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RHYTHMIC ACTIVITY IN SKELETAL MUSCLE FIBRES.

By E. D. ADRIAN and S. GELFAN[1].

(*From the Physiological Laboratory, Cambridge.*)

THESE observations deal with certain features of the rhythmic discharge which may be set up in striated muscle by non-rhythmic stimulation or treatment with various salt solutions. They were made in the hope of finding evidence which would apply to such discharges in general and particularly to those occurring in the central nervous system. Rhythmic activity in muscle has much the same character as that in sensory end-organs and in nerve cells, and muscle discharges have the advantage that they can be recorded at or near their point of origin. A disadvantage arises from the fact that in muscle there is a mechanical as well as an electrical response. This has introduced some uncertainty, but we have found several unexpected features in the muscular discharge and some indication of the conditions which produce spontaneous activity.

Since we have had to record slow as well as rapid changes, we have used a direct coupled amplifier leading to a Matthews's oscillograph. The arrangement is that described by Adrian [1931] with slight modifications.

No great sensitivity is needed to record action currents in single muscle fibres, and as a rule the amplifier has been arranged to give at maximum sensitivity a deflection of 10 mm. for 25 microvolts. A tapped volume control gives various fractions of this sensitivity, and it is usually set to give 1/4 or 1/10. With a metallic resistance in the input circuit there is no appreciable drift of the base line at maximum sensitivity. With the electrodes and preparation in circuit slow drifts appear from time to time, *e.g.* when the composition of the fluids is altered, but these are rarely troublesome. Glass U-tube electrodes were used, with silver, silver chloride leads. These must be shielded from light, as an unequal illumination produces a slow change of potential. A condenser coupling was used in some experiments in which it was necessary to eliminate slow changes. The usual rotating mirror and loud-speaker arrangements were used.

[1] Guggenheim Memorial Fellow.

Rhythmic discharges in NaCl *solution.* The twitching which occurs in a frog's sartorius bathed in 0·6 p.c. NaCl solution is accompanied by action currents of the familiar type, and as these are readily amplified it is much easier to follow the course of the activity by electrical than by mechanical recording. To secure continued action the muscle must be bathed in a large volume of the solution; if the volume is too small (as when the muscle is suspended in air on the electrodes) the activity soon ceases, but it is renewed by irrigation with fresh solution. The work of Dulière and Horton [1929] makes it likely that this is due to a diffusion of K from the muscle fibres: unless the excess is removed

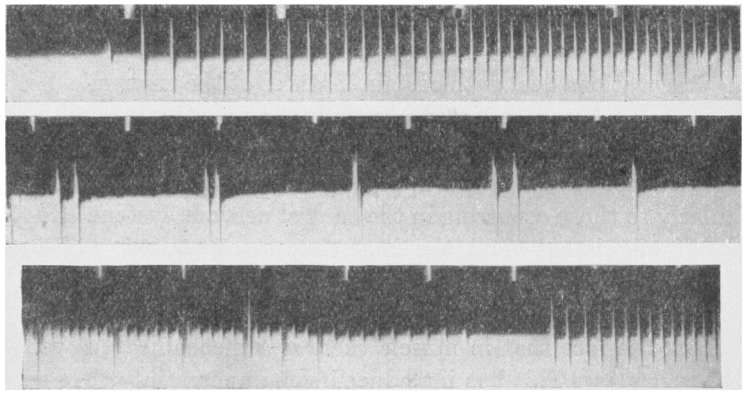

Fig. 1. Spontaneous discharges in frog's sartorius muscle after immersion in 0·6 p.c. NaCl solution. Records made with direct-coupled amplifier and Matthews's oscillograph. The action potentials are due to single muscle fibres. Time marker gives intervals of 0·25 sec. in this and all records.

the activity comes to an end. By making use of this effect it is easy to secure conditions in which there are only one or two series of impulses at a time, *i.e.* only one or two units in action. With frequent renewal of the solution spontaneous activity may continue for an hour or more, each renewal causing a fresh outburst which declines slowly.

Typical records of the discharges are given in Fig. 1. The muscles lay in a bath divided by a slot to form two electrodes, or were suspended in air on U-tube electrodes with cotton-wool plugs soaked in the solution. They were under enough tension to prevent visible movement but were not interfered with except during irrigation. The units responsible for each series of action potentials are, in most cases, the individual muscle fibres, for the discharges occur in curarized muscle, and in normal muscles

some of them are found to arise from the pelvic end beyond the region of nerve endings. The magnitude of the potential varies from one series to another, but the average size is of the order to be expected from a single muscle fibre.

The sartorius contains about 400 fibres and the whole muscle gives a potential (monophasic) of about 40 mv. Thus the average potential from one fibre should be 0·1 mv. [Watts, 1924]. The values recorded range from about 0·01 to 0·3 mv. The variation is probably due in part to the greater short circuiting of the fibres in the interior of the muscle.

The frequency of the impulses in a single series may range from about 1 to 80 a sec. (at 15° C.). The high-frequency discharges usually last for a much shorter time than the low-frequency, though the duration varies widely with the condition of the muscle in regard to irrigation. Discharges which attain a high frequency usually cease when the frequency has fallen to 10–20 a sec. Grouped discharges sometimes occur, each group made up of two or more impulses closely spaced. When several units are in action each preserves its own rhythm and there is no tendency to synchronization.

The behaviour of a muscle in NaCl solution is strongly reminiscent of that observed in the isolated nerve ganglia of insects [Adrian, 1930*b*, 1931]. These give spontaneous discharges with the same mixture of slow and rapid rhythms, which rise and decline in much the same way. The activity is often increased by irrigation with Ringer's fluid and it seems likely that the irrigation acts, as with muscle, by removing something which diffuses from the cells and tends to check their discharge.

The most significant evidence as to the cause of the activity in NaCl solution is that given by Mines [1908]. He found that a muscle in 0·6 p.c. NaCl was much more excitable to currents of long duration than one in Ringer's fluid, though to currents of short duration there was no difference. Thus in NaCl there is a much less rapid adaptation to an electric stimulus: as a result a weak constant current might produce a continued excitation and a repeated discharge of impulses. Potential gradients due to inequalities in the surface of the fibres might form the necessary stimulus. But eventually a stimulus of this kind might be unnecessary, for if there is normally an equilibrium between a reaction tending to produce the state of excitation and one tending to counteract it, a failure of the latter would be enough to start a discharge.

Mechanical stimulation. Stretch. When a fresh muscle has been for some minutes in NaCl solution a light touch on its surface or a slight

stretch will often produce considerable activity. When it has become sensitive to very slight mechanical stimulation of this kind there are usually a good many fibres discharging spontaneously; as these confuse the record we have usually worked with the muscle in a less excitable state. It is also necessary to use a condenser coupling in the amplifier to minimize potential changes of long duration.

The response to moderate stretch may then take several forms, illustrated in Fig. 2. Rapid discharges may start in one or more fibres

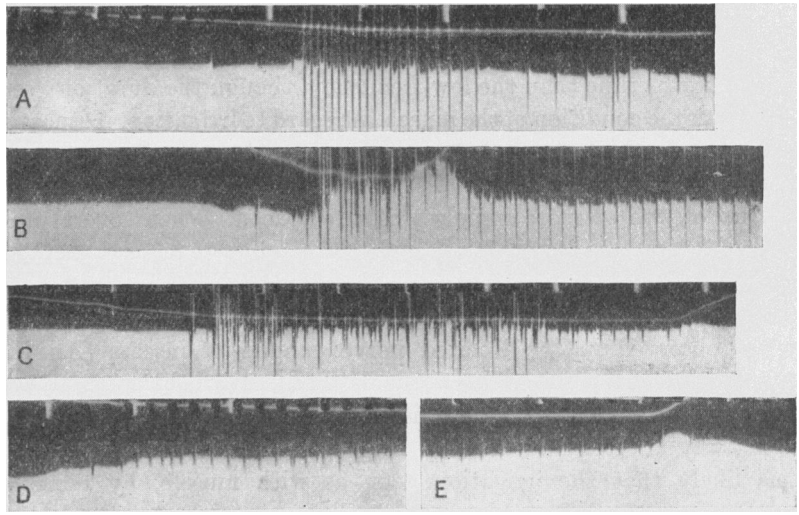

Fig. 2. Discharges produced by stretching muscles treated with NaCl solution. The stretch is shown by the white signal line. In A one fibre ceases to discharge before the stretch is relaxed; in B one begins to discharge at relaxation. In C, D and E, relaxation stops the discharge. D and E are from the same record with an interval of 2 sec. between them. Condenser coupling in the amplifier to eliminate steady potential changes.

and these may come to an end whilst the stretch is still in being (Fig. 2 A) or may persist for a variable time after it is over without any marked change of frequency at relaxation. The relaxation sometimes causes a fresh discharge (Fig. 2 B). But it is a common experience to find the discharge in some fibres persisting throughout the stretch and ceasing abruptly at relaxation (Fig. 2 C, D and E). The amount of extension needed to start the discharge varies with the state of the muscle, but that due to a weight of 1–2 g. is usually enough.

The result is chiefly remarkable in showing that a muscle fibre after treatment with NaCl solution behaves in much the same way as a sensory

nerve ending. A stretch receptor (*e.g.* a muscle spindle or a vagal ending in the lung) gives a rhythmic discharge on extension, and the chief difference is that with the sensory ending the frequency varies smoothly with the stretch, whereas the muscle fibre discharge shows much less flexibility. A spontaneous discharge of low frequency sometimes becomes more rapid when the muscle is stretched, but usually the frequency rises and declines abruptly and once the discharge has started an increase in the stretch has no further effect on it. This lack of grading is not surprising. The sole function of the sensory end-organ is to translate a stretch into an impulse message of graded frequency and its mechanism must work as flexibly as possible. The muscle fibre has no such function: if it is to be under complete control by the nervous system it must not react on its own account to a moderate stretch, and normally it does not. By treatment with NaCl it can be made to do so, but it is small wonder that the mechanism is jerky and inflexible.

Some idea of the mechanism may be gathered by considering the different kinds of discharge produced by stretch. The commonest type is the discharge which, once started, runs its course without further regard to the stimulus, ceasing before or after relaxation and showing no change of frequency when relaxation occurs. Here the exciting factor seems to be an injury which is perhaps healed by time but is not healed by relaxation of the stretch. An injury such as that caused by cutting or tearing the fibre gives a long discharge in NaCl, and the electric forces at the injured region would be an adequate stimulus. Clearly a transient injury would account in the same way for the discharges which cease at relaxation. A breakdown of the polarized surface might repair itself when the mechanical strain is removed, and if the breakdown involved complete depolarization the discharge would not vary in frequency with the stimulus. If the sensory ending has the same kind of mechanism we must imagine that its surface is much less rigidly constructed and so can be made to give a graded change of polarization according to the amount of mechanical strain. It may be noted here that the discharge of a stretch receptor agrees with that of a muscle fibre in regard to the action of salts, for immersion in NaCl prolongs the discharge and there is something which diffuses from the tissues and inhibits activity if the fluid is not changed from time to time [Matthews, 1931].

If it is true that mechanical stimulation acts by causing a local injury or depolarization of the fibre, we might expect to find evidence of steady potential changes due to the stretch. Unfortunately it is not possible to localize the effect of a stretch so that the discharge may be trusted

to start from the neighbourhood of one of the electrodes. There are considerable potential changes between the electrodes, sometimes coinciding with the extension and sometimes outlasting it, but so many factors might produce them that the observation has little value.

A possible method of testing the point seemed to arise from the fact that a discharge can be produced by localized pressure. Experiments with this form of stimulation are described below.

Stimulation by pressure. The sartorius was set up in a moist chamber with the tibial end in contact with the input electrode. The pelvic half of the muscle lay on a small glass plate with its upper surface in contact with the earthed electrode. This had a rigid end which could be pressed against the muscle to give the necessary stimulus.

It was made from a small block of vulcanite with a hole drilled vertically through it and plugged with a fragment of unglazed porcelain, sealed in with wax. The projecting end of the porcelain was ground flat so that it would lie evenly on the muscle. The hole was filled with NaCl solution and a spiral of silver wire coated with silver chloride was dipped into it from above. The electrode could be pressed on to the muscle by a weighed lever or by a positive screw movement.

A typical record, made with low amplification, is given in Fig. 3 A. The muscle had been bathed in NaCl, but was quiescent before stimulation. The movable electrode was held so that it made electrical contact with the muscle but exerted no pressure: it was then gradually pressed down by a fine screw adjustment. The result is a rapid fall of potential (indicated by the upward movement of the base line) and an outburst of impulses in many fibres. The pressure has produced an injury potential and the discharge is presumably set up by this.

With this form of stimulation we have not succeeded in recording a reversible excitation, a discharge which subsides as soon as the pressure is removed. There is often a slight reduction of the injury potential, but some permanent damage has always been produced, and so many fibres remain in action that it is difficult to be sure that any cease discharging when the pressure is relaxed. All that can be said is that in a muscle previously uninjured there is no sign of any production of impulses by pressure before the first appearance of the injury potential, no sign, that is, of a discharge which is not associated with a local depolarization of the fibre. The results are more erratic if the muscle has been damaged by previous stimulation and the fall of potential may then be masked by changes due to the movement of the region already injured.

But the records, although not as conclusive as we had hoped, have shown another feature of greater interest. This is illustrated in Fig. 3 B,

C and D. As the injury potential increases the discharge may suddenly change its character. The small, irregular fluctuations give place to large regular waves with a potential of several millivolts. Their size shows that they are due to a number of muscle fibres acting synchronously; the number cannot well be less than 10 and must often be 20 or more. The degree of synchronization varies, for the form of the waves may differ little from that of the action potential of a single fibre or it may

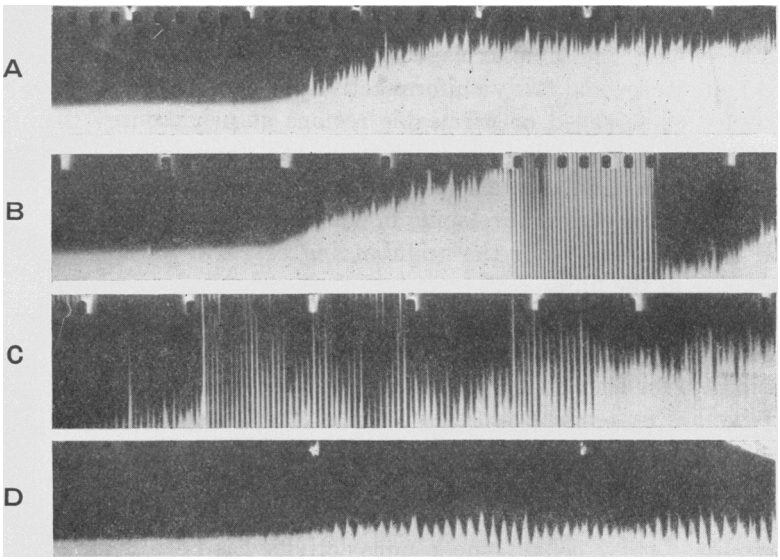

Fig. 3. Discharges due to pressure applied by one of the electrodes. Direct coupled amplifier. An upward movement of the base line denotes a fall of potential at the electrode which is pressed on the muscle. The discharge does not begin until some injury potential has developed. In B, C and D, large synchronous waves take the place of the smaller oscillations. In D the sensitivity is very much reduced, and the speed of the film increased to show the form of the waves.

be more like a smooth sine curve. The waves only occur at high frequencies: the maximum has varied from 90–120 a sec. and the minimum has never been less than 60. When the frequency has fallen to this value the discharge breaks up into the usual rapid, irregular type, though an occasional large wave may appear from time to time.

The synchronization of the muscle fibres is not due to the stimulus acting *via* the nerve, for it occurs after curarization and the pressure may be applied at the pelvic end beyond the region of nerve endings. Treatment with NaCl is not essential, for synchronous waves can be

produced in a muscle irrigated with Ringer's fluid, though the discharge lasts for a much shorter time. Evidently the phenomenon is characteristic of injured muscle and is closely related to the synchronization which occurs in injured nerve fibres [Adrian, 1930*a*]. In the latter the frequency of the waves is naturally higher (300–500 a sec. at 37° C.), and they may occur either at the moment of injury or some time after it, from slight changes of temperature, irrigation, etc. It has been argued that the synchronization in nerve is brought about by the electrical forces at and near the cut ends of the fibres and it is most likely that the waves in muscle have the same explanation. The essential conditions seem to be (*a*) an intense and fairly uniform activity in several fibres, and (*b*) the existence of damaged or permeable regions at neighbouring points in them. These would bring the interiors of the fibres into free electrical communication and give a chance to the group to behave as a single unit. An active region developing in one fibre close to the injury would tend to activate not only the neighbouring points in the same fibre but also those in the fibres next to it, and thus a rhythmic discharge in one fibre might come to dominate the rhythm of its neighbours. Erlanger and Blair have shown recently [1932] that this is more than a theoretical possibility, for they find that although in an uninjured fibre a wave of activity has no tendency to excite other fibres, there are distinct signs of interaction if the fibres are damaged.

The synchronization in these muscle and nerve discharges is of interest from the light it may throw on the synchronization which occurs in groups of nerve cells. Synchronous activity has been found in motor discharges [Gasser, 1928; Adrian and Bronk, 1928], in the retina [Adrian and Matthews, 1928] and in the optic ganglion of insects [Adrian, 1932]. The usual conditions for its appearance are that the excitation should be uniform and of high intensity. In muscle and nerve we have to add the condition that there should be a steady depolarization at neighbouring points in the fibres; we may expect, therefore, that a similar depolarization occurs at some point in strongly excited dendrites or nerve cells.

Changes at the point of origin of the discharge. The activity caused by severe pressure is certainly associated with a persistent depolarization of the fibre at the stimulated point. That caused by stretch, and ceasing when the stretch is over, seems likely to be due to a reversible depolarization, but the evidence is not conclusive. The discharges which occur spontaneously are often indistinguishable from those due to mechanical stimulation and the high frequency discharges might well be due to a

sudden breakdown in some part of the fibre. But many of the spontaneous discharges have a very low frequency and it is unlikely that these can be explained in the same way unless there can be minor degrees of breakdown with a very slight stimulating effect.

The general state of polarization of the fibre surface (apart from localized breakdown) cannot be responsible for the tendency to activity, for some of the solutions which produce it increase, and some decrease the potential difference between an intact and an injured region. In NaCl, for instance, the injury potential is slightly greater than in Ringer's fluid, and if the fibre is uninjured a region bathed in NaCl is a few millivolts positive to a region bathed in Ringer. On the other hand solutions of 0·6 p.c. Na citrate, tartrate or oxalate cause great

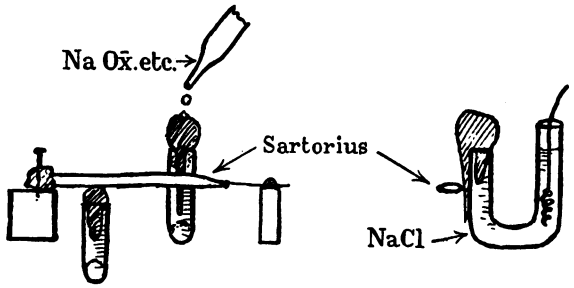

Fig. 4. Arrangement used for recording potentials developed at the point of origin of the discharge, showing method of applying salt solutions to the muscle by way of the electrode.

spontaneous activity, but a region bathed in them is negative to a region bathed in Ringer. It is probable, however, that there is the common factor of a slow rate of adaptation, for with all these solutions the concentration of calcium ions will be less than in Ringer's fluid. With all of them, therefore, the reaction which opposes the development of the excitatory state is likely to take place more slowly than in normal fibre, and in the end the excitatory state might develop from the mere absence of the opposing factor.

To collect more evidence as to this it seemed essential to record the electric changes occurring at the point of origin of the discharge. An application of NaCl solution limited to a few millimetres of the fibre cannot be relied on to cause spontaneous activity, but solutions of Na citrate, tartrate or oxalate will do so. After various trials we adopted the simple arrangement shown in Fig. 4. The sartorius is suspended horizontally and makes contact with two U-tube electrodes. These are

filled with 0·6 p.c. NaCl solution and plugged with cotton wool. The plug on the "active" electrode is pulled out into a tail which is turned down so that it lies against the side of the glass tube and touches the side of the muscle. Solutions dropped from a pipette on to the upper part of the plug flow down by way of the tail and drip off the bend in the U below; thus the fluid in contact with the muscle can be changed in composition with very little disturbance, and only a small length of the fibre is exposed to it. With this arrangement the addition of a few drops of 0·6 p.c. Na citrate, tartrate or oxalate at the top of the plug

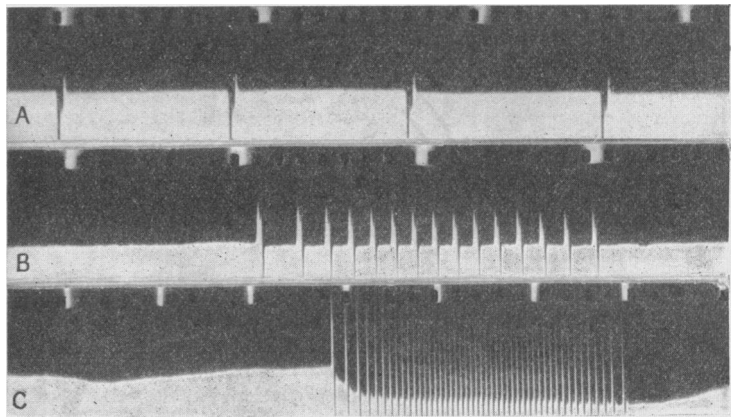

Fig. 5. Control records, made with direct-coupled amplifier, to show the form of the action potentials when the discharge starts from a point beyond or between the electrodes. The potential changes develop suddenly from a horizontal base line. In C there is a movement of the base line due, probably, to the contraction.

is usually enough to start a discharge of impulses in several fibres and it can be stopped again by washing with Ringer's fluid. Control experiments were made by applying the solutions at points beyond or between the electrodes, and the control records differ so markedly from those with the solution on the electrode that there is no doubt of the localization of the effect.

Typical controls are given in Fig. 5 A and B. They show the usual diphasic action potentials rising sharply from a horizontal base line. The action potentials in a series are all alike, and as a rule the movements of the contracting fibre have no effect on the record. Fig. 5 C is unusual in showing a displacement of the base line, but it appears as a smooth curve on which the action potentials are superimposed.

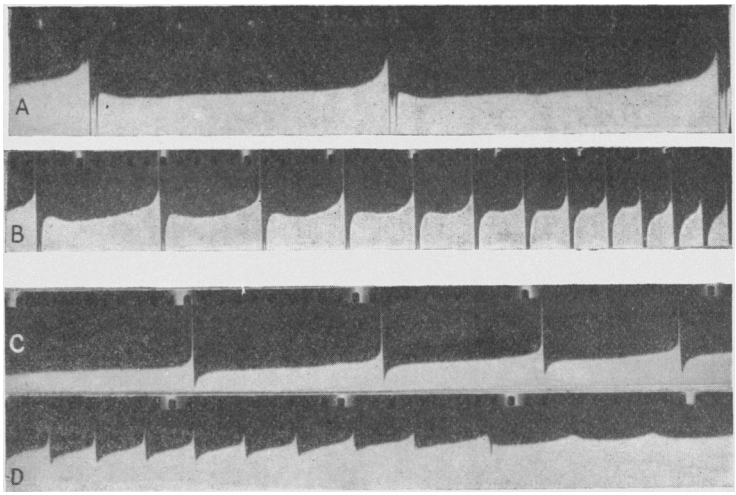

Fig. 6. Form of potential change when the discharge starts from one electrode. In A, C and D, 0·6 p.c. Na oxalate was applied to the electrode, in B, 0·6 p.c. Na citrate. An upward movement of the base line shows a fall of potential at the active electrode. There is a slowly developing fall of potential before each conducted wave and in D at the end of the discharge only the slow changes are left. C and D show the beginning and end of one discharge. Direct coupled amplifier.

Typical records made with the solution applied to the electrode are given in Figs. 6 and 7. The main difference from the controls is that there is now a series of slow potential changes, each leading up to one of the rapid diphasic waves. In Fig. 6 A the frequency is so low that the after effects of each wave are not likely to influence the form of the next, and each wave begins with a gradual fall of potential (shown by the rise of the base line) starting at least 0·1 sec. before the culmination of the wave. Fig. 6 C and D show the beginning and ending of a discharge; there is the same slow rise of the base line before each of the rapid deflections, and at the end the rapid deflections disappear leaving three or four slow waves which are evidently a continuation of those occurring throughout the discharge. The same result is shown in Fig. 7. The appearance of the slow waves alone at the end of a discharge is not a very common occurrence, but the slow change before each impulse is almost invariable. It occurs with Na citrate, tartrate or oxalate, and with 0·6 p.c. NaCl solution in muscles which will respond to a local application.

The records show other peculiarities, but the first point to decide is whether these slow changes of potential are due merely to movement of

the fibre or whether they indicate actual changes of potential at its surface. The fibre will certainly move when each impulse travels down it, but the potential begins to fall a long time before the conducted wave leaves the electrode. The fall of potential must therefore represent a slowly developing activity of some kind localized to the region of the active electrode. This may well involve both a contraction and a change of surface potential, but as the initial change is always in the same direction (a fall of potential at the electrode) we may reasonably conclude that it does imply a gradual depolarization of the muscle fibre.

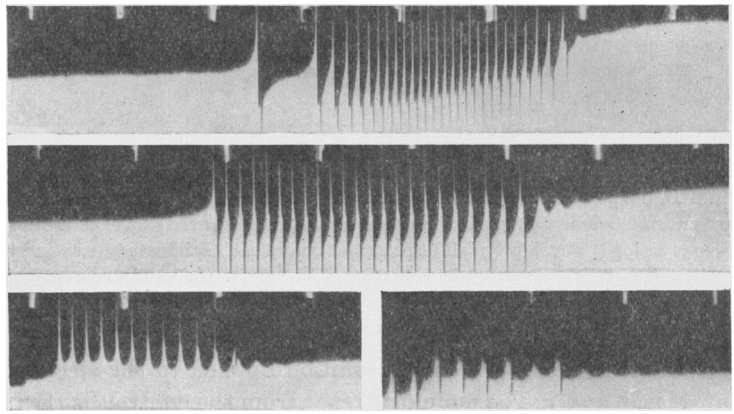

Fig. 7. High frequency discharges starting from one electrode (0·6 p.c. Na oxalate). The initial slow changes and the terminal oscillations are clearly visible. Direct coupled amplifier.

It is difficult to follow the course of the change at the active electrode after the impulse has passed down the fibre. Allowance must be made for the effects of movement, for the action potential at the distal electrode and for the electrical complications due to the presence of inactive tissue and fluid surrounding the active point. The latter probably explains, on the lines elaborated by Craib [1928], the appearance in some records of polyphasic excursions and the difficulty of obtaining pure monophasic potentials. To minimize the short circuiting effects of the inactive tissue we have made several experiments with thin strips cut from the side of the muscle and not much thicker than a frog's sciatic nerve. These are much less active than the whole muscle, owing, probably, to the substances which are constantly diffusing from the injured fibres. Records

from muscle strips and some from the whole muscle are given in Fig. 8 to show the variations in the form of the wave. In many preparations, after the initial slow rise of the base line has culminated in the spike of the action potential, there is a rapid decline to a lower level than before. In terms of potential this means that the active electrode becomes slowly and then rapidly negative to the distal electrode and

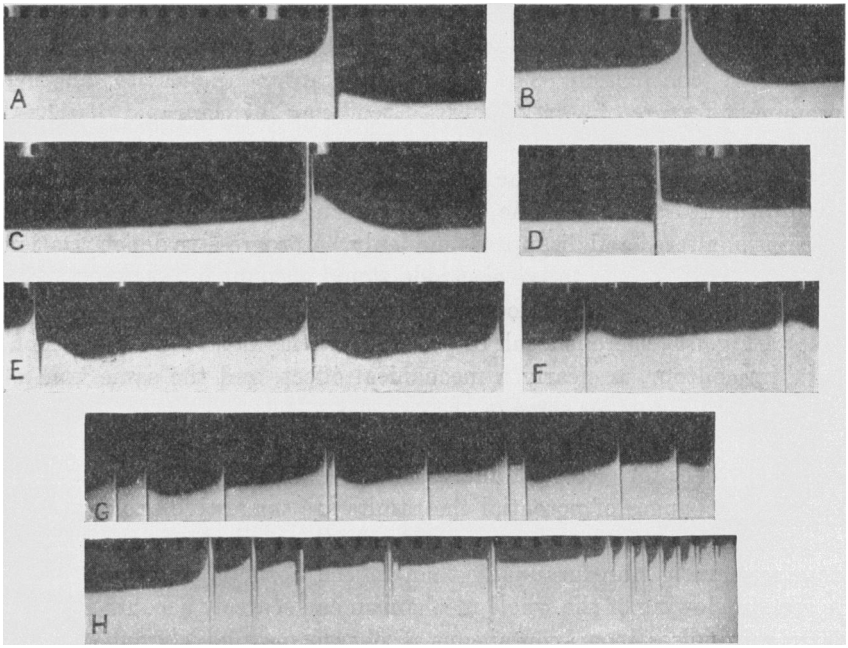

Fig. 8. Various forms of potential change when the discharge starts from the electrode. A, B and C are from a thin strip of the sartorius and are made at a higher speed than usual. D is from the same record, but the wave has started from the distal end of the strip and the gradual development is absent. E, F and G are from other preparations in which the form of the slow change is well marked. In H the waves are polyphasic. Direct coupled amplifier.

then more positive than it was at the start. It returns gradually to its previous value and the cycle is then repeated. In others there is no positive after effect and the negativity subsides slowly. The impulse may be discharged at the peak of the wave or near its beginning. Occasionally a single slow wave is associated with two or three impulses very closely spaced.

It is impossible to say how far the contraction and relaxation of the

fibre influence the exact shape of the wave. In normal muscle the rapid decline of the action potential is followed by a long tail, coinciding in time with the mechanical response [Bishop and Gilson, 1927], and the tail may be larger in the conditions of these experiments. At low frequencies the decline of each slow wave often looks suspiciously like an effect of mechanical relaxation, but at the end of a rapid discharge there is usually nothing to correspond to the relaxation after a tetanus. In Fig. 7 for instance there is no fall after the waves have ceased, though their frequency (15 a sec.) should have been high enough to give a summated contraction. The same uncertainty applies to another prominent feature of some records, a tendency for the rapid discharge of impulses to be accompanied by a fall of mean potential. With this there is a progressive decline in the size of the upward spike, though the downward spike (*i.e.* the potential change at the distal electrode) remains unaltered and disappears suddenly. A progressive depolarization of the fibre under the active electrode would account for these changes, but the fall of potential does not always take place. In the control record, Fig. 5 C, there is a fall of potential at the distal electrode which, from its contour, is clearly a mechanical effect, and the same kind of effect may account for some of the changes mentioned above.

It is clear that a tissue which responds mechanically is not the most suitable object for electrical analysis. But even if we leave out all but the initial changes of potential the results are suggestive enough. They imply that at the point of origin of the rhythmic discharge the activity develops much more gradually than in the normal part of the fibre. A general slowing of the whole mechanism can scarcely account for this, for the impulses in a spontaneous discharge may have frequencies as high as 80 a sec. The maximum frequency at which a normal fibre of the frog's gastrocnemius can respond to indirect excitation is about 150 a sec. (at 15° C.) and that for direct excitation cannot be far different. But a twofold increase in time relations would not be nearly enough to explain the slow development. The most likely explanation is that it is a consequence of the slow rate of adaptation. In the absence of $Ca^{\cdot\cdot}$ the reaction which opposes excitation is slowed down and a gradual building up of the active state becomes possible. The activity which is expressed by the fall of potential is probably the culminating event in a series of reactions, for at very low frequencies the potential may remain steady for the greater part of the interval between successive waves. This agrees with the finding that in a fragment of frog's auricle the potential does not rise or decline appreciably between the beats [Adrian, 1931].

Something which leads to excitation must be taking place in these intervals, but it is only towards the end that changes of potential become evident. For this reason we can scarcely equate the development of the potential change with the building up of the "excitatory state" in the sense used by Eccles and Sherrington for the rhythmic discharge of nerve cells, though no doubt the two are closely related.

It is interesting to find that at the point of origin of the muscle discharge the potential changes develop much less explosively than in the normal fibre, for slow potential changes, rhythmically oscillating or steady, are met with in the central nervous system, and the muscle records can often be paralleled very closely by records of the activity in groups of nerve cells (cf. Adrian, 1932). But this may be no more

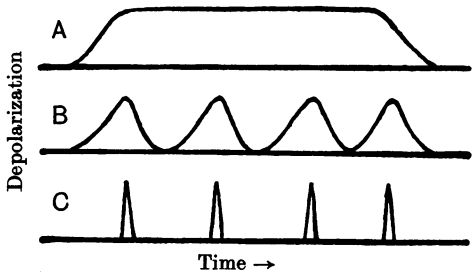

Fig. 9. Three possible types of electrical activity. C is characteristic of normal muscle and nerve fibre. It is suggested that both A and B may occur at the point of origin of rhythmic discharges.

than a casual likeness, and it would be a waste of time to discuss it until the same result has been found with a preparation which does not respond mechanically.

The conclusion must be tentative and it is summarized briefly in Fig. 9. It is suggested that the electrical activity involved in a rhythmic discharge may be of three types, (1) a steady depolarization like that due to permanent or transient injury, (2) an oscillation between the polarized and depolarized condition, and (3) an abrupt depolarization with an almost immediate recovery. In the normal muscle or nerve fibre only the third kind of activity is possible (apart from injury). A rhythmic discharge may be evoked by injury, but the adaptation to the stimulus makes it rapidly ineffective. But with a slower rate of adaptation the active state may rise less abruptly, it may need a smaller stimulus to evoke it, or even no stimulus at all, and a steady stimulus

(*e.g.* a steady depolarization at some point) will cause a persistent oscillation between rest and activity. By local treatment of a muscle with solutions which remove calcium we can produce a slowly adapting region of this kind, and it seems quite probable that similar regions may exist in nerve cells, dendrites and sensory endings.

Summary.

1. Records have been made of the electrical activity of the frog's sartorius muscle treated with NaCl and other salt solutions which lead to spontaneous activity. The action potentials in the individual muscle fibres appear in rhythmic discharges like those from sensory nerve endings and from nerve cells.

2. Stretching the muscle (in NaCl solution) may excite some of the fibres, but in comparison with a sensory nerve ending the muscle fibre is a much less flexible receptor.

3. Stimulation by pressure gives a local depolarization and a discharge of impulses. At the height of the discharge the different muscle fibres may begin to respond synchronously. The synchronous discharge is compared with that from injured nerve fibres and from groups of nerve cells.

4. Spontaneous discharges may be produced by local application of Na citrate, tartrate or oxalate. When solutions of these are placed on one of the electrodes the potential changes can be studied at or near the point of origin of the discharge. They differ considerably from the potential changes in other parts of the fibre, beginning always with a very slow fall of potential which leads up to the rapid conducted wave. At the end of a discharge the conducted waves may fail, leaving only the slow, local oscillations.

It is concluded that a gradual development of the active state is made possible by a slowing of the rate of adaptation in the muscle fibre. The decline of the active state cannot be followed with certainty owing to the movement of the fibres.

The expenses of this research were defrayed by a grant from the Foulerton Committee of the Royal Society.

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