

A PHYSICAL ANALYSIS OF THE RELATION
BETWEEN THRESHOLD AND INTERPOLAR
LENGTH IN THE ELECTRIC EXCITATION
OF MEDULLATED NERVE.

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MANY observations, both ancient and recent, have been made upon the current necessary to excite different lengths of medullated nerve, and there is now unanimity of opinion that, whether the nerve is in air or in fluid, the current necessary to excite is greater the closer together the electrodes. When the interpolar length is greater than about 20 mm. there is no further lowering of threshold however great the distance, and I have verified this statement upon the nerves of the American bull frog, where distances of 100 mm. and more can easily be obtained.

The determination of the relation between threshold and interpolar length of nerve in air is complicated by the fact that change of interpolar length alters the resistance of the stimulating circuit, hence the threshold voltage which is read gives no direct indication of the threshold current. This difficulty has been overcome by Tschirjew [1877], who ligated the nerve between the electrodes and moved the nerve so that the distance from cathode to ligature (= interpolar length) was varied, but the total length of nerve between the electrodes remained constant; by Cardot [1914], who placed in series with the nerve a resistance large enough to swamp that of the nerve; and in the present paper where a galvanometer has been used of sufficient sensitivity to read the threshold current directly.

This difficulty does not arise if the interpolar length is varied by immersing the nerve in a fluid bath through which the current is passing. Marcuse [1877] varied the interpolar length by altering the amount of nerve which dipped into the solution, and the writer [1927] by altering the field in the fluid through shifting the plate electrodes. As was shown graphically in the former paper of the writer [1927, Figs. 2 and 3] all these workers by their different techniques obtained essentially the same relation between threshold and interpolar length.

The explanation of this relation has naturally been that the polar activity at the cathode from which excitation results is in part neutralized by an opposite activity at the anode and that this neutralization occurs

to a greater extent the closer the electrodes. So far the explanation amounts to little more than a restatement of observation, it is when we ask whether the neutralization is chemical or electrical, whether it is propagated from one electrode to the other as a wave, or whether the state develops as instantaneously as the current, that we find divergence of opinion and vagueness of idea.

In a former publication [Rushton, 1927] the writer investigated a concept which is explicit, simple, and which accurately fitted the observations. According to this view a nerve fibre is regarded as having a relatively conducting core surrounded by a very resistant sheath. For definiteness we may regard the axis cylinder as the core and the myelin sheath as the surrounding insulator. Outside the sheath there is interstitial fluid which becomes practically infinite in amount when the nerve is immersed in Ringer's fluid, but which cannot be reduced to negligible proportions by any form of blotting or drying compatible with maintenance of nerve excitability.

Owing to the high resistance of the myelin sheath, it is assumed that the current can flow in the interstitial fluid among the fibres so much more readily than it can penetrate to the axis cylinder, that each nerve fibre will be affected similarly and in each case the flow of current will be radially symmetrical about the axis of the fibre. Since excitation occurs at the cathode, it is assumed to be produced by the current which leaves the core by passing through the sheath at that place.

Now with regard to the relation between threshold and interpolar length, the assumption is of the simplest. It is supposed that the same current has to leave through the sheath at the cathode whatever the interpolar length. When the electrodes approach one another the threshold rises because a smaller fraction of the applied current crosses the sheath at the cathode. In a rough way this can easily be appreciated, for if Fig. 1 represents the resistance plotted against interpolar length (*a*) of the interstitial fluid, (*b*) of the nerve fibre, it is seen that the former is proportional to the length, but the latter resistance is made up of two parts, that due to the double transversal of the sheath (horizontal line) plus the resistance of the core which is proportional to the length. It is thus obvious that for short interpolar lengths (*b*) becomes many times as resistant as (*a*), and consequently only a small fraction of the applied current will enter the nerve at all; the greater part will flow entirely in the interstitial fluid.

But though the above considerations are well enough as a means of getting a rough idea of the variation of current distribution with inter-

polar length, it would be quite misleading to apply this concept (as unfortunately has been done not infrequently) as a quantitative basis for investigation.

For the current does not enter and leave through the sheath merely at the points under the two electrodes, but in some degree over quite a length of the nerve. The reason for this can be seen very easily, for, if the current all crossed the sheath at one point, the current density here would be infinite and hence the potential drop across the sheath would

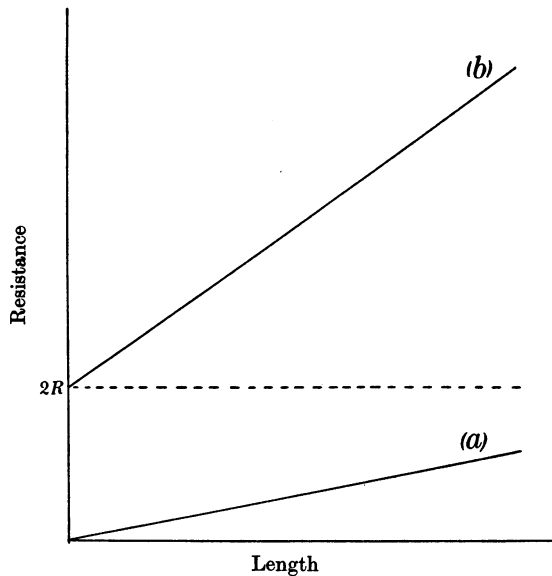


Fig. 1. Schematic representation of resistance as a function of length of nerve. *a*, resistance of interstitial fluid; *b*, of nerve fibre.

also be infinite; whereas this drop can only be a fraction of the applied potential. Again, since both in the interstitial fluid and in the core the potential does not vary suddenly from point to point, the potential difference across the sheath will not vary suddenly, and hence the density of current crossing the sheath will fall off but gradually from the maximum value under the electrodes to zero at the points midway between them and far away in the extrapolar regions.

It thus appears that a quantitative study demands somewhat closer attention to the distribution of current in the nerve than is possible from intuitive consideration, and in the former publication this was supplied by a mathematical treatment, which, though correct, was clumsy and

unnecessarily forbidding. As a result of this treatment a theoretical relation was obtained between threshold and interpolar length, which fitted the observations excellently, as is seen from Fig. 2 of the former paper [Rushton, 1927] which gives the experimental results and the theoretical curve. From these results it follows that the rise of threshold with shorter interpolar lengths can be quantitatively explained as the result of the smaller fraction of the applied current which actually crosses the sheath at the cathode in these circumstances.

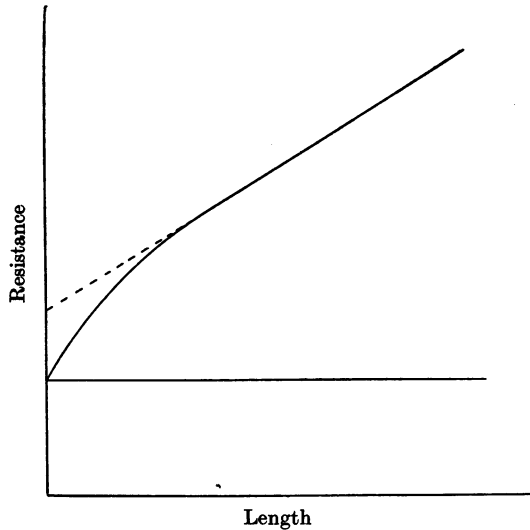


Fig. 2. Diagrammatic relation between resistance of nerve and interpolar length.

Now before any theoretical curve can be compared with experiment, suitable values have to be assigned to the theoretical constants. In the present case the resistances of the various parts of the nerve enter into the equation as a single constant

$$\lambda = \sqrt{\frac{\text{resistance of sheath} \times \text{mm.}}{\text{resistance of core/mm.}}}$$

This constant λ was called "the analytical unit of length" and was found to have a value of about 5 mm. But since λ is a definite physical constant, it should be possible to measure it by purely physical means, so that if it turns out to have a value not of 5 mm. but of 500 or 0.05 mm. it is clear that the theory of current distribution is quite inadequate to explain the strength-length relation, for the coincidence between theory and observation would vanish utterly upon correct scaling. If on the contrary λ was found physically to have the value required to fit the

excitability curves, then the above explanation of the strength-length relation becomes no longer theory but fact.

Unfortunately λ is not at all easy to measure, and I have only recently found a method which will yield results. The principle of this method is as follows.

If the resistance of a nerve is found for different interpolar lengths it is not proportional to the length as (*a*) Fig. 1, nor is it linear as at (*b*). It has in fact the shape shown in Fig. 2. For great lengths it is straight, but for shorter lengths the slope of the curve becomes steeper and steeper. It cuts the vertical axis at a point representing the resistance of the electrodes, circuit, etc. This shape of the curve is to be expected from the assumption already made as to current distribution, for with short lengths the current is mainly in the interstitial fluid, but with great lengths the axis cylinders also contribute to the conduction. Hence the greater the length, the greater the contribution of the cores, the less the resistance of nerve per length, and hence the lower the gradient of the curve.

Now by analysis of this curve it is possible to derive the three resistances which the theory involves—that of the core, the sheath and the interstitial fluid—and hence to determine λ by purely physical measurements.

The objects of the present investigation were therefore to make upon one preparation in comparable conditions the following observations:

- (*a*) The relation between threshold and interpolar length when the nerve is in Ringer's fluid.
- (*b*) This relation when the nerve is in air.
- (*c*) The relation between resistance and interpolar length in air.

These three relations should each fit the appropriate theoretical curve and the constants should all be deducible from (*c*).

Resistance measurements of different lengths of nerve have been made by many workers, but I know of none in which the current was comparable to that used to give rise to a single impulse.

When a constant current has been used and the steady galvanometer deflection read as in the investigation of Rosenberg and Schnauder [1923], the polarization resistance measured may be very different from that existing during the first few milliseconds when alone the constant current possesses stimulating efficacy. When alternating currents are used as in the work of Lullies [1930] a similar current has to be used for the corresponding excitation measurements. This has the disadvantage that with symmetrical electrodes there is danger of obtaining the threshold from the movable electrode, thereby complicating the results by introducing the local variation of threshold from point to point along the nerve. There is also the question of the rapid "inhibition" which a nerve

exhibits on repeated stimulation [Bugnard, 1934], which, though of the greatest interest, obviously complicates the problem.

It is interesting, however, to note that the relation between resistance and interpolar length obtained by both these methods is of the same form as that to be described in the present paper.

METHOD.

The technical difficulties of the present problem fall under two heads, (a) electrical sensitivity, (b) satisfactory electrodes.

(a) The "resistance" of the nerve which is to be measured will not be entirely ohmic, but will be largely made up of a back E.M.F. due to the polarizing action of the current. The resistance will thus be largely dependent upon the duration and form of the current used to measure it. Consequently, if we wish to measure the resistance responsible for current distribution during stimulation, it is essential to employ a current of the same form and duration as that used to stimulate. For reasons mentioned later, this current was a rectangular pulse (*i.e.* brief constant current) of 0.8 millisecc. duration. Now the threshold current for large interpolar lengths was about 2 microamperes, hence the quantity of charge passing through the electrodes was less than 2×10^{-9} coulomb. It was therefore necessary to employ an electrical system of sufficient sensitivity to deal with such a small quantity.

I was fortunate enough to be allowed the use of one of Prof. A. V. Hill's Downing moving magnet galvanometers. The instrument had an internal resistance of 12,000 ohms and a sensitivity of 2.8×10^{10} mm. per coulomb at 2 m. scale distance. I found the galvanometer ready set up and so reliable that though quite inexperienced I never had the slightest trouble with it.

Now when a current is passed through a nerve a polarization is produced which discharges again immediately the current ceases. It was important that this discharge should not enter the galvanometer, since in that case the deflection would be compounded of charge and discharge in a confusing manner. For this reason rectangular pulses were used in which the break of the circuit simultaneously stopped the excitation and cut off one galvanometer terminal from the tissue. The resistance of the circuit was thus found by passing the current pulse from a known constant voltage through nerve and galvanometer in series. The resistance of the circuit was taken as the ratio voltage : current through the galvanometer.

Now for sensitivity it is important that the nerve should be the principal resistance in the circuit: hence the presence of 12,000 ohms internal resistance of the galvanometer was undesirable. But, worse,

this resistance is highly inductive, hence its value will appear greater when the resistance of the rest of the circuit becomes less (*i.e.* short distance between the electrodes).

Both these objections were overcome by placing a large capacity of $10\ \mu\text{F}$ across the terminals of the galvanometer. This in effect completely short-circuited the galvanometer during the brief passage of the stimulus, thereby abolishing both its resistance and inductance, but the

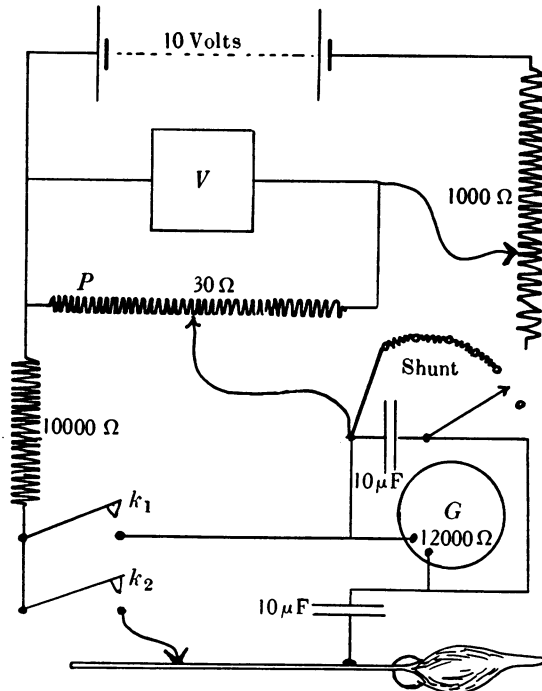


Fig. 3. Circuit diagram. *V*, voltmeter; *P*, potentiometer; *G*, sensitive galvanometer; k_1 , k_2 , keys of Lucas pendulum.

whole current stored in the condenser was discharged through the galvanometer within the subsequent fraction of a second. The circuit constructed on the above lines is shown in Fig. 3.

The voltage drawn from an accurately divided potentiometer of $30\ \Omega$ resistance was known from the reading of the voltmeter across the terminals. The duration of current flow was controlled by the keys k_1 , k_2 of a Lucas pendulum. $10,000$ ohms in the circuit rendered the resistance of k_1 negligible. $10\ \mu\text{F}$ capacity across the galvanometer terminals had the advantages mentioned above, and a similar series capacity both

protected the instrument in case of k_2 accidentally being closed before k_1 , and abolished the steady deflection which would have been present owing to imperfections in the contact of k_1 , nerve injury potential, etc. The galvanometer shunt was a useful protection, but never employed during the actual measurements treated in this paper.

(b) The question of satisfactory electrodes has been the main difficulty in this investigation, and though the results have been fairly consistent the question cannot be said to be satisfactorily answered.

The first essential is that electrodes should be really non-polarizable. Otherwise there are two objections; in the first place there arises in series with the nerve an effective resistance whose value varies with the resistance of the rest of the circuit in a manner difficult to assess, and in the second, there follows stimulation a fast "creep" due to changes

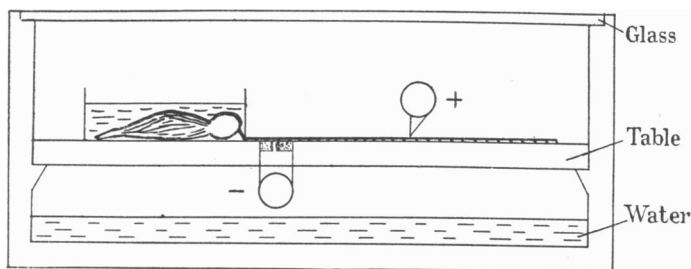


Fig. 4. Stimulating chamber. Electrode tubes from calomel half-cells seen end-on as circles.

at the electrodes, which makes any accuracy of galvanometer reading impossible. Ag-AgCl electrodes prepared and used with all precaution proved much too polarizable to be serviceable. On the other hand calomel half-cells were entirely satisfactory from this point of view. They had the disadvantage of being of high resistance and difficult to apply accurately to the nerve. They were connected to wide tubes filled with Ringer's fluid and plugged with agar-Ringer.

The gastrocnemius-sciatic preparation of the frog (Hungarian *Rana esculenta*) was set up as shown (Fig. 4).

The muscle was placed in a little detachable box, with a slot to allow the nerve to leave. This exit point was sealed with gelatine-Ringer and made watertight. The nerve was blotted free of most of the adherent superficial moisture and arranged on the table of the trough lying stretched parallel to its axis. Ringer's fluid was poured into the detachable box to cover the muscle. The fixed cathode was applied to the

nerve as follows. A circular hole in the table received the upward-bent extremity of the electrode tube. A piece of blotting card with plane normal to the position of the nerve was inserted through the hole, sealed to the tube with agar-Ringer, and left projecting just above the plane of the table top. The agar did not completely fill the hole, and over all was poured a little molten paraffin wax. When this was set, it was shaved off flush with the table top revealing the moistened blotting card tightly set in insulating medium, the whole being a level surface upon which the nerve could be placed. The nerve therefore made a "point" contact with the edge of the card where it lay across it. The resistance of the electrode here was high, but immediately below the thin layer of wax the current entered the wide-bored tube. This electrode was satisfactory. The movable anode was applied to the nerve from above by a prismatic block of agar-Ringer, sealed into the electrode tube and strengthened and made rigid by blotting card and sealing wax. The prism edge slid easily over the nerve without dragging it, though to ensure good contact the nerve was pressed upon somewhat. Even so it is difficult to be satisfied that the resistance at the point of contact was always the same, and to avoid the possibility of some instrumental variation being added to the variation of resistance with interpolar length, which is to be measured. The most serious defect, however, was connected with surface tension; for there was some tendency for moisture to collect about the electrode and be conveyed along the nerve when this was moved.

These errors are not very gross, but the actual quantitative values should be accepted with diffidence.

It was of prime importance that the stretch of nerve investigated should be unbranched and uniform. This condition was satisfied more or less by the sciatic nerve of large Hungarian frogs in which 25 mm. could be obtained between the knee and the large branch to the adductor muscles, though there was commonly one very fine branch given off from this stretch.

The actual course of an experiment was as follows. The nerve was dissected out, set up as described and left for some hours to reach hygrometric equilibrium.

The galvanometer deflections were found for various interpolar lengths when a rectangular pulse of constant voltage was applied which always was either subthreshold or just above threshold for great lengths (the resistance appeared uninfluenced by the presence of a nervous impulse). The deflections were calibrated by substituting known instru-

mental resistances for the nerve and its electrodes. The threshold voltages were then found for the same interpolar lengths. The measurements were repeated and varied in certain ways to be described.

Sometimes the threshold current and not voltage was read, sometimes resistance measurements were taken with voltages which were made just subthreshold for each electrode position, instead of being kept constant. None of these changes seemed to have any effect upon the result. The system appeared to obey Ohm's Law and the procedure first described was found most convenient.

RESULTS OF RESISTANCE MEASUREMENTS.

From the foregoing section we have seen that two quite distinct observations were determined upon the same preparation in precisely the same conditions:

- (a) The relation between resistance and interpolar length.
- (b) The relation between excitability and interpolar length.

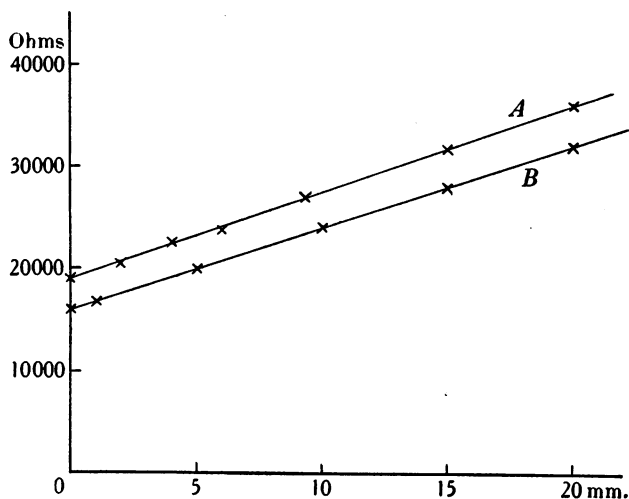


Fig. 5. Relation between resistance and interpolar length of: *A*, rod of agar-Ringer; *B*, uniform strip of Ringer-moistened filter paper.

(a) is a purely physical measurement having nothing to do with excitable structures. It may be made upon a uniform rod of agar-Ringer in place of nerve, the results in this case being shown in Fig. 5*A* or a uniform strip of Ringer-moistened filter paper (Fig. 5*B*). (b), on the contrary, depends upon the excitable properties of living nerve.

Now if we consider Fig. 5 it is clear that the resistance at zero interpolar length is that due to the electrodes and contact with the surface of the rod. Assuming this to be the same for all interpolar lengths the resistance of the rod is given by the height of ordinate above this zero value, *i.e.* the excess of total resistance over the electrode resistance. This is exactly proportional to the interpolar length as was to be expected in the case of a homogeneous conductor like the agar rod.

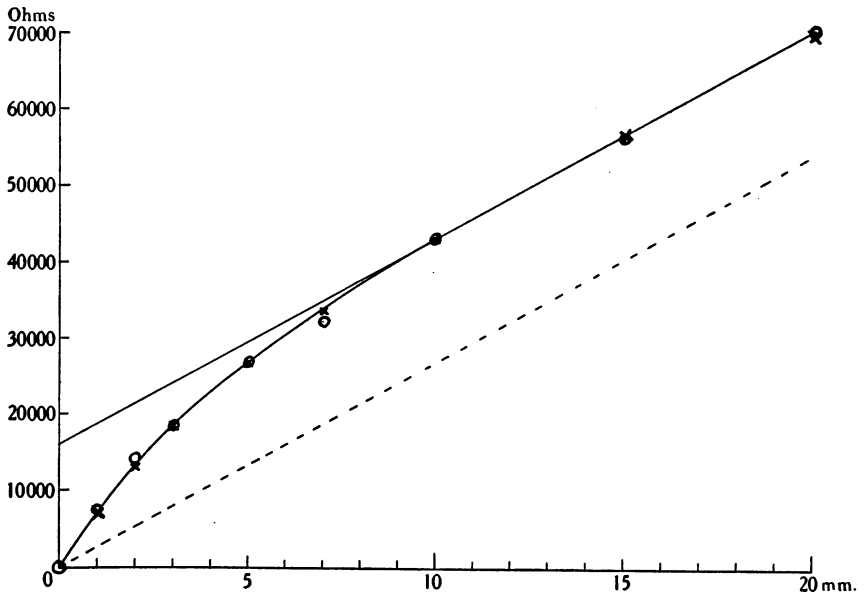


Fig. 6. Relation between resistance and interpolar length of nerve. Continuous line drawn asymptotic to curve for great lengths. Intermittent line drawn through origin parallel to continuous line.

Consider the curve of Fig. 6 on the other hand; this is straight for interpolar distances greater than 10 mm., but for shorter distances the resistance decreases faster than linearly and a curve is obtained of the form anticipated in Fig. 2. The circles (Fig. 6) are obtained by reading the galvanometer deflection for the corresponding interpolar length, and finding the corresponding resistance from the galvanometer calibration. The horizontal axis is drawn through the point where the curve cuts the vertical axis, *i.e.* ordinates represent resistance of nerve free from electrode resistance.

The fact that the resistance of nerve is not proportional to its length

has often been attributed to the added resistance of contact between electrodes and nerve. This, however, would give the linear result of Fig. 5. The curve of Fig. 6 depends upon a more complicated question, namely the distribution of current across the sheath between core and interstitial fluid.

With regard to the theoretical shape of the curve (Fig. 6), I do not think that it can easily be determined except through mathematical considerations. These are given in simplified form in a later section of the present paper. The considerations are identical with those of the former paper [Rushton, 1927] except that the present case is a little more general, and the treatment much less cumbrous. In the case treated the resistance of the sheath is assumed to be uniform. Actually it seems very likely that the current enters through the nodes of Ranvier more easily than elsewhere. This appears probable *a priori*; it would account for the observed differences in the shape of the strength-duration curves of nerve and muscle, and for the relative independence of excitation time of the former and dependence of the latter tissue upon electrode size.

The distribution therefore should be considered with reference to nodal leaks as well as leaks across the sheath in the internodal regions. This adds so considerably to the mathematical complexity that I have not here given this treatment, which I hope to publish shortly elsewhere. Suffice it to state that the forms of the curves considered in this paper are mathematically identical in the two cases, and that the argument worked out here on the assumption of a uniform leak is in no way affected if we consider the current to enter largely through the nodes of Ranvier.

Now the results of this mathematical analysis are very simple and are described in non-mathematical language in the summary to the mathematical section. The resistance for great interpolar lengths should coincide with a straight line, and for shorter lengths the ordinate difference between curve and line should vary in an exponential manner. Fig. 6 shows that the theory is more or less justified by the facts, but in order to test whether the curve is accurately exponential we plot the logarithm of the ordinate difference against interpolar length and the result should be a straight line.

This has been done in Fig. 7¹, where it is seen that the points in question (circles) fall very exactly upon a straight line. We thus observe

¹ Actually the circles of Fig. 7 correspond to the crosses of Fig. 6. The significance of these will appear later, but it is clear that they lie on the same curve as the circles, but with less random error. Hence this curve is an exponential.

that the form of the curve relating resistance and interpolar length is quantitatively exactly as predicted on the cable assumptions.

We can, moreover, obtain the three resistances in the tissue—that of sheath, of core, and of interstitial fluid—from the following three measurements:

- (i) The slope of the straight line in Fig. 6.
- (ii) The point where this line cuts the vertical axis.
- (iii) The slope of the line in Fig. 7.

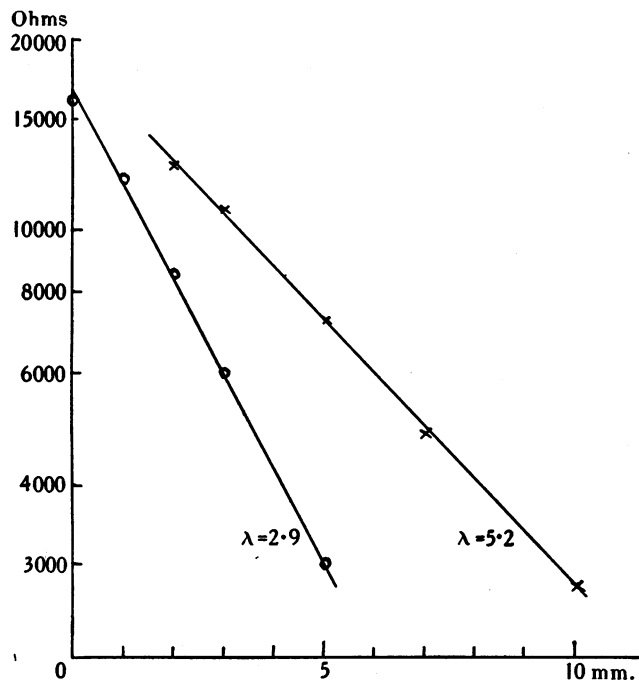


Fig. 7. Abscissæ: interpolar length (uniform scale). Ordinates, circles: resistance of nerve in air (logarithmic scale). Ordinates, crosses: reciprocal threshold in arbitrary units of nerve in Ringer's fluid (logarithmic scale).

All these measurements may be made with fair accuracy, and hence the constants of the equations are no longer arbitrary but physically determined.

RESULTS OF EXCITABILITY MEASUREMENTS.

Turning now to the question of excitability, the experimental measurements give either the threshold galvanometer deflection, or else the threshold voltage, which, in conjunction with the known resistance of the nerve, also allows the threshold current to be obtained.

This is the current which flows through the electrodes, and then largely passes outside the nerve in the interstitial fluid. What interests us is that fraction of the current which traverses the sheath at the cathode for each position of the electrodes. Let us name this the "penetrating fraction" at the cathode. This fraction may be calculated, free from arbitrary constants, by the equations in the Mathematical Section into which the appropriate values of the various resistances have been inserted. But the result may be appreciated very readily by reference to Fig. 6. If from the origin we draw a line (intermittent) parallel with the continuous line already drawn, then the ordinate difference between the curve and this line is proportional to the penetrating fraction at the cathode. We see that at small interpolar lengths practically none of the current crosses the sheath, and that the quantity crossing is increased by increasing interpolar length but only up to about 10 mm., beyond which length the fraction remains constant. Thus, to find the cathodal penetrating current for any interpolar length, we must multiply the ordinate difference of Fig. 6 by the observed threshold current through the electrodes for that length or (what is the same thing) divide the ordinate difference by the reciprocal threshold.

Now the reciprocal threshold current is plotted in Fig. 6 as an ordinate measured from the intermittent line for each interpolar distance, and the results are shown by the crosses which are seen exactly to coincide with the curve already obtained. This means to say that the ratio

$$\frac{\text{ordinate difference}}{\text{reciprocal threshold}} = 1$$

for all interpolar distances, or the threshold current crossing the sheath at the cathode is always the same.

The fact that the above ratio is unity rather than any other number is merely due to the scaling of the reciprocal thresholds, because the coincidence of the curves of crosses and circles is much easier to appreciate than merely a constant ratio of their ordinates.

The significant feature is that the ratio is constant (permitting coincidence by suitable scaling), and hence involving necessarily that the same current always crosses the sheath at the cathode in the condition of threshold excitation, no matter what the interpolar length.

We may thus conclude that the assumptions and interpretations of former papers [Rushton, 1927, 1928*a, b*] were correct, that the "analytical unit of length" has the physical significance formerly given to it, and that the rise of threshold which occurs when electrodes are close together is not due to any chemical or "physiological" neutralization, but is merely due to the anticipated and measured alteration in current distribution.

NERVE IMMERSSED IN RINGER'S FLUID.

When a nerve is immersed in Ringer's fluid, the surrounding interstitial fluid may be considered of infinitesimal resistance (so much fluid being present in parallel), and hence the conditions of current distribution should be at once obtained from the measurements in air by substituting zero for the previous value of the interstitial fluid resistance. It is clearly profitless to make any resistance measurements upon immersed nerve, since one will only in fact be measuring the resistance of the Ringer, but excitability measurements may be made for different interpolar lengths precisely as in the former paper [Rushton, 1927].

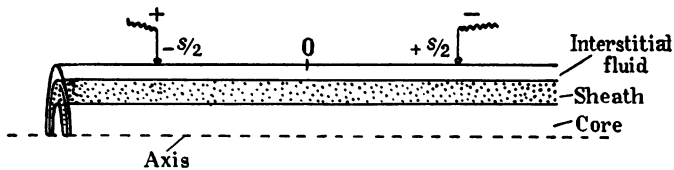
The preparation in Figs. 6 and 7 was in fact set up in a trough, and thresholds obtained for various interpolar lengths in the immersed condition. If the reciprocal of these thresholds were plotted on Fig. 6 they would lie on a curve which did not coincide with the curve of crosses. The form of this curve, however, is better displayed by plotting it in Fig. 7, where it is seen to lie also on a straight line (crosses) though of different slope from the line of circles.

In fact the line in question was not drawn with a slope to fit the points, but with the slope deduced from the resistance measurements on the nerve before it had been placed in Ringer.

Thus not only do the theoretical concepts fit the observations in a quantitative fashion, but also the actual physical significance of these concepts appears to be correct in so far as they have been checked by physical measurement and change of physical conditions.

MATHEMATICAL SECTION.

The object of this section is to calculate from the assumptions of the foregoing paper the current distribution in nerve, and in particular to obtain expressions for the two relations which have been experimentally obtained, namely that between interpolar length and resistance,



and that between interpolar length and that fraction of the applied current which crosses the sheath at the cathode, *i.e.* the penetrating fraction.

- Let r = resistance of interstitial fluid/length to axial currents;
 σ = resistance of core/length to axial currents;
 R = resistance of sheath \times length to radial currents;
 T = resistance of nerve as measured between the electrodes;
 $\lambda^2 = \frac{R}{\sigma + r}$;
 x = distance measured along nerve from mid-point between electrodes;
 s = distance apart of electrodes;
 V_x = potential of core at x ;
 U_x = potential of interstitial fluid at x ;
 i_x = current in core at x ;
 $I_x - i_x$ = current in interstitial fluid at x ;
 I_0 = current through electrodes.
 $\therefore I_x = I_0$ when $-s/2 < x < s/2$, otherwise $I_x = 0$.

Now by Ohm's Law

$$\frac{dV}{dx} = -\sigma i, \quad \frac{dU}{dx} = -r(I - i) \quad \dots\dots(1).$$

Also
$$T = -\frac{U_{s/2} - U_{-s/2}}{I_0} = -\frac{1}{I_0} \int_{-s/2}^{s/2} \frac{dU}{dx} \cdot dx$$

$$= \frac{r}{I_0} \int_{-s/2}^{s/2} (I_x - i_x) dx = rs - \frac{r}{I_0} \int_{-s/2}^{s/2} i dx \quad \dots\dots(2).$$

But from (1)
$$\frac{dV}{dx} - \frac{dU}{dx} = rI - i(r + \sigma) \quad \dots\dots(3).$$

Integrating we obtain

$$(V - U)_{s/2} - (V - U)_{-s/2} = rI_0s - (r + \sigma) \int_{-s/2}^{s/2} i dx.$$

Substituting in (2)

$$T = rs - \frac{r}{I_0(r + \sigma)} \{rI_0s - (V - U)_{s/2} + (V - U)_{-s/2}\}$$

$$= \frac{r\sigma s}{r + \sigma} + \frac{r}{I_0(r + \sigma)} \{(V - U)_{s/2} - (V - U)_{-s/2}\}.$$

This result has been obtained without reference to R , the resistance of the sheath, which may consequently vary in any manner from point to point without affecting the result.

If we consider the conditions at the cathode to be equal and opposite to those at the anode then $(V - U)_{s/2} = -(V - U)_{-s/2}$ and we get the simplification

$$T = \frac{s}{\frac{1}{r} + \frac{1}{\sigma}} + \frac{2r(V - U)_{s/2}}{I_0(r + \sigma)} \quad \dots\dots(4).$$

Thus T plotted as a function of s the interpolar length is made up of two terms. The first is proportional to s and is plotted as straight line

through the origin (intermittent line, Fig. 6). The second term to be added to this is proportional to the potential difference across the sheath at the cathode, which in turn is proportional to the current crossing the sheath at this point.

Now if we assume that R is a constant:

Current leaving the core at x

$$= -\frac{di}{dx} = \frac{V-U}{R} \quad \dots\dots(5),$$

therefore
$$\frac{d^2i}{dx^2} = -\frac{1}{R} \left(\frac{dV}{dx} - \frac{dU}{dx} \right),$$

which from (3)
$$= \frac{i_x}{\lambda^2} - \frac{r}{R} \cdot I_x,$$

therefore
$$i_x = \frac{\lambda r}{2R} \left\{ e^{-x/\lambda} \int_{-\infty}^x e^{x/\lambda} \cdot I_x dx + e^{x/\lambda} \int_x^{\infty} e^{-x/\lambda} \cdot I_x dx \right\},$$

as may be verified by differentiation, the particular integral being that which causes i to vanish for $x = \pm \infty$.

Current crossing the sheath at the cathode

$$= -\left(\frac{di}{dx}\right)_{s/2} = \frac{r}{2R} \left\{ e^{-s/2\lambda} \int_{-\infty}^{s/2} e^{x/\lambda} \cdot I_x dx - e^{s/2\lambda} \int_{s/2}^{\infty} e^{-x/\lambda} \cdot I_x dx \right\}.$$

But since in the present case $I_x = I_0$ when $-\frac{s}{2} < x < \frac{s}{2}$ and zero elsewhere

$$\begin{aligned} -\left(\frac{di}{dx}\right)_{s/2} &= rI_0 e^{-s/2\lambda} \int_{-s/2}^{s/2} e^{x/\lambda} dx \\ &= \frac{r\lambda I_0}{2R} (1 - e^{-s/\lambda}) \quad \dots\dots(6). \end{aligned}$$

Combining (6) with equations (5) and (4) we obtain

$$T = \frac{s}{\frac{1}{r} + \frac{1}{\sigma}} + \frac{r^2\lambda}{r+\sigma} (1 - e^{-s/\lambda}) \quad \dots\dots(7).$$

From (7) we see that the observed resistance T as a function of s , the interpolar length, for great values of s coincides with the straight line (continuous line, Fig. 6)

$$T = ms + c,$$

where

$$m = \frac{r\sigma}{r+\sigma}, \quad c = \frac{r^2\lambda}{r+\sigma} \quad \dots\dots(8).$$

When s is small T diverges from the straight line by a quantity which is an exponential function of s .

Hence when this is plotted on semi-log paper as in Fig. 7 the relation becomes linear. The gradient of this line which can be measured accurately is $-1/\lambda$.

The gradient m above, and the intercept c on the vertical axis can also be accurately measured.

From these three constants, r , σ , R may be found. For from (8)

$$\left. \begin{aligned} m + \frac{c}{\lambda} &= \frac{r}{r + \sigma} (\sigma + r) = r \\ \frac{1}{\sigma} &= \frac{1}{m} - \frac{1}{r} \\ R &= \lambda^2 (\sigma + r) \end{aligned} \right\} \dots\dots(9).$$

When the nerve is immersed in Ringer's fluid $r=0$, σ and R remaining unchanged.

Let λ become λ_0 , where

$$\left(\frac{\lambda_0}{\lambda}\right)^2 = \frac{\sigma + r}{\sigma} = 1 + \frac{c}{m\lambda} \dots\dots(10).$$

Thus the change in λ on immersion is found from the three constants in air.

In the case in Figs. 6 and 7

$$\left. \begin{aligned} c &= 16,000 \text{ ohms} \\ m &= 2650 \text{ ohms/mm.} \\ \lambda &= 2.9 \text{ mm.} \end{aligned} \right\} \begin{aligned} \therefore \text{ from (10), } \left(\frac{\lambda_0}{2.9}\right)^2 &= 1 + 2.08. \\ \therefore \lambda_0 &= 5.1 \text{ mm.} \end{aligned}$$

As is seen from Fig. 7, λ_0 was found to be 5.2 mm.

Summary of mathematics.

Assuming that the nerve is a uniform leaky cable without capacity, we derive the following relations:

(a) The resistance as a function of interpolar length is as represented by the curve of Fig. 6. For great lengths it coincides with a straight line; for shorter lengths it diverges from the line exponentially (formula (7)).

(b) The fraction of the applied current which crosses the sheath at the cathode is the same exponential function of the length (formula (6)).

(c) From this same formula it appears that if $\left(\frac{di}{dx}\right)_{s/2}$ (*i.e.* the penetrating current at the cathode) is constant, the reciprocal of I_0 is proportional to the same exponential. Thus the resistance, T , is the sum of a quantity proportional to s (the intermittent line, Fig. 6), and a quantity proportional to $1/I_0$, *i.e.* when the reciprocal thresholds are added to the ordinate of the intermittent line (giving the crosses, Fig. 6) they should coincide with the curve of resistance (circles).

The fact that this is the case substantiates the assumption that $\left(\frac{di}{dx}\right)_{s/2}$ is constant and that the foregoing treatment of current distribution is valid.

(d) From the curve of resistance against interpolar length, the resistances of the core, the sheath, and the interstitial fluid may easily be found (formula (9)).

(e) When the nerve is immersed in Ringer's fluid, the exponential constant will change in a manner easy to compute (formula (10)).

The experimental data throughout are accurately fitted by the theory.

DISCUSSION.

The structure and electrical properties of any irritable tissue are so complex that some degree of simplification becomes imperative if physical concepts are to be applied profitably. In the present instance a very great limitation has been set to the phenomena observed in that the stimulus has in all cases been a constant current of 0.8 millisecon. duration. But this brings the immense simplification that the time function of the excitation process is removed from our present considerations. We have in fact to deal with efficacy of excitation as a function only of the spatial distribution of current. In the conditions of these experiments we may, without serious error, speak of the "resistance" of the sheath and the core of the nerve, but it will almost certainly be found that these "resistances" are functions of the duration of current flow, and that they will have different values when the stimulating current has a different time course. Capacitative systems are known to have a "resistance" whose value depends upon the time course of the current resisted, and a nerve is known to be in this sense a capacitative system.

These considerations, however, while pointing the way to an important development of the present investigation, in no way affect the argument of the present paper. We have here noted the constant applied E.M.F. and measured ballistically the total current flowing in the given 0.8 millisecon., and the resistance has been defined as the ratio of these two quantities. All the foregoing arguments relative to current distribution are therefore essentially correct if by "current" we understand the average current flowing during the 0.8 millisecon. interval, and by "resistance" we understand the average value of the momentary resistance to current flow during this interval. With this understanding we may review the results of this paper.

We set out with a simple physical concept of the structure of nerve from an electrical point of view.

The measurement of the resistance as a function of the interpolar length gave a curve which accurately fitted the derived equation. From

this it was possible to calculate the current distribution in the nerve and its surroundings both in air and when immersed in Ringer's fluid. In particular it was possible to compute what fraction of the current measured in the galvanometer actually crossed the nerve sheath at the cathode. This in conjunction with the measurement of threshold currents allowed the threshold cathodal current to be computed. It was found that excitation was brought about by the same current crossing the sheath at the cathode no matter what the interpolar length—that in fact the observed variations in threshold were merely compensations for the variations in current distribution with different electrode positions. Accepting, now, the constancy of the threshold cathodal current, the variation of threshold with interpolar length was calculated with the altered current distribution consequent upon immersion of the nerve in Ringer's fluid.

In all these measurements there has been complete accord between theory and observation, and the only arbitrary constant involved has been the absolute value of the cathodal penetrating current necessary to excite, which cannot be computed from physical considerations.

It is hardly necessary to remark that the constancy of the cathodal penetrating current relates only to a given fixed point on the nerve, and a given fixed duration of current flow. Variation of the former probably and of the latter certainly will necessitate a new value of this current, but when the only variation in question is the position of the other electrode, the cathodal penetrating current is constant.

Finally, I must repeat that the electrode system here employed was far from ideal, and no undue weight should be attached to the actual numerical results. A small alteration in the slope of the straight line in Fig. 6, for instance, results in considerable changes in the deduced resistances of core, sheath and interstitial fluid.

But of the main conclusions of this paper, I think, there can be little doubt, since theory and observation appear to agree so closely when tested in several ways.

It is hoped that an improvement of the electrode system will allow this work to be extended.

SUMMARY.

In a former paper [Rushton, 1927] the dependence of threshold upon interpolar length was explained upon the basis of the distribution of current in nerve. The explanation fitted the observations quantitatively with the aid of two assumptions—the threshold current leaving

the cathode was supposed to be the same whatever the interpolar length, and the ratio, resistance of sheath:resistance of core, was assumed to have a certain value which fitted the observations.

In the present paper both these assumptions are investigated and found to be correct.

The resistance of nerve is measured using a subthreshold constant current of 0.8 millisecc. duration, and from the relation between resistance and interpolar length the current distribution in nerve is found free from arbitrary constants.

Measurements of threshold current in identical conditions allow the threshold current crossing the sheath at the cathode to be found, and it proves to be the same for all values of interpolar length.

Accepting this, the strength-length curve may be calculated both for nerve in air and in Ringer's fluid. Both curves coincide with the observed results.

Thus the assumptions of the former paper are justified and the relation between threshold and interpolar length is merely dependent upon the distribution of current in the cable-like structure of nerve.

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