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EVIDENCE FOR SALTATORY CONDUCTION IN PERIPHERAL MYELINATED NERVE FIBRES

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Lillie (1925) suggested that, in myelinated nerve fibres, excitation and the processes which maintain the propagated action potential take place only at the nodes of Ranvier. On this view, the myelin is an insulator, and its function is to increase the conduction velocity by making the local circuits act at a considerable distance ahead of the active region. Much evidence in favour of this theory has accumulated since that date. Thus, many agents which cause stimulation or affect conduction have a stronger action at the nodes than in the internodal regions. This has been shown for electrical stimulation (Kubo, Ono & Toyoda, 1934; Tasaki, 1940), for blocking by electrical polarization (Erlanger & Blair, 1934; Takeuchi & Tasaki, 1942), and for blocking by various ions, ion-free solutions and narcotics (Erlanger & Blair, 1934, 1938; Tasaki, Amikura & Mizushima, 1936). Tasaki & Takeuchi (1941) obtained action currents from a short length of an isolated fibre between two narcotized regions if, and only if, the unnarcotized stretch contained a node of Ranvier. Pfaffmann (1940) obtained larger action potentials from nodes than from internodal regions.

These results all support the theory of saltatory conduction, but there are two respects in which the evidence they provide is not compelling. In the first place, they are consistent also with the hypothesis that only the axis cylinder is concerned with conduction, and that it is shielded by the myelin against external agents at all points except the nodes. In the second place, all except Pfaffmann's results refer only to the initiation or blocking of an impulse, and not directly to normal conduction. If, however, the results are taken together with the evidence that the impulse is propagated by local circuits (e.g. Hodgkin, 1937*a*, *b*, 1939; Tasaki, 1939) they provide strong evidence in favour of saltatory conduction. On the other hand, there are certain difficulties which have prevented the theory from being universally adopted. Thus, Sanders & Whitteridge (1946) conclude that conduction velocity does not depend on the

spacing of the nodes, while a simplified theory of saltatory conduction (Offner, Weinberg & Young, 1940) predicts that the velocity will increase with node spacing. Another difficulty is that, according to many authors (e.g. Maximow & Bloom, 1942; Grundfest, 1947), the myelin sheaths of fibres of the central nervous system are uninterrupted except at points where the fibres branch. If this is true, the saltatory theory cannot apply to central fibres. Bielschowsky (1928), however, insists that many authors have described interruptions in the sheaths of central fibres, and regards their existence as certain. But whichever view may be correct, this point cannot be decisive in a question which concerns peripheral nerve fibres, since it is still possible, though unlikely, that the mechanism of conduction is different in the myelinated fibres of the central and peripheral nervous systems. The other objection is likewise an indirect inference, and cannot stand against direct evidence.

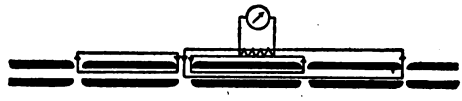

Fig. 1. Diagram illustrating principle of method.

On balance, the evidence seemed to favour the theory of saltatory conduction, but was not sufficiently direct for a certain conclusion to be reached. The object of the main experiment described in this paper (already briefly reported elsewhere, Huxley & Stämpfli, 1948) was to test the theory further by observing the distribution of current around a single fibre during the passage of an impulse. The principle of the method was suggested by Mr A. L. Hodgkin of Cambridge, who pointed out that, if current can enter or leave the axis cylinder only at the nodes of Ranvier, the current along the axis cylinder must be the same at all points in any one internode at any one moment. If a single fibre is used and the recording system passes no appreciable current, the longitudinal current outside the fibre must be equal and opposite to that in the axis cylinder. This external current can be detected by raising the external resistance over a short length of the fibre, and amplifying the potential difference which is developed across this resistance (Fig. 1). If this recording stretch can be made short compared with the length of an internode, the longitudinal current can be observed at different positions in each internode by moving the recording stretch along the fibre. Records from different positions in one internode should then be identical, while records from different internodes should be similar in form but displaced in time.

In addition, a simple experiment giving further evidence that the impulse is transmitted by local circuits is described.

METHOD

Preparation of single nerve fibres. Single myelinated fibres were isolated from the sciatic nerves of large specimens of *Rana temporaria* and *R. esculenta* by the method described by Kato (1934) and modified by one of us (Stämpfli, 1946). A few further modifications were introduced. Thus, dark-ground illumination was employed, making the fibres clearly visible whatever their direction. The oblique illumination from above that was previously used only showed up fibres that ran nearly perpendicularly to the direction of illumination. Also, the motor branch from which the fibre was to be isolated was not separated from the sensory branch with which it runs. This eliminated a difficult step in the preparation, and considerably reduced the time required.

Fibres were usually isolated for about 15 mm. After the dissection the nerve trunk was moved so that the fibre lay straight on the slide, which was placed on an ordinary microscope. The positions of the nodes of Ranvier were determined by means of the mechanical stage, and the external diameter of the fibre was measured with an eyepiece micrometer, using a 4 mm. objective and 20 × eyepiece.

The distance between adjacent nodes was fairly regular in each fibre (within ±20% except for one or two instances), but the mean distance varied from about 1·5 to 3 mm. in different fibres. It appeared not to depend on fibre diameter, which usually lay between 12 and 15 μ., while one fibre had a diameter of 18 μ.

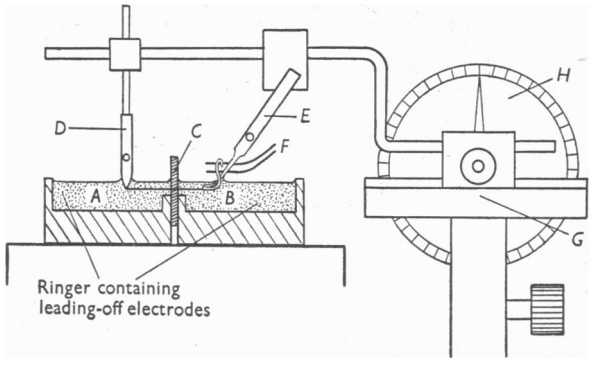

Fig. 2. General arrangement of apparatus. *A* and *B*, troughs cut in 'Perspex' blocks. *C*, partition. *D* and *E*, forceps. *F*, stimulating electrodes. *G*, micromanipulator. *H*, dial.

Apparatus. The general arrangement of the apparatus is shown in Fig. 2. The troughs *A* and *B* were cut in 'Perspex' blocks, and the channel between them was closed by a partition *C*. The fibre lay in the Ringer solution in the two troughs, passing through a hole in the partition. In order to draw the nerve fibre through the hole, a fibre of nylon or silk was pushed through, knotted round the distal end of the nerve fibre, and pulled back. The nylon or silk fibre was gripped in the forceps *D*, and the cut end of a branch of the nerve trunk was gripped in the forceps *E*. The free (central) end of the nerve trunk was lifted out of the Ringer solution and placed in contact with the stimulating electrodes *F*. These were made of silver wire, and were attached to the forceps *E*.

Both pairs of forceps were mounted on a bar carried on the horizontal movement of a micro-manipulator *G*. Thus, by operating the rack and pinion, the fibre could be moved forward or back through the hole. Displacements of the fibre were measured on a dial *H* attached to the pinion shaft. The scale was divided to 0·1 mm., and intermediate values could be estimated to 0·01 mm. The forceps *E* could be moved along the bar by another rack and pinion (not shown) in order to get the fibre just stretched out. Excessive tension damaged the fibre immediately.

Trough *A* was fixed to a base-plate, while trough *B* could be moved by means of a screw. The partition was sealed in place by smearing vaseline on the opposed ends of the blocks, placing the

partition in between with its hole in line with the open ends of the troughs, and bringing the blocks together with the screw.

The partition was designed so that the resistance to current passing between the troughs outside the fibre should be fairly high (0·5–10 megohms), but that the high-resistance part of the path should extend for only 0·4–0·8 mm. along the fibre. The two ways in which this was done are shown in Fig. 3. The earlier type of partition ('oil-gap') is represented by diagram A. It consisted of two coverslips, cemented together along three of their sides with spacing pieces. A hole of diameter between 80 and 400 μ. was drilled through both, and the space between them filled with liquid paraffin. The nerve appeared to move through the holes without being damaged by touching the sides. This type of partition proved to have the following disadvantages:

(*a*) The resistance of the film of Ringer solution outside the fibre was greatly affected by small pieces of connective tissue, etc., adhering to the fibre.

(*b*) The resistance of the film was so high (of the order of 10 megohms) that stray capacities distorted the record. The distortion was prevented by inserting an external shunt, but this must have affected the distribution of current crossing the sheath in the region surrounded by oil.

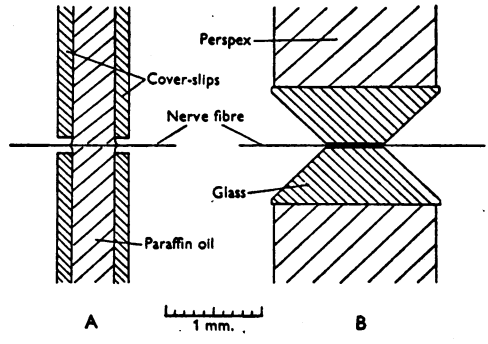

Fig. 3. Partitions. A, oil-gap. B, capillary. Approximately to scale.

(*c*) We tried to confirm the finding of many investigators (e.g. Kato, 1936; Erlanger & Blair, 1938) that conduction is rapidly blocked if the Ringer solution surrounding the fibre is replaced by an isotonic sugar solution, and were surprised that the fibre continued to conduct normally for about half an hour after this treatment. On the other hand, a freshly dissected fibre, which had not been in contact with paraffin oil, was blocked within 1 sec. We concluded that the oil had in some way hindered the diffusion of ions away from the film of fluid surrounding the fibre. If this was so, it was likely that the electrical properties of the fibre would also have been affected.

For these reasons the later experiments were made with partitions of the 'capillary' type shown in diagram B (Fig. 3). A piece of glass capillary tubing was drawn out so that its internal diameter was about 40 μ. Its external diameter was measured, and a hole of the same diameter was drilled through a piece of 'Perspex' sheet 1·7 mm. thick. The capillary was cemented into this hole and cut off flush with each side of the 'Perspex'. The two ends of the capillary were then opened out with a conical drill until only the central 0·5 mm. or so had the original diameter. This type of partition had a resistance of about 0·5 megohm, giving a rather low signal/noise ratio. Capillaries of smaller diameter were tried, but the fibres appeared to be damaged in passing through them.

Electrical recording system. We used the amplifier and cathode-ray oscillograph described by Hodgkin & Huxley (1945). This was built as a direct-coupled balanced amplifier. Since we were concerned only with rapid changes of potential, one of the stages was coupled by resistance and capacity with a time constant of about 0·5 sec. It was also found unnecessary to use it as a balanced instrument, and one of the inputs was connected to earth throughout these experiments.

The input stage was a cathode follower, placed with the grid cap of the valve within 5 cm. of the preparation. Fig. 4A shows the circuit finally employed when the oil-gap partition was in use.

The effects of stray capacities were reduced by the following means. The capacity of the control grid to earth through the screen grid and anode was reduced by connecting the screen grid to the cathode through an h.t. battery of the appropriate voltage. The potential of the screen grid was thus made to follow the changes in potential of the control grid, so that practically no current passed through the capacity between them. The effect of the capacity of the live electrode to the stand and other earthed objects was similarly reduced by connecting the stand, micromanipulator, etc., to the cathode instead of to earth. Finally, the preparation was shunted by a resistance of 2·7 megohms, which brought the time constant down to about 20 μsec. Further reduction of the shunt resistance did not appear to affect the shape of the action-current record.

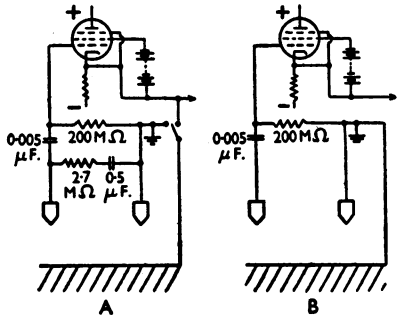

Fig. 4. Input circuits used (A) with oil-gap and (B) with capillary type of partition.

Condensers were inserted in the positions shown to prevent steady currents from passing through the preparation as a result of either the grid current of the valve or the residual potential difference between the electrodes. The grid leak was 200 megohms.

Fig. 4B shows the input circuit used with the capillary partition. The resistance of the preparation was only about 0·5 megohm in this case, so that the stray capacities did not produce serious effects.

The electrodes were pieces of silver sheet, coated electrolytically with silver chloride. The earth electrode was fixed in trough *B*, while the leading-off electrode was fixed in trough *A* (Fig. 2).

The nerve trunk was stimulated by short thyratron discharges at a frequency of about 40 shocks/min. throughout the experiment. The strength of the shocks was adjusted to about twice the threshold for the isolated fibre.

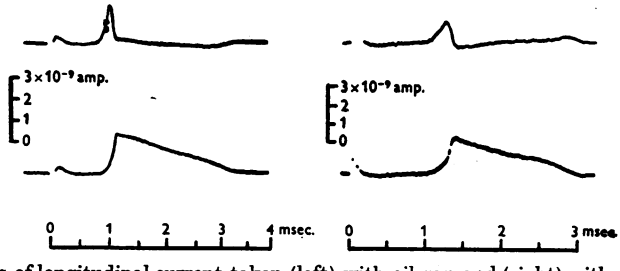

Fig. 5. Records of longitudinal current taken (left) with oil-gap and (right) with capillary type of partition. In each case, upper record taken just proximal to, and lower record just distal to, last working node.

RESULTS

Shape of action-current records. Typical records of the action current at about the middle of an internode are shown in Fig. 5. The left-hand pair of records was obtained with the 'oil-gap', the right-hand with the 'capillary' partition.

The upper record in each case is taken from a point on the fibre which is far enough from the damaged distal end to give a normal action current. The lower records are from points beyond which there is no activity, and the impulse is conducted decrementally for a few millimetres by electrotonic spread. On the theory of saltatory conduction, it would be said that, in the upper records, the node at each side of the recording stretch becomes active, while in the lower records the node of the proximal side of the recording stretch becomes active while that of the distal side does not.

It will be seen that these records are very similar in shape, amplitude and duration to those published by Tasaki & Takeuchi (1941). The upper records correspond to their 'binodal action current' and the lower records to their 'mononodal action current'.

Action currents at various positions in an internode. Fig. 6 shows a series of action-current records taken at different positions along a fibre with the capillary partition. The positions are chosen so that there are three records from each internode, one as near as possible to its proximal end, one near the middle, and one as near as possible to its distal end. There is never a node of Ranvier within the recording stretch.

It will be seen that the three records from any one internode are practically synchronous, while records from different internodes are displaced in time. This is also shown in Fig. 7, where the times of certain features of the first phase of the record, measured from the shock artefact, are plotted against distance. These conduction times increase discontinuously at certain definite positions on the fibre. This was an invariable finding, and the spacing between the discontinuities always agreed with the measured spacing between the nodes. In a number of cases the nodes were located with a microscope while the fibre was in the apparatus and records were being taken. It was then found that the discontinuities occurred when a node was in the recording stretch. We shall assume that this was also the case in the experiments where the nodes were not located visually after the fibre had been mounted in the apparatus.

The velocity of conduction in the isolated part of the fibre is the reciprocal of the mean slope of either of the two lowest graphs in Fig. 7. It is found to be 23·2 m./sec. The detailed analysis described later was carried out on records obtained from this fibre and from three others which gave velocities of 22·2, 24·3 and 23·1 m./sec. These values are normal for frog fibres of 12–15 μ. diameter, at temperatures of 18–20° C. (Erlanger & Gasser, 1937), indicating that the fibres cannot have been seriously damaged by the dissection and other experimental procedures. Most other fibres gave somewhat lower velocities (not less than 12 m./sec.). It is possible that these had been damaged, but in all qualitative respects the results they gave were similar to those described here.

So far, this is what would be expected if current entered or left the axis cylinder only at the nodes. But if that were actually the case, the records would be identical in shape and amplitude, as well as in time, at different positions in one internode. The records in Fig. 6 show that this is not the case. The amplitude

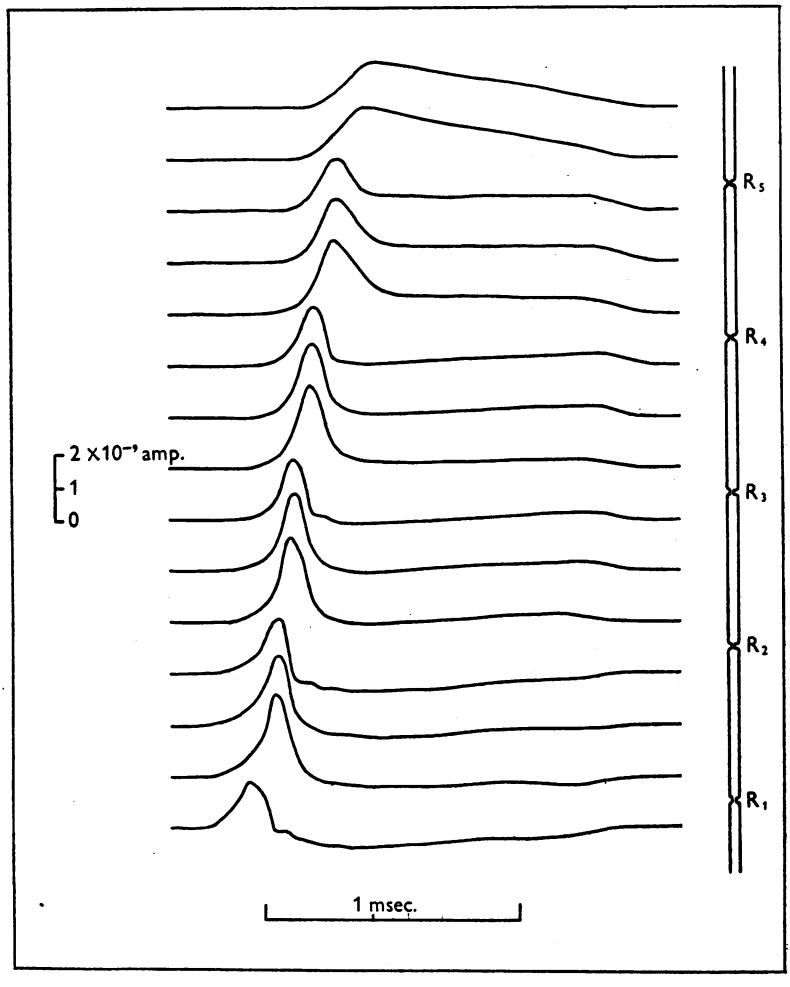

Fig. 6. Tracings of records obtained at a series of positions along one fibre, with capillary partition. Stimulus artefact has been subtracted. Diagram of fibre on right-hand side shows position where each record was taken.

of the first phase decreases from the proximal towards the distal end of each internode. This is better seen in the upper graph of Fig. 7. Also, the shape of the record is different at the different positions. The peak of the first phase is sharpest at the proximal end of each internode, while the angle where the record becomes flat at the end of the first phase is sharpest at the distal end of

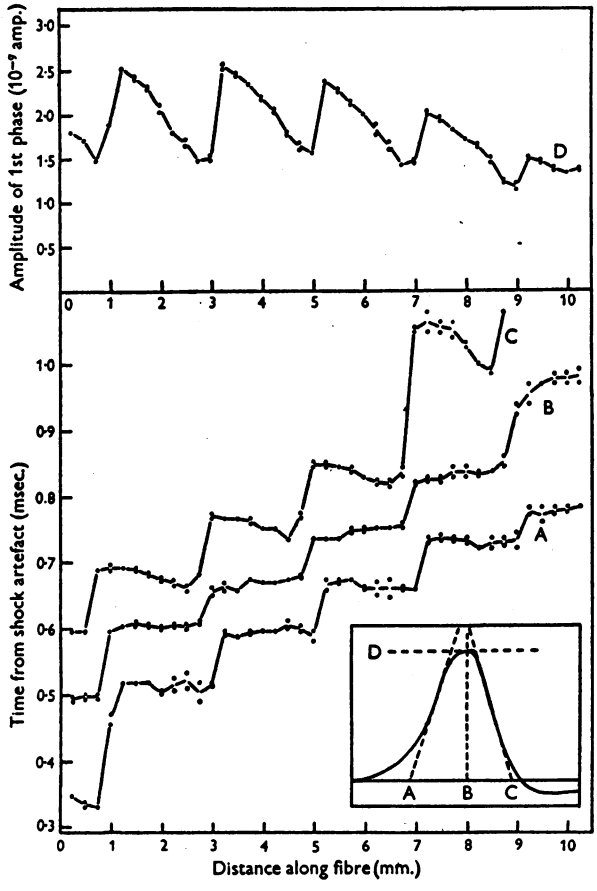

Fig. 7. Lower section: conduction times of (A) upstroke, (B) peak, and (C) downstroke of first phase of record, plotted against distance along fibre. Upper section: amplitude of first phase, plotted against distance along fibre. Inset: diagram of first phase showing how each quantity was measured. From same records as Fig. 6.

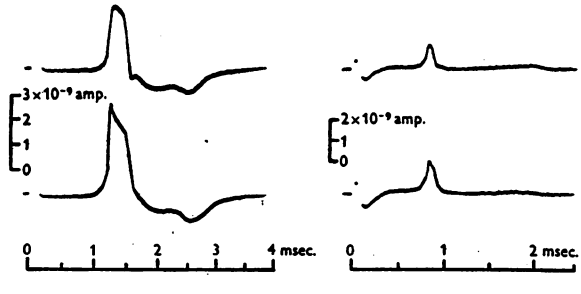

Fig. 8. Longitudinal current at proximal end (lower record) and distal end (upper record) of one internode. Left-hand pair of records obtained with oil-gap, right-hand with capillary type of partition.

the internode. Two pairs of records showing this difference clearly are shown in Fig. 8. These differences between the records obtained at different positions within one internode mean that some current does pass through the myelin sheath. Without further analysis these results are therefore not unequivocal evidence in favour of saltatory conduction. It might be, for instance, that conduction is extremely rapid in each internode, and that a delay occurs at each node because the membrane capacity and conductance are higher there than in the internodes.

The analysis required to clear up this point is carried out in the section entitled 'Determination of membrane current', and shows that the current through the myelin can be explained as a passive current driven through a resistance and a capacity in parallel by the change in potential in the axis cylinder. On this basis the fact that the graphs in Fig. 7 are not horizontal straight lines in each internode can be interpreted as follows. As regards the graph of amplitudes the potential in the axis cylinder is rising and causing current to flow outwards through the electrostatic capacity of the myelin during the first phase of the current record. The longitudinal current is directed forwards in the axis cylinder, so that outward current through the myelin makes the amplitude of the longitudinal current decrease from the proximal to the distal end of each internode.

The graphs of times, with the surprising feature that the descending phase occurs earlier at the distal than at the proximal end of the internode, are best understood by considering the spread of longitudinal current due to the potential change at one node. The rapid rise of potential in the axis cylinder at the node causes, in the axis cylinder of the internode on the distal side, an increase in forward current whose peak is roughly indicated by the peak of the first phase of the record. In the more proximal internode, however, it causes a decrease in the forward current whose peak is given approximately by the end of the first phase, or by the time which is plotted as graph C. Thus, graph C in one internode and graph B in the next more distal internode represent different aspects of the same disturbance spreading symmetrically from the node separating them. This spread takes place with a finite velocity (not necessarily constant), so that graph B becomes later, and graph C earlier, towards the distal end of each internode.

Results when recording stretch contains a node. Consider first the results that would be expected when the recording stretch contains a node, on the hypothesis that current enters and leaves the axis cylinder principally at the nodes. The potential difference across the recording stretch is built up partly by the current in the more proximal of the two internodes separated by this node, and partly by that in the more distal one. As a simplified case we shall first assume that the longitudinal current is the same at all points in one internode at any one moment. The situation is illustrated by Fig. 9.

Let s = length of recording stretch,
y = distance of node from proximal end of recording stretch,
i_a = longitudinal current in axis cylinder of more proximal internode,
i_b = longitudinal current in axis cylinder of more distal internode,
r_1 = resistance per unit length of fluid surrounding fibre,
v = potential on distal side − potential on proximal side.

Then v = potential drop between C and B + potential drop between B and A
$= r_1(s-y)\,i_b + r_1 y i_a$
$= r_1 s\,(i_b + (i_a - i_b)\,y/s)$.

v is therefore a linear function of y, and is equal to $r_1 s i_b$ when $y=0$, and to $r_1 s i_a$ when $y=s$. If the recording stretch is shunted by a resistance, it is easy to show that the same result holds, except that the coefficient $r_1 s$ is replaced by the parallel resistance of $r_1 s$ and the shunt.

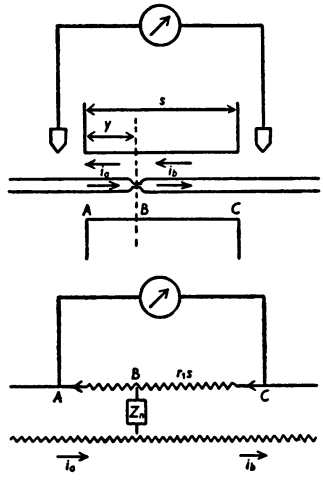

Fig. 9.

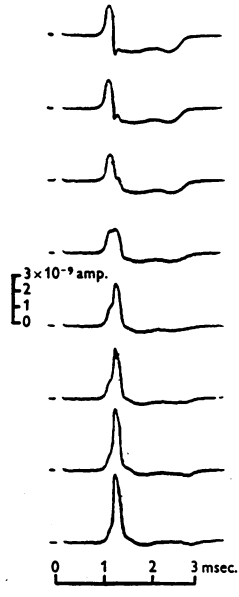

Fig. 10.

Fig. 9. Diagram of situation when recording stretch contains a node. Z_n = impedance of membrane at node. For meaning of other symbols, see text. Proximal end of fibre is to the left.

Fig. 10. Records taken as a node passed through the recording stretch. Fibre moved 0·1 mm. between successive records. Oil-gap type of partition.

This relation cannot be expected to hold exactly in a real case for three reasons. The first is that some current does cross the myelin, so that i_a and i_b are not constants, but depend on distance from the node. The second is that unless r_1 is small compared with the resistance per unit length of the axis cylinder, the values of i_a and i_b at given positions in the fibre will change as the fibre is drawn through the recording stretch. The third is that r_1 may not be the same at all points on the fibre.

The first of these factors is probably unimportant. If i_a and i_b can be sufficiently represented as linear functions of the distance x along the fibre, then the expression for v contains a term in $y(s-y)$ proportional to $(di_a/dx - di_b/dx)$. The values of these differential coefficients can be obtained from records taken in the internodes, and calculation shows that the resulting deviation from linearity of the relation between v and y is negligible.

The second factor probably has an appreciable effect on records taken with the oil-gap, but not on those taken with the capillary, in which the value of r_1 is of the order of $\frac{1}{30}$ of the resistance per unit length of the axis cylinder.

The third factor probably also caused appreciable errors with the oil-gap but not with the capillary. With the oil-gap, the resistance of the external fluid film was affected by local variation in fibre diameter, and, probably more important, by connective tissue fibrils, etc., adhering to the fibre. This factor would be expected to cause irregularities in the relation between observed potential and distance also in the internodes; this is sometimes detectable in records taken with the oil-gap, but not with the capillary.

These sources of error are therefore probably not serious, but may cause deviations from the quantitative predictions of the simple theory when the oil-gap partition is used. We should thus expect that, as the node goes from one side of the recording stretch to the other, the measured potential will change steadily from its value in the proximal to that in the distal internode, but that the change may not be exactly linear, especially in records taken with the oil-gap partition.

Fig. 10 shows a series of records taken at various positions as a node of Ranvier passed through the recording stretch. In order to see whether the transition between the two forms of action potential takes place as predicted,

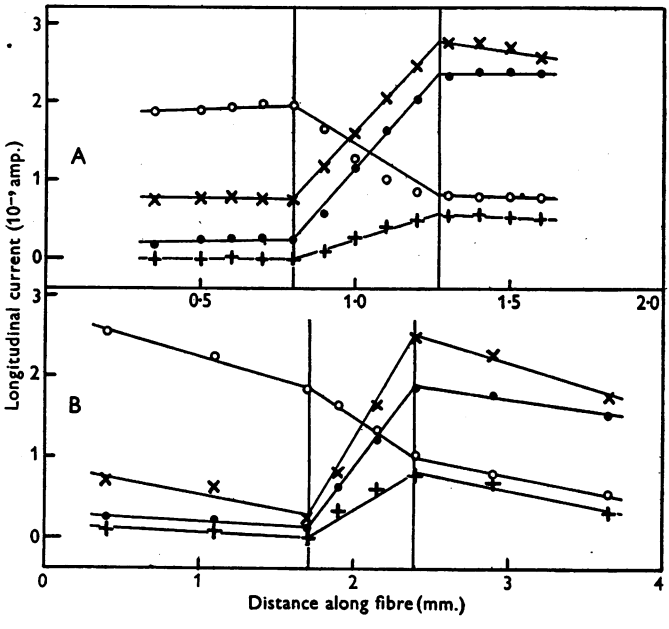

Fig. 11. Longitudinal current plotted against distance along fibre, as a node passes through recording stretch. Each graph corresponds to a constant time after the stimulus. A, oil-gap; B, capillary type of partition. ○—○, near peak of first phase in proximal internode; ×—×, near peak of first phase in distal internode; ●—●, during downstroke of first phase in distal internode; +—+, near end of first phase in distal internode. In A, scale of ordinates is only approximate.

the observed potential is plotted in Fig. 11 against distance along the fibre. Each graph in Fig. 11 corresponds to a particular time after the stimulus. The ordinates are the deflexions at that time in the records taken at varying

positions as the fibre was drawn through the recording stretch. The records from which Fig. 11 A was made were taken with the oil-gap, at intervals of 0·1 mm. The exact length of the recording stretch could not be determined, as the menisci of the oil could not be seen. The positions at which the node enters and leaves the recording stretch are, however, clearly seen on the graphs, and on the simple theory the points in between these should lie on the straight lines joining the ordinates at those positions. Fig. 11 B was constructed from records taken with the capillary partition at intervals of 0·25 mm. The capillary was 0·60 mm. long, but end-effects would be expected to increase its apparent length to about 0·68 mm. The vertical lines in the figure are drawn at this distance apart, and on the simple theory, the points between them should lie on the straight lines which have been drawn, joining the ordinates on the vertical lines. By good fortune, records were obtained when the node was only just outside each end of the recording stretch. It is evident fron the graphs that the potentials at these positions are unaffected by the proximity of the node to the recording stretch.

In both cases the prediction is fulfilled as closely as could be expected from the approximations in the theory and the errors of measurement. This is evidence that the large currents which are shown to enter and leave the axis cylinder in the neighbourhood of the nodes do so within a distance which is short compared with the recording stretch.

Determination of membrane current. The potential recorded by the method described in this paper is proportional to the average, taken over the recording stretch, of the longitudinal current in the axis cylinder. This average is equal to the value of the current at the middle of the stretch if the longitudinal current can be adequately represented, over the stretch, as a linear function of distance along the fibre. This condition is certainly fulfilled so long as the recording stretch does not contain a node of Ranvier. With this proviso, we can therefore say that the observed potential is proportional to the longitudinal current in the axis cylinder at the middle of the recording stretch. If this current is found to be different at two positions on the fibre, at the same moment, then the difference between these currents must have entered the axis cylinder (or left it, as the case may be) in between these positions. We shall refer to this difference as the 'membrane current'.

Thus we can find the current entering or leaving the axis cylinder by taking the difference between the potentials recorded at two nearby positions on the fibre. With our apparatus it was not possible to lead off potentials simultaneously from two stretches of the nerve fibre. We therefore took a record at one position, moved the fibre, and took another record. We then took the difference between the potentials in these two records at the same time after the stimulus. This procedure may have introduced some errors, since the action currents at any one position on the fibre may not have been identical when the two records were taken. In particular, with the oil-gap method, the position of the recording stretch on the fibre probably affected the current distribution. This objection probably does not arise with the capillary method, since the resistance of the fluid

outside the fibre in the recording stretch was small compared with that of the axis cylinder. The results obtained with the two types of partition are very similar, but we shall rely chiefly on the capillary method both because of this objection to the oil-gap method, and because of the other objections mentioned under the heading 'Apparatus'.

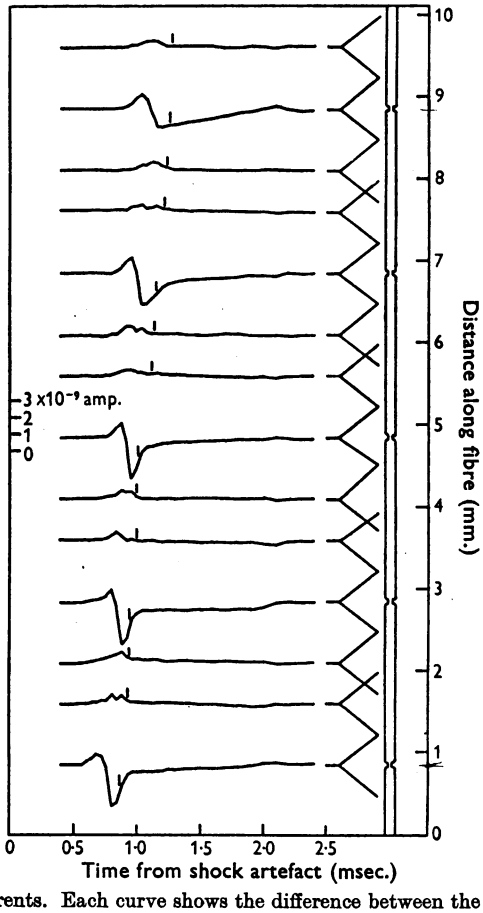

Fig. 12. Membrane currents. Each curve shows the difference between the longitudinal currents at two points 0·75 mm. apart on the fibre. The positions of those two points relative to the nodes is indicated on the diagrammatic fibre on the right. The vertical mark above each graph shows the time when the change in membrane potential reached its peak at that position on the fibre. Outward current is plotted upwards.

Fig. 12 shows a series of results obtained with the capillary partition. It is at once obvious that each graph which refers to a stretch of the fibre containing a node of Ranvier has a large inward component, while the other graphs do not. These curves correspond to the records obtained with tripolar recording by Tasaki & Takeuchi (1941 for nodal, 1942 for internodal stretch), as regards both the principle of the method and the form of the results. With the apparatus used by those authors, however, it was not possible to obtain series of records from different points on the same fibre. Also their recording stretches were

longer than ours, so that a record containing the membrane current at a node contained also the current through the myelin sheath of a greater length of the fibre. This makes the first, outward, current pulse larger, and the second, inward, current pulse smaller and of shorter duration, in Tasaki & Takeuchi's records than in ours. In our records, the nodal stretch includes a length of fibre equal to that from which each internodal record was obtained. The current through the myelin sheath of this stretch must therefore be nearly equal to the mean of the internodal currents observed on either side of the nodal stretch. The current entering or leaving the axis cylinder at the node itself could be obtained by subtracting this mean current from the total current observed in the nodal stretch. This procedure would evidently decrease further the size of the first, outward, pulse of current, and increase the size of the second, inward, pulse, without appreciably altering the times at which they occur.

In order to interpret these curves it is necessary to know approximately the time course of the potential difference between axis cylinder and external fluid at each position where the membrane current is measured.

We did not obtain records of this potential directly, but its form can be obtained by integrating with respect to distance the recorded action current at a constant time after the stimulus. The fluid outside the fibre between the recording stretch and the distal end was practically equipotential, so that

$$\partial V_m/\partial x = r_2 i,$$

where V_m = potential difference across myelin sheath = potential in surrounding fluid − potential in axis cylinder, V_0 = resting value of V_m, x = distance along the fibre, r_2 = resistance per unit length of axis cylinder, and i = observed current = deviation of longitudinal current in axis cylinder from its resting value.

Hence

$$V_m - V_0 = r_2 \int i\,dx.$$

The integration should be taken from a point where no action potential is detectable to the position where the result is required.

This integration was carried out numerically on several sets of records. The conclusions were similar in all cases, but the best results were obtained with the records from which Figs. 6 and 12 are constructed. In this case there was some decremental spread of action current beyond the position where the most distal record was taken, and an allowance for this had to be estimated and added to the result of integration. The main conclusion which is drawn, however, is quite independent of these estimates.

The time at which the potential change across the membrane reached its maximum was read from the curve obtained for each position, and is marked on the corresponding membrane current curve in Fig. 12.

Each of the curves in Fig. 12 taken from a length of the fibre which does not include a node is closely similar to the current which would flow if the calculated membrane potential change were applied to a resistance and capacity in parallel. In the rising phase, the currents through both elements are outward, and add to give the definite outward pulse which is seen in the records. During

the falling phase, however, the current through the capacity is inward, while that through the resistance is still outward. The net current in this phase is therefore small and may be either inward or outward, according to the rate at which the potential falls and the size of the product of the values of the resistance and capacity.

All these 'internodal' records can be explained in this way. In each record from a length of fibre which contains a node, however, there is a large inward pulse of current which begins and indeed reaches its maximum while the internal potential is still rising. This cannot be explained as a passive current being driven through any ordinary circuit element by the change in membrane potential, and must be regarded as current produced 'actively' by the nerve.

Determination of resistance and capacity of myelin. The time course both of the current through the myelin sheath and of the change in the potential difference across it were determined by the methods described in the previous section. The results suggested that the myelin behaves like a membrane with finite conductance and capacitance in parallel. If it is assumed that this interpretation is correct, and, further, that the conductance and capacitance are linear and constant at each point on a fibre, it should be possible to calculate the values of these circuit elements at each position where the current and potential difference curves have been found. This was done at a series of points on each of four fibres. The method used was as follows:

Let i_m = current entering axis cylinder per unit area of myelin,
G_m = conductance of myelin per unit area,
C_m = capacitance of myelin per unit area.
V_m, V_0, and r_2 have the same significance as in the preceding section.

Then
$$i_m = G_m (V_m - V_0) + C_m \frac{\partial V_m}{\partial t}.$$

Integrating this with respect to time,

$$\int_{t_1}^{t_2} i_m dt = G_m \int_{t_1}^{t_2} (V_m - V_0)\, dt + C_m \left[(V_m)_{t_2} - (V_m)_{t_1} \right].$$

To find the conductance, the integration was taken from the beginning of the action potential ('foot') to the time when the potential difference had returned to its initial value ('end'). Then

$$(V_m)_{t_1} = (V_m)_{t_2} \quad \text{and} \quad G_m = \int_{\text{foot}}^{\text{end}} i_m\, dt \Big/ \int_{\text{foot}}^{\text{end}} (V_m - V_0)\, dt.$$

To find the capacitance, the integration was taken from the beginning of the action potential to the time when the potential change was a maximum ('peak'). Then

$$(V_m)_{t_2} - (V_m)_{t_1} = \text{height of action potential},$$

and
$$C_m = \frac{\int_{\text{foot}}^{\text{peak}} i_m\, dt - G_m \int_{\text{foot}}^{\text{peak}} (V_m - V_0)\, dt}{\text{height of action potential}}.$$

The value used for G_m in this equation was that determined at the same position on the fibre.

Membrane currents were obtained by differencing the observed longitudinal current, as described in the previous section. Each value was divided by the area of the myelin from which the current was obtained in order to give i_m, the membrane current per unit area.

The values of $(V_m - V_0)$ and of the height of the action potential were determined by the integration method described in the previous section. The results of this method are proportional to the value taken for r_2, the longitudinal resistance per unit length of the axis cylinder. This was not measured, and the value used was calculated from the dimensions of the axis cylinder, using the specific resistance of Ringer solution. The values of the potential change thus obtained are too small by the factor α by which the specific resistance of the axoplasm exceeds that of Ringer solution. The values of conductance and capacitance must therefore be divided by this unknown factor α. The specific resistance of Ringer solution was taken as 94 ohm-cm. at 18° C., 92 ohm-cm at 19° C. and 90 ohm-cm. at 20° C. These values were based on data kindly provided by Dr B. Katz, of University College, London.

The results of this analysis are given in Table 1, together with other particulars of the data on which it was carried out.

TABLE 1. Results of complete analysis of membrane currents of four fibres. α = (specific resistance of axoplasm)/(specific resistance of Ringer solution, taken as 90 ohm-cm. at 20° C.)

Date of experiment	5. xii. 47	17. xii. 47	4. i. 48	7. i. 48
Type of partition used	Oil-gap	Oil-gap	Capillary	Capillary
Species of frog	*Esculenta*	*Temporaria*	*Esculenta*	*Temporaria*
External diameter of fibre (μ.)	14·5	15·0	14·5	12·0
Thickness of myelin assumed (μ.)	2·0	2·0	2·0	1·5
Temperature (° C.)	18	19	20	20
Conduction velocity (m./sec.)	22·2	24·3	23·1	23·2
Highest action potential (mV.)	106α	93α	79α	109α
Mean capacity of myelin sheath (μF./cm.^{2})	0·0023/α	0·0030/α	0·0035/α	0·0035/α
Dielectric constant of myelin	5·1/α	6·8/α	7·9/α	6·0/α
Resistance of myelin sheath (megohms-cm.^{2}) (reciprocal of mean conductance)	0·082α	0·109α	0·167α	0·158α
Specific resistance of myelin (ohm-cm. $\times 10^8$)	4·2α	5·5α	8·4α	10·5α
No. of positions on fibre where resistance and capacity were measured	5	8	5	6
Standard error of mean capacity (% of mean)	34	10	9	3
Standard error of mean conductance (% of mean)	18	12	12	30

Experiment to test local circuit theory. Two microscope slides were supported end to end on insulating blocks screwed to an earthed base-plate. A single-fibre preparation was chosen in which stimulation of the nerve trunk, proximal to the isolated stretch, caused a visible contraction in the muscle, which was left attached to the nerve. The preparation was laid in a pool of Ringer solution on the slides, so that the muscle lay on one slide and the nerve trunk on the other, with the isolated fibre crossing the junction. The slides were drawn apart, making a gap of 1–2 mm. which was bridged by the isolated fibre. Care was taken that the part of the fibre in the air-gap should not contain a node of Ranvier. The pools of Ringer solution on the two slides could also be connected by laying a thread, moistened with Ringer solution, across the gap. The nerve trunk was stimulated by means of galvanic forceps. It was found that the muscle twitched when the nerve was stimulated if, but only if, the thread connecting the fluids on the two sides of the gap was in place.

The only effect of putting the thread in place was to make an electrical

connexion between the two pools of Ringer solution. Conduction was thus impossible if the longitudinal resistance outside the fibre was above a certain value. This demonstrates that the transmission of the nervous impulse depends on currents flowing outside the myelin sheath, the circuit being presumably completed by the axis cylinder. In non-medullated nerve fibres, whose properties are the same at all points along their length, a change in external resistance affects only the velocity of conduction, and transmission should still be possible however high the external resistance. In a discontinuous system this is not the case. The explanation of this difference of behaviour is as follows.

In a continuous system, the velocity is proportional to $1/(r_1+r_2)^{\frac{1}{2}}$, where r_1 = resistance per unit length of external fluid, and r_2 = resistance per unit length of the axis cylinder. This relation has been derived for certain particular sets of assumptions by Rushton (1937) and by Offner *et al.* (1940), but can also be shown to be a direct consequence of uniform propagation by local circuits, as mentioned by Hodgkin (1947). The time course of the potential change is unaltered, so that its length scale is also proportional to $1/(r_1+r_2)^{\frac{1}{2}}$. The potential gradient is therefore increased in proportion to $(r_1+r_2)^{\frac{1}{2}}$, and the longitudinal current, which is equal to (potential gradient)/(r_1+r_2), is reduced in proportion to $1/(r_1+r_2)^{\frac{1}{2}}$. The length of nerve in front of the active region which has to be depolarized in order to excite it is, however, also reduced in the same ratio, so that the current is sufficient. But in a discontinuous system the membrane (at a node) which has to be depolarized has a fixed capacity and conductance. Its distance from the active node is also fixed, so that the longitudinal current is proportional to $1/(r_1+r_2)$. If r_1 is increased sufficiently, this current will therefore become insufficient to excite.

The experimental result that an increase of external resistance can cause a block might therefore be taken as evidence not only that the impulse is transmitted by local circuits, but also that the system is discontinuous. This point will not be pressed, however, for two reasons. In the first place, it is possible that the part of the fibre which was in air might have been damaged, so that the fibre was made discontinuous by the experimental conditions. In the second place, although a continuous system could in principle conduct in a region where the external resistance was indefinitely high but uniform, it might block at a point where the external resistance drops suddenly from a high to a low value.

DISCUSSION

Evidence for saltatory conduction. The results described in this paper include three more or less independent pieces of evidence in favour of the view that 'activity' takes place only at the nodes of Ranvier.

(*a*) The amplitude and time of occurrence of the main action current wave change discontinuously at each node of Ranvier.

(*b*) The membrane current through the myelin can be explained as a passive current through a resistance and capacity in parallel, but the membrane current at a node of Ranvier has a component which cannot be so explained.

(*c*) Conduction can be blocked by raising the external resistance.

It was pointed out in the 'Results' section that alternative explanations could be produced for observations (*a*) and (*c*). We do not believe that these alternative explanations are correct, but the fact that they exist reduces the value of these pieces of evidence. We shall therefore rely chiefly on the analysis of the distribution of membrane current during the passage of an impulse.

In the region covered by the nerve impulse, the interior of a nerve fibre is more positively charged relative to the exterior than when it is in its normal state. The sheath of the fibre has a finite conductance, so that this charge tends to leak away. For non-decremental conduction, this leakage must be replaced, and the process by which this takes place is called 'activity'. It occurs predominantly in the front of the region carrying the charge, so that the impulse moves forward. If this inward transfer of positive charge could be detected as such, it would be the most direct criterion of activity. But we can only measure the total current entering or leaving the axis cylinder (membrane current), and this contains the currents through the conductance and capacitance of the sheath as well as the current due to 'activity'. If, therefore, we are to locate the regions in a nerve fibre where 'activity' takes place by observing the membrane current, we must first deduce relations in terms of membrane current which are characteristic of 'activity'.

We could evidently say that a region of a nerve fibre does not take part in 'activity' if all the currents in it during an impulse can be explained by the observed potential change acting on known passive conductances and capacities. The resistance and capacity of the myelin sheath have not yet been measured, so that the most that could be said now is that there is no evidence of activity if the currents during an impulse can be explained by the observed potential change acting on plausible values of resistance (not necessarily linear or constant) and capacity. By 'plausible' is meant, for instance, that the capacity should not be so low as to imply an improbable value for the dielectric constant of the myelin.

It would, however, be unsatisfactory to locate 'activity' solely by the failure to satisfy this condition. We shall therefore try to find a characteristic way in which the membrane current of an 'active' region differs from the current to be expected in the absence of activity.

Consider the membrane current to be expected during non-decremental conduction of an impulse in a core conductor whose sheath has resistance and capacity. These passive elements are assumed to be in parallel with each other and with the mechanism which produces the 'active' current; this schematic circuit is not fundamentally different from that which represents 'activity' as a change in the e.m.f. in series with the resistance, but is somewhat more general.

Let x = distance along fibre,

r_1 = longitudinal resistance per unit length of fluid around fibre,

r_2 = longitudinal resistance per unit length of axis cylinder,

i_1 = longitudinal current outside fibre, positive in direction of increasing x,

i_2 = longitudinal current in axis cylinder, positive in direction of increasing x,

V_1 = potential in fluid surrounding fibre,
V_2 = potential in axis cylinder,
G_m = conductance of sheath per unit length,
C_m = capacitance of sheath per unit length,
i_m = current entering axis cylinder per unit length,
V_m = potential difference across sheath $= V_1 - V_2$,
V_0 = resting value of V_m,
u = velocity of conduction, assumed positive so that impulse travels in direction of increasing x.

We shall take first the case of a fibre whose properties are uniform along its length. We assume that during the action potential, $(V_m - V_0)$ is negative and has only one minimum. Then

$$r_1 i_m = -r_1 \partial i_1/\partial x = \partial^2 V_1/\partial x^2 \quad \text{and} \quad r_2 i_m = r_2 \partial i_2/\partial x = -\partial^2 V_2/\partial x^2,$$

so that

$$\partial^2 V_m/\partial x^2 = \partial^2 V_1/\partial x^2 - \partial^2 V_2/\partial x^2 = (r_1 + r_2)\, i_m.$$

During steady conduction, $V_m = f(t - x/u)$, so that

$$\partial^2 V_m/\partial x^2 = 1/u^2 . \partial^2 V_m/\partial t^2 \quad \text{and} \quad i_m = 1/(r_1 + r_2)\, u^2 . \partial^2 V_m/\partial t^2.$$

The membrane current is therefore outward when the graph of V_m against t (the action potential plotted with its peak downwards) has a downward curvature, and inward when it has an upward curvature. The curvature begins downward, but must become upward before the peak of the potential change in order for $\partial V_m/\partial t$ to be zero at the peak. Hence, there must be inward membrane current before the peak of the potential change. During the whole of this phase the currents through the membrane conductance and capacitance are both outward, since both $(V_m - V_0)$ and $\partial V_m/\partial t$ are negative. Hence the inward membrane current must be produced by some 'active' process. This active process must, of course, produce a greater inward current than this, since it is only the excess over the currents through the conductance and capacitance which can be observed as 'membrane current'.

Now consider the more difficult case of a nerve fibre in which activity takes place only at certain small areas of the sheath, which we shall refer to as 'nodes'. We shall assume as before that $(V_m - V_0)$ is negative during the impulse and has only one minimum, and that the time course of the potential change is the same at each position where activity occurs, though occurring later the greater the value of x. The distribution of potential along the fibre will then be roughly as shown in Fig. 13. In each internodal stretch,

$$\partial^2 V_m/\partial x^2 = (r_1 + r_2)\, i_m = (r_1 + r_2)\, \{G_m(V_m - V_0) + C_m \partial V_m/\partial t\},$$

which must be negative throughout the rising phase, so that the curvature of the graph is downward between each two successive nodes.

When the value of V_m at a particular node is at its minimum, and for a finite time before and after, the point on Fig. 13 representing it must lie below the straight line joining the points representing the values of V_m at the neighbouring nodes. Hence $\partial V_m/\partial x$ must be algebraically greater just beyond the node than just before it, and the same is true of i_2, since $i_2 = 1/(r_1+r_2).\partial V_m/\partial x$. The membrane current at the node itself must therefore be inward, by Kirchhoff's first law. Hence, at the points where activity occurs, the membrane current becomes inward before the peak of the potential change at that point, while at all other points this is not the case.

This argument depends on the assumption that the amount of activity is the same at all points where activity occurs. But if, at points between the nodes, a slight degree of activity existed which was insufficient to make the membrane current inward before the peak of the potential change, then the argument and its conclusion would be unchanged. We can therefore conclude that points

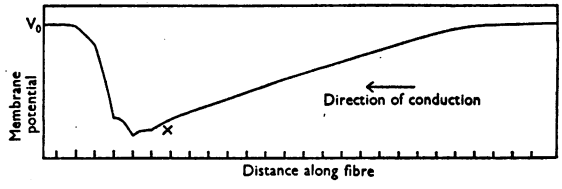

Fig. 13. Diagram showing form of distribution of membrane potential along a nerve fibre with nodes. Positions of nodes marked on horizontal axis. The part of the curve to the left of the point X was obtained by the integration method from actual records of longitudinal current.

must exist where the membrane current becomes inward before the peak of the potential change, and that these are the points where at least the main part of the activity is located. It was shown in the 'Results' section that the membrane current at each node of Ranvier behaved exactly in this way, while that through the myelin sheath did not. We take this as proof that the main part of the 'activity' in these nerve fibres occurs at the nodes of Ranvier.

The question remains whether or not a slight amount of activity occurs in the internodal regions. The 'active current', if any, would be sufficient only to reduce the losses, and not to contribute directly to the current which passes forward in the axis cylinder to depolarize the sheath ahead of the active region. The only criterion we can apply in this case is whether or not the membrane current through the myelin can be explained without postulating activity. As stated in the 'Results' section, the membrane current agrees qualitatively with the current which would flow if the membrane potential change were applied to a resistance and capacity in parallel. The agreement is in fact closer than was indicated at that point. The two peaks frequently seen in the membrane current curves during the rising phase of the potential change correspond to two detectable maxima in the rate of rise of potential, as determined by our

integration method. This agrees with the finding of Tasaki & Takeuchi (1942) that each of these peaks is due to activity at the node at one end of the internode under observation, and not in the internode itself. Also, the small pulse of inward current at the very end of the impulse corresponds to a rapid fall in the calculated potential curves.

Inward current due to activity would make the conductance of the myelin appear lower than its true value. If, as would be expected, the activity occurred chiefly in the rising phase of the potential change, it would also reduce the apparent value of the capacity. It would therefore be evidence of 'activity' in the myelin if the apparent capacity or conductance of the myelin were improbably low for a passive membrane of its thickness. Values of these quantities deduced from our records, and given in Table 1, are uncertain in that they include an unknown factor α, the ratio of the specific resistance of the axoplasm to that of the surrounding medium. The value of this ratio has been determined for axons of certain invertebrates; it is about 1·4 in the giant axon of *Loligo* (Cole & Hodgkin, 1939), 3·0 in *Homarus* axons (Hodgkin & Rushton, 1946) and 4·5 in *Carcinus* axons (Hodgkin, 1947). A value between 1·4 and 1·8 seems likely for the fibres used in our experiments; this would imply that the action potential is about 130–170 mV. in amplitude (Table 1). But even if α is as high as 2·2, and the action potential is about 210 mV. the specific resistance of the myelin is only about 2×10^9 ohm-cm., which does not seem improbably high, and the apparent dielectric constant is about 3. The value found by our method for the capacity, and hence that for the dielectric constant, would be considerably affected if the resistance of the myelin sheath changed during the impulse or were non-linear. If either of these effects existed and were in the same direction as was observed in *Loligo* by Cole & Curtis (1939) and Cole & Baker (1941), it would make the capacity appear smaller than its true value. Thus, our results make it unlikely that the dielectric constant of the myelin was less than 3, which does not seem improbably low. We conclude that the currents through the myelin are adequately explained without postulating an 'active' process there as well as at the nodes.

All our analysis so far has been made on the assumptions that the longitudinal current in the axis cylinder is equal and opposite in direction to that in the fluid outside the myelin, and that the axis cylinder is a uniform ohmic conductor. These are standard assumptions of the membrane theory, but it will be well to see if there is any reason to doubt them, and, if so, whether our analysis is affected.

As regards the first of these assumptions, it is conceivable that some current flows either between a surface membrane of the axis cylinder and the myelin or between the lipoid layers of the myelin itself. If these were merely passive currents, in parallel with either that in the axis cylinder or with that in the external fluid, they would be negligible in magnitude because of the extremely

high resistance of such pathways. On the other hand, such currents might be produced locally by a conduction process taking place entirely within the myelin sheath and axis cylinder. It was in order to test this possibility that we carried out the experiment described in the last part of the 'Results' section. This showed that conduction could be prevented by raising the external resistance. This result agrees with those of Hodgkin (1937 *a*, *b*, 1939) and Tasaki (1939) in indicating that conduction depends on external currents. We conclude that there is no conduction process entirely within the myelin sheath and axis cylinder, and that it is justifiable to assume that the current in the axis cylinder is equal and opposite to that flowing in the external fluid.

As regards the second assumption, the axis cylinder is not uniform since it is markedly constricted at the nodes of Ranvier. The constrictions extend for so short a distance along the fibre, however, that it is justifiable to neglect their effect on resistance. Our analysis might, however, be seriously affected if the axis cylinder is interrupted by transverse membranes across which potential differences can be developed, as suggested by von Muralt (1945). It is difficult to say how this theory would alter our analysis, since it has not yet been given quantitative expression. We are inclined to think that the theory would predict action currents similar qualitatively to those required by the usual theory of a membrane concentric with the axis of the fibre, so that our results do not provide evidence either way concerning the theory.

Node spacing and conduction velocity. Sanders & Whitteridge (1946) found that a large change in node spacing could occur without an appreciable change in conduction velocity. This is generally regarded as evidence against the theory of saltatory conduction. This argument depends on the assumption that a saltatory system will always conduct faster the greater the distance between nodes, as in the simplified case treated by Offner *et al.* (1940). The following examples show that this is by no means necessarily so.

Consider first the case where the conductance and capacitance of the myelin and the conductance of the membrane at a node are negligible. The active node has then to charge the membrane capacity of adjacent nodes through the longitudinal resistances of the axoplasm and the fluid surrounding the fibre.

Let C_n = capacity of membrane at a node,
l = distance between adjacent nodes.
V_m, V_0, r_1, r_2 have the same significance as in the preceding section.

Suppose that as soon as V_m at a node reaches a fixed value V_c it drops instantaneously to a lower value V_a and stays at that value for a time long enough for subsequent changes to have no appreciable effect on the conduction velocity. If, then, the equations and boundary conditions defining the time course of $(V_m - V_0)/(V_a - V_0)$ are expressed in terms of a time variable $T = t/(r_1 + r_2)\, lC_n$, they do not contain r_1, r_2, l or C_n. The interval between the

moments at which successive nodes reach V_c is therefore constant in units of T, whatever values those parameters may have. It will depend only on $(V_a-V_0)/(V_c-V_0)$, so that we can say

$$\Delta T = f\left\{\frac{V_a-V_0}{V_c-V_0}\right\}.$$

Hence
$$\Delta t = (r_1+r_2)\, lC_n f\left\{\frac{V_a-V_0}{V_c-V_0}\right\},$$

and the velocity is

$$l/\Delta t = \frac{1}{(r_1+r_2)\, C_n f\left\{\frac{V_a-V_0}{V_c-V_0}\right\}},$$

which is independent of node spacing.

The simplifications on which this result depends are certainly too drastic both for very short and for very long internodes. In the former case, our assumptions would require the currents to become very large. Real conditions will therefore be represented better if we imagine that the source of potential which charges each node from V_c to V_a has an internal resistance r. The dimensional argument will now apply only so long as $r/(r_1+r_2)\, l$ is constant, and then, for given values of V_c and V_a,

$$\Delta T = \phi\left\{\frac{r}{(r_1+r_2)\, l}\right\}.$$

Clearly an increase in r will delay the charging of the next node, so that $\phi\left\{\frac{r}{(r_1+r_2)\, l}\right\}$ increases as $r/(r_1+r_2)\, l$ increases. The velocity is

$$\frac{l}{\Delta t} = \frac{l}{(r_1+r_2)\, l\, C_n \phi\left\{\frac{r}{(r_1+r_2)\, l}\right\}} = \frac{1}{(r_1+r_2)\, C_n \phi\left\{\frac{r}{(r_1+r_2)\, l}\right\}},$$

which increases with l, approaching for large l the constant value it would have if $r=0$.

When the internodes are long, the distributed capacity of the myelin must become important, and in the limit the capacity of the nodes will be negligible in comparison with it. In that case,

$$1/(r_1+r_2).\partial^2 V_m/\partial x^2 = C_m \partial V_m/\partial t,$$

where C_m = capacity of myelin sheath per unit length of the fibre. If we now define

$$X = x/l \quad \text{and} \quad T = t/(r_1+r_2)\, l^2 C_m,$$

this equation becomes

$$\partial^2 V_m/\partial X^2 = \partial V_m/\partial T,$$

and the boundary conditions do not involve r_1, r_2, l or C_m. Hence the time per internodal distance is constant in units of T, and proportional to $(r_1+r_2)\, l^2 C_m$

in units of t. The conduction velocity is therefore proportional to $1/(r_1+r_2)lC_m$, which actually decreases as node spacing increases. At still greater internodal spacing, the conductance, both of the myelin and of the nodes, may become important, reducing velocity still further and eventually causing a block.

On this set of assumptions, therefore, one would expect that the conduction velocity will have a maximum at a particular node spacing, and that it might be a very flat maximum. Natural selection will probably have made the normal spacing fall near this optimum, so that considerable deviations from the normal spacing would cause only small changes in velocity.

Sanders & Whitteridge compared the velocity in normal fibres with that in fibres with considerably reduced internodal lengths. We should expect the difference in velocity to be least if the normal spacing were somewhat above, and the reduced spacing below, the value which would give maximum velocity. There is, in fact, some evidence to suggest that, at least in frog and toad fibres, the normal spacing is above the value for maximum velocity. Thus, Tasaki & Takeuchi (1941) recorded 'mononodal' action currents from a node both when only one and when both of the neighbouring nodes were narcotized. The records were practically identical, suggesting that the internal resistance of the active node, the factor which makes conduction velocity increase with node spacing, is negligible. Further, our membrane current records (Fig. 12) show that the capacity of the myelin in an internode is greater than the capacity of the nodal membrane, so that the conditions approach those in which it was shown above that velocity is inversely proportional to node spacing.

SUMMARY

1. The longitudinal current which flows in the external fluid when an impulse passes was recorded at various positions along a fibre isolated from the sciatic nerve of *Rana esculenta* or *R. temporaria*.

2. The conduction time of the longitudinal action current was found to be practically constant in each internode, and to increase stepwise as each node of Ranvier was passed.

3. The amplitude of the first phase of the longitudinal current was found to fall steadily from the proximal to the distal end of each internode, and to increase suddenly as each node was passed.

4. The current crossing the myelin sheath during the impulse could be explained as a passive current due to the potential change acting on a resistance and capacity in parallel.

5. At each node, positive current began to enter the axis cylinder before the potential change had reached its maximum. This relation is impossible in a system of resistances and capacities and is shown to be a necessary characteristic of the points which maintain decrementless conduction in a cable-like structure. It is concluded that the process which gives rise to the action

potential takes place at the nodes of Ranvier, confirming the theory of saltatory conduction.

6. Conduction was blocked reversibly by increasing the external resistance between two adjacent nodes. It is concluded that the action potential at each node excites the next node by current flowing forward in the axis cylinder and back in the fluid outside the myelin sheath.

7. The finding of Sanders & Whitteridge that a large decrease in node spacing can occur without a drop in conduction velocity is shown not to conflict with the theory of saltatory conduction.

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