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IDENTIFICATION OF LUCAS'S α EXCITABILITY.

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From the experiments of Lucas [1907–8], Jinnaka and Azuma [1922–3], Davis [1922–3] and Watts [1924–5], it appeared that the chronaxie of muscle might assume values very different from that of the nerve. These results were formerly contested by Lapicque and his followers, but as the results of recent experiments made by Lapicque and myself, there is complete agreement on the following points:

(*a*) In certain circumstances a strength-duration curve can be obtained whose time relations are much longer than that of the nerve. This curve is called α (after Lucas).

(*b*) The conditions for obtaining α may be secured by using large fluid electrodes, especially when the cathode falls at the extremity of the muscle.

(*c*) Conditions giving rise to an α curve do not necessarily exclude an excitability (γ) with excitation time (chronaxie) the same as that of nerve. Thus the strength-duration curve may be made up of these two curves meeting at a kink (see figures in former papers, Rushton [1930, 1931]).

With regard to the γ curve which obtains in these circumstances I have recently [1932 *c*] attempted to identify the structure responsible for it with some histological element in the muscle. A very brief summary of this and other investigations relating to the present problem is given later in this paper, suffice it here to state that various kinds of excitability relations, the effect of curare, and of excision of some of the nerve twigs, all unite to indicate that the γ curves arise from the direct excitation of the intramuscular nerves.

This analysis was conducted throughout with large fluid electrodes, and the conclusions are not necessarily valid when applied to results

with needle or capillary electrodes. But in those circumstances where it is possible to obtain an α curve, it appears that the γ curve is there always due to nerves, and the question next arises as to the identity of α. The conclusion that α is due to the excitability of the muscle fibres themselves is so obvious that it requires no very detailed discussion, but we are still faced with the question as to whether the excitation in this case may not be qualitatively of a different kind from that in nerve and in muscle when small electrodes are used.

I am indebted to Prof. Lapicque and to Prof. Adrian for pointing out to me two possibilities which bear upon this matter:

(i) Is the α excitability due to the excitation at the opening of a constant current?

(ii) Is the α excitability associated with the local cathodic contracture and not with the propagated disturbance?

It will therefore be convenient to consider these various questions under separate headings as follows:

Part I. Identification of the α excitability with the muscle fibres.

Parts II and III. Examination of the two above-mentioned possibilities.

This paper concludes the series in which I have attempted to identify the α and γ substances without the use of drugs, fatigue or other abnormal physiological conditions which might alter the chronaxie. In order to bring together the results of this study, Part IV of this paper will include a summary of the chief experimental results together with such conclusions as seem legitimate. Finally in Part V a hypothesis will be advanced to account qualitatively for the great effect of electrode size upon the excitation time of muscle.

Part I. Identification of the α excitability.

Since the γ excitability has been identified with nerve twigs, the presumption that the α excitability is muscle is so great that a detailed investigation as in the case of the γ fibres would be tedious. With hardly any new experiments we may summarize certain conclusions from former papers.

(*a*) The α excitability is found in the nerve-free pelvic end of the sartorius, it persists after curare, and has an excitation time (chronaxie) 10–100 times that of nerve, and therefore it is not nerve or nerve ending.

(*b*) The threshold-angle results [1930, 1932 *c*] show that the α fibres run in the direction of the muscle fibres.

(*c*) The muscle fibres contracting to an α stimulus account for practically all the tension developed by a twitch.

(*d*) These muscle fibres are in a normal condition in that they are supplied by nerves, are found in all muscles, and in all states of survival of the muscle from the intact condition in the spinal animal to the equilibrium state after remaining 24 hours in Ringer's fluid.

(*e*) Bremer has shown that in certain circumstances a muscle (frog's gastrocnemius) may exhibit a contraction very different from the familiar twitch. This phenomenon, which he calls "neuro-muscular contracture," is characterized by the fact that the contraction is very slow, the tension developed slight and the excitation time of the underlying excitability long. He finds in fact that the excitation time is about a hundred times as long as that for the motor nerve [Bremer, 1930, p. 315], which is just the order of magnitude of the α excitation time. The question therefore arises as to whether the α contraction is to be identified with the neuro-muscular contracture.

It has already been shown [Rushton, 1932*a*] that the tension time of the α contraction is the same as that of the ordinary twitch, whence it was concluded that the α contraction was an ordinary one. If this is correct α cannot be a neuro-muscular contracture which is much slower and weaker [Bremer, 1930, p. 315]. But since it is conceivable that Bremer's contracture might have the same tension time as a twitch—gaining in duration what it lost in intensity—tension time alone will not definitely exclude the identification with the α contraction; for this exclusion an isometric α record is required. In a former paper [Rushton, 1931] it was remarked in a footnote that the isometric twitch was identical whether the excitation was through the nerve or the α substance. The experimental evidence in support of this statement has not been presented and is as follows.

The sartorius muscle was set up as usual in a trough with fluid electrodes of the "block" type applied to the pelvic end with the anode towards the pelvis. The tibial tendon was attached to a rather stiff insensitive tension lever writing on a smoked drum. A strength-duration curve was obtained as shown in Fig. 1 plotted in double logarithmic coordinates. The curve is obviously composed of γ and α portions which may be extrapolated as shown with fair accuracy. Five isometric records were now taken, when the direct stimulus to the muscle was of strength and duration indicated by the triangle, circles and crosses in Fig. 1. It is seen that the crosses are above the γ threshold but below the α, whereas the remainder are above the α threshold but below the γ. Fig. 2

shows the five isometric twitches arising from these stimuli. The amplitude of the tracings was small and Fig. 2 gives the result of measuring the records under a lens, scaling to a common maximum and replotting.

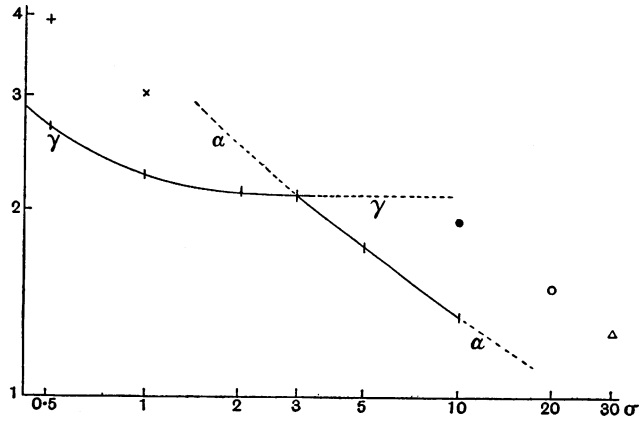

Fig. 1. Strength-duration curve of sartorius. Ordinates, current strength in arbitrary units scaled in logarithms; abscissæ, durations in σ scaled in logarithms.

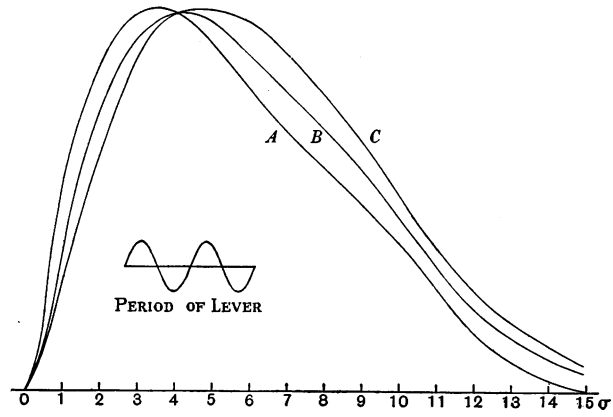

Fig. 2. Isometric twitches of muscle of Fig. 1. *A*, *B*, *C*, when stimuli were crosses, circles and triangles respectively (Fig. 1). Abscissæ: time in σ. Inset: natural period of lever with muscle attached.

The curves from the two stimuli indicated by a cross in Fig. 1 were practically identical (*A*), also the two circles gave nearly coincident curves (*B*), the triangle is represented by *C*. The natural period of the lever with muscle attached is inset. It is seen at a glance that to a first approximation the isometric twitch is identical whether elicited through

γ or α, and it is quite out of the question to suppose that the α contraction has the time course of Bremer's contracture. With regard to minor details in Fig. 2 it is seen that the longer the duration of the stimulus the later lies the maximum and the relaxation phase of the curve. This is easily accounted for by the fact first that the branching nerve fibres cause the γ stimulus to spread quickly all over the muscle, whereas the α excitation is propagated relatively slowly along the muscle fibres. Second, that when the duration of the stimulus is long the various fibres are not all excited at the same moment. Consider, for instance, the strength and duration represented by the triangle (Fig. 1). When this current has only lasted 12σ the threshold fibres respond, and more and more fibres enter over the next 18σ. Clearly this scatter in the moments of reaching the threshold will cause just the observed kind of modification in the shape of the isometric twitch.

Thus in spite of the crudeness of the lever employed it may safely be concluded that the twitch has the same time course whether elicited from an α stimulus or a γ one (*i.e.* through the nerve), and since the tension time is also the same, so must be the tension developed.

The α contraction therefore cannot be the same as Bremer's neuromuscular contracture, since both the time course and the tension developed are of quite different orders of magnitude.

We may thus conclude that the α excitability is that of the ordinary muscle fibres, that all the muscle fibres exhibit this excitability, and that the fibres are in good physiological condition.

Part II. Is the α curve due to the opening excitation?

It is classical that a tissue can be excited as the result either of the closing or the opening of a constant current. Normally the closing is so much more effective than the opening that if threshold currents are used, the latter effect does not enter. By using a dense anode, and a diffuse cathode however, or by killing the nerve under the cathode, the reverse may be the case, and a brief constant current now stimulates at the anode as the result of the cessation of the current. The strength-duration curve in this case has been investigated by Cardot and Laugier [1912], who found a "chronaxie" much longer than normal, and Prof. Lapicque was good enough to point out to me that the α curve might well be due to this phenomenon. He himself was investigating the question at the time of writing, and in a subsequent paper he has stated that the suggestion was not borne out by experiment

[Lapicque, L. and M., 1930], but since he does not mention what experiments he performed, it may not be superfluous here to describe a few which I made at the same time and which confirm his conclusion that the α excitation is brought about by the closing not the opening of the current.

My experiments were of six kinds, the first three showing that excitation occurred at the cathode, relying upon the validity of Pflüger's Law for its application to the present problem, and the second three showing directly that excitation was not the result of the cessation of the current.

(i) *The effect of temperature.*

The sartorius muscle of the frog was set up as shown in Fig. 3, upon the floor of a rectangular bakelite trough; a 1 cm. block was placed

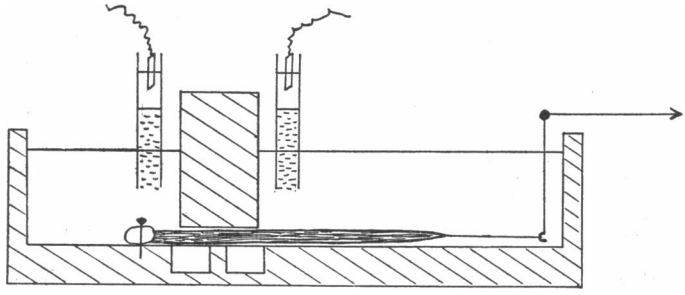

Fig. 3. Apparatus for warming and cooling anode and cathode with "block" electrodes. Note channels for hot and cold water in floor below block separated by mica sheet from fluid in trough.

above it near the pelvic end and non-polarizable (Zn-$ZnSO_4$-Agar-Ringer) electrodes arranged so that the current passed under the block, the cathode being near the pelvis. The floor of the trough below the block was cut away as shown to make two channels. These channels were completely separated from the interior of the trough, however, by very fine sheets of mica. In this way water at various temperatures could be passed through the channels without flowing into the trough, but the muscle, lying on the mica sheet, came intimately into contact (at the lower surface at least) with the temperature of the water. It was thus easy to warm or cool the anode or cathode independently and observe the effect upon the α curve.

The procedure was as follows. The muscle was set up and allowed to rest for an hour. The strength-duration curve was then taken at room

temperature (I). Then cold or hot water flowed below the cathode and anode as indicated below.

	Cathode	Anode
(II)	Cold	Cold
(III)	Cold	Hot
(IV)	Hot	Cold
(V)	Hot	Hot

Finally water at room temperature was passed through both channels (VI) as a control upon progressive changes. Fig. 4 shows the result of

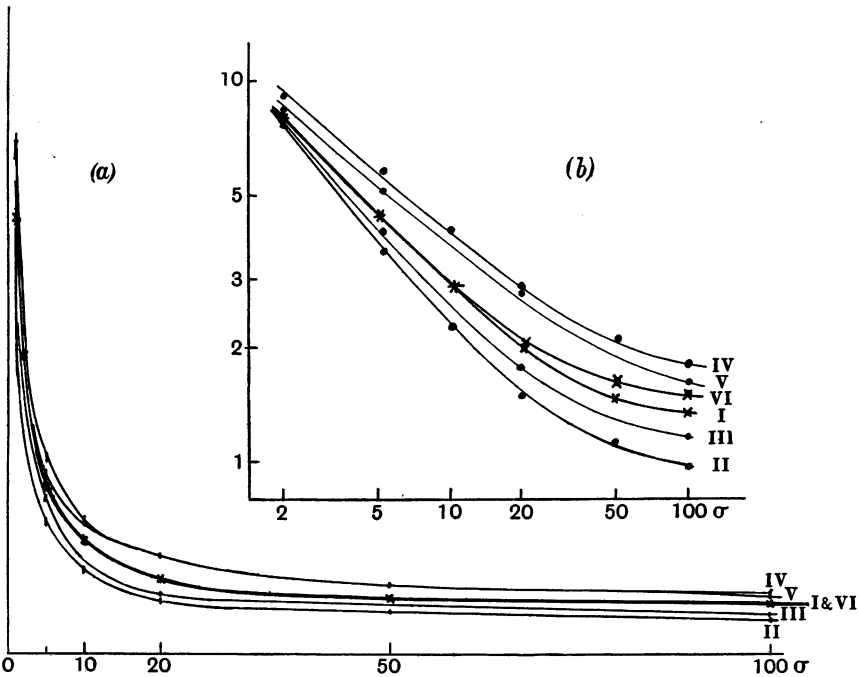

Fig. 4. (*a*) Strength-duration curves at various temperatures of anode and cathode (see text). Linear coordinates. (*b*) Curves of Fig. 4 *a* replotted in logarithmic coordinates.

an experiment where the room temperature was 10° C., and the cold and hot water in the channels was at 4° C. and 32° C., though the muscle probably did not attain these extremes. The complete set of observations took about 2 hours to accomplish, and at the end of that time the threshold had risen some 15 p.c.; to minimize the appearance of this progressive change in Fig. 4 it is assumed that the change occurred at constant rate, and each set of readings is reduced accordingly. Since

the temperature variations of threshold which concern us are greater than 100 p.c., the above assumption cannot in any case involve great error.

It is seen at once from Fig. 4 that when the cathode is cooled (curves II and III) the curve lies below that at room temperature (crosses), no matter whether the anode is hot or cold. Similarly when the cathode is warm (IV and V) the curve lies above, independent of the temperature of the anode. It is thus clear that the cathode is the region which characterizes the α threshold.

It may be wondered why threshold has been used above as criterion rather than excitation time. The latter measure involves an accurate knowledge of the rheobase, which in these α curves is an unreliable measurement, for the current has often to flow for a whole second or more before the contraction occurs, and the resulting polarization produces a change of threshold which is irreversible, or but slowly reversible, so that the rheobase is the least accurate of all points on the curve, and quite unsuited to take part in a characteristic constant.

Another application of temperature alteration to the present problem was as follows. The strength-duration curve for the sartorius was obtained with the same apparatus at room temperature, and then the current was reversed, and a second curve obtained. This second curve (as usual) showed a γ portion, but α was still prominent, and in one typical experiment the threshold lay on the α curve at a duration of 10σ. Thus at 20σ the threshold was undoubtedly α, whatever the direction of the current. The fluid was then withdrawn from the trough and a few drops of hot Ringer's fluid (40–50° C.) were dripped on to the muscle near the pelvic end of the block. Then the withdrawn fluid was replaced and the thresholds again determined for both directions of current at 20σ duration.

The results were as follows:

Initial threshold when cathode lay towards pelvis	14–13·5
,, anode ,,	17–16

After hot drops:

Threshold when cathode lay towards pelvis	20–19
,, anode ,,	18–17

It is clear that the treatment by heat caused no appreciable change in threshold when the anode lay towards the pelvis, but caused a marked decrease in excitability when the current flowed in the other direction. That is to say the excitability was affected by change at the cathode but not by change at the anode.

(ii) *The effect of electrotonus.*

The apparatus was that of Fig. 3, but in this case two additional electrodes were added. They were in the form of silver plates chlorinated and placed at a distance of 2 or 3 mm. apart close up to the block, both on one side or both on the other. When the Ag-AgCl electrodes were placed on the pelvic (cathodic) side of the block the polarizing current greatly affected the height of contraction resulting from an α stimulus sent in through the Zn-$ZnSO_4$ electrodes and localized under the block. The α stimulus was first adjusted to give a moderately small twitch when the polarizing current was not flowing. Then this current was turned on with the anode towards the block, and while the polarization continued the α stimulus was again sent in. The contraction now was abolished or much reduced. Reversal of the polarizing current on the contrary caused a considerable increase in the size of the twitch above the initial value. These results were not obtained, however, when the anode of the α stimulus was polarized, for when the polarizing electrodes were placed on the tibial side of the block it was found that the polarizing current had no effect upon the threshold or height of contraction resulting from the α stimulus. We must therefore conclude again that the condition of the cathode is responsible for the α excitability.

(iii) *Measurement of conduction time.*

The apparatus used for this experiment is that described more fully later in this paper (Part III (*b*)). Suffice it here to say that the sartorius muscle was firmly clamped at the middle, and each end was attached to a lever writing on a fast-moving smoked drum. The usual block electrode was placed over the pelvic end and a duration of stimulus used which elicited an α contraction for either direction of current. Since the stimulus is applied in all cases to the pelvic third of the muscle the pelvic lever will move before the tibial one will, and this difference in latent period will obviously be more pronounced when excitation occurs at the pelvic end of the block than when the current is reversed and excitation occurs nearer the middle of the muscle.

A typical experiment gave the following results at a temperature of 20° C.:

	Difference of latent period
Cathode towards middle	15·8 σ
Repeated	16·3 σ
Cathode towards pelvis	25 σ
Repeated	26 σ

There is no question but that the latent period is greater when the *cathode* is the more eccentric, again showing that the α excitation arises from the cathode.

(iv) *A rheobase current.*

Turning now from the polar properties of the α excitation to direct temporal considerations, the simplest and perhaps the most convincing proof that the α excitation is not an opening excitation lies in the fact that the α strength-duration curve may be obtained as a smooth curve down to the rheobase, and the rheobase current certainly does not stimulate by an "opening excitation," for the stimulation is obtained

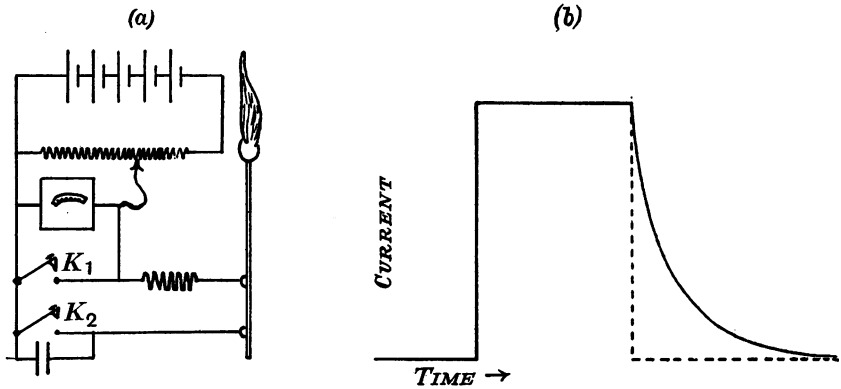

Fig. 5. (*a*) Circuit for stimulating with a current of the form shown in Fig. 5 *b*. (*b*) Rectangular current with exponential tail. Ordinates, intensity; abscissæ time.

equally when the current is allowed to flow on indefinitely. In fact I have never been able to obtain an opening excitation at all, since before the requisite intensity is reached the muscle goes into a prolonged closing tetanus which makes further increase of current valueless.

(v) *An exponential finish to the constant current*[1].

It is well recognized that the efficacy of a current of given intensity is very much reduced if it rise slowly rather than abruptly to its constant value. In the same way the efficacy of the opening excitation is greatly diminished if the current subside but gradually. By placing a condenser (as shown in Fig. 5 *a*)[2] across the second key of the usual strength-duration

[1] I am indebted to Dr Monnier of the Sorbonne (at this time passing through Philadelphia) for this elegant method.

[2] In a former publication [Rushton, 1932*b*] Fig. 6 contains an error which, however, does not affect the text. R_2 should obviously be connected not to the extremity of the potentiometer, but to the slider, as in Fig. 5 (*a*) above.

apparatus, the current will not cease immediately upon opening K_2, but will decline exponentially as the condenser charges (Fig. 5 *b*). The effect of the condenser will clearly be twofold. In the first place it will cause a gradual decline instead of a sudden one, in the second it will cause an increase in the total quantity of electricity flowing.

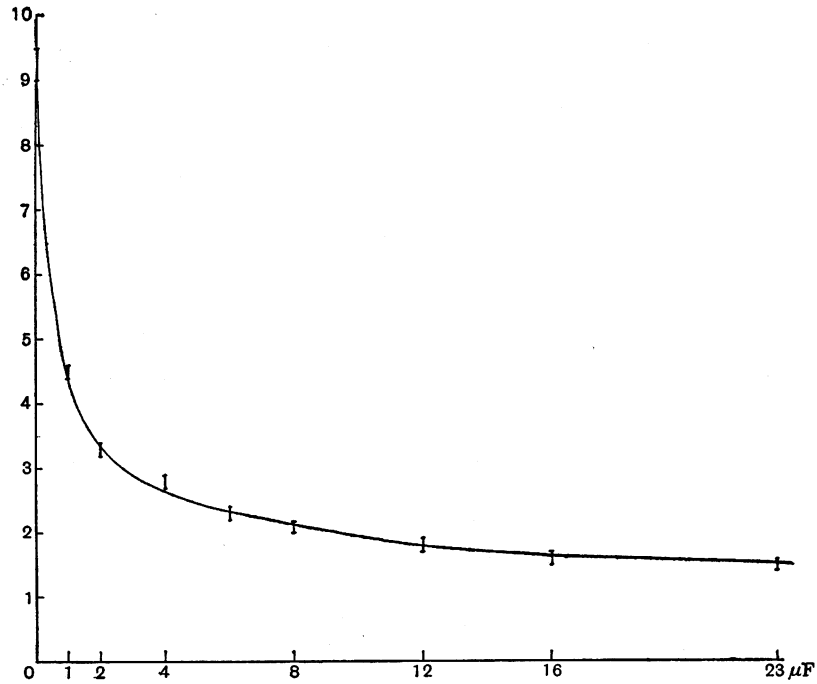

Fig. 6. Relation between strength (ordinates) and capacity in microfarads (abscissæ) for threshold stimulation by a current of the form shown in Fig. 5 *b*. Duration of constant current = 5 σ, resistance through which condenser discharged = 30,000 ohms.

In view of the first it will cause an opening excitation to be less effective; in view of the second it will cause a closing excitation to be more effective. We may easily see whether in fact the condenser increases the efficacy or the reverse and hence learn whether the excitation is opening or closing.

From the experiment it at once appeared that the larger the capacity the more effective was the stimulus, showing that at all durations (and in this case especially the short ones) the α curve involves the closing excitation. Fig. 6 shows threshold plotted against capacity for a dura-

tion of constant current of 5σ; the lowering of threshold with increasing capacity is beyond question.

(vi) As a particular case of the foregoing we may consider the condition when there is zero duration of constant current, *i.e.* the ordinary voltage capacity curve obtained with condensers. As has already been published [Rushton, 1931] this curve resembles the α strength-duration curve in its long time relations as compared with nerve. There is no possibility that in this case we are concerned with the opening excitation since the threshold is lower when the stimulus declines more slowly, and thus those results confirm all the foregoing.

From the several kinds of evidence put forward we may certainly conclude with Lapicque that his earlier suggestion to account for the slow α time relation is not the case, and that the α excitation is elicited from the cathode by the processes set in operation at the start, not the cessation of a current.

PART III. IS THE α CONTRACTION PROPAGATED?

It is known that the direct excitation of muscle may give rise to two kinds of contraction, one propagated and the other localised at the cathode (Tiegel's contracture). Prof. Adrian was good enough to point out to me the possibility that the γ excitability might be correlated with the propagated contraction and the α with the contracture. This would obviously be a very satisfactory explanation of certain difficulties which are involved in reconciling the α phenomena with the views of Lapicque. The slow contracture would have a slow excitation time, the propagated contraction would be isochronous with the similar phenomenon in nerve. Unfortunately, however, this is not the solution of the difficulties for the α contraction is propagated. To show this I used two well-known methods, (*a*) by recording the thickening of the muscle at a point distant from the electrodes, (*b*) by clamping the muscle in the middle, stimulating in one half and noting the shortening of the other half. We proceed to a more detailed description.

(*a*) *Investigation of local thickening.*

The sartorius muscle was set up in a trough as usual and excited by the current concentrated below an ebonite block placed over the pelvic end of the muscle with the cathode towards the pelvis. The muscle was either attached by the tibial end to a light tension lever in the usual way (recording total shortening) or else it was looped loosely on the floor of

the trough, and over the tibial end rested a light small aluminium plate connected by a highly magnifying lever system to a pointer which would record by movement any thickening of the muscle under the little plate. In some experiments the muscle was tied down between the loop and the plate, to avoid any residual mechanical tug from the local con-

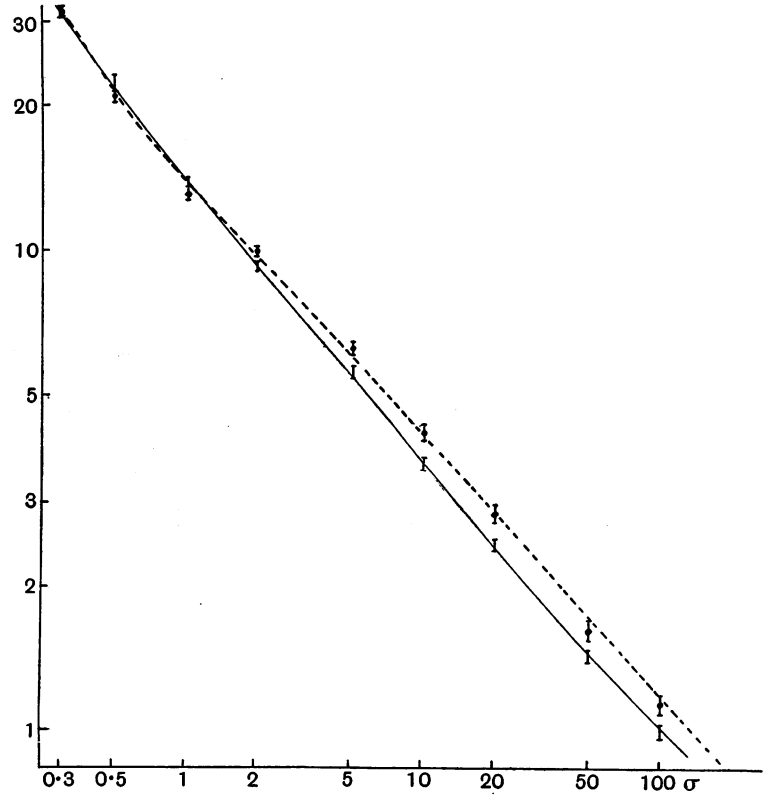

Fig. 7. Strength-duration curves of sartorius clamped in middle plotted logarithmically in both scales. Left of each pair of vertical lines represents threshold for pelvic contraction, right represents threshold for tibial contraction. Thresholds are identical throughout.

tracture, but the control indicated that there was no such tug. Strength-duration curves were obtained using as index either total shortening (continuous line, Fig. 7) or tibial thickening (intermittent line), and the results show clearly first that an α curve could be obtained equally by either method, second that the two curves were almost identical. The results are plotted in double logarithmic coordinates for clearness.

The slight divergence from identity in the two curves has no significance. The room temperature of 33–37° C. at this time made it necessary to conduct the experiment in a cooled box at about 15° C. The box had to be opened and the muscle trough withdrawn in order to change from one type of lever to the other, and thus a disturbance of temperature equilibrium as well as a difference of resting tension and exact localization of the cathode, all contributed to the slight difference observed in the two curves. These errors do not enter into the second type of experiment to be described, and here the two curves are absolutely identical.

(*b*) *Double lever experiment.*

A special trough was constructed which allowed the sartorius muscle to be clamped firmly at its middle, and to have both extremities attached to levers. I was not able to clamp the muscle rigidly without damaging some of the fibres, but a form of clamp which was found satisfactory was formed by a soft rubber strip in the floor, and above the muscle a hard rubber block about 3 mm. thick and as wide as the cross-section of the trough, having blunt teeth on the lower surface (Fig. 8). This was gently lowered on to the muscle until it gave a twitch, whereupon the block was clamped in that position. The muscle was attached to the two levers before clamping, so that the two halves of the muscle were at approximately the same tension. A 1 cm. block was placed over the pelvic portion of the muscle as usual and Ag-AgCl plates served as electrodes on either side of it, cathode towards pelvis, care being taken that neither block nor electrode touched the muscle. A strength-duration curve was then obtained using as index first the tibial then the pelvic lever, but in practice it was found that both levers moved together or not at all in nearly every case. Fig. 9 shows the results of one typical experiment, where the strength-duration curve is plotted in double logarithmic coordinates; each experimental "point" consists of two vertical lines representing the thresholds indicated by each lever. The experimental error (length of line) is seen to be about 5 p.c., and within those limits the threshold is identical for the two levers at all durations. There was practically no exception to this in any experiment, the greatest observed divergence being one of 10 p.c., where the threshold for tibial contraction was consistently higher by this amount. The explanation was no doubt that in this particular case the most excitable pelvic fibres were crushed at the clamp. If these results are accepted, therefore, it shows in a most convincing way that the α contraction is propagated.

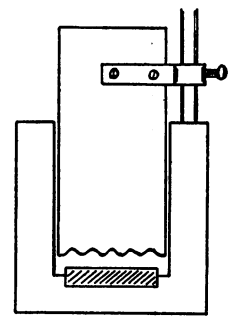

Fig. 8.

But the results cannot be accepted until we are satisfied that the movement of the tibial lever was not due just to passive pull under the clamp, and the real experiment consists in providing this evidence. In every case where the above determinations were made, two or more different controls were made as to the firmness of the clamp, and in no case was any slipping found to occur with tensions many times greater than those

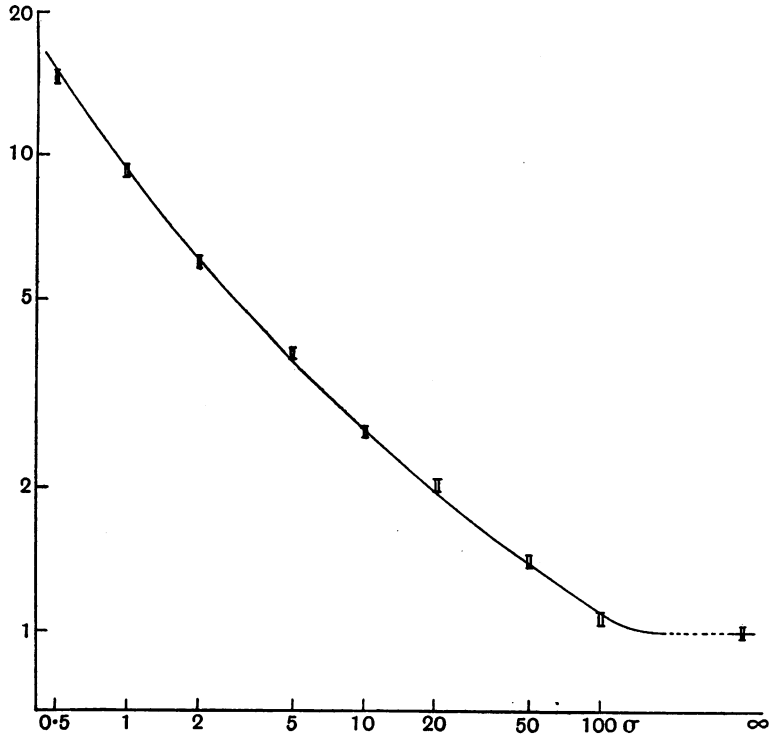

Fig. 9.

developed in these threshold measurements. The controls employed were as follows:

(*a*) Moving by hand the pelvic lever to far greater amplitudes than those actually involved, caused no movement of the tibial lever. The movements applied were sudden flicks to resemble the muscle twitch as far as possible.

(*b*) The muscle was killed with a hot iron applied along a transverse line on the tibial half not far from the clamp. A moderately strong

pelvic contraction now gave no movement of the tibial lever, though the increased rigidity of the killed portion would facilitate the propagation of a mechanical wave. It was finally ascertained that the opacity and swelling did not extend as far as the clamp, so that the muscle was not clamped more firmly by the process of killing.

Temperature coefficient of latent period difference.

The difference in the latent period of the two levers was due to the time occupied in the propagation of the contraction or of the passive tug from the pelvic to the tibial half. It would be expected that the temperature coefficient of propagation would be high, but that of a passive tug would be near unity. The latent period difference was easily measured from tracings on a fast-moving smoked drum, and from repetitions at various temperatures the temperature coefficient was obtained. Most of the observations fell in the region 15–25° C., in which range the Q_{10} lay between 1·5 and 2·3. The error is rather large, but even the lower limit is high for the effect of temperature upon a mechanical tug. Moreover, though flicking the pelvic lever causes no movement of the tibial one, yet often the contraction of the muscle causes equal excursions of the two levers, which is very difficult to explain unless the contraction is propagated.

Dependence of contraction upon local temperature.

If the two halves of the trough contain fluid at different temperatures, the rate of contraction of the pelvic half will be faster the higher the pelvic temperature. The rate of contraction of the tibial half on the other hand will be faster the higher the tibial temperature only if the contraction is propagated; clearly if it is due to a slipping at the clamp then it will be faster when the pelvic temperature is higher. The tracing (Fig. 10) shows clearly that the rate of contraction of the tibial lever is greater with higher local temperature but lower pelvic temperature, hence the contraction is propagated.

In view of these several controls, therefore, we may safely conclude that the muscle clamp was firm and that movement of the tibial lever signified a propagated contraction. This section therefore confirms and extends the results of section (*a*), and since in these experiments at least there was no appearance of Tiegel's contracture below the threshold for a propagated wave, it is clear that the α curve is not due to the use of this contracture as index of excitation.

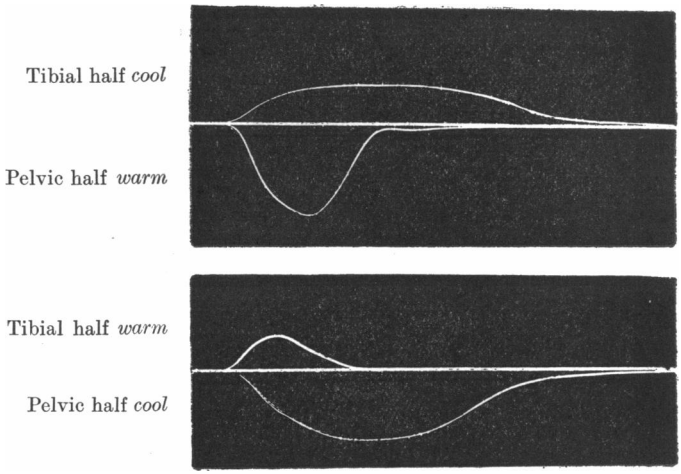

Fig. 10. Tracing of contraction of sartorius clamped in middle; read left to right. Each pair is a simultaneous record of contractions of two halves of muscle. Tibial above shortening upwards, pelvis below shortening downwards.

PART IV. CONCLUSIONS REGARDING α AND γ EXCITABILITIES.

The literature of muscle excitation contains a considerable body of work upon the change of muscle chronaxie with drugs, fatigue, etc. In the majority of these cases it is not clear whether the tissue actually excited is muscle or nerve, or (more misleading still) whether the rheobase current excites muscle and one of twice this intensity at its minimum effective duration (*i.e.* chronaxie point) stimulates nerve, the chronaxie in this case being mainly dependent upon the relative accessibility of the two tissues to the stimulating current. This confusion, it appeared to me, was largely the result of using small "stigmatic" electrodes whereby the excitation time of muscle approaches that of nerve so that the two excitabilities are almost inevitably confused even when the whole strength-duration curve is plotted. In those experiments (unfortunately the majority) where the whole curve was not plotted but the determinations merely restricted to two points—the rheobase and double this intensity—the chronaxie measurement gives very little certain information. If observations have been such, for instance, that the authors have concluded that the muscle chronaxie has increased, it may be alternatively either that the nerve chronaxie has increased, or that the rheobase of the nerve has increased more than the muscle

rheobase has (or decreased less). But as this latter type of change is very likely to occur as the result of slight shifting of the electrode contacts, drying, etc., and especially if the tissue has to be removed, bathed, or manipulated, as is often essential for treatment with drugs, etc., these experiments require far more rigid controls than most accounts suggest have in fact been employed.

It was with the object of developing a technique to distinguish muscle from nerve, and rheobase change from chronaxie change that I undertook the investigation described in the series of papers [Rushton, 1930–2]. The essence of the difference between this method and that of Lapicque was the use of large fluid electrodes, which, as Lucas had shown [1907–8], give a long excitation time to muscle whilst leaving that due to nerve brief. Since Lucas's results had been questioned by Lapicque [1926] it was necessary first to confirm them in such a way as to meet Lapicque's criticisms. Next it was important to be able to obtain α and γ curves alone or combined as required, and finally to identify α and γ with muscle and nerve respectively in a more conclusive manner than had been done hitherto. Nearly all these experiments were made upon fresh surviving, undrugged muscles in what is generally considered good physiological condition. When for certain controls curarized muscles were used, it was left an open question as to whether the drug changed the chronaxie or not. The results of these experiments may therefore be applied without prejudice to future work upon the action of drugs and abnormal conditions.

Since the various phases of the argument are necessarily rather scattered in different numbers of this *Journal*, it may not be out of place to summarize here the principal steps.

(i) *The presence of two excitabilities was detected as follows:*

(*a*) The strength-duration curve when free from kinks was of one or other of two kinds, either γ with an excitation time the same as nerve, or α with a much longer excitation time [1930].

(*b*) When the strength-duration curve exhibited a kink, it consisted of γ at short durations and α at long durations, and the proportion of the two could be altered at will [1930].

(*c*) Threshold angle curves showed two excitabilities, one corresponding to fibres parallel to muscle and having α time relations, the other corresponding to fibres in quite a different direction (or directions) having γ time relations and being removed from activity by curare [1930, 1932 *c*].

(*d*) When the strength-duration curve appears to be nearly ex-

clusively γ, the appearance of α when present may be conclusively confirmed by latent period measurements [1931].

(*e*) In such cases also a double contraction arises from a constant current, the first due to γ excitation, the second to α more than 30σ later [1931].

(*f*) Kinks cannot be due to faulty contacts, etc. (cf. criticism by Hou [1931] of observations by Kodera [1928]), for in addition to the above evidence, results were obtained with four different pendulums, and with excitation by condenser discharges, and the kinks varied systematically with the position of the electrodes on the tissue [1930, 1931].

(ii) *The suggestion that α is due to some abnormal condition of the muscle appears to be incorrect on the following grounds:*

(*a*) An α curve of the usual form was present in spinal animals and in excised muscles at various times from excisions till 24 hours later [1930].

(*b*) The α substance is in physiological connection with its motor nerves [1932 *a*].

(*c*) The α curve may be elicited from all of a dozen different muscles investigated [1931].

(*d*) The α excitation is not due to the cessation of the exciting current (opening excitation) [*this paper*].

(*e*) The α contraction is not a Tiegel's contracture, but is propagated [*this paper*].

(*f*) It is not Bremer's neuromuscular contracture [*this paper*].

(iii) *The γ excitability obtained with fluid electrodes is due to the intramuscular nerves* [1932 *c*], *since:*

(*a*) The γ excitability has the same excitation time as nerve.

(*b*) The γ excitation time is like that of nerve nearly independent of electrode size.

(*c*) The γ substance is in the form of fibres.

(*d*) In the sartorius these fibres start their course at the exact place where the nerves enter.

(*e*) They run in this muscle towards tibia and towards pelvis for 8 mm. or more.

(*f*) In the sartorius they run in many directions, in the sterno-cutaneous strip they run in the direction of the nerve twig, and more or less perpendicular to the muscle.

(*g*) They are absent from the nerve-free pelvic extremity of the sartorius.

(*h*) When the strength-length curves from the sartorius show more than one excitable point, these always correspond to sharp bends in the nerves, and are closely correlated with nerve distribution despite the great variation from preparation to preparation.

(*i*) When the nerve is carefully removed by dissection from the surface of the sartorius, the γ curve initially very prominent disappears entirely from the cleared region.

(*j*) The action of curare upon the γ excitability is to abolish it completely by the time the indirect excitation (through the nerve) has failed.

(iv) *The α excitability is due to the muscle fibres themselves, since:*

(*a*) The α excitability is found in the pelvic (nerve-free) end of the sartorius, it persists after curare, and is due to fibres running in the direction of the muscle fibres (threshold angle results) [1930, 1932 *c*].

(*b*) The muscle fibres contracting to an α stimulus account for practically all the tension time developed by a twitch, and exhibit the same time tracing as a twitch [1932 *a*, and *this paper*].

In view of the experiments summarized above, the object of the investigation appears to be achieved, in that it is certainly possible by using fluid electrodes to obtain the strength-duration curve either of muscle or of intramuscular nerve fibres separately and without fear of confusion. This technique therefore avoids all those errors mentioned earlier which may invalidate the results when stigmatic electrodes are employed. Moreover the fluid electrode is particularly suited to the investigation of tissues in various conditions, for not only are errors due to drying eliminated, and variations in the exact contact of the electrodes excluded, but also these electrodes are better than most for investigations involving changes in the fluid bathing the muscle, since the fluid may be exchanged or circulated without affecting the contact between electrode and muscle.

An objection to the use of fluid electrodes, however, has been recently raised by Lapicque [1931 *a*, *b*], who claims that a strength-duration curve obtained in this way does not characterize the condition of the muscle as does the curve obtained when one of his forms of electrode is used. The original basis of this claim was that all truly characteristic curves must fit a certain empirical formula (Lapicque's Canon), but this argument loses its force when it appears [Rushton, 1932 *b*] that Lapicque's own method as applied to the frog's sciatic nerve does not satisfy the Canon, and that the divergence from the Canon which Lapicque's experiments show is real and not due to inductance errors, as he had supposed.

In a recent publication, however, Lapicque [1932] has put forward in a preliminary account, a theory to explain the "α effect," a correct understanding of which effect will naturally lead to the appreciation of the value and limitations of fluid electrodes. It will therefore be better to leave further discussion of this matter until a more complete development of Lapicque's theory has appeared.

In any case, whatever property of the muscle the α excitability characterizes, this method of excitation has the very considerable advantages that muscle is not confused with nerve, and the results are accurately reproducible.

PART V. A PHYSICAL EXPLANATION OF THE "α PHENOMENON."

Perhaps the most interesting question which arises in connection with the α excitability is why the excitation time varies over so wide a range depending upon the type of electrode used. Now it may be shown that some variation of this kind necessarily follows from the physics of current distribution in muscle according to certain widely accepted ideas concerning excitation, but I had not intended to put forward this explanation before obtaining further proof of a quantitative nature. Since, however, an alternative hypothesis is being developed by Lapicque it seems of value to state here as briefly as possible the essential of the other for comparison.

The hypothesis I wish to put forward rests upon the following assumptions:

(*a*) A muscle fibre is a cylinder with a conducting core and a relatively resistant and polarizable sheath.

(*b*) Excitation results from the cathodal polarization of this sheath, which polarization must attain a critical value at some point.

(*c*) Ions are concentrated against the sheath owing to the applied electric field; the concentration is dissipated owing to the concentration gradient and potential gradient developed by the redistribution of ions.

If the current polarizing a large plane membrane is uniformly distributed over the whole of its extent (Fig. 11 *A*), then the motion of ions must be entirely perpendicular to the membrane (except near the edges where lateral diffusion may occur). If on the contrary the polarizing current is greater at one point (*P*) (Fig. 11 *B*) than others, the motion of ions will no longer be linear, for though the concentrating force is still along the normals to the membrane, yet, since the concentration at *P* is greater than at all other points in the neighbourhood,

diffusion will take place in a lateral as well as a normal direction. If now we imagine the plane rolled into a cylinder (with axis in the plane of the paper) so as to include the arrows, we obtain the condition of muscle excitation represented in the foregoing assumptions. The current passes through the sheath radially, and the above argument still holds. The conclusion is that if the muscle fibre is sufficiently long for the end corrections to be negligible, or if the ends of the cylinder are closed, then normal back diffusion alone will occur so long as the current leaving the sheath is the same at all points. If this polarizing current is localized to the neighbourhood of one point (by a stigmatic cathode for instance), then a lateral diffusion will be added to the normal back diffusion, and

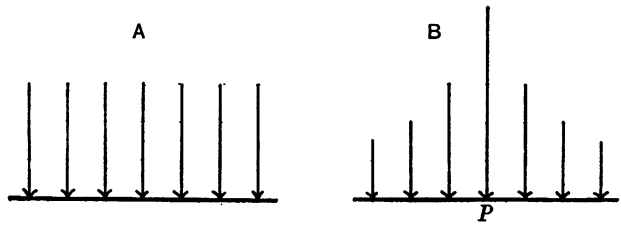

Fig. 11. Diagram of electric field forcing ions up against a membrane. Length of arrow represents magnitude of force at this point.

clearly this lateral diffusion will be more prominent the more localized the stimulus.

It remains to show that increase in lateral diffusion causes shortening of excitation time. For this argument it will be assumed that the amount of polarization developed by a given current in a fixed time is proportional to the intensity of the current.

This relation, introduced here as an assumption, follows as a necessary consequence of the application of linear differential equations to the excitation process. Since linear differential equations govern such phenomena as the flow of electricity in capacitative networks, continuous media, etc., and also the diffusion of particles and the propagation of waves, it would not be surprising to find that they also govern the excitation process which is supposed to depend upon these physical manifestations. In fact the theories of Nernst, Cremer, Hill, Ebbecke, etc., all express themselves in linear equations, and hence the above assumption may be deduced from each of them but is by no means limited to any one.

Let us consider two cases A and B (Fig. 12) where the current polarizing the membrane has the same maximum h in each case, but where the current falls off laterally much more rapidly in A than in B. Then the development of polarization at points A and B will depend

partly upon the polarizing current (the same for each at this point) and partly upon the normal and lateral diffusion. At the start, the concentration developed will be insignificant, hence the back diffusion will be negligible, and both polarizations will initially develop along the straight line *OP*, Fig. 13. But since lateral diffusion is much more pronounced in *A* than in *B*, the opposition to the linear increase in concentration will develop sooner and more markedly in case *A*, and curve *A* (Fig. 13) will diverge the sooner from *OP* and will reach the horizontal at a lower level than *B*. But since it is assumed that the amount of polarization produced is proportional to the intensity of the polarizing current, then

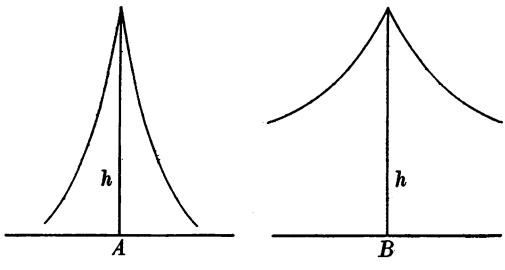

Fig. 12.

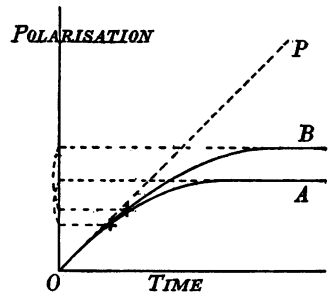

Fig. 13.

Fig. 12. Diagram of electric field forcing ions up against membrane. Ordinates of curves correspond to arrows in Fig. 11, *i.e.* to magnitude of force at various points along the membrane.

Fig. 13. Diagram of development of polarization in case *A* and *B*, Fig. 12. *OP* = development in absence of back diffusion. Crosses represent excitation times in two cases: greater lateral diffusion produces shorter excitation time.

the curves in Fig. 13 may be interpreted as follows. To produce a given threshold polarization, a long-lasting current (rheobase) must be higher in case *A* than in case *B*, but with currents of very short duration, the thresholds will be the same in the two cases. Hence *A* is relatively easier to excite at short durations, *B* at long durations. But it is known experimentally that tissues with short excitation times are those relatively easier to excite by brief currents, and *vice versa*; consequently, the greater the lateral diffusion, as in case *A*, the shorter the excitation time.

In view of these considerations we may conclude that the foregoing very generally accepted assumptions, without any new hypothesis, necessarily involve that the excitation time from stimulation with stigmatic electrodes will be less than from stimulation with large fluid electrodes. Whether the difference in the two cases is of the right order of magnitude

or not cannot be deduced from this qualitative analysis, but it seems worth while before postulating new conditions and mechanisms to see how far the foregoing concepts will take us.

It is interesting to note that lateral diffusion may explain also, qualitatively at least, three other well-known questions in nerve-muscle excitation.

(i) Nernst in his classical development of a Law of Excitation assumed that diffusion was only normal to the membrane. This we have seen is not in fact the case and lateral diffusion plays a very conspicuous part when stigmatic electrodes are employed (as in most of the experiments to test Nernst's Law). If Nernst's equation is solved for the two dimensional case

$$\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} = \frac{1}{\kappa}\frac{\partial c}{\partial t}$$

with boundary conditions similar to his, it is found that a strength-duration curve is obtained which is not asymptotic to the axis of durations but which has a finite rheobase, thus removing the most obvious and classical of the objections to Nernst's theory.

It is not unlikely that Nernst's neglect of the back E.M.F. of polarization was more serious than his neglect of lateral diffusion, but it is interesting to note that a finite rheobase may be deduced with no modification of Nernst's assumptions other than the obvious one that the cathode is more intensely polarized than other neighbouring points.

(ii) It has been known for many years that the excitation time of nerve depends upon the distance apart of the electrodes [Cardot and Laugier, 1914], and Lapicque [1931 *b*] recently has claimed that the same occurs with muscle excited through fluid electrodes. These observations are exactly what we should expect from the concept of lateral diffusion, for when the electrodes are close together there must obviously be a very rapid falling off in concentration from the critical exciting value at the cathode to zero at a point about half-way between the electrodes (Fig. 14), whereas the variation will be spread over a much greater distance with great interpolar lengths. Consequently in the former case there is a great lateral diffusion between anode and cathode which causes the excitation time to be shorter with shorter interpolar lengths.

(iii) The behaviour of nerve differs strikingly from that of muscle in regard to a change from stigmatic electrodes to fluid ones. Unless the present hypothesis is able to account equally for the comparative constancy of the nerve excitation time as for the great variability of the muscle excitation time, it obviously is inadequate. As a conducting

medium for electricity the medullated nerve differs from muscle most obviously in that it is surrounded by a thick insulating sheath pierced only at relatively long intervals by "faults"—the nodes of Ranvier. The obvious suggestion is that current enters the nerve principally through the nodes and stimulates there. But this suggestion, so evident on histological grounds, is exactly the condition to explain the different behaviour of muscle and nerve with various electrodes, for the lateral diffusion in nerve will almost entirely depend upon the size of the node and will be comparatively unaffected by the size of the electrode which leads the current to the outside of the node.

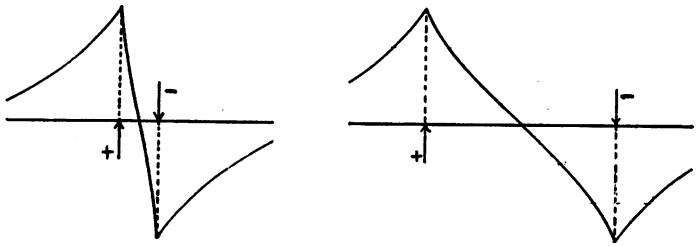

Fig. 14. Diagram of electric field forcing ions up against muscle membrane with electrodes near together or distant. Curves plotted as in Fig. 12.

In conclusion: the hypothesis which has been put forward fits qualitatively the facts of excitation of muscle and nerve with different kinds of electrodes, and this without having to postulate any new concept. It moreover admits of quantitative development to cover a very extensive range of excitability phenomena in a precise and fairly satisfactory manner (unpublished). It therefore appears that unnecessary complication may arise if an entirely new kind of excitation process be supposed to exist before evidence arises to show that the generally accepted process is inadequate.

Summary.

1. Reasons are given for concluding that the α excitability in muscle is the excitability of the normal muscle fibres themselves.

2. The isometric twitch is practically identical whether elicited by an α or γ stimulus. The rapidity of this α twitch excludes the possibility of identifying it with Bremer's neuro-muscular contracture which is very slow.

3. By several different methods the α excitation is shown to arise at the cathode due to the closing (not opening) of a current.

4. The α contraction is not a local Tiegel's contracture but is propagated.

5. The conclusions regarding the α and γ excitabilities derived from the present and former papers are tabulated.

6. Finally a hypothesis is put forward to explain qualitatively the dependence of muscle excitation time upon the nature of the electrodes and the relative independence of nerve.

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