colleges and other establishments where measurements of many subjects are being taken, such as institutions for children, institutions for special classes of defectives and abnormals, insurance companies and the recruiting stations of the army and navy.

(7) To the furtherance of the same methods, instruments, etc., in other countries.

(8) To the development of physical anthropology as a well-organized branch of science in order to insure its greatest practical value and educational benefits for future generations.

(9) To the popular dissemination of the results of scientific research in physical anthropology.

(10) To the furthering and assisting, in our museums, universities and colleges, of the best possible exhibits in human phylogeny, ontogeny, variation and differentiation.

(11) To the aid of advanced and worthy students to original research and field work. And,

(12) To the eventual establishment, in the most favorable location, of the "American Institute of Physical Anthropology," which would serve both as the home and library of the association, and as the center of anthropometric instruction and of dissemination of anthropological knowledge.

The association will consist of active and associate members.

The condition of active membership will be sound original work in or closely related to physical anthropology. Associate members will be all such persons from collateral sciences, or at large, who may, through sympathy with the objects of the association or a desire to benefit from its activities, wish to join its ranks; they will have the privilege to participate in the meetings of the association, without voting.

The annual membership dues, for both active and associate members, are fixed at $2.00 per year. There will also be patrons and life memberships. Applications for membership should be addressed to Professor D. J. Morton, secretary-treasurer, Department of Anatomy, College of Physicians and Surgeons, Columbia University, 630 W. 168th St., New York City.

ALEŠ HRDLIČKA
*Chairman p. t. A. A. P. A.*
U. S. NATIONAL MUSEUM

## SPECIAL ARTICLES

### CIRCUIT TRANSMISSION AND INTERFERENCE OF ACTIVATION WAVES IN LIVING TISSUES AND IN PASSIVE IRON

THE material in which the primary chemical reactions of stimulation take place in living irritable tissues, such as nerve and muscle, is evidently not in homogeneous solution; the indications are that it is situated (*e.g.*, adsorbed) at the protoplasmic phase-boundaries, *i.e.*, forms part of the thin, electrically polarizable surface-layers of the protoplasmic structures concerned. This is implied by such general facts as the universal responsiveness of these reactions to the electric current and their sensitivity to the presence of surface-active compounds (narcotics). According to the chief prevailing conception (membrane theory) of the primary stimulation process, the material in question is a component of a thin, continuous interfacial film or membrane which undergoes both chemical and structural change during stimulation. Two constant features in the response of an irritable tissue to stimulation are (1) that the reaction never remains localized but tends automatically to spread, often rapidly and to an indefinite distance, as in nerve, and (2) that the tissue is always inert and irresponsive for a brief period after excitation (refractory period). The recovery which occurs during this period is an index of the restoration of the reactive surface-layer to its original structure and composition. It is as if one had a thin sheet of explosive material which is completely broken down in each reaction ("all-or-none" behavior) and is then immediately renewed. Evidently in a system so constituted the reaction occurring at any point is temporary, and maintained activity is necessarily intermittent or rhythmical. In the muscle or nerve the state of chemical and other activity resulting from a single localized stimulation travels along the irritable element in the form of a wave. When the excitation process at any point is rapid, as in nerve, only a limited area is occupied at any instant by the reaction; this active stretch constitutes the excitation wave (contraction wave, nerve impulse); in a vertebrate motor nerve it is at most only a few centimeters in length.

If the anatomical relations are such that the excitation wave can return to its starting-point, as by passing around a continuous circular path, it may continue its motion indefinitely, provided the tissue has recovered sufficiently in the interval between successive circuits. Such circuit transmission is not normally found in the intact animal, but it can readily be obtained experimentally in certain instances. Hitherto it has been studied chiefly in circular strips of neuromuscular tissue cut from the hearts of the larger cold-blooded vertebrates and the subumbrellar tissue of medusæ. A contraction wave started in one direction in such a strip will often continue its circular motion for hours or even days. These tissues are alike in having relatively slow rates of transmission and well-marked refractory periods. I have also observed striking instances of the phenomenon in strips of ctenophore tissue containing a row of swimming plates; such strips (*e.g.*, 3 to 5 cm long) often round off in sea-water in such a way as to bring the opposite ends of the row close together; waves of ciliary movement then cross the gap and travel uninterruptedly around the ring, often for hours at a time.[1] In rings cut from the heart of the loggerhead turtle Garrey obtained circus contractions lasting continuously for hours, and Mines made similar observations on the hearts of sharks and rays.[2] In the medusa Cassiopea Mayor and Harvey obtained "trapped" contraction waves which continued steadily for days at rates of 15 to 60 cm per second, traveling distances estimated at many miles.[3] Such experiments are of interest as illustrating the perfect regularity and automaticity of the processes underlying stimulation, transmission and recovery in these tissues. It should be noted that trapped excitation waves of this kind may become a source of deranged coordination in organs whose normal activity depends on regular transmission in one direction; thus both Garrey and Mines have pointed out the intimate relations of this phenomenon to cardiac fibrillation; and the possibility should be considered that similar types of derangement may occur in the central nervous system.

Two chief conditions for circuit transmission are as follows: (1) The excitation wave must be of limited length, so that at any instant it occupies only a restricted portion of the circuit; and (2) its rate of movement must be relatively slow, so that the time required for the wave front to travel the distance of the circuit (less the length of the wave itself) is greater than that occupied by the recovery process (refractory period) of the tissue. Under these conditions the activation wave is continually entering a region of tissue which is sufficiently recovered to permit of further transmission. Hence its progress continues automatically until it is arrested by some secondary change of condition, such as interference, exhaustion or injury. The length and speed of the excitation waves are usually such that the ring must be of considerable size, *e.g.*, some inches in diameter, if the circular transmission is to continue indefinitely; this, according to Garrey, is the reason why only the larger hearts readily undergo fibrillation. According to his conception, reached independently also by Mines, fibrillation is a result of the formation of local closed circuits in which contraction waves may circulate without interference. Evidently the length of any such circuit must be greater than that of the excitation wave if the conditions for the periodic renewal of the wave on its completion of the circuit are to be met (see Mines's diagram, *loc. cit.*, p. 374). Analogous conditions are found in passive iron wires; irregular waves of activity resembling fibrillation are readily obtained in longer lengths of Armco wire in $HNO_3$ of 78–80 v. per cent. concentration[4] but not in shorter lengths.

Attempts to obtain circuit transmission of a similar kind in rings of passive iron wire in nitric acid have hitherto met with only partial success, chiefly because the two necessary conditions, short length of simultaneously active region (activation wave) and rapid recovery of transmissivity, were never found combined in a single wire. Either the non-transmissive period immediately following activation was too long (as in the steel wires used in my earlier experiments),[5] or the duration of the local activity was too great in relation to the speed of transmission, so that the whole wire became simultaneously active. I have tried increasing the concentration of acid; this change of condition shortens the duration of the local reaction, thus decreasing the length of the wave, without greatly affecting the rate of transmission; but unfortunately this procedure also rapidly lengthens the period of recovery, so that the return of the wave finds the wire still non-transmissive. In steel wires the non-transmissive period is so long—some minutes in 70 v. per cent. $HNO_3$ at 20°—as to make any practicable arrangement quite impossible.[6]

Recently, however, I have found that pure iron wire of low carbon content (electrolytic iron or Armco iron) has a very brief recovery period,[7] measured in fractions of a second in 70 to 80 v. per cent. $HNO_3$ at 20°; it thus becomes possible, without unduly prolonging the refractory period, to use acid so strong that the active stretch of wire during transmission is only a few centimeters in length. When the temperature, concentration of acid, and interval since previous activation are properly adjusted, activation waves 10 to 20 cm long are obtained which travel at moderate speeds, of 10 to 30 cm per second. In rings of wire not more than 20 cm in diameter the recovery time is less than the time taken by the wave to complete the circuit, so that under appropriate

1 Observations on Eucharis and Beroe in the Naples Zoological Station in 1904–5 (*cf.* Carnegie Year-book for that year).

2 Garrey, *Amer. Jour. Physiol.*, 1914, 33: 397; Mines, *J. of Physiol.*, 1913, 46: 349.

3 Mayor, Carnegie Inst. Bull. Publ., 1908, 102: 113; Harvey, *ibid.*, 1910, 132: 29, and Carnegie Year-book, 1911, 10: 130.

4 Volumes of $HNO_3$ (C. P. sp. gr. 1.42) in 100 volumes of solution.

5 *J. Gen. Physiol.*, 1920, 3: 107, 129; and 1925, 7: 473.

6 *J. Gen. Physiol.*, *loc. cit.*

7 SCIENCE, 1928, 67: 593.

conditions typical continued circuit transmission is readily obtained.

The wire used in the present experiments was the pure low carbon wire known as Armco,[8] 2 mm in diameter. In order to secure the conditions for a regular progressive movement of a trapped activation wave it is necessary to have the ring of wire surrounded by a continuous column of acid of uniform and not too great width—*i.e.*, by a ring or sheath of acid—instead of lying free in a large continuous volume, as in an open dish. In the latter case it is impossible to keep the activation wave sharply defined and limited in length, because of distance action between the active area and the passive area on the opposite side of the dish. Contact of the wire with the walls or bottom of the vessel must also be avoided, because of irregular local activity set up at such regions.[9] These conditions have been satisfactorily met by the following arrangement. The wire ring is freely suspended by thin glass hooks in a circular trough, *ca.* 2 cm in diameter, containing the acid. This trough is made by cementing a section of glass cylinder, *ca.* 5 cm high and 20 cm outside diameter (cut from a large bottle), to the bottom of a crystallization dish of 24 cm inside diameter and 6 cm depth. The bottom of the trough is covered by a layer of paraffin (to protect the cement against the action of the acid). A satisfactory apparatus has also been made by partly filling a crystallization dish with paraffin and cutting out a trough around the margin. The wire ring (*ca.* 22 cm in diameter) is suspended at *ca.* 1.5 cm from the bottom in a layer of acid 3 cm deep. The temperature is regulated by a water-bath. The wire ring is *ca.* 70 cm in circumference. It is made most conveniently by cutting the required length of wire, bending it into a circle and hooking the two ends together. Usually it is necessary to insert a small piece of platinum wire at the junction where the two surfaces of iron are in contact; otherwise a persistent action is likely to be set up at this region, from which rhythmical waves of activity spread over the wire in both directions, making regular circuit transmission impossible. In some experiments the two ends of the wire have been welded to make a continuous ring. In certain respects this procedure is preferable, but the welded region often acts at first as a block to transmission, apparently because of the formation of iron oxides. If, however, such a ring be kept in strong $HNO_3$ for some time the block disappears and the activation wave then passes the junction smoothly.

The concentration of $HNO_3$ suitable for circuit transmission under these conditions is 75–80 v. per cent. In weaker acid the active stretch of wire (*i.e.*, the activation wave) is too long; in stronger acid the wave is shorter but the return of transmissivity is too gradual. In acid of 78–79 v. per cent. at 15° the activation wave is typically 12–15 cm in length and its speed is about 15 cm per second. Any single region of the metallic surface thus passes through a cycle of chemical change lasting about one second, consisting in a reduction and dissolution of the passivating surface film followed by its reformation under the oxidizing influence of the acid and local electric circuit. By the time the wave has completed the circuit the wire is sufficiently recovered and transmission continues uninterruptedly.

### INTERFERENCE OF ACTIVATION WAVES

When the passive wire, arranged as above, is touched with zinc at any point two activation waves are started which travel in both directions from the contact; these meet on the opposite side of the ring and there immediately extinguish one another, the whole wire becoming again passive. This experiment may be repeated as often as desired at intervals of two or three seconds with always the same result. A similar interference of excitation waves in living tissue has long been known, and is shown clearly in rings cut from large hearts or medusæ. Two equal contraction waves traveling in opposite directions and intersecting undergo mutual extinction.[10] In the passive wire interference is also readily demonstrated in a long straight wire immersed in acid and touched simultaneously at opposite ends, or in a vertically suspended wire over which a thin stream of acid is kept flowing from a siphon; in the latter case the movement of the waves is slow (2 to 4 cm per sec.) and the details of the phenomenon can be observed more closely. The effect itself is a direct consequence of the intersection or superposition of the two oppositely oriented local electric circuits of the two waves; the associated electric currents annul one another by compensation and the dependent chemical action ceases. Electrochemical interference of this type is a possibility in the case of any reaction occurring at an interface under the influence of a local circuit. The fact that it is equally characteristic of activation waves in living tissues constitutes further evidence that the primary chemical reactions of excitation and transmission in protoplasm are surface reactions controlled by local bioelectric circuits.

[8] American Rolling Mill Co. The carbon content is given as less than 0.1 per cent. This wire was also used in my experiments on rhythmical action: *Archivio di Scienze biologiche*, 1928, 12: 102, and SCIENCE, 1928, *loc. cit.*

[9] R. S. Lillie, *loc. cit.*, 1928.

[10] *Cf.* Mines and Mayor, *loc. cit.*

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When the passive wire is held at one region with a pair of platinum-tipped forceps and is then touched at a neighboring point with zinc, the activation wave thus started is blocked at the platinum, while its progress in the other direction is unhindered. If the platinum be withdrawn before the circuit is completed an isolated activation wave is left in the wire; this continues its movement in a manner analogous to the trapped excitation waves in living tissues. The spectacle is a striking one; the dark, slightly effervescent area corresponding to the active stretch retains a nearly constant length (*e.g.,* 15 cm), and moves with remarkable uniformity round and round the wire in one direction. Unless some accidental condition interferes, or the materials are depleted, the movement continues indefinitely. At any time the progress of the wave can be stopped by contact with platinum; the whole wire then becomes passive.

The following are typical speeds of transmission observed in a single wire in the same bath of acid (79 v. per cent.) at different temperatures:

| Temperature | Speed (cm per sec.) |
|---|---|
| 8° | 8 |
| 13–14° | 13–14 |
| 18° | 24–25 |
| 23° | 33–35 |

It is noteworthy that the $Q_{10}$ values (2.5–3) are higher than those usual with nervous transmission or transmission in fully recovered passive iron. This is because the rate of travel of the wave in circular wires is limited by the degree of recovery which the wire has reached in the interval between successive circuits. The temperature coefficient of recovery, both in living tissues and in passive iron,[11] is typically high ($Q_{10} = 2.5$–$3.0$). The speed of the activation wave in passive iron is slowest immediately after the return of transmissivity and gains its final value by a progressive increase, following a curve resembling a parabola.[11] A similar behavior is seen in heart muscle (Mines)[12] and in nerve (Forbes).[13] The return of the definitive or final rate of transmission at any temperature is thus determined by the rate of recovery. What is illustrated by the foregoing observations is in reality the temperature coefficient of recovery; the coefficient of transmission in wires that have reached a stationary condition is much lower ($Q_{10} = 1.4$–$1.5$ in steel wires between 5° and 20°).[11] A relatively low temperature coefficient is also characteristic of transmission (as distinguished from recovery) in nerve and muscle.

With regard to the chemical aspects of the phenomenon certain general features may here be briefly considered. As is well known, transmission in passive iron depends on the cathodal reduction and consequent breakdown of the thin, passivating surface-film of oxidation-product at the region adjoining the already active area. The repassivation which follows automatically in stronger acid is an effect of the reformation of the film by the oxidation of the exposed metal. Any area of metal is thus only momentarily active in strong acid; and since active areas are anodal, the electrochemical oxidation there occurring must be recognized as an essential factor in the repassivation process. This process restores the wire to its original state, and in this sense is comparable with the recovery process in living tissues. As the activation wave travels over the surface of the wire there is an alternation of reduction and oxidation at each point reached. The reduction corresponds to the activation, which is automatically transmitted in the manner indicated. The oxidation plays no direct part in the transmission, but is immediately responsible for the return to the passive or resting state, *i.e.,* for the recovery part of the local cycle of processes. In the general nature of the chemical processes constituting the reaction cycle there is here seen a broad correspondence with the conditions in living tissues such as nerve and muscle; in the latter case also the primary process of excitation appears to be independent of oxidations; these, however, are essential to recovery, as is indicated by the importance of free oxygen to this process. It would thus appear that in both the living and the non-living systems the renewal of the chemically reactive surface layer in which the essential process of activation occurs depends on the formation of some oxidation product or products. In the case of passive iron we know experimentally that when this product is rapidly reduced there follows a structural change, disruption of the film, giving rise directly to the local electrical change which forms the primary condition of activation and transmission. Conversely, oxidation restores the film, rendering transmission again possible. The structural, chemical and electromotor changes in the surface layer are interdependent; the law of polar activation, applicable to both systems, thus becomes intelligible. The specific nature of the chemical processes associated with excitation and transmission in living tissues, such as nerve, can be determined only by special investigations on the metabolism of these tissues during rest and activity.

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[11] R. S. Lillie, *J. Gen. Physiol.,* 1925, 7: 473.

[12] Mines, *loc. cit.*

[13] Forbes, Ray and Griffith, *Amer. J. Physiol.,* 1923, 66: 553.