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IDENTIFICATION OF THE GAMMA EXCITABILITY IN MUSCLE.

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When a muscle is excited through large fluid electrodes it may exhibit at least two excitabilities characterized by very different time relations (excitation times)[1]. Lucas [1907–8], who was the first to demonstrate this, called γ the excitability resembling nerve in its excitation time, and α the excitability which was much slower. He believed γ to be due to the intramuscular nerve twigs, since in addition to its resemblance in excitation time it was absent from the nerve-free part of the sartorius and was abolished by curare; α he supposed to be the excitability of the muscle fibres themselves. Until the last year or so this view was strongly opposed by Lapicque, who used a different electrode system, never obtained α, and concluded that nerve and muscle have the same short excitation time, and that Lucas's results were due to experimental errors.

The work of Jinnaka and Azuma, Davis, and Watts shows clearly that the excitation time of muscle diminishes very greatly with diminution in size of the electrodes employed, though with nerve this effect is small; hence by the use of smaller and smaller electrodes the muscle excitation time will diminish much faster than will that of the nerve, and consequently the two will approach.

Now if the detection of two excitabilities rests upon the observation of a kink in the strength duration curve, it is necessary that the two curves in question should in the first place meet and in the second place meet at a significant angle. But if the two excitation times are nearly the same,

[1] Since Lapicque has insisted that the name "chronaxie" is not to be applied to the constant derived from strength duration curves unless they fit an empirical formula which he has introduced, I have recently proposed [1932] that Lucas's term "excitation time" be used to designate the constant in all cases whatever, and thus the chronaxie is a particular excitation time which satisfies Lapicque's requirements.

there is very little chance of the curves meeting, since one is apt to lie completely above or below the other, and if intersection does occur it is little likely to be noticed on account of the insensitiveness of the usual method of representation.

From these considerations it is clear that, if we wish to be sure of the presence of both α and γ excitabilities, it is important to use sufficiently large electrodes for the α excitation time to be long, for γ resembles nerve in that its excitation time is relatively independent of electrode size.

With this in mind I have recently reinvestigated the question of whether the α phenomenon represents a separate excitability, or whether it is due to some error or abnormality [1930]. Using fluid electrodes with interpolar length of 1 cm. or more, the α curve can be obtained from any voluntary muscle, and all the evidence points to its being a normal constituent of the tissue. The question then arises, if the α excitability is a normal muscle element, what is the γ? Is it a different normal muscle element, is it the same element but excited differently (*e.g.* when excitation is elicited from the middle, not the end of a muscle fibre as suggested by Moore and Brücke [1931]), is it nerve, or is it junctional tissue? It is this question which the present investigation sets out to answer, but at the outset one point must be made clear. The γ excitability to be identified is that element which gives a γ curve in experiments with uniform electric fields when the irregularities at the terminations of muscles are screened [cf. Rushton, 1930, p. 331]. The fact that a curve with γ time relations may be obtained with the use of a pore electrode does not necessarily mean that the substance there excited was the same as that to be investigated in the present paper. It is hoped that this study of comparatively simple and regular cases may throw some light on the difficult cases of non-uniform fields.

Localization of the γ excitability.

(*a*) *The size of the γ substance.*

By γ "substance" is meant the tissue which is directly excited by a γ stimulus and whose time relations characterize the γ curve. As a first step towards identifying this substance with some definite histological entity, we proceed to enquire as to the size of the substance, whether for instance it be small or large compared with 1 mm. Light upon this matter is thrown by the relation between threshold and position of the electrodes. This relation was determined upon two species of frog, *R. pipiens* (U.S.A.) and *R. temporaria* (England). The results in each case lead to the same

conclusions, but those with *R. temporaria* are more straightforward and will be considered first.

In order to expose any given region of the muscle to a uniform electric field whilst keeping each end of the muscle equipotential, the excised sartorius was held by its ends on the floor of a rectangular trough filled with Ringer's fluid [Rushton, 1927, Fig. 1]. The pelvis was fixed and the tibial tendon attached to a light tension lever. Silver plates which fitted the cross-section of the trough (except for a gap below for the muscle) served as electrodes, and could be moved at will over any part of the muscle. Since there was a uniform field between the plates and an equipotential region beyond, they fulfilled the conditions of the present investigation so long as they did not move to the extremities of the muscle and extend the field to the irregularities there. In series with the electrodes was a non-inductive resistance of 10,000 ohms. Current strengths were controlled by a high resistance potentiometer used in conjunction with a voltmeter; durations of current by a Lucas pendulum. In order that the silver electrodes should be non-polarizable they were coated with chloride in the usual manner, but in this condition they appeared to have some toxic properties.

When freshly chlorinated electrodes were placed in Ringer's fluid just above the muscle, it was found that spontaneous rhythmic contractions resulted. Sometimes these started within a few seconds of applying the electrodes, sometimes not until current had been passed between them. The spontaneous contractions when once started continued a long time in spite of removal of electrodes and changes of fluid. This difficulty in former experiments led me to abandon the Ag-AgCl type of electrode and use Zn-$ZnSO_4$ Agar-Ringer. For the present experiment it was necessary to use plate electrodes, and so I returned to the question of these spontaneous contractions. The electrodes were made of pure electrolytic silver, the soldered connections were coated with paraffin wax, and after chlorination the electrodes were washed for an hour in running water. The contractions still appeared, and it seems probable that they are due either to the AgCl, or to the Ag^+ ion which, according to the theory of the non-polarizable electrode, must be present in the solution round the electrode in appreciable concentration. Seeing how commonly this type of electrode is used it might seem remarkable that the present observation is not of general occurrence, but in the first place there is often a wad of cotton-wool or clay between electrodes and tissue, and in the second, nerve is the tissue more often investigated, and this tissue is not much affected. I have never noticed any effect upon the nerve in these circumstances which may perhaps be attributed to the thick connective tissue sheath. Feng and Gerard [1930] have shown what part this sheath may play in withstanding the diffusion of substances, and if a nerve trunk is left overnight in 2 p.c. $AgNO_3$, and the sheath removed next day, after washing, the fibres within are not stained.

In the present experiment, therefore, the electrodes after chlorination were coated with Agar-Ringer, in which condition they were found never to give rise to spontaneous twitchings.

In the apparatus described above, it is the E.M.F. of the exciting circuit which is read, but what we require to know is the current or potential gradient in the solution. In order to obtain the relation between these two it is necessary to calibrate the apparatus for various positions of the electrodes. Both physical and physiological calibrations agreed in showing that the variable fluid resistance was so small a fraction of the fixed resistance of the circuit that the current was always proportional to the E.M.F. correct to 1 p.c.

The physical calibration was made either directly by placing a milliammeter in series and reading the current flowing in the various cases, or by finding the resistance of the electrode system in an A.C. bridge (1000 cycles) and calculating the variation in the final circuit. In the physiological method a sciatic nerve bent double on itself was substituted for the muscle in the trough. The anode was placed over the nerve a few millimetres from the bend and the cathode placed at various distances away so that the bend always lay in the region between the two electrodes. In this arrangement the physiological cathode always lies at the bend, the interpolar length remains constant, and hence the threshold always corresponds to some definite value of the current in the trough. It was found that the threshold E.M.F. was independent of the distance apart of the electrodes.

We may therefore take the voltmeter readings as proportional to the potential gradient in the trough.

The experiment was performed as follows. The sartorius was set up as described with the deep surface uppermost, and the cathode was placed over the muscle near the pelvic end. The anode was placed near the other extremity of the muscle, and a strength duration curve taken. The γ curve was always prominent, and a stimulus duration of 10σ usually was sufficiently short to avoid confusion with the α threshold. Some shorter duration, usually 1 or 2σ was taken and used throughout the experiment, and the threshold was found for different positions of the electrodes. Fig. 1 shows the results of one experiment, where ordinates give the voltmeter readings of the threshold (size of "point" gives limit of error) and abscissæ show the position of the variable electrode.

Consider first curve A, which corresponds to a cathode fixed at O at the pelvic end of the muscle and movable anode. At first, diminution in interpolar distance is unaccompanied by any threshold change, but soon the curve rises smoothly to become vertical at an electrode separation of 17 mm. This result is very regular and can be repeated accurately. In many experiments (cf. Figs. 3 and 9) the vertical part of the curve is met by a new horizontal line corresponding to an excitability unaffected by further movement of the anode until the electrodes lie only 2 or 3 mm. apart. With regard to this horizontal part of the curve it may at once be stated that it is the α excitability, and we find again the well-known

observation that (with large electrodes) α alone is present at the pelvic extremity. In order to learn whether it be possible that the γ substance be small compared with 1 mm., let us assume this to be the case and interpret the results of Fig. 1 in terms of this hypothesis. It is clear that, if the most excitable γ element lies somewhere between the electrodes,

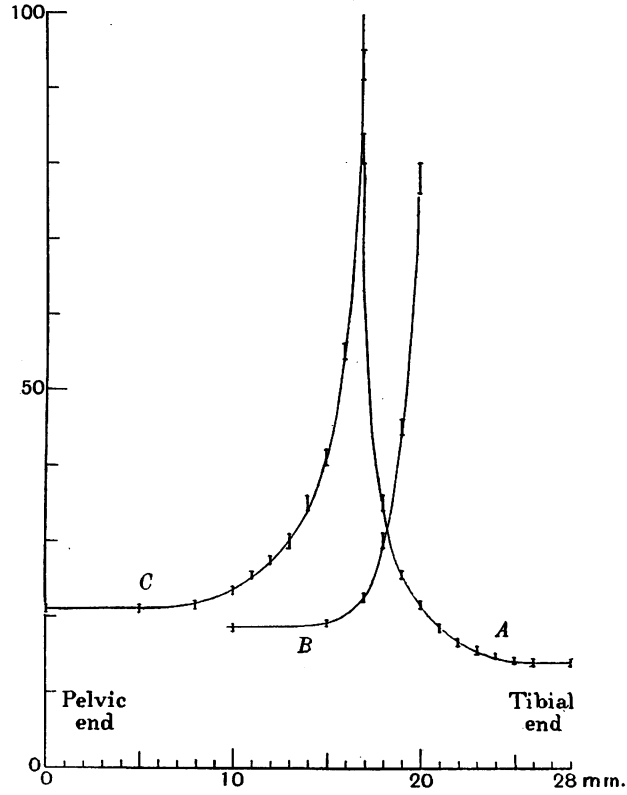

Fig. 1. Strength-length curve (*R. temporaria*). Abscissæ length in millimetres, ordinates current strength in arbitrary units. *A*, *B*, *C*, see text.

the observed threshold will depend simply upon the current in the neighbourhood of this γ element, and hence will be unchanged by movement of the electrodes until one of them passes over this element and excludes it from the field, when the threshold will promptly rise to that of the most excitable element now remaining in the field. Interpreting Fig. 1, curve *A*, in this manner, therefore, we must conclude that the most excitable γ elements are situated near the extreme tibial end of the muscle, and that

those with increasing threshold are distributed with surprising regularity as we approach the centre of the muscle; the pelvic half is very inexcitable, since in general no γ excitability is revealed when the anode lies on the pelvic side at the place where curve A becomes vertical. This may not have an air of great probability, but the evidence so far is not definitely incompatible with the hypothesis of small γ elements; by a further experiment, however, we may completely exclude this hypothesis.

Fig. 1, curve B, is the result of repeating the observations on the same preparation, but with the anode now fixed at the point marked 22 mm. and with the cathode at the various positions shown by the abscissæ. On the hypothesis of small γ elements we must again suppose that the variation of threshold is due to the exclusion, one by one, of the most excitable elements from the field, and since curve B rises as we move towards the tibia, it follows that in this case the most excitable fibres lie on the pelvic side. But this introduces the contradiction that, in that region of abscissæ where the two curves are both sloping markedly and in opposite directions, the γ elements must be assumed for A to be more excitable towards the tibia, for B, more excitable towards the pelvis. Specifically, in the region between 17 mm. and 20 mm. a movement of the anode (curve A) causes a sharp change of threshold, showing that the γ elements in the neighbourhood of this electrode are more excitable than any other elements in the field. But if instead of moving the anode the cathode is moved (curve B), there is also a sharp threshold change, indicating that the elements in the cathode neighbourhood are the most excitable. Since the two conclusions are necessarily incompatible we are left no option but to reject the assumption that the γ elements are small, and to conclude first that the observed thresholds are affected by the length of the γ substance exposed to the field, and second that the lengths in question must be at least of several millimetres.

(*b*) *The position of the γ substance.*

Granted that the γ substance has extension of several millimetres it is not surprising to find that the threshold depends upon how much of this length is exposed to the stimulating current. Experiments upon the relation between interpolar length and threshold have been made by a large number of workers, who have agreed that the curve obtained resembles the strength duration curve (thresholds plotted vertically in each case) in that it becomes asymptotic to the vertical axis and to a line parallel to the horizontal axis but above it. An example of a strength-length curve obtained upon nerve by the method of the present paper is shown in Fig. 2

of a former paper [Rushton, 1927], and some results of earlier workers are shown there in Fig. 3.

Now, in the present case, we have seen that the γ substance must have several millimetres extension, and thus it must have a cylindrical structure, for no other kinds of excitable structures of that size are present in the sartorius. But, as I have attempted to show [1927], the very cylindrical structure will account for the exact form of the strength-length curve on the simplest physical assumptions. Hence it is natural to suppose that the γ fibres will exhibit a strength-length curve of the usual shape. This is seen in Fig. 1 to be the case. As the electrodes approximate, no matter which is moved, the threshold rises and curve A, where the cathode is fixed, is seen to resemble closely the corresponding curve for nerve shown in the former paper. It is not to be supposed that the γ fibres necessarily stretch all the way between the electrodes in every case, but fibres must run towards the tibia at least as far as the point where the curve A becomes horizontal, for if they ended at some earlier point we could not account for the continued fall in threshold as the anode moved from this point to the 25 mm. mark. By the same argument the γ fibres must run towards the pelvis at least as far as the point where the curve A becomes vertical. But, whereas it is possible that the fibres extend tibially even further than the point where curve A becomes horizontal, it is not possible that these fibres run further towards the pelvis than the vertical asymptote. Both from theory and experiment with excised nerves it is found that the curve only becomes vertical when the interpolar length becomes infinitesimal, and we may therefore conclude that the γ fibres stimulated in curve A run towards the pelvis only as far as the vertical asymptote; between this point and the pelvis the length of fibre is infinitesimal, hence the fibre either here ceases altogether, or else turns and runs no further in the pelvic direction. From this analysis we may, therefore, conclude that the histological elements which give rise to the γ curve A, are fibres which start at a fixed point 17 mm. and run in the tibial direction for at least 8 mm.

When the experiment of Fig. 1, curve A, is repeated with the current reversed and the cathode now fixed at the tibia, curve C, Fig. 1, results. In this case the cathode was kept fixed at 28 mm. and the anode moved to points as indicated by the abscissæ. The curve obtained is in all respects similar to A and may be shown like A to be due to the change in interpolar length and not to the exclusion from the field of small excitable structures. All the former analysis of A applies equally to C, and we must conclude that a second series of γ fibres exist starting at a definite point and running

in the opposite direction. We note, moreover, that the vertical asymptote for curve A is the same as for that of curve C, whence we conclude that at this point, which we may call the "origin" of the γ fibres, they start and run, some towards the pelvis and some towards the tibia for distances of at least 8 mm. We must also accept the remarkable fact that when the whole muscle is placed in a uniform field (parallel to the axis of the muscle) only those γ fibres which lie on the anodic side of their "origin" respond, whichever the direction of the current.

(c) *Direction of γ fibres.*

One deduction from the cylindrical structure of the γ fibre is the form of the strength-length curve; this as we have seen is experimentally verified. Another deduction [Rushton, 1927] is the relation between threshold and the angle between fibre and direction of current. It appears that, if a straight fibre is immersed in a uniform electric field at any angle, it will be excited proportionally to the component of the field resolved in the direction of the fibre. Experimentally this has been found by many workers both in muscle and nerve, and results obtained with the apparatus of the present investigation are given for nerve [Rushton, 1927, p. 371], for muscle [1930, p. 332], where former work is discussed. In particular the method of plotting in polar coordinates has considerable advantages, as the relation between angle and threshold appears as a straight line perpendicular to the direction of the fibres. It is, therefore, clear that we may find the direction of unknown straight fibres by obtaining this line from the threshold-angle results in polar coordinates, and drawing a perpendicular to it.

Experiments exactly upon these lines have already been described [Rushton, 1930], and Fig. 14 of that paper shows a set of results with the sartorius, where it is seen that the γ fibres (in contradistinction to the α fibres whose thresholds lie within the heavy curve) run in a great many directions. This result is always obtained, and similar threshold-angle curves are shown here in Fig. 5 (upper half) and in Fig. 9 (bottom). The actual curves vary greatly from one preparation to another, but always agree in that the γ fibres run in a great many directions. The complexity of the results with the sartorius makes a detailed analysis unprofitable, but further light on this question will be thrown by the comparatively simple case of the sterno-cutaneous strip, considered in a later section of this paper. For the present suffice it to remark that the γ fibres are by no means restricted to the direction of the muscle fibres, but run in many different directions and vary greatly from one preparation to another.

Comparison with histology.

There are several other lines of investigation which may be employed to identify further the γ fibres, but since the foregoing analysis would suggest very strongly that these fibres are not muscle but nerve fibres (even if this conception had not already been supported by the evidence of Lucas), it will be convenient to consider this hypothesis at once. In this way it will first be shown that the results so far considered fit in detail, and then the further analysis may be presented in connection with the histology of the nerve fibres, so that the correspondence may be more directly appreciated.

We have seen from the evidence of Fig. 1 that the γ substance is in the form of fibres which start from a point, their "origin," and run some towards the pelvis, some towards the tibia for a distance of about 8 mm. or more. If all the muscle fibres ran from one end of the sartorius to the other, this evidence would exclude the muscle fibres from being identified with the γ substance, but since some fibres certainly end in the body of the muscle, it might conceivably happen that these were more excitable than the others, and thus account for the observation. However, the evidence concerning the *direction* of the γ fibres excludes this possibility, and microscopic examination does not show any large number of muscle fibres ending at the γ origin, but it does show that the γ origin corresponds exactly with the point of entry of the nerve trunk.

This correspondence cannot be regarded as a coincidence. The localization can easily be made in the fresh preparation during the actual stimulation, correct to $\pm$ 0·5 mm., and in all of a large number of experiments with different kinds of technique the correspondence has been exact within these limits. Fig. 2 shows quite a different form of apparatus similar to Lucas's. It is less accurate and more troublesome than that already described, but it is interesting as affording a control upon the other method, since in this case "deformation of current" is of quite a different kind from that where the muscle is completely immersed, and also because the zinc electrodes are separated from the muscle by side tubes filled with Agar-Ringer, so that poisoning and potential discontinuities are eliminated. The interpolar length of the muscle is the part in air between the two liquids. This was varied by opening the tap to cistern *A*, and for each position of the liquid the threshold voltage and also the A.C. resistance of the circuit were measured (1000 cycles). Fig. 3 shows the muscle (*R. pipiens*), stained for nerves by May's method, and also

the strength-length curve with cathode fixed at the pelvis. The strengths are proportional to the calculated current intensities. It is seen that, by this method also, the vertical asymptote coincides with the point of nerve entry. The horizontal line to the left of the vertical was found to be due to the α excitability. Fig. 4 shows the curves of Fig. 1 together with the corresponding preparation stained for nerves by May's method, and we see the verification of the earlier deductions that fibres start at the point

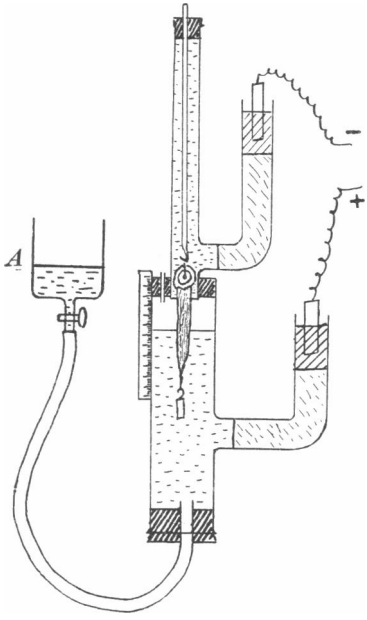

Fig. 2.

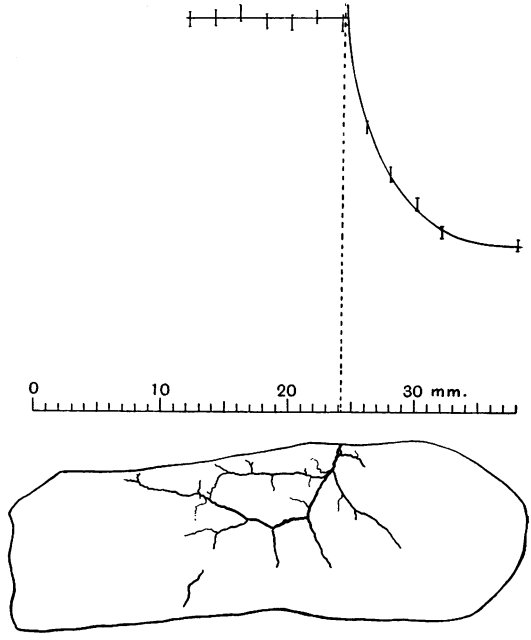

Fig. 3.

Fig. 2. Second form of apparatus.

Fig. 3. Strength-length curve from apparatus of Fig. 2. Sartorius muscle (*R. pipiens*) drawn to the scale of the horizontal axis.

"17 mm." and run for at least 9 mm. to the left. With regard to the fibres running to the right, they should run at least 4 mm. further than appears in the tracing. This discrepancy is probably due to the fact that the peripheral nerve twigs do not always take the stain very well, and it is easily possible that some long fine branches may run for several millimetres further to the right without appearing in the tracing. As a result of the foregoing experiments, therefore, we may conclude that

the nerve fibres fit the requirements of the γ substance to the following extent.

(*a*) They are in the form of fibres.

(*b*) These enter the muscle at the exact point where the γ fibres start.

(*c*) They run in both directions a distance of some 8 mm. measured along the axis of the muscle.

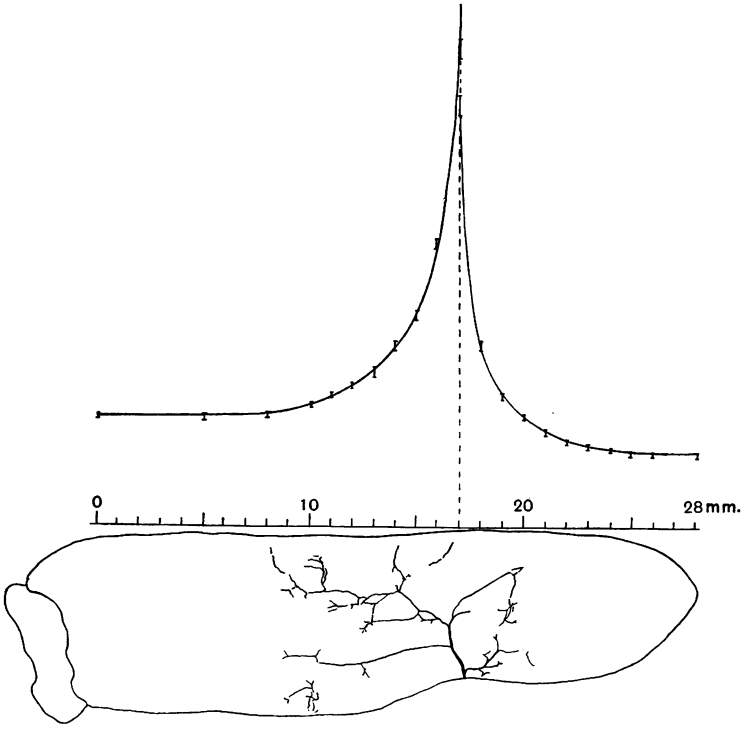

Fig. 4. Strength-length curves from Fig. 1 and sartorius muscle (*R. temporaria*) drawn to scale.

(*d*) They run in many directions.

(*e*) They are absent from the pelvic extremity.

(*f*) They have the same excitation time as nerves.

This identification may be yet considerably strengthened by experiments with the sartorius of the American green frog and the sterno-cutaneous of the American bull-frog, but before describing this work it will be well to consider the critical question: "Are the γ fibres undetectable after curare?"

Curare.

I do not wish to discuss at any length the action of curare until a later publication, but if γ fibres are nerves the abolition of their action by the drug is so obvious a consideration that it clearly deserves investigation in this place. Without the necessity of entering into details, however, it may

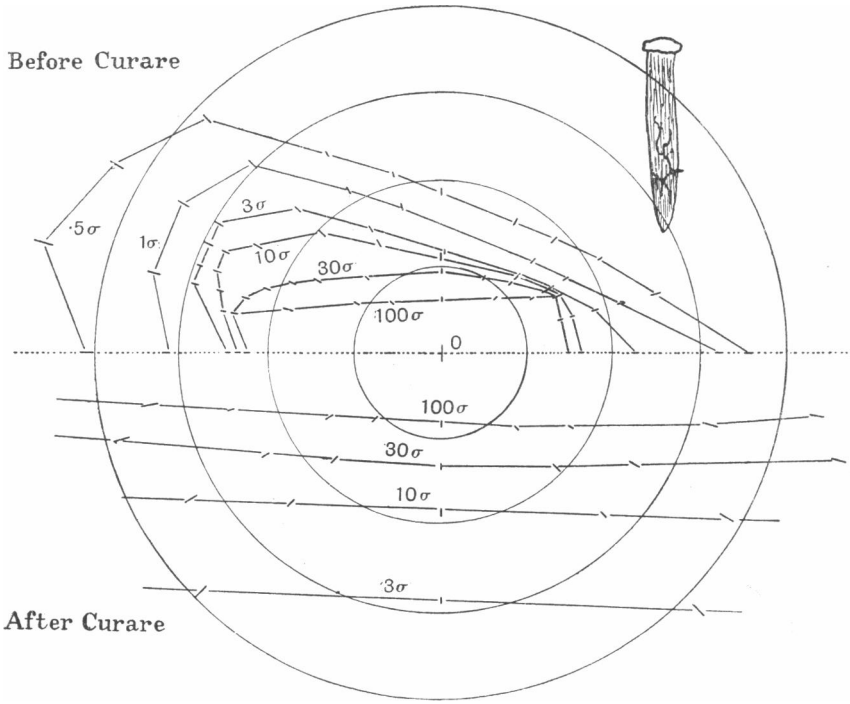

Fig. 5. Threshold-angle results for various durations of stimulus. Results before curare above horizontal, results after curare reflected below. Distance of "point" from *O* is proportional to threshold, direction of line from "point" to *O* is the direction of the current with respect to the muscle shown diagrammatically (*R. pipiens*).

at once be stated that no case was ever encountered where the γ excitability remained after curarization. These observations upon the action of curare are in complete agreement with the present hypothesis, but they fit equally the theory of Lapicque that the γ substance may be muscle, and that the γ excitability vanishes after curarization, not because the excitable fibres are no longer operative, but because their excitation time has lengthened and no longer has the γ time relations. The following experiment decides against Lapicque's explanation.

The threshold-angle curve of a sartorius was determined at various durations of current flow, and the results are shown in Fig. 5 plotted as usual in polar coordinates. The upper half of the circle shows the results before curare (cathode towards pelvis), the repetition of the same after curarization is shown for clearness reflected about the horizontal diameter, and they thus appear below.

These lower results are, therefore, uncomplicated by the irregularity of nerve structure, and appear exactly as would be expected—a set of parallel straight lines, indicating fibres running in the direction of the muscle fibres.

Now since curare cannot alter the direction of a fibre, the upper results of Fig. 5 should also be a set of horizontal parallel lines if Lapicque were right, and the fibres excited initially were the same as those after curarization. But these upper results indicate quite a different set of fibres running in various directions in the way that has already been shown to be normally the case with γ fibres. It is, therefore, clear that the action of curare upon the γ fibres is not to alter their time relations as Lapicque suggests, but to remove their activity altogether and to leave a new set of fibres (α) with different time relations, and a different direction, namely the direction of the muscle fibres. The identification of γ with nerves, therefore, is strongly supported by the effect of curare, which was always found to have abolished the action of the γ excitability at the moment when excitation through the nerve failed.

Sterno-cutaneous muscle.

It was remarked in a former paper [Rushton, 1930] that the irregularities which obscure results with the sartorius can be largely overcome by using a strip of sterno-cutaneous muscle, and Fig. 12 of that paper shows some threshold-angle results. Fig. 6 of the present work shows the results of a similar experiment with the tracing of the corresponding muscle strip (on the right) stained to show its nerve. The experimental details are given in the former publication, and it will here suffice to say that the strip of muscle was cut from the medial border of the sterno-cutaneous of a bull-frog, by a clean snip parallel to the muscle fibres. The threshold-angle results were obtained in the usual way, and then the preparation was stained by May's method, mounted in gelatine and a tracing made from an optical projection.

With regard to Fig. 6 we notice that the excitability represented by the horizontal lines changes threshold greatly between 100σ and 30σ

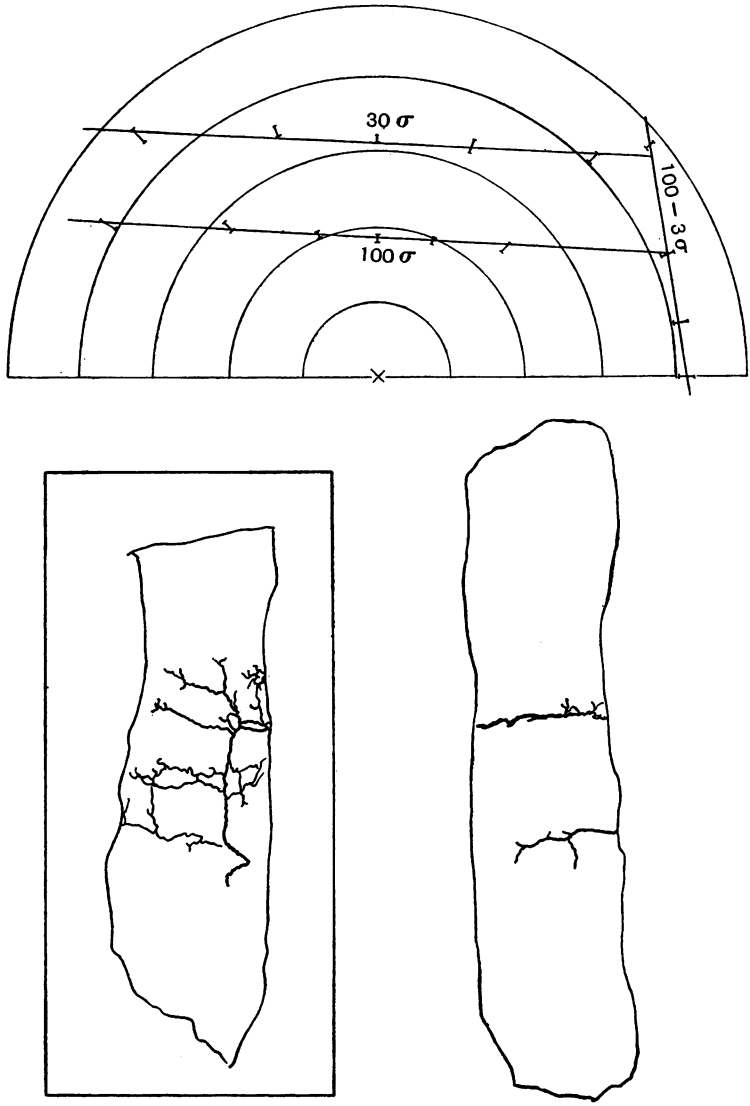

Fig. 6. Threshold-angle results for the sterno-cutaneous strip, shown below (right). Sterno-cutaneous strip from another frog (left). Plotting as in Fig. 5 (bull-frog).

duration, and hence must be α which again corresponds to fibres in the direction of the muscle, as in the case of the sartorius. The other excitability, on the contrary, has a utilization period of less than 3σ and is therefore γ which is seen to make an angle of 75° with this direction. It is clear from the tracing (right) that the directions of the muscle and the nerve fibres are very nearly perpendicular to those of the α and γ lines respectively. Other experiments confirm this; the angle between the γ and α lines varies from preparation to preparation, but there is always a corresponding variation in the angle between nerve and muscle.

On one occasion the γ line instead of being straight was quite curved, indicating fibres in many directions. When this preparation was stained and examined it presented the appearance shown traced in Fig. 6 (left).

The action of curare is also clearer here than in the case of the sartorius, since the pronounced difference in the directions of the γ and α fibres makes it easy to see that the γ are removed and α left [cf. Rushton, 1930, Figs. 11 and 12]. The results of the experiments with the sternocutaneous, therefore, bear out in all particulars the less satisfactory results with the sartorius, and confirm and extend the correlation of the γ excitability and the nerve twigs.

Excision of nerve twigs.

An obvious if crude test for the present hypothesis lies in the effect of removing by dissection some of the principal intramuscular nerve branches in the sartorius. This is much easier with *R. pipiens* than with *R. temporaria*, since, with the former, the nerves after they enter the muscle lie very superficially and but slightly bound down by connective tissue. This was easily slit with a sharp cystotome and the nerve, lifted by the end with forceps, could then be freed from the subjacent tissue, for several millimetres along each branch, and then cut. This operation removes the nerve with very little damage to the muscle, and when the final stained preparation was examined, the muscle fibres could be seen intact, the nerve fibres cleared from the region of the nerve entry, and the place where they had been, approximately marked by the rows of the pigment cells which follow the nerve branches here very closely.

When this operation is performed and the strength-length curves determined before and after, according to the method of Fig. 1, it is found that the γ excitability initially present is completely removed and that α alone remains. No figure is here given in illustration of this state-

ment, since the initial γ curves are of course normal and the subsequent γ curves being absent cannot be represented.

The experiment, however, gives a very different proof of the identity of γ and nerves.

The analysis of complex cases.

If a sartorius is stimulated as in the experiment of Fig. 1 with nearly the whole length of the muscle exposed to the current, we might expect that a γ excitation could be elicited from a great many points among the ramifications of the γ fibres, and that the actual point giving the threshold would be merely that particular place where the excitability was greatest to the stimulus in question. The simplicity of the results so far considered depends upon the fact that the "γ origin," which appears always to be a highly excitable point, in these cases is so much more excitable than any other place, that the only γ excitation which appears at all arises from here. By this I do not mean that it is impossible by any placing of the electrodes to elicit a γ response from elsewhere, since curve *B*, Fig. 1, is a ready instance to the contrary, but when the cathode lies at either extremity of the muscle, then this impossibility arises in all those muscles so far considered. Convenient as this is in simplifying the analysis, it is so singular that we should expect some preparations to exhibit other excitable points. *R. pipiens* nearly always shows two or more such points, and with *R. temporaria*, though this is not so common, the same may often be found.

It is natural to enquire what places are the most excitable in the conditions of these experiments, and the answer must involve two factors:

(*a*) The local excitability of the point in question, *i.e.* the amount of polarizing current required to excite this point.

(*b*) The current distribution in the fibre at the point in question, *i.e.* the proportion of the field current which is flowing in a direction to polarize the fibre at this point.

With regard to (*a*) little can be said. I see no reason why the local excitability could not vary at random from point to point, though actually the variations do not seem very great. Superimposed upon these there is the well-known hyperexcitability of a fibre in the neighbourhood of the cut end after recent section, probably correlated with the catelectrotonic effect of the injury current [Gotch, 1900]. This may in part explain the hyperexcitability of the "γ origin," if we identify γ with nerves.

With regard to (*b*) more can be said than is suitable in this place. The distribution of current in cylindrical fibres is a physical problem which

admits of an accurate solution. I have already published [1928] a general formula which covers all cases with which we may here be concerned (except for three or more fibres branching from a point, which requires a slight extension of the method), but it suffers from two objections. In the first place solutions involving definite integrals do not recommend themselves to some physiologists; in the second, the data in practice are presented in the form of a traced curve (*e.g.* the course of the intramuscular twigs) while the formula requires it in the form of an analytical expression. I have recently been able to overcome both these objections by a method of solution which gives the results graphically from a simple construction with pencil and scale, and which involves no mathematical technique. This method I hope to publish in the near future and to apply it to the more detailed analysis of γ and other excitability measurements, and therefore certain statements in the present paper will rest merely upon their general probability, waiting for the subsequent work for a more complete justification.

Chief among these are the ideas connected with excitation at the bend of a fibre. If in Fig. 7 the current flows in the direction of the arrow, and the fibre ABC is immersed in this field, the most excitable point will be B, for this is the most cathodic of all the points in the fibre. The sharper the point at B, and the closer the lines AB, CB to the direction of the current, the more excitable will B be; thus in a complex ramification of fibres we should expect sharp bends to be the most excitable points, provided that the current flows into the angle as in Fig. 7. An experimental verification of the idea together with a theoretical treatment has already been published for the case of bent nerve [Rushton, 1928].

Now if the cathode of the trough used for Fig. 1 lies to the left of B, Fig. 7, and the anode approaches B in the direction of the arrow, this anode may be represented as a line which is perpendicular to the current direction and which moves in the direction of the arrow. Thus the interpolar lengths BA_1, BC_1 will be shortened, and hence the usual strength-length curve will be obtained with this difference, that 1 mm. movement of the electrode will cause much more than 1 mm. diminution in BA_1 and BC_1, owing to the foreshortening of the fibre. Thus the strength-length curve obtained will be foreshortened to the same extent, and the threshold plotted against position of the electrode will rise very much more sharply than usual. An example of this will be considered later (Fig. 9).

Before turning to the experimental results there is one more point the consideration of which will elucidate the principal features of these observations. If in Fig. 8 two fibres A, B end at the distance O and both run to

the right for some way, then they will both give similar strength-length curves, A, B, but if B is less excitable than A, curve B will always lie above A and will never be found by ordinary threshold measurements. Suppose now that the whole fibre B is moved to the left (B_1) so that it ends at O_1, then the strength-length curve will similarly be moved an equal distance to the left (B_1), and hence will now cross A and be seen in threshold measurements as a kink in the strength-length curve. We may locate the two points O and O_1 whence the two excitations arose by extrapolating the curves A and B_1, till they become vertical, as is seen at once from Fig. 8.

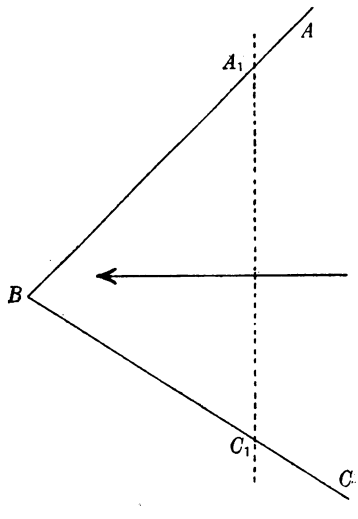

Fig. 7.

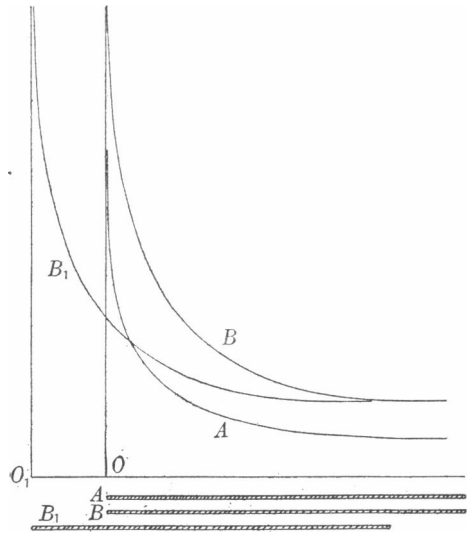

Fig. 8.

To summarize this analysis, therefore:

(*a*) A kink in strength-length curve signifies two excitable points.

(*b*) The point whence excitation was elicited for each portion of the curve lies where the extrapolation of this portion becomes vertical.

(*c*) The foreshortening of each portion of curve as compared with a standard[1] strength-length curve is equal to the foreshortening of the corresponding fibre when projected on to the direction of the current.

[1] The standard curve would be that obtained from a straight γ fibre running 1 cm. or so parallel to the muscle. In practice this standard is seldom found, and (*c*) is useful rather in respect of the corollary that if one experimental curve is more foreshortened than another, the fibre corresponding to the first is more oblique to the current than that corresponding to the second.

(*d*) The points whence excitation is elicited are likely to be either where fibres end, or where they bend sharply in such a direction that the current flows into the concavity of the bend.

We may now turn to the experimental results and, using the principles which have been somewhat justified above, we may continue the correlation between γ excitability measurements and the histology of intramuscular nerves.

Analysis of experimental results.

Fig. 9 shows the results of an investigation upon the sartorius of *R. pipiens*. First the muscle was excised, and strength-length curves were obtained in the usual way with the cathode fixed first at 0 mm., then at 40 mm. These curves are shown in the upper part of Fig. 9 where the millimetre scale gives the zero of ordinates. The muscle was then transferred to the rotating trough and the threshold-angle curve obtained using the same duration of stimulus (2σ). These results are shown at the bottom of Fig. 9, plotted as usual in polar coordinates, where O is the polar origin, and where the direction of the muscle is represented by the horizontal broken line. Finally the muscle was fixed and stained according to May's method, mounted in glycerine jelly and traced from an optical projection at magnification of five diameters[1]. The course of the nerves was subsequently verified by microscopic examination of the preparation and comparison with the tracing. This tracing is shown in the middle of Fig. 9.

Turning now to an analysis of the results, it is seen that the strength-length curve with the cathode at the tibial end of the muscle is made up of two parts A and B. The simplest justification for making a kink at 24 mm. in this curve is derived from the curve of reciprocal thresholds (shown below as a curve dipping down to the millimetre scale). This latter curve may be regarded as giving the excitability of the preparation for various positions of the electrodes, and it is seen at once that the point at 24 mm. lies below the smooth curve which might be drawn through the other points. The deviation would correspond to an experimental error of at least 15 p.c. in the threshold, which I do not think is admissible. The curve with the cathode at the pelvic end is obviously composed of three parts, of which C and D are due to the γ excitability, but the remaining

[1] Five diameters is the ratio of the size of the projected image to that of the fresh tissue, as obtained by noting the distances between the principal nerve branches before fixing. In this way errors due to shrinkage during staining are largely reduced.

portion gave an α strength duration curve. This latter portion is a good illustration of the relative independence of the α threshold upon interpolar length, since there is no further change in threshold after this length has exceeded 3 mm.

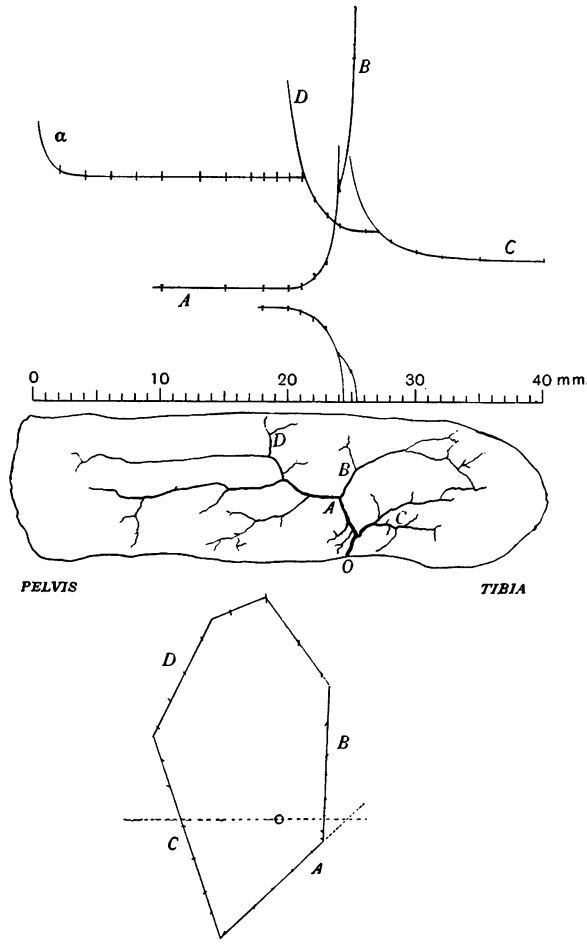

Fig. 9. Strength-length curves, sartorius muscle (*R. pipiens*) drawn to scale, and threshold-angle curve (with coordinate circles omitted for clearness).

Applying now the principles of analysis formulated above we conclude that each of the four curves *A*, *B*, *C*, *D* corresponds to excitation at a different point in the muscle. These points may be found by extrapolating the curves until they become vertical; hence *A* is just to the left

of 25 mm., *B* just to the right of this point, *C* coincides with *A* or lies a little to the left, while *D* is just to the left of 21 mm. Observing now the foreshortening of the curves, it is obvious that *A* and *B* rise very much more steeply than *C* and *D*, therefore the fibres excited in the former case must run much more obliquely to the muscle fibres than in the latter case. These conditions are satisfied approximately if we suppose that curves *A* and *C* represent excitation at *O*, the point of entry of the nerve, the excited fibres in each case being those running from *O* to *A* and *C* respectively in the tracing. It is clear that as predicted branch *AO* is much more oblique than branch *CO*. Curve *B* represents excitation at the point *B* in the tracing, the fibres in question being those running from *A* to *B* and then bending back slightly to the left. Since the current flows into this bend the point is likely to be an excitable one, and the obliquity of both branches should produce a foreshortening of the curve similar to that of curve *A*. Finally curve *D* represents excitation at point *D* in the tracing, the fibres in question running from *A*, bending round *D*, and returning a short way towards the tibia. Curve *D* should be no more foreshortened than curve *C*.

From the foregoing, therefore, we have obtained a definite correlation between the excitation curves and the histology of nerves; it is of interest to compare these conclusions with the threshold-angle results. These results may be all included in six straight lines (as shown), indicating that when the muscle is freely immersed in a uniform field at various angles there are six different points whence excitation is elicited. To identify these we note that the broken line through *O* represents the direction of the muscle, hence the sides of the hexagon cut by this line represent the excitable points when the field is parallel to the muscle. This case, therefore, is the same as that of the strength-length curves above when the interpolar length is very great (*i.e.* the whole muscle exposed). Thus the side of the hexagon marked *C* represents the threshold excitability when the current flows from *O* to the left, which corresponds to the curve $CD\alpha$ in the upper figure, which has *C* for the threshold with great interpolar length. But we have identified the excitable point *C* as being *O* on the tracing, the point of entry of those nerve fibres which run in the direction *OC*. From the threshold-angle results, the fibres of the excitability *C* should run in a direction perpendicular to the direction of the side *C* of the hexagon (see p. 180), which is an adequate agreement considering that this simple result is based upon the assumption of a straight fibre.

Applying this analysis to current flowing parallel to the muscle towards the tibia, we learn from the strength-length results that *A* is the

threshold excitability with large interpolar length. This we have identified with O, in the tracing, the point of entry of those nerve fibres which run in the direction OA, and hence the corresponding side of the hexagon should be more or less perpendicular to this direction. It is seen that there is such a side marked A, but this is not the one first cut by the broken line through O. The explanation for the discrepancy is probably as follows. One reason for the presence of the cut nerve end as a principal excitable point in all these experiments is due to the initial hyperexcitability following section. As is well known this excitability declines fairly rapidly, and in the interval between the strength-length and threshold-angle measurements it is probable that the excitability of A and C fell as compared with that of other points not situated at the cut end. Thus the sides A and C of the hexagon moved out from O (keeping the same directions of course), but the other sides remained more or less constant. The lengths of broken line from O to C and from O to A (produced) are in the same proportion as the thresholds for C and A in the strength-length figure, as would be expected. If this explanation is accepted the side A fits the conditions previously postulated for A and we may turn to consider the excitability B.

Excitability B we have supposed to arise from B in the tracing due to the nerve branches lying to the left of this point. When the current excites a nerve at a bend (as distinct from exciting at its termination), the threshold-angle results in polar coordinates give a straight line which is perpendicular to the bisector of the angle of bend in the case where the two limbs are straight and equal. Both theoretical and experimental justification for this statement has been given in a former publication [Rushton, 1928], and applying the results to excitation at B where the assumptions are approximately accurate, we perceive that the bisector of the angle lies in the direction of the muscle, and hence the corresponding side of the hexagon should be perpendicular to this. It is seen that the side marked B fulfils this condition. Excitability D may be analysed similarly, whence we conclude that the corresponding side of the hexagon should be perpendicular to the bisector of the angle at D. The side marked D runs more or less in this direction, and it was recorded when making the observations that the excitability represented by this side gave a barely perceptible twitch, indicating that only a few muscle fibres were activated by the excitability in question, as would be expected if we identify it with the nerve fibres running from D upwards and to the right. The threshold, however, is somewhat higher than might have been expected. With regard to the two upper sides of the hexagon, that on the left gave a very small

twitch and corresponds to some bend of a nerve twig near its termination, but that on the right gave a big contraction and probably corresponds to excitation at *A* in the tracing, the fibres involved being those which do *not* go in the direction of *B*, for the bisector of the angle which the remainder make at *A* is more or less perpendicular to this last side of the hexagon.

This analysis has been considered at some length, not so much for the confirmation which it brings to the γ identification of this paper, as for the analysis itself which, as far as I am aware, has not been previously described and which may have considerable application in various excitability problems. Certain defects in the method are apparent. Localization of electrodes and irregular shrinkage during staining may introduce a possible localization error of $\pm$ 0·5 mm. or even more. The extrapolation of the portions of strength-length curves is somewhat arbitrary, though more reliable when the extrapolation is performed upon the reciprocal curves. Even given approximately the position on the axis of the muscle, where an excitable point is to be located, there may often be several possible branches to choose from, and this possibility will be enormously multiplied if we include those fine terminal nerve twigs which usually do not take the stain in the three hours during which the muscle was generally treated. However, this error is not so great as one might suppose, for it appears to be a general rule that *ceteris paribus* the larger a nerve trunk the more excitable it is, hence the small unstained fibres are not those excited at threshold strengths. However, in spite of this, ambiguity may arise in some cases, which the foreshortening of the strength-length curves and the nature of the threshold-angle curves may help to settle. The threshold-angle curve itself is open to the objection that, since the nerves are not of simple geometrical form, the rules so far applied are more or less inaccurate. Both this and the extrapolation of the strength-length curve are, however, susceptible of more accurate treatment (as it is hoped to show in a future publication); hence the localization can become considerably more determinate than might at first sight appear.

In fact the fourfold correlation—the foreshortening of the strength-length curves, the position of their vertical asymptotes, the nature of the threshold-angle curve, and the histology of nerve distribution in muscle—affords a strong presumption that the basis of the analysis is sound, and that the localizations effected are correct. And when each muscle investigated is found to have a different histology of nerve twigs, a different threshold-angle curve and different numbers and positions of the kinks in the strength-length curves, and yet when these differences are all inter-

correlated in the manner of Fig. 9, there seems little room to doubt that the earlier conclusion of this paper is confirmed in detail and that the γ excitability is to be identified with nerve.

Discussion.

The identification of the γ excitability in muscle is liable to be needlessly complicated owing to the fact that two distinct meanings can be assigned to the expression "γ excitability," and that the identification will depend upon which is adopted. The matter becomes clear from a brief survey of the history.

Lucas [1907–8] showed that when large fluid electrodes are used, α and γ curves may appear, where by γ he meant the curve that he obtained having a short excitation time. Later Jinnaka and Azuma [1922–3], Davis [1922–3] and Watts [1924–5] investigated the effect of size of electrode upon the α excitation time and showed that, as the size of cathode decreased, the α excitation time diminished to about the value which γ had initially. Watts repeated this investigation upon nerve and found that electrode size had a very insignificant effect upon excitation time. With regard to the effect of electrode size upon the excitability which gave a γ curve in Lucas's experiments (large electrodes), these investigators gave little information, as they applied the small cathode almost exclusively to the pelvic end of the sartorius which Lucas had shown to be free from γ.

Upon this head, however, evidence is furnished by the work of Lapicque [1926], who excited the sartorius and other muscles at various points with small cathodes and never found any excitation time different from that nerve. We may, therefore, conclude that γ resembles nerve in that its excitation time is but slightly dependent upon electrode size.

Now, in the conditions of Lucas's experiments, the meaning of "γ excitability" is unambiguous, and the same applies to my own work where the conditions are essentially the same, but when we consider the quickening of the α excitability by the use of small electrodes until the α curve resembles γ, it now becomes merely a question of definition whether we call this altered α curve a γ curve and the responsible excitability a γ excitability or whether we restrict the name "γ" to that excitability which gave γ with large electrodes. In fact, the names α and γ may either be used to describe the behaviour of an excitable element or to distinguish the natures of different elements. It does not matter which definition is adopted, provided the matter is made clear. Actually in this

and in my former papers I have adopted the second alternative, and by γ excitability I mean that element which gives a γ curve when large electrodes are used; the curve obtained by a small electrode from the pelvic end of the sartorius may then unambiguously be described as a γ-like α curve or an α curve of short excitation time.

I much regret that, owing to my failure to be explicit in this matter earlier, Lapicque [1931*a*, p. 202] has evidently supposed my statement that "γ cannot be obtained from the pelvic end of the sartorius" to be a denial of the work of Jinnaka and Azuma and the other workers mentioned above, and has been put to the trouble of repeating their work and confirming that a γ-like curve may be elicited using small electrodes. As a result of these experiments he concludes [1931*b*, p. 219], "I cannot admit that γ corresponds only to the nerve excitability and that the muscle's own excitability corresponds to α," and later, p. 236, "From the above facts, we know that the γ curve is not only concerned with the nervous substance but also with the muscular one." There is no conflict between these statements and the present paper's identification of γ with nerve only, for what Lapicque means (as shown by the nature of his evidence) is merely that muscle can, with stigmatic electrodes, give a γ-like curve. In one of his experiments, however, Lapicque obtains evidence that at first sight does seem to establish that γ may be muscle, for he finds [1931*a*, p. 208] in a curarized muscle without the use of stigmatic electrodes an excitability with rather a short excitation time. The explanation of this case involves a factor of prime importance in the study of α curves, as it may cause the greatest variations in the form of the curve. In my first experiments I found that the α curve varied considerably from one angle to another [1930, Fig. 2]. Subsequent work revealed that the error was due to the irregular terminations of the muscle fibres which were excited by the free immersion of the muscle in fluid. Screening these irregularities from the field allowed of very much more consistent results to be obtained, and I therefore pointed out in my paper that this error was present in the early results but absent from the later ones, and that screening these irregular terminations was essential for consistent results. Unfortunately this observation appears to have been overlooked by Lapicque, for he does not mention it in his criticism of these curves [1931*a*, p. 198], and in his own experiments he has not taken the necessary screening precautions. In fact he writes [1931*a*, p. 199]: "As a first approximation, we considered that the accuracy of parallelism was not necessary, so that I used a round trough," and he proceeds to describe his form of electrodes which not only exposes the ter-

minations of the muscle, but exposes them to an electric field which is anything but uniform. With this arrangement he obtains curves which are seen to vary considerably in shape and to be but poorly reproducible. The question of the variability in the shape of the α curve hardly lies within the scope of the present paper, except in so far as the shape may approach that of the γ curve and be confused with it. This effect I also found in my early experiments when the muscle terminations were not screened, for in experiments with curarized sterno-cutaneous strips sometimes a very brief excitability would be found. The direction of this excitability as given by the threshold-angle relation was always oblique to the muscle, and indeed it was the attempt to identify this oblique excitability that called my attention to the oblique terminations of many muscle fibres. As already mentioned, these γ-like curves did not occur in curarized strips when screened. Moreover, the explanation of the effect is simple, for if we suppose (as Lapicque has already pointed out) that the excitation time of the α curve is greatly diminished by decreasing the interpolar length, then in the case where a parallel fibred muscle is excited by a very oblique current, since the excitable portions of fibre will be those very short terminal irregularities which happen to lie more or less in the direction of the current, they consequently will have the excitation time corresponding to their short length.

Now the case quoted by Lapicque [1931*a*, Fig. 13] where a γ-like curve was found from curarized muscle without a stigmatic electrode is exactly in the category just considered. For not only are the unscreened ends of the muscle exposed to this error, but in comparing the results at the two angles it appears that, whereas the α threshold rises for the oblique current, the γ-like threshold falls, indicating that the direction of the γ-like excitability is oblique to the muscle axis, and therefore certainly cannot refer to normal muscle fibres. It was to avoid the complications produced by these irregularities that at the outset of this paper the conditions were restricted to uniform fields and screened muscle terminations, and in these conditions I do not know of any evidence to controvert the conclusion that γ is always nerve.

Quite a different effect of the muscle terminations upon the excitation time has recently been brought to light by the experiments of Moore and Brücke [1931]. They stimulated the single muscle fibres in the basihyoid membrane of the frog, and found that the excitation time when the cathode lay at the terminations of the fibres depended upon the diameter at this point: thin terminations had long excitation times. They suggested that this might be correlated with α and γ excitabilities in that the γ

might be elicited from the middle of the fibre, and α from the thin end of it. This would fit the observation that in practice α and γ are found more or less in these respective parts of the fibre, and it allows of an isochronism between nerves and the γ excitability of that part of the fibre where the nerve enters. Unfortunately this hypothesis does not accord well with the detailed results of varying the position of the electrodes. When a 1 cm. block is placed over the muscle at various points and the strength duration curve obtained as, for instance [Rushton, 1930, Fig. 8], we do not find that the curve is simple and gradually changing in form from α at the extremity to γ near the centre, but, on the contrary, it is made up of two parts, α and γ, each of which has more or less the same excitation time at all points of the muscle, but the relative prominence of which varies in such a way that γ is absent in the neighbourhood of the extremities, but is present nearly to the exclusion of α in the neighbourhood of the nerve entry. This clearly speaks for two different kinds of excitabilities, not for a continuous variation of one kind, and with regard to α it suggests that it has the same sort of value for its excitation time all over the muscle. With regard to γ, we have the evidence of the present paper which is quite contrary to the suggestion that γ is muscle, since the direction, the action of curare, and all the other features which have been discussed, point strongly to the identification of this excitability with nerve. The suggestion of Moore and Brücke, therefore, will not explain the difference between α and γ, but their observations are valuable in showing that the α excitation time can vary within wide limits depending upon the size of fibre at the point whence excitation is elicited. It is not unlikely, however, that this difference is more marked in the rather heterogeneous fibres of the basihyoid membrane, than in the more uniform fibres of the sartorius.

Conclusions.

This paper set out to identify the γ excitability. Only three excitable elements have been recognized in muscle, the muscle fibre, the nerve fibre and a possible intermediary substance. The latter cannot be identified with γ for the experiments of Fig. 1 show that the γ substance has extension of several millimetres, and consequently must be muscle or nerve. Lapicque [1931, *a*] and Moore and Brücke [1931] have suggested identification with the former, but as was indicated in the foregoing discussion, it is probable that Lapicque's evidence does not relate to what is here called "γ" at all but to a modified form of α, whereas the suggestion of Moore and Brücke is not as satisfactory as the alternative hypothesis

that γ is nerve. This latter view which is that originally advocated by Keith Lucas is very strongly supported by the evidence of the present paper, the conclusions from which may be summarized as follows:

(*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 γ 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 that indirect excitation (through the nerve) has failed.

As a result of this summary there can be no question I think, but that the γ fibres in all my experiments were the intramuscular nerve twigs. With regard to the possiblity that in the foregoing experiments it so happened that the nerves and the α excitability between them were always more excitable than some hypothetical γ muscle fibres, so that the latter were never investigated, little need be said. If these hypothetical fibres never enter into threshold measurements we are justified in neglecting them when concerned with threshold determinations, and it will be time enough to consider their nature when some reason is found for supposing they exist. To quote from Lapicque [1926, p. 265], "Était-il besoin d'entreprendre la démonstration complète? Une démonstration négative est toujours bien laborieuse; la preuve incombe à ceux qui affirment."

SUMMARY.

When a muscle is excited through large fluid electrodes, two excitabilities α and γ are found. The present paper set out to identify γ in conditions where the irregular terminations of the muscle are not excited and where the stimulating electric field is uniform. In these circumstances a variety of experiments with movable electrodes justify the ten conclusions summarized in the preceding section, whence it appears that the γ excitability is certainly nerve.

It is a pleasure to express my appreciation of the help afforded me by Prof. Bronk during my stay in Philadelphia. I am also indebted to the Government Grants Committee of the Royal Society for enabling me to obtain some of the apparatus used in this research.

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