period reaction is all set and ready to go, and requires only that the light change S into P and A so that the latter can catalyze the transformation of L into T, which is the end-product of the sensory process. The whole photosensory mechanism may then be summed up in the two reactions

$$S \rightarrow P + A; \quad L \| P + A \| \rightarrow T,$$

in which the symbol $\| P + \mathrm{A} \|$ means catalysis by one or both of the precursor substances. The first of the two reactions occurs during the sensitization period; the second during the latent period.

IX

This hypothesis of photoreception is rather concrete. The concreteness of the conceptions has however proved a useful tool in the acquisition of knowledge in this field. Time does not permit the description of experiments designed to test the hypothesis in numerous ways. I can, however, mention just a few to indicate its fruitfulness.

The latent period is assumed to be a simple, chemical reaction, perhaps as hydrolysis or an oxidation. Its behavior with the temperature should therefore follow quantitatively the rule deduced by Arrhenius for the relation between the velocity constant of a reaction and the absolute temperature. This means more than a mere determination of the temperature coefficient for 10 degrees; it means a continuous relationship between temperature and velocity, following certain theoretical considerations. Experiments showed that the reaction $L \rightarrow T$ follows this prediction accurately, and that the value of the constant, $\mu = 19{,}680$, for our reaction is in accord with those usually found for hydrolyses, saponifications, etc., in pure chemistry.

Another test concerns the interrelations between the exposure and the latent period. I have mentioned that the velocity of the latent period reaction is directly proportional to the exposure (t), provided the intensity (I) is kept constant. This may be written

$$V = k_1 t.$$

If now we keep the time of exposure constant and vary the intensity we find that

$$V = k_2 \log I$$

or that the velocity is proportional to the logarithm of the intensity. Ordinary mathematical reasoning indicates that if we combine these two equations—which means experimentally that we vary simultaneously both the time and the intensity—it should be true that

$$V = kt \log I.$$

Experiments prove that this expected relationship indeed holds good.

Still another and perhaps more significant application of the proposed hypothesis has been made. This concerns the dark adaptation of the human eye. A careful analysis of the data of dark adaptation in terms of the principles discovered in these investigations has shown that dark adaptation and protoreception in the human retina are fundamentally similar in principle to the process in *Mya* and *Ciona*. As a result there has been opened up a new field of investigation in retinal photochemistry which may some day enable us to possess a reasonable theory of vision.

Selig Hecht

Physiological Laboratory,
Creighton Medical College,
Omaha, Neb.

THE MECHANISM OF INJURY AND RECOVERY OF THE CELL[1]

Some of the fundamental ideas of biology are extraordinarily difficult to analyze or define in any precise fashion. This is true of such conceptions as life, vitality, injury, recovery and death. To place these conceptions upon a more definite basis if is necessary to investigate them by quantitative methods. To illustrate this we may consider some experiments which have been made upon *Laminaria*, one of the common kelps of the Atlantic coast.

[1] Address for the Symposium on General Physiology at the meeting of the American Society of Naturalists, December, 1920.

It has been found that the electrical resistance of this plant is an excellent index of what may be called its normal condition of vitality. Agents which are known to be injurious to the plant change its electrical resistance at once. If, for example, it is taken from the sea water and placed in a solution of pure sodium chloride it is quickly injured, and if the exposure be sufficiently prolonged it is killed. During the whole time of exposure to the solution of sodium chloride the electrical resistance falls steadily until the death point is reached; after which there is no further change. If we study the time curve of this process, we find that it corresponds to a monomolecular reaction (slightly inhibited at the start).

This and other facts lead to the assumption that the resistance is proportional to a substance, M, formed and decomposed by a series of consecutive reactions. On the basis of this assumption we can write an equation which allows us to predict the curve of the death process under various conditions. This involves the ability to state when the process will reach a definite stage, *i.e.*, when it will be one fourth or one half completed. This can be determined experimentally with considerable accuracy.

This curve is of practical, as well as of theoretical importance, since it allows us to compare the degree of toxicity of injurious substances with a precision not otherwise attainable. The best way of doing this is to proceed as a chemist might in such cases and express the degree of toxicity by the velocity constants of the reaction (*i.e.*, of the death process) under various conditions.

From this point of view we must regard the death process as one which is always going on, even in an actively growing normal cell. In other words the death process is a normal part of the life process. It is only when it is unduly accelerated by a toxic substance (or other injurious agent) that the normal balance is disturbed and injury or death ensues.

If we wish to put this into chemical terms we may say that the normal life process consists of a series of reactions in which a substance O is broken down into S, this in turn breaks down into A, M, B and so on. Under nomal conditions M is formed as rapidly as it is decomposed and this results in a constant condition of the electrical resistance and other properties of the cell. When, however, conditions are changed so that M is decomposed more rapidly than it is formed the electrical resistance decreases and we find that other important properties of the cell are simultaneously altered.

Hence it is evident that injury and death may result from a disturbance in the relative rates of the reactions which continually go on in the living cells.

It is evident that we can follow the process of death in the organism in the same manner that we follow the progress of a chemical reaction *in vitro*. In both cases we obtain curves which may be subjected to mathematical analysis, from which we may draw conclusions as to the nature of the process. This method has been fruitful in chemistry and it seems possible that it may be equally useful in biology.

If we suppose that resistance depends on a substance, M, it may be desirable to discuss briefly certain assumptions which have been made in regard to it. The protoplasts of *Laminaria* are imbedded in a gelatinous matrix (cell wall) which offers about the same electrical resistance as sea water or dead tissue. Since the electrical resistance of the living tissue is about ten times as great as when it is killed it is evident that the living protoplasm must be responsible for the increased resistance. The living cells consist for the most part of a large central vacuole surrounded by a delicate layer of protoplasm: the sap which fills the vacuole seems to have about the same resistance as the sea water. The high resistance of the living tissue must therefore be due to the layer of protoplasm surrounding the vacuole, a layer so extremely thin as to be comparable to what is commonly called the "plasma membrane." Since the current is due to the passage of ions through

this extremely thin layer of protoplasm[2] it would seem that the electrical resistance may be regarded as a measure of the permeability of the protoplasm to ions. It is of interest in this connection to find that the measurements of the permeability of the protoplasm by a variety of other methods (plasmolysis, exosmosis, diffusion of salts through the tissue, entrance of dyes, etc.) confirm the results obtained by electrical measurement.

In view of these facts the simplest assumption which we can make concerning M is that it is a substance at the surface of the protoplasm which determines the resistance: as M increases in amount and forms a thicker layer the resistance increases, and vice versa.

Tissue which has developed under normal circumstances is found to be rather constant in its electrical resistance. This is of considerable practical importance as it enables us to test material as it comes into the laboratory and to reject any which has been injured or is in any way abnormal.

We may therefore speak of a normal degree of resistance as indicating a normal state of the tissue. If injury occurs and the resistance falls we may consider that the loss of resistance gives a measure of the amount of injury. Thus if the tissue loses ten per cent. of its normal resistance we may say that the injury amounts to ten per cent. This enables us to place the study of injury upon a quantitative basis.

In the case of *Laminaria* we find that if the injury in a solution of sodium chloride amounts to five per cent. the tissue recovers its normal resistance when replaced in sea water. If however the injury amounts to twenty-five per cent. the recovery is incomplete: instead of rising to the normal it recovers to only ninety per cent. of the normal. The greater the injury the less complete the recovery. When injury amounts to ninety per cent. there is no recovery at all.

[2] Some of the current passes between the masses of protoplasm (*i.e.*, in the cell wall) but allowance can be made for this since the relative proportion of cell wall and protoplasm remains unaltered throughout the experiment.

This is of practical interest in view of the fact that in physiological literature it seems to be generally assumed that when recovery occurs it is always complete, or practically so, as if it obeyed an "all or none" law. It is evident that partial recovery may be easily overlooked unless accurate measurements are possible. This may serve as another illustration of the fact that quantitative methods are indispensable in the study of fundamental processes.

It is evident that injury presents two aspects. One is the temporary loss of resistance which disappears, wholly or in part, when the tissue is placed under normal conditions: this may be called temporary injury. The other is the permanent loss of a part of the resistance which is observed after more prolonged exposure: this may be called permanent injury. By exposing tissue for various lengths of time to a toxic solution and observing the amount of recovery each time we may construct a time curve of permanent injury. This curve may be subjected to the same kind of mathematical treatment as the time curve of temporary injury, already discussed. The mathematical analysis leads to the conclusion that if we adopt the scheme $O \rightarrow S \rightarrow A \rightarrow M \rightarrow B$ we must regard temporary injury as due to the loss of M while permanent injury is due to the loss of O. Recovery occurs when the loss of M is replaced by a fresh supply of M derived from O, but if O is itself depleted recovery will be incomplete.

It may be added that an equation has been found which enables us to predict the recovery curves under a great variety of conditions with considerable accuracy.

If we accept the conclusions stated above we are obliged to look upon recovery in a somewhat different fashion from that which is customary. Recovery is usually regarded as due to the reversal of the reaction which produces injury. The conception of the writer is fundamentally different; it assumes that the reactions involved are irreversible (or practically so) and that injury and recovery differ only in the relative speed at

which certain reactions take place. Thus in the series of reactions

$$O \rightarrow S \rightarrow A \rightarrow M \rightarrow B,$$

if the rate of $O \rightarrow S$ becomes slower than the normal, injury will occur, while a return to the normal rate will result in recovery. Injury could also be produced by increasing the rate of $M \rightarrow B$, or decreasing the rate of $S \rightarrow A$ or $A \rightarrow M$.

If life is dependent upon a series of reactions which normally proceed at rates bearing a definite relation to each other, it is clear that a disturbance of these rate-relations may have profound effects upon the organism, and may produce such diverse phenomena as stimulation, development, injury and death. It is evident that such a disturbance might be produced by changes of temperature (in case the temperature coefficients of the reactions differ) or by chemical agents. The same result might be brought about by physical means, especially where structural changes occur which alter the permeability of the plasma membrane or of internal structures (such as the nucleus and plastids) in such a way as to bring together substances which do not normally interact.

In the case of *Laminaria* death may occur in two ways. In the first there is a loss of resistance which continues until the death point is reached, as, for example, in sodium chloride. In the second, as in calcium chloride, there is an increase of resistance followed by a decrease. Both of these methods may be predicted by means of the scheme already outlined.

If we mix sodium chloride with calcium chloride we do not get a result which is merely intermediate for we find that long after death has occurred in pure sodium chloride or pure calcium chloride the tissue still survives in a mixture of these salts (made in certain definite proportions). The facts lead us to assume that both sodium and calcium combine with a constituent, X, of the protoplasm, forming a compound Na_4XCa. According to the laws of mass action we may calculate the amount of this compound which will be formed in each mixture of sodium and calcium chlorides. These calculations indicate that the speed of all the reactions is regulated by the amount of Na_4XCa (it is also found that certain reactions are accelerated by calcium chloride).

This enables us, by means of the equations already mentioned, to predict the time curves of injury and death in mixtures (in addition to those in pure salts) as well as the recovery curves when tissue is transferred from such mixtures to sea water.

It is evident therefore that the theory not only explains why pure sodium chloride and calcium chloride are toxic but also why they antagonize each other in mixtures. Moreover the explanation which it furnishes is a quantitative one, *i.e.*, it shows just what degree of antagonism is to be expected in each mixture.

Extremely interesting results are obtained when the tissue is first exposed to sodium chloride, then to calcium chloride, then to sodium chloride or to sea water and so on. By varying the conditions of the experiment a very complicated set of curves may be obtained. It is rather remarkable to find that all of these may be predicted with considerable accuracy by means of the equations already referred to. A detailed statement of the results will be found in recent papers in the *Journal of General Physiology*.

Throughout these investigations the aim has been to apply to the study of living matter the methods which have proved useful in physics and chemistry. The attempt presented no serious difficulties after accurate methods of measurement had been devised: nor does there seem to be any real obstacle to a general use of methods which lead biology in the direction of the exact sciences.

It is evident that if the facts have been correctly stated such fundamental conceptions as vitality, injury, recovery and death may be investigated by quantitative methods. This leads us to a quantitative theory of these phenomena and a set of equations by which they can be predicted. It may be added that the

predictive value of these equations is quite independent of the assumptions upon which they were originally based.

This investigation of fundamental life processes shows that they appear to obey the laws of chemical dynamics. It illustrates a method of attack which may throw some light upon the underlying mechanism of these processes and assist materially in the analysis and control of life-phenomena.

W. J. V. Osterhout

Harvard University

ISAO IIJIMA

Professor Isao Iijima, head of the department of zoology in the Imperial Uinversity, died of apoplexy at his home in Tokyo on March 14. His father, a Samurai of the Daimyo Inouyé of Shizuoka, was one of those devoted to foreign learning in the decades before the restoration: proceeding to Nagasaki, he studied European ideas through the medium of the Dutch language—later suffering imprisonment on account of these interdicted studies. The son Isao, born Bunkyu-ni-nen (1860), followed the father's footsteps, was early a student of foreign languages and science, and was eager to master physiology and anatomy. So he found his way presently to the Imperial University of Tokyo, which then was beginning its famous career. Here he came under the guidance of the American zoologist, Professor Edward S. Morse, whose inspiration soon turned him from medical studies to pure science. Thereafter he went to Leipsic, where he took his doctorate with Professor Leuckart. Returning to Japan about 1885, he was appointed a member of the faculty of the Imperial University, where he was to remain until the day of his death; in the last years he was also professor in zoology at the Nobles' College, Tokyo. Foreign zoologists will always remember Iijima, side by side with Kakichi Mitsukuri, as taking foremost and genial place in all zoological matters in Japan. His knowledge of the general subject was unusually wide: a fluent lecturer, an attractive personality, he popularized zoology and brought help to it from many sides; for not only was he the trained morphologist, but the old school naturalist as well, bird expert notably, having among his friends collectors and gunners in all part of Japan; his hobby took him everywhere, and as a good shot he was as welcome in the hunting parties of the Emperor as with the pheasant-stalking peasants on the hillside near Misaki—where for many years he spent his summers. Here was the seaside laboratory of his zoological department, and offshore were the great depths of Okinosé (6,000 meters) from which many a red-turbaned fisherman, and Kuma Aoki especially, brought him the rarest of glass-sponges. These Iijima made his life-long study: and he dealt with them in memoirs which, published in the main in the *Journal of the Science College,* are classics, indeed—though Iijima himself would be apt to add, in his joking way, that this was not as great a feat as it seemed, since he was the only life-long specialist in the field! In point of fact, these sponges were poorly represented throughout the world (large museums had sometimes not more than a few small specimens—usually a ragged Hyalonema, or a defective Venus-basket), till the discovery was made of many species, genera, and even families of them in Iijima's district of the Pacific where nature seemed to have taken many pains to keep them alive in an early geological "garden."

In a practical direction Iijima's studies carried him to the culture of "artificial" pearls, and several of his students, the late Dr. Nishikawa especially, developed this industry with great success—having devised new modes of causing the pearl oyster to produce hemispherical, more-than-hemispherical, and in the latest time completely spherical pearls.

Bashford Dean

SCIENTIFIC EVENTS

EX-SECRETARY MEREDITH ON RESEARCH

(From a correspondent)

The organization of research is now receiving so much attention that the fear is ex-