National Academy of Sciences

Abstracts of Papers To Be Presented at the Annual Meeting, 22–24 April 1957, Washington, D.C.

Thyroxin, Transhydrogenase, and Oxidation of Reduced Triphosphopyridine Nucleotide

Previous reports from our laboratory have dealt with a purified preparation from heart muscle which contains all the components of the cytochrome electron transmitter system. Electron micrographs of this preparation taken by Russell Barrnett indicate that it is composed largely of mitochondrial membranes. In the presence of this preparation, succinate and DPNH react rapidly with oxygen, but no reaction whatsoever occurs with TPNH, whether it is added as such or is generated by the glucose-6-phosphate dehydrogenase system. However, oxidation of TPNH does occur if a small amount of DPN is added. It thus appears that the preparation lacks TPN-cytochrome c reductase but contains the enzyme transhydrogenase, which catalyzes the reaction.

$$\text{TPNH} + \text{DPN} \rightleftharpoons \text{DPNH} + \text{TPN}$$

This DPN-mediated oxidation of TPNH requires cytochrome c and is inhibited by cyanide and the naphthoquinone SN 5949. The pathway of electron flow is thus characteristic of that for the oxidation of DPNH or succinate by the same enzyme preparation. A 30-percent and 85-percent inhibition of this oxidation of TPNH has been obtained with L-thyroxin at concentrations of $4.5 \times 10^{-6}M$ and $4.5 \times 10^{-5}M$, respectively.

Experiments are under way to see whether this inhibition by thyroxin occurs *in vivo*. If so, it could lead to an increase in the amount of TPNH oxidized by the alternate TPNH-cytochrome c reductase pathway and so induce a rise in activity of this reductase [see Philips and Langdon, *Biochim. et Biophys. Acta* **19**, 380 (1956)]. If this alternate pathway is less productive of high-energy phosphate [see Kaplan *et al., Proc. Natl. Acad. Sci.* **42**, 481 (1956)], an increased oxygen consumption in the hyperthyroid animal would follow.

ERIC G. BALL, OCTAVIA COOPER
Harvard Medical School

On the Structure of an Intermediate in the Demethylation of Lanosterol

In the conversion of lanosterol to cholesterol by animal tissues, three methyl groups are oxidatively removed. The sequence of steps in this demethylation process has been partially elucidated by the isolation of a sterol of a hitherto unknown type. The new sterol is an efficient precursor of cholesterol. Although it is available only in trace amounts, the substance could be structurally characterized and shown to be a 4,4-dimethyl cholestadienol (14-nor-lanostadienol). Of the two double bonds in the molecule, one is located between C_{24} and C_{25}; the other, though not yet definitely assigned, is known to extend from C_8 to either C_7, C_9, or C_{14}.

Clarification of this remaining structural detail is being attempted by organic synthesis of the three isomeric 4,4-dimethylcholestenols under consideration. The natural sterol, labeled with C^{14} by biosynthesis and after conversion to the 24,25-dihydro derivative, cocrystallizes and is chromatographically identical with 4,4-dimethyl-$\Delta^{8,14}$-cholestenol. It is shown to differ, by the same procedures, from the $\Delta^{7,8}$ isomer. The mechanism of the demethylation of lanosterol is discussed in the light of these findings.

K. BLOCH, F. GAUTSCHI
Harvard University

Group Vibrations

Many complex molecules contain "characteristic groups," such as CH_3, whose group frequencies and approximate vibrational modes are reasonably well known in advance of calculation. A method is desirable whereby these "group vibrations" may be eliminated from the vibrational problem once and for all, in advance, and whereby the reduced problem of "framework" vibrations may be simply written without considering the complete molecular problem. This paper presents such a method and illustrates its application.

BRYCE CRAWFORD, JR., WILLIAM T. KING
University of Minnesota

Regulation of Gastric Secretion

Food taking stimulates gastric secretion by reflexes over the vagus nerves and through the liberation of a secretory stimulating hormone from the antrum of the stomach. When the acidity of the stomach contents reaches *p*H 3, further secretion is inhibited. This inhibition is due to the prevention of the formation and release of gastrin rather than to the release of an inhibitory hormone. When acidified food reaches the duodenum, pancreatic secretin is liberated. This hormone stimulates pancreatic secretion and, at the same time, inhibits gastric secretion dependent on the stimulating action of gastrin. There is thus a protective mechanism which under normal conditions prevents exposure of the stomach and duodenum to excessively acid gastric content.

LESTER R. DRAGSTEDT,
HERBERT B. GREENLEE,
ENRIQUE H. LONGHI
University of Chicago

Dependence of Yield of Photosynthesis in Long-Wave Red on Wavelength and Intensity of Supplementary Light

The yield of photosynthesis of the green alga *Chlorella* from a band of red light centering at about 644 mμ is not increased by supplementing the red light with additional illumination from a different source. We have tried supplementary illumination at wavelengths from 644 mμ to 436 mμ and intensities sufficient to give photosynthesis approaching 10 times the rate of respiration.

On the other hand, the yield of photosynthesis from a band of red light of longer wavelengths (most of the energy being of wavelengths longer than 690 mμ) can be increased by supplementary light of shorter wavelengths. We have measured the increase in yield as a function of intensity and wavelength of the beam of supplementary light. Higher intensities of supplementary light lead to greater improvements in yield of photosynthesis from long-wave red up to a point of saturation.

To compare different wavelengths of supplementary light, we used intensities below the region of saturation. At each wavelength we adjusted the intensity of the supplementary beam to give the same rate of photosynthesis. We then measured the increment in photosynthesis brought about by addition of the band of long-wave red light. Of wavelengths so far tested, the yellow mercury line at 578 mμ is most effective, the red cadmium line at 644 mμ is next, followed by the green mercury line at 546 mμ. Least effective is the blue mercury line at 436 mμ.

Comparison of these observations with the absorption spectra of chlorophylls *a* and *b* shows that there is a possibility of interpreting the differences in effectiveness of different wavelengths as evidence that chlorophyll *b* is the sensitizer for the action of supplementary light.

The collaboration of Ruth Chalmers and Carl Cederstrand and support from National Science Foundation grant G-1398 are gratefully acknowledged.

ROBERT EMERSON
University of Illinois

Color Discrimination by the Turtle Retina

The retinas of fresh-water turtles have few rods, and their function is dominantly that of cones. Earlier experiments showed

that a sudden shift of illumination from one color to another evokes an electric response that cannot be abolished by any balancing of intensities [Forbes *et al., J. Neurophysiol.* **18**, 517 (1955)]. We have conducted two kinds of experiments to determine what types of receptors are involved.

Spectral sensitivity curves were calculated from the height of electroretinograms recorded with gross electrodes from the excised, dark-adapted retina. With moderately bright light, peak sensitivity occurred at about 645 mμ, with shoulders at approximately 620 mμ and 575 mμ. With extremely dim light, peak sensitivity lay somewhere in the blue-green.

Quantitative study of the shift response in relation to difference in wavelength between two beams was made with one of four interference filters for the fixed color (675, 570, 540, and 510 mμ) and a monochromator for the variable color. The energy of the two sources was adjusted to equalize the height of the on-effect *b*-waves. Shifts from the fixed to the variable color and back produced larger responses as the difference in wavelength became greater. Increases in size of shift response occurred in steps. These rises were steepest at 620 to 640 mμ, 585 to 605 mμ, and 540 to 560 mμ, suggesting the activation of three types of cones, sensitive to red, orange, and yellow-green, and rods, sensitive to blue-green.

ALEXANDER FORBES,
HELEN WENDLER DEANE
Harvard University

Element Synthesis in Supernovae

On the assumption that an intense flux of neutrons ($\sim 10^{32}$/cm^2 sec) becomes available in a supernova explosion [F. Hoyle *et al., Science* **124**, 611 (1956)] heavy elements ($A > 60$) are synthesized, primarily from the iron group elements, by a rapid succession of neutron captures interspersed with negative beta decay. The capture path in the charge-mass (Z–A) plane passes through unstable neutron-rich nuclei whose neutron binding energies (~ 2 Mev) are such that equilibrium is reached between the (n,γ) and (γ,n) processes involving these nuclei at the temperature ($\sim 10^9$ degrees) and neutron density ($\sim 10^{24}$/cm^3) at which synthesis takes place. Abundances have been assumed to be proportional to the beta decay lifetimes ($\tau_\beta \sim W_\beta^{-5}$), which have been calculated for these nuclei by using extrapolations of empirical beta decay energies (W_β).

Reasonable agreement is found with the abundances of Suess and Urey [H. E. Suess and H. C. Urey, *Revs. Modern Phys.* 28, 53 (1956)] for the neutron-rich stable isobars at a given A which result from the subsequent beta decay of the nuclei produced at A. The abundance peaks at $A \approx 80$, 130, and 196 have been attributed [C. D. Coryell, *Lab. for Nuclear Sci. Ann. Rept.* (1956); P. Fongg, *Bull. Am. Phys. Soc.* **2**, 15 (1957)] to neutron magic numbers $N = 50$, 82, and 126. The critical dependence of the shape of these peaks on the conditions at synthesis raises the question whether the observed neutron-rich heavy nuclei of the solar system might have been produced in a single supernova.

Supernova synthesis is capable of building radioactive elements, and we have calculated the relative abundance of the progenitors which decay to U^{235} and U^{238} by subsequent beta and alpha decay. The production ratio is $U^{235}/U^{238} = 1.8$, assuming that spontaneous fission occurs rather than alpha decay for A (odd) $\geqq 259$, A (even) $\geqq 250$. From the present U^{235}/U^{238} ratio and the relative decay rates, it is thus possible to calculate the date of a single-event synthesis as 6.7×10^9 years ago. Synthesis in a series of supernovae requires an even longer time scale, $\sim 10^{10}$ years.

This work was supported in part by the joint program of the U.S. Office of Naval Research and the Atomic Energy Commission.

WILLIAM A. FOWLER, F. HOYLE,
G. R. BURBIDGE, E. M. BURBIDGE
California Institute of Technology

Genetic Control of Adenylosuccinase in Neurospora crassa

Combined genetical and biochemical studies have been performed on a series of adenine-specific mutants in *Neurospora crassa*. Twenty-one mutants of independent origin have arisen as a result of mutation at a single locus (*ad-4*) in linkage group III between two closely linked marker genes. Crosses between the various mutants tend to be sterile and yield few or no homocaryotic adenine-independent recombinants. Biochemically, all the mutants have been found to be blocked in the terminal step in adenine biosynthesis, involving the splitting of adenosine monophosphate succinate (AMP-S) to adenosine monophosphate (AMP) and to lack or have impaired activity for the AMP-S splitting enzyme, adenylosuccinase. One of the mutants is temperature sensitive and produces an adenylosuccinase which in crude extracts is much more thermolabile than that from wild type. Certain of the *ad-4* mutants are capable of reverse mutation to adenine-independent phenotypes, and these have been shown to possess restored adenylosuccinase activity, although at levels (or of stabilities) below that of wild type.

These results establish that in this instance forward mutation at a single locus in the wild type to adenine requirement results in the loss of activity of a specific enzyme involved in adenine biosynthesis, and that reverse mutation to adenine-independence results in the restoration of this activity. Additionally, changes at this locus, arising from either forward or reverse mutational events, may produce diverse mutant and revertant types as judged by qualitative and quantitative tests of enzyme activity.

Certain combinations of *ad-4* mutants have been found to form heterocaryons (dicaryons) able to grow in the absence of adenine. Although the individual mutants lack detectable adenylosuccinase activity, this enzyme is synthesized by the dicaryons. Possible mechanisms for this unexpected type of complementation between alleles in enzyme formation are considered along with its implications for biochemical genetic theory in general.

NORMAN H. GILES, C. W. H. PARTRIDGE,
NORMA J. NELSON
Yale University

Experimental Investigation of the Effect of Air Pollution on the Initiation of Rain

Warm or unnucleated supercooled clouds will not usually precipitate unless moderate numbers of large cloud droplets (about 15 to 25 μ radius) are formed high above the cloud base. These droplets fall down through the cloud and grow into raindrops by accretion.

New measurements in a giant expansion chamber show that the size of newly formed cloud droplets depends critically on the cleanliness of the processed air. Droplets formed in ordinary air are too small to grow, but droplets large enough to precipitate are immediately formed by condensation whenever the condensation nuclei density is sufficiently reduced. Since the activated nuclei density is usually observed to decrease rapidly with increasing altitude, the probability of generating droplets sufficiently large to initiate rain increases as the vertical development of a cloud system increases. The population densities of the large cloud droplets usually observed near the tops of precipitating clouds may be explained in terms of the cooling of an overlaying parcel of air that is initially relatively free of nuclei.

Since pollution is swept out of the atmosphere by diffusion onto cloud droplets and by droplet movement, it is suggested that periods of general cloudiness and precipitation act to reduce the original nuclei density. This permits the subsequently formed droplets to grow still larger, thus increasing the probability of appreciable precipitation. The rain-producing cycle is, therefore, provided with a feedback or regenerative mechanism which usually proceeds, in a given mass of air, until the air is appreciably desiccated.

Condensation nuclei, as well as water vapor, usually accumulate simultaneously in fair weather. The presence of these nuclei may delay the initiation of precipitation until sufficient vertical instability can be established to lift or cool the relatively clean overlaying layers. The precipitation cycle may then be reestablished.

ROSS GUNN, B. B. PHILLIPS
U.S. Weather Bureau

Effects of Ground on Shaking in Earthquakes

Damage from earthquakes depends on properties of earthquake waves, effects of the ground (investigated here), and properties of the shaken structures. Five identical seismographs have been operated temporarily at about 20 locations near Pasadena, and their records have been compared with those of an identical rou-

tine instrument at the Pasadena Seismological Laboratory of the California Institute of Technology.

The ratio of amplitudes recorded at locations on fairly dry alluvium more than 500 feet deep to those written simultaneously at the Seismological Laboratory (on crystalline rock) is frequently 5 or more for earthquake waves having periods of about 1 sec. For much shorter waves (periods of ± 0.1 sec) and much longer waves (periods of more than 10 sec, length more than 10 mi) the corresponding differences in amplitudes are usually small. On water-saturated soft ground amplitudes may be more than 10 times those recorded at the laboratory. Usually the period of waves for which the relative response is greatest decreases as the thickness of the alluvium decreases and is about ¼ sec at stations on alluvium ± 100 feet thick. On Mount Wilson (on crystalline rock) the ground motion is slightly greater than at the laboratory.

On alluvium relatively strong shaking lasts a few times as long as on crystalline rock; usually, its duration in a given shock decreases with decreasing thickness of the alluvium. Ground effects may produce appreciable differences in duration and amount of shaking at sites less than 1 mi apart.

B. GUTENBERG
California Institute of Technology

Cross-Reactions of Anthrax and Cryptococcus-A Polysaccharides in Type-XIV Antipneumococcal Horse Serum

Anthrax polysaccharide from bacilli grown in guinea pigs precipitated the antiserum, while that from *in vitro* cultures did not. Forssman antigen, known to cross-react, was not responsible, since absorption of the antiserum with sheep erythrocytes did not prevent the precipitation. Removal of antibody precipitated by anthrax greatly reduced precipitation by carob mucilage, a galactomannan in which galactose occurs only as nonreducing end-groups. Carob-absorbed antiserum also gave less precipitate with anthrax. Galactose end-groups might, therefore, account in part for the cross-precipitation, particularly since the type-XIV pneumococcal polysaccharide, the antigenic determinant responsible for the production of the antibodies under investigation, has now been found to contain the galactose end-groups predicted from the cross-reactions of carob and tamarind seed polysaccharides in type-XIV antipneumococcal serum. It is therefore likely that the anthrax polysaccharide also contains galactose end-groups.

The specific polysaccharide of cryptococcus A was found by Evans to contain mannose, xylose, glucuronic acid, and a little galactose, present possibly as a contaminant. The cross-reaction of the polysaccharide in anti-XIV was used in order to resolve this question. Comparison of the original and antibody-precipitated substances showed that the latter (2 percent) contained 3 times as much galactose, twice the glucuronic acid, and one-half as much mannose as the original material. This therefore contains at least two polysaccharides, one richer in galactose and glucuronic acid than the other. Quantitative data on these findings are given.

M. HEIDELBERGER
Rutgers University
S. A. BARKER
University of Birmingham, England
P. A. REBERS
Rutgers University

Inhibition of Growth of Mammary Tumors of the Rat by Administration of 3-Methylcholanthrene

In the present experiments on neoplasms of the albino rat, it was found that 3-methylcholanthrene retards the growth rate of transplanted mammary tumors owing, in part, to a selective depression of certain functions of the hypophysis.

Certain mammary tumors are characterized by a high degree of dependence on ovarian hormones, since their growth is profoundly retarded by ovariectomy or by the administration of certain compounds in the androstane series. The administration, oral or intramuscular, of 3-methylcholanthrene, 2 mg daily for 50 days, caused a considerable depression of growth of these tumors.

Other mammary tumors are more malignant than the afore-mentioned ones, since their growth rate is more rapid and it is little affected by the removal of the ovaries. The administration of androstane derivatives or 3-methylcholanthrene restrained the growth of these tumors only slightly. The concurrent injection, daily, of dihydrotestosterone (1 mg) and 3-methylcholanthrene (2 mg) caused a profound depression of the growth of these malignant tumors.

With reference to uninjected controls the administration of 3-methylcholanthrene, 2 mg daily for 50 days, resulted in a decrease of weight of ovaries, uterus, preputial glands, and the hypophysis. Estrus was not always abolished. Body growth was not significantly retarded, and the adrenals were similar to the controls. 3-Methylcholanthrene caused a profound decrease of content of alkaline phosphatase in the mammary glands of the tumor hosts. The compound did not promote growth of hormonal targets.

CHARLES HUGGINS, LUCIO POLLICE
Ben May Laboratory for Cancer Research, University of Chicago

Action of Thyroxin on Mitochondria

It has been postulated that the primary action of the thyroid hormone is to act as a biological uncoupling agent since thyroxin added *in vitro* under certain conditions inhibits the phosphorylation of ADP which is coupled to respiration in isolated mitochondria. However, reports from this laboratory have established that thyroxin does not have a detectable inhibitory action on the enzymes involved in coupled oxidative phosphorylation as it occurs in fragments of the mitochondrial membrane separated from digitonin extracts of mitochondria. On the other hand, it has been shown that thyroxin does cause changes in the structure of isolated mitochondria, leading to uptake of water and swelling.

This paper deals with a more detailed study of the action of thyroxin on the structure of rat liver mitochondria *in vitro*. With some refinement of experimental conditions, the swelling action of thyroxin can be detected at a concentration of $1 \times 10^{-8} M$, which is approximately that existing in the tissues. A number of factors influence this reaction, among which are *p*H, ionic, and non-ionic constituents of the medium and tonicity. The reversibility of the action of thyroxin is considered. The oxidation-reduction state of the respiratory carrier enzymes of the mitochondria appears to be a major factor in conditioning the response of the mitochondria to thyroxin and also the rate of the exchange of inorganic P^{32} with ATP. These findings suggest that the action of thyroxin on mitochondria is on factors linking the enzymes concerned in electron transport and phosphorylation with what appear to be contractile elements of the mitochondrial membrane.

ALBERT L. LEHNINGER, BETTY LOU RAY
Johns Hopkins School of Medicine

Learning Elicited by Electric Stimulation of Subcortical Regions in the Unanesthetized Monkey

It has been demonstrated that an animal can learn to operate a switch in order (i) *to start* a train of electric stimuli [Olds and Milner, Brady *et al.*] or (ii) *to stop* a train of stimuli [Delgado, Roberts and Miller] in different regions of the unanesthetized brain. In our experiments, we have tested and mapped approximately 500 zones in the brains of three restrained, unanesthetized monkeys (*Macaca mulatta*) within approximately 6 mm of the midplane in experiments lasting from 3 to 12 months. The "start-the-stimulus" zones are found to be much more numerous than the "stop-the-stimulus" ones.

To date, "start" zones can be found in the septum, caudate, globus pallidus, and putamen; "stop" zones, in the preoptic and anterior hypothalamic regions. To date, most of the neocortex appears to be relatively neutral.

Stimulation of a "start" zone can function as a reward for lever pressing, alternation, delayed alternation, and quasi-counting. With a proper choice of stimulus parameters, stimulation of a "stop" zone can be shown to function as a punishment; the animal can learn to turn off the stimulus train without any external clues and without exhibiting any of the clinical signs of "fear" or "pain" which are elicitable at higher values of current. In most of the "start" zones, mild "searching" or "hallucinating" behavior is elicited and attack or escape actions are inhibited. In the "stop" zones, either pain-

like or fearlike behavior can be reproduced in different regions with inhibition of feeding, grooming and similar types of spontaneous activity. During stimulation of these animals, the various clinical syndromes elicited do not allow a secure diagnosis of either the presence or absence of a subjective concomitant.

JOHN C. LILLY
National Institute of Mental Health

Behavior of Two Protein Antigens in Mice during Inhibition of Antibody Formation by Cortisone

This report describes an attempt to learn more about the mechanisms of antibody formation by determining whether or not certain procedures that inhibit the process achieve this end by affecting the way in which the body deals with antigens.

The dosage of cortisone large enough to inhibit all antibody formation in mice, which were vigorously stimulated to form antibody, was first determined. Other mice, while under the influence of this dosage of the hormone, were then injected with a tracer antigen obtained by coupling a blue dye to bovine γ-globulin. In these animals, the spleens and lymph nodes, organs which normally form antibody, were reduced to about one-sixth or one-eighth of their usual weight, and no antibody was formed. Nevertheless, these diminutive organs, and other tissues throughout the body which were relatively unaffected by cortisone, took up quite as much of the tracer antigen as was found in the same tissues of normal animals. Moreover, mice injected with the native protein, bovine γ-globulin, instead of the tracer antigen, while under the influence of cortisone—and maintained under its influence and unable to form antibody for 3 weeks—readily produced antibody when the hormone was withdrawn.

Apparently, the cortisone did not inhibit antibody formation by affecting the ability of the tissues to take up the tracer antigen, nor was the antigenicity of the native protein, bovine γ-globulin, destroyed more rapidly than it seems to be in normal animals.

PHILIP D. MCMASTER
Rockefeller Institute for Medical Research
JOSHUA L. EDWARDS
University of Florida College of Medicine

Interaction between Tobacco Mosaic Virus and Formaldehyde

The rate of reaction of formaldehyde with a masked strain of tobacco mosaic virus (1 mg/ml) was determined at three temperatures by means of HCHO—C^{14} in nine concentrations ranging between 25 μg HCHO/ml and 19.86 mg/ml. At all concentrations, relatively rapid initial reaction was followed in approximately 15 hours by a slower increase in formaldehyde uptake which was observed to be linear in time. After 3 to 4 days the reaction became still slower but never ceased during the 36 days' duration of these experiments.

The slopes (F) of the intermediate linear portion of the reaction curves, as well as the intercepts (I) with the ordinate, were proportional to initial formaldehyde concentration (C_0). This behavior suggests the intervention of a diffusion process. Considering the virus as an infinite cylinder, application of diffusion mathematics to the case of simultaneous radial diffusion (diffusion coefficient D cm^2 sec^{-1}) and irreversible first-order reaction with respect to formaldehyde (k sec^{-1}) within the virus leads, after simplification, to the following expression for formaldehyde retention (M_t) in micrograms per milliliter of virus at time t:

$$\frac{M_t}{C_0} = 0.278\left[1 + kt - \left\{\sum_o \frac{-Da_n^2 t}{a_n^2}\right\}\frac{1}{\sum \frac{1}{a_n^2}}\right]$$

from which values of k and D may be deduced. Here α_n's are obtained from roots of the Bessel function $J_0(r\alpha_n) = 0$ in which r theoretically is the radius of the cylindrical virus. Experimental values of $\Sigma 1/\alpha_n^2$ correspond to a diffusion path shorter than the actual radius. The activation energy of the reaction is 9000 to 10,000 cal/mol. The maximum formaldehyde retention observed was 8.4 μg/mg after 36 days at $C_0 = 9950$ μg/ml, which corresponds to 14,000 molecules of HCHO per TMV molecule (mol wt. 5×10^7).

HENRY T. MERIWETHER,
CHARLES ROSENBLUM
Merck, Sharp & Dohme
Research Laboratories

Experimental Study of Increased Susceptibility to Salmonella Infection following Antibiotic Therapy

Mice which have been treated the day before inoculation with a single large dose of streptomycin by stomach tube can be infected (by stomach tube) with about one 100-thousandth of the number of *Salmonella enteriditis* required to infect normal untreated mice. This increased susceptibility to *Salmonella* infection is believed to be caused by some change in the composition of the normal microflora of the intestinal tract resulting from the antimicrobial action of the drug. It is presumed that the normal intestinal flora includes microorganisms which in some way hinder the establishment of *Salmonella*.

In vitro, the multiplication of *Salmonella* is inhibited by bacteria-free filtrates of suspensions of feces from normal mice but not by similar filtrates of feces from streptomycin-treated mice. This inhibitory effect is demonstrable only under anaerobic conditions. It does not occur under aerobic conditions, or in the presence of an abundant supply of nutrients. The enhanced susceptibility of streptomycin-treated mice can be reduced by introducing into the gastrointestinal tract fecal suspensions from normal mice or anaerobic cultures of such suspensions.

Our observations thus far suggest that the presence of certain Gram-negative, nonsporulating, streptomycin-sensitive anaerobes in the mouse's intestinal tract acts as a deterrent to the establishment of *Salmonella*. If this be true, their presence must play a significant role in the maintenance of the normal degree of resistance to infection with this microorganism which is a natural pathogen for the mouse.

C. PHILLIP MILLER,
MARJORIE BOHNHOFF, DAVID RIFKIND
University of Chicago

Some Differences in the Stellar Population of Galaxies

Recent work carried out jointly with N. U. Mayall at the Mount Wilson and Lick Observatories indicates that there is a well-marked relationship between the spectra and forms of the galaxies. Those having pronounced nuclear bulges seem to owe most of their light to yellow giant stars; on the other hand, systems with little or no central condensation are composed principally of blue and white stars —as far as their light is concerned.

These differences in stellar types are probably associated with different stages in evolutionary development. A promising field for investigating the physical nature of galaxies is indicated from studies of galactic spectra.

W. W. MORGAN
Yerkes Observatory

Ocean Waves of Very Low Frequency

We have obtained some energy spectra of pressure fluctuations on the sea bottom at a depth of 60 fathoms off Guadalupe Island, Mexico. For frequencies higher than 1 cycle in 20 seconds, the spectra consist of peaks whose frequency increases by about 10 percent per day; sequences repeat once every 3 or 4 days. These dispersive signals are believed to originate from very distant cyclones in the storm belt of the Southern Hemisphere. The earliest arrivals are of the order of 1 mm high and 1 km long; there is some indication that they originated in the Indian Ocean and have traveled through the Tasman Sea. Later arrivals were generated in the South Pacific. For frequencies lower than 1 cycle in 20 seconds, the spectra reveals a series of well-defined bands with fine structure. The features repeat themselves from day to day without changes in any essential details.

WALTER H. MUNK, FRANK SNODGRASS
Scripps Institution of Oceanography

Heteroplastic Grafting between Rat and Chick Embryos

Martinovitch has shown that experiments utilizing auto- and homografts can be performed in chick embryos before the establishment of the circulatory system. In the light of this work, it was deemed necessary to reinvestigate heteroplastic

grafting between widely different species to test the capacity of tissue healing, to test the capacity for graft differentiation, and to test the current theories of tissue specificity.

Rat embryos of varying ages were transplanted into chick embryos after the host had been prepared for the transplantation by the excision of the forebrain at the mid-mesencephalic level. The tissues of the host and graft heal well initially and, in the best cases, form masses which are chimerically combined with the tissues of the host. When it is only partially connected with the host, the graft may form an independent embryonic vesicle.

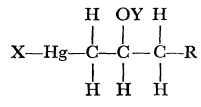
Differentiation occurs in the graft tissues definite with reference to both specific tissues and organs. It is more nearly complete than in chorioallantoic grafts, and specific embryonic form is more frequently secured.

According to theories now current, the blood content is specific for graft tolerance. In our series, the fate of the graft is influenced by a number of factors of which vascularity is but one. There is not in the embryo the antagonistic specificity that has been reported for heterografts in adults.

J. S. Nicholas, Petar Martinovitch
Yale University

Structure-Diuretic Activity Relationships of Organic Compounds of Mercury

Mercurial diuretics in common use today exhibit certain basic similarities in structure. All are addition products of mercury and substituted propyl compounds and may be represented as follows:



Friedman and others have shown that the nature of OY within limits of hydroxy, methoxy, or ethoxy has little effect on the basic diuretic properties of these compounds. X, although a determinant of acute toxicity (cardiac arrhythmias), is otherwise of little significance. It is commonly halogen, theophylline, or thioglycollate. R, on the other hand, has a pronounced effect on both toxicity and diuretic potency. It is commonly a complex substituent, the simplest representative being urea in the compound Chlormerodrin.

Not all organic compounds of mercury have diuretic properties. In an attempt to define the simplest structure consonant with diuretic activity and to describe the essential pharmacological properties of such a drug, we have synthesized 12 organic compounds in which the mercury is attached by one valence bond to a 1, 2, or 3 carbon chain or to a benzene ring.

If one disregards mercuric chloride, which is moderately effective as a diuretic, the structure which we have found to be associated with diuretic activity includes (i) a chain of not less than 3 carbon atoms, (ii) an atom of mercury attached to the terminal carbon of this chain, and (iii) some hydrophilic group not less than 3 carbons distant from the mercury. It is possible that mercury and the hydrophilic group with this critical spatial configuration bind at two sites to some renal tubular enzyme concerned with reabsorption of salt and water. Inactivation of this enzyme results in diuresis.

Robert F. Pitts, Richard H. Kessler, Rodolfo Lozano
Cornell University Medical College

Scientific Apparatus: Unwritten Documents of the History of Science

Written and published accounts of experimental work tell only part of the story of scientific investigation. They reflect what the scientist thought he was doing; this, in some cases, may be very different from what was actually the case. At the time of making an experiment, one may be very conscious of the capabilities and limitations of one's apparatus, but later generations see the story divorced from this governing influence. Only by the study of former instruments can we fully relive the atmosphere of previous scientific work and gain an understanding of why and how things happened when they did. Too often, important pieces of apparatus have been lost by neglect and cannibalization; even in some cases where they have been preserved and cared for, they cannot be studied to advantage without a range of comparative material.

The role of the museum of science is thus more than a pedagogic device for teaching science or a reliquary of scientific heroes; it is an essential tool in our understanding of the way in which advances are made.

Examples are adduced from Classical Greece, from the Middle Ages, and from Modern Times to show how such evidence is important to studies of the history of science and even to science itself.

Derek J. Price
Smithsonian Institution

Normal Proclivities and Neoplastic Disabilities as Determinants of the Course of Tumors

Tumors are habitually appraised in terms of powers gained, not of lost powers or retained normal traits; yet their influence can bulk large.

Carcinogens elicit many "benign" epidermal excrescences on rabbit or mouse skin for every cancer arising. These papillomas are telltales of cancers to come, which take off from some of them; but they have failed heretofore on transfer and eventually regress unless stimulated.

Six papillomas from tarred mice, implanted subcutaneously in sucklings, have now flourished for more than a year in successive hosts, inducing no obvious resistance, and usually proving fatal. Single in kind, they differ in capabilities. Type-A tumors have able-bodied cells, keratinizing and spreading on bare surfaces, like normal epidermis. They line graft pockets with a velvety layer and pack them with keratin, thus turning the papillomas outside in. Keratin accumulation renders the cysts huge; the overlying skin mummifies; and the uninvasive growths, lacking anchorage, are extruded to the surface, forming massive horns there, broad, keratinizing discs, or giant papillomas.

Type-C tumors have crippled cells, unable to spread but producing keratin. This inflames the adjacent tissue, and an ever-enlarging, fluid-filled cyst forms, having bare walls except where a stalked or cauliflower papilloma protrudes. Eventually the cyst ruptures; fluid escapes; and fatal infection follows. Type C grades into type A. The many carcinomas derivative from both lack spreading power. Hence, those on the walls of type-A cysts are outstripped laterally by the extending papilloma tissue, which kills through incessant keratin production.

Peyton Rous, Raymond A. Allen
Rockefeller Institute for Medical Research

Ramifications of Studies on African Amphibians

Studies on the amphibians and reptiles of Africa, begun by one of us (K. P. S.) in 1916, continue in a formal report on a collection of some 70,000 frogs, of 40 species, from the Belgian Congo. The report is undertaken at the instance of Victor Van Straelen, director of the Institut des Parcs Nationaux du Congo Belge, and concerns material obtained in the new Parc National de l'Upemba, in the southeastern Congo.

New studies, with large series of specimens, make possible great improvements in the definition of the species, for secondary sex characters are defined, are followed through their ontogenetic and seasonal development, and are distinguished as genetic and hormonal. These studies have involved separate anatomical studies by one of us (R. F. I.).

The food habits of African frogs are for the first time examined with sufficient material to place chance records in perspective and to discern the seasonal cycle in foods taken.

The sharpened definition of the species of frogs brings us in contact with a remarkable "species swarm" in the subgenus *Ptychadena* of the common frog genus *Rana*. There are some 35 species of this group in Africa, of which a great number are sympatric. Their definition renews interest in the field ecology of many abundant forms.

Exact definition of the species involved brings out the geographic relations of the southeastern Congo. There is an east-west savanna province south of the central African forest, extending from Angola to Lake Tanganyika, corresponding to the east-west Sudanese province 1000 miles to the north.

Karl P. Schmidt, Robert F. Inger
Chicago Natural History Museum

On the Theory of the Bubble Chamber

The bubble chamber invented by Glaser employs superheated liquids in which bubbles are nucleated by the passage of charged particles. The mechanism of nucleation appears to depend on the production of point thermal "spikes" produced as a consequence of the transfer of kinetic energy from the moving particle to the electrons or nuclei of the liquid. Glaser [D. A. Glaser and D. C. Rahm, *Phys. Rev.* **97**, 474 (1955); D. A. Glaser, D. C. Rahm, C. Dodd, *ibid.* **102**, 1653 (1956)] and his colleagues have quoted an example in which about 16 bubbles were formed per centimeter of path in propane by positive pions having momenta near 900 Mev/c. This corresponds to a cross section per molecule in the range associated with the transfer of about 1 Kev or more to the electronic system by coulomb encounters, whereas it corresponds to the transfer of 0.1 ev or more to the protons.

Three components of energy enter into the formation of a bubble which can expand: (i) surface energy of the bubble, (ii) heat of sublimation of the gas in the bubble, (iii) energy required to sustain the pressure needed for production of the bubble in competition with thermal conductivity. In hydrocarbons and heavier rare gases, each of these appears to be of the order of 1 Kev under conditions described by Glaser and his associates. In hydrogen, the first two are of the order of 1 ev, whereas the third is nearer 100 ev and apparently is the limiting factor.

It is proposed that energetic electrons are responsible for the great majority of bubbles. Their kinetic energy is transferred to the molecules and produces localized thermal spikes in a sphere of radius 10^{-6} cm or less.

FREDERICK SEITZ
University of Illinois

High-Melting Fibers

Since early in 1951, I have been directing researches on the production of high-melting glass fibers. High-melting oxides and minerals and their mixtures have been changed to glass directly, since no classical glass-melting furnaces were capable of attaining the necessary temperatures. The raw materials were mixed with suitable binders, wetted and converted to a plastic mass that was extruded downward, in continuous rods or tubes, by a screw feed. These, on descending, were dried and baked by convection currents and then passed through suitably designed high-temperature burners. The lower end of the baked extruded material was melted instantly and homogeneously to glass, which was either blown by compressed air or steam into bulk fibers, or drawn into monofilaments.

A pilot plant has already produced 200 pounds per day of superior bulk fiber, which has remained unchanged after baking 2.5 days at 2350°F and subsequent storing for 3 years. These fibers are longer, softer and more durable than any others of approximately their nature resulting from earlier efforts in the fiber glass field. The capacity of the production unit can be increased to 1 ton per day.

Researches are underway toward the production of fibers with melting points up to and beyond 5000°F. Special heating systems, besides oxygen-acetylene, are under consideration.

The entire principle depends on the very rapid passing of transition points and the retention of high-temperature properties. The products are intended largely for use in jet craft and guided missiles.

ALEXANDER SILVERMAN
University of Pittsburgh

Magneto-Ionic Expander Isotope Separator Applied to Uranium

In the ionic centrifuge [J. Slepian, *J. Appl. Phys.* **26**, 1283 (1955)] and the magneto-ionic expander isotope separator [J. Slepian, *J. Franklin Inst.* (Feb. 1957)] the random energies of the ions and of the electrons remain equal to each other at each point of space; hence, these devices have no space-charge current limitation whatsoever. In the ionic centrifuge, however, the random energy of the ions goes up with the energy of mean motion of the ions. Hence, there can be only small enrichment of isotopes in the various deposits.

In the mageto-ionic expander, on the contrary, the large adiabatic expansion received by the ions and electrons makes their final random energy small compared with the energy of final mean motion of the ions. Hence, very high isotopic enrichment is found among the deposits.

When applied to uranium the cost per gram of U^{235} in the expander is approximately $\$1 + \$700/I$, where I is the number of amperes in the arc. We have used $I = 100$ experimentally, which would make the cost \$8 per gram of U^{235}.

At present the price per gram of U^{235} 90-percent enriched is \$17.07 as offered by the 1956 AEC price list. This is obtained by the multistage gaseous-diffusion process, to which the magneto-ionic expander is therefore a strong competitor.

JOSEPH SLEPIAN
Pittsburgh, Pennsylvania

Effect of Pressure on Electric Properties of Polymer Solutions

An apparatus for measuring the dielectric properties of liquids at pressures up to 1200 atm over the frequency range from 10^2 to 10^6 cy/sec has been constructed. The electric measuring system imitates that described by Cole and Gross. Our principal objective is to study relaxation processes in high-polymer solutions.

The effect of pressure on the dielectric constant and loss of a 50 weight-percent solution of poly-p-chlorostyrene in toluene has been determined over the temperature range from −20° to 30°C. The breadth of the dispersion region is slightly greater than that predicted by Kirkwood and Hammerle for a dilute polymer solution and is nearly independent of temperature and pressure in the range studied. At constant pressure, the temperature-dependence of the frequency of maximum loss corresponds to a heat of activation of 14 kcal/mole for the relaxation process, while the pressure-dependence at constant temperature gives a "volume of activation" of about 50 ml/mole.

With the aid of available density and compressibility data, we find that the aforementioned results correspond to an energy of activation of about 10 kcal/mole for the relaxation process at constant volume. This figure is much higher than constant-volume activation energies for diffusion, viscosity, or dielectric relaxation in simple liquids and suggests that energy barriers to internal rotation of the polymer chain play a significant role in limiting the relaxation rate.

WALTER H. STOCKMAYER,
MARTIN E. FULLER II,
ROBERT L. CLELAND,
JAY H. VREELAND
Massachusetts Institute of Technology

Energy Transmission in Biological Systems

Newer knowledge of the structure of contractile proteins makes it increasingly difficult to picture contraction as a classical chemical reaction. The possibility was considered earlier that the bond energy of ATP is transformed into electronic excitation ere it produces contraction. It was found that the steric relations of the ATP molecule are such as to make it possible for the terminal phosphate to form a coordination complex with the purine of the same molecule, the two being coordinated by a magnesium atom through which excited electrons could pass. The question of how the excitation energy is transmitted from purine to the contractile protein was left open.

Acridin orange can be excited by light to a singlet which emits a green fluorescent light. If two acridin orange molecules dimerize, then they are excited to a triplet which emits a red phosphorescence. If a glycerinated muscle is stained with acridin orange, as shown by Karreman and Mueller, it becomes red phosphorescent, indicating that the dye has formed a dimer with some constituent of the muscle proteins. The question arises whether ATP does not transmit its energy to the muscle proteins by dimerizing, similarly, with some group on the protein, the dimer thus formed being capable of a triplet excitation. If the hypothetical dimerizing group would be identical with the one binding acridin orange, then acridin orange should inhibit contraction and the inhibition should show the properties of competitive adsorption. The experiments show this actually to be the case.

These observations bring the possibility closer that ATP transmits its energy to

the contractile proteins by dimerizing with some group, possibly histidine, the dimer being capable of a triplet excitation into which the energy of the ~ P is transformed.

ALBERT SZENT-GYÖRGI
Marine Biological Laboratory, Woods Hole

Recrystallization Textures in Experimentally Deformed Marble

At 300° to 600°C and confining pressures of 3000 to 5000 atm, pure calcite marble is highly ductile. Shortening of cylinders by 50 percent and local elongation by 500 percent are achieved in experiments of 1 or 2 hours' duration. The main mechanism of deformation is plastic —twin gliding on $\{01\bar{1}2\}$ and translation on $\{10\bar{1}1\}$. This is accompanied by rotation of grains and adjustment of grain boundaries. The process and resultant microscopic fabric are closely analogous to those of cold-worked metallic aggregates. As in the latter, the component grains show strong preferred orientation, which attains a stable pattern in highly strained material.

Even at high temperatures (500° to 800°C) recrystallization involving growth from new nuclei is surprisingly inconspicuous, except in highly strained specimens. In these we have observed partial recrystallization within some grains; and in one specimen clusters of new granules have developed along old grain boundaries. Part, at least, of recrystallization occurred while deformation was in progress (the equivalent of hot-working). The new grains, contrary to prediction based on consideration of strain energy at room temperature, tend to be oriented with [0001] parallel to the compression, or normal to the elongation axis.

Moderately strained specimens held for 2 weeks at 450°C in an atmosphere of CO_2 and water (confining pressure 600 atm) show no sign of annealing recrystallization.

Observed resistance of experimentally strained marble to annealing and the minor role of hot-working in our range of experiments contrasts sharply with the prevalence of what seem to be completely recrystallized (annealed) textures in naturally deformed (metamorphic) marbles.

F. J. TURNER, D. T. GRIGGS
University of California

Manipulation of Cerebral Serotonin and Its Relationship to Mental Disorders

In 1954 Woolley and Shaw first produced evidence which suggested that the hormone serotonin played a role in mental processes. The induction of a specific deficiency of serotonin in the brain (by means of antimetabolites of this hormone) led to psychotic episodes in human beings. Since that time considerable additional evidence to support such a view has appeared.

Woolley and Shaw further suggested that the naturally occurring derangements, such as schizophrenia, possibly were due to a lack of serotonin in the brain. This lack could arise from some metabolic failure to produce enough of it in the central nervous system. They demonstrated that such a lack could not be corrected by peripheral administration of serotonin, because such administration did not result in passage of the hormone into the brain in detectable amounts. Consequently the problem arose of how to increase cerebral serotonin by peripheral medication. This has been accomplished by combined use of the special antimetabolite called BAS plus Udenfriend's precursor of serotonin—namely, 5-hydroxytryptophane.

The hydroxytryptophane increases the serotonin in both periphery and brain, and the BAS, which does not readily enter the brain, counteracts the peripheral effects which otherwise are severe. The result is to increase selectively the functioning serotonin content of the brain alone. This has provided a means for direct test of the serotonin-deficiency postulate about the causation of schizophrenia. Preliminary clinical trials on mental patients have suggested that this combined use of BAS and hydroxytryptophane suppresses the disease. Further trials will be needed to establish the point.

D. W. WOOLLEY
Rockefeller Institute for Medical Research

Visualization of Molecular Order in Organic Crystals

It has recently been shown possible [J. W. Menter, *Proc. Roy. Soc.* **236 A**, 119 (1956); L. W. Labaw and R. W. G. Wyckoff, *Proc. Konink. Acad. Amsterdam* **59**, 449 (1956)] to see with the electron microscope what appear to be the molecular separations (of the order of 10 A) in very small and thin crystals of phthalocyanin and its copper and platinum compounds. The visibility of this molecular detail in an organic compound having a molecular weight of no more than about 500 offers many new possibilities for electron microscopy at high resolution.

We have been examining a variety of crystalline organic compounds in the attempt to determine the conditions under which such molecular detail can be seen. Certain of the indanthrene dyes have proved to be favorable objects for this investigation; some of the results thus far obtained with them are described and illustrated

RALPH W. G. WYCKOFF, L. W. LABAW
National Institutes of Health

New Books

Radioactive Isotopes in Agriculture, a Conference. Sponsored by the Council of Participating Institutions of Argonne National Laboratory. U.S. Atomic Energy Commission, Washington, 1956 (order from Supt. of Documents, GPO, Washington 25). 416 pp. $3.

An Introduction to Electrostatic Precipitation in Theory and Practice. H. E. Rose and A. J. Wood. Constable, London, 1956 (order from Essential Books, Fair Lawn, N.J.). 166 pp. $2.80.

Disturbed Communication. The clinical assessment of normal and pathological communicative behavior. Jurgen Ruesch. Norton, New York, 1957. 337 pp. $6.

Osteology of the Reptiles. Alfred S. Romer. University of Chicago Press, Chicago, 1957. 722 pp. $20.

Atoms for the World. United States participation in the Conference on the Peaceful Uses of Atomic Energy. Laura Fermi. University of Chicago Press, Chicago, 1957. 227 pp. $3.75.

In-Service Education for Teachers, Supervisors, and Administrators. Fifty-sixth yearbook, pt. 1. Nelson B. Henry, Ed. National Society for the Study of Education, 1957 (distributed by University of Chicago Press, Chicago, Ill.). 376 pp. Paper, $3.25; cloth, $4.

General Geography for Colleges. O. D. Von Engeln and Bruce C. Netschert. Harper, New York, 1957. 681 pp. $7.50.

Dairy Microbiology. Edwin M. Foster, F. Eugene Nelson, Marvin L. Speck, Raymond N. Doetsch, Joseph C. Olson, Jr. Prentice-Hall, Englewood Cliffs, N.J., 1957. 492 pp. $5.65.

Experimental Psychology and Other Essays. I. P. Pavlov. Philosophical Library, New York, 1957. 653 pp. $7.50.

The Economic Consequences of Automation. Paul Einzig. Norton, New York, 1957. 255 pp. $3.95.

Neoplasms of the Domesticated Mammals, a Review. Review Series No. 4 of the Commonwealth Bureau of Animal Health. E. Cotchin. Commonwealth Agricultural Bureaux, Farnham Royal, Bucks, England, 1956. 100 pp.

Research Project for the Study and Treatment of Persons Convicted of Crimes Involving Sexual Aberrations, Final Report. June 1952 to June 1955. Bernard C. Glueck, Jr., Director. University of Minnesota Medical School, Minneapolis, 1956. 401 pp.

Philosophy of Science. The link between science and philosophy. Philipp Frank. Prentice-Hall, Englewood Cliffs, N.J., 1957. 394 pp. $7.65.

Flotation. A. M. Gaudin. McGraw-Hill, New York, ed. 2, 1957. 573 pp. $12.50.

The Road to Inner Freedom. Baruch Spinoza. Introduction by Dagobert D. Runes, Ed. Philosophical Library, New York, 1957. 215 pp. $3.

Vitamin B_{12} and Intrinsic Factor. H. C. Heinrich, Ed. Enke, Stuttgart, Germany, 1957. 576 pp.

Vergleichende Physiologie. vol. III, *Ernahrung, Wasserhaushalt und Mineralhaushalt der Tiere.* W. von Buddenbrock. Birkhauser, Basel, Switzerland, 1956. 677 pp. DM. 66.

Handbuch der Physik. vol. XX, *Electrical Conductivity II*; 491 pp.; DM. 112. vol. XXX, *X-rays*; 384 pp.; DM. 88. S. Flugge, Ed. Springer, Berlin, 1957.

Chemical Engineering Reports. How to search the literature and prepare a report. Kenneth A. Kobe. Interscience, New York, ed. 4, 1957. 175 pp. $3.