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DEPOLARIZATION OF SENSORY TERMINALS AND THE INITIATION OF IMPULSES IN THE MUSCLE SPINDLE

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It has been shown by several authors (Adrian & Gelfan, 1933; Fessard, 1936; Arvanitaki, 1938; Hodgkin, 1948) that the rhythmic response of a muscle or nerve fibre to an electrical or chemical stimulus is initiated by a local preliminary depolarization which re-develops after each discharge and which varies with the strength of the stimulus. It has been suggested that similar local potential changes intervene between the various forms of sensory stimuli and the initiation of afferent impulses (Pantin (1937, p. 418); Granit's 'generator potential' (1947); Stevens & Davis's 'transducer effect' (1938)). The existence of local potential changes in sense organs, e.g. the electro-retinogram, or the cochlear microphonic effect, has been known for many years, but their exact significance and relation to the discharge of impulses has not been established with certainty. Recently, important evidence was obtained by Hartline & Graham (1932), by Granit (1947) and by Bernhard (1942), who showed that visual stimulation of the eye gives rise to electrotonic potentials in the optic nerve (see also Parry, 1947). In the present paper, further evidence is presented using the muscle spindle of the frog. It will be shown that stretching of the muscle produces a depolarization of the sensory nerve endings which spreads electrotonically along the axon and varies directly with the rate and amplitude of the mechanical stimulus. By a suitable dose of a local anaesthetic the sensory nerve impulses can be abolished and the spindle potential obtained separately. The local spindle potential appears to be an essential link between input and output of the sense organ, and the mechanism whereby a mechanical deformation is converted into this electrical membrane change will be discussed.

METHOD

Preparation and method of recording have been described in preceding papers (Katz, 1949*a*; 1950*b*). The electrode arrangement is shown in Fig. 1. To apply a synchronized stretch to the muscle, two procedures were used. In some experiments where only qualitative information was required the preparation was stretched by stimulating another frog muscle which had been placed in series with the preparation. Usually, however, one tendon was connected via a lever to a magnetic relay. The

velocity of stretching was adjusted by varying the energizing current or a viscous resistance which opposed the motion of the lever. The mechanical excursion could be registered together with the electric response of the sensory axon on a double-beam oscilloscope. The movement of the lever was recorded without noticeable delay by using a photocell with cathode follower output.

Several checks were made to discriminate against electrical artifacts which might accompany stretching of the muscle. Such artifacts could arise from resistance changes in the presence of grid current, but tests with a blocking condenser at the input (Katz, 1950*b*) showed that this effect was quite negligible.

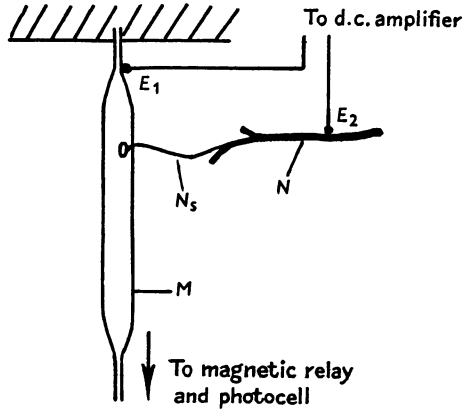

Fig. 1. Electrode arrangement. *M*. M. extensor longus dig. IV.; N_s, isolated sensory axon; *N*, peroneal nerve.

A more serious possibility of error arose from the fact that a portion of the muscle was included between the recording electrodes (Fig. 1), and any potential change occurring in the muscle would vitiate the experiment. Artifacts of this kind were checked by short-circuiting the sensory axon (letting it lie along the muscle) or by crushing it at the point of entry into the muscle (see, for example, Figs. 7 (3); 9 (7)). In this way, electric potential differences in the sensory nerve were eliminated, and artifacts due to the muscle were recorded alone. In many preparations, the potential changes were abolished by this procedure, and this showed that the electric response to stretching originated wholly in the spindle. In some instances, however, small residual potential changes in the muscle were observed, and it was then safest to discard the experiment altogether. Artifacts of this kind appeared to be due to local injury or to tissue debris which had been left on the muscle. The best way of avoiding this difficulty was clean and careful dissection.

It is worth mentioning that in a few experiments an intact motor axon was isolated instead of a sensory fibre. In these cases, no potential change could be recorded while the muscle was stretched, and this provided a satisfactory additional check.

RESULTS

Qualitative observations

Fig. 2 shows the electric response in the peripheral end of a sensory axon during a transient lengthening of the muscle. The stretching was produced by the contraction of a sartorius muscle to which single shocks of varying strength were applied. Records 2–4 were obtained with increasing shock intensity, 'diphasic' as well as 'monophasic' records being shown. During 'rest' there were occasional discharges of either propagated impulses showing the usual

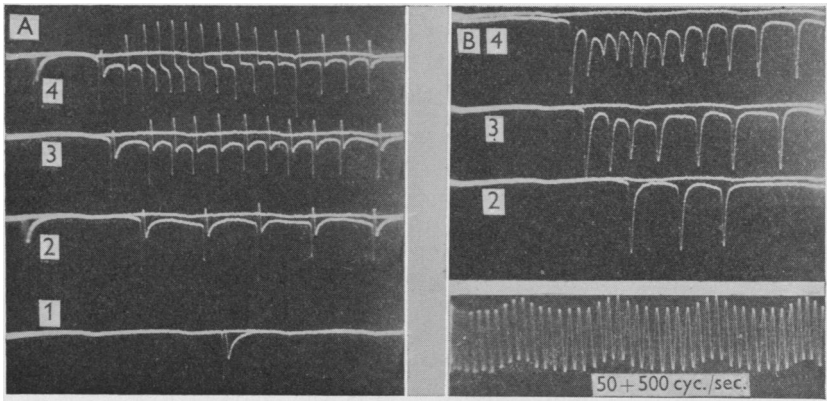

Fig. 2. Potential changes in a sensory axon when the muscle is subjected to a transient stretch. The stretch was applied by a sartorius muscle contracting against the M. extensor dig. IV. All records in this paper read from left to right and show 'spindle negativity' (i.e. a positive potential difference between electrodes E_2 and E_1) as a downward deflexion. A: usual recording from uninjured axon. 1, at 'rest'; 2–4, with increasing intensity of stretching. B: the records have been made monophasic by crushing the central portion of the axon. *Note.* In this preparation, the axon divided into two branches before entering the muscle. Occasional alternations in spike size (e.g. record A, 2) are probably to be attributed to impulses starting along alternate branches of the axon.

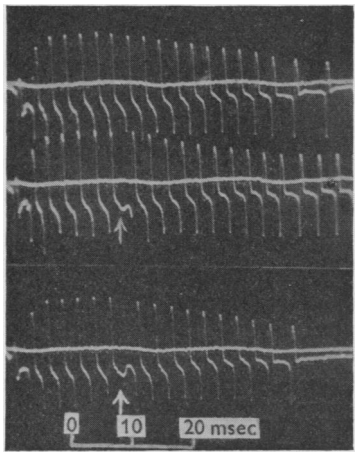

Fig. 3. Occasional 'block' during intense depolarization. Same experiment as in Fig. 2. The places where an impulse has dropped out are marked by arrows.

triphasic pattern or of small abortive impulses (Katz, 1950*b*). During the stretching, a burst of propagated spikes occurred, superimposed on a slow depolarization which was localized at the peripheral lead. The amplitude of this depolarization and the frequency of the spike discharge increased with the intensity of the mechanical stimulus.

It is interesting to note that during the intense depolarization in Fig. 2, record 4, the size of the spike diminished. This cannot be attributed simply to the refractory state left behind by preceding impulses, for the *diphasic* record indicates that, after conduction to the proximal lead a few millimetres away, the spikes have reached their normal amplitude. The reduction in spike height must be the result of the local depolarization—an effect which has previously been described as a cathodic depression (e.g. Hodgkin, 1948; Lorente de Nó, 1947). This depressing action can become so intense that spikes fail to propagate (see Fig. 3), so that during a vigorous stretch impulses may appear to drop out of an otherwise regular series.

A curious fact, invariably observed, was the marked difference in size between the small initial depolarization which precedes the first impulse and the conspicuous potential change leading up to the second and later impulses of a series. In fact, in some experiments (e.g. Fig. 4B), no distinct step could be seen preliminary to the first discharge, while there was always a large depolarization preceding the later impulses. The significance of this observation will be discussed at a later stage (pp. 273–4), but it is necessary to dispose at once of an important objection. It might be argued that the local depolarization in Fig. 2 is not the direct result of stretching, but a cumulative effect of after-potentials left by a train of nerve impulses. It has previously been shown that the spike is followed by a local negative after-potential at the nerve endings (Katz, 1950*b*), but it can now be shown that the depolarization during stretching is a separate phenomenon: (*a*) in many experiments (e.g. Figs. 2, 3 and 4A), there is no doubt that a small initial depolarization occurs *before* the first spike arises; (*b*) the depolarization builds up gradually during the interval between spikes *after* the negative after-potential has declined (Figs. 2, 4–6 and 12); (*c*) spikes and after-potential can be eliminated by a local anaesthetic without affecting the depolarizing effect of stretching (p. 269); (*d*) when an intense depolarization has been produced by stretching (Figs. 4 and 5), the negative after-potential becomes reduced or even disappears. Evidently we are dealing with a direct action of the mechanical stimulus on the nerve membrane, without the intervention of a nerve impulse.

Dynamic and static stretch effects

The time relations between stimulus and response were examined by using a double-beam oscilloscope and recording the change of length of the muscle simultaneously with the electric changes in the sensory nerve.

In Fig. 4B, an experiment is illustrated in which a small test stretch, of 1·3 mm. amplitude, was applied at various speeds to a muscle of 17·5 mm. initial length. There is a discharge of nerve impulses superimposed on a slow

depolarization. The most striking phenomenon, however, is the apparent separation of the electrical changes into two phases: (*a*) a relatively intense dynamic effect which coincides with the period of initial lengthening, and (*b*) a final static effect during which the local depolarization and the rate of discharge are maintained at a lower level (see also Figs. 6, 7 and 9, and Katz, 1949*b*).

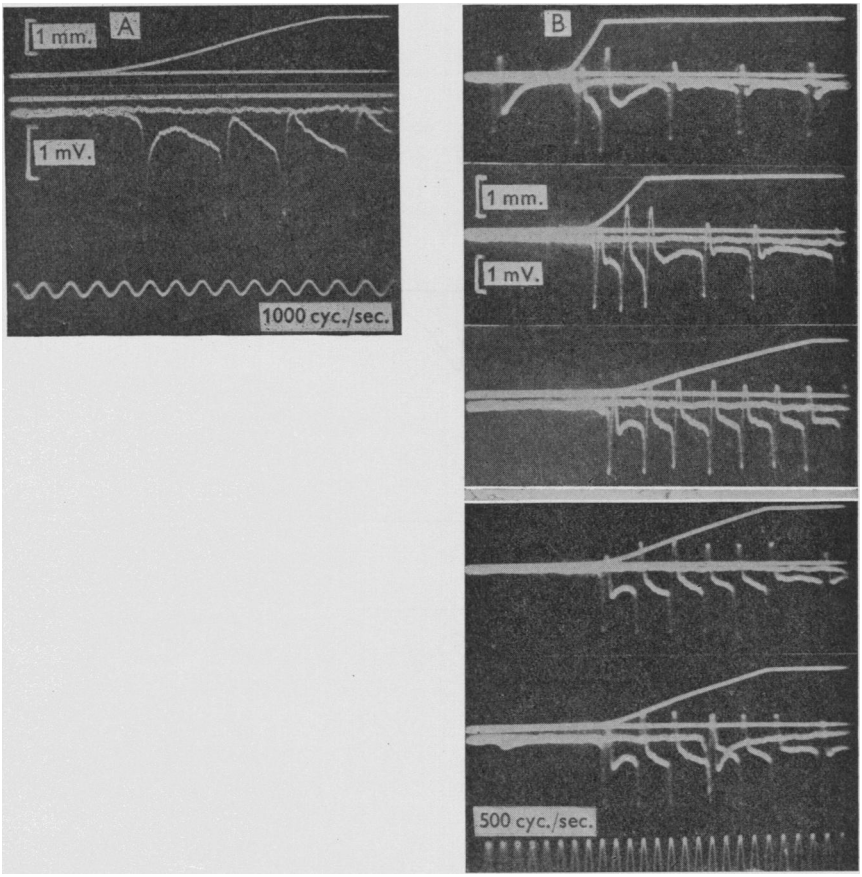

Fig. 4. Double-beam recording of mechanical lengthening (upper trace) and electric potential changes (lower trace). A, fast time base. Monophasic recording. Initial muscle length 16 mm. B, another preparation. Slower time base, Diphasic recording. Initial length 17·5 mm. Occasionally an impulse from the 'resting spindle' is superimposed on the record of the stretch response. Each record consists of two exposures, (i) a 'base-line' (with an occasional impulse appearing on it) and (ii) the stretch response.

It is noteworthy that the discharge of impulses begins as soon as stretching commences; in fact, the first impulse is often discharged when the mechanical record has barely risen from its base-line. It should be remembered, however, that the 'resting' spindle is on the verge of firing and that, therefore, the initiation of the first impulse may require only a minute stimulus.

The intensity of local depolarization can be measured during the interval between impulses. This measurement is somewhat arbitrary because the potential does not remain at a steady level. In practice, the 'flattest' portion

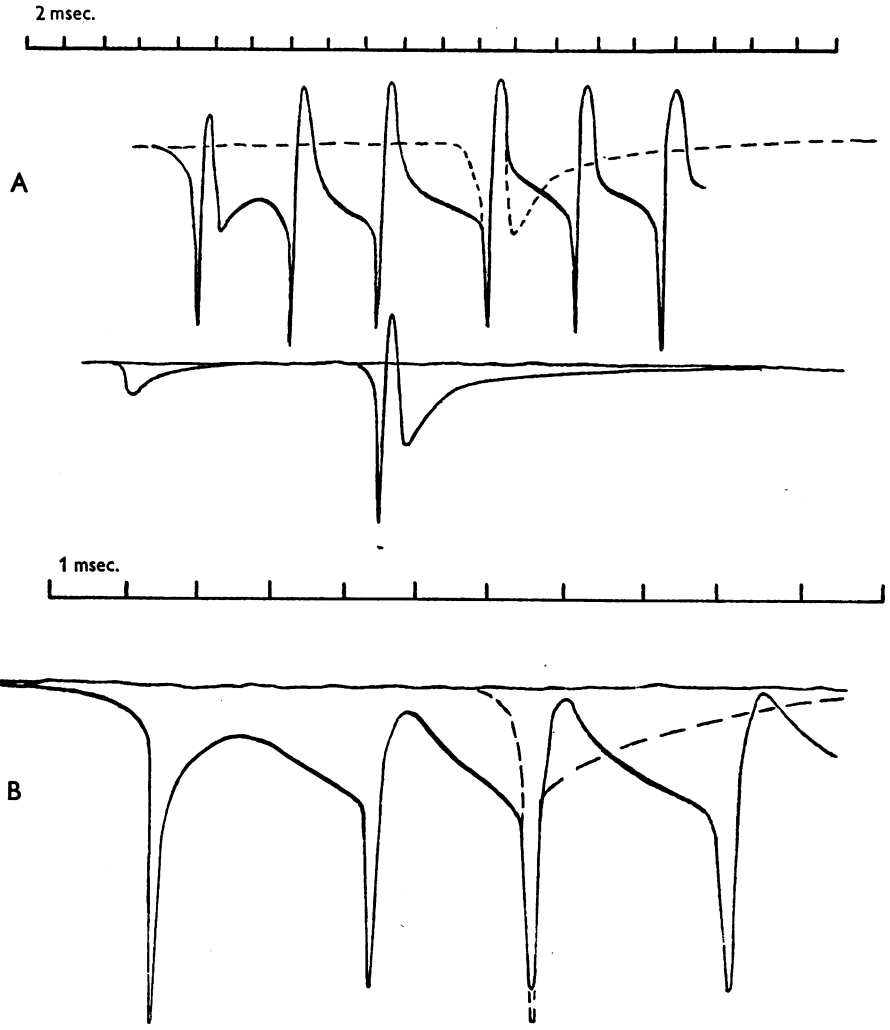

Fig. 5. Stretch response and resting discharge in a sensory axon. Note the reduction of the negative after-potential during stretching. A, upper record: continuous tracing shows the response to stretching. Broken line tracing shows an impulse from the 'resting' spindle. Lower record shows an abortive and a propagated spike from the 'resting' spindle. B, stretch response (continuous tracing) and 'resting' discharge (broken line) in another preparation. Records were monophasic in this instance.

of the curve between successive spikes was chosen for measurement and mean values were determined in each record (*a*) for the 'dynamic' and (*b*) for the 'static' depolarization (see also Katz, 1950*a*). The 'dynamic' effect with various

rates of stretching is plotted in Fig. 8. These results were taken from a single preparation; in seven other experiments similar results were obtained. The

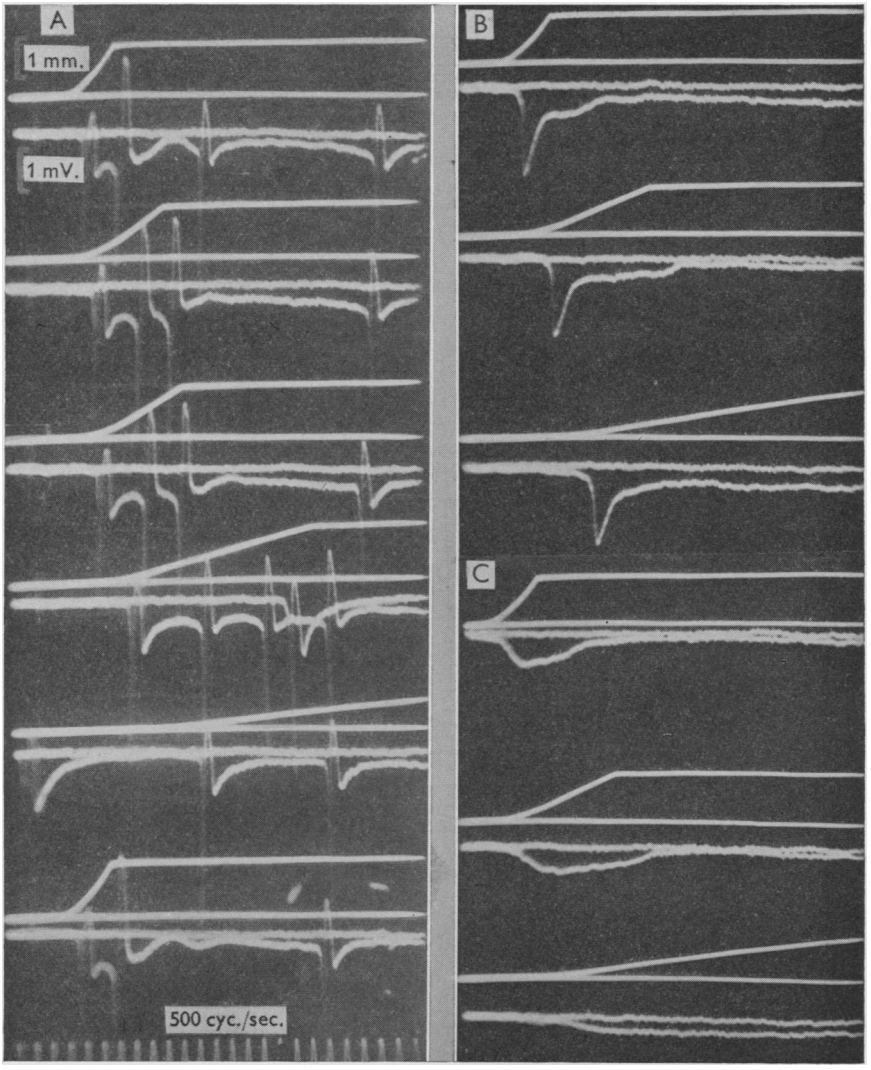

Fig. 6. Effect of procaine on the stretch response. A, normal preparation. Various rates of stretching. B, after application of 0·25% procaine. C, after application of 0·5% procaine. Note the initial non-propagated spike in B.

depolarization increases with the velocity of stretching up to a maximum which, in the case of Fig. 8, was 0·75 mV., or about 20% of the recorded spike height. When the muscle was stretched at a rate greater than 1–1·5% per msec.

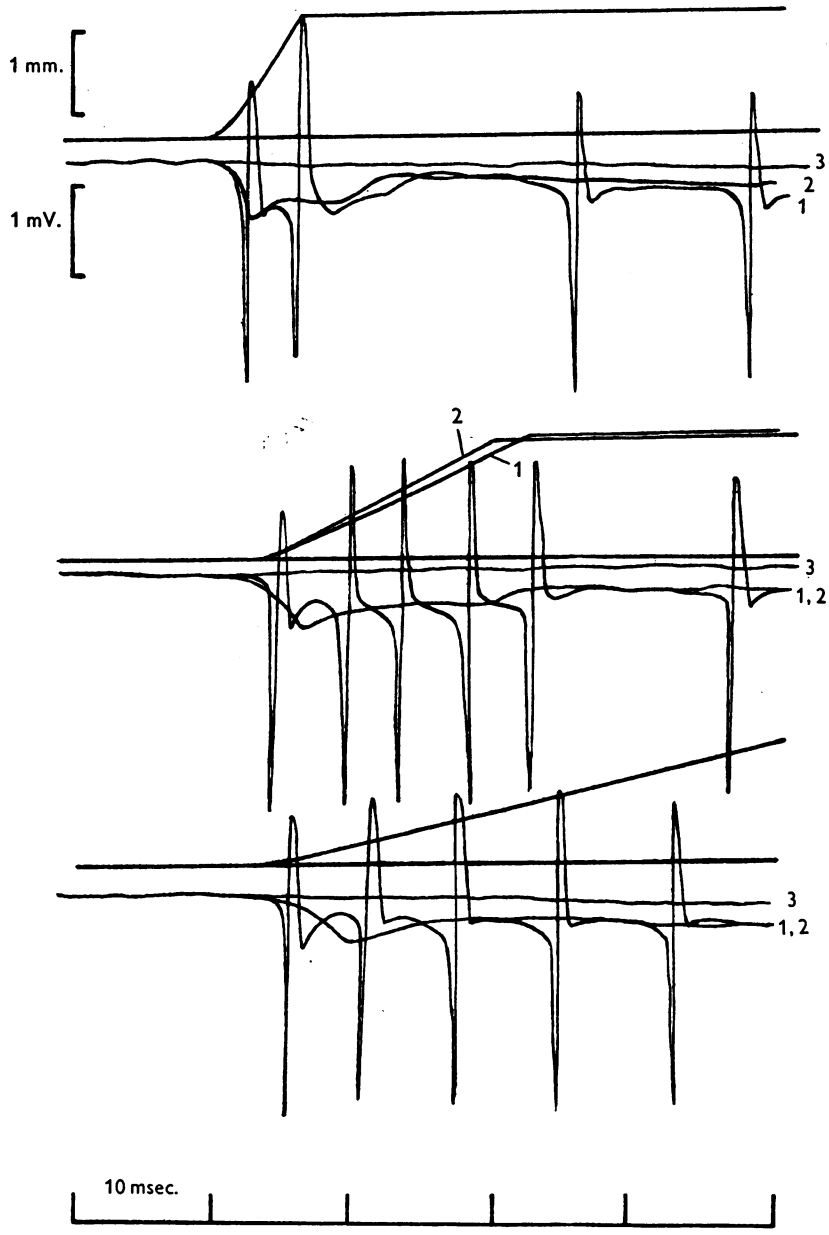

Fig. 7. Superimposed tracings of stretch responses before and during local anaesthesia. Three different rates of stretch shown approximately in the upper drawings. The electrical potential changes were recorded (1) in the normal preparation, showing repetitive spikes and local depolarization; (2) after application of 0·35 % procaine showing only local depolarization (with a trace of an initial local spike); (3) after crushing the axon at its point of entry into the muscle, the record becoming now indistinguishable from a base-line.

no further increase in the local depolarization occurred. A half-maximal effect was produced by stretching at a rate of 0·28% per msec. (mean of eight experiments, at 16–20° C.: 0·23% per msec., S.E. of mean ±0·034% per msec.). The 'static' effect of a 1·3 mm. extension (about 8% of muscle length) amounted to 0·26 mV.: an equivalent 'dynamic effect' was produced by stretching the muscle at a rate of 23 μ. (0·15% of its length) per msec.

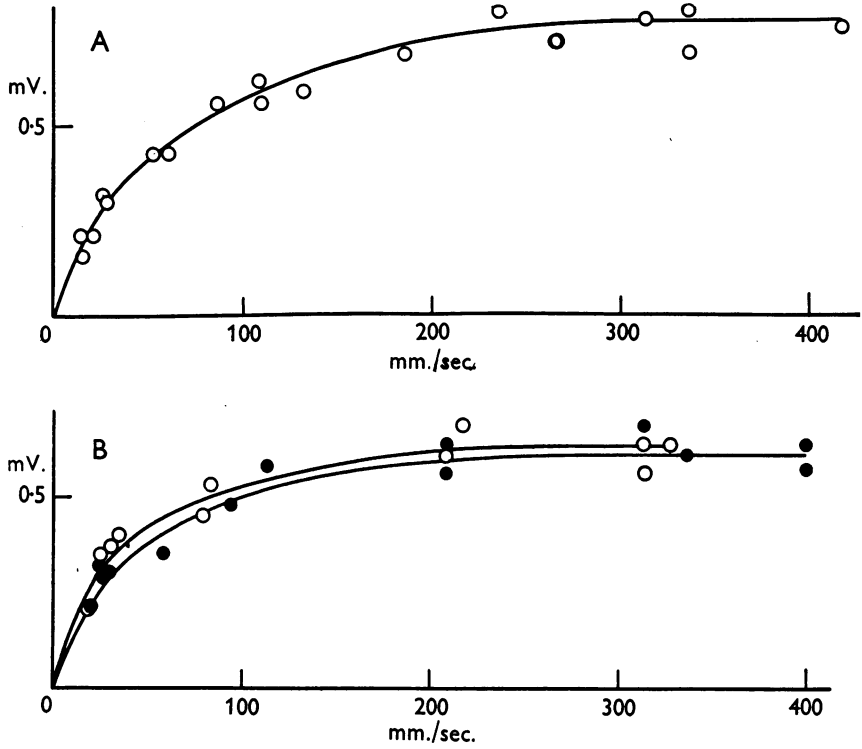

Fig. 8. 'Dynamic' effect of stretching. Initial length of muscle 15·5 mm. Abscissae: rate of stretching of muscle. Ordinates: local depolarization. A, normal preparation. B, anaesthetized preparation. Hollow circles, 0·25% procaine. Full circles, 0·5% procaine.

The effect of local anaesthetics

When the preparation was soaked for several minutes in a buffered solution of procaine/Ringer, the impulse discharge was curtailed or abolished, according to the concentration of the anaesthetic. With 0·1% procaine, a single propagated impulse usually remained: with 0·2% there was evidence of a residual non-propagated spike: with higher concentrations all signs of excitatory activity usually became extinguished while the prolonged depolarization during stretch was either unaffected (with concentrations up to 0·3%) or somewhat reduced (0·4–0·5%). Similar effects were seen when the preparation was treated with a sodium-free solution (0·12 M/l. choline chloride plus the usual

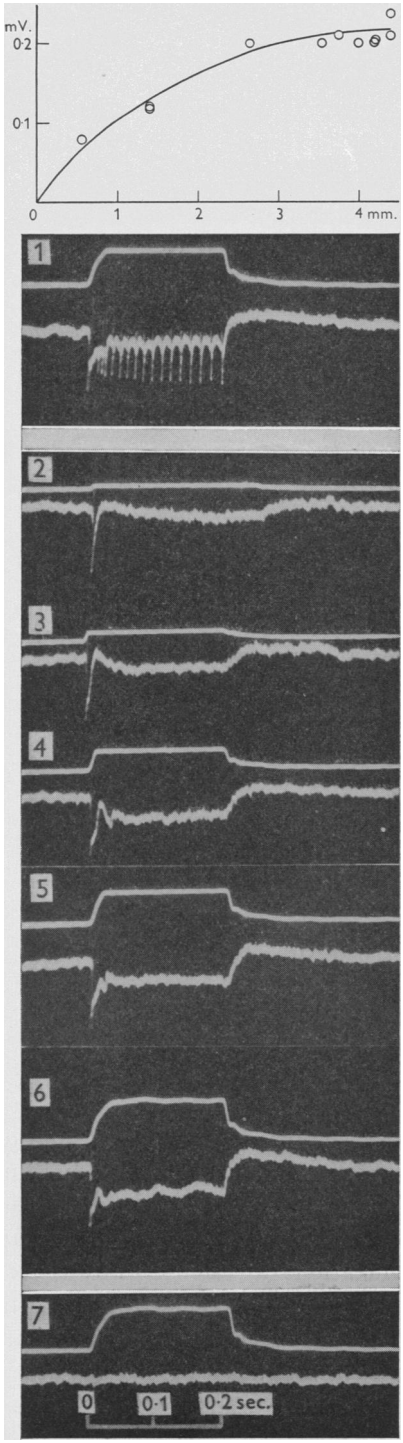

Fig. 9. 'Static' effect of stretching. The diagram shows the relation between extension (initial length 16 mm.) and local depolarization in the anaesthetized preparation (cf. records 2–6). In records 1–7, the upper trace indicates change of length of the muscle, the lower trace shows potential changes in the sensory axon. Record 1, normal. Records 2–6, after 0·1% procaine. (An initial spike remains.) In record 6, the slight mechanical oscillations are accompanied by more pronounced (dynamic) potential changes. Record 7, same conditions as in record 6 except that the axon has been crushed at the point of entry into the muscle.

amounts of KCl and $CaCl_2$). After soaking for 10 min. in this medium, a single impulse was seen instead of a burst of discharges; after a further 30 min. immersion, all traces of spikes, local and propagated had vanished while the prolonged depolarization was still obtained.

In Figs. 6 and 7 the effect of procaine is illustrated, and in Fig. 8A and B, the 'dynamic stretch potentials' are plotted before and after paralysis. The two curves are practically the same. When a large dose of procaine (more than 0·4%) was applied, the local stretch potentials diminished in size, and it was often noticed that the 'static' depolarization diminished more than the 'dynamic'.

A number of tests were made (see also Method) to ascertain that the stretch potentials were, in fact, a depolarization of the sensory axon and could not be attributed to artifacts. In many preparations, when the sensory axon was short-circuited, or crushed at the point of entry into the muscle, all electric changes were abolished. This was a satisfactory test and confirmed the view that the stretch potentials were electrotonically conducted into, and recorded from, the sensory nerve. In some preparations electrical artifacts were seen which could be traced to potential differences in the muscle tissue; they varied in sign and were usually not large enough to mask the genuine depolarization of the nerve, but it was considered best to discard such experiments.

Relation between local depolarization and impulse discharge

The stretch potential is closely related, in its time course and amplitude, to the mechanical stimulus: it is presumably the direct result of the deformation of nerve endings and their receptor membranes. The potential change persists even when the excitatory mechanism of the nerve membrane has been paralysed: this suggests that, whatever the mechanism of the electro-mechanical conversion, it does not involve an 'active response' of the nerve endings, at least not of the kind which is associated with the action potential. The discharge of nerve impulses appears to be a secondary phenomenon, initiated by the stretch potential in a manner analogous to electric excitation in nerve or muscle.

This view is supported by the close relation which exists between the intensity of the local depolarization and the frequency of impulses. The relation is obvious from the records, and was tested statistically in one experiment, illustrated in Fig. 10. The intervals between successive impulses were measured as well as the level of depolarization during the intervals. There was a highly significant correlation with a coefficient of 0·97 (ninety-one pairs of observations). The regression line in Fig. 10 was fitted by the usual statistical method and shown to have a highly significant slope.

There is an interesting analogy between the discharge from a muscle spindle and the repetitive response to constant current in a crustacean nerve fibre (Fessard, 1936; Hodgkin, 1948; see also Fig. 11). In both instances, a con-

tinuous stimulus gives rise to rhythmic impulses whose frequency depends upon the stimulus strength. Furthermore, both types of response are mediated by a local depolarization. There are, however, noticeable differences. In the crustacean axon, the level of the depolarization from which successive spikes

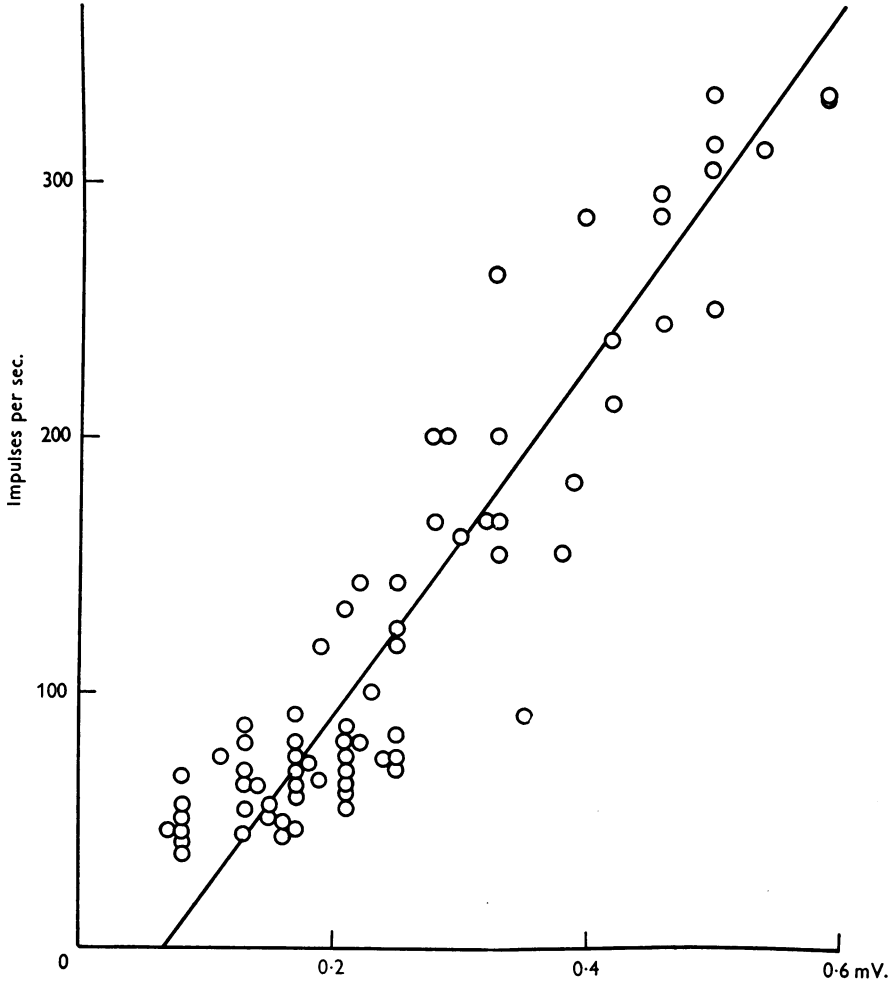

Fig. 10. Relation between local depolarization (abscissae) and frequency of impulses (ordinates). A regression line has been drawn through the results which were obtained from ninety-one pairs of observations. For further explanation see text.

take off remains almost constant: it is practically the same for the first as for the following spikes of a series of impulses, and does not vary much with the frequency of the discharge. In the spindle axon, however, the local depolarization which precedes the first of a series of impulses is always small, and the 'firing level' increases markedly with the frequency of the impulses. An ex-

planation of this difference may be found along the following lines. The recovery from a nerve impulse involves two changes: (i) a restoration of the membrane resistance, and (ii) a gradual return of 'excitability'. The existence of two different processes is indicated by the fact (Hodgkin, 1938) that (1) a stronger current is required during the refractory period to build up a given potential change across the membrane, and (2) a larger potential change is required to evoke a membrane response. How these two factors are coupled is not yet

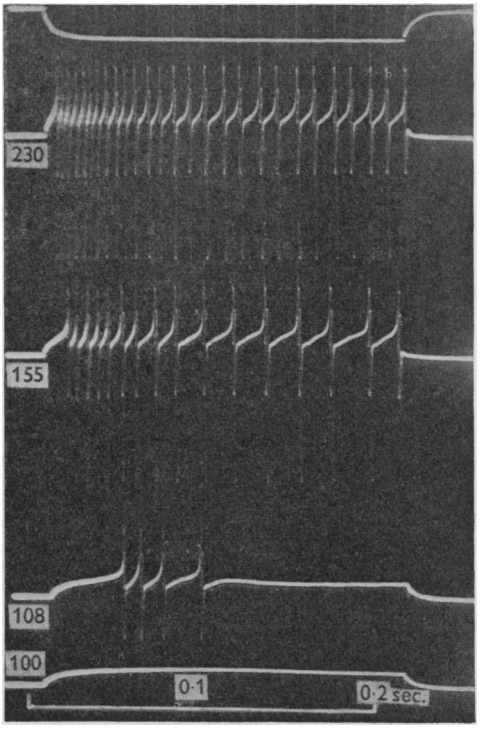

Fig. 11. Response of *Carcinus* nerve fibre to electric currents, recorded at the cathode (cf. Hodgkin, 1948). The numbers indicate relative current strength.

known; they may depend upon different mechanisms, and there is no reason to suppose that they proceed at identical rates or even at the same relative rates in different tissues. If the repair of the membrane leakage were considerably quicker than the return of excitability, a behaviour as seen in the spindle axon would be obtained, for a larger local depolarization would be required before the second, third, etc. impulse of a series could be initiated. If, on the other hand, both recovery processes occurred at approximately the same rate, or the second one were faster, then all the impulses would take off at practically the same level as is found in the *Carcinus* axon.

In this way it seems possible to explain the differences between the electrotonic stretch effects at the spindle and the cathodic potentials in isolated crustacean axons. The depolarization, which precedes the first of a series of sensory impulses, is small, probably because the threshold of the normal 'rested' nerve terminals is low. It should be remembered that the normal 'resting' spindle is on the verge of firing (it does, in fact, discharge impulses at a low irregular rate), and that therefore the initial impulse during stretch may be set up by a very weak stimulus and a very small local depolarization, just enough to trigger the most excitable nerve terminal. The next impulses are initiated at a time when all the nerve endings are relatively refractory, and a much larger depolarization is then required to give rise to a spike. Similarly, a large local stretch potential is obtained when the threshold has been raised by other means, e.g. by the application of an anaesthetic. Thus, the observed relation between local and propagated changes can be explained in simple terms, and there is no reason to suppose that the sensory impulses arise from any agent other than the local stretch potential.

Sensory potential changes accompanying the release of a stretched muscle

It has been shown by Matthews (1931*b*) that during the release of a stretched muscle the discharge of impulses from a spindle drops below its final steady rate immediately after the tension is reduced. It was of interest to investigate the

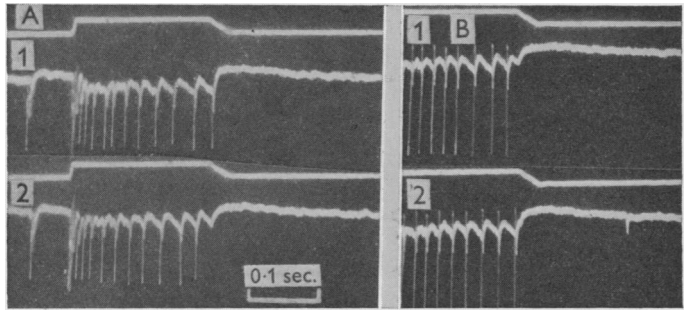

Fig. 12. 'Off-effect' at the end of a period of stretching. Note the appearance of a miniature spike in A 2 and B 1.

local potential changes which accompany this phenomenon. When a normal muscle is released, the depolarization in the sensory axon suddenly falls and the discharge of impulses stops (Fig. 12). This 'cut-off' occurs without noticeable lag; the depolarization falls, in fact, so quickly that a local 'miniature spike' is formed when the mechanical release happens to coincide with the preliminary rise which precedes the firing of an action potential (Fig. 12). There is evidence for a transient *positive* potential change, i.e. a dynamic 'off-effect'. Examples are shown in Fig. 13. The positive spindle potential is usually smaller

and more prolonged than the 'on-effect', but this is to be expected, for the mechanical conditions during release are not the exact converse of those during forcible extension. The speed at which the sense organ returns to its initial shape depends upon its own elastic restoring forces and viscous resistances rather than upon the speed of the applied lever and, therefore, the effects of stretch and release can be compared only qualitatively.

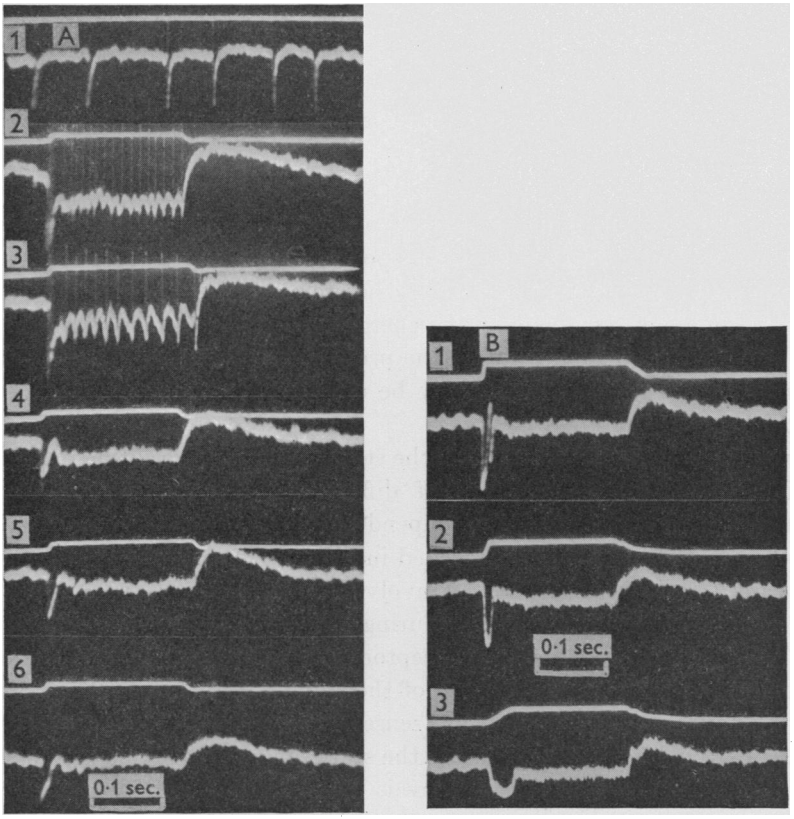

Fig. 13. 'Off-effect' at the end of a period of stretching. A, initial length 15–16 mm. In records 2–6 a 1·8 mm. stretch was applied. Records 1–3, normal preparation, initial length being slightly less in 3 than in 1 and 2. Record 1 shows 'resting' discharge. Records 4 and 5, after application of 0·15% procaine; record 6, after 0·3% procaine. (In records 4 and 5 an initial spike was present, but is not visible in the reproduction.) B, another preparation, treated with 0·3% procaine. Initial length 15 mm. Three stretches of 1·3 mm. amplitude, applied at different rates. (In B1 an initial spike was set up in the region between the recording leads.)

The 'off-effect', in Fig. 13, might be interpreted in various ways: (*a*) it might be an after-potential left behind by the preceding train of impulses; (*b*) there is 'adaptation' during the static period of stretch shown by the gradual fall in the discharge rate: if 'adaptation' were due to some process opposing the

local depolarization, a positive 'off-effect' could appear as a consequence; (c) it might be the counterpart of the dynamic 'on-effect' as suggested above, associated with a relatively slow return of the sensory structure to its initial length.

It is possible to decide between these suggestions by the use of procaine (Fig. 13). In the absence of sensory impulses, the positive potential change is still obtained; hence it cannot be an after-effect of nerve activity. Nor can it be ascribed to 'adaptation', for this would require a slow decline of the depolarization during the static period of stretch, and no such decline is observed. It is, therefore, more likely that the positive potential change is a dynamic 'off-effect', similar to the dynamic depolarization described above (p. 265).

DISCUSSION

The spindle potentials described in this paper can be satisfactorily explained as a local link between stimulus and response, arising in the terminal receptor membrane and giving rise, in turn, to discrete messages in the attached nerve fibre. The problem remains how the energy of the mechanical stretch is converted into a local depolarization. The present experiments provide no direct evidence on this matter, but it may be of interest to consider some simple hypotheses.

If we compare the time courses of the stimulus and the resulting depolarization, it is clear that a certain degree of 'differentiation' has taken place, a large component of the spindle potential depending upon rate rather than magnitude of stretch. This might be accomplished in different ways and two factors will be discussed both of which may be involved.

The 'differentiation' could occur during the mechanical transmission of the stimulus from the tendon to the receptor membrane (see Matthews, 1931*a*). For example, if the sensory portion of the spindle were less viscous than the muscular portion in series with it, the sense organ would suffer greater deformation during the dynamic than during the static phase of stretching. While this possibility cannot be dismissed, there is another way of explaining the differentiation of the time course as well as the origin of the spindle potential.

When the polarized surface membrane of a nerve or muscle fibre is stretched, electrical changes may arise in several ways: first, there may be a transient fall in the membrane potential while the membrane is being stretched and its capacity increased (cf. Ramsey, 1947). This action would be similar to that of a 'condenser microphone'. If we knew the time constant of the membrane, its resting potential and rate of stretching, the resulting depolarization could be calculated as shown in the Appendix. Secondly, the membrane permeability may be altered by stretching, ionic pores, for instance, might be enlarged and consequently the resting potential may fall. Thirdly, chemical changes may take place in the interior of the cell as a result of stretching (cf. Feng, 1932), and

these may subsequently affect the distribution of ions and the potential across the surface membrane. The capacitative effect seems almost inevitable, provided that the membrane is initially in an expanded state. If it were not, stretching would merely straighten out some folds without altering the electrical properties. But the surface area of an expanded membrane would increase and its thickness diminish when it is stretched, and one would therefore expect that the capacity (C) of the membrane becomes greater, and its transverse resistance (R) less, as the fibre is lengthened. The increase of capacity must be accompanied by an immediate fall of the membrane potential; but this would be a transient effect and the membrane would be recharged, at a rate depending upon its time constant RC, to its resting potential at the new length.

Thus, it is conceivable that the dynamic component of the spindle potential is simply the result of a change in membrane capacity. The ensuing static component may be due to a different mechanism, namely a change in membrane permeability. It is not intended to pursue these speculations seriously until more evidence is available to support them, but a method of calculating the 'dynamic component' of this receptor model is shown in the Appendix. As a point of interest, the observed depolarization is too great to be explained without some mechanical amplification of the applied stretch. Unless the deformation of the receptors were larger than that of other parts of the muscle, the present hypothesis would be untenable, but this difficulty would be removed, if the sensory structure of the spindle were more 'compliant' than the rest of the intrafusal bundle.

It may be objected that this hypothesis unnecessarily invokes two different mechanisms for the dynamic and static response. This assumption, however, is not entirely unfounded. There were indications in several experiments that the two components are affected differently by large doses of procaine, the static potential change being reduced more drastically than the dynamic change. Furthermore, the discharge of impulses frequently occurs in two discrete groups, corresponding to the dynamic and static phases of stretch (cf. Matthews, 1931*a*). This is seen in Fig. 7 and further illustrated in Fig. 14. There is a gap between the two groups of impulses, and this gap corresponds to a 'dip' in the stretch potential observed in the procaine-treated preparation (Fig. 7). This would agree with the suggestion of two separate components of the potential change, the 'static' effect developing more slowly and at times rising after the quick 'dynamic' effect has already begun to decline. These observations are not conclusive but they would fall into line with the idea of two separate components of the stretch potential, and would be more difficult to explain on the idea of a simple mechanical differentiation (p. 276).

The mechanism of the stretch receptor suggested here does not invoke any specific properties other than those found in nerve or muscle fibres. The factors which distinguish mechanical receptor endings from ordinary nerve or muscle

membranes may be of a rather simple nature: first, as suggested above, the nerve endings may be subject to greater deformation than the adjacent tissue. Secondly, the surface membranes of muscle fibres, and of nerve axons *in situ*, may not be in the fully extended state without which the theoretical mechanism could not work (cf. Katz 1950*a*). Finally, the threshold at the nerve endings might be lower than elsewhere so that a relatively small amount of depolarization would be sufficient to start an impulse. While such factors would suffice

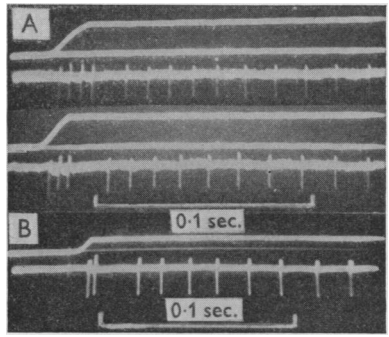

Fig. 14. The 'gap' between the dynamic and static discharge of impulses. A and B, two different preparations. Amplitude of stretching: A, 17%; B, 8% of the initial length.

to explain the differentiation of the spindle receptors, one cannot dismiss the possibility of a specially adapted molecular mechanism, for example some piezo-electric substance, being responsible for the conversion of stretch into a spindle potential. The problem thus remains whether muscle spindles and mechanical receptors generally work on a specific molecular basis, like most photo- and chemo-receptors, depending upon specific chemical reactions, or, as suggested here, like an ordinary electro-mechanical converter system, as condenser microphones or resistance strain gauges.

SUMMARY

1. When a frog muscle is stretched, its sensory nerve endings become depolarized, and a local potential change can be recorded from the sensory axon at a point close to the spindle.

2. This potential change varies with the rate and amplitude of stretching, and gives rise to repetitive impulses in the sensory nerve.

3. By applying a local anaesthetic it is possible to abolish the nerve impulses without affecting the local electric reactions to stretch. There is evidence for two distinct components of the potential change associated with the dynamic process of stretching and with static extension respectively.

4. When a stretched muscle is released, a transient potential change in the opposite direction (i.e. a positive variation at the nerve endings) is observed.

5. The local potential change appears to arise from a direct action of the mechanical stimulus on the sensory nerve endings and to be a link between the mechanical input and the rhythmic output of impulses from the sense organ. The mechanism whereby the mechanical deformation is converted into an electrical membrane change is discussed.

APPENDIX

The immediate effect of stretching on an electrically charged membrane may be represented by a simple model (Figs. 15, 16). A membrane element of capacity C_0 and conductance G_0 ($=1/R_0$) is normally charged to the resting potential E.

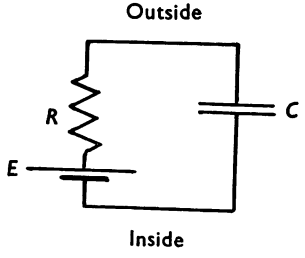

Fig. 15.

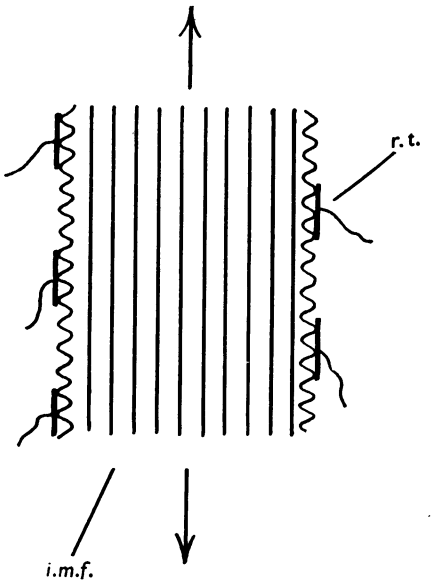

Fig. 16.

Fig. 15. Electrical model of the receptor membrane.

Fig. 16. Schematic diagram of intrafusal muscle fibre (*i.m.f.*) with several receptor terminals (*r.t.*) on its surface. Arrows indicate direction of stretching.

When the tissue is stretched, the volume of the stretched elements remains constant but their surface area increases and thickness diminishes (provided that these elements are fully extended and their surface membrane is in an unfolded state). The terminal membrane of the sensory nerve is assumed to change in this manner when the muscle is stretched.

If it be assumed further that the dielectric constant and specific conductivity of the membrane material remain unaltered, then the total capacity and conductance of the membrane must become greater as its surface area increases and its thickness diminishes. In a cylindrical structure, area and reciprocal

thickness vary as the square root of length, hence the membrane capacity and conductance, being proportional to both variables, would change in direct proportion to the length.

If the muscle is subjected to a constant rate of stretching ('dynamic' phase), the length of the muscle varies according to

$$l = l_0 (1 + kt), \tag{1}$$

where l is varying length, l_0 the initial length of the muscle, t is time and k a velocity constant determining the rate of stretching. The changes in capacity and conductance of the membrane are then described by equations (2) and (3):

$$C = C_0 (1 + kt), \tag{2}$$

$$1/R = G = G_0 (1 + kt), \tag{3}$$

where R and C are the varying values of membrane resistance and capacity. It is seen that the membrane time constant RC remains constant during the stretch ($= R_0 C_0$; cf. Ramsey, 1947). Current will flow from the source E into the capacity tending to keep it charged to the resting potential. The flow of charge dQ/dt is described by equation (4):

$$\frac{dQ}{dt} = p\frac{dC}{dt} + C\frac{dp}{dt} = \frac{E-p}{R}, \tag{4}$$

where p is the varying potential across the membrane. From equation (2)

$$\frac{dC}{dt} = kC_0; \tag{5}$$

hence

$$\frac{dp}{dt} = \frac{E-p}{RC} - \frac{pk}{1+kt}. \tag{6}$$

The solution of equation (6), for which I am indebted to Dr E. J. Harris, is given by

$$p = E\left[1 - \frac{kRC}{1+kt}(1 - e^{-t/RC})\right] \tag{7}$$

for $p = E$, at $t = 0$. The 'dynamic depolarization' is given by $E - p$, and its relative value by $(E-p)/E$:

$$\frac{E-p}{E} = \frac{kRC}{1+kt}(1 - e^{-t/RC}). \tag{8}$$

To find this value we must know the time constant RC and the rate of stretching k. When k is made very small compared with $1/RC$, the depolarization, i.e. $(E-p)/E$, develops exponentially with time constant RC to a value given approximately by kRC, and with continued stretching it slowly declines. Tentatively, one may, therefore, derive an approximate value of RC from the initial development of the depolarization with low rates of stretch (p. 267, Fig. 6C), the result being of the order of 3 msec.

With a rate of stretching of 20 mm. per sec. and an initial length of 16 mm., k is 1·25 sec.$^{-1}$. The maximum depolarization in this case should be only 0·4% of the resting potential. Experimentally, a depolarization was observed which amounted to about 10% of the recorded spike, and the value at the terminal membrane must have been even greater on account of the inevitable attenuation in the terminal axon branches.

It is clear that with a total extension of 10% of the muscle length the membrane capacity, according to equation (2), could not increase more than 10% and, therefore, the depolarization could not exceed this value, no matter at what rate the muscle was being extended.

For very fast 'instantaneous' stretches at which k becomes very large, and t very small compared with RC, equation (8) reduces to

$$\frac{E-p}{E}=\frac{kt}{1+kt};$$

hence a 10% stretch (i.e. $kt=0{\cdot}1$) could reduce the resting potential of the membrane, at the most, by 9%.

In the experiments, however, depolarizations of up to 30–50% of the spike potential were found. Although there are uncertainties in comparing the amplitudes of local, and propagated, potential changes (see Katz, 1950*b*, Method), the observed stretch effect must involve a large reduction of the resting potential at the sensory terminals. The fact that the depolarization reaches a maximum level with rates of 0·2 m. per sec. indicates that at this and higher rates of stretching the local depolarization may be complete. All these observations suggest that the electrical effect of stretching is much greater than that calculated on the simple condenser hypothesis. This hypothesis, therefore, must either be discarded or coupled with a further assumption, namely that the mechanical deformation of the nerve endings is greater than that of the adjoining muscle tissue (see p. 277).

My thanks are due to Prof. A. V. Hill for the facilities provided in his laboratory and to Mr J. L. Parkinson for his invaluable assistance. I am also indebted to Dr E. J. Harris and Mr D. A. Scholl for frequent discussion and advice.

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