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TRANSMISSION OF ACTIVATION IN PASSIVE METALS AS A MODEL OF THE PROTOPLASMIC OR NERVOUS TYPE OF TRANSMISSION

ONE of the most remarkable peculiarities of irritable living cells and cellular elements like nerve fibers is the readiness with which chemical or metabolic influence may be transmitted, without accompanying transfer of material, between regions differing in the degree or character of their physiological activity. Thus one region of a muscle or nerve which is in a physiologically more active or "stimulated" state transmits its activity regularly to another more or less distant resting region. The state of activity aroused in the irritable living system by a localized stimulus does not itself remain localized, but tends to spread; the region immediately stimulated imparts a similar state of activity to adjoining regions, these then activate the next adjoining, and in this manner a wave of activation or excitation is propagated over the entire irritable element, often to a long distance from its point of origin. In many cases, as in nerve, there is no decrease in the intensity of the local process as it passes along the element; its characteristics are reduplicated both qualitatively and quantitatively at each point which it reaches in its course; the local excitation is temporary and quickly dies out, each successive region of the tissue becoming active and then returning automatically to its original state of rest. Transmission of this type is known to physiologists as "conduction," and is exhibited in its most highly developed form in the nerves of higher animals. It is, however, by no means peculiar to these structures; any cell or cell element which reacts as a whole to a local stimulus illustrates the same phenomenon; some disturbance affecting the metabolism and functional activity of the living system is radiated from the original point of stimulation and activates the whole. The characteristic functional manifestation then appears—contraction in a muscle cell, motor reaction in a protozoon, cell division and development in a resting egg cell, etc. Conduction is in fact a widely general if not universal cell process. Excitation may thus be transmitted not only between different regions of the same cell or cellular element but also between different cells or elements which are in contact with one another; the transmission between neurones in the central nervous system and from a nerve to its muscle or other terminal organ illustrates this type of conduction. It is thus possible to distinguish between intracellular and intercellular conduction, although there is probably no essential difference between the two types.

Physiological transmission of the kind described seems to have in it something mysterious and specifically vital; in fact the problem of the essential physico-chemical nature of nerve conduction—the type phenomenon of this class—is still regarded by most physiologists as unsolved, and apparently by many as insoluble. The difficulty of the problem has been accentuated by the apparent lack of any close analogies with known inorganic processes. Comparisons with the electric current, with the transmission of mechanical influences such as elastic strain or vibration, and with the propagation of explosive waves or of germ-effects like crystallization in supersaturated solution, have all proved inadequate and often highly misleading. Yet it would seem that any phenomenon which is so universal in organisms and upon which many of their most characteristic activities directly depend—especially in animals—must have some general physico-chemical basis present also in inorganic nature. The problem is to find some simple and readily reproducible inorganic process, involving transmission of chemical influence, which is similar in its most general features to the conduction process in living cells, initiated under similar conditions, and dependent upon the same fundamental factors. What is to be looked for is not complete or detailed identity of the physiological process with its inorganic model, but rather a class resemblance of a definite and unmistakable kind; the inorganic process should exhibit peculiarities which stamp it clearly as a phenomenon of the same essential kind as the physiological process. If the comparison is a true one, the transmission of chemical influence to a distance in cells or nerve fibers and the transmission of similar influence in the inorganic model should take place at similar rates, be influenced similarly by external conditions, be initiated by the same means, have the same external manifestations, and be dependent upon the same underlying physico-chemical factors. Just as the passage of the pulse wave in an artery and that of a distension wave in a simple elastic tube are both determined by general physical factors common to both objects, so the transmission of chemical or metabolic influence along a living conducting element like a nerve should—in the case of a valid comparison—depend upon certain fundamental features of physico-chemical constitution present also in the inorganic model. Is there in fact any known general class of non-vital physico-chemical phenomena to which we can thus assign the phenomenon of protoplasmic conduction?

In the stimulation of an irritable living structure by an external agent, the primary or releasing event is undoubtedly a surface process of some kind; the characteristic activation or "response" of the whole irritable element follows automatically upon this surface change. In most irritable cells any local mechanical or chemical alteration of the protoplasmic surface layer (or "plasma membrane"), or a slight change in its electrical polarization due to an electrical current, may cause excitation. There is little doubt, however, that the essential determining factors in any form of stimulation are *electrical;* and that mechanical and chemical stimuli excite the cell indirectly by means of the local electrical effects which they produce. The stimulating agent alters locally the structure or composition of the surface film; the state of electrical surface polarization is there changed; and the bioelectric circuit arising between altered and adjoining unaltered regions completes the activation. This view at once explains why the electric current is the most universal stimulating agent. It is well known that stimulation of any cell, by whatever means induced, is always accompanied by an electrical variation of the cell surface, or current of action; and we find the same to be true of the propagation of the excitation wave. This last process, which is evidently essential to the stimulation of the cell as a whole, is apparently dependent upon the bioelectric circuit formed at the boundary between the active and inactive regions of the cell surface; that part of the local current which traverses the still inactive regions stimulates these electrically; the regions thus secondarily excited act similarly upon the resting regions next adjoining; the process repeats itself automatically at each new active-inactive boundary as it is formed, and in this manner the state of excitation spreads continually from active to resting regions. A wave of activation thus travels over the surface of the element.[1]

If this theory of conduction is well founded, the chemical alteration of a surface film of material under the direct influence of local electrical circuits would seem to be indicated as the essential basis for the transmission. Changes of this kind are in fact a frequent phenomenon at the surfaces of metals in contact with solutions; and in a recent paper[2] I have called attention to the many striking analogies between the effects of such local electrolytic action in metals and the effects of local stimulation in living cells. For example, in the rusting of iron in aqueous solutions the formation of local electrical circuits between different regions of the metallic surface is now generally recognized to be the chief factor in the process. The surface layer of metal is typically not homogeneous, but exhibits local anodal and cathodal areas; at the former regions the ions of the metal enter solution and are precipitated as oxide or carbonate, while nascent hydrogen and alkali are presumably formed at the cathodal regions. Each of the areas of local chemical action thus represents an electrode-area in a local electrical circuit; and electrolysis at these areas is what determines the chemical changes there taking place. Now electrolysis is a process in which the transmission of chemical influence to a distance without transfer of material is an essential and constant characteristic; the very flow of the current depends in fact upon this condition. Any electrochemical change at one electrode of a battery or other electrical circuit due to chemical action necessarily involves a corresponding change of a chemically opposite kind at the other electrode. Oxidation, the general effect at the anode, thus involves simultaneous reduction at the cathode; an oxidizing substance placed in contact with one electrode will thus instantly oxidize a reducing substance at the other electrode. Spatial separation of the two regions is a matter of indifference except in so far as it increases the electrical resistance of the circuit, thus retarding the rate of the electrochemical process. The transmission of the chemical influence between the electrodes is automatic and instantaneous.

This "chemical distance action"[3] suggests a possible basis for the protoplasmic type of transmission, since distance action is a feature of all electrochemical circuits, including those present in local action at metallic surfaces. If therefore it could be shown that the cell surface can act like a metallic surface the essential difficulties of the problem of protoplasmic transmission might be regarded as overcome. An inconsistency, however, appears in the fact that the transmission of electrochemical influence in a circuit is instantaneous (*i. e.,* 3×10^{10} cm. per sec.), while the most rapid protoplasmic transmission—in the motor nerves of mammals—is only 120 meters per second; again, the intensity of chemical distance action decreases with the distance between the electrodes, because of the increase in electrical resistance, while in the nerve impulse there is normally no decrease in intensity (or "decrement") as the local change

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[1] *Cf. Amer. Jour. Physiol.,* 1915, Vol. 37, p. 348; 1916, Vol. 41, p. 126.

[2] *Loc. cit.,* 1916.

[3] *Cf.* Ostwald, *Zeitschr. physik. Chemie,* 1891, Vol. 9, p. 540.

passes along the fiber. Such difficulties are only apparent, however; in nerve conduction it is quite certain that an entirely new state of activity is aroused at each successive region of the fiber as the impulse passes; and all of the evidence indicates that the speed of transmission is determined mainly by the sensitivity and local rate of response of the nerve,[4] and not at all by the rate of transmission of the electric current in the bioelectric circuit. It is probable that in the local bioelectric circuit set up by the initial stimulus the direct chemical influence of the current extends for only a short distance, at most a few centimeters from the original site of stimulation; but one of its effects is to originate a new and similar circuit in the adjoining regions of the fiber; this process repeats itself as already indicated, and in this manner the impulse spreads. The observed speed of the activation-wave has thus nothing to do with the speed of the purely electrochemical distance effect. What we seem to observe is a local electrical circuit which travels along the nerve together with the activation wave; but in reality there is a succession of new circuits, each of which automatically arises at the boundary between resting and active regions as the front of the activation wave advances. The relatively slow rate of movement of the impulse and the absence of a decrement may thus be understood.

The rapid passage of a wave of chemical decomposition (probably oxidative in nature and involving some structural change) over the surface of the reacting element, followed immediately by a reverse change which restores the original or resting condition, is what appears to take place in a nerve or other living structure during conduction. Associated with the chemical process is a local electrical circuit by whose electrolytic action the chemical change is apparently determined. Have we examples of similar processes in inorganic systems? It appears in fact that this general type of process is not unusual in metals in contact with solutions. Especially clear and striking examples are seen in the transmission of the state of activity over the surface of metals, especially iron, which have been brought into the temporarily non-reactive or "passive" condition by immersion in strong nitric acid (or other suitable oxidizing agent) and are then placed in dilute acid and made to react. It has long been known that iron which has been thus "passivated" becomes resistant or refractory to reaction and (for example) no longer dissolves spontaneously when placed in dilute nitric acid (s. g. 1.20). But if while immersed in the dilute acid it is touched momentarily with a baser metal, or with a piece of ordinary non-passive iron, it is at once "activated" and reacts vigorously with the acid until dissolved.[5] The experiment is a striking one and easily performed. In my own demonstrations a piece of pure iron wire (No. 20 piano wire, bent at one end into a hook for handling) is passivated by immersion in strong nitric acid (s. g. 1.42) for a few seconds, and is then placed (by means of a glass hook) in a flat dish containing dilute acid (s. g. 1.20). The wire if left undisturbed remains bright and unaltered for an indefinite time. If then it is touched at one end with a piece of ordinary iron, or with zinc or another baser metal, the bright metallic surface is at once darkened (through formation of oxide) and active effervescence begins; this change is transmitted rapidly, though not instantaneously, over the entire length of the wire; the velocity of transmission varies with the conditions, and is of the order of 100 or more centimeters per second in this experiment. The wave of activation may also be initiated *mechanically, e. g.,* by bending the wire or tapping it sharply with a glass rod; or *chemically, e. g.,* by contact with a reducing susbtance such as sugar; or *electrically, e. g.,* by making the wire (while immersed in the acid) the cathode in any battery circuit (of two or more volts potential), preferably with another piece of passive iron wire as anode;

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[4] *Cf. Amer. Jour. Physiol.,* 1914, Vol. 34, p. 414; Vol. 37, p. 348.

[5] For a recent extended study of the passive state in metals with full references to the literature, *cf.* Bennett and Burnham, *Jour. Physical Chem.,* 1917, Vol. 21, p. 107.

the cathodal wire is instantly activated, while the anodal wire remains unchanged. Activation with the electric current is thus typically a polar phenomenon, just as is the excitation of a living irritable element like a nerve.

Activation by contact with active iron or a baser metal is in reality an instance of electrical activation, the activating metal forming the anode of the local circuit arising at the region of contact. At the local cathode, *i. e.,* the adjoining passive iron, the metal is at once activated, and the effect spreads in the manner already indicated by means of the circuit which automatically arises at the boundary between active and passive areas. Any metal which thus activates by contact must be of such a nature that the passive iron becomes the *cathode* of the local circuit formed. A metal which is nobler than passive iron, like platinum, not only does not cause activation, but it renders the iron locally more resistant to activation; thus the passage of the activation wave may be blocked by the contact of a platinum wire. This latter effect depends upon the formation of a local circuit of the reverse orientation, the iron becoming anodal, a condition which furthers passivation and hinders activation. Active iron is a base metal in relation to passive iron, being more negative that the latter by *ca.* 0.75 volt in 1.20 HNO_3; hence when any region of a passive wire is rendered active it immediately activates the adjoining areas.

In passivation the surface layer of the iron is modified in a peculiar manner, apparently by the formation of a thin resistant layer of higher oxide. Any condition that interrupts locally this surface film of altered iron forms necessarily a local circuit by whose action the whole metal is activated in the manner just described. Apparently at any cathodal area the surface film of oxide is reduced to metallic iron; contact of a reducing substance has a similar effect; while a mechanical agent breaks the continuity of the film and exposes the unaltered iron beneath, thus forming the local circuit. The reason why mechanical, chemical and electrical influences all produce the same effect is thus evident. The parallel to the living irritable tissue is plain; local alteration of the protoplasmic surface film produces effects of a closely comparable nature, which spread in an analogous manner by means of the local electrical circuits formed. We are thus enabled to understand why any rapid local alteration of the cell surface may activate the whole cell—in other words why the cell is so characteristically "irritable." The iron wire in its passive state may be compared to the irritable living element in a state of rest. The state of inactivity continues in both cases only so long as the surface layer is intact and homogeneous. The reason why the *whole* cell (or the whole iron wire) responds completely to a local stimulus is simply because transmission over the entire surface follows automatically and inevitably upon local activation. The "all-or-none" behavior thus becomes intelligible.

Under normal conditions an irritable nerve or muscle returns spontaneously to an inactive or "resting" state after stimulation, and for renewal of activity a second stimulus is required. The resting condition thus represents a condition of equilibrium, which is temporarily disturbed by the stimulating agent. The same is true of the passive condition of iron in *strong* solutions of nitric acid. In weaker solutions, of s. g. 1.20 and less, the reaction once initiated continues unchecked until all of the iron is dissolved; but in stronger solutions *the reaction is temporary and the metal returns spontaneously to the passive condition.* A wave of temporary activity thus sweeps over the surface of a passive iron wire which is activated (*e. g.,* by touching with zinc) in nitric acid of s. g. 1.25 or higher; the state of local activity lasts in such a solution for a brief period only, which is the shorter the higher the concentration of the acid. An interesting gradation of effect may thus be shown by activating a series of passive wires in different dilutions of strong (s. g. 1.42) acid, *e. g.,* 90, 80, 70, 60 and 55 volumes per cent. (*i. e.,* 90 c.c. 1.42 HNO_3 *plus* 10 c.c. water, etc.). When a wire immersed in pure 1.42 acid is touched at one end with a piece of zinc a momentary flash-like wave of activation is seem to pass rapidly along the whole wire; the local reaction lasts for only a small fraction of a second and is instantly reversed; a slight temporary darkening of the metallic surface and a trace of brown coloration (due to reduction of the acid to lower nitrogen oxides) are the only visible effects; in 90 per cent. acid a similar though somewhat more prolonged reaction takes place; in 80 per cent. acid there is slight visible effervescence for a fraction of a second; in 70 per cent. the effervescence lasts for about one second and the darkening of the metallic surface is more pronounced; while in 60 per cent. the reaction occupies two or three seconds and in 55 per cent. five seconds or more, and a considerable accumulation of brown oxide is formed at the surface of the metal. It would thus appear that in the stronger solutions the oxidation which forms the protective surface film takes place so rapidly that only a momentary reaction of the metal with the acid is possible; as the concentration of acid decreases the surface film forms more slowly and the reaction lasts longer, until at a certain critical concentration (about 50 per cent.; *ca.* 1.20 s. g.) the surface oxidation becomes so gradual that its passivating influence is insufficient to interfere with the continued solution of the metal in the acid.

Two chemical reactions of opposite character thus take place successively as the activation wave passes any region of the metallic surface; first, the local cathodic reduction which removes the protecting layer of oxide and enables the metal to react with the acid; and second, the immediately succeeding oxidative process which reforms the protective surface film and arrests the reaction. A factor of importance in this process of repassivation is apparently the electrochemical oxidative action at the local anode. As the activation wave advances, the surface film is disintegrated at the cathodal region immediately in advance of the wave front; this region then instantly becomes active, *i. e.,* anodal; in other words, it undergoes a change of condition which in itself tends to check or arrest the reaction. This is because of the characteristic passivating influence at the anode; the reaction of a piece of active iron wire in 1.20 HNO_3 may in fact be brought to rest and the wire rendered passive by passing a strong current through it as anode for a few seconds.[6] As the activation wave passes, each region of the metallic surface thus becomes alternately cathodal and anodal. Making the passive metal cathode has an activating effect, while making the active metal anode tends to passivate. This latter electrochemical action is added to the direct passivating action of the acid. Hence in acid of a sufficient strength the local reaction is automatically self-limiting as well as self-propagating. This peculiarity depends directly upon the properties of the surface film, which when the metal is cathode undergoes dissolution, and when the metal is anode is reformed. Apparently in strong acid the metal is in a condition where a slight local increase of reducing influence initiates the activating reaction and a slight increase of oxidizing influence inhibits it. We have here another parallel to the condition in an irritable element like a nerve fiber, where cathodal polarization promotes and anodal polarization inhibits the local reaction (electrotonus). In both cases the alternate disintegration and reformation of a surface film under electrochemical influence appear to be the essential features of the local process.

The passage of the wave of activation can be observed with especial clearness in a passive iron wire which has been dipped in a test-tube containing 1.42 HNO_3 and is then suspended vertically in air and touched at its lower end with zinc. The adhering layer of acid is so thin as to increase greatly the resistance of the local circuit between active and inactive regions, and the local reaction spreads with corresponding slowness, at a rate of only a few (5 to 10) centimeters a second. As the

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[6] Contact of a piece of platinum foil with a reacting iron wire has the same effect; near the platinum the iron soon ceases reaction and becomes passive, and the effect then spreads over the whole wire. This phenomena is biologically interesting, as a case of transmission of inhibitory influence.

reacting region extends upward the bright surface of the iron is darkened locally for a distance of two or three centimeters; behind this advancing active region the wire again becomes bright and inactive. The visible effect is that of a slight temporary darkening or clouding which travels upward along the wire. After the wave has passed over the whole length of the wire the latter, when tested by dipping in 1.20 acid, is found to be again passive; the temporary and reversible character of the activation is thus shown. A similar slow spreading of the active state takes place in a passive wire dipped in weaker (1.20) acid and then activated as above, but in this case there is no spontaneous return to passivity; the whole wire remains dark, and when again placed in 1.20 acid at once reacts vigorously in the usual manner of active iron. Spontaneous reversal thus takes place only in the strong acid.

In the experiment just cited the rate of transmission is lowered by increasing the electrical resistance of the local circuit, but in other respects there is no essential difference from the conditions observed in immersed wires. A noteworthy feature of these phenomena is that after a wire has been activated while immersed in strong acid (*e. g.,* 80 per cent. 1.42) some time elapses before a complete reaction can be again excited; *i. e.,* a period of insensitivity and imperfect transmission always follows the spontaneous return of passivity. Contact with zinc within the first four or five minutes after activation causes typically only a local reaction which may be transmitted slowly for a few centimeters but then dies out; some minutes later transmission takes place more rapidly and through a longer distance; but it is usually only after ten or fifteen minutes (the exact time varying with the conditions) that perfect transmission through an indefinite distance becomes again possible. The recovery of the original condition thus requires some time, the exact interval varying with the concentration of acid, and in general decreasing with decreasing concentration. This phenomenon also has its biological analogies, and may be compared to fatigue, or possibly to the refractory period which typically follows stimulation in all irritable tissues. Evidently the reformed surface film regains its former sensitive properties by a progressive and somewhat gradual process.

This tendency to an automatic restoration of the protective surface layer of oxide after local removal is probably the essential condition underlying another characteristic feature of the electrical activation of passive iron, namely, that a slowly increasing current passed through the wire (as cathode) is much less effective in causing activation than a current of similar strength which attains its full intensity rapidly or instantaneously. In this respect also the passive metal resembles the living irritable tissue. If the current leading to the two passive wires immersed in 1.20 HNO_3 is derived by means of a stationary and a movable zinc electrode from a bath of zinc sulphate solution forming part of a circuit of several storage cells—an arrangement enabling the potential of the "shunt current" to the iron wires to be varied at will—it is found that a gradual increase of the current, from near zero to an intensity which in itself is amply sufficient to activate with sudden closure, is typically without effect. Evidently a *sudden* change of surface polarization is needed; if the change is gradual it seems that the oxidative action of the acid in contact with the metal has time to reform the passivating protective layer as fast as it is reduced by the cathodal action.

The chief of the foregoing resemblances between the passive iron wire and the irritable living element may now be briefly summarized as follows: (1) Mechanical, electrical and chemical agencies have the same activating effect; (2) electrical activation is a polar phenomenon (analogy to the law of polar stimulation); (3) the local state of activity is propagated along the wire at a velocity which is similar in its order to that of the excitation wave in living tissues; (4) whenever activation is excited by any means in a passive wire immersed in a definite solution of acid (*e. g.,* 70 per cent. 1.42 HNO_3) the *whole* wire is involved and the reaction lasts for a definite time; *i. e.*, the character, intensity and duration of the reaction are independent of the nature of the activating agent; the metal either reacts completely or not at all (analogy to the "all-or-nothing" behavior of irritable living elements); (5) a wire which is polarized anodically while immersed in acid is activated with difficulty and the activation wave tends to travel for only a short distance (analogy to anelectrotonus in nerve); (6) the spontaneous return of passivity in strong acid is immediately succeeded by a period during which the metal is less responsive than before (analogy to fatigue effect or refractory period); (7) a current which reaches its full intensity gradually is less effective than one which reaches the same intensity suddenly; and finally (8) the local chemical surface reaction of activation is constantly associated with a variation of electrical potential, the active region becoming negative relatively to the inactive regions (analogy to the bioelectric variation or "action current" of an active living tissue).

The chief characteristics of this electrical variation are readily demonstrated as follows. When two iron wires connected with the binding-posts of a voltmeter of suitable scale are passivated and placed side by side in a vessel containing 1.20 HNO_3, no potential difference is shown. If then one wire is activated the instrument at once indicates a P.D. of 0.7 to 0.8 volt, with the active wire negative; this P.D. remains constant while the reaction continues in the one wire; if then the other wire is also activated the P.D. again falls to zero. The active wire is thus anodal, the passive wire acting like a noble metal. If the same experiment is performed with stronger acid (55 per cent. 1.42 or higher) a similar but *temporary* excursion of the needle is seen, lasting for the period of the reaction. In acid of 55 or 60 per cent. the potential exhibits irregular rhythmical fluctuations for the few seconds during which the reaction continues, and the needle swings by degrees back to zero and somewhat beyond as the reaction subsides and ceases. Immediately after the return of the passive condition the activated wire is always found slightly more positive than before, usually by *ca.* 0.02 volt; after an interval of some minutes—corresponding apparently in its duration to the insensitive or refractory period above described—the original potential returns. The wire may then be again reactivated and the same process is repeated. This tendency to overpass the original potential after the return of passivity recalls the similar phenomenon in nerve known as the "positive after-variation," and suggests a similarity in the general conditions under which the surface film is reconstituted in the two cases.

The variation of potential associated with the transmission of the activation wave may be demonstrated in a single wire which is connected near its opposite ends with a sensitive string galvanometer (by means of thin passive iron wires) and immersed in 70 or 80 per cent. acid. If the wire is activated at one end the string shows a quick excursion, first in the one direction, then in the other, the deflection showing that at each leading-off region the wire becomes first negative and then positive. The curve of movement is thus comparable to the typical "diphasic" action current curve of a nerve conducting an impulse.

The amplitude of these variations of potential in metals is of course much greater than that found in living tissues, but in their general characteristics both classes of phenomena give unmistakable evidence of being conditioned in the same manner. In the case of the metal it is certain that the effect depends upon a sudden alteration of the electromotor properties of the surface layer. In living tissues and cells there is also much evidence that a change in the protoplasmic surface layer (or so-called plasma-membrane) involving increased permeability and altered metabolism is constantly associated with stimulation, and that the variation of electrical potential is due primarily to this change. Thus in both living system and metal the electrical variations are the expression or indication of changing chemical and structural conditions in the surface layer. The local interruption or removal of the surface film of oxide in the metal is comparable with the increase of permeability in the living element.

A significant general analogy to physiological conditions is also to be seen in the readiness with which the active state is transmitted from an active to a passive metal by *contact*. Transmission of excitation from one cell or cell element to another by contact is frequent in organisms; and many characteristic structural arrangements, especially in the nervous system, give evidence that such transmission is a normal and constant physiological process; the interlacing of dendrites from different neurones, contact of nerve cells with one another by "end-feet" and similar structures, the histological characters of the myoneural junctions and other nerve endings—which typically form contact with the *surface* of the cell—may serve as examples. Instances of transmission by contact in metals have been given above. A good demonstration is the following: if a number of passive iron wires are placed in contact with one another in a dish of nitric acid, and any single wire is touched with zinc, *all* immediately become active. A long fine passive wire in contact at one end with a large piece of passive iron, *e. g.*, a nail, will on activation at its other end rapidly conduct and transmit the state of activation to the terminal object. Another remarkable feature of this phenomenon is that the transmission between different metals may be *irreciprocal;* this may be shown by using wires of the two metals, iron and nickel, which differ in the readiness and rate with which activation takes place. A momentary contact with active nickel will instantly activate a piece of iron wire in 1.20 HNO_3, but under the same conditions a piece of passive nickel is activated slowly and only after prolonged contact. Consequently, while briefly touching passive iron with active nickel immediately and completely activates the iron, touching passive nickel with active iron is typically ineffective or has only slight local effect. In other words, transmission of activation takes place rapidly and readily from nickel to iron, but not in the reverse direction. The difference depends upon the relative slowness of the activation process in nickel; in this metal the local reaction tends to start slowly and to reach its maximum slowly, and the rate of transmission is correspondingly gradual. Such facts suggest the possibility that the characteristic irreciprocality of transmission in reflex arcs may depend upon similar differences in the time factors of excitation of the interacting neurones at the synapses. The recent work of Lapicque and Keith Lucas has shown clearly the fundamental importance of the time factor in the excitation process.[7]

It seems clear that variations in the electromotor properties of the surfaces concerned—respectively the metallic surface and the cell surface—form the essential feature of activity which is common to both types of system and upon which the above various similarities of behavior depend. These variations are due to changes in the physical and chemical character of the surface layer, which in both cases is water-insoluble, chemically unstable, and in contact with an electrolyte solution. Experiment shows that in the passive metal this surface film is in a characteristic state of equilibrium which is readily disturbed, and the same appears to be true of the protoplasmic surface film in an irritable cell or cell element.

This general similarity probably explains another peculiarity of behavior common to both systems, namely a tendency to automatic rhythmical fluctuations of potential and chemical action; this phenomenon is seen in the solution of many metals in nitric acid, and also in the well-known rhythmical catalytic decomposition of hydrogen peroxide in contact with mercury. Alternation of activity and passivity, due to rhythmical formation and dissolution of a surface film of oxide or other protective material, appears to underlie these phenomena in metals. In living organisms rhythmical action is also highly characteristic, and is presumably due to analogous conditions.

The general view that the semi-permeable

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[7] Similarly with transmission from element to element. Lapicque's work indicates that the failure of transmission from nerve to muscle in curare poisoning is due to "heterochronism."

cell surfaces may have electromotor properties similar in certain respects to those of metallic surfaces has long been familiar to physiologists; and the so-called "membrane theory" (or theories) of the bioelectric potentials, which originated in a suggestion of Ostwald in 1890 and has been developed in considerable detail by Bernstein, Höber and others, has referred the physiological variations of potential to variations of permeability or to other changes in the plasma-membrane. It seems best, however, to avoid for the present too special conceptions of the precise nature of the processes concerned in these phenomena and to regard the latter from a broader and more generalized point of view. Variations of phase-boundary potentials, with associated or dependent chemical effects, appear to constitute the general type of phenomenon involved. More recently the work of Haber, Beutner and especially of Loeb and Beutner in collaboration, has demonstrated many fundamental resemblances between such potentials and the bioelectric potentials, and is of the highest interest in relation to this general problem. The work of Loeb and Beutner, together with that of Macdonald, indicates that organic membranes and cell-surfaces behave as if reversible (in the electrochemical sense) to cations as a class; in this respect they resemble the surfaces of solutions of lipoids in organic solvents; and it seems probable that the demarcation-current potentials are thus to be explained. I am inclined, however, in view of the conditions in passive iron as well as for more purely biological reasons, to regard the local bioelectric circuits accompanying normal cell activity as representing primarily some type of oxidation reduction element. In general the physiological effects observed at the respective regions where the electric current enters and leaves the cell-surface are *opposite* in character, and the same must be true of the underlying chemical or metabolic processes. Oxidation at one area, simultaneously with reduction at another area—these chemical changes involving synthesis as well as decomposition—seems to be a more probable source of the normal currents of action, especially when the dependence of vital phenomena on oxidation and synthesis and the interdependence of the two latter processes are considered. Further discussion of the possible relations between the bioelectric processes and cell-metabolism, with a fuller account of the facts described in this article, must be reserved for a more complete paper.

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THE INTER-ALLIED SCIENTIFIC FOOD COMMISSION[1]

The Inter-Allied Scientific Food Commission now sitting in London has already at previous meetings accomplished a good deal of work, and if its recommendations are carried out, the provisioning of allied countries will be placed on a sound scientific basis. That its recommendations will be carried out seems to be more or less guaranteed by the fact that it was established as a result of a decision of the Inter-Allied Conference held in Paris last November. The Conference directed that the inter-allied scientific commission should consist of representatives of France (Professors Gley and Langlois), Italy (Professors Botazzi and Pagliani), United States (Professors Chittenden and Lusk), and the United Kingdom (Professors E. H. Starling and T. B. Wood). It was instructed to meet periodically in order to consider from a scientific point of view the food problems of the Allies and in agreement with the inter-allied executives to make proposals to the allied Governments. The commission held its first meeting in Paris on March 25, and its second in Rome on April 29. Before its present meeting in London a representative of Belgium, Professor Hulot, was added. A memorandum upon the work of the commission, furnished to us by the food controller, contains some particulars enlarging the information published in previous issues.

At its first meeting last March in Paris the commission came to an agreement as to the minimum food requirements of the average man. It was laid down that for a man weigh-

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[1] From the *British Medical Journal*.