fined gold of royalty. But a man so generally popular as Dr. Gill gets all the praise that is good for him, anyway; so it may be observed that there are some things in which this book may yet be improved. The illustrations are better than none, but not much; and the directions for using flash-test apparatus are not quite as complete as a beginner ought to have. It should always be remembered that a metallurgical or cement chemist, for example, skilled in using ordinary apparatus, may know nothing at all about a flash-test; and it is in little details that the manipulation of the expert excels and has its greatest value. In most cases the directions given in this book are full and clear.

The inclusion of refractive indices would probably be generally approved, since the refractometer has come into general use. In general, the book would be better if there were more of it; and while its value is partly due to leaving out information not useful to the analyst, some further remarks as to the nature of the various oils, as well as to changes produced by reagents, from one so experienced as the author, would be of much use to the student.

Somewhat more than half of the book is given to physical and chemical tests; then there are descriptions, including preparation, uses, tests and constants for the chief petroleum products, for seventeen vegetable and nine animal oils, and certain waste fats and greases. There is an appendix of tables and other information. The book has been largely rewritten and has a good index; it appears to be free from typographical errors.

A. H. Sabin

SCIENTIFIC JOURNALS AND ARTICLES

The American Naturalist for May presents two papers, and notes: "The Categories of Variation," by S. J. Holmes, in which the author discusses the differences between fluctuating variations and mutations; going to some length in the analysis of elementary species, retrograde varieties and fluctuations, as distinguished by De Vries; with the general conclusion that the evidences, so far presented, do not sufficiently distinguish between unstable mutations and fluctuations. "The General Entomological Ecology of the Indian Corn Plant," by S. A. Forbes. "Notes on Some Recent Studies on Growth," by Raymond Pearl; "Cuénot on the Honey-bee," by T. H. Morgan; "Poulton and Plate on Evolution," by V. L. K[ellogg].

The American Naturalist for June presents four papers, and notes: "Heredity and Variation in the Simplest Organisms," by H. S. Jennings. "The Color Sense of the Honeybee: is Conspicuousness an Advantage to Flowers"? by John H. Lovell; with the adduced evidence that the query is to be answered affirmatively. "Variation in the Number of Seeds per Pod in the Broom, *Cytisus scoparius*," by J. Arthur Harris. His conclusion is that for this species variability due to habitat is not more noticeable where it is introduced than where it is native. "Present Problems in Plant Ecology." These are presented in two articles read before the Botanical Society of America at the Baltimore meeting, 1908: (1) "The Trend of Ecology," by Henry C. Cowles, and (2) "Present Problems of Physiological Plant Ecology," by Burton E. Livingston. Under "Notes and Literature" V. L. K. makes note, under the heading of Evolution, on the retirement of Ernst Haeckel from his chair in the University of Jena, with emphasis upon the establishment and care of his new Phyletic Museum. He also notes the recent German discussion of mechanical versus vital basis for explaining phenomena of nature. George H. Shull notes the literal translation into French of Hugo De Vries's "Species and Varieties: their Origin by Mutation." J. F. McClendon presents a note on "The Totipotence of the First Two Blastomeres of the Frog's Egg."

SPECIAL ARTICLES

ON THE CONNECTION BETWEEN STIMULATION AND CHANGES IN THE PERMEABILITY OF THE PLASMA MEMBRANES OF THE IRRITABLE ELEMENTS

Evidence of a varied and highly conclusive kind now exists that the phenomena of stimulation in irritable or contractile tissues depend primarily on a temporary and readily reversible increase in the permeability of the surface films or plasma membranes of the constituent cells or elements. This evidence is essentially as follows.

1. Those motile organs and tissues in plants where movement is due to changes in the turgor of the cells present perhaps the clearest case (osmotic motile mechanisms: sensitive plants, *Dionæa,* stamens of Cynareæ, etc.). In *Mimosa pudica* (*e. g.*) the movement results directly from a sudden loss of turgor in the pulvinus cells, due to the escape of a fluid containing considerable dissolved matter. This effect indicates very clearly a sudden increase in the permeability of the protoplast in relation to the dissolved substances of the cell-sap. Movement in these plants is excited by the usual stimulating agencies and is accompanied by an electrical change or "negative variation" similar to that observed in the irritable tissues of animal during stimulation (Burdon-Sanderson). These conditions show (1) that in resting cells, at least of turgid plants, the normal state is one of almost absolute impermeability to the dissolved crystalloid substances within the cell combined with free permeability to water—otherwise the maintenance of turgor would be impossible; and (2) that during stimulation this semi-permeability is temporarily lost.

2. In animal cells the evidence of increased permeability during stimulation is less direct. That in this case also a high degree of impermeability characterizes the plasma membranes is shown by the phenomena of plasmolysis, by the inability of many dyes to enter the living cell, and by the failure of many dissolved crystalloid substances (sugars, neutral salts) appreciably to enter the suspended cells in fluids like blood (Hedin's researches). That stimulation is associated with an increase of permeability is indicated by the fact that most stimulating agencies (heat, various chemical substances, mechanical action, electrical shocks) also visibly increase the permeability of pigment-containing cells like blood-corpuscles, as shown by their laking action. Direct evidence of increased permeability during strong stimulation is also seen in certain favorable organisms, *e. g., Arenicola* larvæ (see below).

3. Evidence that semi-permeable membranes are concerned in stimulation is seen in Nernst's proof that the stimulating action (s) of alternating currents decreases with an increase in the number of alternations per second according to an apparently quite definite rule ($s = i/\sqrt{m}$, where $i =$ intensity of current and m number of alternations). This indicates that changes in ionic concentration at the semi-permeable surfaces of the irritable tissue—*i. e.,* at the plasma-membranes—are an essential condition of electrical stimulation. A corollary of this theory is that if during stimulation the permeability is increased so that the semi-permeability of the membranes temporarily vanishes, stimulation should become temporarily impossible; the existence of a refractory period is thus indirect, but strong evidence of a marked increase in ionic permeability at the height of stimulation.

4. The assumption that stimulation is associated with an increase in the permeability of the semi-permeable membranes also explains the characteristic electrical phenomena of irritable tissues. If the irritable element, *e. g.,* muscle-cell, be regarded as a concentration-element in which the potential-difference between exterior and interior is due to a separation of ions at the plasma membrane, which is assumed to be readily permeable during rest to certain cations (probably hydrogen ions) but not to anions (Ostwald-Bernstein "membrane-theory")—the sudden fall of the demarcation-current potential during stimulation (negative variation or action-current) is at once explained by assuming that at this time the membrane becomes freely permeable also to anions. Free permeability to ions during stimulation is indicated by the refractory period, as already pointed out. The increase in permeability following death or injury is accompanied by an electrical change similar to that associated with stimulation—a fact which

again supports the view that permeability is temporarily increased during stimulation.

5. A close inorganic parallel to certain characteristic phenomena of stimulation is seen in the pulsating mercury hydrogen peroxide catalysis of Bredig and his collaborators. The electrical rhythm accompanying the rhythm of oxygen-evolution has been shown by Antropoff to run parallel with the formation and dissolution of a surface-film of mercury peroxidate. Here we have apparently an actual instance of a rhythmical change of potential which is due to rhythmical alteration of a surface-film; the marked resemblance in time-relations and in other respects to many rhythmical processes in organisms supports the view that a similar surface-change is the basis of the electrical variations accompanying automatic rhythmical stimulation in living tissues. The alternate formation and dissolution of the film over the mercury surface would correspond respectively to the alternate decrease and increase of permeability in the living cells.

The following special observations and experiments, made chiefly during the past summer at Woods Hole, furnish, it is believed, strong confirmatory evidence of the truth of the above general view. The organisms used were the larvæ of the annelid *Arenicola cristata*, which are readily obtainable in large quantity at Woods Hole. These are bitrochal larvæ *ca.* 0.3 millimeters in length with three setigerous body-segments; they swim actively by their cilia, showing pronounced positive phototaxis, and have a well-developed muscular system; and the cells are remarkable for containing large quantities of a water-soluble yellow pigment. This substance serves as an index of increased permeability by diffusing at such times from the cells and coloring the medium; such loss of pigment occurs during intense stimulation, after death, or under the influence of cytolytic substances (chloroform, etc.), but not during the normal activities of the animal; the phenomenon indicates therefore an abnormally great increase of permeability.

When *Arenicola* larvæ are transferred from sea-water into pure isotonic solutions of various alkali and alkali-earth salts (*e. g.*, $NaCl$, KCl, NH_4Cl, $LiCl$, $CsCl$, $RbCl$, $SrCl_2$, $BaCl_2$) they contract strongly to almost half the normal length and remain contracted for several seconds. During this interval the yellow pigment diffuses freely from the cells and colors the solution. Isotonic $CaCl_2$ and $MgCl_2$, on the other hand, have no such intense stimulating action and cause no loss of pigment; in these solutions the larvæ remain straight and extended and muscular movements cease (anesthethic action). Addition of a little $CaCl_2$ (1 volume $m/2$ $CaCl_2$ to 24 volumes $m/2$ $NaCl$) to isotonic $NaCl$ solution prevents the initial stimulating action of the pure salt and at the same time the loss of pigment; in this mixed solution larvæ remain living and active for greatly prolonged periods (antitoxic action of Ca ions). Both the stimulating action and the toxicity of the pure sodium salt are thus associated with a marked increase of permeability; if this last is checked, as by the presence of appropriate bivalent cations (Ca, Mg, etc.), the two former effects also disappear. Solutions of $MgCl_2$ and similarly acting salts and anesthetics appear, on the contrary, to *decrease* the normal permeability. Stimulation is thus associated with an increase and inhibition with a decrease of permeability.

The electrolytes affect permeability presumably by influencing the state of aggregation of the colloids composing the plasma membrane. The consistency of the latter may also be changed by altering the condition of its lipoid constituents. It was found that relatively strong solutions of lipoid-solvents in sea-water, or even in $m/2MgCl_2$ solution (one half to one third saturated chloroform; saturated ether or benzole), also produce strong muscular contractions accompanied by loss of pigment. Solutions of this concentration are rapidly destructive to the larvæ; in *lower* concentrations the lipoid-solvents have the opposite action, checking activity (anesthetic action) without stimulation or loss of pigment. In general, the lipoid-solvents in *low* concentration appear to decrease permeability and hence temporarily to suspend activity without toxic action (anesthesia); in *higher* concentrations they stimulate strongly, cause visible increase of permeability, and show pronounced toxicity. It would thus appear that marked increase of permeability, if prolonged for more than a short time, is highly injurious to cells—presumably on account of the diffusion of essential protoplasmic constituents to the exterior and the resulting chemical disorganization. Decrease of permeability, on the other hand, can have no such injurious effect, but merely checks interchange of material across the plasma membrane for the time being.

In isotonic sugar solutions muscular contractility is gradually lost. On transfer to solutions of various electrolytes contractions return. Of the pure solutions of the alkali salts the most favorable in restoring contractility are those of sodium; lithium and cæsium, while less favorable, resemble sodium in their general action; rubidium and potassium produce temporary contractions, but are much more toxic than the others. The order of increasing favorability for the cations is thus: K and Rb $<$ NH_4 $<$ Li $<$ Cs $<$ Na. The various sodium salts vary in their action according to the nature of the anion; the order of increasing favorability for anions is: I $<$ Br $<$ NO_3 (and ClO_3) $<$ Cl $<$ HPO_4 $<$ $C_4H_4O_6$ $<$ SO_4 $<$ $COOCH_3$. Of the alkali earth chlorides $MgCl_2$ produces no return of contractions; $CaCl_2$ and $SrCl_2$ cause slight contractions lasting some time; $BaCl_2$ almost immediately destroys all muscular contractility.

In explanation of the above effects it is assumed that in the non-electrolyte solution the normal permeability is decreased; hence the inhibitory or anesthetic action. The above electrolytes, by their action on the colloids of the plasma membrane, increase the permeability of the latter and so stimulate. On this interpretation, *any* substance which alters the plasma membrane in the direction of increased permeability should *ipso facto* restore contractility in larvæ from sugar-solution. It was found that weak solutions of acids (HCl, H_2SO_4, $HCOOCH_3$ in concentrations of $n/3{,}200$ to $n/12{,}800$) in isotonic sugar solutions restore almost normal contractions for a certain time. Acid causes also marked increase in the state of tonic muscular contraction. Alkali, on the other hand, has little power of restoring contractility, and induces decrease of muscular tone or lengthening. Weak acid thus appears to increase and alkali to decrease the permeability of the plasma membranes in larvæ from sugar solution.

Experiments on the influence of different electrolytes in restoring contractility in larvæ from isotonic $MgCl_2$ solution gave results essentially similar to the above, with the difference that the restorations of contractions by pure solutions of the above electrolytes is, as a rule, less readily effected. Presumably $MgCl_2$ solutions decrease the normal permeability to a greater degree than sugar; anesthesia appears more rapidly and is more profound in solutions of this salt than in those of dextrose or other sugar.

The question why increase of permeability should correspond to stimulation and decrease to inhibition is answered in essentially the following manner. It is assumed that during periods of increased permeability the loss of carbon dioxide from the cell will be more rapid than normal; the energy-yielding oxidative reactions of which this substance is the end-product are thus accelerated as a direct consequence of the increased rate of removal of the reaction-product from the system; hence the increased contractile activity or other energy manifestation during stimulation. Conversely, decrease of the normal permeability means decreased loss of carbon dioxide and hence retarded oxidation and energy-production; stimulation is more difficult at such times because of the greater difficulty of increasing the permeability to the critical degree required. This general view ascribes primary importance to the plasma membrane as probably the chief means by which the velocity of the oxidative energy-yielding reactions in the cell is varied. The promptness and vigor of the response to stimulation in highly irritable and active tissues like muscle are to be regarded simply as evidence of the high velocity with which the energy-yielding process, when unimpeded by the accumulation of reaction-products, proceeds in such cells. The grounds of this high velocity are imperfectly understood at present. If we assume, however, that the reactions in the living cell progress rapidly to equilibria, and that in the resting cell, with a plasma membrane offering considerable resistance to the passage of CO_2, a condition of approximate chemical equilibrium prevails—it is clear that any disturbance of equilibrium, as by a more rapid removal of reaction-products (*i. e.*, CO_2), must be followed by a corresponding prompt acceleration of the reaction concerned. Such a system would respond to variations in the rate of removal of CO_2—*i. e.*, to variations in permeability—in a manner which under favorable conditions might well be very sensitive.

The *positive* electrical variation during inhibition (Gaskell)—as well as the negative during stimulation—receives consistent explanation on the membrane-theory if the polarizing electrolyte is assumed to be carbonic (with possibly other) acid. For further discussion the reader is referred to the complete paper in the *American Journal of Physiology*, Volume 24, April, 1909, page 14.

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June 15, 1909

THE FORTIETH GENERAL MEETING OF THE AMERICAN CHEMICAL SOCIETY

THE fortieth general meeting of the American Chemical Society was held at the Detroit Central High School from Tuesday, June 29 to July 2, 1909. About 300 chemists were present, making this the most largely attended summer meeting in the history of the society.

On Tuesday evening the visiting chemists enjoyed a complimentary smoker given by the Detroit Society of Chemists.

On Wednesday afternoon and evening the visitors were guests of Parke, Davis & Co. In the afternoon the chemical laboratories were inspected and luncheon was served in the evening. This was followed by a moonlight ride on the river.

On Thursday morning a special train carried the visitors to Ann Arbor on the invitation of the regents of the University of Michigan. A subscription dinner was given at the Hotel Pontchartrain on Thursday evening.

On Friday excursions were made to the following manufacturing establishments: Acme Lead and Color Works, paints, white lead by new process; Morgan & Wright, auto tires and mechanical rubber; Detroit Salt Company, rock salt mine, 800 feet deep; Murphy Ice Company, distilled water, artificial ice—ozonizing plant in connection; Peoples' Ice Company, artificial ice plant; Packard Automobile Company; Detroit City Gas Company, manufacturers of illuminating gas; Cadillac Motor Car Company, auto manufacturers; The Herpicide Company; Goebel Brewing Company; Hiram Walker & Sons, distillery; American Electric Heater Company; Hoskins Manufacturing Company, pyrometers and electric furnaces; Sibley Quarry Company, limestone and sand-lime bricks; Peninsular Engraving Company, engravers and printers; The Clark Wireless Telegraphy Company, manufacturers of wireless equipment; Berry Brothers, varnish manufacturers; Detroit Iron and Steel Company, blast furnace.

The following papers were read before the general meeting:

Optical and Quartz Glass; their Chemical and Physical Properties: H. E. HOWE.

The Chemistry of Phosphorescing Solids: WILDER D. BANCROFT.

The following papers were read before the Section of Chemical Education:

A Place for Chemistry in the American College: ALEXANDER SMITH.

Some Ideals, Some Difficulties and a Compromise for a First Course in Chemistry: S. LAWRENCE BIGELOW.

A First College Course in Chemistry: ARTHUR JOHN HOPKINS.

College Chemistry beyond the Elementary Course: LAUDER W. JONES.

Laboratory Instruction in Industrial Chemistry: HARRY MCCORMACK.

Teaching by the Lecture System: NORMAN A. DUBOIS.

The following papers were read before the various sections:

BIOLOGICAL CHEMISTRY

Samuel C. Prescott, chairman

The Determination of Urea in Urine: F. W. GILL and H. S. GRINDLEY.

This paper gave the results of a somewhat complete comparative study of the Folin, the Benedict-Gephart and the hydrolysis-aeration methods for the determination of urea. The following are the most important conclusions: First, creatinine and hippuric acid are not at all decomposed by heat-