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THE RELATION BETWEEN CONDUCTION VELOCITY AND THE ELECTRICAL RESISTANCE OUTSIDE A NERVE FIBRE

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Nervous transmission is generally believed to depend upon an electrical process, but the precise way in which one section of a nerve fibre activates another is still uncertain. According to the membrane theory, restimulation is brought about by the local electric currents which spread in advance of the active region. In the conventional form of the theory the current is assumed to flow in one direction along the core of the fibre and to return through the conducting fluid outside. If this view is correct, the velocity of transmission should vary with the electrical resistance outside a nerve fibre. Thus in Lillie's iron wire model, the velocity of propagation may be altered over a wide range by changing the volume and hence the total conductance of the fluid outside the wire [Lillie, 1924]. The experiments to be described in this paper were undertaken in order to decide whether the rate of propagation in a nerve fibre can be affected in a similar way. Single fibre preparations from crab or squid were employed, and the external resistance was changed by lifting the fibres out of sea water into a layer of aerated paraffin oil, or in the case of the squid fibres into an atmosphere of moist air. In sea water the fibres are shunted by a large volume of conducting fluid, but in oil or air they are surrounded by a thin film of saline, so that the external resistance would be high. This method of changing the external resistance has the advantage that the fibres are always in contact with a layer of sea water, so that their immediate environment remains unchanged throughout the experiment. Hence any changes in velocity produced by this treatment must be entirely due to the alteration in electrical resistance and cannot be attributed to chemical or ionic effects.

Experiments with crab axons

Single fibres were isolated from the limb nerve of *Carcinus maenas* by a method which was described in a previous paper [Hodgkin, 1938]. An account of the stimulating and recording apparatus was also given in this paper, so that they need not be described here. The arrangement for comparing conduction velocity in oil and in sea water is shown in Fig. 1. It consisted of four platinum electrodes (*B–E*), a fine glass hook (*G*) and two holders (*A*, *F*) which were made from fine-tipped forceps. When the dissection was complete, the electrode system was lowered into the sea water and one end of the fibre was gripped by the holder *A*. The other end was then seized with a needle and the intermediate stretch looped above the electrodes and beneath the glass hook.

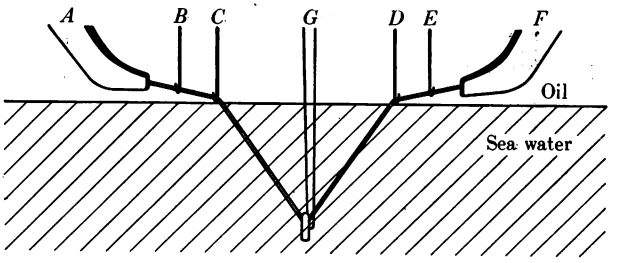

Fig. 1.

Finally, the free end of the fibre was gripped in the second holder *F*, and the glass hook was gently lowered until the fibre was taut. The whole system of holders and electrodes was firmly attached to a movable stage which could be raised or lowered by means of the screw adjustment on a Palmer stand. In order to measure the conduction velocity in sea water, the fibre was raised until the electrodes *C* and *D* were just clear of the interface. At this point both stimulating and recording leads were insulated by oil, but the greater part of the intermediate conduction distance was immersed in sea water. In order to determine the conduction velocity in oil it was only necessary to raise the electrode system until the whole of the fibre had passed through the interface.

The results of a typical experiment are illustrated by Fig. 2. In *A* the intermediate conduction stretch was immersed in sea water and in *B* it was raised into oil. This had a marked effect on the conduction rate, since the velocity was about 30 % greater in *A* than in *B*. The change was completely reversible, for the conduction rate returned to its original value when the fibre was replaced in sea water (*C*).

In order to make certain that the observed changes were not due to alterations in latency, the leads were arranged so that the action potential could be recorded before it entered the sea water as well as after. Measurements of this kind gave an entirely satisfactory result, for they showed that the latency did not change by more than 50 μsec., whereas the total conduction time might alter by as much as 1000 μsec.

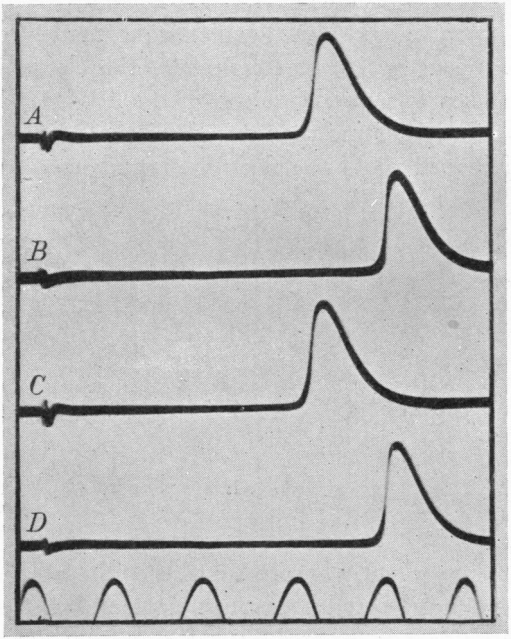

Fig. 2. *A* and *C*, action potential recorded with sea water covering 95 % of intermediate conduction distance, *B* and *D*; fibre completely immersed in oil. Conduction distance 13 mm. Time msec.

By lowering different fractions of the nerve fibre into sea water it was possible to show that the increase in conduction rate must occur to a uniform extent throughout the fibre. Fig. 3 illustrates the result of an experiment of this kind. In *A* the entire conduction distance was surrounded by oil, and in *B* 95 % of it was covered by sea water. In *C* one-third was raised into oil and two-thirds were left in sea water, whereas in *D* two-thirds were in oil and only the central third remained in sea water. Finally, in *E*, the entire conduction distance was again raised into oil. This experiment shows that the decrease in conduction time is roughly proportional to the length of nerve immersed in sea water, as

it should be, if the effect depends upon a uniform increase in conduction velocity.

In some of the records in Fig. 3 the base-line is disturbed by small irregularities which occur between the application of the stimulus and the arrival of the action potential. These disturbances usually occur at the moment when the action potential crosses the oil-sea water interface or passes some other discontinuity on the nerve. They are to be regarded as artifacts and occur because the potential difference between the ends of the nerve fibre undergoes a sudden change at the moment when the action potential enters or

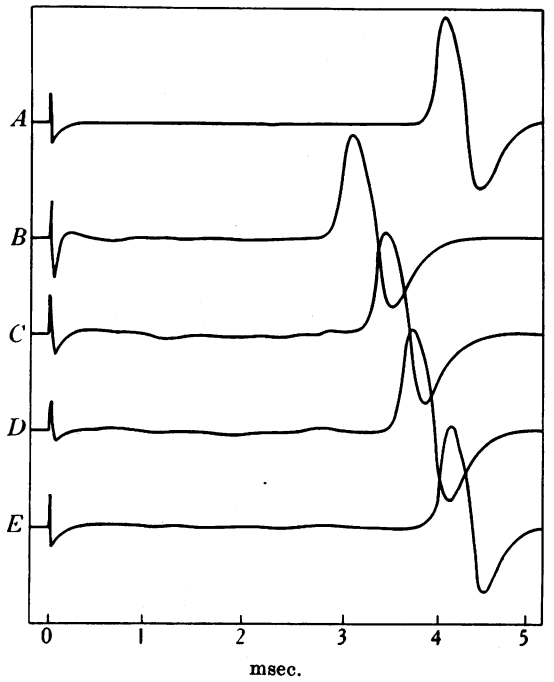

Fig. 3. *A*, *E*, fibre completely immersed in oil. *B*, 95 % of conduction stretch in sea water. *C*, 67 % in sea water. *D*, 33 % in sea water. Conduction distance 13 mm.

leaves the sea water, thus producing a transient flow of current through the stray capacities between the stimulating and recording leads. Artifacts of this kind were not observed in similar experiments with the squid giant fibre, because this has a much lower resistance, so that effects due to stray capacity are relatively unimportant.

The process of transferring a fibre from oil to sea water occupied only a few seconds, so that a large number of observations could be made on one fibre. A series of measurements extending over a period of 30 min. is shown in Fig. 4, and provides a good demonstration of the speed and reversibility of the velocity change.

Table I summarizes the results of the experiments with crab fibres and shows that there is considerable variation in the magnitude of the velocity change. This probably depends upon differences in the amount of connective tissue left on the fibres, since any adherent tissue must lessen the external resistance in oil and so facilitate the propagation of the action potential.

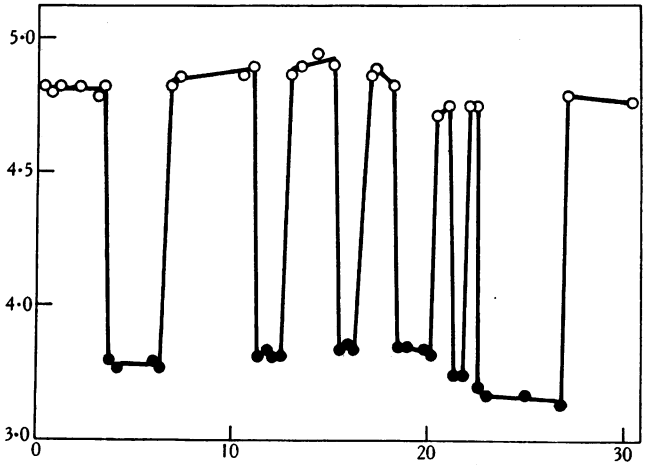

Fig. 4. Abscissa: time in minutes. Ordinate: conduction velocity in m./sec. Hollow circles: velocity in sea water. Full circles: velocity in oil.

TABLE I. Conduction velocities of crab fibres in oil and sea water. The diameter of the axis cylinder of these fibres was about 30 μ. Temperature about 21° C. In certain cases the conduction distance was not measured, so that the absolute values for velocity were unknown, although the percentage increase could be obtained from the conduction times.

Velocity in oil m./sec.	Velocity in sea water m./sec.	Percentage increase
—	—	35
—	—	33
2·8	3·9	40
4·1	5·3	30
3·8	4·9	28
—	—	33
3·4	4·5	33
—	—	25
3·6	4·1	14
3·4	4·0	18
3·5	4·0	15
3·0	3·9	30
2·6	3·1	20
4·4	5·5	26
4·0	5·2	30
3·5	4·5	29

Experiments with the squid giant axon

The giant fibres used in this work were obtained from the hindmost stellar nerve of *Loligo pealii* [Young, 1938] by the method described by Cole & Curtis [1939].

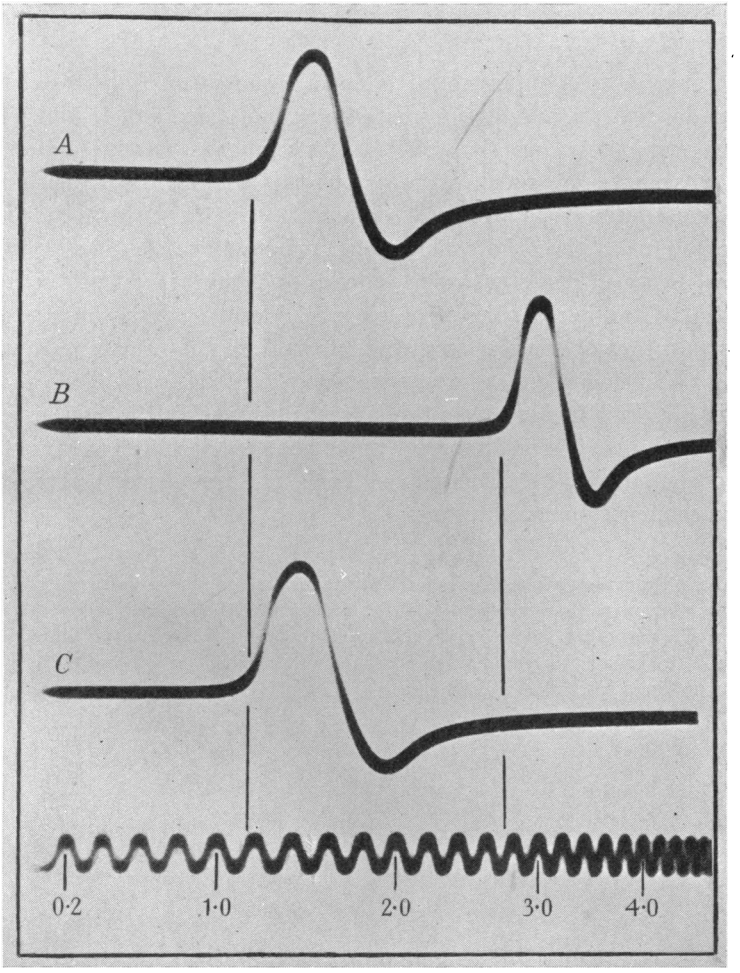

Fig. 5. *A*, *C*, velocity with 95 % of conduction distance in sea water. *B*, whole fibre in moist air. Time base 5000 cycles. The figures give the time in msec. after the shock. Note that the sweep is exponential. Conduction distance 26 mm.

The stimulating and recording apparatus were slightly different from those used in the previous experiments, but need no special description.

The electrode system was similar in principle to that in Fig. 1, except that the leads were sealed into a wax cell and the axon was immersed in sea water by raising the interface instead of by lowering the electrodes. The giant fibre survived quite well in an atmosphere of moist air, so that it was unnecessary to use oil as an insulating medium and the external resistance could be changed by lowering the sea water until the whole fibre was surrounded by air.

The results of a typical experiment are shown in Fig. 5. Record *B* was made with the conduction distance in moist air, and *A* and *C* with the sea water covering about 95 % of its length. In this experiment there was no visible shock artifact, but this was of little consequence, since the stimulus was arranged to coincide exactly with the beginning of the sweep, so that the conduction time could be obtained from the interval between the start of the sweep and the arrival of the action potential. Thus a comparison of records *A* and *C* with the time base shows that the conduction time was 1·15 msec.[1] In *B* it was 2·75 msec., so that the velocity must have been about 140 % greater in sea water than in air. This increase was the largest observed in the present work, but it was by no means abnormal, since changes of 100 % or more have been observed on several occasions. Table II summarizes the results of the experiments on squid axons.

TABLE II. Conduction velocities of squid fibres in air and sea water. The axis cylinders of these fibres were between 480 and 520 μ. in diameter. Temperature, about 20° C. The low velocities in the second experiment probably occurred because this fibre was kept for 11 hr. before being used. One preliminary experiment in which a 60 % increase was obtained has not been included.

Velocity in air m./sec.	Velocity in sea water m./sec.	Percentage increase
11·7	25·0	114
(5·6)	(10·6)	89
9·5	22·6	138
13·8	26·8	97
11·3	25·5	134

These large changes could only be obtained when the axons were very carefully cleaned from all loose connective tissue. A good illustration of this is afforded by an experiment in which measurements were made before the final cleaning of the fibre had

[1] Conduction times were measured between the beginning of the shock and the moment when the action potential rose to 5 % of its maximum.

been completed. Under these conditions the following values were obtained:

Velocity in sea water = 25·4 m./sec.
Velocity in air = 17·7 m./sec.
Increase = 44 %.

The fibre was then replaced in sea water for 3 hr. and as much connective tissue as possible removed from it. When this operation was complete the velocities were again measured and found to be as follows:

Velocity in sea water = 25·0 m./sec.
Velocity in air = 11·7 m./sec.
Increase = 114 %.

This experiment shows that the removal of connective tissue had no appreciable effect on the velocity in sea water, and indeed there is no reason why it should, since the resistance of a large volume of sea water is so low that the velocity would be limited only by the internal resistance of the axis cylinder. However, in air the adherent tissue plays an important part, since it lowers the external resistance and thus allows the action potential to propagate faster than it would in a cleanly dissected fibre. Similar considerations also account for the quantitative difference between crab and squid fibres, since the ratio of adherent material to axis cylinder is greater in crab fibres, so that the velocity change should be smaller than in the squid preparation.

Velocity in nerve trunk

Experiments with whole nerve trunks showed that the velocity of the giant axon *in situ* was approximately equal to the velocity of the same axon in a large volume of sea water. This result seems reasonable, since the resistance of the nerve trunk would be low compared with that of the axis cylinder, so that the electrical conditions would approach those of an isolated axon in sea water.

Similarity in the action of oil and air

In most of the work on squid axons air was used as an insulating medium, but on two occasions oil was used, in order that its action might be compared with that of air. These experiments showed that both media produced approximately the same decrease in velocity, which is a satisfactory result since it indicates that the effect of paraffin oil is solely due to its properties as an insulator.

ALTERATION OF CONDUCTION VELOCITY BY METALLIC CONDUCTORS

A few experiments were made in order to discover whether the conduction velocity could be accelerated by means of a metallic short circuit. This was done by placing a grid of platinum strips between the stimulating and recording leads. These were sealed into the moist chamber and arranged so that they could be connected together by means of a mercury switch (Fig. 6). The fibre was mounted in position, and the

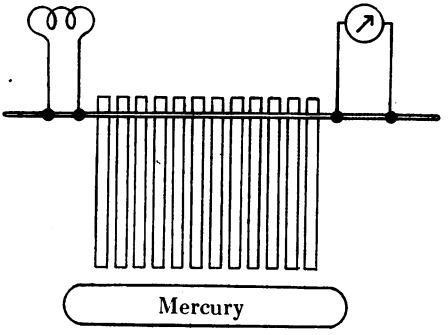

Fig. 6. Diagram of apparatus for short-circuiting giant fibre with metal conductors.

conduction velocity measured with the switch first in one position and then in the other. This method of changing the external resistance has the advantage that the fibre itself remains in a constant environment and the only condition altered is the position of a switch outside the moist chamber. Measurements were made on three axons and in each case the conduction velocity was found to be greater when the metal strips were connected together (Table III). The effect was not large, but

TABLE III. The velocities given are the average velocities between stimulating and recording leads. In the first case, the conduction distance was not measured.

Velocity with strips disconnected	—	14·7 m./sec.	12·5 m./sec.
Velocity with strips connected	—	17·8 m./sec.	14·3 m./sec.
Percentage increase	12	21	14

it was striking to watch on the oscillograph screen, since it took place within the fraction of a second required to move the switch. Table III shows that the change in velocity was much smaller than that observed in the air sea-water experiments. There are two good reasons for this difference. In the first place, the metal bridges are polarizable, so that

they offer an appreciable resistance to the action potential; and in the second place they only connect certain discrete points on one side of the fibre, instead of short-circuiting the entire surface as sea water does.

Metal bridge experiment

One preparation afforded an opportunity for observing a phenomenon which resembled that in the *Nitella* salt bridge experiment [Osterhout & Hill, 1930]. A fibre was left in the electrode chamber at the end of an experiment, and after a little time it was found that a spontaneous block had developed between two of the platinum strips. This was only effective when the strips were disconnected; if they were joined by the mercury contact, the action potential was able to traverse the injured region and so reach the recording leads. This condition did not last long, because the intensity of the block soon deepened to a point where it could no longer be relieved with the short circuit. There is no reason to doubt this effect in spite of its transient nature, for the result is an obvious corollary to the preceding experiments.

Discussion

The results of the present research are very similar to those obtained by Auger [1933, 1936]. Auger measured the velocity of propagation in *Nitella*, and showed that it could be accelerated by covering the *Nitella* cell with a strip of moist filter paper. He considered that the increase in velocity could only be due to the decrease in external resistance, and concluded that his results constituted strong evidence for the local circuit theory. With the exception of this experiment on *Nitella*, all previous attempts to demonstrate a relation between conduction rate and electrical conductance have depended upon altering the chemical composition of the fluid bathing the tissue. Thus Pond [1921] immersed skeletal and cardiac muscle in solutions of low salt content and showed that this treatment led to a reduction in conduction velocity. This experiment is suggestive, but is not completely conclusive, because the observed change in velocity might have been due to an alteration in membrane excitability resulting from the decrease in salt content. This objection can be raised to any method which depends upon altering the constitution of the external medium. It does not apply to the present experiments, because in them the external resistance was changed by altering the volume and not the chemical constitution of the fluid outside the nerve fibre.

SUMMARY

The following experiments show that the speed of propagation depends upon the electrical resistance outside a nerve fibre:

1. The conduction rate of an isolated crab fibre was 14–40 % faster in sea water than in oil. The external resistance was increased by oil, because the fibre was surrounded by only a very thin film of salt solution.

2. The velocity in the giant axons of the squid was 80–140 % faster in sea water than it was in air or oil.

3. A giant axon was laid on a series of metal strips which could be joined by a mercury contact. The velocity was accelerated by 12–21 % when the strips were connected together.

These results strengthen the local circuit theory of nervous transmission.

The work on squid axons was made possible by the kindness of Dr Cole and Dr Curtis who demonstrated the dissection of the giant fibre and allowed me to use their equipment at Wood's Hole. I wish to express my gratitude to them, and at the same time to Dr Gasser for assistance and hospitality in New York.

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