THE ANALYSIS OF COMPLEX EXCITABLE TISSUES BY THEIR RESPONSE TO ELECTRIC CURRENTS OF SHORT DURATION.

By KEITH LUCAS, *Fellow of Trinity College, Cambridge.*

(*From the Physiological Laboratory, Cambridge, and the Laboratory of the Marine Biological Association, Plymouth.*)

I. *Theory of excitation by currents of short duration.*

When the duration of an electric current sent through a muscle or a nerve is decreased beyond certain limits, the current strength which just suffices to produce an excitation is increased. This fact was first observed by Fick in 1863[1]. It has led many physiologists to abandon the doctrine, which du Bois-Reymond[2] originally maintained, of the paramount excitatory value of current variation, and to seek for a relation between the excitatory effect and some factor such as the current strength, the electrical energy expended, or the quantity of electricity passed. Formulæ have actually been put forward by Hoorweg[3], Weiss[4], and M. and Mme Lapicque[5], connecting the excitatory effect with these various factors. And at first sight it does seem as though some such factor, which varies with the time of passage of the electric current, would have to be taken into account; for in Fick's experiment the excitatory effect became less when the duration of the current was alone decreased. But Fick[6] also observed a similar effect if for duration of current he substituted duration of break in a constant current. He passed a constant current through a muscle,

[1] Fick. *Beiträge zur vergl. Physiologie der irritabelen Substanzen*, p. 20. Braunschweig. 1863.

[2] Du Bois-Reymond. *Untersuchungen über thierische Elektricität*, I. p. 258.

[3] Hoorweg. *Arch. f. d. ges. Physiol.* LII. p. 87. 1892.

[4] Weiss. *Arch. Ital. Biol.* XXXV. p. 438. 1901.

[5] M. and Mme Lapicque. *Journ. de Physiol. et de Path.* V. p. 991. 1903. For an account of other work dealing with the same subject see Weiss *loc. cit.* pp. 413–528.

[6] Fick. *loc. cit.* p. 21.

and cut off this current for variable times: the shorter the time during which no current passed, the less was the excitatory effect. The fundamental importance of this experiment seems to have been overlooked entirely, until Woodworth[1] made the same experiment independently while working on amphibian smooth muscle. Woodworth's observation was confirmed by Stewart[2] for mammalian smooth muscle. The interpretation which Woodworth gave to his experiment was that the opposed effects of make and break upon the muscle interfered one with the other more and more as the time interval separating them was made less. And this seems a most reasonable supposition. For we have ample evidence that at each electrode the effect of make is opposite to that of break. At the cathode, for example, make of the current produces excitation, break produces inhibition. And if make follows break at so short an interval that the inhibitory effect of the break has not yet died out when the make occurs, it is clear that the make-excitation will have to contend against an existing inhibited condition of the tissue, and so will be less effective. Indeed this seems to be the only explanation which will fit the experiments made with short intervals of no current. For in such cases the factors such as energy and quantity, which have been called in to explain the action of short currents, actually become less as the interval becomes longer and the excitation greater.

If then the interference of the effects of make and break is a factor of sufficient importance to explain the inefficacy of short intervals of no current, may it not also account for the fact that currents of short duration become less effective as they become shorter? Currents of short duration excite at the cathode[3] only, so that in considering how the effects of make and break may interfere, we may consider first what goes on at the cathode. The make of the current sets up an excitation at the cathode, the break causes inhibition. It does therefore seem possible that the break-inhibition may quash the make-excitation if it occurs before the latter has reached its full development. And the earlier during the development of make-excitation that the break-inhibition occurs, the more potent will the latter be in arresting the former. At the anode of course inhibition precedes excitation, and it may be that the failure of the anodic break excitation to appear with

[1] Woodworth. *Amer. Journ. Physiol.* III. p. 41. 1900.

[2] Stewart. *Amer. Journ. Physiol.* IV. p. 197. 1901.

[3] Cf. Lapicque. *C. R. Acad. des Sciences*, CXL. p. 537. 1905.

minimal strength of current is due to the start which the anodic make inhibition gets.

The interference of the effects of make and break affords therefore a possible explanation of the behaviour both of currents of short duration and of short intervals of no current. Any explanation, on the other hand, which rests upon such factors of the current as energy or quantity can at best explain only the case of currents of short duration. It seemed to me worth while to enquire whether the relation of the duration to the voltage required for minimal excitation presented the same peculiarities when short durations of no current were used as it does with short durations of current. For the form which that relation takes cannot be ascribed in the case of short currents to the importance of energy or of quantity as the determining factor of excitation, if it holds also for short intervals of no current, in which the effects of energy or quantity cannot exist. If indeed this is found to be so, we shall have strong evidence that the interference of the effects of make and break is the important factor in both cases.

The fundamental points which all experimenters have found by determining the minimal voltages required for excitation at various current durations are the following[1].

1. As the duration of the current is decreased the voltage increases at first slowly, and then more and more rapidly.

2. As the duration of the current is decreased the quantity decreases approximately along a straight line.

3. As the duration of the current is decreased the energy falls to a minimum and then again increases.

In the following section are described some experiments which show that these relations are also found when one uses short intervals of no current. Of course in this case it is absurd to speak of quantity and energy, since no quantity and no energy pass during the interval; but the point on which I wish to lay stress is that the value of tv and the value of tv^2 (where t is the interval between make and break, and v the voltage at which minimal excitation occurs) change in the same way with changes in the value of t whether tv and tv^2 represent actual quantity and energy or are meaningless. For, this being the case, we must infer that the relation between the value of t and the values of tv

[1] These three points are illustrated by Hoorweg, *Arch. f. d. ges. Physiol.* LII. p. 87. 1892 (spec. Fig. 3, p. 97), and many examples may be seen in Weiss, *Arch. Ital. Biol.* XXXV. p. 428, 1901, or in M. and Mme Lapicque, *Journ. de Physiol. et de Path.* V. pp. 843, 991. 1903.

or tv^2 is not due to any actual part which quantity or energy play in excitation, but is due to some cause common to the case of short currents and the case of short intervals of no current. What that common cause probably is I have already indicated.

II. *Experiments with breaks of short duration.*

Woodworth's experiment was of a very simple nature, owing to the long intervals between break and make necessary to excite smooth muscle. But with intervals of the short duration required by nerve it is no longer possible to make circuit directly by pressing two metal contacts together; the risk of the contacts rebounding is too great[1]. Every change in the circuit must be brought about by means of a break of contact. I therefore arranged the circuit as shown diagrammatically in Fig. 1. The three wires *ABC*, each a metre long

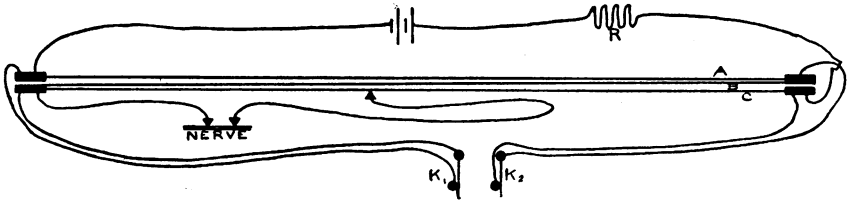

Fig. 1. Arrangement of circuit for obtaining short breaks in a current.

and of about 5 ohms resistance, are in parallel in the battery circuit as long as the two keys k_1 and k_2 are closed. When k_1 is opened the greater part of the current flows along *A* and through k_2, that which flows by *B* and *C* being negligible owing to the much lower resistance of the path by k_2. When k_2 is also opened, the three resistances *ABC* are in series. By suitable adjustment of the resistance *R* the potential difference between the ends of the wire *C*, which is used as the potentiometer wire, can be made practically identical whether k_1 and k_2 are both closed or both open. If then the keys k_1 and k_2 are closed at the start, there will be a current flowing through the derived circuit in which the nerve lies; when k_1 is broken this current will cease; and when k_2 is also broken the current will resume its former value.

The mechanism used for breaking the keys k_1 and k_2 at the required intervals of time is shown in Fig. 2. A heavy pendulum *M*, 100 mm.

[1] Cf. M. and Mme Lapicque. *Journ. de Physiol. et de Path.* VI. p. 867. 1904.

in length, swings on the ball-bearing axle *A*. The pendulum carries a light steel arm *E* 547 mm. long. The hook *H* retains the pendulum in a position 102° from its vertical position. The hook *H* carries two notches, the lower of which is used for releasing the pendulum, while the upper automatically catches it after it has made one double swing. The key k_2 is moveable along a slide *S* placed tangential to the arc described by the extreme end of *E*, touching that arc at the point

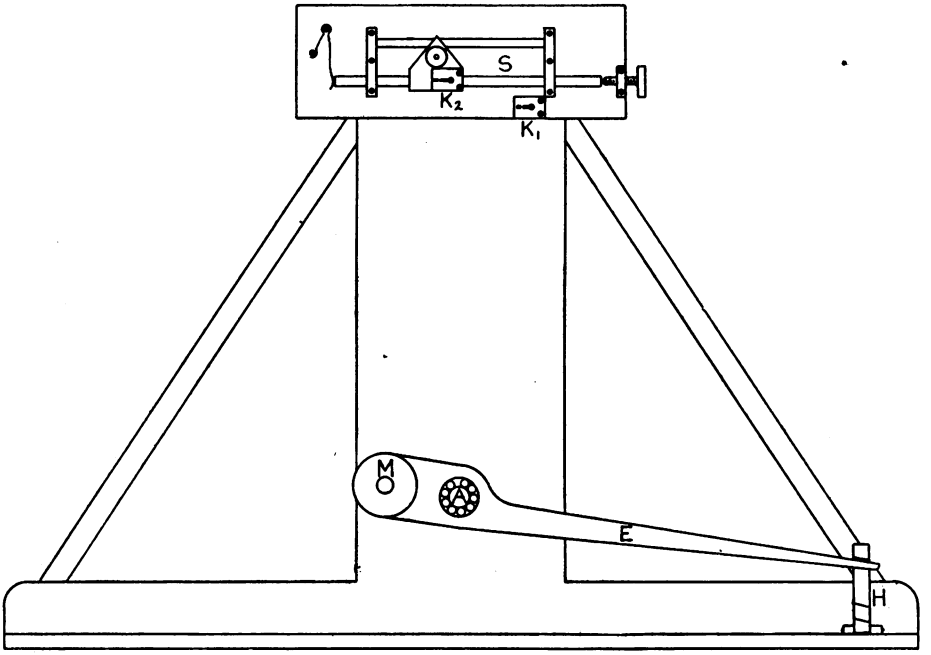

Fig. 2. Pendulum used for opening keys at the required intervals of time.

where the pendulum is vertical. The key k_1 is struck by the arm *E* at about 50 mm. before the vertical position of the latter. The travel of k_2 along its slide allows the two keys to be struck open by *E* either simultaneously or at any interval up to 150 mm. The carriage on which k_2 slides is furnished with a scale of millimetres read by a microscope (not shown in the figure). The time which intervenes between the opening of the keys k_1 and k_2 is calculated from the observed time of swing of the pendulum and the tangential distance separating k_1 and k_2. The velocity of the extreme end of the arm *E* at the instant after k_1 has been struck is 5760 mm. per sec.

In the experiments made upon the sciatic nerve I used the

fluid electrodes described in a previous paper[1]. The gastrocnemius muscle was used as an index of excitation of the nerve.

The procedure was to determine first by means of the potentiometer wire (*C*, Fig. 1), the minimum voltage at which the make of current was effective when acting alone. The keys k_1 and k_2 were then set so that the make was preceded by a break at some chosen short interval of time, and the minimum voltage was determined again. The current was a descending one, so that make alone was effective, while break alone was ineffective. Below are given the details of an experiment of this type. The cases in which the time interval between break and make is given as ∞, are those in which the make alone was used.

Exp. 1. Sciatic of Frog. Temperature 8·1° C. Resistance of nerve and electrodes 66000 ohms.

Time interval between break and make	Voltage required for minimal excitation
∞	0·094 volt
0·017 sec.	0·142
∞	0·091
0·017	0·139
∞	0·088
0·0087	0·183
∞	0·094
0·0087	0·205
∞	0·094
0·0052	0·334
∞	0·094
0·0052	0·334
∞	0·091
0·0026	0·567

The minimum voltage for make alone was tested before and after every observation made with a short interval between break and make, and the results are sufficiently concordant to show that the nerve remained in good condition throughout the experiment. The mean results of the observations are:—

Time interval between break and make	Voltage required for minimal excitation
∞	0·092 volt
0·017 sec.	0·140
0·0087	0·194
0·0052	0·334
0·0026	0·567

[1] Keith Lucas. This *Journal*, xxxiv. p. 375. 1906.

The results of this experiment are plotted in Fig. 3, the abscissæ measuring values of t (interval between break and make), while as ordinates there are shown the corresponding values of v (minimal voltage), of tv, and of tv^2. It will be observed that as the values of t decrease:—

(1) v increases slowly at first and then more and more rapidly;

(2) tv decreases approximately in a straight line;

(3) tv^2 is increasing with the three smallest values of t. No marked minimum is shown in the plotted points, but it is evident that tv^2 must previously have decreased with decreasing values of t, for with $t = \infty$ the value of v is not much less than it is with $t = 0{\cdot}017$ sec. It is therefore probable that the value of tv^2 corresponding to $t = 0{\cdot}017$ sec. lies on the decreasing limb of the curve. The actual minimum shown in the curve of Fig. 3 is obtained by interpolation of values of tv^2 from values of v found at several points along the curve relating t to v, between the values of $t = 0{\cdot}017$ sec. and $t = 0{\cdot}0087$ sec.

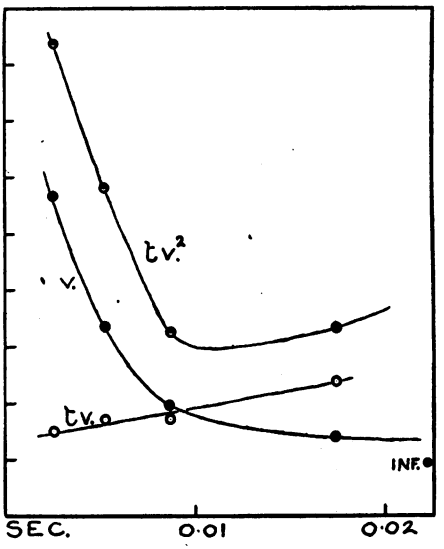

Fig. 3. Exp. 1. Sciatic of Frog. Variable durations of no current. Relation of values of v, tv, and tv^2 to values of t. Abscissæ, 1 division = 0·01 sec. Ordinates for v, 1 division = 0·1 volt. For tv 1 division = 0·001 tv; for tv^2 1 division = 0·0001 tv^2; where t is in seconds and v in volts.

It is to be regretted that the experiment could not be carried over a larger range of t, but the prolonged passage of constant current through the nerve is apt to cause irregularity. The actual values plotted are:—

t (sec.)	(v volts)	tv	tv^2
∞	0·092	∞	∞
0·017	0·140	0·0024	0·000333
0·0087	0·194	0·0017	0·000326
0·0052	0·334	0·0017	0·000581
0·0026	0·567	0·0015	0·000833

The same three facts are observed in Exp. 2, the details of which are tabulated below and plotted in Fig. 4. In this case the minimum of tv^2 is more clearly shown than in Exp. 1.

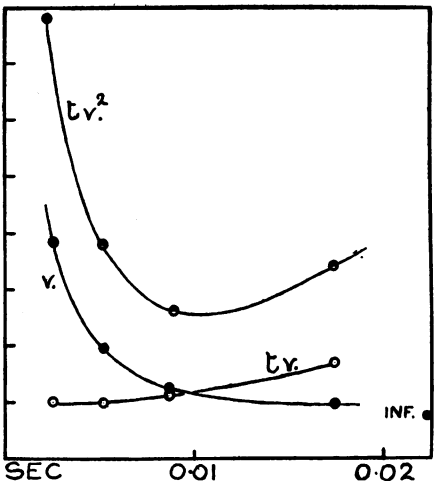

Fig. 4. Exp. 2. The values of ordinates and abscissæ are the same as in Fig. 3, except for tv^2, which is doubled to avoid confusion with the other curves.

Exp. 2. Sciatic of Frog. Temperature 8·1° C. Resistance of nerve and electrodes 56000 ohms.

Time interval between break and make	Voltage required for minimal excitation
∞	0·074 volt
0·017 sec.	0·099
∞	0·074
0·017	0·099
∞	0·077
0·0087	0·122
∞	0·080
0·0087	0·125
∞	0·077
0·0052	0·195
∞	0·077
0·0052	0·198
∞	0·077
0·0026	0·384

Mean values:

t (sec.)	(v volts)	tv	tv^2
∞	0·077	∞	∞
0·017	0·099	0·0017	0·00017
0·0087	0·123	0·0011	0·00013
0·0052	0·196	0·0010	0·00019
0·0026	0·384	0·0010	0·00039

It appears then from these experiments that the same general relation between the time interval and the values of tv or of tv^2 holds whether current passes during the interval or does not pass. I conclude that the form of the relation between the duration of the interval and the minimum voltage is determined mainly by the interference of make and break in both cases, not by the excitatory effect of energy or of quantity of electricity.

Moreover, as I shall now attempt to show, the interference of make and break affords a satisfactory explanation of the correspondence which has been observed to exist between the rapidity of the excitation process in any tissue and the shortness of current at which an increase of the minimum voltage is first observed. And this correspondence receives no satisfactory explanation on the view that the energy or the quantity of electricity is the important factor in excitation.

III. *The relation of current duration to minimum voltage as affected by the rapidity with which excitation develops.*

Much detailed work has been done recently upon the exact relation between the duration of a current and the minimal voltage which suffices for excitation. The investigation of this relation in many different animals—the work of M. and Mme Lapicque[1] and of Weiss[2] —has led to the generalisation that the duration of current at which the voltage necessary for excitation begins to increase is proportioned to the duration of the contraction in each tissue. In one paper M. and Mme Lapicque[3] speak of a similiar relation to the duration of excitation, and Weiss[4] points out that the voltage begins to increase at a duration of current which is about equal to the latent period of the tissue concerned. But no satisfactory hypothesis has been put forward

[1] M. and Mme Lapicque. *C. R. Acad. des Sciences*, CXXXVI. p. 1147, 1903; CXXXVI. p. 1477; CXL. p. 801, 1905. *Journ. de Physiol. et de Path.* v. pp. 843, 991. 1903.

[2] Weiss. *Arch. Ital. Biol.* XXXV. pp. 434–436. 1901.

[3] M. and Mme Lapicque. *C. R. Acad. des Sciences.* CXL. p. 801. 1905.

[4] Weiss. *Journ. de Physiol. et de Path.* IV. p. 823. 1901.

to account for these relations. If, however, we suppose that the excitatory disturbance, which is directly caused by the stimulus, reaches its full development in a time which is roughly proportional in each tissue to the duration of contraction and to the duration of the latent period, a supposition which is probably just, then the interference of the effects of make and break will account for the relation which is observed to exist between the duration of contraction or of latent period and the duration of current at which the voltage begins to increase. For as the duration of the current is decreased, the inhibition produced at the cathode by breaking the current can only begin to render less effective the excitatory disturbance previously set up by the make, if it occurs before the latter has reached its full development. In this way the time interval at which break following make just begins to render necessary an increased voltage for excitation is seen to be equal to the time which the excitatory disturbance requires for its full development.

IV. *The use of the relation last discussed for the analysis of complex excitable tissues.*

Not only the tissues of different animals, but also the different tissues of one animal show regular differences in the relation between the duration of the exciting current and its minimal voltage. And these differences are due, if the view which has just been put forward is correct, to the different rates at which the excitatory disturbances proceed. For example, I have found the following relations from experiments made on the sciatic nerve and on the nerveless part of the sartorius muscle in the Toad.

The apparatus used for obtaining short currents of variable duration was in the main that already described. The pendulum and keys, k_1, k_2, were those shown in Fig. 2. The circuit was arranged as in Fig. 5. The wires A and B are each one metre long. A is of about 5 ohms resistance, B of negligible resistance. The battery current is led to the brass pieces C and D which form the extreme ends of A, with a series resistance R of about 40 ohms. The slider S makes contact between A and B, and is used for varying the potential difference between D and E. As long as k_1 and k_2 are closed, D and E are short circuited, so that practically no current flows by the circuit through k_2 and the nerve. When k_1 is opened, while k_2 remains closed, current flows through k_2 and the nerve. When both k_1 and k_2 are

opened the nerve is cut out of circuit. The time during which current flows through the nerve is therefore the interval between the opening of k_1 and the opening of k_2. In principle this method is identical with that used by Weiss[1], and the particular arrangement of the circuit shown in Fig. 3 was adopted in order that self-induction might be reduced to a minimum by the twisting together of the several pairs of leads in which the current undergoes large variations.

The tissue to be excited was set up in the fluid electrodes previously mentioned.

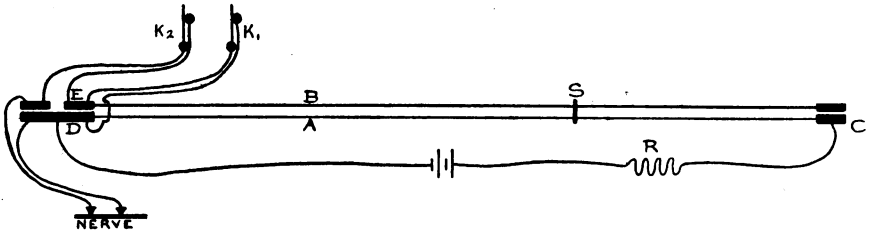

Fig. 5. Arrangement of circuit for obtaining currents of short duration.

Two experiments made on the trunk of the sciatic nerve in the Toad gave the following results.

Exp. 3. Sciatic nerve of Toad. About 8 mm. of nerve between electrodes. Descending current. Temperature 10·1° C.

Duration of current	Voltage required for minimal excitation	Duration of current	Voltage required for minimal excitation
0·0070 sec.	0·102 volt	∝	0·080
0·0070	0·104	0·0017	0·154
∝	0·096	0·0017	0·152
0·0035	0·130	∝	0·080
0·0035	0·130	0·0035	0·110
∝	0·093	0·0035	0·106
0·0017	0·154	∝	0·077
0·0017	0·150	0·0070	0·080
∝	0·091	0·0070	0·080
0·00087	0·180		
0·00087	0·182	Mean values:	
∝	0·088	∝	0·086
0·00043	0·240	0·0070	0·091
0·00043	0·250	0·0035	0·119
∝	0·083	0·0017	0·152
0·00087	0·178	0·00087	0·179
0·00087	0·178	0·00043	0·245

[1] Weiss. *Arch. Ital. Biol.* xxxv. p. 432. 1901.

Exp. 4. Sciatic nerve of Toad. Descending current. Temperature 10·2° C.

Duration of current	Voltage required for minimal excitation	Duration of current	Voltage required for minimal excitation
∞	0·083 volt	∞	0·080
0·0070 sec.	0·086	0·00052	0·211
0·0070	0·086	0·00052	0·210
∞	0·085		
0·0035	0·109	Mean values:	
0·0035	0·109	∞	0·082
∞	0·081	0·0070	0·086
0·0017	0·126	0·0035	0·109
0·0017	0·126	0·0017	0·126
∞	0·083	0·00087	0·158
0·00087	0·158	0·00052	0·211
0·00087	0·157		

In Fig. 6 are plotted the results of Exp. 3. It will be observed that the voltage required for minimal excitation is doubled when the duration of the current is reduced to about 0·001 sec. A like increase of voltage is reached in Exp. 4 with the duration 0·0008 sec.

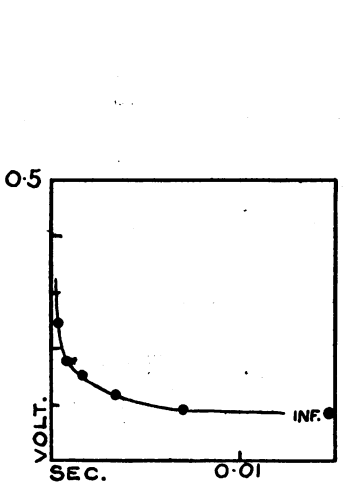

Fig. 6.

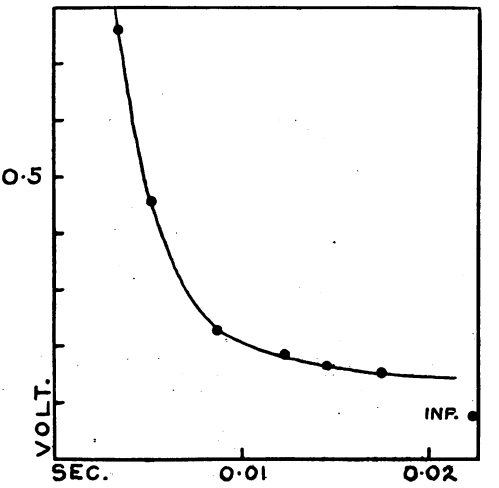

Fig. 7.

Fig. 6. Exp. 3. Relation of current duration to minimum voltage in the sciatic nerve of the Toad.

One division of the ordinate = 0·1 volt.
One division of the abscissa = 0·01 second.

Fig. 7. Exp. 5. Relation of current duration to minimum voltage in the nerve-free pelvic end of the Toad's sartorius. One division of the ordinate = 0·1 volt, one division of the abscissa = 0·01 second.

Exp. 5, which is tabulated below and plotted in Fig. 7, was made upon the nerve-free end of the Toad's sartorius. The voltage required for excitation is doubled at the duration 0·017 sec. This duration is more than ten times as great as that found above in the experiments made upon the nerve trunk.

Exp. 5. Nerve-free pelvic end of Toad's sartorius. Temperature 10·1° C.

Duration of current	Voltage required for minimal excitation	Duration of current	Voltage required for minimal excitation
∞	0·076 volt	0·0052	0·484
0·017 sec.	0·149	∞	0·076
0·017	0·153	0·0035	0·760
∞	0·081		
0·012	0·183	Mean values :	
0·012	0·183	∞	0·077
∞	0·076	0·017	0·151
0·0087	0·229	0·012	0·183
0·0087	0·225	0·0087	0·227
∞	0·076	0·0052	0·458
0·0052	0·432	0·0035	0·760

There is then a marked difference between the curve relating current duration to minimum voltage in the nerve-trunk and the corresponding curve for the nerveless muscle, a difference which is due, if we have viewed correctly the action of currents of short duration, to the greater rapidity with which the excitatory disturbance develops in the nerve. And this difference may be used for determining what excitable substances are called into action when currents of short duration are applied to that part of the sartorius where nerves enter. The following results, obtained from an experiment made on the region of nerve-entry in the same muscle as was used in Exp. 5, show how this analysis can be made.

The results of Exp. 5 B are plotted in Fig. 8. The curve is complex, but consists obviously of a series of curves similar in general form to those of Fig. 6 or Fig. 7. Consider first the portion of the curve lying between *B* and *C*. It resembles fairly closely the simple curve of Fig. 6 obtained by stimulation of the sciatic nerve. The voltage in this case is constant for durations exceeding about 0·01 sec., and is doubled with a duration of 0·003 sec.; in Fig. 6 the voltage is constant for durations exceeding about 0·009 sec., and is doubled at 0·001 sec. On the other hand there is a very wide divergence between either of these curves and that obtained from the nerve-free muscle (Fig. 7), where the voltage is changing considerably at 0·02 sec., and is doubled with a duration as long as 0·017 sec. Therefore it appears

Exp. 5 B. Same muscle as that used in Exp. 5. Electrodes applied to the region of nerve entry. Temperature 10·2° C.

Duration of current	Voltage required for minimal excitation	Duration of current	Voltage required for minimal excitation
∞	0·093 volt	∞	0·102
0·026 sec.	0·161	0·00052	0·404
0·026	0·166	0·00052	0·404
∞	0·093	∞	0·102
0·017	0·161	0·00026	0·433
0·017	0·161	0·00026	0·429
∞	0·093	∞	0·119
0·012	0·166	0·000087	0·595
0·012	0·166	0·000087	0·608
∞	0·098		
0·0087	0·170	**Mean values:**	
0·0087	0·166	∞	0·101
∞	0·102	0·026	0·163
0·0052	0·191	0·017	0·161
0·0052	0·195	0·012	0·166
∞	0·102	0·0087	0·168
0·0035	0·297	0·0052	0·193
0·0035	0·297	0·0035	0·297
∞	0·102	0·0017	0·397
0·0017	0·399	0·00087	0·399
0·0017	0·395	0·00052	0·404
∞	0·102	0·00026	0·431
0·00087	0·399	0·000087	0·601
0·00087	0·399		

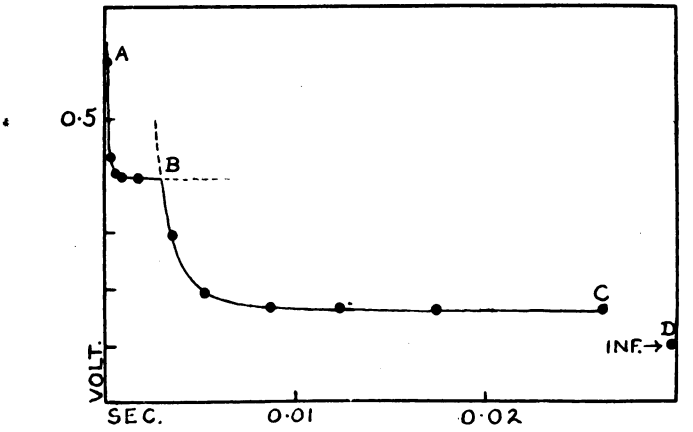

Fig. 8. Exp. 5 B. Relation of current-duration to minimal voltage in the middle part of the Toad's Sartorius. One division of the abscissa = 0·01 second, one division of the ordinate = 0·1 volt.

probable that the portion of the curve lying between B and C is obtained by excitation of the substance which I have called the substance γ of the nerve-trunks[1].

Between C and D the voltage changes considerably, and such a change does not occur in the corresponding part of Fig. 6, where the nerve-trunk alone is being excited. But the curve of Fig. 7, obtained by excitation of the nerveless muscle, does show a change of voltage going on at the longest durations tested, so that the change of voltage between C and D may well be due to the excitation of the substance α of the muscle, may be in fact a portion of a curve similar to that of Fig. 7[2].

Between A and B there is a portion of a curve in which the voltage is constant at durations exceeding 0·0009 sec. and is doubled at about 0·00005 sec. This must be due to the presence of an excitable substance whose excitatory disturbance develops in about one-tenth of the time occupied by that of the nerve. It is probable that this is the substance which I have previously described as the substance β, for that substance was always, in experiments made with condenser discharges, excited by the discharges of shortest duration.

In this way the application of a series of currents of different durations serves for the analysis of a complex excitable tissue. The present method is easier of application than the method of condenser-discharges which I have previously used[3], partly owing to the difficulty of maintaining standard capacities true to their values, and partly because the present method does not require a knowledge of the resistance of the tissue used.

I have previously used the time of discharge at which energy is at a minimum as the label for each excitable substance found, and this method might of course be applied as well to the results obtained from the present short currents as to those obtained from condenser-discharges. For example in Exp. 5 the energy (volts^2 × duration) is at a minimum when the duration is 0·00087 sec. The relation of the minimum of energy to a duration-voltage curve such as that of Fig. 6 may be regarded in the following way. At durations exceeding about

[1] Keith Lucas. This *Journal*, xxxv. p. 111, 1906. See note below.

[2] The apparatus at present available does not afford range enough of current durations to permit the precise exploration of this part of the curve. I hope soon to have an instrument giving wider range. The experiments described here are used merely as illustrations of the method of analysis, and do not claim to deal exhaustively with the tissues upon which they are made.

[3] Keith Lucas. This *Journal*, xxxiv. p. 372, 1906, and xxxv. p. 103. 1906.

0·007 sec. the voltage (v) is practically constant, so that as the duration (t) is decreased from infinity to 0·007 sec. v^2 will scarcely change, and therefore the product v^2t, which measures the energy, will decrease. On the other hand at durations less than about 0·0004 sec. v is obviously increasing extremely rapidly for very small decreases in the value of t, and v^2 is increasing more rapidly still, so that at these durations the value of v^2t increases with decreasing values of t. At some point between the durations 0·007 sec. and 0·0004 sec. the change from decreasing to increasing values of v^2t will take place, and at this point energy will be at a minimum. On comparing Fig. 6 with Fig. 7 we see that in the latter both the part of the curve in which v is constant, and the part in which v is increasing very rapidly for small changes of t, are displaced considerably to the right. In Fig. 7, therefore, the minimum of energy which lies between these parts of the curve occurs at a much larger value of t than in Fig. 6. In fact the minimum is at a value larger than $t = 0{\cdot}017$ sec., the largest value of t used in the experiment. In this way the value of t at which energy is at a minimum comes to bear a relation to the value of t at which v just begins to change, and so to the time in which the excitatory disturbance develops.

But the duration at which the voltage is doubled can be determined more precisely and with less calculation than that at which energy is at a minimum[1]. I propose then to adopt as a label for each excitable substance the duration at which the minimal voltage is doubled. And since this duration will bear in each tissue a relation to the time in which excitation reaches its full development, I shall speak of it as the 'excitation-time' of the tissue. The excitation times determined in this paper will be approximately,

for the substance	α	0·017 sec.
,, ,,	γ	0·0008—0·003 sec.
,, ,,	β	0·00005 sec.

when the temperature is between 10° and 11° C.

The whole possibility of applying currents of short duration, whether battery currents or condenser-discharge to the analysis of a complex excitable tissue depends upon the remarkable fact that in such a tissue the minimum voltage which will excite each substance is

[1] M. and Mme Lapicque (*C. R. Acad. des Sciences*, CXL. p. 803, 1905), have proposed to use the duration at which the voltage is just perceptibly increased, but it is obviously difficult to determine this with precision.

inversely proportional to the excitation-time of the substance. For example in Exp. 5 B, the minimum voltages are, for α 0·10 volt, for γ 0·16 volt, and for β 0·40 volt. If this order were reversed, so that β had the lowest minimum voltage, it is obvious that for all durations of current β would alone be excited by a minimal voltage, and the method of analysis would fail.

In order to test whether this relation between excitation-time and minimal voltage held good in any tissues other than the sartorius muscles of the Frog and the Toad, I made experiments upon the muscles and nerves of the Lobster.

V. *Experiments on the muscles and nerves of the Lobster.*

These experiments were made at a time when the apparatus for obtaining short galvanic currents was not yet available. The method of condenser-discharges was therefore used, the circuit being arranged in the manner which I have described in a previous paper[1].

The claw of the Lobster was removed, separation taking place at the joint between the basipodite and the ischiopodite. Non-polarisable kaolin electrodes were applied, one to the open end of the ischiopodite, the other to a hole bored in the shell of the meropodite. The positions of the electrodes are the shaded areas *A* and *B* in Fig. 9. The limb was

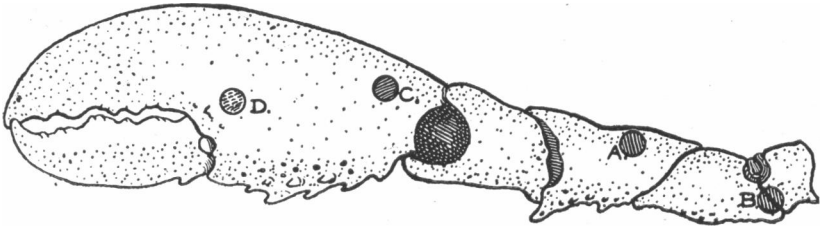

Fig. 9. Claw of Lobster showing the points at which the shell was bored for the application of non-polarisable electrodes. The hole *D* is on the further side of the claw. Left claw seen from below.

clamped to a stand, and a lever, attached to the dactylopodite, was arranged either to move over a scale or to write on a smoked drum. The tendon of the abductor muscle was cut, so that the movements of the adductor only were recorded.

[1] Keith Lucas. This *Journal*, xxxiv. p. 374. 1906. Fig. 2.

Since the experiments were made during September, at temperatures ranging from 18° to 20° C., the muscle was free from tone, and inhibition was not obtained with any stimuli used.

Exp. 6 is a typical example of the results obtained from stimulating in this way the nerve to the adductor muscle. The first column shows the voltage to which the condenser was charged, the second the minimum capacity in microfarads at which excitation was obtained, the third the time (T)[1] taken by the current in falling to one-tenth of its original value, the fourth the energy of the discharge in ergs, and the fifth the character of the muscle-contraction.

EXP. 6. Nerve to adductor of Lobster's claw. Tendon of abductor cut. Electrodes in ischiopodite and meropodite. Movement of dactylopodite taken as index of excitation. Resistance through which condenser was discharged 4240 ohms. Temperature 18·5° C.

Observation	V (volts)	F (microfarads)	T seconds	$5V^2F$ (ergs)	Character of contraction
1	2·53	18·95	0·186	608	slow
2	2·80	14·9	0·145	586	,,
3	3·14	11·4	0·112	562 min.	,,
4	3·57	8·9	0·087	566	,,
5	4·13	6·8	0·067	580	,,
6	4·90	5·3	0·052	637	,,
7	6·03	4·2	0·041	764	,,
8	7·84	3·15	0·031	798	,,
9	11·2	2·23	0·022	1396 max.	,,
10	14·2	1·17	0·0115	941	quick
11	19·5	0·41	0·0040	622 min.	,,
12	21·1	0·34	0·0033	758	,,
13	25·2	0·239	0·0023	758	,,
14	31·2	0·162	0·0016	787	,,
15	40·9	0·106	0·00104	887	,,
16	48·5	0·098	0·00096	1152	,,

In Fig. 10 the results of this experiment are plotted to show the relation between the minimum voltage and the duration of the discharge. There is a break in the curve at B, giving the appearance of two curves crossing at that point, as the dotted lines suggest. If this interpretation of the curve is correct, we have here a fresh example of the association of shorter excitation-time with higher minimum voltage; for the continuation of the curve AB beyond B will obviously lie above the curve BC, so that the curve AB will have been obtained by the excitation of a substance having a shorter excitation-time,

[1] $T=\frac{FR}{0\cdot434}$, where F is in farads, R in ohms, and T in seconds.

and a higher minimum voltage than the substance which gave the curve *BC*.

An examination of the energy used for excitation also points to the presence of two substances, one excited in observations 1—9, a second excited in observations 10—16. For there is a relative maximum of energy at observation 9, and a well-marked minimum of energy on each side of this.

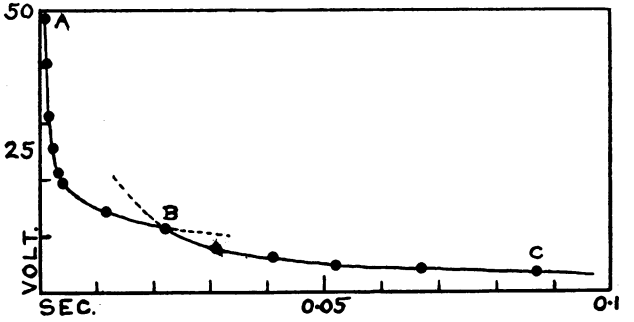

Fig. 10. Exp. 6. Relation of current-duration to minimal voltage in nerve to adductor muscle of Lobster's claw. Ordinates, 1 division = 10 volts, abscissæ, 1 division = 0·10 sec. Observations 1, 2 and 3 are not plotted.

Now the view that the point where two curves intersect, or the point where energy reaches a relative maximum, marks the transition from one excitable substance to another, finds confirmation in a remarkable fact which the experiments on Frogs and Toads did not show. In observations 1—9 of this experiment the contraction was uniformly slow; at observation 10 it suddenly became about five times as rapid, and it maintained the latter character during observations 10—16. The change in character of the response therefore coincided exactly with the crossing of the curves at *B* and with the relative maximum of energy. An example of this change in the character of response is given in Fig. 11, which is taken from Exp. 7.

Exp. 7. Resistance = 3740 ohms. Temperature = 19·5° C. Rate of movement of recording surface 82 mm. per sec.

	V (volts)	*F* (microfarads)	*T* (seconds)
Upper curve	14·2	20·0	0·17
Lower curve	77·0	1·1	0·0095

This coincidence of the crossing of the curves and of the relative maximum of energy with the change in character of the muscular response was regularly observed in all experiments in which the nerve was excited. It was observed whether the electrodes were placed across

the nerve only as at *A*—*B* (Fig. 9), or across the muscle itself, as at *C*—*D* (Fig. 9). An example of the latter sort is given in Exp. 8. A repetition of this experiment (8 A), made about half an hour later, is also

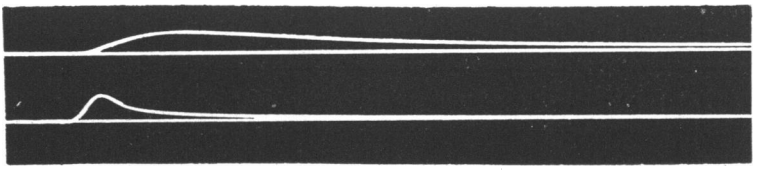

Fig. 11. Exp. 7. Two contractions of adductor muscle of Lobster's claw, showing the change in the character of response with change in the duration of condenser discharge.

Upper curve, $T = 0{\cdot}17$ sec.
Lower curve, $T = 0{\cdot}0095$ sec.

Exp. 8. Adductor muscle of Lobster's claw. Tendon of abductor cut. Electrodes on opposite sides of propodite. Resistance through which condenser was discharged 5640 ohms. Temperature 19·5° C.

Observation	V (volts)	F (microfarads)	T (seconds)	$5V^2F$ (ergs)	Character of contraction
1	8·9	11·0	0·143	4360	slow
2	10·3	5·6	0·073	2980	,,
3	11·2	4·2	0·055	2630	,,
4	14·2	2·25	0·029	2280 min.	,,
5	16·0	1·82	0·024	2320	,,
6	18·2	1·46	0·019	2410	,,
7	21·1	1·19	0·0155	2650	,,
8	25·2	0·89	0·0116	2820	,,
9	31·2	0·70	0·0091	3400	,,
10	40·9	0·42	0·0055	3510 max.	quick
11	48·5	0·271	0·0035	3190	,,
12	59·5	0·179	0·0023	3170 min.	,,
13	77·0	0·117	0·0015	3470	,,

Exp. 8 A. As 8, experiment made half an hour later.

Observation	V (volts)	F (microfarads)	T (seconds)	$5V^2F$ (ergs)	Character of contraction
1	8·9	10·5	0·136	4160	slow
2	10·3	5·3	0·069	2820	,,
3	11·2	4·0	0·052	2500	,,
4	14·2	2·17	0·028	2200 min.	,,
5	16·0	1·77	0·023	2260	,,
6	18·2	1·43	0·0186	2360	,,
7	21·1	1·15	0·0149	2560	,,
8	25·2	0·865	0·0112	2740	,,
9	31·2	0·690	0·0090	3350	,,
10	40·9	0·416	0·0054	3480 max.	quick
11	48·5	0·274	0·0036	3220	,,
12	59·5	0·180	0·0023	3190 min.	,,
13	77·0	0·115	0·0015	3410	,,

given in order to show how steady the condition of the adductor preparation remains. It will be seen that the minimum capacities found for each voltage, and the positions of the maxima and minima of energy correspond very closely in the two experiments.

I bring forward these experiments on the Lobster only because they bear upon the method of analysis by currents of short duration. They show that the relation between excitation-time and minimum voltage, on which the possibility of the method hangs, holds good outside the amphibia; and they strengthen the interpretation which I have placed upon the complex curves which a mixed excitable tissue yields. Towards the analysis of the neuromuscular apparatus in the Lobster they do not yet go far. It appears probable that the nerve to the adductor contains two excitable substances, each linked to a separate contractile substance in the muscle. But whether the separate substances are contained in separate nerve-fibres and in separate muscle-fibres, and whether stimulation across the muscle itself excites directly the nerves alone, are questions which I leave aside.

SUMMARY.

When currents of short duration are employed for the excitation of muscle or nerve, decrease of the duration beyond certain limits renders necessary an increase of voltage if excitation is to result. This fact has led physiologists to look for some relation between excitation and either the energy expended or the quantity of electricity employed in the exciting current.

But Woodworth has shown that the same is true for intervals of no current interrupting a constant current. In this case there can be no question of energy or quantity becoming less as the interval becomes shorter, since no current passes during the interval. He has proposed the explanation that the shorter intervals are less effective as stimuli because in them the opposed effects of make and break interfere more with one another.

Experiments described in this paper show that the same relations are observable between the values of t (the duration of the interval) and the values of tv or tv^2 (where v is the minimal voltage), whether the interval be one in which current passes or one in which current does not pass. From this it is inferred that the energy expended and the quantity of electricity employed are not factors of importance in

excitation by currents of short duration, but that the relations above mentioned are determined both for currents of short duration and for short intervals of no current by the interference of the opposed effects of make and break.

Moreover the probability that the latter view is correct is increased by its ability to explain the observed relation between the duration of current at which minimum voltage begins to increase and the rapidity with which the excitatory processes go on in any tissue.

The difference exhibited by different tissues in this relation of current duration to minimum voltage can be used for the analysis of mixed excitable tissues. Experiments are described in which this relation is determined for the nerve, the nerve-free muscle, and the region of nerve-entry in the muscle of the Toad. The curves relating current duration to minimum voltage in the first two are simple, whereas that obtained from the region of nerve-entry is complex, and appears to consist of at least three curves superposed. Two of the superposed curves can be recognised as the curves of nerve and of nerve-free muscle, while the third is probably that of the 'substance β' described in a previous paper. It is shown how the minimum of energy, used in previous experiments for the identification of different excitable substances is related to the simple duration-voltage curve, and so to the rapidity of the excitatory process.

The possibility of using this method of analysis depends upon the fact that excitable substances whose excitatory processes develop more rapidly require a higher voltage for their excitation. A similar relation is shown to occur in the nerves of the Lobster.

In the experiments made on the Lobster confirmation is obtained of the view that each break in the continuity of a duration-voltage curve, or each passage from one minimum of energy to another, implies a change in the excitable substance immediately affected by the stimulus. For a break of continuity in the curve, and a relative maximum of energy between two minima, are found to coincide with an abrupt change in the character of the muscular response.

The work on the Lobster was carried out in 1906, while I held the Cambridge University Table at Plymouth. I wish to give my cordial thanks to Dr Allen and to the Staff of the Laboratory.