established response patterns. Although in various of their publications (2) they emphasized the role of acetylcholine levels in "adaptive" behavior in new situations, they did not make explicit the latter part of the hypothesis.

Yet, the data about the effects of pentobarbital sodium to which they referred at first seem compatible with that hypothesis and with our own results. We have difficulty, however, in reconciling the data reported by them on the effects of pentobarbital sodium with the explanations and hypotheses they offered. During the first four days, their drugged group (group II) displayed an extremely marked preponderance of light hypotheses, and a consistent mode of behavior was established. They attributed this effect to depression of cortical acetylcholine metabolism by the drug. They further reported that when the drug was discontinued, light hypotheses diminished, presumably as a consequence of restored acetylcholine levels.

To us, this seems to constitute a paradox: Although cortical acetylcholine levels are presumed not to affect the performance of established response patterns, a pattern established with a cortical acetylcholine level altered by a drug becomes modified when the acetylcholine level is restored after the drug is discontinued. Further, they reported that subsequent administration of the drug after the animals had been run for two days without drug again raised lightgoing choices. These various considerations, together with the complete failure of intracerebral eserine to alter hypothesis behavior in our experiments, seem incompatible with their major hypoth-

With respect to the additional questions raised by our colleagues, two comments seem in order. No data were discarded, as suggested in their point 3. Animals were run so long as their physical condition permitted. Finally, while we agree that the effects of diisopropyl fluorophosphate (DFP) persist for some time, the results of DFP experiments were essentially comparable to results obtained with eserine, and certainly the failure of DFP to alter hypothesis behavior cannot be attributed to its subsequent prolonged effects on cholinesterase activity.

We have no explanation to offer for the interesting discrepancy between the effects of pentobarbital sodium before and after appreciable maze experience. Certainly other consequences of this drug besides altered acetylcholine synthesis are well known and might equally well be relevant to these effects, just as factors besides cholinesterase concentrations are relevant to the regulation of acetylcholine metabolism. In view of the inconsistencies outlined above, we doubt that effects on acetylcholine levels play an important role in the phenomenon. We agree that it would be of interest to observe the effects of anticholinesterase injections at the outset of maze experience. Since our current research activities lie in other areas, and since Rosenzweig, Krech, and Bennett are admirably qualified to pursue such problems, we look forward to the publication of further data which will clarify these issues.

K. L. Cноw E. R. John

Department of Physiology, University of Chicago, Chicago, Illinois

- 1. K. L. Chow and E. R. John, Science 128, 781 (1958).
- D. Krech, M. R. Rosenzweig, E. L. Bennett, B. Krueckel, Science, 120, 994 (1954); M. R. Rosenzweig, D. Krech, E. L. Bennett, Science 123, 371 (1956); D. Krech, M. R. Rosenzweig, E. L. Bennett, J. Comp. Physiol. Psychol. 49, 261 (1956) 261 (1956).

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Meetings

Subcellular Particles

The 13th annual meeting of the Society of General Physiologists was held at the Marine Biological Laboratory, Woods Hole, Mass., 9–11 June. Contributed papers were presented, and the annual business meeting was held, 9 June. A symposium organized by Teru Hayashi of Columbia University on the "Function of Subcellular Particles" was held 10–11 June.

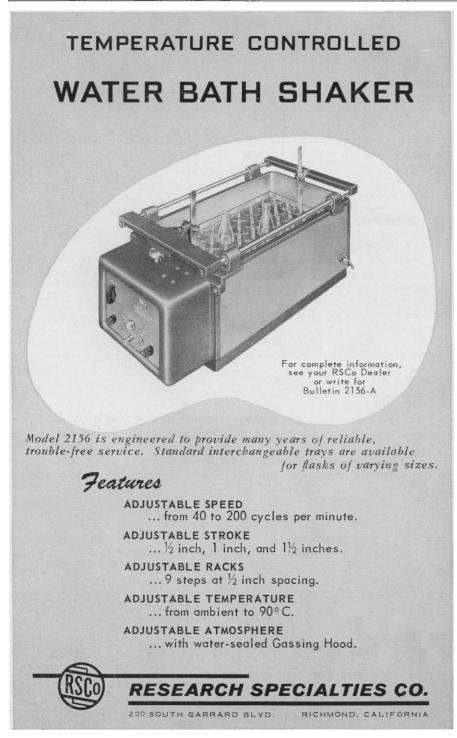
The society has, from its birth,

brought together animal, plant, and microbial physiologists to discuss functions of cells which are common to all organisms. This policy has resulted in interesting and stimulating symposia, often revealing relations between different fields which had not been appreciated. This year's symposium served to bring to the attention of general physiologists recent developments in the study of functional aspects of subcellular particles, particularly the biochemical activities of these entities. On the other hand, the biochemists had an opportunity to become acquainted with the effects of surface and structural factors in biochemical reactions. Arrangements have been made to publish the 1958 symposium in the monograph series of the American Physiological Society. Four previous symposia sponsored by the Society of General Physiologists have been published in this series.

The tone of the symposium was set in a critical review by the first speaker, A. B. Novikoff (Albert Einstein College of Medicine). His comprehensive examination of the work of various investigators working on the physiology of submicroscopic structures put the problems facing workers in this field in sharp focus. The next two speakers of the initial session dealt with the effects of surfaces as structural factors and their effect on biochemical reactions. A. D. McLaren and K. L. Babcock (University of California) presented striking evidence of localized differences in pH at intracellular interfaces and gave examples of the effect of such differences on biochemical reactions. The nonapplicability of classical kinetics for these phenomena was stressed. S. Siegel (Rochester University) then presented experimental evidence for the view that surfaces per se, depending on their nature, may act as "catalytic agents" for such physicochemical reactions as the polymerization of certain substances, such as lignin. He showed clearly that the formation of lignin in the plant and in in vitro systems is dependent on the same surface factors.

In the second session, G. E. Palade (Rockefeller Institute), with a series of technically brilliant electron micrographs, illustrated the morphological changes of subcellular particles correlated with the physiological condition of the cells. Especially noteworthy were the changes in the zymogen granules of the pancreas and changes in the endoplasmic reticulum depending on the secretory activity of the cells. He was followed by E. L. Kuff (National Institutes of Health), who presented work on the isolation and identification of the Golgi apparatus and the biochemical properties of this subcellular entity. D. E. Green (University of Wisconsin) next summarized the work of the Wisconsin group on the fragmentation and analysis of the mitochondrion. He postulated that the mitochondrion is composed of subunits which can be separated by mechanical means, each subunit being composed of enzyme moieties separable only by drastic chemical means. Most interesting was the prominence given to the lipoproteins and their possible function, especially in the electron transport particle. He concluded that the molecular parts of the mitochondrion appeared to be held in a stable structure, and that their reactions did not seem to depend on thermal collisions, as in a free solution.

The final paper of this session, by M.



100 SCIENCE, VOL. 129

Kodak reports on:

finding a trivially named organic in a pedantically named list . . . a device with enormous potentialities for inventiveness . . . tocopherol, three years and 1384 papers later

PAN—PAR

We have been counting on a man who needs a reagent for copper and zinc to go unerringly to our catalog and look up $o-\{2-[\alpha-(2-Hydroxy-$ 5-sulfophenylazo) benzylidene hydrazino benzoic Acid Sodium Salt (Eastman 7199) in the alphabetical listing. To work like that, a man needs to be very smart in an overspecialized sort of way. By neglecting to list this compound under its trivial name Zincon (zinc and copper, get it?) we haven't shown much brilliance ourselves. Our devotion to Chemical Abstracts nomenclature is commendable, justifiable, and sometimes fatuously self-sacrificing. We are holier than most chemical houses. Why, we know of some producers of dyestuffs very useful in the laboratory who refuse orders written in the systematic nomenclature, much less encourage them!

Between trademarks—which specify only commercial origin for merchandise otherwise named as to kind—and systematic but pedantic chemical names lies the convenient middle ground of trivial names (trivial: three roads, i.e., the fork where the people meet to chat, get that?). Some are trademarks abandoned by their owners, some are pronounceable combinations of letters from the systematic name, some

are little slogans concocted by enthusiastic chemists who discovered the uses

It has suddenly struck us that a few of the names neither crossreferenced in our catalog nor familiar to everybody gabbing at the crossroads, should be put in the hands of every chemist interested enough to ask. Sample entries:

PAN—1-(2-Pyridylazo)-2-naphthol (Eastman 7192)

PAR—4-(2-<u>P</u>yridyl<u>a</u>zo)<u>r</u>esorcinol (Eastman 7714)

Tiron—4,5-Dihydroxy-m-benzenedisulfonic Acid Disodium Salt (Eastman 7062), reagent for <u>ti</u>tanium and <u>iron</u> (Also called sodium catecholdisulfonate)

Thoron—o-(2-Hydroxy-3,6-disulfo-1naphthylazo)benzenearsonic Acid Disodium Salt (Eastman 6748), reagent for thorium

Topo—<u>Tri-n-octylphosphine</u> Oxide (Eastman 7440)

Pyrocatechin Violet—

Pyrocatecholsulfonephthalein (Eastman 7589)

Blue Tetrazolium-

2,3,5-Triphenyl-2H-tetrazolium Chloride (Eastman 6533)

Handy little reference book when transcribing notes from a cocktail napkin. You get a copy from Distillation Products Industries, Eastman Organic Chemicals Department, Rochester 3, N. Y. (Division of Eastman Kodak Company). To use it the way we want you to, you must also have a copy of Eastman Organic Chemicals, List No. 41, which gives the prices and package sizes for all the 3700 organics we stock.

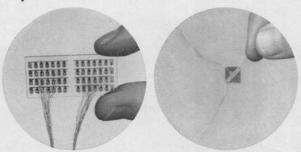
The wordy vitamin

In the three years 1955 through 1957, there have appeared to our knowledge 119 papers in the world's scientific literature on the occurrence and distribution of vitamin E. 60 on the determination of vitamin E, 148 on its chemistry, 362 on its relation to physiology and pathology, 85 on its pharmacology, 275 on its role in nutrition and metabolism, and 335 on its medical and therapeutic uses. There has been an international congress on vitamin E in Venice, and the vitamin has been definitely related to the hatchability of turkey eggs, with weighty consequences for turkey economics.

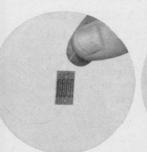
Because we like to think of ourselves as a potent force in the investigation and commercial production of vitamin E, one or the other of us has, with varying degrees of belief, read every one of these papers. We have subsequently prepared an annotated bibliography of them for distribution by the National Vitamin Foundation, 149 East 78th Street, New York 21, N. Y., the fourth such we have done. If you have use for a copy, you can state your case to the Foundation.

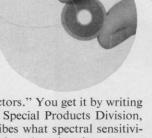
Now that it is printed, we have at least one regret. On page 56 we see the word "preventative." Rhetoricians deplore the word "preventative."

They transduce



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phlet, "Kodak Ektron Detectors." You get it by writing Eastman Kodak Company, Special Products Division, Rochester 4, N. Y. It describes what spectral sensitivities and time constants can be selected and very, very briefly summarizes the circuitry considerations—a little rough, perhaps, for persons with casual interest in this sort of thing. It does tell enough to place an order for breadboarding purposes or a request for quotation.

This is another advertisement where Eastman Kodak Company probes at random for mutual interests and occasionally a little revenue from those whose work has something to do with science



Kamen and J. Newton (Brandeis University), dealt with their investigations on photosynthesis phosphorylation in bacterial chromatophores. They compared the activity of their bacterial particle system with the particulates from green plants and found that, despite the anaerobic nature of the bacteria, definite similarities existed. A promising immunochemical technique opening the way to a molecular localization of the active portions of the particulates was also described.

Christian DuDuve (Louvain, Belgium) gave a comprehensive review of

the concept of the lysosome as an intracellular particle containing hydrolase enzymes. He first outlined the evidence for the concept and then the evidence pointing to the possible function of lysosomes in the cell in digestion (as related to pinocytosis), autolysis, and necrosis. DuDuve was followed by Mary Stephenson, who, together with J. Littlefield, L. Hecht, R. B. Loftfield, and P. C. Zamecnik (Harvard University), presented a summary of the reactions preceding the advent of the ribonucleoprotein particle in protein synthesis. They envisage a reaction which involves, first, the activa-

tion of the amino acid by a specific enzyme, requiring adenosinetriphosphate; second, a soluble ribonucleic acid which incorporates specific nucleotide end groupings and which then can bind the amino acids. This soluble ribonucleic acid can then, presumably, transfer the bound amino acids to microsomal ribonucleic acid and microsomal protein.

Polynucleotide synthesis, studied in situ by high-resolution autoradiographic techniques, was presented by J. H. Taylor and P. Woods (Columbia University). They demonstrated that tritiated cytidine appears first in the nucleolus (although with longer incubation periods the label appears in the chromosomes also). They concluded that polynucleotide synthesis, presumably ribonucleic acid, as indicated by ribonuclease digestion, takes place in the nucleolus.

The final paper of the symposium was presented by V. Allfrey (Rockefeller Institute) and dealt with the biochemical properties of the isolated nucleus. Activities including amino acid uptake and turnover of energy-rich phosphate could be demonstrated. A lively discussion of the conditions for centrifugal isolation of the nuclei and retention of these biochemical activities, and of an interesting salt dependence of the isolated nuclei, followed the presentation of the paper.

Results of the mail balloting for officers and council were announced at the business meeting. C. Ladd Prosser became president, and William D. McElroy was elected vice president. A. C. Giese and T. Hayashi were elected to serve 2-year terms as councilors.

The abstracts of the contributed papers are to be published as a supplement in the October issue of the *Journal of Gellular and Comparative Physiology*.

TERU HAYASHI

Department of Zoology, Columbia University, New York, New York

F. G. SHERMAN

Department of Biology, Brown University, Providence, Rhode Island

Forthcoming Events

February

9-11. American Acad. of Allergy, Chicago, Ill. (B. Rose, Royal Victoria Hospital, Montreal, P.Q., Canada.)

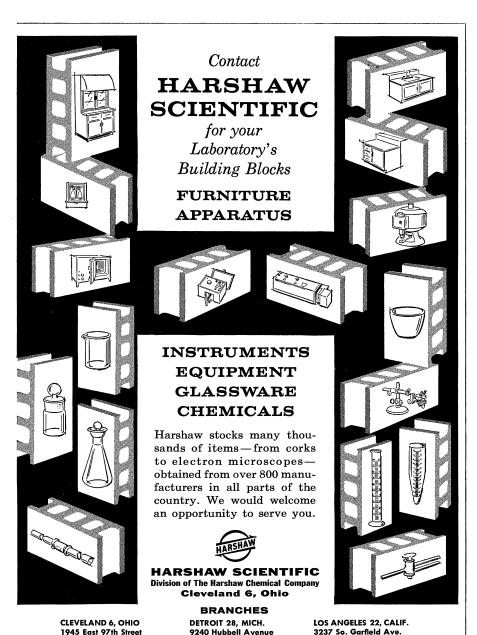
9-11. Nature of Coal, symp., Bihar, India. (Director, Central Fuel Research Inst., P. O. Fuel Research Inst., Dhanbad District, Bihar.)

9-24. Pneumoconiosis, intern, conf., Johannesburg, South Africa. (S.A.C.S.I.R., 18 London House, Loveday St., Johannesburg, S.A.)

11-13. American Acad. of Occupational Medicine, Boston, Mass. (L. Blaney, 1608 Walnut St., Philadelphia, Pa.)

12-13. Solid State Circuits Conf., Philadelphia, Pa. (A. B. Stern, General Electric Co., Bldg. 3, Syracuse, N.Y.)

14. Short Range Navigation Aids, Montreal, Canada. (Intern. Civil Avia-



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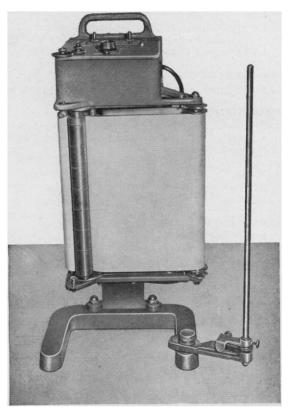
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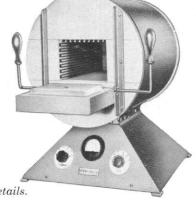
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tion Organization, Maison de l'aviation internationale, Montreal.)

14-21. Planned Parenthood, 6th intern. conf., New Delhi, India. (Secretary, 1 Metropolitan House, Dadabhari, Naoroji Rd., Bombay 1, India.)

15-19. American Inst. of Mining, Metallurgical, and Petroleum Engineers, annual, San Francisco, Calif. (E. O. Kirkendall, AIME, 29 W. 39 St., New York 18.)

16-19. Problems in Field Studies in Mental Disorders, intern. work conf., New York, N.Y. (J. Zubin, American Psychopathological Assoc., 722 W. 168 St., New York 32.)

20-21. Epidemiology in Mental Disorders, annual meeting of the American Psychopathological Assoc., New York, N.Y. (J. Zubin, APA, 722 W. 168 St., New York 32.)

23-27. American Concrete Inst., 55th annual, Los Angeles, Calif. (W. A. Maples, A.C.I., 18263 W. McNichols Rd., Detroit 19, Mich.)

25-26. Midwest Industrial Radioisotopes Conf., Manhattan, Kan. (J. Kitchens, Dept. of Continuing Education, Kansas State College, Manhattan.)

25-27. Biophysical Soc., annual, Pittsburgh, Pa. (G. Felsenfeld, Dept. of Biophysics, Univ. of Pittsburgh, 325 Clapp Hall, Pittsburgh 13.)

26-28. American Acad. of Forensic Sciences, annual, Chicago, Ill. (W. J. R. Camp, AAFS, 1853 W. Polk St., Chicago 12.)

26-28. Genetics and Cancer, 13th annual symp. on fundamental cancer research, Houston, Tex. (Editorial Office, Univ. of Texas, M. D. Anderson Hospital and Tumor Inst. Texas Medical Center, Houston 25.)

27-1. National Wildlife Federation, 23rd annual convention, New York, N.Y. (NWF, 232 Carroll St., NW, Washington 12.)

March

1-2. Pennsylvania Acad. of Sciences, Gettysburg. (K. Dearolf, Public Museum and Art Gallery, Reading, Pa.)

1-5. Gas Turbine Power Conf., Cincinnati, Ohio. (O. B. Schier, ASME, 29 W. 39 St., New York, N.Y.)

8-9. American Broncho-Esophagological Assoc., Hot Springs, Va. (F. J. Putney, 1712 Locust St., Philadelphia, Pa.)

8-9. American Laryngological Assoc., Hot Springs, Va. (J. H. Maxwell, University Hospital, Ann Arbor, Mich.)

8-12. Aviation Conf., Los Angeles, Calif. (O. B. Schier, ASME, 29 W. 39 St., New York, N.Y.)

10-12. American Laryngological, Rhinological and Otological Soc., Hot Springs, Va. (C. S. Nash, 708 Medical Arts Bldg., Rochester 7, N.Y.)

13-14. American Otological Soc., Hot Springs, Va. (L. R. Boies, University Hospital, Minneapolis 14, Minn.)

13-15. Alabama Acad. of Sciences, Auburn, (H. M. Kaylor, Dept. of Physics, Birmingham-Southern College, Birmingham, Ala.)

15-20. American College of Allergists, San Francisco, Calif. (M. C. Harris, 450 Sutter St., San Francisco.)