

THE EFFECT UPON THE THRESHOLD FOR NERVOUS
EXCITATION OF THE LENGTH OF NERVE
EXPOSED, AND THE ANGLE BETWEEN
CURRENT AND NERVE.

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THE EFFECT OF INTERPOLAR LENGTH UPON NERVOUS EXCITATION.

Introduction. It is well known that the minimum current required to excite a nerve decreases when the distance between the electrodes is increased. Various explanations have been proposed in the past, but since most of the work was done some fifty years ago, they are somewhat unsatisfactory from the present standpoint.

The general ideas of nervous activity then in vogue have since been modified and made more precise by two conceptions in particular.

First the work of Lucas and others distinguished between the two forms of activity, "the local excitatory process," and "the propagated disturbance." The threshold for excitation was shown to depend upon purely local phenomena, and the remoter parts of the nerve had no other effect on the success or failure of a stimulus than sometimes to block the propagated disturbance which had already been initiated.

Second, the ionic hypothesis elucidated the nature of the passage of electricity in media such as those of which the tissues are composed, and showed that any change which was brought about must occur through the action of ions.

Nernst⁽¹⁾ applied this concept to the problem of nervous excitability, and, assuming that movement of ions *per se* could have no effect, he was immediately brought to his membrane hypothesis. According to this a stimulating current acts only through the changes in ionic concentration which are brought about, and such changes can only occur in the neighbourhood of something which opposes the flow of ions, *e.g.* a semi-permeable membrane.

Nernst made the further assumption that not only did the local excitatory process depend upon the ionic concentration, but that this concentration was always the limiting factor in excitation. He therefore

concluded that if the requisite concentration was attained, excitation would certainly occur (this assumption was modified a little to account for the results of stimulation with currents of long duration).

Nernst's theory is well supported by the results of stimulating a nerve with constant currents of various durations, and with alternating currents of various frequencies. Except when the time intervals are great, the value of the minimum exciting current lies very close to that calculated from the above assumptions.

The advantage of a theory such as Nernst's is obvious, for it allows a theoretical relation to be worked out in terms of the known properties of ions. The assumptions, moreover, are simple and precise.

Since Nernst was not concerned with changes in the position of the electrodes, it was unnecessary to make any assumptions as to the extent of membrane against which the ions had to be concentrated. For the purpose of the present investigation, however, the following assumption on this point will be made.

"Excitation will occur at any point in the membrane, when the ionic concentration at that point attains a certain value."

It is the object of this paper to see to what extent Nernst's theory is able to explain the variations of excitability consequent upon changes of interpolar length.

Variation of threshold with interpolar length. It has long been known that a current is more efficacious the longer the stretch of nerve it traverses. This is entirely confirmed by the following observations, which are in complete agreement with the older work, and have the advantage that they were obtained by a method which avoids any manipulation of the nerve during the experiment.

Apparatus. An ebonite trough filled with Ringer's fluid was used, of the following construction (Fig. 1):

The trough was deep at one end to hold the muscle, and a cork was provided to receive the pin through the knee. This deep part was 3 cm. in length. The rest of the trough, 6 cm. in length, was shallower by about the thickness of the knee, so that the upper surface of the knee was just above the floor of the shallow part. The centre of this floor was grooved by a longitudinal slot, of such a size that it would just easily contain the nerve. When the preparation was set up, therefore, the nerve lay in the groove and passed horizontally to the knee, and the muscle lay below in the deep part of the trough.

The electrodes were plane vertical plates of bright silver, which fitted exactly the section of the trough. The plate near the muscle was

always kept fixed, and was the cathode. The anode was movable. The interpolar length was read off directly from a scale (not shown in diagram).

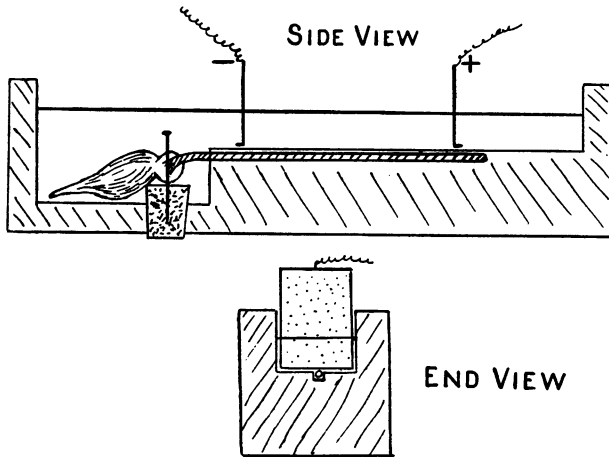


Fig. 1. Apparatus for strength-length determination.

It was assumed that there was a uniform potential gradient in the fluid from one electrode to the other, and that each extrapolar region was equipotential.

The currents used were constant currents lasting about $\cdot 0002$ sec., hence the polarisation at the electrodes was not excessive. Moreover, it was not cumulative, since the electrodes were connected by a short circuit between each observation, and hence would dissipate any charge they might have acquired.

Experiment. A frog's sciatic-gastrocnemius preparation was used. The nerve was ligatured near the cord, and cut through central to the ligature. The preparation was then set up in the apparatus as described, and left for about an hour to attain a steady state.

The duration of the current was controlled by a Lucas pendulum and the strength by leading off from a low resistance potentiometer wire. Two strengths were recorded usually differing by 5 p.c., the upper of which caused a perceptible twitch of the muscle whilst the lower did not. The results are recorded graphically as the line joining the two points corresponding to these two strengths.

The experiment was performed with the interpolar length being made gradually shorter; then it was repeated with the length increasing, and finally the first was again repeated.

If these three did not on the whole agree to 10 p.c., they were all rejected without any further analysis. In the other event all three were accepted and no further rejection was done. As a matter of fact the apparatus was found reliable, and after the technique had been acquired no rejections were necessary.

Results. It was found that the longer the interpolar length the more excitable the nerve up to a point, but that after 20 mm., an increase to 40 mm. had no further favourable effect.

Taking the strength of this lower limit as two units (for reasons which will appear later), the relation between length and threshold is fairly constant from nerve to nerve, and if we plot the threshold in these units against the length in arbitrary units which differ slightly from nerve to nerve, the results of all the experiments can be made to lie on the same curve (Fig. 2).

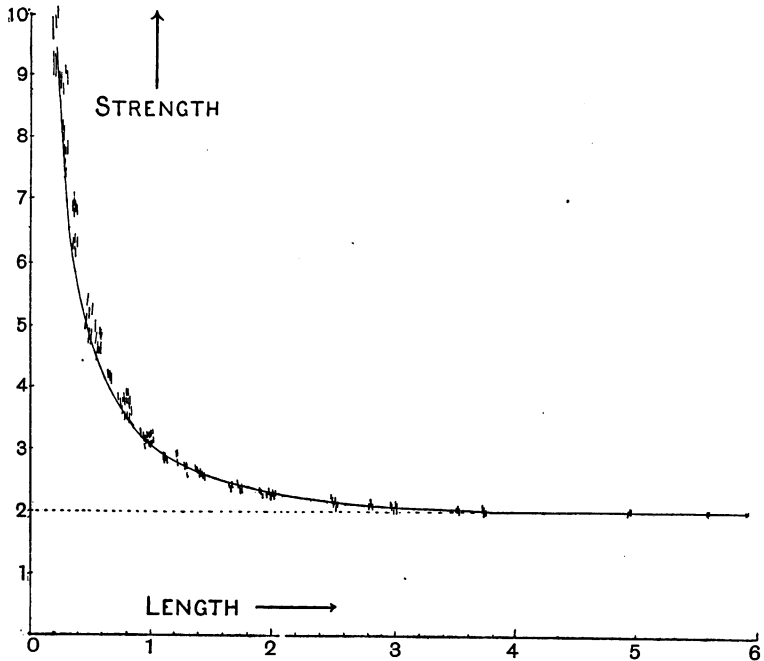


Fig. 2. Strength-length relation. Lengths measured in "analytical units" of about 5 mm. Equation of curve, $y = 1 + \coth x/2$.

Significance of strength-length relation. If the ineffectiveness of the current flowing through a short length is to be explained in terms of ionic movement, there are two possibilities.

(1) The electric field must be inadequate to concentrate the ions much when the length is short.

(2) The back diffusion must be too great to allow of much concentration.

These two cases are not mutually exclusive, and that the second certainly is in operation is seen from the effect of interpolar length upon the chronaxie.

It has been shown by many workers in France⁽²⁾ that the chronaxie becomes less as the interpolar length is diminished, and this is confirmed by one or two experiments with the above apparatus, where it was found that the strength-length curve was to some extent changed when the duration of current flow was altered. It is impossible, however, to estimate whether the alteration of back diffusion is sufficient to account for the change in threshold unless a definite conception of the exact movement of ions is assumed. If, however, it is assumed that the change of threshold is mainly dependent upon changes in the electric field, this assumption may be given a plausible basis, and be made to yield a quantitative explanation.

Dependence of electric field upon interpolar length. Hermann⁽³⁾ and Hering working on the question of internal polarisation in nerves came to the conclusion that their phenomena could be explained on the assumption that the medullated nerve fibre was a cylinder with a resistant sheath and a conducting core.

Hermann made a model nerve with a platinum wire as core, and with a relatively resistant $ZnSO_4$ solution for the sheath.

Hering's model was a piece of grass soaked in saline, the solution being the core, and the grass envelope the resistant sheath.

There is obviously nothing like metallic conduction in a nerve so that Hering's model is a more accurate representation, but both models realised the phenomena of internal polarisation, for both satisfied the essential condition of a resistant sheath and a conducting core. If this model is accepted, then, the membranes responsible for internal polarisation are cylinders co-axial with the nerve.

It will be further assumed that these membranes are also the ones which are responsible for nervous excitation on Nernst's theory.

Nernst himself specified only that the membrane might be considered at an infinite distance from any other. Hill⁽⁴⁾ on the other hand worked out a modification wherein two membranes were assumed close together. But neither investigator assigned to the membranes any definite position in the structure of the nerve.

The alternative suggestion that the membranes are placed transversely is not supported by any histological evidence, and is difficult to reconcile with the classical observation that at "make," the excitation is localised at the cathode.

The inability of transverse currents to excite will be considered later in this paper.

Accepting therefore the above assumptions, it will be possible to calculate the distribution of current in the nerve when it is placed in an electric field, and hence to estimate the force concentrating ions against the cylindrical membrane.

It must be added that the theoretical treatment which follows does not claim to be more than a first approximation, suitable only to explain the observations which are under discussion. It is hoped that it will be possible later to develop it to embrace a wider range of phenomena.

MATHEMATICAL TREATMENT OF RESISTANCE OF NERVE.

Definitions. The nerve fibre is assumed to be a cylinder with a relatively well-conducting core, and a relatively non-conducting sheath. The current is therefore supposed to enter radially through the sheath, and then to pass longitudinally up the core.

It is assumed that all points in the system take up a steady potential immediately the circuit is closed.

Now the resistance of the core to longitudinal currents varies directly as its length, whereas the resistance of the sheath to radial currents varies inversely as the length of the sheath through which the current passes. There must therefore be a certain unique length l , such that the longitudinal resistance of l mm. of core = the radial resistance of l mm. of sheath.

For the purposes of the mathematical analysis which follows, it is convenient to measure all lengths in terms of this length l as unit length, and similarly to measure resistance in terms of the resistance of l mm. of core as unit resistance.

It is not possible to measure l directly, but it will be shown that the value can be deduced from the strength-length curves.

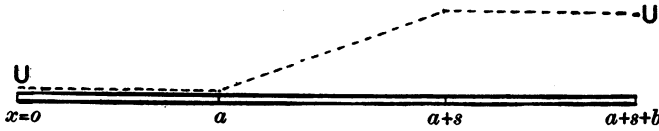
Expressed in these units, let

x = lengths measured along axis of nerve,

U = potential applied to outside of sheath at any point x

V = potential of core at any point x .

The problem is assumed to be radially symmetrical.



The system is defined as follows:

The potential U is 0 from $x = 0$ to $x = a$

$$vx \quad x = a \quad x = a + s$$

$$vs \quad x = a + s \quad x = a + s + b.$$

The two extremities $x = 0, x = a + s + b$ are supposed to be closed by transverse membranes of resistance $\tanh \alpha, \tanh \beta$ respectively, according as $< 1; \coth \alpha, \coth \beta$ respectively, according as > 1 .

Consider first the part from $x = a$ to $x = a + s$.

The current leaving the core at any point $= \partial^2 V / \partial x^2$ but also $= V - vx$.

The solution of this differential equation is

$$V = A \cosh x + B \sinh x + vx$$

as may easily be verified.

It is readily seen that $\partial^2 V / \partial x^2$ may be expressed as $k \sinh \overline{x - c}$ where k, c are constants

For since $\partial^2 V / \partial x^2$ is positive at the anode and negative at the cathode and is also a continuous function of x between these two limits, it follows that at some point c intermediate $\partial^2 V / \partial x^2 = 0$.

$$\therefore B \cosh c [A/B + \tanh c] = 0.$$

And since $B \cosh c \neq 0$,

$$\therefore A = k \sinh (-c)$$

$$B = k \cosh (-c).$$

$$\therefore \partial^2 V / \partial x^2 = k \cosh x \sinh (-c) + k \sinh x \cosh (-c) = k \sinh \overline{x - c}.$$

Thus since $\sinh \overline{x - c}$ increases with x for all values of $x, \partial^2 V / \partial x^2$ has a greater value at the cathodic extremity than at any other point in the range over which the equation holds (*i.e.* from a to $a + s$).

But since the membranes are assumed to be longitudinal $\partial^2 V / \partial x^2$, which is the current leaving the core, is the current concentrating cations against them.

Thus cations will most be concentrated at the cathodic extremity of the range, and the excitatory value of the current is given by

$$(\partial^2 V / \partial x^2)_a = A \cosh a + B \sinh a.$$

Now introduce a new variable ψ defined as follows:

$$\frac{\partial^2 V}{\partial x^2} / \frac{\partial V}{\partial x} = \tanh \psi \text{ according as } < 1; \text{ coth } \psi \text{ according as } > 1.$$

Then since $\partial^2 V / \partial x^2$, $\partial V / \partial x$ are both continuous functions of x whatever continuous function U may be, ψ will also be a continuous function.

In the present case

$$\tanh \psi = \frac{A \cosh x + B \sinh x}{A \sinh x + B \cosh x} \text{ between } x = a, x = a + s.$$

If ψ_a , ψ_{a+s} are the values which ψ assumes when $x = a$, $a + s$ respectively we may write the two corresponding equations and solve for A and B .

Then substituting these values in

$$(\partial^2 V / \partial x^2)_a = A \cosh a + B \sinh a$$

$$\text{we obtain } \left(\frac{\partial^2 V}{\partial x^2} \right)_a = v \sinh \psi_a \cdot \frac{\sinh s - \psi_{a+s} + \sinh \psi_{a+s}}{\sinh s + \psi_a - \psi_{a+s}}.$$

Now the regions from $x = 0$ to $x = a$; $x = a + s$ to $x = a + s + b$ are particular cases of stretches exposed to constant potential gradients, namely, when the gradient is zero.

Hence

$$\tanh \psi = \frac{A_1 \cosh x + B_1 \sinh x}{A_1 \sinh x + B_1 \cosh x} = \frac{A_1 / B_1 + \tanh x}{A_1 / B_1 \tanh x + 1} = \tanh \overline{x + c}$$

when $\tanh c = A_1 / B_1$.

$\therefore \psi - x = c$, a constant over the whole range.

$\therefore \psi_0 - 0 = \psi_a - a$.

Also $\psi_{a+s} - (a + s) = \psi_{a+s+b} - (a + s + b)$.

Now

$$\begin{aligned} \tanh \alpha = \text{resistance of end at } x = 0 &= \left(\frac{\partial^2 V}{\partial x^2} / \frac{\partial V}{\partial x} \right)_0 = \tanh \psi_0, \\ &\therefore \alpha = \psi_0. \end{aligned}$$

$$\begin{aligned} \tanh \beta = \text{resistance of end at } x = a + s + b &= - \left(\frac{\partial^2 V}{\partial x^2} / \frac{\partial V}{\partial x} \right)_{a+s+b} \\ &= - \tanh \psi_{a+s+b}, \quad \therefore \beta = - \psi_{a+s+b}. \end{aligned}$$

Substituting these values in the above two equations

$$\begin{aligned} \psi_a &= (a + \alpha), \\ \psi_{a+s} &= - (b + \beta). \end{aligned}$$

These may now be substituted in the equation for $(\partial^2 V / \partial x^2)_a$ giving

$$\left(\frac{\partial^2 V}{\partial x^2} \right)_a = v \sinh \overline{a + \alpha} \cdot \frac{\sinh s + b + \beta - \sinh b + \beta}{\sinh s + a + \alpha + b + \beta}.$$

This formula holds provided that $\tanh \alpha$, $\tanh \beta$ obtain.

If $\coth \alpha$ obtains each term containing α becomes \cosh instead of \sinh ; if $\coth \beta$ obtains each term containing β becomes \cosh instead of \sinh ; if $\coth \alpha$ and $\coth \beta$ obtain each term containing α and β remains \sinh , others become \cosh .

Application to strength-length curve. The interpolar length is represented by the length s which is exposed to the constant potential gradient, the extrapolar lengths being the parts in the equipotential solutions.

We have seen that the current concentrating ions against a longitudinal membrane is given by the value of $\partial^2 V / \partial x^2$ and that this continually increases from one end to the other of the interpolar stretch. It may also easily be shown that the values in the extrapolar regions are always intermediate between the two extremes of the interpolar stretch, hence, according to the assumption at the beginning of the paper, excitation should occur at the cathodic extremity of the interpolar stretch. On similar assumptions but supposing the membranes to be transverse, excitation should occur approximately in the centre of this stretch, where $\partial^2 V / \partial x^2$ vanishes.

Experiments with the local application of weak alcohol showed that excitability was only affected when the application was at the cathodic extremity of the interpolar stretch.

Now since the interpolar length was in all cases altered by moving the anode,

\therefore "a," the cathodic extrapolar stretch remains constant.

Hence $s + b = \text{constant} = c$.

$$\therefore \left(\frac{\partial^2 V}{\partial x^2} \right)_a = v \sinh \frac{c}{a} \cdot \frac{\sinh \frac{\beta+c}{a} - \sinh \frac{\beta+c-s}{a}}{\sinh \frac{a+a+\beta+c}{a}} \text{ or } \cosh, \text{ etc.}$$

Now if $c > 6$ we may convert these hyperbolic functions into their exponential equivalents and obtain

$$(\partial^2 V / \partial x^2)_a = (1 \pm e^{-2(a+\alpha)}) (1 - e^{-s}) v / 2$$

correct to less than 1 p.c., or, regarding $(\partial^2 V / \partial x^2)_a$ as attaining a constant value whenever the threshold is just reached,

$$\begin{aligned} v &\propto 1 / (1 - e^{-s}), \\ &\propto 1 + \coth (s/2). \end{aligned}$$

The experimental results when plotted at the scale of about 5 mm. to the analytical unit fit this equation well. And since $c > 30$ mm. $\therefore c > 6$ units and the above condition is realised.

Method of finding value of analytical unit in each case.

The threshold potential gradient corresponding to each interpolar length is expressed in units such that the value corresponding to infinite length = 2.

The curve $y = 1 + \coth x/2$ is drawn. y is then made equal to each of the threshold potential gradients in turn, and the corresponding value of x is read off.

Thus to each potential gradient there corresponds on the one hand the observed inter-polar length in mm., and on the other the derived value of x .

These latter two quantities when plotted against each other are found to lie upon a straight line which passes through the origin. The gradient is easily seen to be the analytical unit of length expressed in mm.

COMPARISON WITH EXPERIMENTAL RESULTS.

The conclusion of the mathematical treatment shows that the strength-length curve, expressed in units such that the minimum threshold strength was 2, is a curve involving a single arbitrary constant—the value of the analytical unit of length. If all nerves had the same unit, all should have the same strength-length curve; actually, however, we should expect that there would be a slight variation from nerve to nerve. But when the lengths (in mm.) were divided each by their own unit, we should expect that they all fell upon the same curve.

This has already been quoted as fact when considering the experimental results.

Furthermore, the curve in question should coincide with

$$v \propto 1 + \coth (s/2).$$

That this is the case with considerable accuracy may be seen from Fig. 2. The curve here is that corresponding to the above equation, and the experimental lines are seen to fit it within the general limits of the experiment. The lengths are plotted in analytical units, and the strengths in units such that the minimum is two.

It therefore appears justifiable to regard the strength-length curve as due largely to the variation in current distribution consequent upon the resistant sheath of each fibre.

The change of chronaxie with different lengths shows that the rate of dissipation must play some part in altering the threshold, but this part need not be very great since the strength-length curve is capable of being explained quantitatively without reference to it.

COMPARISON WITH FORMER WORKERS.

MARCUSE⁽⁵⁾. The first results that I know of which can be studied quantitatively are those of Marcuse. In principle his apparatus was similar to mine, but the extrapolar regions of the nerve were lifted out of the solution. This must involve errors due to handling, and the meniscus makes it impossible to read the inter-polar length to an accuracy greater than 1 or 2 mm.

Fig. 3 shows my theoretical curve and all the results of Marcuse where the cathode was kept fixed. Those where the cathode was moved would include errors from variations of local excitability from point to

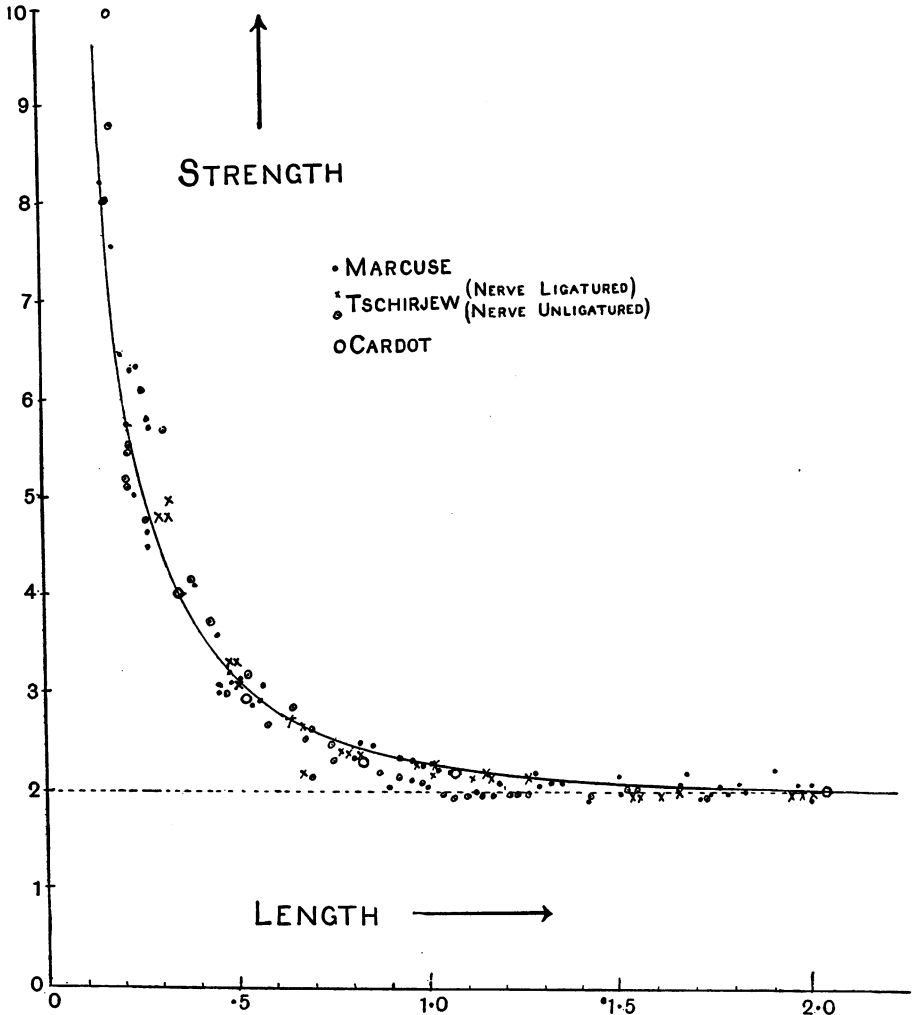


Fig. 3. Strength-length relation. Results of former workers. Units as in Fig. 2.

point, besides the deviation due to the fact that the theoretical curve for this case is not the same as for the former.

The results given show a fair agreement with the theory, and suggest a fairly large random error, but no consistent divergence.

Marcuse found that some of his curves exhibited a minimum threshold corresponding to a certain length: lengths greater than this required a higher threshold. He thought that those curves which did not show this would do so were the length sufficiently increased. However, if we consider only the results with cathode fixed this minimum is not much in evidence, and, as has been mentioned, the other results are not strictly comparable.

TSCHIRJEW'S(6) results were published in the same year as Marcuse's, and apparently quite independently.

His method was quite different. Electrodes were applied to the nerve in air, and the interpolar length varied by two methods.

(1) The electrodes were moved.

(2) The nerve was ligatured in the interpolar region, and the whole nerve was moved across the electrodes.

Thus, though the length of nerve substance between the poles was constant, the length of nerve between the ligature and the electrode nearer the muscle was varied.

These results when plotted are seen to agree with the theoretical curve about as well as those of Marcuse.

Tschirjew's formula $v = a + b/s^m$ where a , b , m are constants is one which would fit any curve of this type within the rather wide limits of error. It has one more arbitrary constant than mine, has no theoretical basis, and hence need not be considered.

CARDOT(2). Comparatively recently the same investigation has been carried out by Cardot. Electrodes were applied to the nerve in air, and the interpolar length altered by moving the anode. A large resistance was placed in series with the nerve. Unfortunately he only gives one result, but that is seen to fit excellently the theoretical curve.

To summarise the results of these workers:

The large variations of Marcuse and Tschirjew allow of no conclusion other than that the results are not inconsistent with the theory.

Cardot's curve may be taken as confirmatory.

VARIATION OF THRESHOLD WITH ANGLE BETWEEN CURRENT AND NERVE.

The foregoing results have been explained on the assumption that excitation is brought about by the concentration of ions against a membrane which is cylindrical and co-axial with the nerve. A few *a priori* reasons in favour of this assumption have been given, and it is now necessary to deal with what appears to be a serious objection.

From the time of Galvani onwards it has been recognised that a

nerve is nearly or quite inexcitable to currents perpendicular to the axis. This seems to favour the assumption of a transverse membrane, for at first sight it would appear that the transverse direction would be the most efficient for concentrating ions against a longitudinal membrane.

Determinations were made on the relation between threshold and angle between current and nerve, and the results are in agreement with previous workers. These experiments were all completed before the development of the foregoing mathematical theory with which they are in close accord.

Apparatus. A frog's sciatic-gastrocnemius preparation was used. The nerve was ligatured near the cord, and cut through central to the ligature. It was stretched horizontally in a trough of Ringer's fluid, through which a current was passed between two non-polarisable Ag-AgCl plates. Seen from above, the trough was square, and the plates occupied the whole of two opposite sides.

The lines of flow of the current were therefore all parallel to each other, and perpendicular to the two plates. It is this direction which is referred to as the direction of the current, though the actual direction in the nerve is different.

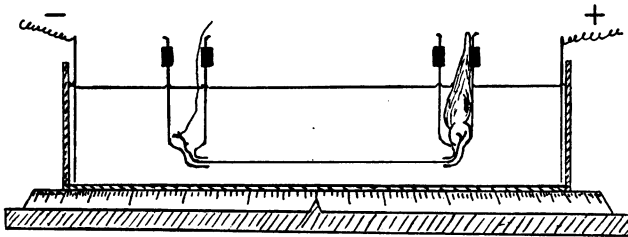


Fig. 4. Apparatus for determining relation between threshold and angle.

The trough and electrodes were mounted on a small turn-table graduated in degrees.

Both ends of the nerve entered the capillary ends of two tubes, and the muscle rested in the wider body of one of them. A screw controlled the distance between the tubes by operating upon the arms which held them. These arms were attached to a rigid stand so that they remained fixed when the turn-table rotated. By this means the angle between current and nerve was varied.

The advantages of holding the nerve in this way are:

- (1) The portion of nerve exposed to the current is confined to the part between the tubes.
- (2) This length may be varied accurately and easily.
- (3) The nerve is entirely straight in the exposed part.

Proof of (1) is derived from three sources:

- (a) If current entered it would have to leave by the same opening.
- (b) The strength-duration curve shows no α curve.
- (c) If the nerve is completely withdrawn into the tube with the muscle no contraction can be produced.

Experiment. A frog's sciatic-gastrocnemius preparation was set up in the tubes as described, and was left for about a quarter of an hour to attain a steady state before the determinations were made.

The stimulus was in all cases a constant current usually of about .002 sec. duration delivered by a Lucas pendulum; the strength was controlled by leading off from a low resistance potentiometer wire.

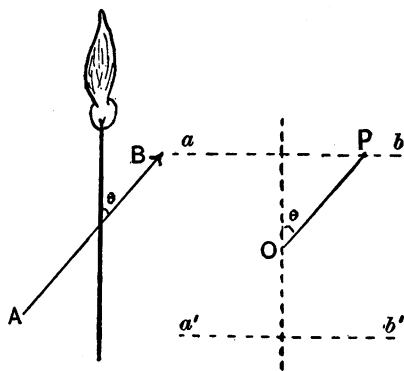
At every 10° in the whole revolution, measurements were taken of the least potential led off which would bring about a perceptible contraction of the muscle. The limits of experimental error are recorded as in the strength-length determinations.

In order that the readings of the turn-table should give the angle between the current and the nerve, it was necessary that the nerve should be set parallel to the plates when they were set at an angle 90° . In the earlier experiments this was done by eye, but later silver wires were inserted into the mouths of the two tubes and each connected to a terminal of a sensitive galvanometer. The current was then passed between the plates of the trough, and the tubes adjusted to give no deflection in the galvanometer. Their openings are now in a line perpendicular to the lines of flow.

Results. From the first it was clear that the excitability was roughly proportional to the cosine of the angle between current and nerve. It was therefore thought well to plot the results in polar co-ordinates, for, not only is a cosine relationship represented by this method as a straight line, but also any zero error which there might be will do no more than rotate the graph about the centre through an angle equal to this error.

The following convention is therefore adopted.

If the current is flowing through the nerve in the direction AB , draw from the origin, O a line parallel to AB . And if the strength of the current necessary to excite is 38 units, then draw the line OP 38 mm. long. The point P will



therefore represent the two related variables, the strength of current given by the distance OP and the direction given by θ , the angle which OP makes with the direction of the nerve.

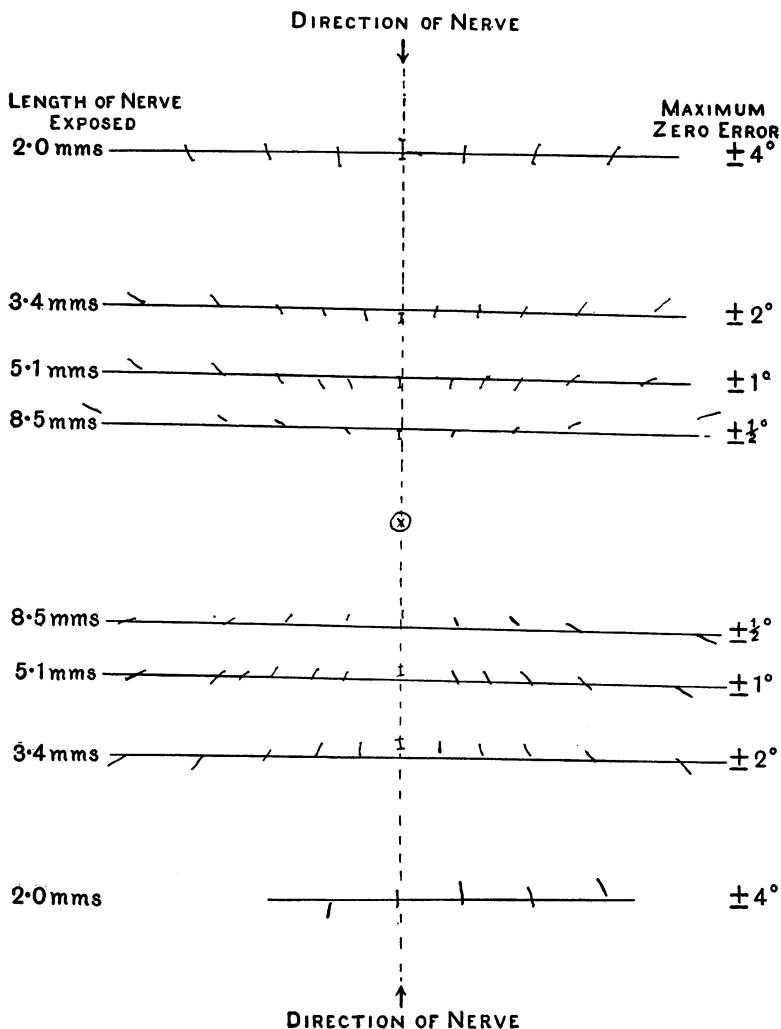


Fig. 5. Relation between threshold and the angle which the current makes with the nerve.

If then the length OP is always inversely proportional to the cosine of the angle it makes with the nerve, P must always lie on a straight line perpendicular to the direction of the nerve (as ab , $a'b'$).

The results show that this is very nearly the case. The actual figure

(Fig. 5) gives several experiments performed upon different lengths of nerve from the same frog.

Some experiments give closer approximations to straight lines, but the above is typical.

The divergence of the results from two straight lines perpendicular to the direction of the nerve seems to be of three types:

(1) The lines were sometimes straight and parallel but not perpendicular. This is what would be expected as the result of zero error. It was found most pronounced in the earlier experiments when the zero was set by eye. In the later ones, where the galvanometer was used the error was never greater than that recorded beforehand as the maximum possible error from the galvanometric reading.

(2) In the earliest experiments it was often found that the lines were not straight, but markedly concave towards the origin.

Experiments directed to the investigation of this phenomenon showed that it was not caused by skewness of the tubes holding the nerve nor by any sort of progressive change taking place throughout the course of the experiment.

It was noticed in a preparation which showed the phenomenon most markedly, that the nerve was hanging loosely between the tubes, and that it was bent somewhat at the place where the branch to the hamstring muscles leaves the sciatic trunk, so that the two halves of the exposed nerve were in slightly different directions.

To see whether this was the cause the following experiment was performed (Fig. 6).

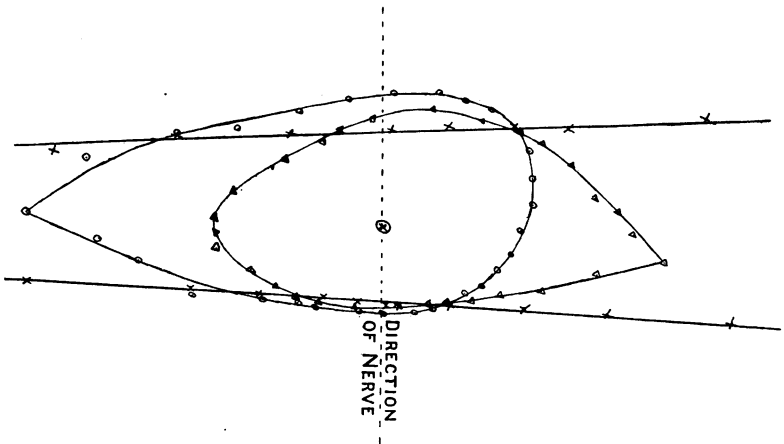


Fig. 6. Effect of bending nerve.

A preparation was set up slightly stretched so that there should be no appreciable bend, and a set of determinations made. The results gave straight lines as shown by the crosses. Then the nerve was artificially bent by pulling the centre to one side. The determination gave results very similar to those obtained accidentally before; the main features were that the two branches of the curves were concave towards the origin, and met in a rounded curve at one end and a point at the other, as shown by circles. The nerve was then bent the other way and the results showed that the round and pointed ends had been reversed (triangles). It was therefore concluded that the concavity towards the origin when present was caused by the bending of the nerve.

This conclusion was confirmed by all the subsequent experiments; in these the nerve was kept slightly stretched, and this concavity never appeared.

This source of error is of importance in criticising the earlier work on this subject, for it was never expressly mentioned, and, I believe, not recognised by those whose results showed this concavity towards the origin.

(3) The later results, which were free from these two errors, were usually not quite straight, but slightly convex towards the origin. The effect seemed to be diminished or abolished when special precautions were taken to ensure that the nerve lay in the centre of the capillary tubes.

In any case this error in most cases only just exceeds the experimental error, and it will probably not be far wrong to conclude that the component of the current in the direction of the nerve is alone effective as a stimulus. The component at right angles has practically no effect, but such as it has seems to be *inhibitory*.

Independence of cosine relation on length of nerve or duration of current. In order to be the more certain of the generality of the cosine relation, it was thought well to show that this relation was not dependent upon the particular length of nerve exposed to the current, or the particular duration of current employed.

Length. The lengths used for the previous determinations varied over the range of 2 mm. to 20 mm., and, as is clear from the results shown, though the actual values of excitability are greatly changed by variations of length, the cosine relation is unaffected.

Duration. To find what effect other durations of current have upon this relation it would have been possible to repeat the former experiments, using currents of different durations.



The procedure actually adopted, however, was to find the strength-duration curve at different angles between nerve and current.

The curve was determined after the method of Lucas. A given length of nerve was taken, and set parallel to the current, and the strength-duration curve was obtained. Then the curve was repeated at one or two other angles. Finally the first curve was repeated.

If each of the strength-duration curves is reduced so that the strength at infinite duration is 1, then all the curves coincide remarkably well. In fact, there was never a greater divergence between the first curve and any subsequent one, than there was between it and its repetition at the end of the experiment.

Significance of the cosine relation. From the foregoing results it seems justifiable to conclude that du Bois Reymond was correct in his suggestion that the threshold was inversely proportional to the cosine of the angle between current and nerve, and it appears that the transverse component is ineffective no matter what the length of nerve exposed, nor what the duration of current employed.

Now we have already seen the way in which threshold is related to interpolar length, and it is clear that if transverse stimulation is equivalent to an interpolar length of the order of the diameter of a nerve fibre, then the strongest currents which were used would be quite inadequate.

This statement may be made quantitative on the lines of the foregoing mathematical treatment.

We have already seen in the case of stimulation with longitudinal currents that v , the threshold potential gradient, and $\partial^2 V/\partial x^2$, the corresponding potential difference across the sheath, are related by

$$\left(\frac{\partial^2 V}{\partial x^2}\right)_a = v \sinh \overline{\alpha + a} \cdot \frac{\sinh \overline{\beta + b + s} - \sinh \overline{\beta + b}}{\sinh \overline{\alpha + a + \beta + b + s}} \text{ or cosh, etc.,}$$

$$\text{or when } s = 6 = (1 \pm e^{-2(\alpha + a)}) (1 - e^{-s}) v/2,$$

$$\text{or when } a > 1 = \text{order of } v/2.$$

Thus, if a transverse current is to be effective as a stimulus, the applied potential gradient v' must be at least sufficient to produce a potential difference across some point in the sheath equal to $v/2$.

Now if the external diameter of a nerve fibre is $2r$, at no point in the sheath is the potential difference across it $> v'r$.

Therefore the minimum value of v' is defined by

$$v'r = v/2.$$

$$\begin{aligned} \therefore v'/v &= 1/2r \text{ where } r \text{ is measured in analytical units} \\ &= 5/2r \text{ where } r \text{ is measured in mm.} \end{aligned}$$

Now r = order of 8/1000 mm. $\therefore v'/v$ = order of 300.

We thus conclude that the transverse current is ineffective because, to produce the same ionic concentration as a longitudinal current, it needs to be more than 300 times as strong.

The strongest currents used in my experiments were far weaker than this.

COMPARISON WITH FORMER WORKERS ON VARIATION OF EXCITABILITY WITH ANGLE.

(1) FICK(7). He investigated the relation over the range from 34° to 90° by a method which depended upon the nerve dipping into a solution through which a current was passing in parallel lines. The results were in very good agreement with the cosine relation and Fick concluded that this law described them. He found, however, that a transverse current was always capable of exciting, though the strength required was much greater than any used in my experiments.

The explanation of this is probably due to the fact that the nerve, supported at two ends, looped down into the solution. It therefore behaved as in my experiments when the nerve was not slightly stretched. As has been described, this condition gives rise to results which diverge from straight lines by being concave to the origin. This is the very divergence from the cosine relation which Fick obtained.

(2) ALBRECHT and MEYER(8). These workers did not study the relation at various angles but contented themselves with finding whether a nerve can be excited by a strictly transverse current.

They confirmed the above speculation by showing that when great precaution is taken that the current shall be perpendicular to the nerve at all points, the nerve is quite inexcitable.

(3) TSCHIRJEW(6). The results of this worker are in complete disagreement with those of all others. This is probably due again to the failure of the precaution to keep the nerve stretched straight. When plotted in polar coordinates these curves strongly suggest badly bent nerves, and since his nerve was tied by threads to the surface of a glass plate, the extremities would probably be lying in any direction, and this would account for the results.

These results, then, appear to be valueless, and on the whole the earlier work confirms the cosine relation.

The theoretical interpretation of the cosine relation is well summed up by Hermann in his *Handbuch*. He here puts forward three reasons why it is useless to try to establish a relation between excitability and angle.

(1) The nerve is not a homogeneous conductor, and hence the distribution of current in it will vary with angle.

(2) The transverse resistance is greater than the longitudinal, and hence the nerve will appear more excitable to longitudinal currents.

(3) To compare longitudinal and transverse excitability, equal lengths of nerves must be taken, hence in the longitudinal case a length of .01 mm. must be used.

But these objections are only valid if no attempt is made to compensate for the various factors. In the present work, however, each of these is taken into account, and, instead of them rendering the results valueless, they are at the basis of the explanation.

The inefficacy of a transverse current has been shown to be due to the great resistance which a nerve offers to the passage of a current in a transverse direction. So obvious a possibility was not overlooked by the earlier workers, but definitely rejected by them owing to an error which seems to have been peculiarly widespread.

Hermann placed a large number of nerves parallel to each other and found the electrical conductivity of the mass when a current was passed parallel to the fibres, and when perpendicular to them.

The conductivity in the former case was five times that in the latter.

From this it appears to have been very generally concluded that the alteration of conductivity between the longitudinal and transverse directions will only account for an alteration of excitability of 1 : 5.

This, however, is only valid if this ratio represents the variation of current at the place where excitation occurs.

Now on the basis of the above calculations the conductivity of a single fibre to a transverse current is extremely small, and consequently in Hermann's experiment the conductivity measured would be merely that of the fluid between the fibres. The results therefore give no information about the conductivity of the *fibres* themselves, and cannot be applied to this question.

SUMMARY.

(1) The relation between threshold and interpolar length is determined, and the results are given in Fig. 2.

(2) The experimental results accord well with the theoretical curve calculated from the following assumptions:

(a) The nerve is a cylinder with a resistant sheath and a conducting core.

(b) Nernst's assumptions regarding the dependence of excitation upon ionic concentration are accepted.

(c) Excitation is brought about by the current leaving the nerve through the cylindrical sheath.

(3) The relation between threshold and angle is determined and the former is found to vary inversely as the cosine of the angle between the current and nerve.

(4) This cosine relation obtains for different lengths of nerve and different durations of current.

(5) The cosine relation is directly deduced from the mathematics put forward to explain the relation between threshold and interpolar length.

(6) Observations of former workers on these two relations are not inconsistent with the quantitative results of this explanation.

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