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THE LOCAL ELECTRIC CHANGES ASSOCIATED WITH REPETITIVE ACTION IN A NON-MEDULLATED AXON

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One of the most striking properties of crustacean nerves is that they readily give rise to repetitive discharges when stimulated with weak constant currents. Fessard (1936) and Arvanitaki (1938) have made extensive studies of the repetitive discharges which can be recorded in multifibre preparations from *Carcinus maenas* and *Cancer pagurus*. The present experiments deal with the behaviour of isolated axons from *Carcinus maenas*. The results obtained are in general agreement with those of Fessard and Arvanitaki, but give more precise information about the local electric changes associated with repetitive action than can be obtained from studies of whole nerve trunks. The repetitive discharges of crustacean axons are of general interest for two reasons. In the first place the characteristics of the discharge are often very similar to those recorded from sensory receptors or motor neurones. Great caution must be exercised in applying conclusions about invertebrate nerve to the excitable cells of vertebrates. But vertebrate receptors and motor neurones resemble crustacean nerve in at least one important respect. According to Cajal (1899) most sense organs or motor neurones contain a short stretch of non-medullated axon, and this may behave in a manner that is more closely simulated by the thinly myelinated axons of crustacea than by the heavily myelinated nerve fibres of vertebrates. The repetitive discharges of crustacean nerve are also important because they raise an interesting physical question. It will be shown that an axon with a spike duration of 1 msec. and a relative refractory period of less than 10 msec. may repeat at frequencies as low as 5/sec. The frequency of such a discharge must be regulated by a process which has slower time relations than the spike or the recovery cycle and the experiments of Arvanitaki (1936) indicate that this process has an electrical sign. In her more recent work Arvanitaki (1939) has shown that the repetitive discharges of decalcified *Sepia* nerve are associated with the oscillations of a local electric process. A similar conclusion may be drawn from the work of Adrian & Gelfan (1933) on decalcified frog's muscle or from that of Brink, Bronk & Larrabee (1946) on the

decalcified nerves of frog and squid. The subthreshold potentials of *Carcinus* axons show little tendency to oscillate provided that weak currents are employed and that the axons are kept in solutions of normal ionic content. But axons repeat without these special conditions and it is with the local electric changes which accompany such repetition that this paper is concerned.

METHOD

The apparatus employed did not differ materially from that described in former papers (Hodgkin, 1938; Hodgkin & Rushton, 1946; Hodgkin, 1947*a*). A single fibre was mounted on three silver chloride electrodes which terminated in fine agar wicks. Current was applied to the central electrode and to one of the adjacent electrodes through a resistance of 10–300 MΩ. Electrical changes were recorded from the central electrode and the remaining electrode with a d.c. amplifier of high input impedance. The central electrode was earthed and the usual precautions to avoid leaks or artefacts were employed. Electrical changes recorded in this way may be taken as being roughly proportional to those at the point where impulses arise. The absolute magnitude of the membrane potentials must have been reduced to about one-half by the short-circuiting effect of the external fluid (Hodgkin, 1947*a*; Hodgkin & Rushton, 1946) but no distortion of time course was introduced by this cause. The recorded changes were slightly distorted by the potential drop resulting from the flow of applied current in the common stimulating and recording electrode. With the type of electrode employed the magnitude of this effect normally amounted to about 3 % of the subthreshold potentials and to less than 1 % of the spike. It could therefore be ignored with safety. Another source of error arose from the finite width of the central electrode. The potential difference across the nerve membrane was recorded from the extrapolar edge of the central electrode whereas impulses probably arose at the interpolar edge. The difference between the membrane potentials at the two sides of the central electrode probably amounted to about 6 % since the electrode width was of the order of 200 μ. and the appropriate space constant for these axons was about 2·5 mm.

The stimulating current consisted either of an electronically generated rectangular pulse or of a constant current applied by means of a morse key. Determinations of the refractory period and recovery curves were made with an electronic circuit which generated two short pulses of variable spacing and amplitude.

Axons were normally kept in sea water before being raised into paraffin oil. A few preliminary experiments were made with *Carcinus* Ringer (Hodgkin, 1947*b*) but did not reveal any obvious difference in the pattern of repetitive behaviour.

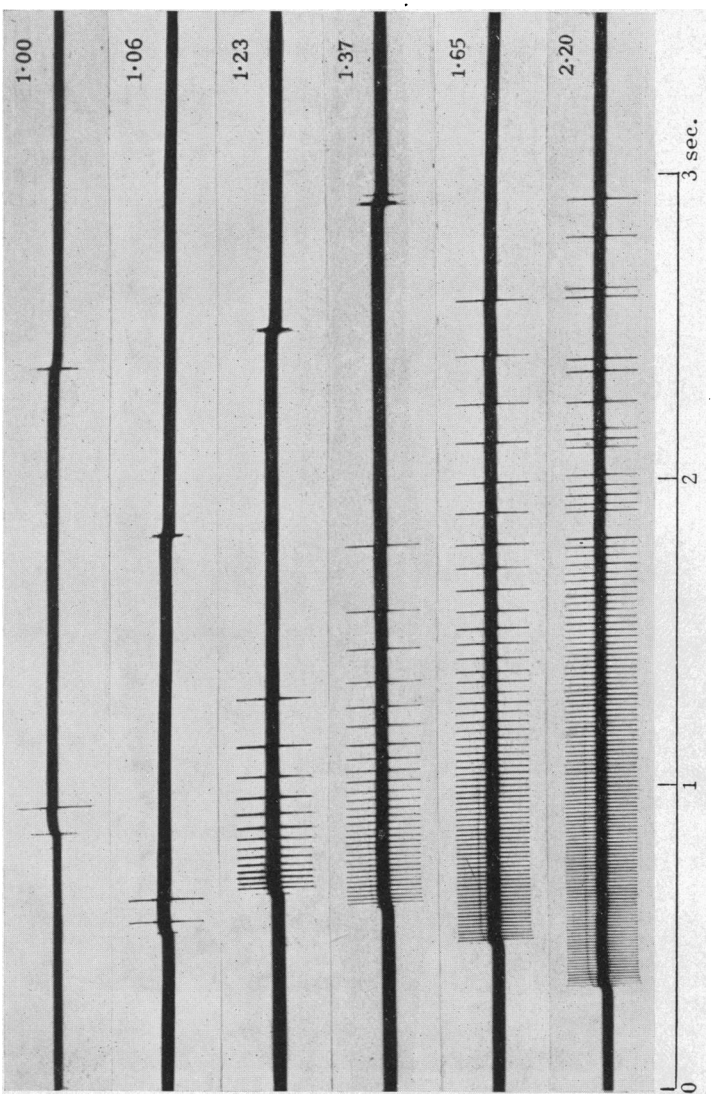
The experiments were made at temperatures between 14 and 16° C.

RESULTS

The characteristics of the response to a constant current varied considerably in different axons (cf. Fessard, 1936; Arvanitaki, 1938). The preparations encountered could be divided into three main groups:

(1) Axons in which the recovery cycle showed no significant supernormal phase and which were capable of repetition over a wide range of frequencies. In such axons the frequency varied smoothly over a range of about 5–150 impulses per sec.

(2) Axons with a pronounced supernormal phase. This class usually gave a train of impulses of frequency 75–150/sec. which was relatively insensitive to changes in the strength of the applied current.



Electrical changes at stimulating electrode produced by sudden application of constant currents. The numbers give the current strength relative to the rheobase. Transient artefacts are visible at make and break.

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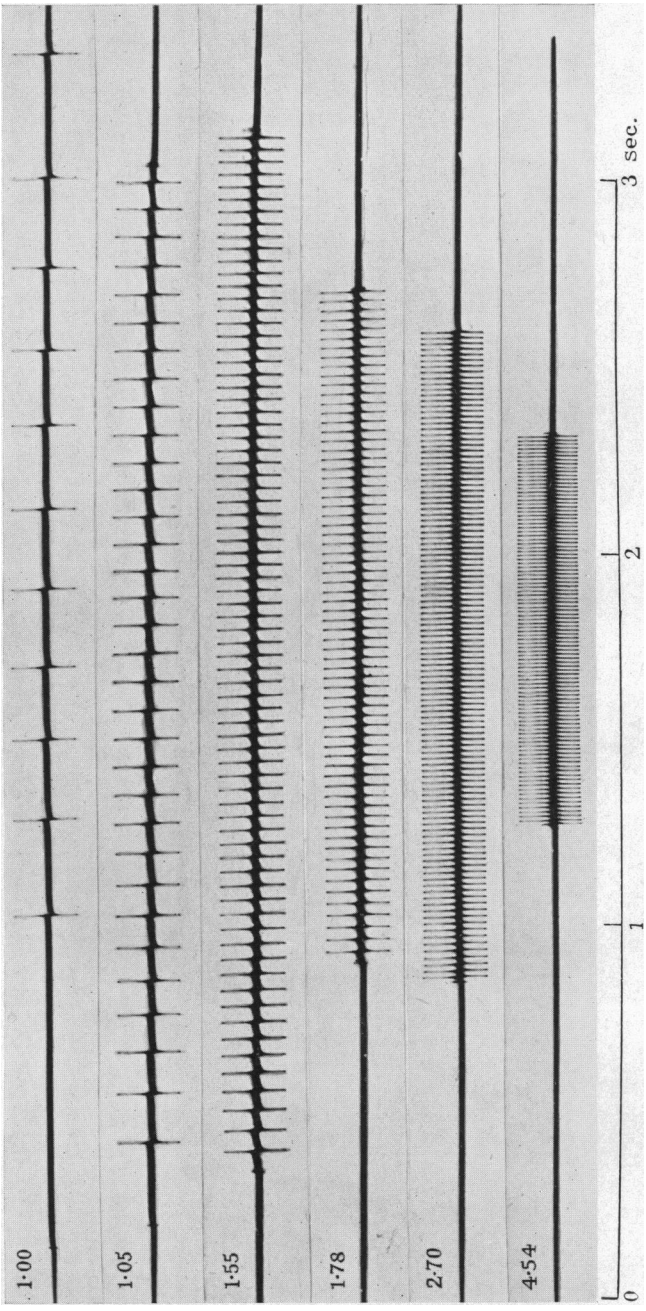


Electrical changes at stimulating electrode produced by sudden application of constant currents with strengths shown relative to rheobase. The absolute magnitude of the rheobase was about $3{\cdot}5 \times 10^{-9}$ amp. The beginning and end of the applied current is marked by a slight artefact.

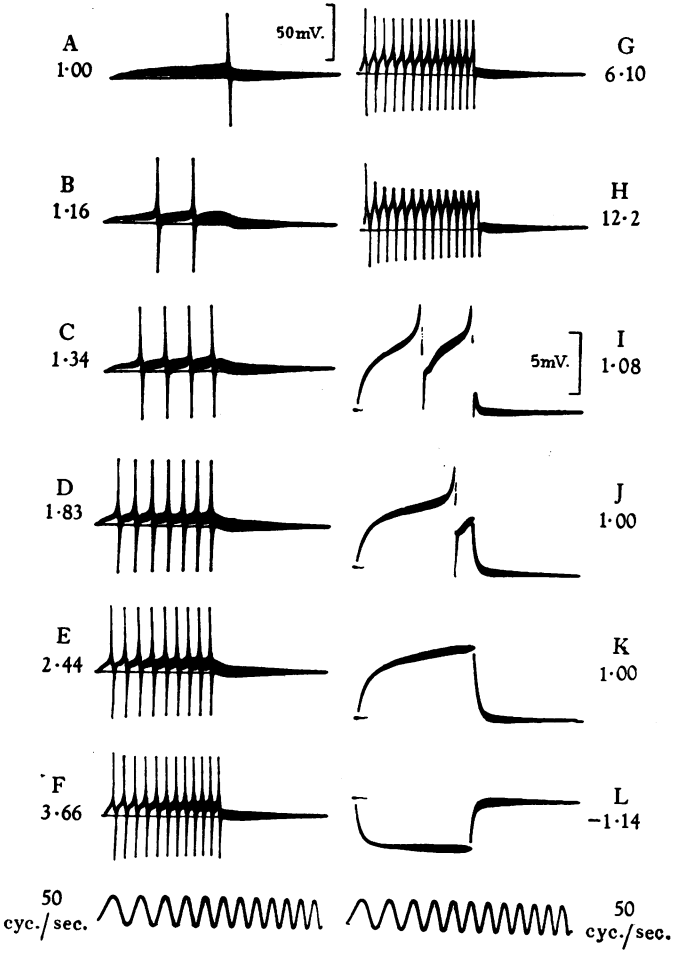
(3) Axons with high threshold and low safety factor which either failed to repeat or succeeded only if the current strength was much greater than rheobase. The response time of these axons never reached such large values as that of axons in the first two classes.

This classification was based on the present experiments, but is similar to that adopted by Arvanitaki (1938). Arvanitaki recognized a class of axons which repeat only with difficulty and which give an immediate response, while she divided the axons which repeat into two groups that are not unlike those defined in the present paper. The classification is in any case of an arbitrary nature since there are transitional stages between the various groups and a single axon may show different types of behaviour during the course of one experiment. Thus an axon which has been left in oil or sea water for many hours usually passes through a stage in which it fails to repeat before becoming inexcitable.

Axons in Class I

The first group of axons is considered to be of the greatest interest because it affords an opportunity of studying a type of behaviour which is similar to that of motor neurones and sensory receptors. About 50 % of the axons studied were in this class. The general resemblance between the response of a crab fibre and that of a sensory receptor is illustrated by Pl. 1 which has several properties in common with records obtained by Adrian (1932), Matthews (1931) and Hartline & Graham (1932). Thus the response to a constant stimulus started at a frequency which might be as high as 80/sec. and declined slowly to a lower limit of about 6/sec. With a strong stimulus the response tended to become irregular and a stable low frequency discharge did not occur; similar behaviour has been observed by Matthews (1931) in the frog's muscle spindle. Sensory receptors such as those in the carotid sinus (Bronk & Stella, 1932), the endings of the vagus in the lung (Adrian, 1932) or certain types of muscle spindle (Matthews, 1931, 1933) adapt very slowly and often discharge continuously throughout the entire period of stimulation. Barron & Matthews (1938) found that motor neurones responded in a similar way to a constant current and showed that the frequency of the response varied smoothly with the applied current over a range of 5/sec. to 70/sec. This type of behaviour and that of the slowly adapting sense organs finds a parallel in certain *Carcinus* axons which give steady repetitive discharges for long periods. An example is provided by Pl. 2. Not only did this axon give little sign of accommodation or fatigue, but the frequency of the discharge showed an initial increase with time. The increase in frequency must have been due to some progressive rise in excitability or 'warming-up' process, but no attempt was made to discover the nature of the progressive change which was observed on infrequent occasions. The repetitive train seen in the uppermost record of Pl. 2 ended with the last impulse shown. In the remaining records the repetitive response was terminated only by the

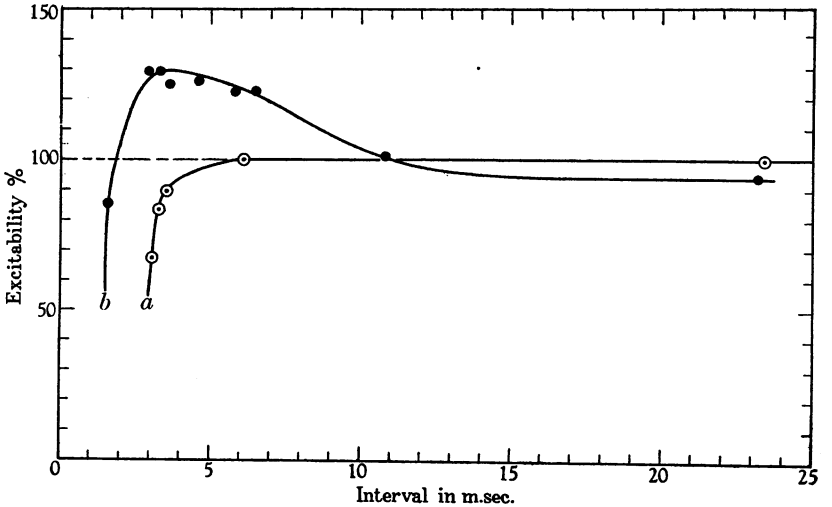
removal of the stimulating current. Records taken earlier from this axon indicated that the repetitive discharge produced by a 1·4 rheobasic current was maintained at a frequency of about 16/sec. until the end of a stimulus lasting 17/sec. The stimulus was not continued for a longer period because it was feared that prolonged activity might cause an irreversible change in the characteristics of the axon.



Text-fig. 1. Electrical changes at stimulating electrodes produced by rectangular currents with strengths shown relative to rheobase. The voltage calibration in A applies to records A–H and that in I to records I–L. The rheobase in I–L was 22 % higher than that in A–H. The absolute magnitude of the current in A was about 8×10^{-9} amp.

Details of the response to a rectangular current are given in Text-fig. 1 which illustrates a number of important points. In the first place it can be seen that the local subthreshold potentials were small compared to the

propagated action potential. Thus the depolarization produced by a just subthreshold current (record K) amounted to about 6·2 mV. whereas the spike amplitude was 57 mV. Another point of interest is that the response time was extremely long when the strength of current was weak. The delay in A amounted to 98 msec. and it is probable that longer delays would have been observed if the pulse could have been increased in duration. Further, the interval between the beginning of the current and the first spike in records B–F was of the same order as the interval between impulses in the repetitive train. This observation suggests that response time rather than refractory period is the primary factor in determining the frequency of repetition when the current



Text-fig. 2. Curve *a*. Recovery curve of an axon in class 1. Curve *b*. Recovery curve of an axon in class 2. Abscissa. Interval between two shocks in msec. Ordinate (normal threshold)/(threshold during recovery period).

is weak. Fessard (1936) and Arvanitaki (1938) came to a similar conclusion in their studies of whole nerve trunks from *Carcinus maenas* and other crustacea. The hypothesis receives support from a number of directions. The relative refractory period has been found to occupy less than 10 msec. in an axon which was capable of repetition at 5/sec. An example is afforded by Text-fig. 2*a* which gives the recovery curve of the axon used in obtaining the records in Pl. 2.

The recovery curve was not determined with great precision and it might be argued that recovery from refractoriness was not quite complete at the end of 10 msec. and that it remained incomplete for 200 msec. This argument is not a plausible one and it breaks down completely when the effect of currents appreciably greater than rheobase is considered. If recovery from refractoriness were the sole factor in determining repetition rate the axon of Text-fig. 2*a* and

Pl. 2 should discharge at 240/sec. when the current was 5 % above rheobase. The actual repetition rate was about 13/sec. at this strength. Persistent changes in excitability such as the subnormal period and the second period of supernormality described by Gasser (1937) may have a considerable effect in modifying the rhythm set by the rate of growth of the local response, but they do not appear to be the most important factor in crustacean axons.

In order to explain the low repetition frequencies in terms of response time it would be necessary for this time to be of the same order of magnitude as the repetition interval. A rough comparison between the two intervals was made by examining a large number of photographic records and determining the greatest response time and repetition interval observed in any one experiment (Table 1). Such a procedure must be exceedingly rough because the magnitude

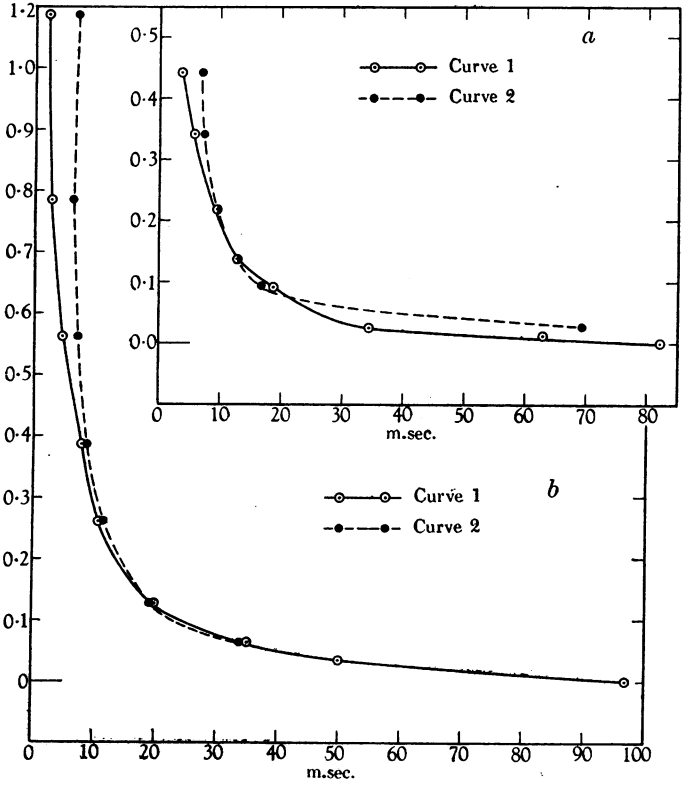
TABLE 1. Longest response times and repetition intervals recorded in different experiments. Results obtained on axons with supernormal phase (class 2) have been omitted. Bracketed figures were obtained from the same axons at different times

Longest response time (msec.)	Longest repetition interval (msec.)
755	789
1980	604
109	584
160	112
82·1	210
70·6	49
98	51
24·6	34·4
4·4	7·62

of the greatest interval observed is largely determined by the number of trials. A nerve fibre appears to pass through a region of unstable equilibrium before it propagates and the length of time for which it can remain in this condition is plainly incapable of precise definition. But Table 1 indicates that the maximum response time is usually of the right order of magnitude to account for the longest repetition interval observed in any particular experiment. There is also an obvious correlation between the two sets of figures and the correlation coefficient between the logarithms of the two quantities was found to be 0·88 which can be shown to be a highly significant result.

A better method of comparing response time with repetition interval is to plot these quantities against the strength of current. The relation between response time and current strength is illustrated by curve 1 of Text-fig. 3*a* and *b*, while curve 2 shows the effect of current on the initial repetition interval. The two intervals were usually not identical and showed considerable deviations near rheobase, but both were affected by current in a comparable manner and the general similarity between the two curves suggests that both were determined by a common process. The refractory period became important when the current strength was large and the repetition frequency was high. Strong

currents reduced the response time towards zero but the repetition interval never became less than 6·5 msec. and in one case actually increased when the current was raised sufficiently. An explanation of this phenomenon may be that recovery from refractoriness is hindered by strong cathodal depolarization (cf. Bishop & Erlanger (1926)). The decrease in action potential height which

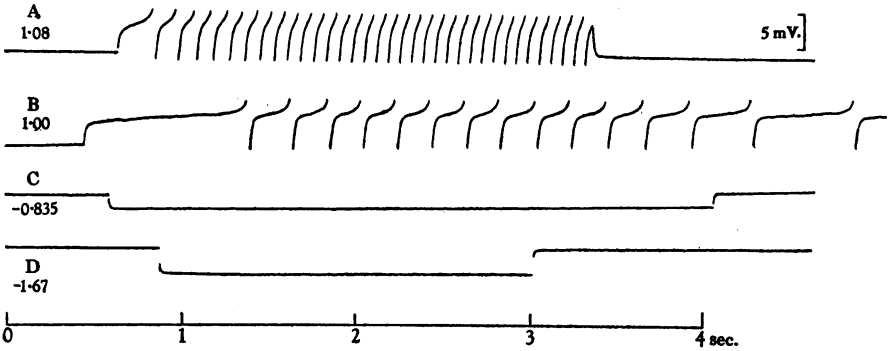


Text-fig. 3*a* and *b*. Effect of current strength on response time and repetition interval in two axons. Curve 1, interval between make of current and appearance of first impulse; curve 2, interval between 1st and 2nd impulses. Abscissa: interval in msec. Ordinate $\log_{10}$ (current/rheobase).

can be seen in Text-fig. 1 is probably another sign of the depressant action of excessive depolarization. The resemblance between the two curves in Text-fig. 3*a* and *b* would have been less if the process of accommodation had been more rapid. Arvanitaki (1938, p. 52) presents experimental data of this kind but shows that the entire family of curves relating current strength to the intervals which precede the 1st, 2nd, 3rd... spikes can be superposed if the current strength is expressed in terms of the individual rheobases of the 1st, 2nd, 3rd... spikes. The excellent fit which she obtaines provides strong

evidence for the hypothesis that the evolution of the first impulse is essentially similar to that of any other impulse in the repetitive train.

The preceding arguments indicate that the large response times observed in *Carcinus* axons are associated with the ability of these axons to give stable low frequency discharges. Hodgkin & Rushton (1946) reported that the long response times of *Carcinus* axons were themselves associated with a prolonged local response. The present work has provided ample confirmation of this conclusion. In every case in which a long response time has been observed there has also been a corresponding electrical sign of subthreshold activity. This prolonged subthreshold activity is superimposed upon the passive depolarization of the nerve membrane which normally approaches a steady state with a time constant of 5–15 msec. The two processes may be distinguished



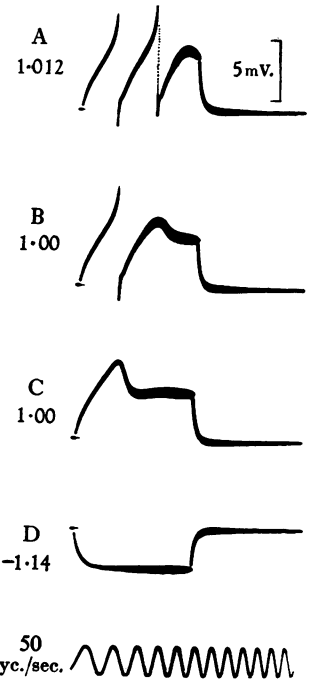
Text-fig. 4. Electrical changes at stimulating electrodes produced by sudden application of constant currents with strengths shown relative to rheobase. The absolute magnitude of the rheobase was approximately 4×10^{-9} amp. All records at same amplification. The height of the action potential was 45 mV. in this experiment.

by comparing the effects of anodic and cathodic currents. Text-fig. 1 record L gives the effect of a weak anodic current while records K and J give the effects of just subthreshold and just threshold currents. The difference between the two curves is most easily explained by postulating a subthreshold process which grows at a rate depending on the applied current until it reaches propagating size.

The rate of growth of the local response may be exceedingly slow if the current strength is only just sufficient to excite. An extreme example is afforded by Text-fig. 4. In this case the local activity developed in a slightly irregular manner but, nevertheless, showed an upward trend during 950 msec. On the other hand, the passive charging process was complete in about 20 msec. as may be seen from records C and D.

The sequence of events in a repetitive discharge may be summarized in the following way. When current is suddenly applied, the membrane charges to

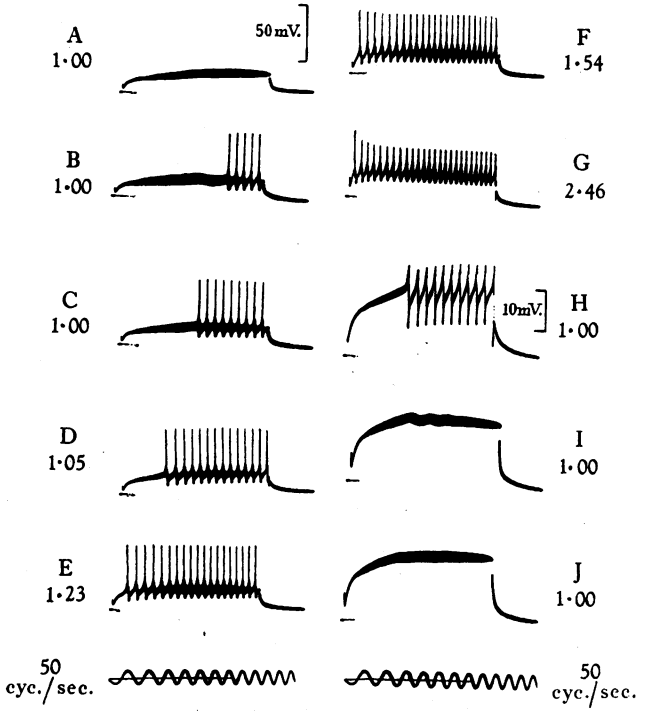
a value determined by the membrane resistance with a time constant of 5–15 msec. Upon this charging process is superimposed the slow growth of the local response. The effect of both processes is to depolarize the axon and a propagated action potential arises when a critical level of depolarization is reached (Hodgkin & Rushton, 1946, fig. 15). The membrane resistance falls to a low value during activity (Cole & Curtis, 1939) and the membrane is discharged. The whole process—passive depolarization and growth of local response—must therefore repeat before a second action potential arises. If this argument is correct there should be a marked resemblance between the potential changes which precede the first impulse and those which precede any other impulse in the repetitive train. The two processes may not be identical because the rate of growth of the local response is exceedingly sensitive to small changes in current strength or in the general level of excitability and a very slight residue of supernormality or refractoriness may modify the rate of growth of the local response to an appreciable extent. Text-figs. 1, 4, 5 and 7 illustrate the general similarity between the initiation of the first impulse and of others in the repetitive train. The similarity is most striking when the axon is made monophasic by crushing at the distal lead. This operation removes the second phase of the action potential which normally obscures the initial part of the recharging process. An illustration is afforded by Text-fig. 5 which was obtained from the same axon as that in Text-fig. 1. Unfortunately the operation of crushing the axon caused some alteration in the characteristics of this axon. The response time at rheobase became shorter and the local response rose to a definite maximum during the rectangular pulse. These changes were probably caused by the spread of depolarization from the crushed point as a result of local circuit action. But the records show plainly that the electrical changes which preceded the first impulse were very similar to those which preceded the second.



Text-fig. 5. Electrical changes at stimulating electrodes produced by rectangular currents with strengths given relative to rheobase. The absolute magnitude of the rheobase was about 8×10^{-9} amp. All records at same amplification.

Axons with pronounced supernormal phase (Class 2)

Text-fig. 6 is an example of the response of an axon with a pronounced supernormal phase. The initial part of the response was not markedly different from that already described, but the first spike was followed by a train of impulses the frequency of which bore little relation to the response time. The frequency of this discharge was relatively insensitive to changes in the applied



Text-fig. 6. Electrical changes at stimulating electrode produced by sudden application of rectangular currents with strengths given relative to rheobase. The voltage calibration in A applies to records A–G and that in H to records H–J. The rheobase in H–J was 2 % higher than that in A–G. The absolute magnitude of the rheobase was about 6×10^{-9} amp.

current. In the experiment illustrated by Pl. 2 the frequency was trebled where the current strength was increased from rheobase to 1·05 rheobase; in the experiment of Text-fig. 6 it rose by only 19 % for an increase from rheobase to 1·23 rheobase. A further point is that it was impossible to evoke a single impulse with a current of long duration. At a constant strength of current the axon gave either a train of impulses of fairly high frequencies or no propagated action potentials at all. Axons of this type were not capable of giving low frequency discharges. When the current was maintained for a long time it evoked a train of impulses which might last for several seconds but which ended

abruptly without giving frequencies lower than about 50/sec. The obvious explanation of this type of behaviour is that each action potential was followed by a supernormal phase which caused another action potential to appear with relatively little delay. Text-fig. 2*b* gives the recovery curve of the axon which has just been considered. It can be seen that the increase in excitability amounted to nearly 30 % and that it was a maximum at about 3·5 msec. after the first stimulus. Supernormality ended at about 11 msec. and the axon then became slightly subnormal. The repetition frequency of this axon varied between 90/sec. at rheobase and 150/sec. for a current of 2·41 rheobase. These figures are unintelligible if the recovery curve is regarded as being the only factor in determining repetition rate. In that case a rheobasic current should give a frequency which would be determined by the time at which the excitability first returned to normal. The curve of Text-fig. 2*b* indicates that this frequency would be 540/sec., which is close to the maximum of which crustacean axons are capable (Hodgkin, 1938). What actually appears to happen is that the local response develops at an increased rate during the period in which the axon is supernormal. This means that the spike arises earlier than it would in the absence of supernormality, but it does not imply that the spike must arise at the crest of the recovery curve, nor need it arise until after the end of the supernormal phase. The timing of the repetitive discharge depends upon the form of the recovery curve and the rate of growth of the local response in a complicated manner and it would be quite impossible to predict the frequency of the repetitive discharge from the recovery curve alone. Record H, Text-fig. 6 leaves little doubt that the development of the local response was much faster after the first spike than it was after the make of the current. This conclusion is supported by other records and by the previous observation (Hodgkin, 1938) that a subthreshold shock of constant strength produced a larger local response in supernormal nerve than it did in normal nerve.

An interesting feature of Text-fig. 6 is the presence in record I of small subthreshold oscillations of frequency 44/sec. The amplitude of these oscillations varied from stimulus to stimulus; extreme limits are shown by records I and J. It is difficult to make any reliable statement about the nature of these oscillations since they have only been observed on a few occasions. But they appear to differ in several respects from the oscillations seen in decalcified nerves or in nerves stimulated with strong currents. In the first place the oscillations seem to occur over a very narrow range of currents and the variation in amplitude suggests that they only occur when the axon just fails to propagate. A further point is that both the amplitude and the frequency of the oscillations are considerably less than those which can occur in decalcified nerve.

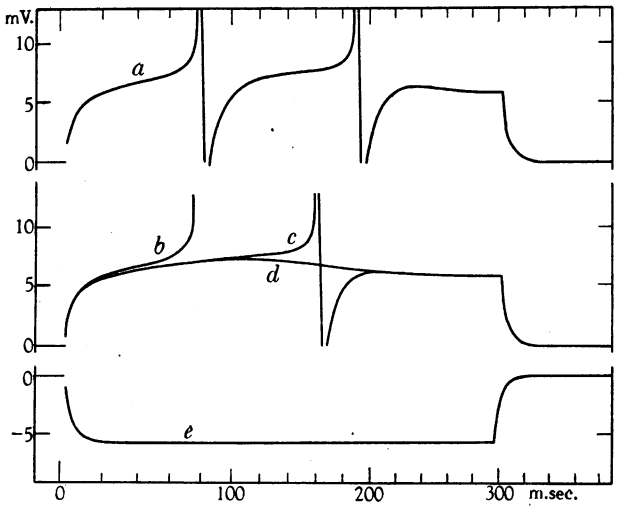
Axons which repeat only with difficulty or not at all (Class 3)

Carcinus axons usually give repetitive discharges if reasonable care has been taken with the dissection. The ability to repeat diminishes if the axons are left in sea water for a long period. Under these circumstances the pattern of the subthreshold potentials alters in a characteristic manner. The response time at rheobase is greatly reduced and the local response rises quickly to a well-defined maximum.

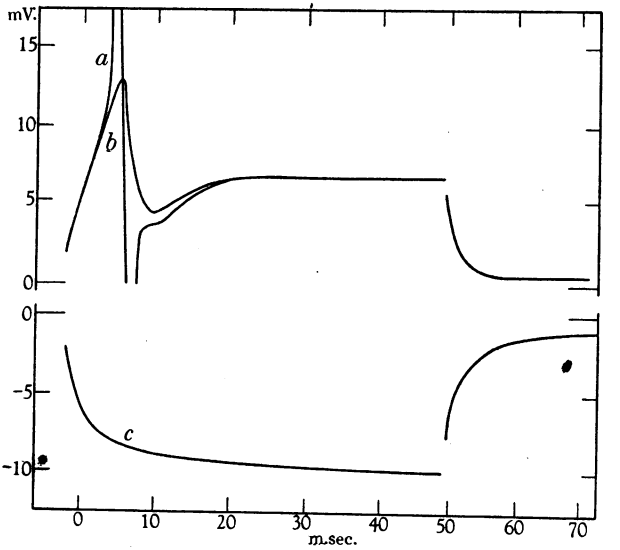
TABLE 2. Properties of an axon at different stages of an experiment. The left-hand column gives values obtained at about 3 hr. after isolation of the axon and the right-hand column gives values at about 6 hr. after isolation

Magnitude of action potential (external recording)	52·9 mV.	36·6 mV.
Critical level of depolarization (external recording—see text for definition)	7·4 mV.	12·9 mV.
Safety factor (see text)	7·15	2·84
Membrane resistance	8200 Ω cm.^{2}	7200 Ω cm.^{2}
Membrane time constant	8·2 msec.	7·0 msec.
Membrane capacity	1·0 μF. cm.$^{-2}$	0·97 μF. cm.$^{-2}$
Current through axon at rheobase	$9{\cdot}3 \times 10^{-9}$ amp.	$24{\cdot}8 \times 10^{-9}$ amp.
Longest response time observed at rheobase	160 msec.	5·9 msec.
Time to crest of local response (extreme recorded)	120 msec.	7·1 msec.
Lowest repetition frequency observed	9/sec.	—
Number of impulses produced by current equal to twice the rheobase	70	1
Initial frequency produced by 2 × rheobasic current	89/sec.	—

The changes in the excitation pattern of one axon are illustrated by Text-figs. 7 and 8 while Table 2 summarizes the results of a number of quantitative measurements on the same axon. The records in Text-fig. 7 were obtained about 3 hr. after the process of dissection had been completed. The behaviour of the axon at this stage clearly falls into the first class. The response time at rheobase amounted to 160 msec. and the subrheobasic local response rose to a rather flat crest in about 120 msec. The subthreshold response appeared to be maintained throughout the entire period of current flow if the difference between cathodic and anodic curves is taken as a criterion of activity. The repetition frequency varied between 9/sec. at 1·0 rheobase and 89/sec. at twice rheobase; while a twice rheobasic current of very long duration gave rise to about 70 impulses. The records in Text-fig. 8 were obtained about 3 hr. later and show that a marked change had taken place in the characteristics of the axon. The response time did not exceed 6 msec. and the local response rose to a sharp maximum in 7 msec. The axon did not repeat at any strength of current up to 2·5 rheobase and the rheobase itself had increased considerably. The steady potential produced by a rheobasic cathodic current was smaller than that produced by the corresponding anodic current whereas it had formerly been greater. This effect can be attributed to a rectification of the type



Text-fig. 7. Traced records of potential changes at stimulating electrode resulting from rectangular currents with strengths: *a*, $9{\cdot}5 \times 10^{-9}$ amp. cathodic; *b*, *c* and *d*, $9{\cdot}3 \times 10^{-9}$. amp. cathodic; *e*, $10{\cdot}5 \times 10^{-9}$ amp. anodic. The later part of record *b* has been omitted; it was similar to the corresponding part of record *c*.



Text-fig. 8. Traced records of potential changes at stimulating electrodes resulting from rectangular currents with strengths: *a*, $25{\cdot}0 \times 10^{-9}$ amp. cathodic; *b*, $24{\cdot}6 \times 10^{-9}$ amp. cathodic; *c*, $28{\cdot}0 \times 10^{-9}$ amp. anodic. The records were obtained from the same axon as those in Text-fig. 7 but 3 hr. later.

described by Cole & Curtis (1941) or Cole & Baker (1941) which may perhaps be a passive phenomenon similar to the rectification described by Blinks (1930) in certain inanimate systems. In the early part of the experiment the current strength was weaker so that the passive rectification should have been smaller and would in any case have been masked by subthreshold activity. Arguments about rectification and activity must be largely a matter of words until more is known about the physicochemical basis of the action potential, but there can be little doubt that, at the end of the experiment, the axon was no longer capable of maintaining a steady level of subthreshold depolarization and that this change was connected with the loss of its ability to give repetitive discharges. At one time these changes in excitation pattern were thought to be associated with the large decrease in membrane resistance which often occurs during the course of a long experiment. And there is still reason to believe that such changes do have a marked effect on the characteristics of the response to a constant current. But in this experiment at least, the decrease in membrane resistance was small and must be regarded as of doubtful significance. The most important change which took place during the course of the experiment was the large change in safety factor (Table 1). The concept of a safety factor was introduced to describe the effectiveness of the action potential as an electrical stimulus (Hodgkin, 1937). The safety factor can be defined quantitatively in several ways. In Table 2 it is taken as the ratio of the peak of the action potential to the maximum depolarization produced by a just subthreshold current of long duration. This definition is clarified by reference to Text-fig. 7. A rheobasic current gives a potential which is produced partly by passive depolarization of the nerve membrane and partly by an actively generated local response. A propagated action potential arises when the total depolarization exceeds a certain level. In the experiment of Text-fig. 7 this was about 7·4 mV. Measurements at a lower amplification indicate that the height of the action potential was 53 mV. The safety factor was therefore taken as 7·15. The argument is not affected by the fact that the membrane action potential is reduced by about 1/2·5 as a result of external short-circuiting, since the same factor operates in reducing the subthreshold potential. Other definitions of safety factor are equally logical. The local response could have exceeded 7·4 mV. without propagating if the current had been switched off before the end of the utilization time. Under these conditions the potential time curve starts to bend upwards, but does not continue to do so in the absence of external current unless the depolarization exceeds by about 50 % the level which is needed for excitation when the current is maintained (cf. Hodgkin & Rushton, 1946, fig. 15). There appear to be two critical levels of depolarization in a nerve fibre. The first defines the maximum depolarization which can occur without giving rise to a propagated impulse when the external current is maintained at a constant value. The second defines the level of

depolarization which must be exceeded before propagation can take place in the absence of external current. Either of these levels could be used in defining the safety factor and the only reason for employing the first is that it was easier to measure with the apparatus at my disposal.

At the end of the experiment the recorded action potential had decreased from 53 to 37 mV. whereas the critical depolarization had increased from 7·4 to 12·9 mV. The safety factor had therefore declined from 7·4 to 2·8. A change of this magnitude must have a marked effect on many phases of nervous activity and there are theoretical grounds for believing that it would lead to a diminution in the ability to repeat. Further discussion of this problem and of the related phenomenon of accommodation must be deferred to a later paper.

A certain number of axons were capable of repetition but did not do so unless the current strength was large. Under these conditions the propagated action potentials might be followed by a damped oscillation which appears to be similar to that described by Arvanitaki (1939). An example of this type of behaviour was given in a former paper (Hodgkin & Rushton, 1947, fig. 14) and requires no further description. Oscillations are also seen in decalcified nerve, but are not easy to observe since removal of calcium often leads to a prolonged and uninterrupted discharge of nervous impulses.

CONCLUSION

The variable nature of repetitive discharges is emphasized by a large body of experimental evidence [e.g. Erlanger & Blair (1935), Adrian & Gelfan (1933), Brink *et al.* (1946), Skoglund (1942), Arvanitaki (1938) and Fessard (1936)] and it is difficult to make generalizations which might be useful in studies of neurones or sensory receptors. The present paper does not attempt to give a comprehensive theory of repetitive behaviour: its object is to emphasize two points of general interest. The first is that the long response times of *Carcinus* axons are associated with the ability of these axons to give regular low frequency discharges; and the second that both response time and repetition interval are determined by the development of subthreshold activity which may be extremely slow under appropriate conditions. The importance of response time and of slowly rising local potentials was emphasized by Fessard (1936) and Arvanitaki (1938) but has often been neglected in studies of sensory receptors. Most writers seem to have adopted the suggestion of Adrian (1928) that the frequency of a repetitive discharge is determined by the refractory period of the sense organ. The experiments described in this paper suggest that the response time of a sense organ to a constant stimulus may be quite as important as its refractory period.

SUMMARY

The initiation of repetitive discharges by constant currents was investigated by recording local electric changes from the stimulating electrode in isolated axons from *Carcinus maenas*.

The following classification was made on the basis of the types of repetition encountered:

(1) Axons which were capable of responding over a wide range of frequencies (5–150/sec.).

(2) Axons with a pronounced supernormal phase. This class gave a train of impulses of frequency 75–150/sec. which was relatively insensitive to the strength of the applied current.

(3) Axons with high threshold and low safety factor which either failed to repeat or succeeded only if the current strength was much greater than rheobase.

Axons which were left in oil or sea water for long periods usually passed through a stage in which they failed to repeat before becoming inexcitable.

The repetitive behaviour of axons in the first class is of interest because it is similar to that of slowly adapting sensory receptors or motor neurones. The frequency of repetition appears to be primarily determined by the rate of growth of a local electric response to the level necessary for propagation. Thus there is a marked resemblance between the potential changes which precede the first impulse and those which precede any other impulse in the repetitive train. The response time of the first impulse is of the same order as the initial repetition interval and both periods are affected by current strength in a similar manner. The rate of growth of the local response may be exceedingly slow and both response time and repetition interval have exceeded 500 msec. on certain occasions.

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