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Transformation of Renal Tumors of Frogs to Normal Tissues in Regenerating Limbs of Salamanders

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(Introduced by Albert F. Blakeslee)

Normal tissues in regenerating limbs dedifferentiate and revert to an embryonic state, after which the cells grow and differentiate into new tissues. Because cancerous tissue seems to be abnormally differentiated, an attempt has been made to obtain its dedifferentiation and subsequent transformation to normal tissue. In order that former cancer cells might be recognized if they did revert to normal, frog tumors with small nuclei were transplanted to limbs of salamanders which have cells with much larger nuclei.

Small pieces of rapidly growing renal tumors from *Rana pipiens* were transplanted subcutaneously to forelimbs of *Triturus viridescens*. After the small pieces of frog tumor were established and had started to grow and invade the tissues of the salamanders' limbs, the limbs were amputated through the cancer. In all cases regeneration was normal. The regenerates, with a section of the old limb, were fixed and studied histologically. During the early stages of regeneration, when the salamander tissues were just beginning to differentiate, patches of unorganized frog cells were observed. In slightly later stages patches of frog muscle, cartilage, and fibrous connective tissue can be seen interspersed and blending with the corresponding salamander tissues. The frog tissues, in addition to having smaller nuclei, were found to stain somewhat differently and are invaded by leucocytes of the host. Most of the patches of normally differentiated frog tissue are adjacent to unchanged tumor remaining in the old part of the limb proximal to the level of dedifferentiation.

Suppression and Facilitation of Angry Behavior by Certain Forebrain Mechanisms

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A state of extreme refractoriness to rage-provoking stimuli, a condition we term placidity, was produced in cats by removal of all neocortex with sparing of the remainder of the forebrain. Throughout long survival periods the animals invariably failed to show any sign of anger when subjected to rough handling or quite strong noxious stimulation. Since cats deprived of the entire forebrain tend to display rage on rather slight provocation, it is evident that in the absence of neocortex one or more parts of the remaining forebrain must con-

tinuously exert a suppressing effect upon the mechanisms in the lower portion of the brain (hypothalamus and mid-brain) which are executively involved in the bodily expression of anger. This inhibitory influence is a specific one, for the placid animals showed no paucity of the many nonemotional activities of which cats without fore-brain are capable. Conversion of the state of placidity to one of ferocity was effected by bilateral removal of either the cortex of the midline (gyrus cinguli and anterior limbic area) or certain parts of the so-called olfactory brain (amygdala, pyriform lobe, and hippocampus). Of a variety of restricted bilateral ablations of forebrain structures, the only one which caused a gentle normal cat to become savage was removal of amygdala and pyriform lobe. This group of experimental facts indicates that the threshold of the rage reactions of a normal animal is determined by several distinct cerebral mechanisms which interact as a series of checks and balances.

Acquisition and Maintenance of Endocrine Functions at High Altitudes

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Four species of rodents transported to, and maintained at, four altitude levels within the range of 600 feet to 14,260 feet, both as immature and mature stock, attained sexual maturity at the usual time and maintained a normal reproductive performance as adults at all altitude levels.

The fact that normal reproduction requires, within fairly close limits, a normal internal secretory function on the part of the pituitary body, thyroid glands, adrenal glands, testes and ovaries assures that normal reproductive activities provide adequate demonstration of lack of impairment of function on the part of these endocrine organs within this range of altitude.

The rat, hamster, mouse, and guinea pig demonstrate great adaptability to diminished oxygen pressures and carry on reproduction when temperature and nutrition are adequate. Altitude levels of greater than 14,260 feet are required to induce marked interference in the vital function of reproduction. Impairment of reproduction and of internal secretory functions have been reported from highland areas of other countries.

Endometrial Growth in Monkeys

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The growth response induced in the uterine endometrium of castrated monkeys by a chronic treatment with estrogen is limited. The endometrium attains its maximal thickness within about 30 days and becomes

considerably thinner by 100 days. The growth response to estrogen is not increased when the possible influence of the muscularis is eliminated by a midventral incision through the wall of the uterus. If, however, progesterone is given concurrently with estrogen, the rate of growth is greatly increased and continues for a longer period. Also, if the muscularis is cut, the endometrium may grow out into the coelom and form an endometrial mass equal in volume to that of the entire uterus.

These effects of estrogen and progesterone also have been observed in uterine fistulas and exteriorized uteri. Endometrial growth produced by estrogen in a uterine fistula is no greater than in an intact uterus, but if progesterone is given concurrently, tongues of endometrial tissue will grow out through the fistular opening. The endometria of uteri that have been exteriorized through the abdominal wall and incised transversely from fundus to cervix show similar growth responses. This is especially true for the endometrium of the cervix which, unlike that of the anterior and posterior walls of the uterus, does not undergo cyclic blushing and blanching but remains cherry red, even during strong uterine contractions, and retains its color both previous to and during active menstruation. These preparations make it possible to observe changes in the endometrium and to obtain biopsies at frequent intervals.

The Differential Effects of Combined Radiations on Chromosome Breakage and Mutation Rate

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(Introduced by B. H. Willier)

One of the important problems of cytogenetics is the relationship between chromosome change and gene mutations. The solution of the problem is difficult, particularly since the usual mutagenic agents, such as X-rays and short ultraviolet light, also alter chromosome structure. A possible avenue of approach is through the use of additional agents which, while ineffective of themselves, can, when combined with X-rays or ultraviolet, increase or decrease the rate of chromosome change without effecting mutation production, or vice versa.

Infrared, when combined with X-rays, increases the rate of chromosome change (in *Tradescantia*) and the rate of morphological mutations (in *Aspergillus*). The chromosome effect is probably due to the infrared affecting the rate of recombination of broken ends of chromosomes but not the initial rate of chromosome breakage. It is likely that the increased rate of mutations is the result of additional chromosome changes having phenotypic effects, since infrared, when combined with ultraviolet (2,537 Å) is ineffective in altering the mutation rate. Infrared, therefore, does not affect the stability of the gene. Ultraviolet, when combined with X-rays, does not alter the X-ray mutation rate but markedly decreases the X-ray-induced chromosome changes.

This selectivity of radiations permits the separation of gene mutations from chromosome changes. The former

result from initial absorptions of energy which are not affected by combined treatments, while the chromosome changes which depend upon initial breakage of chromosomes followed by recombination of broken ends, are influenced by additional agents which effect the recombination rather than the initial breakage phase of chromosome alteration.

Pigments of Yellow-eyed Races of Black-eyed Susan (*Rudbeckia hirta*)

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The floral cone in *Rudbeckia hirta* is dark purple. Two mutants with yellow cones which are indistinguishable phenotypically are known. In one (Black Yellow) the cone is blackened; in the other (Red Yellow) it is reddened on treatment with strong alkali. Breeding tests have shown that these types have the following genetic constitutions:

Purple cone	BY RY
Yellow cone (Black Yellow)	by RY
(Red Yellow)	BY ry and by ry

Cones of Purple types contain a glycoside of the anthocyan pigment, cyanidin. Cones of Black Yellows contain a leuco-substance convertible to cyanidin *in vitro* by acid hydrolysis. Cones of Red Yellows contain neither leuco-substance nor cyanidin. All types contain a yellow anthoxanthin pigment of unknown constitution.

Apparently the last two steps in the production of cyanidin in Purple types are (1) production of leuco-substance by the gene, RY, and (2) conversion of leuco-substance to cyanidin by the gene, BY. When RY is replaced by its allele, ry, the first step is blocked so that neither leuco-substance nor cyanidin can be formed. The cones therefore contain only the yellow anthoxanthin pigment, which gives a characteristic deep-orange color with alkalis (Red Yellow types). When BY is replaced by by (RY being present), the second step is blocked, and the cones contain both anthoxanthin and leuco-substance. The mixed pigments, as also found independently in *Gossypium*, give a dark-green color (black when concentrated) with alkalis (Black Yellow types). The double recessive type, by ry, reacts as Red Yellow, as expected on this interpretation.

The Angiosperm Seed as a Genetic Mosaic

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The developing seed in flowering plants comprises three genetically diverse parts, endosperm, embryo, and maternal tissues. The antipodals constitute a fourth element in the pattern in species in which this tissue remains functional after fertilization. Seeds resulting from fertile matings between different species, or between diploids and their respective autotetraploids, often collapse and die before maturity. This failure is a conse-

quence of the imbalance set up between the genetically different components of the seed as a result of double fertilization by foreign rather than normal sperm. The primary changes leading to collapse occur in the endosperm. The latter structure not only is a nurse tissue to the juvenile embryo but also mediates certain necessary developmental changes in the associated maternal tissues. The endosperm in a seed destined to collapse commonly grows weakly and loses its meristematic character prematurely. Overgrowth of the adjacent maternal tissue is a frequent secondary effect of the subnormal endosperm development. Fertilization by foreign sperm in the *Gramineae* fails to evoke full activity in the persistent antipodals which lie athwart the nutrient stream. Pronounced chromosomal irregularities in the associated endosperm may ensue, thus precipitating breakdown. Death of the embryos in collapsing seeds appears to be a secondary effect of endosperm disfunction rather than a primary result of the embryo genotype. The inherent viability of such embryos has been demonstrated directly by artificial cultivation following excision from the seed. Imbalance between embryo and endosperm, although sometimes apparent, seems to be a minor factor in seed failure as compared with genetic unconformity between endosperm and maternal tissue.

Genes, Cytoplasm, and Environment in the Control of Cellular Heredity

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The view that heredity is exclusively controlled by nuclear genes is not supported by studies on cellular heredity in the one-celled animal, *Paramecium*. In this organism cytoplasm and environment, as well as genes, play decisive and interlocking roles in heredity. What hereditary traits *can* characterize a line of descent is determined by the genes; but which of the *possible* traits *will* characterize any line of descent is under the control of cytoplasmic determinants. For one group of traits, either a gene or the environment may be decisive as to whether the cytoplasmic determinant involved can survive and thereby produce the trait it determines. For another group of alternative traits, the genes seem to control the production of a series of alternative determining cytoplasmic factors or plasmagenes. Which plasmagene and trait will prevail appears to involve competition, or a sort of intracellular "natural selection," among them. The outcome of this competition is determined by specifiable past and present environmental and intracellular conditions. The preceding mechanisms operate on the cellular level of heredity, where the new cells arise from the division of cells with highly differentiated cytoplasm. Higher organisms arise from an egg with relatively undifferentiated cytoplasm, and consequently the cytoplasm ordinarily plays an insignificant role in their heredity. If the results obtained in the study of cellular heredity have any significance for higher organisms, it is probably in suggesting mechanisms, not of heredity, but of differentiation of the persistently diverse cell types that

normally arise in the development of the multicellular body from the egg.

Biochemical Approach to Individuality

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In rare human cases unusual metabolic products are formed and excreted in significant amounts. These phenomena have been long recognized and designated "inborn errors of metabolism."

A program of investigation now under way indicates that what correspond to "inborn errors" are commonplace. Even in the early stages of the investigation, which employs microbiological, chromatographic, and spectrographic methods for analyses of body fluids, it seems clear that every individual possesses a *distinctive* "metabolic personality." By scientific means we can reasonably hope to duplicate the feat of the hound-dog, i.e. identify individuals by their metabolic products. Acquaintance with individual metabolic patterns will lead eventually to their effective classification.

The implications of this type of study are far-reaching because one's susceptibility to numerous diseases, including alcoholism, drug addiction, and mental disorders, is doubtless greatly influenced by his type of metabolic personality. Furthermore, significant correlations between metabolic personalities and psychological personalities will doubtless eventually appear.

Social problems of great magnitude arise out of individuality, and society must be built for real people, not hypothetical average people. In important aspects of sex, for example, normal individuals vary by a factor of 10,000-fold. In such cases a gross average is meaningless; the members of society obviously belong in several separate categories.

Only by supplementing the psychological approach with a biochemical and physiological one and by paying attention to individuality can we make a satisfactory coordinated scientific attack on the problem of human nature—a problem of unparalleled importance.

Effects of Electroconvulsive Shock on Innate and Learned Behavior in Albino Rats

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Controlled experiments indicate that electroconvulsive shocks impair the learning ability of rats. The losses have sometimes been ascribed to the rat's becoming emotionally aroused because of what appears to be increasing aversion to the learning situation. However, there is temporary impairment of intellectual functions in instances wherein emotional disturbance has not been a complicating factor. Recovery is completed within two or three weeks after the course of convulsions is terminated.

Small bilateral lesions in the cortex produced by cautery are more deleterious to maze performance than electroconvulsive shocks. With complicated mazes, ablation

of from 5 to 8% of the cortex causes both more temporary and permanent impairment than a course of daily electroshocks over a period of 12-15 days.

The maternal behavior of the rats also is severely impaired by electroconvulsive shocks. When applied daily from the day of breeding to the 13th day thereafter, pregnancy is never established; but if they run from the 2nd day to the 13th day after insemination, about 30% of the females become pregnant. These carry their young to term but fail to build nests, to suckle their young, and in other ways to manifest the appropriate maternal responses. Similarly, if the course of shocks runs between the 13th day of pregnancy and the time of parturition, there is no maternal behavior whatever. When the shocks begin on the 2nd day postpartum and continue until the 15th day, variable results are obtained. Gradually, nests which have already been built begin to fall apart, any young which are dragged from the nest are not retrieved and die from neglect, and young remaining in the nest are stunted in growth. On the whole, the disturbance of maternal behavior caused by electroconvulsive shocks is more striking than that produced in the more strictly learned responses involved in maze and discrimination problems.

The Bearing of the Living *Metasequoia* on Problems of Tertiary Paleobotany

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A recent study of the environment and plant associates of *Metasequoia* in central China provides significant data for the interpretation of Tertiary floras, of which this genus is a member. Preliminary study of the material now assigned to *Sequoia* indicates that in many instances the fossil leaves and cones are referable to *Metasequoia*, a genus which has survived only in central China but was formerly widely distributed over the northern hemisphere.

Sucrose Utilization by the Plant

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When lack of neither inorganic nutrients nor water interferes with growth of a plant, which processes are limiting or controlling its growth? In the tomato plant it was found (1) that when the light intensity drops below 1,200 f.c., photosynthesis becomes limiting; (2) that because of the peculiar temperature coefficient of sugar translocation (about 0.5, meaning that less sugar is transported upon a rise in temperature) a sugar deficit develops in the growing regions when tomatoes are grown at high night temperatures; (3) that, most actual growth occurring during night, growth is controlled by the night temperature. At low night temperatures (below 15° C) the growth process is slowed down so much that it limits growth, and neither hormone nor sugar applications can increase the growth rate.

Since it was found that sucrose sprayed on leaves of

tomato plants is readily absorbed, from points (1) and (2) it can be concluded that sugar sprays will be effective in increasing growth under conditions of low light intensity and high temperature. This is exactly what was found experimentally. But at low temperatures, especially during night, utilization of the photosynthesized sugar is limited by the slow growth process. This is the usual condition of field-grown plants, which means that the apparent photosynthetic efficiency of plants in nature is very low.

A thorough knowledge of the physiology of crop plants may very well increase their photosynthetic efficiency by increasing their rate of sugar utilization. The dry weight and fruit production of tomato plants, for instance, can be increased several fold by darkening them each afternoon during the spring season. Under those conditions the photosynthates are used much more efficiently.

The Role of the Spleen in the Quinine Treatment of Malaria

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A standard quinine dosage administered to chickens infected with *Plasmodium gallinaceum* was less effective in reducing mortality and parasitemia in splenectomized than in intact chickens. We have found no evidence that the spleen (or the macrophages which it contains) plays any direct role in the chemotherapeutic activity of quinine by virtue of its role in immunity, its metabolic activity, or its localization of the drug. Thus, quinine does not stimulate phagocytosis of parasites by the macrophages of the spleen, liver, and bone marrow. As these are the macrophages chiefly involved in the suppression of infection during innate and acquired immunity, quinine does not act by stimulating the immune mechanism. Quinine apparently acts as such and is not transformed in the body to a more active product. Its chief action is to inhibit the reproduction of the parasite. Splenectomy raises the quinine blood level after a standard dose of drug, and this results in a more effective drug-parasite contact.

Further analysis indicates that three independent antimalarial factors are operative during quinine treatment, viz., innate immunity, acquired immunity, and the antimalarial action of quinine. Splenectomy produces its chief effect by reducing the auxiliary action of acquired immunity. The loss of acquired immunity reduces the overall antimalarial action to such an extent that the probably increased drug action, as indicated by the increase in quinine blood level in splenectomized chickens, is obscured.

Tuberculosis in Germany

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A rise in tuberculosis is a usual aftermath of war and disaster. Germany experienced such a rise after each World War. With the outbreak of World War II, a

previously excellent tuberculosis control program deteriorated rapidly, and by the end of the war conditions were chaotic. Malnutrition and inadequate hygiene paved the way, and crowding, utilization of German tuberculous patients in industry, and the exodus of tuberculous inmates of concentration camps at the end of the war resulted in dissemination of the disease.

After the war, a control program was rapidly revived by newly constituted public health officials with the assistance of the Military Government in the U. S. Zone, and supported by reallocation of beds for tuberculosis, reorganization of out-patient clinics, search for qualified personnel, and new organization of the reporting system for cases. Substantial improvement has taken place in the last two years, and the mortality rate has returned to the prewar level in most of the Zone.

In the city of Berlin restoration to normal has proceeded slowly. The tuberculosis mortality rate is four times that in the U. S. Zone. The excessive rate is the result of a number of factors, including Berlin's disadvantageous position with respect to housing, food supply, and beds for the care of tuberculosis. Some improvement is now evident.

Continued progress is contingent upon political and economic stability, making long-range planning possible.

A New Instrument for Measuring the Thermal Radiation of the Environment

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(Introduced by Eugene F. DuBois)

To determine the total heat load on the human body out-of-doors it is necessary to measure the air temperature and velocity, humidity, and total thermal radiation. Adequate methods are available for measuring humidity, air movement, and temperature, but due to the lack of a proper instrument, information regarding the thermal radiation of the environment is extremely meager. Heat radiation incident upon a man out-of-doors includes that from the sun received directly and reflected from surrounding objects, as well as infrared radiation exchange to and from the surroundings and sky.

To measure the sum of radiation from all these sources we have constructed an instrument which is portable and which can give readings at approximately 2-min intervals. The apparatus consists of two hollow silver spheres 6 mm in diameter, one of which is highly polished and the other blackened. Both spheres contain small heating coils and thermocouples. Electrical energy is put into one or the other sphere to bring them to the same temperature. When the black sphere is receiving radiation from the environment, energy must be put into the polished sphere, and the amount of this energy is equivalent to the difference in the radiation received by the two spheres. When there is a loss of heat by radiation, as, for example, at night, energy is put into the blackened sphere. Data so obtained must be corrected for reflecting power of the skin and clothing in different parts of the spectrum.

Measurements of total radiation with this instrument were made in New York City in summer and winter. These indicated that at 34° C (ordinary skin temperature) in summer a body absorbed radiant heat at a rate of 100 kcal/m²/hr when in the direct sunlight. Under the same conditions in winter there was a loss of heat at a rate of about 50 kcal/m²/hr. This difference in radiation is due to change in temperature of the surrounding objects from summer to winter.

An Interference Method for the Study of Diffusion

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When a boundary, in which a solute is diffusing from the solution underneath into the solvent above, is placed in the path of a lens, the image of an illuminated horizontal slit is spread out into a rectangular pattern of interference fringes. This phenomenon was first observed and explained qualitatively by Gouy in 1880. The lower edge of the rectangle is formed by light that suffers a maximum downward deflection in passing through the layer of solution at the center of the boundary, where the gradient of refractive index is steepest. The interference fringes are formed by rays that pass through layers of equal gradient above and below the center of the boundary, for which the path difference is such as to give constructive interference.

As diffusion proceeds and the boundary spreads, the rectangle of light contracts, without alteration of the number of fringes, by the upward movement of its lower edge. Although previous workers have used this motion to follow the diffusion process, because of diffraction effects this edge is not sharply defined and its location is difficult. The fringes, on the other hand, can be located accurately, and, with the aid of the theory of their spacing recently developed by Kegeles and Gosting, any fringe may be used for the evaluation of a diffusion coefficient. The precision of the method is further enhanced by averaging the results from a large number of the fringes.

Reaction Rates in Physics

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A general expression for the rate of change, R , of a system can be written as $R = \sum_i n_i \nu_i \gamma_i$ where n_i is the number of systems in the i th state; ν_i is the frequency of vibration along the reaction coordinate, and γ_i is the chance of a reaction occurring during each vibration. Nuclear decompositions have been considered by Condon and Gurney and by Gamow, as well as by others, from this point of view. There are now many types of nuclear reactions. The Richardson equation treats thermal emission of electrons. In this case, n_i is calculable from known equilibrium theory with the usual uncertainty about the magnitude of the activation energy, which in this case is the work function. Electrical and thermal

conductivity of metals are well understood in principle. Thermal conductivity of nonmetals still offers difficulties.

Diffusion and viscosity of liquids have been systematized by treating them as examples of reaction rates involving the jumping of molecules from one equilibrium position to another. For this to occur, an empty site must be provided, and the associated activation energy is chiefly the energy required to provide such an empty site. This free energy has been related to the heat of vaporization. The formal theory is a straightforward adaptation of the formalism of chemical kinetics. Dielectric relaxation is treated in the same way.

Deformation of solids was treated by Maxwell as the stretching of springs attached to dashpots. The latter were assumed to relax at a rate proportional to the force. This oversimplification has been rectified by treating dashpot relaxation as one would a chemical rate process. The rate of relaxation is thus found to depend exponentially on the force, as is required by experiment. One of the key problems in plastic deformation is to know to what extent n_1 (the number of flow units in various states) can be calculated from equilibrium theory and how much the n_1 are "frozen in" imperfections. The equilibrium theory leads to a picture of fluctuations in density responsible for flow in metals much like the fluctuation responsible for the blue of the sky. The arguments for this point of view will be briefly summarized.

Reaction Rates in Chemistry

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Arrhenius developed the empirical equation for reaction rates in chemical processes, $k = A \exp(-E/RT)$ in terms of active and normal molecules in equilibrium with one another. Thirty years ago the factor A was interpreted as a "collision number," Z , for spherical molecules. Deviations caused the insertion of a "steric factor," P , to yield an equation $k = PZ \exp(-E/RT)$ for abnormal rates of reaction. When P was found to vary from 10^{-1} to 10^{-8} in "slow" reactions, the concept of a steric factor became indefinite. Eyring, Polanyi, and their co-workers developed a theory of absolute reaction rates which not only interpreted A of the Arrhenius expression but set forth the concept of the activation energy, E , in terms of a potential energy barrier separating reactants and products. The rate was determinable in terms of the concentration of an activated complex at the top of the potential energy barrier, which concentration was calculable by statistical mechanical procedures. The velocity constant was expressible by the equation

$$k = \frac{RT}{Nh} \exp(-\Delta F'/RT) \\ = \frac{RT}{Nh} (\exp(\Delta S'/RT) \exp(\Delta H'/RT)),$$

in which the free energy of activation, $\Delta F'$, the entropy of activation, $\Delta S'$, and the heat of activation, $\Delta H'$, of the

activated complex are explicitly introduced. The equation shows that the collision theory, $k = Z(\exp. E/RT)$, is limited to reaction between two hard spheres. The P factor takes account of the entropy change in activation.

The influence of surfaces in accelerating reactions was formulated by Langmuir in terms of monolayer adsorption on a uniform surface. It can now be shown that actual reactions on surfaces are complex in their nature, since most surfaces are nonuniform, and the rate processes may be governed by the chemisorption of reactants, which may be slow, by rearrangement on the surface or by desorption of the reaction products. New evidence for surface heterogeneity is presented.

Reaction Rates in Biological Processes

Frank H. Johnson

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Biological phenomena are generally dependent upon numerous and complex reactions, ultimately limited by the activity of protein catalysts, or enzymes, with their substrates. Frequently a single enzyme system is largely rate determining. In bioluminescence the luciferin-luciferase oxidative system itself limits the rate under an unusually wide variety of conditions, and the intensity of the emitted light furnishes a unique, instantaneous index to its activity. Normally, two reactions involving the same molecule, the enzyme luciferase, govern the observed result: (1) an equilibrium (K_1) between active and inactive states of the protein, and (2) the catalytic reaction with specific rate constant (k_2). Thus, with other factors constant, the quantitative relation between the brightness (I) of bacterial luminescence and temperature (T) as well as hydrostatic pressure (p) is described by equation (1), in which the equilibrium constant is defined in the usual manner, the rate constant by the Theory of Absolute Reaction Rates (Eyring), and "b" is a proportionality constant:

$$I = \frac{b k_2 [\text{luciferin}] [\text{luciferase}]}{1 + K_1} \\ = \frac{kT}{bkh K_1^\ddagger [\text{luciferin}] [\text{luciferase}]} \\ = \frac{eTe^{\frac{-\Delta E^\ddagger + p\Delta V^\ddagger}{RT}}}{1 + e^{\frac{-\Delta E + p\Delta V - T\Delta S}{RT}}} \quad (1)$$

The equilibrium (K_1) has the large energy (ΔE), volume change (ΔV), and entropy (ΔS) of reaction indicative of protein denaturation. The rate process (k_2) has the moderate activation energy ($\Delta E^\ddagger$), typical of biological oxidations, and a fairly large volume increase of activation ($\Delta V^\ddagger$). Thus, K_1 is more strongly influenced by temperature than k_2 . Consequently, the observed rate increases with rise in temperature, then goes through a maximum, and finally decreases, as in most other biological processes. Likewise, since ΔV is larger than $\Delta V^\ddagger$, the influence of pressure depends upon the temperature, and vice versa. Pressures of a few hundred atmospheres

may strongly retard, have no effect, or greatly accelerate the process at low, optimum, or relatively high temperatures, respectively.

The large volume increases probably indicate an unfolding of the protein, in both the denaturation and the catalytic reaction. In growth, similar volume changes may be expected to accompany the formation of biologically specific molecules, such as genes, viruses, and proteins, by the templet mechanism generally, the first molecule acting as a pattern for the synthesis of a second one just like it. To serve as a templet it would seem necessary for a globular protein first to unfold into a fibrous form, probably with a volume increase. Thus, although equation (1) has been found to describe the rate of bacterial (*E. coli*) reproduction at normal pressure, growth is strongly retarded under 500 atm, regardless of temperature. Reproduction of a large variety of bacteria (except among certain barophilic organisms from the deep sea) is virtually prevented by pressure of the same magnitude.

A drug or other chemical (X), e.g. sulfonamides, may reversibly inhibit the luminescent process by combining with the enzyme independently of the denaturation equilibrium (K_1) through an additional equilibrium (K_2). A different type (U), exemplified by alcohol, ether, urethane, etc., combines in a manner that furthers the denaturation through still another equilibrium (K_3). In both cases the net result is governed by temperature and hydrostatic pressure as well as by the concentration of the inhibitor, in accordance with equation (2):

$$I = \frac{cTe}{1 + \frac{\Delta E^\ddagger + p\Delta V^\ddagger}{RT} + K_1 + K_2(X)^r + K_1K_2(X)^r + K_1K_3(U)^s} \quad (2)$$

With the numerical values of the constants determined from experiments, the relative rate of the process may be calculated with considerable success for the different values of the variables concerned. Equation (2) also describes with some accuracy the rates of aerobic and anaerobic glucose oxidation by certain bacteria in the presence of urethane at various temperatures.

The theory arrived at through the study of luminescence has anticipated results in other connections and has contributed toward an understanding of the fundamental mechanism of rate control in processes of greater and less complexity than luminescence, including growth, muscle contraction, extracted enzyme reactions, specific antibody precipitation, killing of bacteria and spores, denaturation of viruses, and others.

Reaction Rates in Solids

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Reactions in solids involving the motion of atoms represent special cases of chemical reactions in general and as a result can be formulated in terms of the methods developed by Wigner and Eyring to treat reaction rates. Several important types of reactions are discussed on the basis of this formalism, namely, chemical diffusion, plastic flow under stress, nucleation of phase transformations,

and grain growth. Of the reactions considered, diffusion is the most basic, since it is involved, at least as a connecting link, in all reactions in solids other than those which depend only upon a change in electronic configuration. As a result, principal attention is devoted to it. Diffusion can occur by means of either one of three basic geometrical paths, namely, by direct interchange of atoms, by interstitial migration, and by migration of vacant lattice sites. The mechanism which may occur in any given system depends upon the activation energy required for each of the three geometrical possibilities, that requiring lowest energy being preferred. The experimental and theoretical information that is available concerning the mechanism which obtains in the various types of solids is discussed. Direct interchange appears to be forbidden in almost all cases, whereas interstitial and vacancy diffusion occurs commonly in many familiar solids. The role of diffusion in reactions involving solids is surveyed.

Observing the Phases of Light Waves

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The phases of light vibrations cannot be observed. The fringes in the diffraction pattern of a slit, for example, must alternately have reversed phases, but are all seen alike. By projecting this pattern on an evenly illuminated background, however, those fringes that have phases opposite to the background show dark, the others light, thus revealing their phases. Evidently this is an interference phenomenon to be observed only if the background is coherent with the pattern. Different ways of obtaining this are discussed and the results shown.

An application of greater general interest is found in the phase contrast method. A light wave that has passed through a slightly inhomogeneous medium, such as the air flowing around a model in a wind tunnel, has local differences of phase. The classical way of observing these is by the use of an interferometer. In the phase contrast method, the comparison wave which forms the background is obtained in a simpler way by diffraction at a narrow transparent strip. Small changes in phase appear in this way as differences of intensity. Comparable circumstances are found on a smaller scale in microscopic observation of transparent objects. Details of the newest development of this phase microscopy are given and some results shown.

The Energy Source for Light Emission in Fireflies

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(Introduced by E. V. McCollum)

When a water extract is made of firefly "lanterns," a preparation is obtained which is momentarily highly luminous; however, upon standing the light rapidly disappears. The light emission is presumably due to an oxidation of the substrate molecule (luciferin) in the presence of an enzyme (luciferase). According to pre-

vious ideas, the substrate molecule of this reaction is destroyed during light emission. An alternative explanation based upon the source of energy necessary for luminescence has been suggested for this "irreversible" step in the light reaction. In recent experiments on firefly extracts it has been possible to demonstrate that the energy necessary for light production is the limiting factor in luminescence and that this can account for the apparent irreversibility of the light reaction. If energy is supplied to the firefly extract in the form of high-energy phosphate groups (adenosine triphosphate), a brilliant flash of light appears immediately which is maintained for a considerable time in proportion to the ATP concentration. It appears that the light-emitting reaction is "re-established" by the transfer of high-energy groups from the ATP molecule to some component of the light-emitting system, presumably luciferin.

The results demonstrate an additional use of metabolically generated energy-rich phosphate groups in a biological system and support the general principles concerning the liberation and transfer of energy in the form of small, discrete units. It would appear that the simple oxidative step in light production is only the last step of a series of reactions leading to excitation of the luciferin molecules. Reactions prior to light emission are apparently necessary to meet the energy requirements.

Detection of Short-Range Particles From Nuclear Disintegrations by Means of an Electron Multiplier Tube

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The electron multiplier vacuum tube is an amplification device whose action depends on the fact that electrons or heavier ions, striking a metal surface properly prepared, eject secondary electrons. More than one such secondary is emitted per ion, and if these secondaries all strike a second plate, the shower is amplified. In a 12-element tube developed by J. S. Allen and used by us, 7×10^5 electrons arrive at the 12th plate for one electron striking at the first. Many artificially produced nuclear reactions take place in high vacuum when a beam of high-energy ions impinges on a target. In detecting the disintegration products of such a reaction, the produced particles previously had to pass through the vacuum wall of the system, and the existence of particles of low penetrating power, unable to do this, could not be directly proved. With the electron multiplier tube we can detect and study the slow recoil nuclei. The technique may be compared to the study of gunnery by careful measurements on the recoil of the gun tube rather than by following the flight of the projectile. We have detected the lithium nuclei recoiling from the reaction $\text{Be}^9(p,\alpha)\text{Li}^6$ and found that they occur in the three possible states of ionization. The recoiling light helium nuclei from $\text{D}^2(d,n)_2\text{He}^3$ have been measured, giving a new value for the energy of the neutrons, which are difficult to measure accurately. By allowing the lithium nuclei, produced as above, to pass through thin foils,

it is possible to measure their rate of loss of energy and study the probability that the atomic fragments will pick up or lose an electron in the interesting region where the velocity of the moving fragment is comparable to the orbital electronic velocities.

New Vacuum-Tube Developments

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General Electric Company

Three new vacuum-tube developments are described. The first is an efficient, long-life cathode for thyratrons, called a *dispenser cathode*. Its electron emission remains constant during life, which may be many years, and it is uninjured by overloads and short circuits. Experimental cathodes have been made for currents as high as 5,000 amp.

The second new tube is a high-voltage thyatron, for rectifying and controlling currents at high voltages. The high-voltage quality is obtained by insulated grids, mounted between the control grid and anode, which multiply the operating voltage in proportion to their number. An experimental tube with 5 grids, which controlled 40 amp at 70 kv, is described. Possible applications are power supply for television transmitters and direct-current power transmission.

The third new tube is a rectifier which uses cesium both as coating for the hot cathode and as current-carrying vapor. This double use of cesium gives the highest efficiency theoretically obtainable in a thermionic rectifier, combined with unlimited life. Applications include changing alternating current to 110-v direct current.

Experiments With High-Speed Rotors

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The technique previously described (Beams, Young, and Moore. *J. appl. Phys.*, 1946, 17, 886) for spinning steel and other ferromagnetic rotors to high speeds in a vacuum has been improved. The rotors are suspended magnetically and spun by a rotating magnetic field arrangement. With the air or gas, in the chamber surrounding the spinning rotor, at a pressure of 10^{-6} mm Hg, practically all of the frictional drag is accounted for by gaseous friction alone. As a result, the power required to drive the rotor in a high vacuum is very small, and the maximum rotational speed obtained is limited only by the strength of the rotor. Rotors weighing from 5.0×10^{-4} to 10^4 gm have been used.

With a 21-mil-diameter steel rotor, centrifugal fields of 4.3×10^8 times gravity were obtained with a rotor speed of 6.33×10^5 r.p.s. The low frictional drag also makes it possible to drive the rotor in synchronism with a piezo-electric-crystal controlled circuit without "hunting." This should give rotor speeds constant to one part in 10^8 . Symmetrical magnetic stainless steel mirrors are found to be well adapted for rotating mirror experiments. The application of the technique to certain centrifuging problems is outlined.

The Gas Turbine and Its Significance as a Prime Mover

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Massachusetts Institute of Technology

The gas turbine is the fourth of the major prime-mover developments of a century and a half, the other three being the steam engine, the steam turbine, and the internal combustion engine. An early contender in this race, the hot-air engine, failed to reach maturity but contained the basic idea out of which the recent gas turbine developments have grown. This paper gives a brief survey of this development and its significance.

Trajectories and Conics

Edward Kasner

Columbia University

John De Cicco

Illinois Institute of Technology

In the Newtonian field the trajectories are conics, and simple results arise. In general fields of force, the trajectories (paths of free particles) are complicated. The authors use conics which have highest contact with the curves at a given point, and new general theorems are found.

If we start at a fixed point in a fixed direction, the single infinities of trajectories have osculating conics whose centers always lie on a straight line.

If we study catenaries, brachistochrones (least time), and other physical families, the locus of centers of the conics is found itself to be a conic (ellipse, parabola, or hyperbola).

Two Academy Conferences on Theoretical Physics

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Institute for Advanced Study

The National Academy of Sciences has sponsored and supported two small conferences on fundamental problems of theoretical physics. The first was held at Shelter Island in early June of 1947; the second, in the Poconos in early April of 1948. Among the many problems discussed, three were most intensively considered at both conferences: (1) the relation of mesons with nucleons; (2) the electromagnetic properties of nuclear matter; and (3) the development of electrodynamics to form a consistent theory, and the comparison with experiment of its prediction for the reactive corrections in atomic phenomena.

The rapid progress of the last year tended to confirm the earlier conclusions that (a) the paradoxes of electrodynamics were far less serious, and its range of validity far greater, than had long been supposed; (b) far less was known of the essential experimental facts about mesons than imagined; and (c) the unambiguous detection of specific interactions between nuclear matter, on the one hand, and electrons and radiation, on the other, may require a careful analysis of the finer points in the

quantum theory of interacting fields. In the course of the discussion there was speculation about the synthesis of these various areas of experience in the atomic world.

The members of the conference wish to express their great gratitude to the Academy.

Thermochemistry of Ferromagnesium Silicates

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Carnegie Institution of Washington

(Introduced by L. H. Adams)

As an example of the application of thermochemistry to petrology and mineralogy, the simple ferromagnesium silicates, occurring as olivines and orthopyroxenes in rocks, were investigated. The heats of solution in hydrofluoric acid were measured by means of a solution calorimeter constructed for the purpose. A linear relationship was found between the heat of solution and the iron magnesium ratio of the mineral, indicating that the iron magnesium replacement in the structures of these minerals is thermally perfect. The importance and possibility of applying calorimetry to the study of the complicated replacement phenomena in rock-forming minerals is emphasized. On the basis of the results obtained, the stabilities of MgSiO_3 and FeSiO_3 are illustrated.

Hydrothermal Silicate Equilibria

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The accessible part of the solid earth is composed largely of silicates, but molten material from which igneous rocks consolidate is not a simple molten mixture of silicates. In addition to these very refractory substances it contains small amounts of substances which not only melt but even boil at comparatively low temperatures. They are, therefore, commonly referred to as the volatile components. They remain dissolved in the silicate melt or magma in the depths only by virtue of the high pressures that prevail there. Their violent escape when magmas approach the surface is a cause of the explosive phases of volcanic activity. If the magma crystallizes slowly under deep-seated conditions, they are in part retained, to enter into the composition of some of the crystalline igneous minerals, and in part they may escape into surrounding rocks and bring about the formation of metamorphic minerals.

Analyses of the gases that escape from volcanoes and of the minerals that form in and about plutonic igneous masses show that water is the most important of the volatile components. Experimental investigation designed to throw light on the origin of rocks must, therefore, include studies of phase equilibria in silicate melts containing water and of the equilibrium relations of water with crystalline silicates. High pressures as well as high temperatures are required in such investigations. We present some results obtained in melts of the system $\text{K}_2\text{O}-\text{Al}_2\text{O}_3-\text{SiO}_2-\text{H}_2\text{O}$, representing igneous condi-

tions, and others for compositions of the system $\text{MgO—SiO}_2\text{—H}_2\text{O}$, representing metamorphic conditions. In the investigations pressure up to 30,000 lbs/sq in combined with temperatures up to 900° C were employed.

Nuclear Reactions, the Intermediate or Compound Nucleus, and Continuity of Series

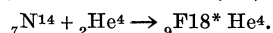
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The University of Chicago

In 1919 Rutherford disintegrated the nuclei of nitrogen by collisions with fast helium nuclei and assumed that the nucleus was split into carbon and hydrogen by the blow. The reaction assumed was a noncapture disintegration: ${}_7\text{N}^{14} + {}_2\text{He}^4 \rightarrow {}_6\text{C}^{13} + {}_1\text{H}^1 + {}_2\text{He}^4$.

The writer considered that a photographic process was essential to determine the mechanism and in 1923 published with R. W. Ryan a method by which, by the use of α -particles of a velocity of 20,600 km/sec and by the first use of the cloud chamber of C. T. R. Wilson for this purpose, this could be revealed. The Chicago method was adopted at Cambridge, and in the few cases photographed the α -particle was captured.

Whereas the experimental results obtained at Cambridge and Chicago were identical, their interpretations were entirely different; at Cambridge disintegrations by noncapture of the projectile were considered possible as late as 1935.

The theory developed at Chicago (Proceedings of the Academy, 1926 and 1936) considered that below the highest energy then known (14 Mev) noncapture disintegrations do not occur. The primary event is not a disintegration but a synthesis of a nucleus, as, for example,



The intermediate fluorine nucleus, after a life period, disintegrates in any one of several ways.

Until 1936 this theory was considered “impossible” by *theoretical nuclear physicists*.

In the reactions of the atomic bomb it is not uranium 235 which fissions, but only the intermediate or compound 236, formed by the addition of a neutron. This provides as much energy as 1,500 tons of coal from 1 lb of U^{235} .

The present paper considers more recent work: the extension of the relations into the region of 100,000,000 electron volts.

Microwave Spectroscopy and Molecular Structure

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Microwave spectroscopy now provides one of the most precise and definite methods of determining the structures of molecules of not too large a size or too complicated a nature. Because of the exceedingly high resolving power and great measurement precision possible in this region as compared with that in the infrared, it is possible in the microwave region to resolve the pure rotational spectra of many molecules whose vibration rotation bands in the infrared are quite unresolvable. The possibility of observing isotope shift, Stark and Zeeman effects, and hyperfine structures due to nuclear quadrupole moments adds further power to this tool. The most difficult part of the utilization of the microwave spectra is the analysis, unless the molecule is linear or symmetrical. It is at present a very laborious process to analyze the spectrum of an asymmetric rotor-type molecule. Nevertheless, many tools are available which can be used in this problem of analysis. The information which can be obtained from a completely analyzed spectrum is discussed along with some of the difficulties and methods for getting around these difficulties. Several molecules which have been studied recently are used as examples.

At the annual dinner of the Academy held in Washington, D. C., April 27, the Henry Draper medal for 1947 was conferred on Hans A. Bethe, professor of physics at Cornell University, in recognition of his contributions to astronomical physics and more especially his researches on the generation of energy in the sun and stars.

The Charles Doolittle Walcott bronze medal and award for 1947 went to Alexander G. Vologdin, a corresponding member of the Academy of Sciences and a distinguished scientist of the Paleontological Institute in Moscow. Dr. Vologdin was selected because of his studies of Pre-Cambrian and Cambrian algae and particularly because of his researches on that most distinctive and enigmatic group of Cambrian organisms, the *Archaeocyatha*.

The Agassiz gold medal and honorarium for 1947 went to Felix Andries Vening Meinesz, professor of geodesy and geophysics, University of Utrecht, and president of the Netherlands Geodetic Commission, for his contributions to oceanography. Professor Vening Meinesz is known for his invention of an apparatus for the determination of gravity at sea, his many measurements of gravity in each of the great oceans, and his interpretation of the physical properties and behavior of the earth's crust beneath and adjacent to the oceans.