

THE IMPULSES PRODUCED BY SENSORY NERVE-ENDINGS. Part 2. The response of a Single End-Organ.

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IN Part I of the present series⁽¹⁾ one of us described an instrument consisting of a capillary electrometer with a 3-valve amplifier, capable of recording the action currents set up in sensory nerve fibres by appropriate stimulation of their end-organs. A preliminary analysis of the results was given, but it was pointed out that an essential step was missing. All the records were made from nerve trunks containing many afferent fibres and it was impossible to tell with certainty what was happening in each fibre, what was the frequency of the response, how it varied with the stimulus, etc. The present paper remedies this defect, for it is concerned with the impulses set up by a single end-organ and travelling in a single afferent nerve fibre. Only one type of end-organ has been investigated, but the results seem to be of such general application that it will be surprising if other types are found to behave very differently.

Preparation employed. The recording instrument has already been described in detail and the only modification introduced has been the provision of a variable shunt to reduce the excursions of the electrometer, should this be necessary. The preparation employed was suggested to us by the papers of Keith Lucas on the all-or-none response of muscle fibre. In these experiments Lucas used the m. cutaneus dorsi of the frog. He found that the nerve supplying this muscle had ten fibres only, of which one or two might be sensory. We have investigated this muscle, but so far we have been unable to detect any action currents in the nerve roots when the muscle is stretched, and we are inclined to think that all the fibres are motor. But in a footnote Lucas mentions another muscle—the sterno-cutaneus—in which there is no doubt of the existence of sensory end-organs. The number of fibres in the nerve supplying the muscle varies from 12 to 25. There is certainly one muscle-spindle in the muscle (it is figured in Cajal's book, *Textura del Sistema Nervioso*, Madrid, 1899, p. 404), and as our results show there are usually three or

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four end-organs which are stimulated by tension in the muscle of a medium-sized frog (*R. temporaria*). We have used this muscle in all the experiments to be described. The preparation is fairly simple. The skin on the chest of the frog is removed except for a small piece in which the cephalic end of the muscle is inserted. This piece of skin serves as the point of attachment of the silk thread by which the muscle is stretched. The origin of the muscle is not interfered with but the fascial investments on either side are cut through. The nerve is derived from a branch of the large brachial nerve, and in dissecting it the brachial nerve is cut high up in the axillary space and again just below the branch which supplies the sterno-cutaneous. This is followed down from the brachial nerve, all side branches being cut, until it becomes reduced to the extremely slender trunk which enters the muscle about half-way down its outer border. The preparation is tested by stimulating the nerve with an induction shock. This should produce a contraction in the sterno-cutaneous and in no other muscle, and as a rule there is no difficulty in securing this condition. The preparation is placed inside the metal box which acts as a shield from electromagnetic disturbances (see Part I), with the nerve slung by a thread from a small wooden peg at the side of the frog. Non-polarisable electrodes of the Ag, AgCl, NaCl, gelatine type are connected to the nerve by short lengths of moist carpet thread embedded in the gelatine. These allow some movement of the nerve to take place (and this is bound to happen when the muscle is extended) without producing changes of potential in the electrometer. For stimulating the end-organs in the muscle we have used weights of $\frac{1}{4}$, $\frac{1}{2}$, 1, 2, 3 and 5 gm. attached to the thread from the muscle and allowed to hang over a light pulley. The maximum tension developed by the sterno-cutaneous of a medium-sized frog in an isometric contraction produced by tetanising the nerve was 2 gm. so that the above range of tensions probably covers the values occurring naturally in the intact animal. In some of the experiments we have used an elastic apparatus which permits of gradual extension. This will be described later. The records of the action current were made with 3-valve amplification (= 1850) on plates travelling at 1 metre per sec. or less and on cinematograph film travelling 10–15 cm. per sec. Since the nerve trunk (*i.e.* the nervus pectoralis proprius, Gaupp) to which the electrodes are applied contains only 50 to 200 fibres, the responses are large and they are sometimes so large that their size must be reduced by shunting the electrometer or by bringing the leads very close together on the nerve, so that the two phases of the response interfere. The latter method is usually preferable,

since a change in the resistance of the electrometer circuit alters the constant used in the analysis of the records.

Results. In our earliest experiments we recorded the responses in the nerve with various weights which were hung on the muscle 10 seconds before the plate was exposed and remained on it during the exposure. The interval of 10 seconds between the moment of application of the weight and the making of the record was chosen to allow the conditions to become steady before the record was made. The records all showed a succession of action currents with the same form and time relations as those found in the frog's sciatic (cf. Part I), occurring in irregular succession at frequencies which were as high as 150 per second with a 2 gm. weight. Most of the action currents conformed to a standard size, but some were larger, and on analysis many of these proved to be made up of two or more responses, separated by a very short time interval. The interval between these responses was often as short as $1/1000$ sec. or less, and this interval is shorter than the absolute refractory period of the frog's sciatic (about .002 sec. 15° C.). It was therefore obvious that the responses were not all produced by the same nerve fibre, and we attempted to diminish the number of end-organs or nerve fibres in action by cutting narrow parallel strips away from the muscle on the mesial side. As a rule the first section produced a considerable reduction in the frequency of the responses for a given stimulus and evidence of regular rhythms began to appear in the records. As more and more of the muscle was cut away the existence of definite rhythms became more and more obvious. The change that occurs is best illustrated by the records from our most successful experiment of this type, Exp. 1 (Fig. 1). This was made from a very large male frog and the muscle and its nerve were isolated from the body, the abdominal muscles from which the sterno-cutaneous takes its attachment being held in a clamp. In *A* the muscle is intact and the load is 2 gm. In *B* the stimulus is the same but the first strip of muscle has been removed and the responses are fewer and more regular. In *C* a second cut has been made and the stimulus was reduced to 1 gm. to avoid damaging the muscle. An analysis of this record shows that the responses occur in four regular series with periods of .035, .042, .045 and .046 sec. After the next cut the responses become completely regular with a period of .030 sec. At this stage of the experiment about two-thirds of the muscle had been removed and the subsequent removal of another small strip abolished the responses completely, though what remained of the muscle would still contract when the nerve was stimulated.

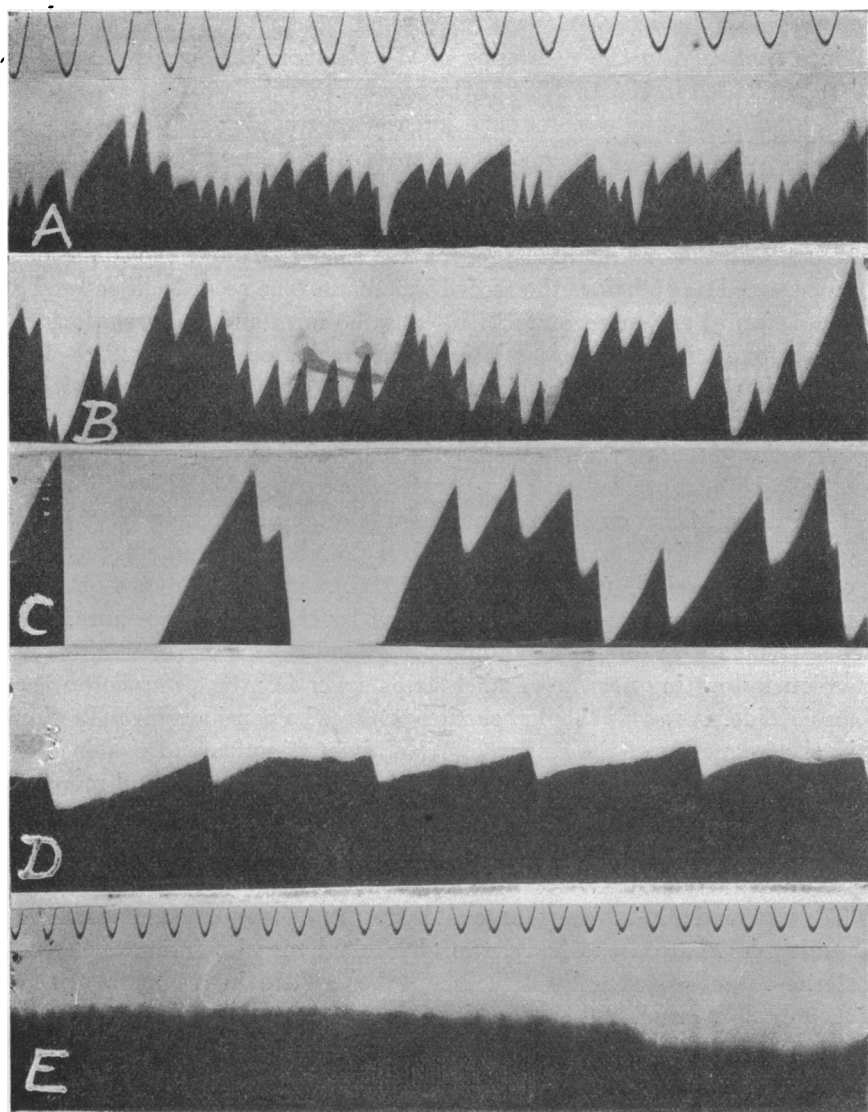


Fig. 1. Exp. 1, 19° C. Afferent responses from nerve when muscle is stretched by a weight applied 10 sec. before record is made. Capillary electrometer with 3-valve amplifier, magnification 490. Time marker gives .01 sec. Responses vary in size, as electrodes are adjusted between each record.

- A. Muscle intact. 2 grm. weight.
- B. First strip removed. 2 grm. weight.
- C. Second strip removed. 1 grm. weight. Impulses in four regular series.
- D. Third strip removed. 1 grm. weight. Single regular series.
- E. Fourth strip removed. 1 grm. weight. Slower plate. No impulses.

Response from single end-organs. We have no direct proof that the regular responses shown in *D* are due to one nerve ending only, but the indirect evidence leaves very little doubt of it. As many of our conclusions are based on this assumption, the evidence needs consideration in some detail. In the first place, the impulses recorded in Fig. 1 *A-D*

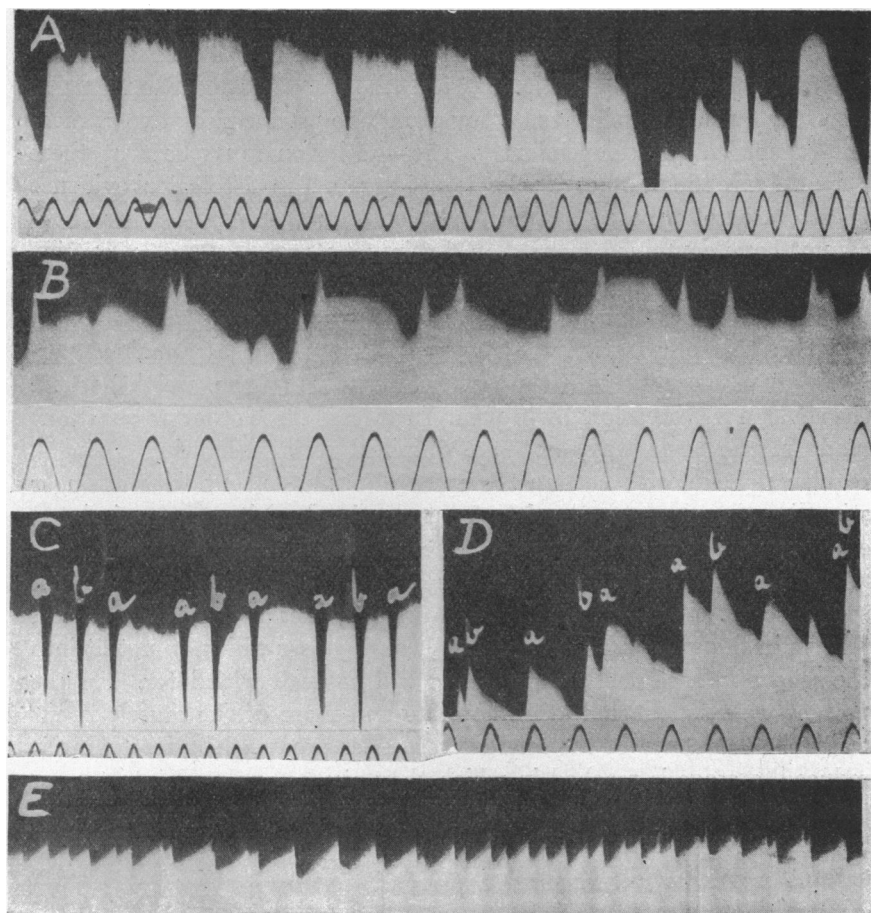


Fig. 2. Examples of rhythmic discharge from different experiments.

- A. Exp. 5. 15° C. Muscle divided. 3 grm., 10 sec. Single rhythm, broken at end.
- B. Exp. 2. 21° C. Muscle divided. 3 grm., 10 sec. Double rhythm.
- C. Exp. 5. 15° C. Muscle divided. 2 grm., 10 sec. Double rhythm.
- D. Exp. 6. 15° C. Muscle divided. 2 grm., 10 sec. Double rhythm, one extra.
- E. Exp. 15. 14° C. Film, speed as in Fig. 5 *D*. Loading just complete. Two rhythms producing beats.

are clearly set up in sensory and not in motor fibres. If traction on the muscle produced impulses in the motor nerve fibres, there is no reason why the removal of little more than two-thirds of the muscle should abolish the responses, for the effects of stimulation showed that the motor nerve supply to the remaining muscle fibres was still intact. When several end-organs are present, as in the intact muscle, there is no indication that they respond synchronously, for the impulses in *A* occur at irregular intervals; and no reason why they should so respond to a stimulus which is continuous and not periodic. Yet in *D* the responses occur so regularly that it is quite impossible that they should be produced by two or more end-organs acting independently. The conclusion must be that these responses are the product of a single end-organ. The histological evidence is certainly not opposed to this conclusion for the preparation used in *D* cannot have contained more than ten intact nerve fibres at an outside estimate, and of these the majority are clearly motor, as may be seen from stained specimens.

With this preparation the rhythm of the responses remained perfectly regular except with the weakest stimulus ($\frac{1}{4}$ grm. weight) where the rhythm was occasionally broken. In at least three other preparations made in the same way, we have obtained records showing a single, regular rhythm with certain strengths of stimulus, but with stronger stimuli, or in other records with the same stimulus, either a few isolated extra responses have appeared or else the record is made up of two or more distinct series of responses side by side. Fig. 2 gives examples of such records. Double rhythms are shown very clearly in *B*, *C*, *D* and *E*, though in *B* and *C* there were one or two responses which do not fit into the scheme. These aberrant responses will be dealt with later. For the present we may conclude that as more and more of the muscle is cut away the frequency of the afferent responses produced by stretching is reduced, a stage is reached in which they can be analysed into two or three regular series and a final stage in which only one regular series is left. Each regular series we take to be the product of a single end-organ.

Production of regular discharges. In these experiments the stimulus, *i.e.* the change of conditions imposed on the muscle, is steady and has no period of its own. To make certain of this we have altered the length of the thread from the muscle to the weight and allowed it to run over a small cardboard bridge placed at various distances from the muscle. These procedures would alter the period of any possible vibrations in the thread, but they have no effect on the rhythm of the response. But it

is not surprising that an end-organ should produce a regular series of discharges under a steady stimulation: it would have been much more so had the discharge been irregular. Indeed, the regular response of the end-organ can be very simply explained without recourse to any other factors than the known properties of excitable tissues in general. In a nerve or muscle fibre a momentary stimulus sets up an impulse which leaves the refractory state behind it. During the absolute refractory period a second stimulus has no effect, but as the refractory state passes away the excitability of the nerve returns gradually. A second stimulus falling during this relative refractory period will succeed in exciting if it is strong enough, and as recovery progresses the strength of the stimulus may be reduced until it is finally no stronger than the threshold value for the resting nerve. The course of events is shown by the "recovery curve" of which many examples have been previously published. The curve in Fig. 3 A is a typical example from a frog's sciatic at 15° C.

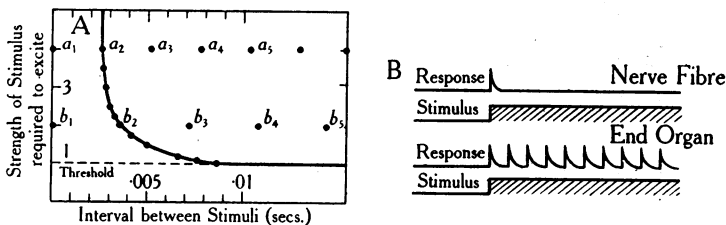


Fig. 3. A. Recovery curve of frog's sciatic at 15° C.

B. Response of nerve fibre and of end-organ to a constant stimulus.

Now if a constant current is used instead of an induction shock, an impulse is set up when the current is turned on, but no further impulses are produced till it is broken again (unless the strength of the current is very great). The impulse leaves the usual refractory state which is recovered from in the usual way, but the constant current does not re-excite, because the nerve has now become adapted to it and it is no longer an effective stimulus. Various hypotheses have been put forward by Nernst, Hill, Lapique, etc. to account for this rapid adaptation, but these need not concern us for the moment. The adaptation is also shown by using a current which increases gradually instead of suddenly. Unless the rate of increase exceeds a certain "liminal current gradient" (Lucas) no impulse is set up.

In most, if not all, sensory end-organs this process of adaptation, if it occurs at all, is evidently a much slower affair. A continued stimulus, such as a state of tension, a light or a sound, produces a continued

passage of sensory impulses to the central nervous system. The sensation diminishes after a time, but it does so very slowly. The difference between the response of a nerve and an end-organ to a constant stimulus can therefore be represented diagrammatically as in Fig. 3 *B*. Now if we assume that the end-organ reacts in exactly the same way as the nerve fibre, with this one exception of a much slower rate of adaptation, it is obvious that a steady stimulus will produce a regular discharge of impulses. When the stimulus is first applied an impulse will be set up and the end-organ will become refractory. It will recover and, as soon as its excitability had returned to the requisite value, another impulse will be set up. If the stimulus has the strength a_1 (Fig. 3 *A*) the impulses

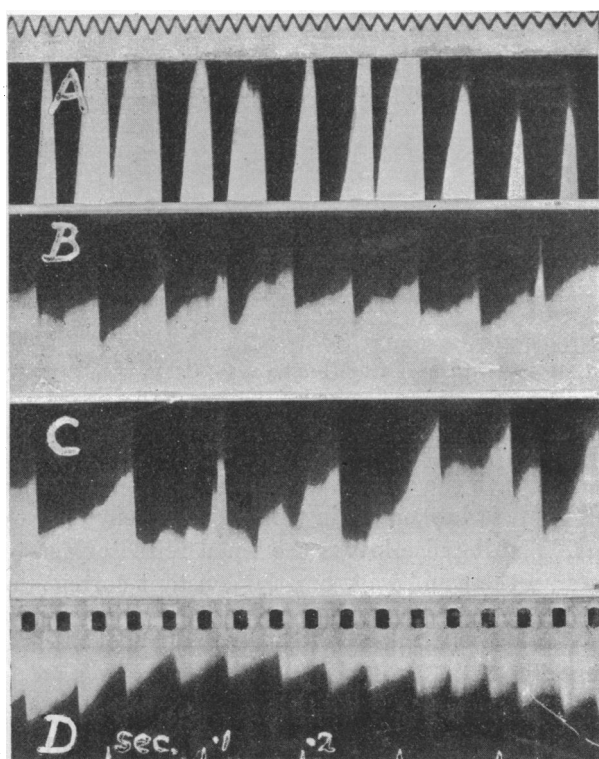


Fig. 4 *A*, *B* and *C*. Exp. 1. Single end-organ in action. Rhythm with various loads.

A. 1 grm., 10 sec. Frequency 33 per sec.

B. $\frac{1}{2}$ grm., 10 sec. Frequency 27 per sec.

C. $\frac{1}{4}$ grm., 10 sec. Frequency 21 per sec. Less regular.

D. Exp. 15. Cinematograph film. Gradual loading and progressive increase in frequency.

will recur at a_1, a_2, a_3, a_4 , etc. If it is weaker, b_1 , the impulses will recur with a slower period b_1, b_2, b_3 , etc. If it increases gradually in strength, the frequency of the impulses should increase too.

The end-organs of the sterno-cutaneous behave as we should expect on this hypothesis. Fig. 4 *A, B, C* shows three sets of responses from Exp. 1 with different weights applied for 10 secs. The weights were 1 grm., $\frac{1}{2}$ grm. and $\frac{1}{4}$ grm. and the corresponding periods are .030, .037 and .046 sec. The records were made at intervals of 1–2 mins. The responses in *A* (1 grm.) are very large and they were reduced in the subsequent records by moving the electrodes closer together. With the $\frac{1}{4}$ grm. weight there are signs of some irregularity in the rhythm, but the dominant rhythm is clearly present. Fig. 4 *D* shows the effect of a gradual increase in the stimulus. In this experiment the weight was lowered very slowly on to the string from the muscle by the movement of a weighed lever controlled by an oil dashpot. There is a gradual increase in frequency and later on a second rhythm begins to appear as the stimulus becomes adequate for a second end-organ.

Recovery curve of end-organ. By plotting the intervals between consecutive responses against the strength of the stimulus we shall evidently obtain a "recovery curve" for the end-organ comparable to the recovery curve of a nerve fibre. A curve constructed in this way for Exp. 1 is given in Fig. 5 *A*. The threshold stimulus—the least tension which will evoke any response—is unknown, so that the strengths of stimuli must be expressed in absolute values and not as multiples of the threshold strength. Similar curves, or portions of curves, from some other experiments, are given in the figure. In some of these the larger weights brought several nerve fibres into action, so that there is some uncertainty in the upper parts of the curve. The general form of the curve apart from its actual time relations can be studied most easily by counting the frequency of the responses from an intact muscle with three or four end-organs, instead of waiting for the lucky chance of a preparation with only one. The average interval between consecutive responses plotted against the strength of the stimulus will give a curve with time relations three or four times as rapid as those of the single organ. The only objection to this method is that a strong stimulus may call into play more end-organs than a weak, and consequently the intervals with strong stimuli will be unduly shortened and the curve will rise more gradually than it would have done if the number of organs in action had been constant. Fig. 5 *B* shows the relation between frequency and weight in an experiment with the muscle intact. The figures opposite each point give the

order in which the records were made. Fig. 5 *C* is the recovery curve constructed from this and the dotted line is the hypothetical curve for

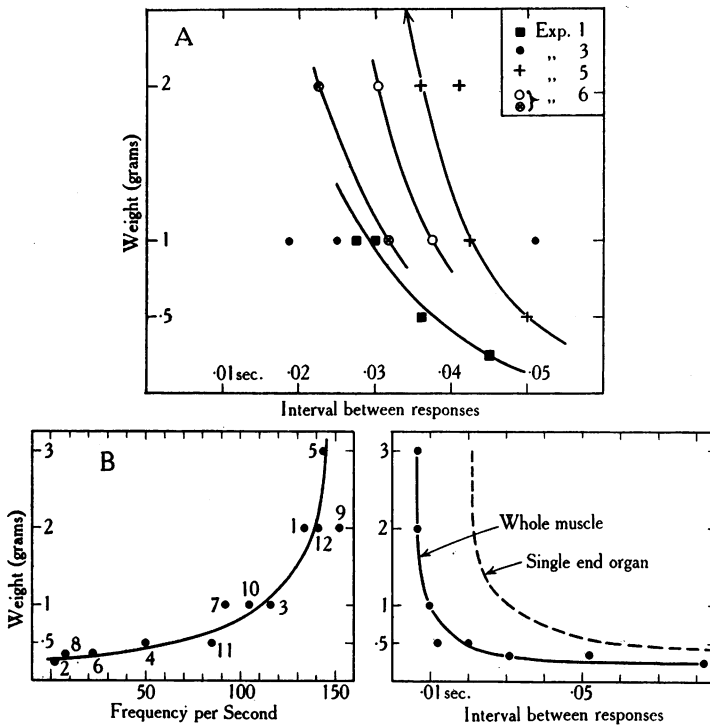


Fig. 5. A. Relation between stimulus and period of rhythmic responses in different experiments.

B. Exp. 9. 17° C. Relation between stimulus and frequency of response, muscle intact.

C. Exp. 9. 17° C. Relation between stimulus and interval between responses for intact muscle. Hypothetical curve for single end-organ.

a single end-organ made on the assumption that three are always in action. Although the curves for single end-organs have to be constructed from very meagre data their general features agree fairly well. With a stimulus of .5 gm. the periods are over .03 sec., and with one of 2 gm. they lie between .03 and .02 sec. An increase to 3 gm. and above reduces the period slightly, but the most rapid period which has appeared is .015 sec.

The time relations of the recovery curve for the end-organ are therefore considerably longer than those for the nerve fibre. In a mixed nerve trunk such as the frog's sciatic, the absolute refractory period, judged by the presence or absence of a second electric response is rarely longer than .0025 sec. at 15° C. The return of excitability has only been

mapped out for the motor fibres, but it is unlikely that it differs much from that of the sensory fibres from the muscle. Erlanger and Gasser(2) have shown that a mixed nerve trunk may contain fibres whose refractory periods may vary from $\cdot 00142$ to $\cdot 00446$ sec. but the phrenic nerve of the dog contains motor fibres and sensory fibres from muscle receptors and they find that all these have the same refractory period. For the motor fibres of the frog the excitability has returned to 95 p.c. of its resting value in less than $\cdot 02$ sec. though the subsequent return to complete resting excitability may be complicated by the development of the super-normal phase. Thus, if we may assume that sensory and motor fibres recover at much the same rate, it appears that the relative and absolute refractory periods last much longer in the end-organ than they do in the nerve fibre connected with it. In fact, the periods in the end-organ and the nerve fibre seem to be so related that the impulses set up will always travel in nerve which has completely recovered from the passage of the previous impulse.

Effects of adaptation. Before this conclusion can be accepted there is another factor which must be taken into account. It was pointed out in Part I that the frequency of the impulses in the sciatic when the gastrocnemius is stretched falls off considerably as the period of stimulation is increased. There is evidently some adaptation of the end-organ to the stimulus, as indeed we should naturally expect. This is true for the single end-organ as well as for the collection of end-organs in the

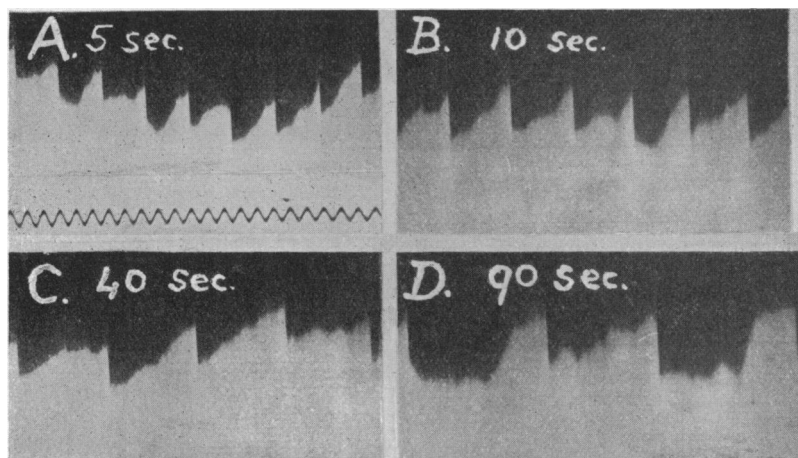


Fig. 6. Exp. 1. Single end-organ. Decrease in frequency of response as duration of stimulus is increased. 1 grm. weight.

gastrocnemius. Fig. 6 gives the responses in Exp. 1 produced by a 1 grm. weight applied for 5, 10, 40 and 90 seconds and the intervals between the responses range from .026 sec. when the weight had been on for 5 sec. to .08 sec. when it had been on 90.

Consequently the recovery curves given in Fig. 5 are only true for an end-organ which has already been stimulated for 10 seconds, and they are only true for this period on the assumption that the rate of adaptation is the same for a strong stimulus as for a weak. We have, therefore, studied the process of adaptation in greater detail with the aid of continuous records on long strips of cinematograph film. In the earlier experiments the weight was lowered by hand so that the tension was applied suddenly. A strip of film was exposed before the loading and another beginning about 1 second afterwards and continuing for 20 seconds or more whilst the weight was in place. At the actual moment of loading there was usually a large excursion due apparently to the movement of the nerve and the impulses were not recorded until this had subsided. An experiment of this kind is shown in Fig. 7. The muscle was intact and the frequencies are reckoned by counting the total number of impulses in each second. With a 3 grm. weight the frequency at the end of 1 second is 145 and at the end of 10 it is 104, *i.e.* it has fallen to 72 p.c. of its former value. With a weight of .5 grm. the frequencies are 58 and 40, *i.e.* a fall to 69 p.c. In another experiment the weight was lowered by the movement of an arm controlled by an oil dashpot. With this method the extension of the muscle occupied about .5 sec. and was smooth enough to allow the record to be made during its progress. The data below give the maximal frequency just after loading and the frequency 10 seconds later with different weights.

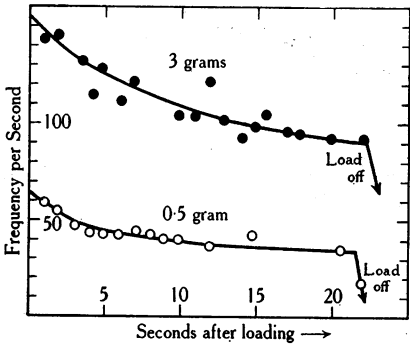


Fig. 7. Exp. 11. Decline in frequency after application of load.

Exp. 12. Temp. 14° C.

Weight grm.	Initial frequency (maximal) per sec.	Frequency after 10 sec. loading per sec.	Percentage of initial frequency
5	190	120	63
5	150	104	69
.5	35	15	43
1	66	37.5	57
2	98	59	60

In this experiment some of the waves were monophasic and some diphasic. These can be distinguished when the frequency is not too high and the rate of adaptation can be checked by counting the monophasic waves only. This gives the following results:

Exp. 12. Monophasic waves only counted.

Weight gram.	Initial frequency (maximal) per sec.	Frequency after 10 sec. loading per sec.	Percentage of initial frequency
2	37	17	45
1	26	16	61.5
.5	14	8	57

Later experiments using an elastic extension apparatus instead of a weight gave results of the same order and the agreement between them is close enough to justify the conclusion that the frequency after 10 seconds of weighing is from 40 to 70 p.c. of the initial frequency and that the percentage fall is much the same whatever the value of the stimulus.

Thus the recovery curves in Fig. 5 are approximately correct for an end-organ which has been in action for 10 seconds and we can obtain the curve for the fresh, unadapted state by halving the time intervals for each point in the curve. This has been done in Fig. 8, taking the recovery

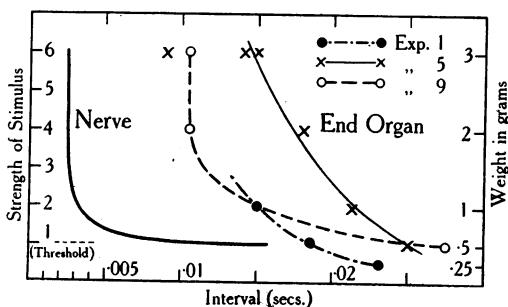


Fig. 8. Recovery curve of frog's sciatic at 15° C. and corrected recovery curves for end-organ at moment of application of load.

curve in Fig. 6 *A* and *C* as a basis, and in the same figure is drawn a typical recovery curve of the motor fibres in the frog's sciatic. Evidently the rate of recovery of the end-organ is so much slower than that of the nerve that the impulses set up by it will always travel in a fibre which has itself almost completely recovered. This conclusion is interesting, for it shows that, on the afferent side at least, the refractory period of the nerve fibre is not one of the factors which determines the size or

frequency of the impulses which reach the central nervous system. Owing to its very rapid recovery the nerve fibre is able to behave alike to all the impulses which reach it from the end-organ. It should be able to conduct all at the same rate and with the same intensity because the path can never become overcrowded by too frequent discharges. Cooper and Adrian(2) have already brought forward some evidence to show that the frequency of impulses reaching the motor neurones is also lower than the maximum frequency to which the motor fibre and the muscle can respond, so that both on the motor and sensory side it seems that the nerve fibres are never pushed to the limit of their power of response.

All-or-nothing response of nerve fibre. As far as the present experiments are concerned there is an interesting corollary to this conclusion. If the afferent impulses are all travelling in nerve fibre which has completely recovered, they should all be of the same size provided that the all-or-nothing principle does apply to the nerve fibre. Since the potential difference developed varies with the degree of moisture on the nerve and the distance between the electrodes, the point must be tested by comparing records in which both these factors are kept constant. In the record shown in Fig. 4 *D* the stimulus is increased gradually, the state of the nerve and electrodes remaining unchanged. It will be seen that the impulses increase in frequency but that the rate of rise of the mercury at each response shows no appreciable change. Records of this kind are unsuitable for analysis, since they are taken on a slowly moving surface, and to test the point more rigorously we have taken a series of responses with different weights on a plate travelling at 1 metre per sec. The weights were hung on for 10 seconds before the exposure was made and records were made as rapidly as possible so as to avoid changes due to the drying of the nerve. The muscle was a large one, containing probably five or more end-organs and half of it was cut away before the records were made. In this state it contained at least two end-organs but the responses were far enough apart for analysis. The data of this experiment are shown below:

Exp. 10. Temp. 14° C.

A. Muscle intact. Frequency of impulses with various loads determined at the moment of loading.

Weight gram.	Frequency per sec.
.25	137, 175, 162
.5	200
1.0	290
2.0	400

Exp. 10. Temperature 14° C. (contd.)

B. Muscle cut. Loading for 10 seconds. Size of responses from analysis of electrometer records.

Order of exposure	Weight gram.	Maximum height of response (arbitrary units)			
1	.25	35,	40		
2	2.0	35,	37		
3	1.0	34,	37,	34	
4	.25	34.5,	29,	39	
5	.5	37,	35		
6	2.0	35,	39,	41	
7	.25	34,	38		
8	1.0	30,	35,	35,	33
Averages		<hr/>			
	.25	35.6			
	.5	36			
	1.0	33.7			
	2.0	37.4			

It will be seen that an eight-fold increase in the stimulus gives no appreciable increase in the size of the response. That the $\frac{1}{4}$ gram. stimulus was not already maximal is shown by the increase in frequency with the larger weights. The experiment seems conclusive enough and a general survey of all our records has detected no sign of an increase in the size of each response when the stimulus is larger.

It is conceivable that the electric response may show no variation although the change which evokes it—the propagated disturbance—does vary, but there is at any rate no doubt that there is an all-or-nothing relation between the stimulus applied to the end-organ and the electric response in the afferent nerve fibre. This result confirms the conclusions already put forward by Adrian and Forbes(4) and gives evidence of a new kind in favour of the all-or-nothing reaction of the nerve fibre.

Grading of effect on central nervous system. To reconcile an all-or-nothing relation in the sensory nerve fibre with the obvious fact that our sensations are graded, it has often been pointed out that the effect on the central nervous system may be determined by two other factors apart from the size of each impulse. These factors are the number of fibres in action and the frequency of the responses in each fibre. Since our preparations contained relatively few end-organs even with the muscle intact, it was nearly always possible to count the total number of impulses per second with stimuli of different strengths.

Some curves relating the total frequency to the strength of the stimulus are given in Fig. 9. In all of these the weight had been on for 10 seconds before the record was made. On the average the frequency rises from about 20 per second with a $\frac{1}{4}$ gram. weight to 200 with 5 gram., but there is considerable variation from one muscle to another. This is

probably due to differences in the number of end-organs, for the muscles of large frogs usually gave the higher frequencies. The form of the curves

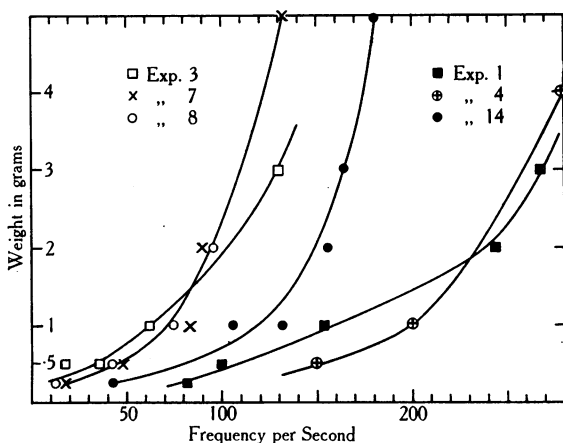


Fig. 9. Relation between frequency and strength of stimulus for various intact muscles.

suggests that most of the end-organs are brought into play by a stimulus of 1 or 2 gm. since there is not much increase in frequency with larger weights. Evidently a much wider range of gradation would be possible in a muscle with many end-organs of varying excitability, and the form of the curve would then depend more on the distribution of thresholds in the different end-organs than on the change of frequency in each fibre. For this reason no general conclusion can be drawn as to the precise relation between the stimulus to a group of end-organs and the total frequency of impulses which will reach the central nervous system.

The smallest stimulus which we have been able to use was the weight of $\frac{1}{4}$ gm. Smaller weights were not great enough to produce any constant degree of extension owing to the friction of the thread and the muscle on the moist surface of the chest. But in the majority of our experiments a slow discharge of impulses continues (as long as some end-organs are present) even though the muscle is perfectly slack. These impulses occur at frequencies ranging from about 3 to 8 per second. The interval between successive impulses often remains constant for half a second or more, but it is hard to trace a definite rhythm over longer periods. An example of these responses is given in Fig. 11. It is conceivable that they may be the basis of the slight tonic contraction present in muscles whose central connections are intact. Their irregularity, and the irregularities which sometimes appear in records from a single end-organ with

a small stimulus (cf. Fig. 4) may be accounted for by supposing that the stimulus is very near the threshold value. The excitability of a nerve returns very gradually when recovery is nearly complete and the mapping of this part of the curve is often a matter of great difficulty owing to slight changes in the threshold. So with the end-organ a slight change in the effective value of the stimulus will produce a considerable change in the rhythm of the response, the change in rhythm may itself disturb the threshold afresh and in this way an irregular discharge will be produced. In fact the end-organ may have the same difficulty in giving a constant response to a weak stimulus as the experimenter has in plotting the final stages of the recovery curve of a nerve.

Nature of adaptation. The gradual decline in rhythm which occurs with a steady stimulus has already been described, but its cause has not been dealt with. It might be due to a gradual decrease in the excitability of the end-organs or to a gradual increase in their refractory period, or to both these causes. If only the former were in action, the effective value of the stimulus would decrease so that longer and longer intervals would have to elapse after each impulse before the end-organ had reached the degree of excitability necessary for the setting up of a fresh impulse. A slowing of the rate of recovery would have the same effect, although the excitability remained unaltered. When a gradually increasing current is applied to a nerve fibre the adaptation which occurs is confined to the mechanism of excitation, for the stimulus may fail to set up an impulse at all if it increases too slowly. Presumably the failure of a constant current to set up more than one impulse is due to the same cause, *i.e.* to the rapid decline in the stimulating value of the current. The rate of recovery may be altered in the region which becomes adapted, and Brücke⁽⁵⁾ has shown that the refractory period of the nerve fibre or nerve ending becomes prolonged when a rapid succession of impulses are passing, but this by itself would not account for the complete failure to set up a second impulse. So, if the decline in rhythm from the end-organ is due to a process of adaptation of the same kind as that occurring in the nerve fibre we should expect to find evidence of a change in excitability with or without a change in refractory period in addition.

In order to study the process more thoroughly we have increased the tension on the muscle at varying rates, recording both the tension on the muscle at each moment and the frequency of the afferent impulses. The tension was applied by a short lever fixed in the centre of a twisted elastic band. A similar lever at one end of the band was rotated at varying speeds through a known angle and its movement was communi-

cated to a pointer moving across the slit of the film camera. The lever in the middle of the band is fixed to the thread from the muscle and can only move through a very small arc, but when the end lever is rotated the tension on the thread is increased and its final value depends on the amount of movement of the end lever. The tension developed for different movements of the end lever was determined by hanging weights on the centre lever and finding the amount of movement required to raise them. Fig. 10 *A* shows the effects of varying the rate at which the tension increases and the records of another experiment are shown in

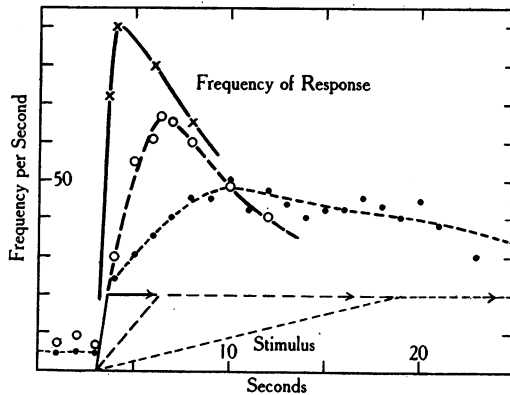
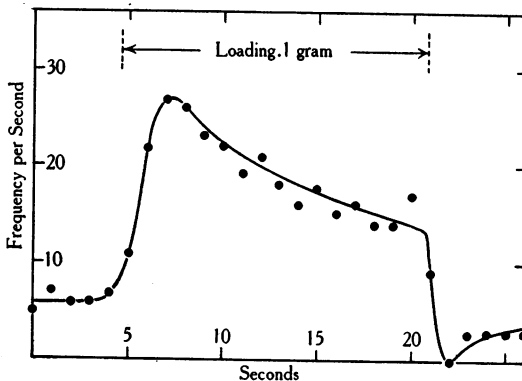
Fig. 10 *A*.Fig. 10 *B*.

Fig. 10. *A*. Exp. 13. 13.2° C. Frequency of responses with various rates of loading, showing effects of adaptation. Maximum tension 1.3 gm.

B. Exp. 12. 14° C. Frequency before, during and after loading. Monophasic waves only.

Fig. 11. With very rapid loading the maximum frequency is reached at about the same moment as the maximum tension, but with more

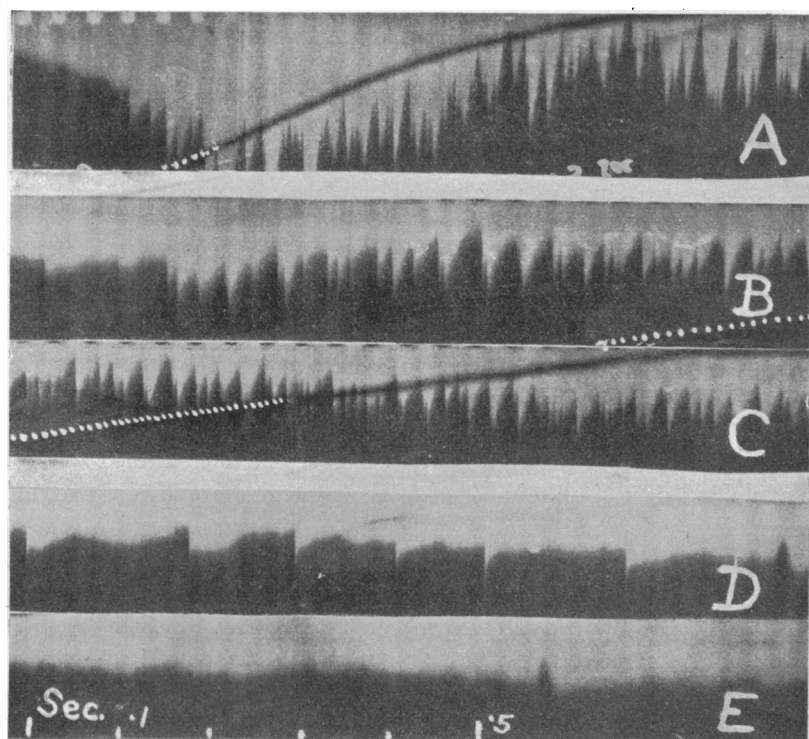


Fig. 11. *A, B and C.* Exp. 13. Tension of 1.3 grm. applied rapidly in *A* and slowly in *B* and *C*. *B* and *C* are portions of the same record with an interval of .75 sec. omitted.

D and *E.* Exp. 12. *D*, immediately before loading, impulses about 7 per sec. *E*, immediately after loading. Pause without impulses. The single excursion is probably an artefact.

gradual loading the maximum frequency is much less and it is reached some time before the stimulus is at its full value. These curves would be the natural result of any process of adaptation and they merely serve to emphasise the fact that the adaptation begins at the moment that the stimulus is applied. A more significant fact is shown in Fig. 10 *B*, which records also the effects of a rapid unloading after the tension had been at its full value for 17 seconds. In all our experiments the result of this has been a complete cessation of all impulses for a period varying from .75 to 1.5 sec. followed by a gradual return to the normal "resting"

frequency of 3-8 per second. In the present experiment the record immediately before and immediately after the stimulus is shown in Fig. 11 *D* and *E*. It is difficult to explain this pause in the discharges without supposing that a true fall of excitability has occurred. During the period of stimulation the frequency has fallen to about half its initial value. If this fall is due to an increase in the refractory period the latter must have risen to about double its initial value, and we should expect to find a discharge at half the initial resting frequency when the stimulus is removed. Actually the initial frequency is 6 per second but there is a pause of 1.3 sec. at the end of stimulation.

We conclude that the decline in the frequency of response is due in part at least to a fall of excitability in the end-organs when the stimulus is continued and their adaptation is thus brought into line with the much more rapid process which occurs in the nerve fibre.

Remarks.

The behaviour of the end-organs which we have examined seems to be explained very simply in terms of the general properties of excitable tissues, in particular by the phenomena of adaptation and of the refractory state. It is probable, therefore, that other types of end-organ will be found to react in much the same way to the particular stimuli which call them into play. This probability is strengthened by the close resemblance of the records of impulses in various types of sensory nerve dealt with in Part I, though an investigation of other single end-organs will be needed to establish it. A point of considerable interest is that the frequency of the discharge from the end-organ is so much slower than the maximum frequency which the nerve fibre can tolerate. If this is true of end-organs in general it means that the frequency of the impulses in the fibres of the auditory and of the optic nerves is lower than is often supposed. This again must wait for experimental confirmation. Finally, it is worth enquiring whether the synapses of the central nervous system may not sometimes react in the same way as the end-organ to the mass of impulses reaching them. The regular succession of impulses obtained by Brevée and Dusser de Barenne⁽⁶⁾ from the spinal cord treated with novocaine is a remarkable instance of rhythmic discharge from motor neurones which may perhaps be brought into line with the phenomena dealt with in this paper.

SUMMARY.

(1) The afferent impulses produced by the receptors in the sternocutaneous muscle of the frog have been recorded with a capillary

electrometer and three-stage amplifier. The receptors were stimulated by stretching the muscle with different weights. There are generally three or more end-organs in the muscle but they may be reduced to one or two by cutting successive strips from the muscle.

(2) The impulses set up by a single end-organ occur with a regular rhythm at a frequency which increases with the load on the muscle and decreases with the length of time for which the load has been applied. The frequency may vary from 5 to 100 a second, though the very low frequencies are usually irregular.

(3) The regular rhythm can be explained as the natural consequence of the refractory period and the subsequent return of excitability in the end-organ, the difference in the response of a nerve fibre and an end-organ to a constant stimulus depending on the much more rapid adaptation to the stimulus in the former.

(4) The "recovery curve" of the end-organ can be determined by comparing the frequencies with different stimuli. It is found to have the same general form as that of other excitable tissues, but its time relations are about five times as long as those of the nerve. The absolute refractory period is probably about .01 sec.

(5) Owing to the more rapid recovery of the nerve fibre the impulses which enter it from the end-organ will always find it almost completely recovered from the effects of the previous impulse.

(6) There is an all-or-nothing relation between the size of the electric response in the nerve fibre and the strength of the stimulus to the end-organ.

(7) The adaptation which occurs when the stimulation is continued is due in part at least to a fall of excitability and it is unlikely that there is much change in the refractory period.

(8) The response of the end-organs in muscle can therefore be brought into line with that of excitable tissues in general. No new properties have to be invoked to explain it, and it seems likely that other types of receptor will be found to react in the same way.

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REFERENCES.

- (1) Adrian. *This Journ.* 61. p. 49. 1926.
- (2) Erlanger and Gasser. *Amer. Journ. Physiol.* 70. p. 663. 1924.
- (3) Cooper and Adrian. *This Journ.* 58. p. 209. 1923; 59. p. 61. 1924.
- (4) Adrian and Forbes. *Ibid.* 56. p. 301. 1922.
- (5) Brücke. *Ztsch. f. Biol.* 76. p. 213. 1922.
- (6) Brevée and Dusser de Barenne. *This Journ.* 61. p. 81. 1926.