J. Physiol. (1940) 97, 471–488 612.813

ELECTRIC INTERACTION BETWEEN TWO ADJACENT NERVE FIBRES

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(*Received* 1 *August* 1939)

Hodgkin's recent work [1937–9] has substantiated the already strong suspicion that the propagation of the nerve impulse is maintained by the stimulating effect of the action current wave. The idea of an electric mechanism of this kind had been alive since Hermann [1899], but the recent experiments have established the order of magnitude of the effect, and have shown that the normal action current is a powerful electric stimulus capable of exciting resting regions in front of the active centre of the potential wave with a considerable factor of safety. These findings raise the questions of whether, and to what extent, an action potential travelling in one or a number of axons might affect adjacent fibres.

The possibility of such an interaction between separate, active and resting, units is of interest from several aspects. (i) Normally, local currents set up in the vicinity of an active region do not, and obviously must not, excite adjacent fibres. Some mechanism apparently is present by which, not only the further propagation of the impulse in the active fibre, but also its "isolated conduction" is ensured. (ii) A *subthreshold* effect of an action potential on an adjacent fibre must be expected, however, since some part of the local current is bound to penetrate the surrounding tissue.

The object of the present paper was to investigate the electric interaction between separate axons in a simple case, using a nerve preparation which contains two fibres only, and determining quantitatively (i) any excitability changes which might take place in one fibre during the passage of an impulse in the other, and (ii) any mutual interaction between impulses travelling simultaneously in both fibres.

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METHODS

Preparation. Using the technique described by Hodgkin [1938], two adjacent fibres were isolated from the limb nerve of a crab (*Carcinus maenas*). In the proximal part of the limb nerve, inside the meropodite, two or more large non-medullated axons (diameter about 30 μ) are usually found running side by side, so that a pair of fibres held together only by sparse strands of connective tissue can be isolated from the remainder without great difficulty. The nerve was dissected in sea water using a binocular microscope of weak (10 ×) magnification, the two fibres were then separated along part of their length so that either of them could be stimulated independently. The ends of the fibres were gripped in the tips of screw-controlled forceps (ordinary ruling pens with tips slightly bent and coated with electric insulation). The preparation was then stretched across the electrodes (bare platinum hooks, in most cases 150 μ thick), and the whole system gently lifted from the sea water into a layer of aerated paraffin oil by means of a Palmer rack and pinion *X* block.

In this situation, each fibre is electrically shunted by the other fibre, by a little interstitial tissue, and by some sea water. In certain experiments the electric conductivity of the surrounding fluid was further reduced by soaking the preparation previously in a solution in which part of the saline was replaced by isotonic cane-sugar. As a rule, the preparation gave consistent results for several hours, much longer than required for the actual experiments. Temperatures ranged from 19 to 25° C.

Stimulation. The arrangement of stimulating and recording leads is shown in Fig. 1. For quantitative threshold tests a short thyratron

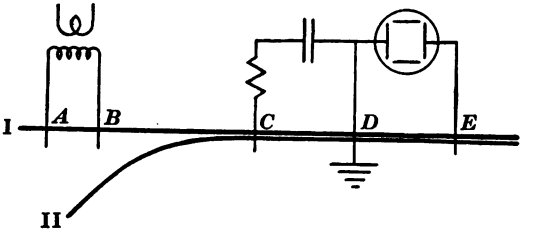

Fig. 1. Electrode arrangement for excitability measurements. I and II, fibres I and II respectively. *A*, *B*, leads for stimulation of fibre I; *C*, *D*, leads for stimulation of fibre II. *D*, *E*, recording leads connecting with amplifier and cathode ray oscillograph.

condenser discharge (time constant *RC* of its subsidence being 30–50 μsec.) was used, for ordinary stimulation a low capacitance transformer was interposed between the thyratron circuit and the nerve.

Two completely independent thyratron stimulator units utilizing thermionic trigger tripping and accelerated recharging were employed. Each of these was independently synchronized electrically with the linear sweep circuit [Schmitt, 1934] so that two stimuli of separately adjustable polarity and strength could be administered at any desired time interval, the strengths of stimuli being unaltered by variations in the time interval between the two shocks or by the frequency of sweep. The time interval between the stimuli was observed directly on the screen of the cathode ray oscilloscope; at any one setting, it was constant within the accuracy of measurement. The rate of stimulation usually employed was 1–2 per sec.

For accurate measurements of thresholds, two *T* pad attenuators were provided in each stimulator unit, one of logarithmic taper, the other linear and fitted with a vernier dial. The logarithmic unit permitted adjustment of the stimulus to the right order of magnitude while the linear control made accurate measurements possible.

Amplifier. The amplifier consisted of three stages of high gain (120, 120, and 500 gain/stage respectively) push-pull, cathode phase inversion, circuit [Schmitt, 1938] preceded by a head amplifier stage, again of the cathode phase inversion type, but in this case arranged as an impedance changer both with respect to input and output. This stage was mounted within a few centimetres of the nerve so that short leads could be used. The input impedance of this unit was equivalent to a capacitance of 3–4 $\mu\mu$F. in parallel with approximately 100 MΩ of resistance. The output impedance of the head amplifier was well below 1000 Ω so that shielded leads could be used between it and the main amplifier without producing appreciable attenuation below 50,000 c./sec.

In most of the experiments where only excitability changes were measured, this head amplifier was not used, as the frequency characteristic of the amplifier in these cases was of no consequence. With the head amplifier the overall voltage amplification was substantially constant to 5000 c./sec. and dropped about 15 % at 10,000 cycles.

Results

I. *Excitability changes in a nerve fibre during the passage of an impulse in an adjacent fibre*

In the case of two adjacent axons mounted in an insulating medium the theoretical effect of an action current in one fibre on the excitability of the other can be stated in simple terms. A diagram of the local circuits, essentially identical with Hermann's well-known scheme, is illustrated in Fig. 2. In the front and the wake of the advancing active

region, the positive current lines which *leave* the inside of the conducting fibre (fibre I) *enter* the adjacent resting axon (fibre II); in the active region itself (i.e. at the points where the membrane of fibre I has become "excited" and its resting potential collapsed) the current *leaves* fibre II and *re-enters* fibre I. At all points where the membrane of fibre II is penetrated by electric currents a change of excitability must be expected, an enhancement at the "cathodal" points where the current leaves fibre II, a depression at the "anodal" points where current enters. The effect therefore will be initiated by a lowering of excitability upon which is subsequently superimposed a rise in excitability and a final depression [Katz & Schmitt, 1939].

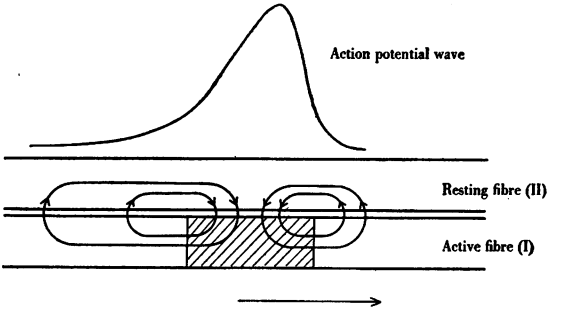

Fig. 2. Local circuit diagram, illustrating the penetration of fibre II by the action currents of fibre I. The shaded area indicates the "active region" of fibre I. Note that the direction of the penetrating current reverses twice.

A more accurate idea of the time course of these expected changes can be obtained by analysing the form of the monophasic action potential of fibre I. It is obvious from Fig. 2 that the external current which penetrates fibre II has essentially the same temporal and spatial distribution as the transverse "membrane current" in fibre I. The latter, however, is proportional to the second derivative d^2P/dx^2 (or d^2P/dt^2) of the monophasic action potential P with regard to distance x (or time t) of its propagation. (This has been shown by Cremer [1929] and others; see e.g. A. V. Hill, 1934; Cole & Curtis 1939.) The function d^2P/dt^2 can be obtained by graphical or by electric differentiation of the monophasic action potential [Schmitt, 1939*a*; see Fig. 5], the first derivative being obtained by placing the lead-off electrodes very close together (about 0·2 mm.), the second derivative by electrically differentiating this first derivative (Fig. 5).

The above expectations were tested in the following way. Fibre I, as illustrated in Fig. 1, was stimulated at AB; at various moments after-

wards, while the impulse approached and passed through the region *CDE*, the threshold of fibre II was tested by a short condenser shock (*RC* 30 to 50 μsec.) applied to *CD*, with cathode at *D*. The time interval between the stimuli was measured from the distance between the shock artefacts on the oscilloscope screen; the threshold index was the appearance of the propagated (diphasic) spike of fibre II.

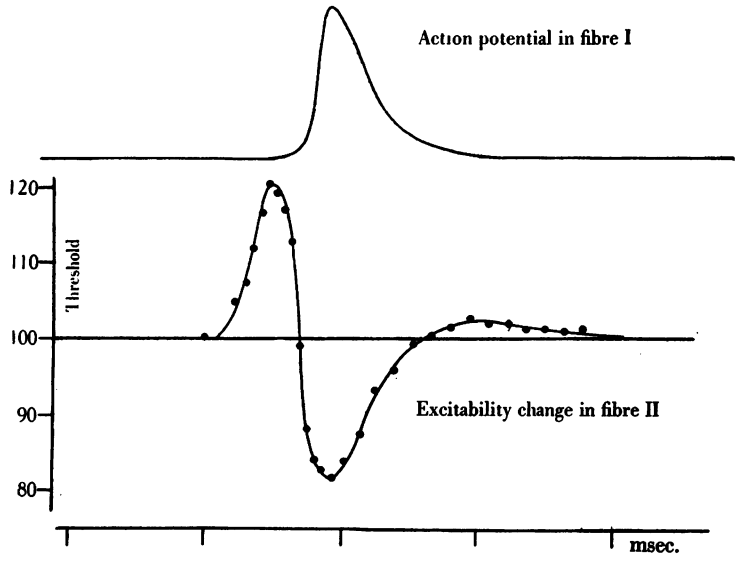

Fig. 3. Excitability changes in fibre II during the passage of an impulse in fibre I (the time course of the latter is illustrated in upper part of figure). Abscissae: time in msec. Ordinates: threshold intensity of fibre II (for a brief shock), in percentage of its "resting threshold".

TABLE I. Peak values (in percentage of "resting threshold") of the three successive phases of excitability change

	1st phase (17 exp.)	2nd phase (17 exp.)	3rd phase (12 exp.)
Mean	117 (110*–122)	89 (82–95)	102 (100–104)

* This exceptionally low value was found in a case in which fibre I was considerably smaller than fibre II.

The observed excitability change consisted of two or three successive phases: a depression at first, suddenly changing into a "supernormal" phase, which was often followed by another period of slightly reduced excitability. A typical result is shown in Fig. 3. The peak values of the three successive phases are given in Table I.

It was found sometimes that this triphasic cycle was followed by another period of slightly raised excitability. This, however, was only observed if, during a period of super-

normal recovery, fibre I became more excitable than fibre II, and so was capable of reducing the threshold of fibre II by its second action potential (see below).

Control experiments. These results, though self-consistent, might be affected by a number of errors. Excitability changes in the resting fibre might conceivably be due, for instance, to a direct effect of the stimulus transmitted by electrotonic currents or through external stray capacities, or to circulation of current through the input leads of the amplifier. Both of these possibilities were eliminated by the fact that neither a reversal of the stimulus, nor a reversal of leads *C* and *E* affected the result. In the former case, there was merely an increase of the conduction interval between the application of shock I, and the arrival of the impulse with accompanying excitability change at *D*. In the latter case, the excitability change remained unaltered, while the action potential was, of course, recorded somewhat sooner (at *CD* instead of *DE*).

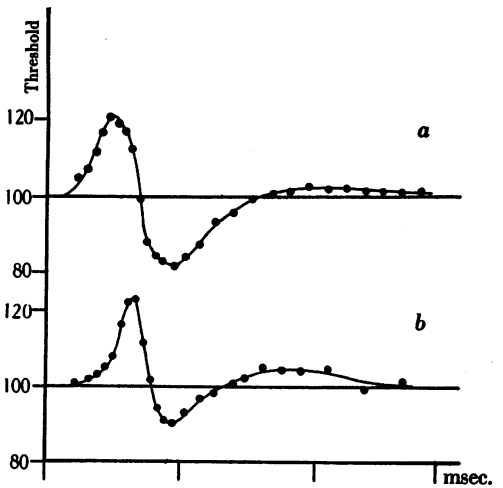

Fig. 4. Effect on the excitability curve of interchanging fibres I and II. Co-ordinates as in Fig. 3. *a*, threshold changes measured in the *more* excitable fibre; *b*, in the *less* excitable fibre. For further explanation see text.

The observed result depends to some extent, however, upon the relative "resting thresholds" of fibres I and II. The preferable arrangement is the one in which fibre II (the "test fibre") has the lower threshold; otherwise one cannot really determine the "base-line" of the excitability curve, viz. the resting excitability undisturbed by action currents in the adjacent fibre. There is strong indication (see also p. 475 above) that, at the point of stimulation, the less excitable axon receives

some encouragement from its active neighbour, and that its apparent resting threshold is really lowered, by a few per cent, by the slightly preceding action potential in the more excitable element. It is easy to appreciate that, with this latter arrangement, the phase of threshold lowering will be apparently reduced in size, since the base line from which the changes are measured is already lowered to some extent; conversely, the phases of increased threshold may be relatively exaggerated. This was verified in several experiments, as illustrated in Fig. 4. As a whole, however, the effect, while changing in details, is not altered essentially by an interchange of fibres I and II.

Time relations between action potential and excitability change. A further observation which requires some comment is the consistent divergence between the durations of the action potential and the accompanying excitability change in the neighbouring fibre. The excitability change precedes, and outlasts, the action potential by about $\frac{1}{2}$ msec.

The longer persistence of the excitability change is, of course, nothing unusual; as in ordinary electric stimulation, the "local excitatory disturbance" subsides only gradually after the stimulating current has ceased. The earlier start of the observed change also conforms to general experience [see e.g. Blair & Erlanger, 1936]. It is known that the response to a threshold shock does not propagate at full speed immediately, but requires about $\frac{1}{2}$ msec. to move away from the point of stimulation. During this interval, a relatively weak anodal shock is capable of preventing propagation. This is exactly what happens in the present case, with the single difference that the anodal shock is provided, not by an external source, but by the wave front of the approaching action potential (see Fig. 2). The strength of the shock applied to fibre II must, therefore, be raised even if the anodal currents, from the action potential of fibre I, arrive $\frac{1}{2}$ msec. later.

Time course and size of the effect. In a general way, the direction and temporal configuration of the observed excitability changes agree with the predictions of the local circuit theory. It is important, however, to inquire whether the quantities are of the right order of magnitude.

The size of the effect depends not only upon the strength of the penetrating current, but also upon the time factor of the nerve fibre (see Hill's excitation theory [1936]). One may assume, using earlier results [Katz, 1937; Hodgkin, 1938], that the time factor k of a large crab fibre is of the order of 0·25 msec., at 20° C. Knowing the approximate configuration of the penetrating current pulse (Fig. 5), it is possible to

reconstruct the approximate time course of the expected excitability change (Hill's "local potential" [1936]).

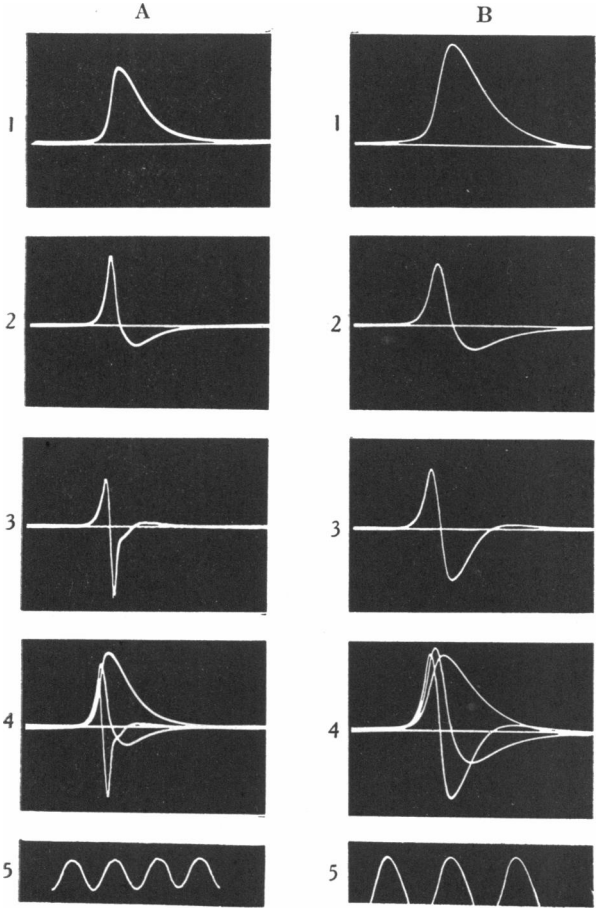

Fig. 5. Time course of "membrane current" obtained by electric differentiation (see p. 474). *A* 1, monophasic action potential, obtained by electric integration of *A* 2 [cf. Schmitt, 1939*b*]. *A* 2, diphasic action potential. Distance between lead-off electrodes 0·12 mm. *A* 3, "membrane current", by electric differentiation of (2). *A* 4, superimposed records of (1)–(3). *B*, a similar series from a different preparation. Inter-electrode distance 0·3 mm. "Imperfect differentiation" in *B* 3, giving a distorted picture of the membrane current which resembles closely the form of the excitability curve (Figs. 3, 6; see also p. 479). Time signals, 2000 per sec. Vertical scale arbitrary. Note that records *A* 3 and *B* 3 resemble curves 1 and 2 of Fig. 6, respectively.

This operation can be done graphically [Rushton, 1937; see Fig. 6], or electrically [cf. Monnier, 1934]. Record *B* 3 in Fig. 5 which was actually obtained by an imperfect electrical

differentiation of the diphasic, differential element of action potential, gives a fair picture of the excitability change, rather than of the membrane current, as this "imperfect" differentiation is substantially the process employed by Monnier and Rushton.

Let us consider two limiting cases: (i) The time factor k is large compared with the duration of the action potential. In this case, the "local potential" is obtained by integrating the membrane current, i.e. its time course is represented by the diphasic action potential, as recorded in Fig. 5. (ii) The time factor is very small; in this case, the "local potential" would follow the tri-phasic changes of the membrane current without appreciable distortion. In practice, some intermediate result must be expected (Figs. 3, 4, 6).

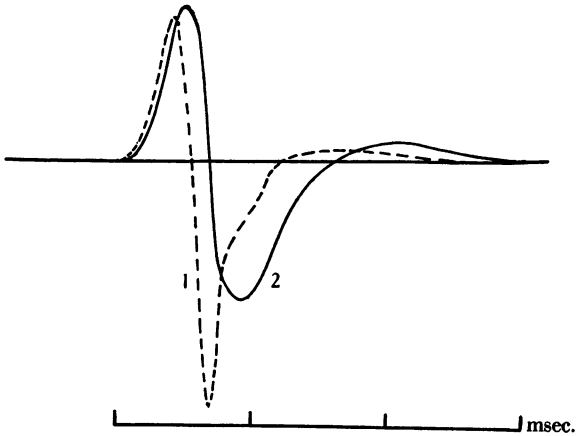

Fig. 6. Excitability change, and stimulating current obtained by graphical analysis. Curve 2 (full line): observed threshold changes. Curve 1 (broken line): time course of stimulating current which, according to Hill's [1936] theory, would produce the observed excitability changes. A time factor k [Hill, 1936] of 0·25 msec. has been assumed. Curve I was derived using Rushton's [1937] graphical method. Note the resemblance between curves 1 and 2, and records $A3$ and $B3$ of Fig. 5, respectively.

The observed excitability curve is very similar to the one reconstructed from the membrane current (Figs. 5, 6); it should be noted, in particular, that the amplitude of the first depression phase is, if anything, greater than that of the period of raised excitability (cf. also Table I), in contrast to the undistorted "membrane current" picture.

To obtain an estimate of the absolute magnitude of the changes to be expected, we must make a number of assumptions regarding the external distribution of the local action currents. From recent measurements by Hodgkin & Rushton (personal communication) it appears that the conductivities, for longitudinal currents, of the "inside" and "outside" of an isolated crustacean axon are about equal. In the case of two fibres, one might expect, therefore, that at least two-thirds of the external action current is taken up by the interstitial fluid and connective tissue while the

remaining third might penetrate the resting fibre. Actually the penetrating fraction would be further reduced by the considerable transverse impedance of the resting membrane [see Cole & Hodgkin, 1939].

Another even more important factor which limits the excitatory effect of the external action currents is the immediate reversal of the membrane current, as soon as it has reached threshold strength in the active fibre [cf. Cole & Curtis, 1939]. This automatic "cut-off" mechanism provides an effective protection of the surrounding elements against any very drastic disturbance.

Taking both factors together, we may assume that rather less than one-third of threshold current enters the resting fibre; assuming further that the excitabilities of both fibres are about equal, this should produce an initial threshold rise of rather less than one-third. The observed values (up to 20 %, see Table I) do not differ very much from this estimate. The subsequent phase of threshold lowering might be of this same order of magnitude but cannot be much larger, as has been pointed out. We can understand, therefore, that even under the present conditions which appear to be ideally suited for electric interaction of fibres, the external stimulating effect of the impulse stays far below threshold, and "isolated conduction" is safeguarded by a good margin.

There seemed some possibility that, by reducing the size of the platinum electrode *D* (Fig. 1) (to 40 μ instead of 150 μ), and by carefully avoiding any accumulation of sea water at the point of contact, the observed effect might become larger, due to removal of the shunt constituted by the width of the electrode and its associated droplet of liquid. This, however, was not the case, presumably because the test shock, in any case, excites at the "inner" edge of the applied metallic, or fluid, contact only. In another attempt to obtain an increased effect, three fibres were used, and the excitability change in one axon measured, while an impulse was travelling in both adjacent fibres. This, again, did not change the result; one could, however, hardly expect it to do so, unless the two action potentials happened to be exactly synchronized.

One should, however, expect a distinct change if the resistance of the outside fluid were raised artificially, and consequently a larger fraction of the action current were forced to penetrate the shunting fibre. This can be verified by soaking the preparation in a mixture of sea water and isotonic cane-sugar before lifting it into oil. In this way an effect was obtained. Replacing half the saline by isotonic sucrose increased the size of the threshold change reversibly, from 22 to 30 %. The effect will be dealt with in more detail in § II below.

II. *Mutual interaction of impulses in adjacent axons*

The previous observations show that, with each pulse of activity travelling in fibre I, an accompanying wave of excitability changes sweeps along the adjacent fibre II. If impulses exist simultaneously in both fibres, one may expect a slowing or speeding to take place depending, at any particular moment, upon the relative phase of the two impulses.

(i) If impulse II lags a little behind impulse I, so that the wave front of II coincides with the active phase of I, then clearly the local membrane currents which leave fibre II are reinforced by the external currents which re-enter fibre I, and the propagation of impulse II will be facilitated. In other words, the stimulating process in fibre II takes place during a period of raised excitability, induced by the action currents of fibre I.

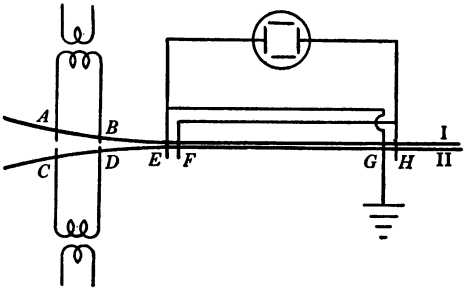

Fig. 7. Electrode arrangement for the measurement of velocity changes. I and II, fibres I and II respectively. *A*, *B* and *C*, *D*, stimulating leads; *E*, *F* and *G*, *H*, two pairs of recording leads. The action potentials of each fibre are recorded before and after the impulses have been travelling beside each other.

(ii) If, however, impulses I and II happen to be accurately in step, then one must expect a mutual interference of the wave-front currents. Stimulation in each fibre would then occur while its excitability is being lowered by the influence of its neighbour and, therefore, propagation would be slowed. One can express it also in the following terms: the action currents of neither fibre can penetrate the adjacent axon because the fibres are mutually equipotential. The only return path available, therefore, is the interstitial tissue; in other words, the synchronous activity of neighbouring fibres acts like an increase in external impedance.

These expectations are borne out by experiment. Two axons were dissected, as before, but mounted in a different way, illustrated in Fig. 7. Fibre I was stimulated through electrodes *AB*, fibre II through *CD*, and

the action potentials were led off from two pairs of electrodes, connected together as shown in Fig. 7. In this way, as pointed out by Schmitt [1939*a*], one can obtain, from a single record, a very accurate measurement of the conduction velocity. In each fibre, a diphasic wave is recorded when the action potential passes the region *EF* and again when passing *GH*. The velocity of the impulse is obtained from the time interval between the two diphasic waves.

The distance *FG* was 12–15 mm. The action potential occupied, at any moment, only about 5 mm. of nerve and required about 3 msec. to travel from *F* to *G*. During this interval, any excitatory disturbance which might have been caused in region *GH* by being connected to leads *EF* would have disappeared. It was considered unnecessary, therefore, to insert any extra resistances in the lead-off circuit.

The interval between the shocks to fibres I and II was adjusted so that the action potentials could be given any desired phase relationship when arriving at the "junction" *E*. With each interval, three different records were superimposed, to facilitate the comparison (see Fig. 8): (i) and (ii), the action potentials of fibres I and II, separately excited, and (iii), the combined potential wave due to simultaneous stimulation.

The results are illustrated in Figs. 8 and 9. It is obvious that the combined action potential recorded at the first pair of leads (*EF*) is simply the sum of the two separate waves without any change in form or position. This was true only if the fibres were kept apart between the stimulating and first pair of recording leads. If the fibres "joined" a few mm. before the leads *EF*, the combined potential wave differed from the sum of the individual waves and showed that an interaction had taken place before the impulses reached the first pair of recording leads.

The second potential pulse, recorded from the points *GH*, reveals the sign and extent of interaction which has occurred while the impulses were propagating beside each other through the intermediate stretch *FG*. The size and direction of this mutual effect depended upon three principal factors: (i) the difference in velocities of impulses I and II, (ii) the phase at the start (i.e. at *EF*), and (iii) the electric conductivity of the interstitial fluid.

The first factor varied from experiment to experiment in an uncontrollable fashion, depending in part upon the relative diameters of the two axons [Erlanger & Gasser, 1937]; the other factors could be varied at will.

Obviously, if the velocities of impulses I and II are widely different, their mutual interaction cannot be very extensive, since the faster action potential will stay side by side with the slower one only for a very short

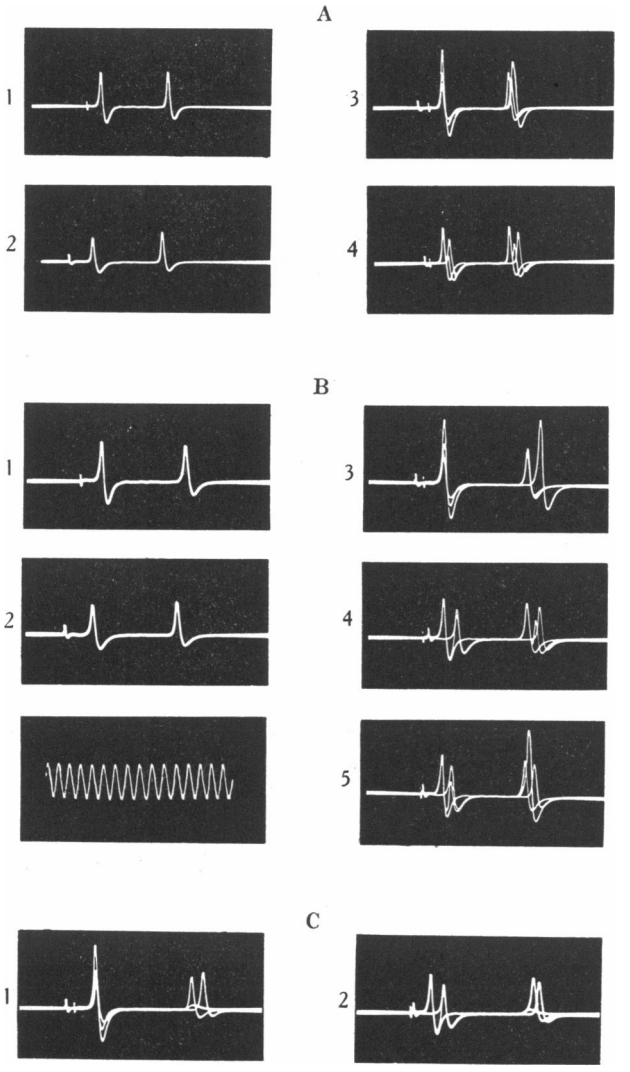

Fig. 8. Mutual interaction of impulses in two separate fibres (see text). *A*, normal preparation. *A* 1, action potential of fibre I, recorded first as it passes electrodes *E*, *F*, then as it passes *G*, *H* (see Fig. 7). The interval between the two spikes is 2·72 msec., the intermediate length of nerve 13·5 mm., the conduction velocity, therefore, 4·95 m./sec. *A* 2, action potential of fibre II. *A* 3 and 4, superimposed records of individual, and combined, action potentials, travelling together in different phase relationships. *A* 3 shows the delay of the combined wave if the impulses are "in step"; *A* 4, the speeding of the later impulse. *B*. Same preparation, in "50 isotonic sucrose/50 sea water". The interaction is more marked; individual conduction is slowed. *C*, same as *B*, but the electrodes *G*, *H* have been moved just beyond a region in which one of the impulses became blocked (only a small monophasic remainder being recorded at *GH*). The combined potential wave at *GH* can be recognized by its larger size. Mutual slowing in *C* 1, speeding of the later impulse in *C* 2. Time signal 2000 per sec.

time and will soon leave it behind. The smaller the velocity difference, the longer will the impulses stay together and, therefore, the better the chances of a thorough interaction.

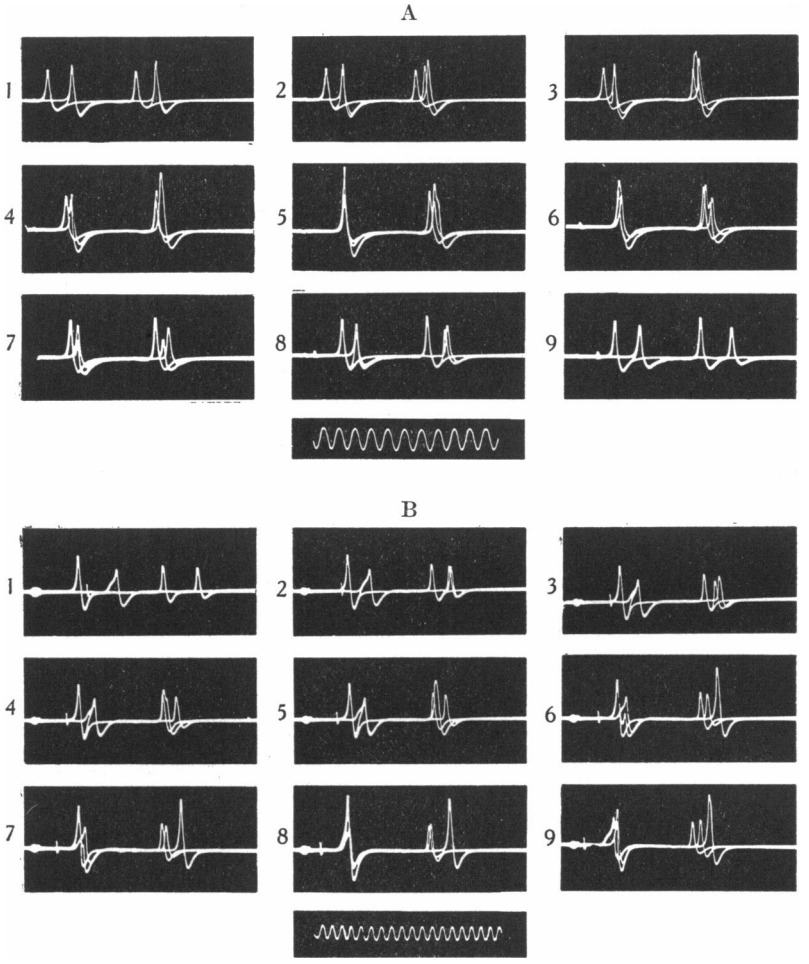

Fig. 9. Interaction of two nerve impulses (see text). *A*, in normal nerve; *B*, with "50 sucrose/50 sea water". Time signals 2000 per sec. *A* 1–9, the phase relationship of the two impulses at the start is varied progressively. Mutual slowing in 4 and 5, speeding of later impulse in 2 and 7. *B* 1–9, "½ sugar" preparation. The effects (especially *B* 8 and *B* 4) are more marked.

In a case, for instance (Fig. 8), in which the velocities of the individual impulses differed by 5 %, the following changes were observed: the quicker impulse, if it was initially behind the slower one, gradually

caught up with the latter. When it had approached it within about ½ msec., it became accelerated until the two impulses had come nearly in step, it then slowed down to less than its initial speed, which it recovered as it proceeded to overtake the slower impulse. However, at this moment, the slower impulse started to speed up a little and in a certain, rather critical, position the velocities of both impulses became equal. From now onwards, the two impulses travelled together at the same speed, and remained in this peculiar, slightly "out-of-phase", position. The quicker impulse acted rather like a pacemaker, dragging along its slower neighbour. As a whole, therefore, if the velocities are only slightly different, the electrical interaction of the two local circuits suffices to make them very nearly, or exactly, equal and to bring about a more or less persistent "synchronization" of the two impulses, though in a characteristic "out-of-step" position.

If the velocities differ by more than about 10 %, the same process of speeding and slowing takes place, but is not sufficient normally to equalize the speeds; sooner or later, therefore, the faster impulse will completely escape from the slower one.

If the individual velocities are equal, the interaction tends to pull the impulses entirely "in step", even if they started somewhat out of phase. The impulse which lags behind is accelerated, catches up, and then a mutual slowing occurs which is most marked in the final, perfectly synchronized, position.

If the two impulses are travelling perfectly "in step", and if the electric conductivities and action potential patterns of both fibres are identical, then the action currents cannot cross from one fibre into the other, but are restricted to the interstitial fluid. This is equivalent to an increase of the resistance on the outside of the nerve fibre which leads to a slowing of the impulse. This effect in single fibres has previously been

TABLE II. Effect of reduced salinity on interaction

Sea water/isotonic cane-sugar	Individual velocity of quicker fibre in m./sec.	Maximum slowing observed during simultaneous conduction in both fibres, %
100/0	5·35	7·7
50/50	3·45	27
33/67	3·05	39
25/75	2·5	45

shown by Hodgkin [1939]. A larger change may be expected if the resistance of the interstitial fluid is raised by the substitution of isotonic cane-sugar solution for part of the sea water. In this case, the adjacent

fibre becomes a more important shunt for the action currents of each axon, and consequently the mutual slowing should be increased. This was verified experimentally (Figs. 8, 9, Table II). The lower the electric conductivity of the interstitial fluid, the more marked was the interaction, in particular the mutual slowing, of two synchronized impulses.

Finally two phenomena may be described which, though observed casually, and under abnormal conditions, are a corollary of the previous results. It was found that an impulse in one fibre was able to help its neighbour across a blocked region if the impulses were set up together and the block was not too strong. Conversely, a fibre which exhibited a hyperexcitable region was started off by the action current in the adjacent axon if it arrived during a supernormal recovery phase.

Discussion

The results described are entirely consistent with the "local circuit theory" of nervous conduction as proposed by Hermann and Cremer, and recently confirmed by Hodgkin and others. The interpretation of the phenomena, in terms of local action currents, entering and leaving adjacent fibres, has been satisfactory, and the good agreement between the predicted and observed effects may be regarded as a further confirmation of Hermann's theory.

The question of stimulating effects of the action currents, and of interaction between separate conducting elements, is almost as old as electro-physiology (one need only refer to the "rheoscopic frog", and to Hering's experiments on the "secondary excitation" of one nerve by another [see Biedermann, 1895]). More recently, Blair & Erlanger [1932] reported that the action potential wave in one part of the dog's phrenic nerve does not appreciably alter the excitability of the other part, while Jasper & Monnier [1938] found that a non-medullated crab nerve, which is on the verge of spontaneous activity, may be stimulated by impulses running in an attached crab nerve. Quantitative observations, however, were not available. The present experiments show that, even under most suitable electrical conditions, the effects of an impulse in one fibre on another non-medullated nerve fibre remain well below threshold (pp. 479–480). To what extent these observations are applicable to the conduction of impulses *in situ*, and to medullated nerve, cannot be said at present. The results described may have some bearing on the phenomena of "synchronization" and "simultaneous firing" of adjacent nerve or muscle fibres, which have not infrequently been described; but it should be remembered that such effects are usually associated with abnormal alterations (e.g.

local hyperexcitability, influence of a nearby injured region; see Adrian [1930], Blair & Erlanger [1932]), which make them less comparable with the present case. The "rheoscopic frog" and Hering's experiments show that under certain conditions a medullated nerve can be excited by the action currents of a muscle or another medullated nerve, but it is equally certain that normally nothing of this kind occurs. Without a sufficient knowledge, in each particular case, of the arrangement of the local circuits, of the distribution of the action currents, and of the excitability of the tissue, it is impossible to make well-founded predictions about either sign or magnitude of the supposed effects. This applies also to the electric theories of synaptic transmission which have been put forward from time to time without, however, much attention having been paid to these factors.

SUMMARY

A preparation consisting of two adjacent fibres was isolated from the limb nerve of the crab *Carcinus maenas*.

During the passage of an impulse in one fibre, subthreshold excitability changes take place in the adjacent fibre. These were measured by applying brief test shocks.

As the potential wave in the active axon approaches, the excitability of the resting fibre is at first reduced, then quickly increased above normal, and finally passes through a second slower period of slight depression. These changes are explained as being due to a penetration of the resting fibre by external action currents from the active fibre, remembering that the direction of these currents, with respect to the nerve membrane, reverses twice and that current lines which leave the active fibre enter the adjacent resting fibre.

When impulses are set up simultaneously in both fibres, a mutual interaction takes place producing various combinations of speeding and slowing, depending upon the phase relationship between the two impulses.

If the impulses are advancing entirely "in step", their local action currents interfere with each other, and the propagation velocity is reduced. If one impulse slightly precedes, it accelerates the conduction rate of the lagging action potential. This effect leads to a "synchronization", and to equalization of speeds of the impulses, if their individual velocities differ only slightly.

The alterations of conduction rate are consistent with the changes of excitability induced by each action potential in the neighbouring fibre, and can be explained by simple summation of the local action currents contributed by the two fibres.

The observed changes can be increased by soaking the axons in isotonic solutions of reduced salinity (sea water/cane-sugar mixtures). In this way, the conductivity of the interstitial fluid is reduced and a larger fraction of the action currents diverted into the adjacent fibre.

The quantities of the observed effects are of an order of magnitude consistent with the electric theory of nervous conduction.

In spite of the powerful stimulating effect of the action potential wave in the conducting fibre itself, the external effects are small, and a large safety margin is provided for the "isolated conduction" of the impulse in each individual fibre. The principal factors by which this mechanism is ensured are discussed.

We are greatly indebted to Prof. A. V. Hill for his kind hospitality and encouragement, and to Mr J. L. Parkinson for his invaluable assistance.

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