THE IMPULSES PRODUCED BY SENSORY NERVE ENDINGS. Part I. By E. D. ADRIAN.

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THIS paper describes an amplifier used in conjunction with the capillary electrometer and some preliminary observations with it on the action currents set up in sensory nerve fibres by appropriate stimulation of their end organs.

Since the introduction of the triode valve a number of workers have used valve amplification in conjunction with the string galvanometer for recording electric responses of very small intensity. The results of Forbes(1) and his co-workers and of Gasser and Newcomer(2) have shown how valuable such a combination may be for studying reflex effects in nerve. There is one serious limitation, however, in the ordinary type of string galvanometer which no amount of amplification can overcome, and that is the limitation imposed by the inertia of the moving system. Owing to the mass of the string the record of its movement does not give a true picture of the changes of electromotive force applied to it and the distortion, though of little account in the record of a muscle action current, is quite enough to obscure the true form of the much briefer response of a nerve fibre. With sufficient amplification this defect might be overcome by the use of a recording system of very high natural period (as in the oscillograph), but it cannot be overcome in the usual type of string galvanometer without very extensive alterations[1]. The magnitude of the distortion and the possibility of correcting the records by mathematical analysis have been dealt with very clearly by Erlanger and Gasser(3) and more recently by Williams(4). The ideal instrument for recording nerve action currents is undoubtedly the cathode ray oscillograph devised by Erlanger and Gasser, for in this the moving system is a stream of cathode rays, the inertia of which is completely negligible. At present, however, the intensity of the illumination from the ray is far too small to allow photographs to be made from a single excursion, and similar excursions must be repeated many times over before the plate or the eye is affected. As a result the cathode ray oscillo-

[1] These objections would not, of course, apply to the beautiful instrument recently constructed by Prof. Einthoven, where the string moves in a vacuum and has a very high natural period.

graph can only be used in experiments where the same sequence of action currents can be repeated over and over again and it is not suitable for recording an irregular series of action currents such as are produced by the activity of the central nervous system. Another instrument in which the inertia factor is extremely small is the capillary electrometer. This has fallen out of favour with the majority of physiologists because its records need analysis and because of its low sensitivity compared with that of the string galvanometer. These objections have now become of little importance. With the advent of reliable valve amplifiers a low sensitivity in the recording instrument is no drawback at all, and the analysis of capillary electrometer records can be made in a few moments by the machine designed by Keith Lucas(5). As will be seen, the combination of valve amplifier and electrometer gives us an instrument of such range and precision that it promises access to fields of investigation which are as yet almost unexplored.

The chief point in which the capillary electrometer has the advantage over the string galvanometer lies in the fact that its records show practically no distortion caused by the inertia of the moving system. In both classes of instrument the moving system has appreciable mass and the movement in both must satisfy the usual equation for a damped oscillation,

$$Cy + D\frac{dy}{dt} + M\frac{d^2y}{dt^2} = f(t), \quad \ldots\ldots(1)$$

where C is the restoring force, and D the damping.

In the capillary electrometer, however, both damping and restoring forces are very large and the third term $M\frac{d^2y}{dt^2}$ is so small in comparison that it is practically negligible. The mercury therefore moves in accordance with an equation which is approximately

$$Cy + D\frac{dy}{dt} = f(t), \quad \ldots\ldots(2)$$

where f is the displacing force (in this case the applied P.D.) at the time t. This equation resolves itself into the well-known formula for the correction of capillary electrometer records,

$$E_{(t)} = y + h\frac{dy}{dt} \text{ or } E_{(t)} = y + k\tan\theta, \quad \ldots\ldots(3)$$

where y is the vertical distance travelled by the mercury at the time t and the angle θ gives the slope of the curve at that moment. Thus the true value of the potential difference at any moment can be calculated without difficulty.

The work of Burch, Gildemeister and others has shown that this

equation is approximately correct for a properly constructed electrometer, but it is naturally no more than an approximation, for it leaves the acceleration term $\left(M\frac{d^2y}{dt^2}\right)$ out of account altogether and assumes that on the application of a P.D. the mercury will pass instantaneously from a state of complete rest to a state of motion beginning with the maximum velocity and slowing down as the distance travelled (y) increases. Actually the mercury must take a finite time in accelerating before the maximum velocity is reached and the equation cannot be used with confidence unless we are sure that this time is very small in comparison with the time relations of the potential charges under investigation. How far this condition is complied with by a given capillary can be tested very simply by producing an instantaneous change of potential and recording the movement of the mercury on a rapidly moving plate. Fig. 3 F shows such a record taken on a plate moving 80 cm. per second. A large change of potential has been established and the initial velocity of movement is considerable, but there is no sign of any rounding of the curve when the movement begins—no sign, that is, of a progressive acceleration before the maximum velocity is reached. Since the plate travels ·8 mm. in ·001 sec. it is clear that the mercury passes from rest to its maximum velocity in much less than $\frac{1}{1000}$ sec. and a careful inspection of this and similar records shows that the time required for accelerating is probably less than ·0001 sec. Thus the equation (3) may be taken as correct even when we employ the electrometer to record changes such as nerve action currents which are over in a few thousandths of a second.

This freedom from distortion by inertia has been insisted on because it enables the capillary electrometer photograph to be analysed without difficulty and so to give a much truer record of nerve action currents than that obtained with the usual form of string galvanometer. There are, however, two other features of the capillary electrometer which make it specially suitable as a recording apparatus in conjunction with an amplifier. One is that its own resistance is practically infinite so that the changes in the effective resistance of the valve circuit can be recorded without diminution. The other is the great practical advantage that very little harm is done to it if a large potential difference is applied by mistake. When valves are used a chance interference with the input circuit may give rise to a current large enough to break the string of a galvanometer[1], but in the electrometer such a current will merely cause

[1] The string could be protected by a fuse, but this would have to be even more delicate than the string.

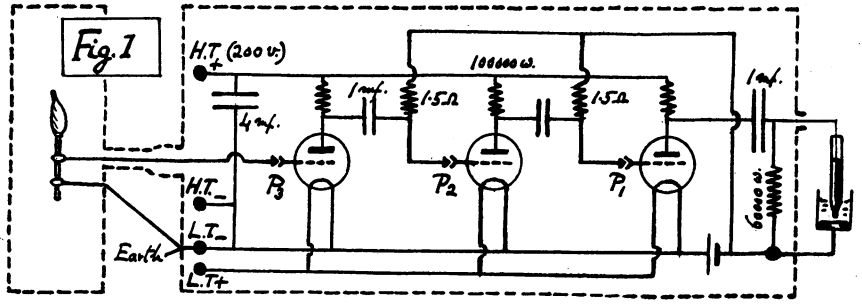
the mercury to run out of the end of the capillary tube, or at the worst will produce some electrolysis and bubbles of gas which are easily cleared by flushing the tube out with mercury. With the present instrument it has never been necessary to take down the tube since the amplifier was installed.

A. *Description of Instrument.*

The electrometer used in the present work needs no description, for it is the original instrument designed by Keith Lucas(6) and described by him in this *Journal*. The only changes which have been made are (1) the substitution of a small clockwork feed arc lamp with a choking coil in series to give a very steady illumination and (2) the substitution in the later experiments of a spring time marker in place of the electrically driven tuning fork. The contacts of the fork sparked considerably and although the records showed no sign of disturbance from this it seemed better to use a time marker which should be above suspicion. This consists of a small strip of clock spring fixed at one end in a massive stand. The other end is bent down and held in a catch released by the same movement which releases the photographic plate. The length of the strip is adjusted so that it makes 100 vibrations per second and it continues to vibrate for 2–3 seconds after it has been released. The capillary tube at present in use has a diameter of ·03 mm. at its working part and a pressure of 14 cm. Hg is needed to bring the mercury to this part.

The amplifier owes much to the great kindness of Prof. Gasser, who supplied me with details of the amplifier used by him in America, and to the staff of Messrs W. G. Pye and Co. of Cambridge, who redesigned an instrument on the same general lines and planned the very compact and well shielded lay-out of the apparatus. It is a three valve resistance-capacity coupled instrument made on conventional lines but designed so as to be as free as possible from extraneous mechanical and electrical disturbances. The arrangement of the circuits is shown in Fig. 1, and it will be seen that only one high tension and one low tension filament battery is used for all three valves. A single switch in the filament circuit turns the amplifier on or off and the change from one to two or three valves is made in a moment by plugging in P_2 and P_1. A 4 M.F. condenser is placed across the terminals of the high tension battery (dry cells) to diminish fluctuations in E.M.F. and the resistances are wire wound and shielded in brass cases. The three valves with condensers and resistances are mounted on an ebonite base and contained in a sheet iron box to which the negative side of the filaments are earthed. The box is housed in the top compartment of a large wooden case (38″ × 18″ × 13″)

which contains the high and low tension batteries and is completely sheathed in lead. The input wire is carried in a metal tube which is con-



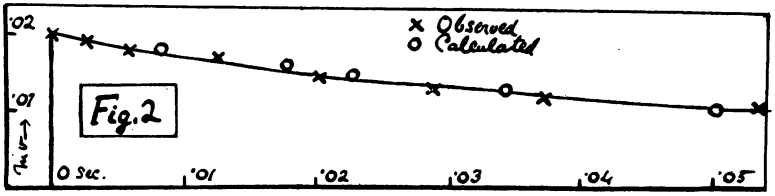


Fig. 1. Connections of preparation, amplifier and electrometer. Metallic shielding indicated by dotted line. The batteries are shielded with the amplifier.

Fig. 2. Calibration curve. Observed and calculated points on applying a steady P.D. of ·02 millivolts through 50,000 ohms (three valves).

nected with the sheath of the amplifier case. The length of the input wire is about 2 ft. The preparation itself is contained in a large box of sheet iron $\frac{1}{8}''$ thick, measuring $24'' \times 12'' \times 12''$ and just large enough to hold a cat or rabbit (it might have been made larger with advantage). The sides of the box are hinged and open downwards to allow access to the preparation and the box is placed on a heated animal table. A carbon lamp inside the box aids the rather inefficient heating when warm-blooded preparations are used. The sheath of the input wire is in metallic connection with the wall of the box. With this arrangement it will be seen that the whole system, preparation, input wire and valves are completely enclosed in a continuous metal sheath which is earthed to the water pipes of the laboratory.

This electromagnetic shielding is all that can be desired, for it is possible to run small D.C. motors 7 or 8 ft. from the amplifier without causing any disturbance, and the sparking of an electrically driven tuning fork 14 ft. away had no appreciable effect on the record. The

complete enclosure of the preparation is usually unnecessary and one of the sides of the box is generally left open during an experiment for convenience in manipulation.

Mechanical Shielding. Each valve socket is attached to the vulcanite base plate by a small flexible rubber support. The base plate rests on rubber sponges in the metal case which is packed into the outer wooden box with a thick jacket of felt. The wooden box is double walled and consists of an inner and outer case of three-ply wood with cotton waste packed between them; the outside is covered with $\frac{1}{16}$" sheet lead and the whole stands on four large rubber feet. The front of the box forms a door which opens to allow access to the valves and batteries.

If the door of the outer box and the door of the small inner valve chamber are both thrown open there is enough mechanical vibration of the valve elements to produce a considerable effect on the electrometer when three valves are used. This shows itself as a regular oscillation at about 260 per sec. with slower beats superimposed on it. A loud noise near the valves increases the oscillations enormously. When both doors are shut there is no sign of any disturbance unless the box is actually tapped and noises of ordinary volume may be made near it with complete impunity.

Connection to Electrometer. The high tension battery produces a large permanent E.M.F. between the filament and plate of the final valve and on this are superimposed the fluctuations which are the amplified image of those in the input circuit. To guard the electrometer from the effect of this steady high potential a 1 M.F. condenser is placed across the output circuit (Fig. 1). The electrometer itself is shunted through a resistance of 60,000 ohms as the damping of its movement depends *inter alia* on the resistance in the circuit and this value gives good results with the particular tube in use.

Amplification. The valves used are Marconi D.E. 5b type, and the voltage amplification with three valves is 1850. With two valves it is 170, but all three valves have always been used in the present work.

When no valves are used the capillary gives a steady deflection of 45 mm. on the screen (magnification = 490) for a potential change of 19 millivolts and with all three valves the same deflection would be given by ·0105 millivolts. The rate of movement under this potential is such that a distinct excursion would be produced on a plate moving at 1 metre a second, even though the potential was applied for $\frac{1}{1000}$ sec. only. Thus with three valves the capillary should be able to detect a change of potential in the input circuit of about ·01 millivolts lasting for

$\frac{1}{1000}$ sec. The resistance of the circuit in which this P.D. is measured may be as high as 500,000 ohms, though the base line becomes unsteady if the resistance is much greater.

Naturally such a change could not be detected except on an extremely steady base line and when viewed by eye the shadow of the mercury column often shows irregular oscillations of a few mm. amplitude. Fortunately these movements are all extremely slow compared with such rapid changes as a nerve action current; their periods are of the order of $\frac{1}{10}$ to $\frac{1}{5}$ sec. or longer and over any given period of $\frac{1}{20}$ sec. the base line remains extremely steady provided that the resistance in the input circuit is not too great (cf. Fig. 3 A and F and Fig. 8 C and F).

Distortion. How far may we assume that the change of potential in the electrometer circuit is an exact reproduction, amplified a thousandfold or more of the change of potential in the input circuit? There are two groups of factors which will cause distortion, one of them important only with very rapid and the other with very slow changes of potential. If the potential in the input circuit alternated at a period of a million times a second an amplifier with wire wound resistances would be unsuitable. The capacities of such resistances are not negligible and at such high frequencies the capacity between the ends of the coil would provide an alternative path for the current and so diminish the impedance of the circuit. Thus the amplification would be much smaller for a high frequency than for a low. In the present case, however, we are concerned with frequencies of the order of a thousand a second instead of a million. With the instrument described the amplification only begins to show perceptible falling off when the input frequency is raised to 5000 a second and therefore a series of nerve action currents is well within its powers. The other factor which may cause distortion depends on the use of condenser coupling between the valves and on the condenser which intervenes between the output and the capillary. These condensers will transmit rapid fluctuations of potential without distortion, but a slow or a permanent change of potential would soon cease to have any effect as the condenser would have time to come into equilibrium by charging or discharging itself. The time taken to charge or discharge is proportional to the capacity of the condenser multiplied by the resistance in the circuit. For the intervalve condenser this resistance is very large ($1{\cdot}5\overset{\sim}{\omega}$) and the rate of discharge is very slow, but in the circuit of the output condenser the resistance is only 60,000 ohms plus the effective resistance of the valve (about 20,000 ohms). If a change of potential is suddenly established between the two sides of this con-

denser there will be a transient current in the resistance R which will start at its maximum and should decline to half its initial value in ·055 sec. The electrometer measures the difference of potential between the ends of the resistance and the change which is recorded will therefore decline at the same rate as the current through R. Fig. 2 shows an analysis of the electrometer record when a P.D. of $\frac{1}{50}$ MV. is suddenly established in the input circuit together with a series of points calculated on the assumption that the decline of the recorded potential is due entirely to the output condenser and that the effect of the intervalve condensers may be neglected. The agreement between observed and calculated points is close enough to justify this assumption and the record shows that in $\frac{1}{100}$ sec. the observed P.D. has fallen to about 85 p.c. of its initial value. Since the changes which we are concerned with are generally over in less than $\frac{1}{200}$ sec. the amount of distortion from this cause will be negligibly small. If it were desired to record the action currents of a muscle instead of a nerve, the distortion would be more important, but it could be reduced easily enough by using an output condenser with a capacity greater than 1 M.F. The only advantage of a condenser of this capacity is its small size and high resistance and the fact that it does not take long to become charged when the amplifier is turned on.

The only other considerable source of error is that introduced in the analysis of the electrometer records in accordance with the equation $E_{(t)} = y + h \tan \theta$. The mechanical analyser designed by Keith Lucas enables this to be done with great accuracy provided only that the photographic image is sharp enough. The essential operation consists in turning the eyepiece of a microscope until the cross wires in it are tangential to the curve traced out by the shadow on the plate. This cannot be done if the image is badly focussed or the negative thin, and for this reason the accuracy of the final result is probably determined more by the quality of the photographic technique than by any distortion in the amplifier or electrometer. Some idea of the accuracy of the analysis under favourable conditions may be gained from records previously published in which condenser discharges of known time relations were photographed with the electrometer and the calculated and observed forms were compared (7).

General points in technique.

Up to the present the apparatus has not been used in any experiment which involves the electrical stimulation of the preparation, so that

there has been no trouble from artefacts due to induction shocks, etc. A small D.C. electric motor is used to run the film camera when a continuous record is to be made, but it is 15 ft. away from the preparation box and it has no appreciable effect on the record. When artificial respiration is used the air is taken from the laboratory compressed air supply through a semi-rotary valve operated by a wind-screen wiper[1] also driven by compressed air.

It is essential that the nerve whose action currents are recorded should not move relative to the electrodes when a record is taken and to ensure this it is usually looped over a small glass hook between the electrodes and the animal (or muscle) with enough slack to prevent a slight movement from pulling on the nerve beyond the hook. The electrodes are plugged with gelatin with a short piece of worsted protruding from the lower end and the nerve is supported by small glass hooks fused to the lower end of the electrode tubes. The tube is filled with Ringer's fluid above the gelatin and the current is led off by a silver wire coated with silver chloride.

Since the electrical effects which are recorded are all extremely small it is essential to make numerous control observations to guard against artefacts. As a routine at the end of each experiment the nerve is killed by crushing or burning between the electrodes and the animal, and a record is made to see if any disturbance can be detected in the electrometer. Almost invariably the base line remains quite steady in these controls. More elaborate control observations will be described in detail later.

B. *Afferent impulses from Muscles. Responses produced by stretching.*

The experiments to be discussed are to some extent preliminary. They suffice to show the capabilities of the instrument but an exhaustive analysis must be left to a later date.

The most complete observations have been made on the sensory impulses produced by the stretching of a muscle. Sherrington's earlier work and its recent extension by Liddell and Sherrington(8) has made it clear that sensory impulses must travel up to the central nervous system when certain muscles are stretched. In 1921 de Meyer(9) reported very small oscillations observed with a string galvanometer in the nerve when the muscle which it supplies is stretched, and quite recently Forbes, Campbell and Williams(10) were able to show

[1] This is a Lucas screen-wiper as fitted on Morris Cars Very few alterations are needed to drive it by compressed air instead of suction.

conclusively that the act of stretching does produce true action currents which travel away from the muscle towards the central nervous system. In Forbes' work the muscle was jerked suddenly by a spring or made to twitch by an induction shock to the nerve and the action currents were recorded with a string galvanometer with or without a single valve amplifier. His records show a group of three or four oscillations diminishing rapidly in amplitude and he was able to prove quite clearly that each oscillation must represent a group of action currents arising in the muscle and having time relations which do not differ greatly from those of the action currents set up by an electric stimulus. This observation is of fundamental importance as the first definite measurement of the action currents set up in proprioceptor fibres by stimulation of their end organs. The procedure of stretching the muscle suddenly has the advantage of stimulating a large number of the receptors more or less simultaneously so that reasonably large action currents appear in the nerve. With the present apparatus these would be needlessly large and the method of stimulation usually employed consists in stretching the muscle by hanging a small weight on the thread attached to the tendon. A frog's sciatic-gastrocnemius preparation is dissected out and placed on an insulated stand in the metal preparation box with the knee joint held firmly in a clamp and the nerve resting on the electrodes. The thread from the tendon passes through a small hole in the side of the box and over a light pulley. When the thread is completely slack (the muscle resting on a glass plate) the electrometer record is very nearly quiet, though there are occasional small oscillations which are not present in the control records after the nerve has been killed. If a weight of 10 gms. or more is hung on the thread and left in position a record made after 10 secs. shows a rapid succession of oscillations (Fig. 3). With a heavier weight these are more frequent and many of them are larger.

Controls. If these oscillations are to be accepted as true action currents they must satisfy certain criteria. A true electric response should consist of a transient fall of potential which passes rapidly along the nerve, in this case away from the muscle. The time relations of the response and its rate of conduction should not differ much from those of the response set up by stimulating the nerve trunk electrically and they should be prolonged considerably by a fall of temperature. Finally the responses should not appear unless we have reason to suppose that the end organs are being stimulated and they should disappear if the nerve is killed between the electrode and the muscle. This last criterion is certainly obeyed. The oscillations only appear in any number when the

muscle is stretched and the control with the nerve killed shows no oscillations whatever the weight hanging on the muscle.

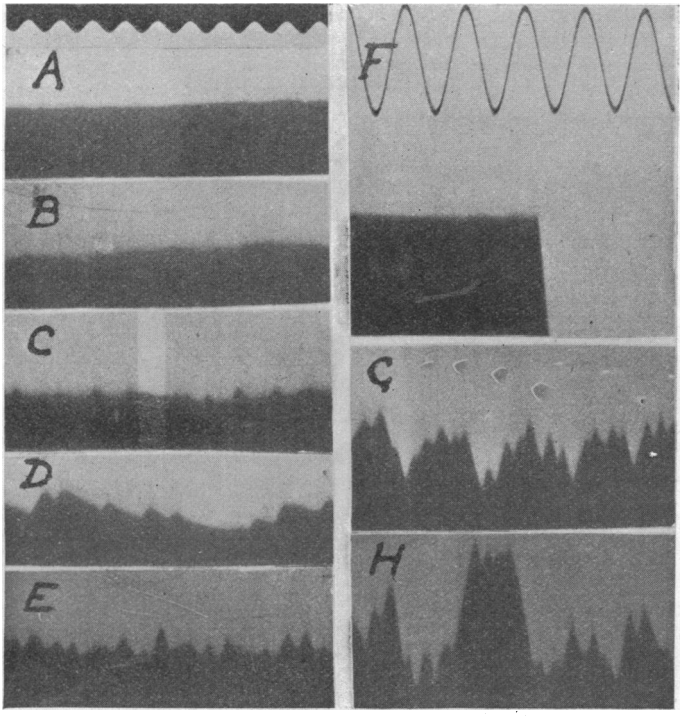


Fig. 3. A–D, G and H, records of action currents in frog's sciatic nerve on stretching gastrocnemius by a weight.

A. Control. Nerve killed near muscle. Tuning fork gives 200 D.V. per sec.
B. Nerve uninjured, muscle relaxed.
C. Weight of 10 gms. for 10 secs. Nerve uninjured (diphasic).
D. Weight of 10 gms. for 20 secs. Nerve injured between leads (monophasic).
E. Weight of 100 gms. for 10 secs. Nerve uninjured.
G. Another preparation. 40 gms. for 5 secs. on gastrocnemius.
H. Same as G. 40 gms. on gastrocnemius and on tibialis anticus.
F. Calibration curve. 0·1 millivolts, 3 valves, showing instant acceleration of mercury. Spring time marker gives 100 D.V. per sec.

Diphasic and Monophasic Responses. The first criterion will be satisfied if we can show that an isolated oscillation is a diphasic change with the first phase indicating negativity at the electrode nearest the muscle, and if we can convert this into a monophasic change by killing the nerve between the electrodes. When the tension on the muscle is

very slight (5 gms. weight, *e.g.*) the oscillations are not continuous but occur as isolated disturbances on a steady base line, and it is then found that the direction of movement of the mercury does show an initial fall of potential at the electrode nearest the muscle. Fig. 4 C gives the analysis of a portion of the record in Fig. 3 C and it will be seen that each oscillation is diphasic. Fig. 3 D and the analysis in Fig. 4 D shows the effect

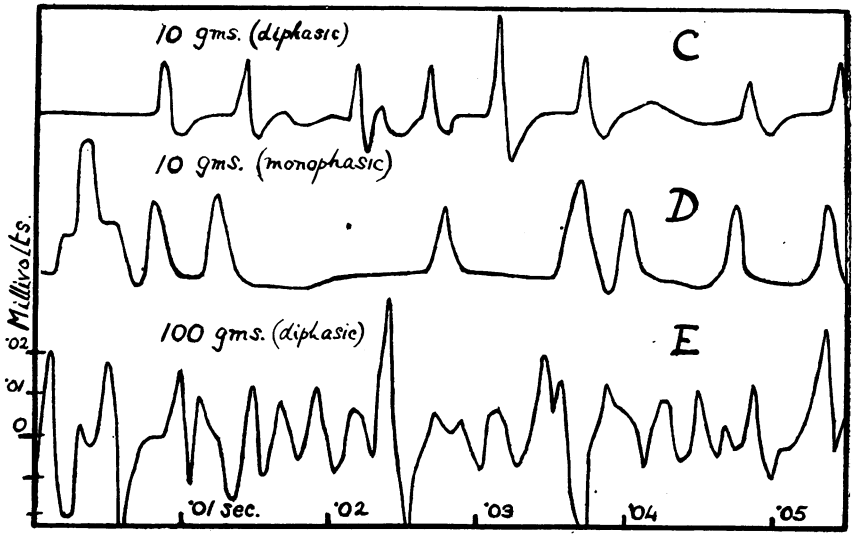


Fig. 4. Analysis of records in Fig. 3 C, D and E.

of killing the nerve between the two electrodes. The electrometer oscillations have a different form and the analysis shows that the response has become monophasic. This change from a diphasic to a monophasic type of response has occurred invariably wherever the nerve is injured between the leads. We have therefore conclusive proof that the disturbances consist of a transient fall of potential passing along the nerve away from the muscle and appearing first under one electrode and then under the other.

Time Relations. Some idea of the time relations of the responses may be gathered from Figs. 3 and 4. Evidently they are not all of the same duration. The larger responses last on the whole for a longer time and some of them are obviously complex. When the oscillations are crowded together (*e.g.* Fig. 4 E), as they are with a strong stimulus, they vary considerably both in duration and amplitude, but in a record where there are pauses between successive oscillations it is noteworthy that the great majority of them have much the same duration and much

the same size. Whether these really represent the activity of a single nerve fibre or whether they are due to a group of fibres acting in unison is a question which must be left open for the present, but they copy one another so closely that we are certainly safe in assuming that their time relations do represent some definite characteristic of the response. Fig. 5

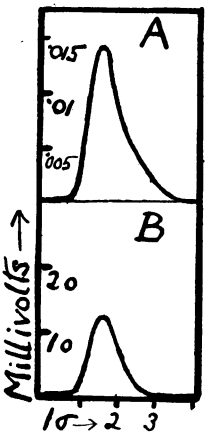


Fig. 5.

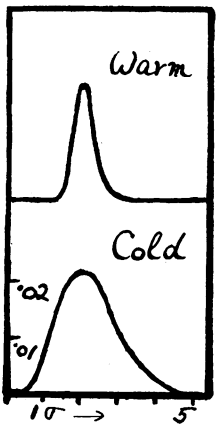


Fig. 6.

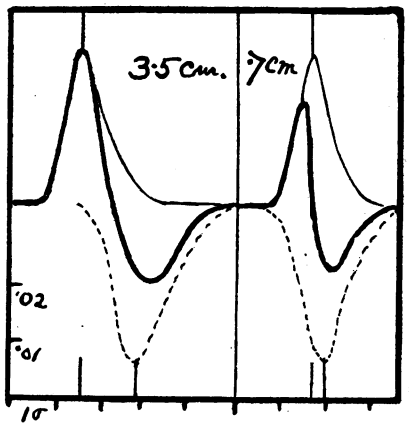


Fig. 7.

Fig. 5. A—isolated monophasic response produced by stretching muscle.
B—response of same sciatic stimulated electrically (no valves).

Fig. 6. Isolated monophasic responses produced by stretching. Nerve warmed and cooled.

Fig. 7. Isolated diphasic responses with varying distance between leads. Thin line gives monophasic response.

gives the analysis of one of these characteristic disturbances on a larger time scale together with the monophasic response produced by stimulating the frog's sciatic with an induction shock and recorded by the same electrometer without amplification. The error in the analysis of the records is fairly large, for with such brief disturbances the whole change only occupies 1–2 mm. on a plate travelling at a metre a second, but the agreement is close enough to justify the statement that the time relations of these responses produced by stretching the muscle do not differ greatly from those of the action current set up by an electric stimulus.

Effects of Temperature. The time relations of a true electric response should be prolonged considerably by a fall of temperature. In some previous work(11) a change from 16° to 6° C. was found to prolong the response of a frog's sciatic to about three times its former value. A careful determination of effects of temperature on the present responses has not been made, but in one experiment the nerve was alternately warmed by pouring Ringer at 25° over it and cooled by placing some ice

about 1 cm. below it, the muscle was stretched by a weight and the monophasic responses were recorded with the amplifier. Fig. 6 shows the analysis of typical responses and there is no doubt that the cooling has increased the duration considerably. It is extremely unlikely that an artefact would be affected so much by a fall of temperature.

Rate of Conduction. A true electric response in the frog's sciatic should be propagated at a rate somewhere between 20 and 30 metres a second at 15° C. Some idea of the rate of conduction of the present responses may be gained from an analysis of the diphasic curves, though here as in the case of the monophasic curves we are met by the difficulty that the larger excursions may have longer time relations and are sometimes obviously complex. But here too if we confine ourselves to isolated excursions we find a fairly constant interval between the two phases and Fig. 7 gives two sets of diphasic curves with different distances between the two electrodes, together with monophasic curves made after the nerve was killed between the electrodes. The rate of conduction works out at 25 m. per sec. The possible error is large, perhaps ± 5 metres per sec., but in any case the value is in very good agreement with the known rate of conduction of the nervous impulse in the frog's sciatic.

Frequency. The oscillations do not occur regularly, but in any given record the numbers appearing in successive periods of $\frac{1}{25}$ sec. are generally very near one another. Now if the oscillations are true action currents their frequency should bear some relation to the state of the end organs, the degree of stimulation, temperature, etc. If they are artefacts depending on the properties of the recording apparatus or on chance disturbances from mechanical or electrical vibrations in the building their frequency would not be affected by the condition of the end organs. The fact that they do not appear at all unless the muscle is under slight tension makes it extremely improbable that they are artefacts and this is confirmed by the fact that their frequency does vary with the degree of tension on the muscle, and if the tension is kept constant with the temperature of the muscle. This is illustrated in the following experiments.

Expt. 1. Frog's sciatic gastrocnemius preparation. At room temperature 16·5° C.

Stimulus	No. of oscillations (estimated by counting for period of ·15 sec.)
(*a*) Weight of 10 gms. hung on muscle for 10 secs. before record was made	210
Weight of 10 gms. on muscle for 20 secs. ...	175
(*b*) Weight of 50 gms. on muscle for 10 secs. ...	290
Weight of 50 gms. on muscle for 20 secs. ...	230

Expt. 2. Frog's sciatic gastrocnemius. Nerve kept at 15° C. Temperature of muscle varied.

Stimulus constant	No. of oscillations per sec.
(*a*) Muscle at 15° C. Weight of 40 gms. for 5 secs.	330
(*b*) Muscle at 5·8° C. Weight of 40 gms. for 5 secs.	190

Evidently the frequency is determined by something happening in the muscle and not by the mechanical or electrical properties of the recording apparatus.

These controls have been dealt with at some length because of the obvious possibility of artefacts in recording changes of potential as small as ·01 millivolts in a high resistance circuit such as a nerve. They leave no doubt that the oscillations are due to nervous impulses travelling away from the muscle and they show what kind of record we may expect from sensory nerve fibres in general. Granting, then, that we have to deal with true action currents we may proceed to discuss the conditions which give rise to them.

Number of fibres in action. The chief difficulty in interpreting these records lies in the fact that we are dealing with a number of afferent fibres and that there is no reason to suppose that they are activated synchronously. It is a point of some importance that the oscillations should appear as clearly as they do, for it is easy to imagine a state of affairs in which the overlapping of impulses in different fibres would be so great that the electrometer record would be smoothed out into a straight line. So far nothing approaching this has been observed in any of the experiments. With a weak stimulus (cf. Fig. 4 C and D) the oscillations are isolated from one another by considerable pauses. As the strength is increased these pauses disappear and the oscillations are much more irregular in size (Fig. 4 E). Evidently there is some overlapping in such records, but even with the strongest stimuli it has not been enough to cut down the average size to any great extent. This must mean that the total number of impulses set up in a given time in all the afferent fibres by a weak stimulus is relatively few—probably not more than 300 in a second, and it is natural to enquire whether the simple, isolated responses such as those in Fig. 4 do not each represent the action current of a single nerve fibre. The fact that they all conform closely to a standard size and a standard duration supports this very strongly, for it seems most unlikely that a continuous stimulus such as a state of tension would activate groups of fibres synchronously. The potential change in these isolated responses usually lies between ·015 and ·025 millivolts, which is about a thousand times less than the potential change

occurring when the whole sciatic nerve is stimulated electrically. The number of fibres in the frog's sciatic lies between three and four thousand, but it is difficult to say what the relation between potential and number of active fibres would be for such extreme cases as the whole nerve trunk and a single nerve fibre. For the present, then, we must be content with the conclusion that only a very few fibres are concerned in producing the isolated responses—almost certainly less than ten and probably only one.

Effects of change in strength and duration of stimulus. This will not be dealt with in any detail on account of the uncertainty in interpreting the results from a nerve containing many afferent fibres. In the near future it should be possible to make use of a preparation containing only one sensory nerve ending, and if this can be done a knowledge of the relation between the stimulus and the frequency of the impulses set up will be far more significant. When many end organs are present, an increase in frequency in the record might be due to an increase in the number of nerve fibres in action, to an increased frequency in each fibre or even to a change from synchronous to asynchronous activity in different fibres. At the same time the results are definite enough and may be stated briefly. In the first place, if the weight is kept constant and is applied at different times before the record is made, it is found that the frequency of the oscillations falls off gradually as the length of the period is increased. This is illustrated in the following experiment.

Expt. Frog's sciatic gastrocnemius preparation. Temp. 16° C. Weight of 50 gms. hung on tendon. Record made at different times after application of weight.

Duration of application (secs.)	No. of oscillations per sec.
5	290
10	270
20	165
40	125
80	60
245	47
615	33 (extremely irregular)

It will be seen that some oscillations can still be recorded even though the weight has been hanging on the muscle for ten minutes. Whether they cease immediately on its removal is a point which has not been tested, but they are certainly absent 5 secs. later. This persistent discharge of impulses when the tension on the muscle is maintained is in striking agreement with the work of Liddell and Sherrington on the stretch reflex which persists in the same way when the tension is maintained.

The gradual decline in frequency makes it necessary to use a stimulus

of constant duration when changes of strength are investigated. If the period of loading is kept constant (5, 10 or 20 secs. as a rule) an increase in the weight causes an increased frequency up to a limiting value of about 400 per second. Thus a weight of 5 gms. for 10 secs. gave a frequency of 120 per sec. and a weight of 50 gms. gave 310. More evidence of overlapping occurs as the frequency increases and the record takes on the character of Fig. 4 E, with a mixture of large and small oscillations. It is an interesting point that in records with smaller weights (or longer durations) where isolated responses can be measured, the magnitude of these appears to be constant and shows no signs of varying with the strength of the stimulus. This result is clearly in agreement with the idea of an all or nothing relation between stimulus and nervous impulse.

Afferent impulses from other muscles. In the decerebrate cat Liddell and Sherrington find that the stretch reflex is only elicited by tension on the extensor muscles. Tension on the flexors, on the other hand, is not without reflex effect, for it inhibits the stretch reflex in the extensors. In the frog tension on the following muscles produces a sustained discharge of afferent impulses in the sciatic: gastrocnemius, tibialis anticus, sartorius, extensors of the thigh and hamstring muscles. There is no obvious difference between the records from the flexors and those from the extensors. In the spinal cat if electrodes are placed on the popliteal nerve (cut high up in the thigh), tension on the gastrocnemius tendon produces a record almost indistinguishable from those given by the frog's sciatic.

C. *Impulses in cutaneous sensory nerves.*

The responses so far discussed have all been initiated in the sensory end organs of muscles, *i.e.* in organs of the proprioceptor class. These are the most easily investigated because the stimulus which excites them is so much more readily controlled and measured than are the stimuli which excite the cutaneous sensory endings. But there is no difficulty in recording the action currents in a cutaneous sensory nerve. The internal saphenous nerve of a spinal (decapitate) cat is dissected out as low down as the knee, ligated and divided high up in the thigh and placed on the electrodes. The leg is allowed to rest on the table, all motor nerves to the limb being divided to prevent reflex movements. A record of the electric effects in the nerve then shows a rapid series of oscillations, and these increase in frequency and amplitude if the skin of the foot is nipped by a pair of artery forceps or pricked by a pin

(Figs. 8 and 10). The oscillations conform to the same tests which were applied in the case of afferent impulses from the muscles. The responses

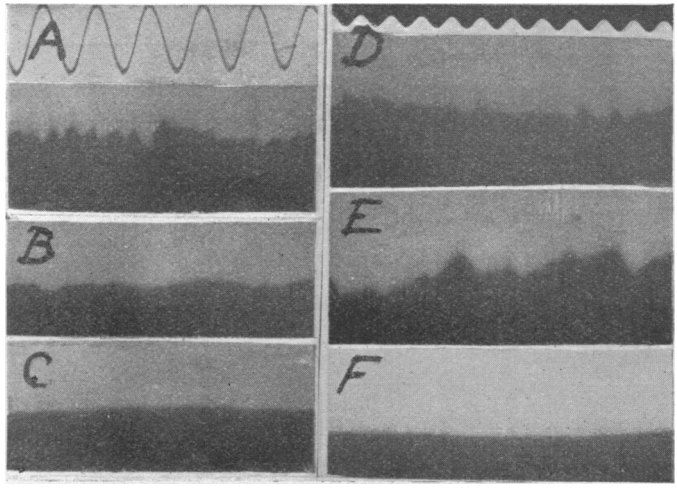


Fig. 8. A, B, C responses from vagus of spinal cat. Time marker gives 100 D.V. per sec.

A. Lungs held inflated for 5 secs. (diphasic).

B. Lungs deflated 5 secs.

C. Control. Nerve killed distal to leads.

D, E, F responses from internal saphenous nerve of spinal cat. Tuning fork gives 200 D.V per sec.

D. Skin of leg pinched by forceps. Diphasic.

E. No added stimulus. Monophasic.

F. Control. Nerve killed distal to leads.

become monophasic when the nerve is injured between the electrodes and they disappear when the injury is distal to the electrodes, though the injury itself sometimes sets up a rapid discharge of impulses lasting several minutes. A further control consists in leaving the proximal connections of the nerve intact and cutting it distally. The record is then quite free from oscillations though the nerve fibres are uninjured and are in connection with the body of the animal. Records have been made from six nerves and it is noteworthy that in all of these a fairly continuous series of oscillations was present, although the leg was not interfered with in any way. The normal environment seems to contain factors which stimulate the cutaneous receptors, such factors being, no doubt, the pressure of the leg on the table, movements of the hairs produced by air currents, etc. The only added stimuli investigated have been those which would cause pain in the intact animal. The increase in

frequency may be relatively small if the frequency is already high in the resting limb. The maximum rate recorded was 420 per sec., the temperature of the limb surface being 25° C. As the temperature of the nerve was not accurately controlled, not much information can be drawn from the time relations of the responses, but there is no indication that the additional impulses set up by a painful stimulus differ much from those with the limb undisturbed which are presumably due to non-painful stimuli[1].

In two experiments on the spinal cat and one on the frog it has been found that pinching the tendon of a muscle with artery forceps produces a series of oscillations of the usual type in the nerve attached to the muscle.

D. *Afferent impulses in the vagus and cardiac depressor.*

Observations of the same preliminary character have been made on these nerves, since their sensory end organs belong to the class of visceral receptors and the impulses set up might conceivably differ from those in sensory fibres from the skin or the skeletal muscles. Einthoven(12) has published string galvanometer records from the peripheral portion of the divided vagus in the dog during the movements of respiration and these show a slow deflection of the string corresponding to the movement of inspiration and a slow return during expiration. On this curve are superimposed a series of more rapid oscillations which are synchronous with the heart beat. The respiratory and the cardiac effects could be separated by leading off from either the vagus or the cardiac depressor in the rabbit. These observations (which confirmed and extended the earlier work of Lewandowski and of Tschermak and Koster) show that the vagus becomes electro-negative during inspiration, as would be expected if afferent impulses were passing up it, but there is nothing to indicate the nature and frequency of these impulses.

The following experiments have been made with spinal (decapitate) and decerebrate cats and with rabbits anæsthetised with urethane. One vagus was divided at the level of the lower border of the thyroid cartilage, and the lower, distal portion was dissected out as far down as the sternum and placed on the electrodes, the distal part of the nerve being looped over a glass hook to prevent the pulsations of the carotid from being transmitted to the electrodes. When continuous records were required the shadow of the capillary was thrown by a train of

[1] Erlanger and Gasser have shown that there are probably differences in the time relations of various classes of sensory impulse, but they are scarcely great enough to be detected in the present records.

mirrors on to the slit of a camera containing cinematograph film driven at a constant rate by an electric motor. The movements of respiration were recorded on the same film by a lever connected by a thread to a flat plate resting on the chest of the animal.

Typical results are shown in Fig. 9. Fig. 9 A and B are from the

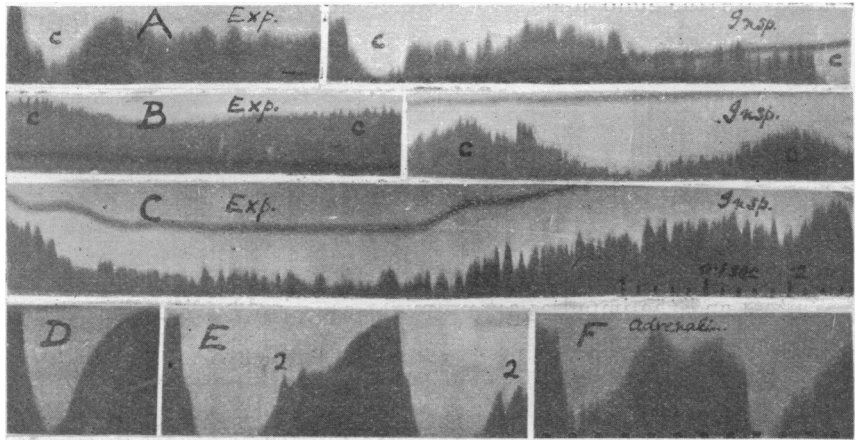


Fig. 9. Portions of continuous records on cinematograph film from vagus and cardiac depressor nerves. Time marker (on C) gives ·02 sec.

A. Spinal cat. Artificial respiration. Record from vagus showing cardiac (*c*) and respiratory impulses.
B. Decerebrate cat. Natural respiration. Cardiac (*c*) and respiratory impulses.
C. Rabbit, urethane. Record from vagus.
D and E. Ditto. Record from cardiac depressor.
F. Ditto. After injection of adrenalin.

cat and impulses of depressor origin are therefore included. These occur in groups at the same rate as the heart beat and each group is marked *c* in the figure, but their consideration may be deferred as they can be studied more conveniently in the rabbit. The respiratory effect is quite clear. Oscillations occur during expiration as well as inspiration, but their frequency and amplitude is greatest at the height of inspiration and least at expiration. The most striking result is the absence of any sign of a renewed discharge of impulses at the moment when the lungs are most deflated. In the records from the cat there is very little activity in the vagus throughout the period of expiration apart from the groups of cardiac impulses. In the rabbit there are more oscillations during expiration though the increase on expansion of the lungs is clear enough.

This difference may be due to the fact that the breathing was shallower and more rapid in the rabbits, so that the lungs were never as completely relaxed as in the cat, but the oscillations might also be due to impulses in sensory fibres coming from other regions than the lung.

Nature of stimulus to vagal endings. The increased flow of impulses during inspiration might be due to the actual movement of expansion of the lungs or to the state of tension produced in the tissues, or to both. In a number of experiments the tube from the trachea was clamped and the lungs allowed to remain in the expanded or relaxed state for several seconds before the record was made. Typical records are given in Fig. 8. In one of these experiments the lungs were allowed to remain inflated for 20 secs., but the oscillations were as clearly marked as in records made during the actual movement of expansion. Clearly then the state of expansion of the lung is an effective stimulus to the vagal endings and the flow of impulses continues as long as the tension is maintained, just as it does in the afferent fibres from a skeletal muscle. Since there is a steady flow of impulses as long as the lungs remain expanded, the total number of impulses reaching the centre will go on increasing until the lungs are relaxed. If the effect of the impulses on the centre is cumulative, this would account for the fact that the contraction of the expiratory muscles becomes greater and greater as long as the breath is held.

If the lungs of a spinal cat are deflated forcibly and the trachea tube is then clamped, a record taken 2–3 secs. after does not show any more oscillations than are present if the chest is merely allowed to deflate itself. Indeed, as far as these records are concerned, there is no evidence that deflation of the lungs is an effective stimulus to the vagal endings.

Nature and Frequency of impulses. Analyses of two records are given in Fig. 10. The time relations are much the same as those in the cat's internal saphenous, though here too the temperature of the nerve was not accurately controlled. The maximum frequency with the lungs inflated has been 450 for short periods.

The close likeness of the records from the vagus, internal saphenous and from the frog's sciatic suggests either that all the sensory fibres concerned are very much alike, or that the characteristic record is an artefact with oscillations determined by the recording instrument. This possibility has been discussed already and rejected, and if further evidence were needed against it, it is supplied by the records from the cardiac depressor which are of an entirely different character.

E. *Impulses in the cardiac depressor.*

The rabbit's cardiac depressor is a very slender nerve made up entirely of afferent fibres from the heart. For this reason the responses in it are large compared with those of a mixed trunk like the vagus or sciatic. Typical electrometer records are given in Fig. 9 D, E and F, and an analysis of one complete cardiac cycle in Fig. 10. The responses occur

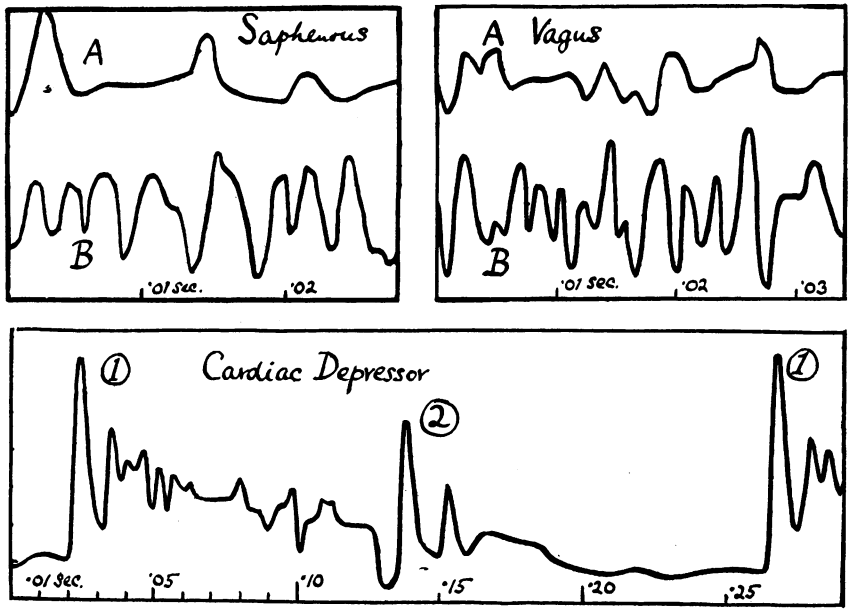


Fig. 10. Analysis of records from internal saphenous, vagus and cardiac depressor.
Saphenous. A. Monophasic, no added stimulus.
B. Diphasic, skin of leg pinched.
Vagus (spinal cat). A. Monophasic, lungs deflated 3 secs.
B. Diphasic, lungs inflated 3 secs.
Cardiac depressor. Rabbit. Initial wave marked 1, "dicrotic" 2.

in groups synchronising with the heart beat with a distinct pause between successive groups. The pause (presumably diastolic) is broken abruptly by one or more very large oscillations of E.M.F. followed by a rapid succession of smaller oscillations. Before these have died out completely there is nearly always another large oscillation (marked 2 in the figures). After a few more small oscillations the diastolic pause ensues. Using an ordinary galvanometer Tschermak and Koster(13) found that a negative variation was produced in the nerve by distension of the aorta, and in view of this we may take the first large outburst of

impulses as due to the rise of pressure in the aorta at the beginning of the ventricular systole and the second to the rise of pressure when the aortic valves close. Records from different animals or from the same animal at different times show a great variation in the number of smaller oscillations. The conditions determining this have not been studied, but an injection of adrenalin (·5 cc. of a ·01 p.c. solution) into the ear vein of the rabbit was made in two experiments and was followed by a great increase in the number of oscillations, the smaller waves continuing throughout the diastolic pause. In the records of the cat's vagus, if the decapitate preparation is used, the groups of oscillations which show the cardiac and not the respiratory rhythm have much the same character as those in the rabbit's depressor, but in the only decerebrate preparation the large initial and "dicrotic" waves are not evident (Fig. 9 B). The obvious need for the correlation of these records with determinations of the blood-pressure makes further discussion premature.

The foregoing results have been put on record more as an indication of the capabilities of the recording instrument than as a contribution to any branch of physiology. All of them suffer from the fact that the preparations employed have contained many afferent fibres and that we do not know how many are in action at a given time. But the instrument is clearly capable of recording the action current of a single nerve fibre even though it is surrounded by a thousand or more inactive fibres in a large nerve trunk, and it should not be a matter of great technical difficulty to isolate a single sensory ending and so to obtain the positive information lacking in the present experiments. Experiments on these lines are in progress and have already reached a great measure of success.

Summary.

The paper describes a combination of a capillary electrometer with a three valve amplifier which is capable of recording rapid changes of potential of the order of ·01 millivolts with almost complete absence of disturbance from mechanical and electrical artefacts. With its aid it has been possible to record the action currents accompanying afferent impulses in the frog's sciatic nerve when the gastrocnemius is stretched by a weight, in the cat's internal saphenous nerve when the skin is pinched, in the cat's and rabbit's vagus when the lungs are inflated and in the cardiac depressor nerve of the rabbit. Numerous control observations have been made to exclude the possibility that the recorded oscillations of potential are due to any other cause than the passage of impulses in the nerve. It is probable that many of the oscillations represent action

currents in a single nerve fibre, and these have the same general form and the same general time relations (allowing for temperature differences) in all the sensory nerves in which they can be isolated sufficiently for measurement. There is no evidence that an increase in the stimulus increases the size of the action currents in single fibres, but the frequency of the impulses in the nerve trunk increases and leads to interference and overlapping of impulses in different fibres. When a muscle is stretched by a weight the discharge of afferent impulses continues for as long as ten minutes, provided that the tension is maintained. Similarly the passage of the impulses up the vagus continues (for as long as 20 secs.) if the lungs are held in the expanded state. No evidence was found of any renewed discharge of impulses in the vagus on deflation of the lungs. More detailed analysis of these results is postponed until experiments have been made on preparations containing a known number of sensory endings, if possible only one.

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