

FACILITATION, INHIBITION AND DEPRESSION AT THE
'ARTIFICIAL SYNAPSE' FORMED BY THE CUT END
OF A MAMMALIAN NERVE

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In a recent paper, 'Fibre interaction in injured or compressed region of nerve', Granit, Leksell & Skoglund (1944) have given a brief account of the historical background of this problem and of their own finding, namely, that electrical stimulation of one of the motor roots of the sciatic nerve (cats) elicits a discharge in the corresponding sensory root to which it has been transmitted from an 'artificial synapse' formed by the cut end of the sciatic or the hamstring nerve. Several controls described in that paper enabled them to localize the point of transmission to this region and to exclude stimulus escape. A very much smaller discharge or none at all is transmitted in the opposite direction, sensory to motor. The unidirectional properties of the artificial synapse of the severed end of the nerve were ascribed to the lower rheobase and accommodation of mammalian sensory fibres as compared with motor fibres (Skoglund, 1942; Kugelberg, 1944; cf. for same result with frogs, Erlanger & Blair, 1936).

In this paper it will be shown that the artificial synapse has several properties of theoretical interest which are of importance for an understanding of synaptic activity in general; moreover, Granit *et al.* (1944) noted that the artificial synapse behaved like a real synapse in its dependence upon the degree of anaesthesia of the animal. If the cats were drugged so that reflex activity was depressed, then the artificial synapse also failed to transmit impulses. Nor did it work in asphyxiated nerves in which the spikes set up by an electrical stimulus were still practically normal. In fact, in order to act as an artificial synapse the cut end must be in very good condition. Decerebrate animals made good preparations unless they had lost too much blood; cats under 'dial' easily became too heavily narcotized. A chloralose narcosis (about 5 c.c./kg. of a 1% solution) was found to give very good enduring preparations.

TECHNIQUE AND PROCEDURE

Fig. 1 is a schematic illustration of the manner in which the experiment was set up. In most cases the stimulating electrodes (*St*) were on the motor root of L7, and the recording leads (*Re*) to the amplifier on its sensory root. In some cases, and, later on in the work, nearly always, the stimulating electrodes were on both L7 and S1 or on each branch of the divided L7. Thus local interference between successive stimuli could be avoided. All branches from the main sciatic stem were severed as far up as possible; all muscles around the spine and the hip were cut across, and the leg completely denervated. These precautions are very important (cf. Granit *et al.* 1944). For quantitative work it is best to cut the whole sciatic stem, including the hamstring, at the same level so as to have a single reflecting cross-section. The effects from two cross-sections can interfere and thus cause complications (Granit *et al.* 1944).

The stimuli were slowly repeated condenser shocks of less than $100\mu\text{sec}$. duration. Two stimuli, conditioning shock plus test shock repeated as a group, have mostly been used. The conditioning stimulus has then been synchronized with the sweep circuit of the cathode-ray oscillograph so that, each time the beam of the cathode-ray passes horizontally across the face of the tube, this movement starts at the moment of stimulation of the nerve. Thus, when the film slowly passes vertically across the beam, a series of successive pictures of its horizontal movement are obtained upon which are superimposed (vertically) (i) the volley elicited by the first stimulus, (ii) the shock artefact of the second stimulus followed by (iii) its volley (see Figs. 7, 8).

The terms 'afferent' and 'efferent' will be used to refer to the regions of the artificial reflex arc wherein impulses travel towards or away from the synapse, independently of whether sensory or motor nerves are involved.

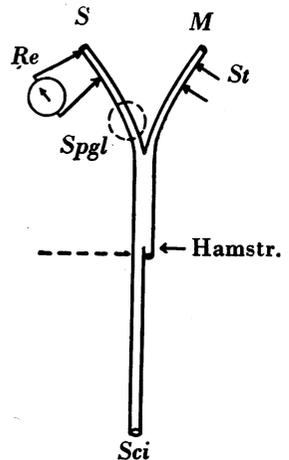


Fig. 1. Diagram illustrating stimulating electrodes (*St*) on motor root (*M*) and recording electrodes (*Re*) on sensory root (*S*). *Sci*, sciatic nerve; *Spgl*, spinal ganglion. In order to avoid interference between two reflecting cross-sections the whole nerve should be severed at the region marked by horizontal broken line.

RESULTS

1. *Two modes of action of the artificial synapse*

Rhythmic synapses. It was noted by Adrian (1930) that the 'injury' discharge from the cut peripheral end of a mammalian nerve is often rhythmically synchronized into beats. The rhythmic discharge gradually disappears. In Fig. 2*a* the discharge, picked up from the sensory root immediately after severance of the sciatic nerve, consists of synchronized beats at about 140 per sec. That these are coming from the cut end of the nerve is easily shown by several tests involving interference of some sort or other with that end. The records *a* show a set of successive pictures taken at the usual rate of 1-2 per sec. Upon these faster beats are superimposed slower rhythms which cause variations in their amplitude. The two upper records *b* were taken in succession, somewhat later after cutting the nerve, by which time the rhythmic discharge had diminished. Then a single stimulating shock to the (*St*) electrodes on the motor root was synchronized with the sweep so

that in the two lower records *b* the shock initiates the sweep movement. The first effect of the shock to the motor root consisted in the appearance of a double volley (two peaks) in the sensory root. This first volley (cf. record) is preceded by a latent period, generally of the order of 3 msec. for nerves cut just above the knee. (For an explanation of the second peak see Granit *et al.* 1944.) The first volley is seen in the record to be succeeded by two large rhythmic beats. As a matter of fact a long train of such beats, gradually damping out, were started by the shock, as if it had operated some trigger mechanism at the artificial synapse, but, in the brief time during which the sweep traversed the face of the tube and was photographed, only two such beats had a chance to become included in the picture.

Now, in Fig. 2*b*, the last record directly succeeds the last but one (another stimulus has been applied) so that the rhythmic beating has been interrupted. It is interesting to note that the fresh stimulus of the last record has reset the whole mechanism of excitation and reiterated the events just described. These facts are typical, regular and easily repeatable, provided that the artificial synapse is of the kind in which the efferent (in this case = sensory) part of the reflex arc happens to be spontaneously beating. As previously pointed out by Adrian (1930) and Skoglund (1942) it is the rule to find the sensory fibres of the freshly severed mammalian sciatic discharging spontaneously, and quite often rhythmically. A new finding here is that activation of the artificial

synapse from the motor end has such a remarkable influence on this kind of spontaneous activity. This raises questions as to the kind of changes of excitability which the shock has left behind in the synapse.

In the experiment of Fig. 2 the rhythm was obvious from the beginning; more commonly, however, and especially if the nerve had been severed for some 5 min. or more, there remained merely an irregular injury discharge. Despite absence of spontaneous rhythm the relayed response, caused by a shock to the motor L7 and recorded at the sensory L7 in the usual manner,

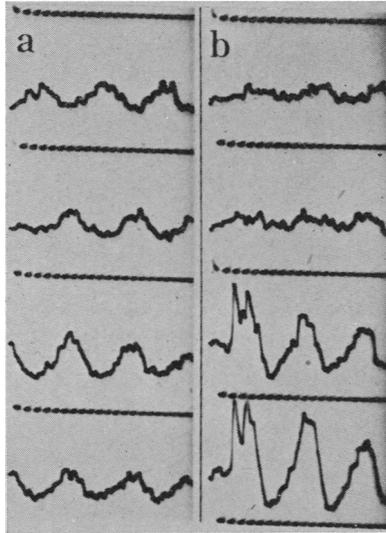


Fig. 2. *a*, spontaneous response from cut end recorded as indicated in Fig. 1. In the beginning of *b* the spontaneous oscillations have diminished but in the two last records of series *b* a shock to the motor L7, and synchronized with the beginning of the sweep to the extreme left, has activated the cut end to discharge a double-peak volley succeeded by a series of oscillations at the rate of the original rhythm. Time in msec. See text.

consisted of two or three beats gradually damping out, the first volley always much larger than the secondary waves (see Figs. 7, 8). Finally, in some cases, when the 'reflex' response was as simple as the original motor volley from L7 and merely differed from it in being spread out over a longer duration, it was nevertheless possible to demonstrate by appropriate tests that periodic changes of excitability took place at the synapse. These will be discussed in the later sections of this paper.

The great majority of artificial synapses show some signs of rhythmic behaviour, gradually becoming less marked in an ageing preparation. But full rhythmic activity may then be restored by the simple expedient of making a fresh section farther up the nerve. For this reason it is suspected that non-rhythmic synapses are merely less active synapses. The easiest way of producing aperiodic synapses is by drugging the animals so deeply that general reflex irritability is depressed.

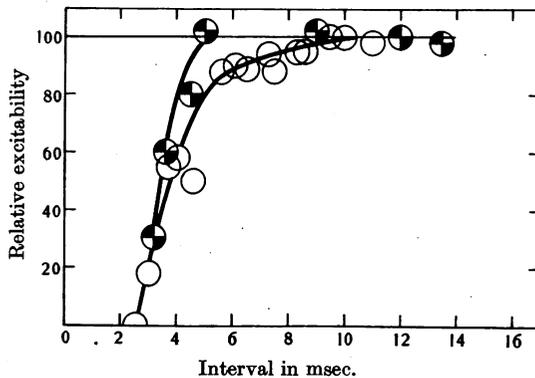


Fig. 3. Non-rhythmic artificial synapse. Abscissae: interval between conditioning shock and test shock in msec. Ordinates: relative excitability = size of second response expressed as percentage of normal control. Two different experiments. See text.

The non-rhythmic synapse. In the experiments of Fig. 3 two stimuli, conditioning stimulus and test stimulus, have been used. The test stimulus approaches the conditioning stimulus and consequently the relayed effect diminishes when the second stimulus falls during the state of refractoriness left by the first. This diminution is illustrated on a percentage basis against interval between the stimuli as abscissa. In the lower curve there is a slight indication of a hump at 5-6 msec. The upper curve is from another experiment with another animal. The refractoriness becomes 'absolute' at an interval between the stimuli of about 2.7 msec. The term 'absolute refractoriness', that here refers to the 'reflex arc', is used as a convenient shortening for 'least interval during which second stimulus is ineffective'. The two consecutive stimuli (causing maximal relayed waves) were in this

case delivered to the same *St* electrodes but a great number of control experiments, demonstrating refractoriness for stimuli to different branches of L7, have shown beyond doubt that the seat of this long 'absolute refractory period' is the synapse (see below).

2. The 'absolute refractoriness'. The 'synaptic delay'

From thirty-seven measurements of the absolute refractoriness of the artificial reflex the statistical distribution curve of Fig. 4 was plotted. The extremes are 1 and 4.5 msec., the arithmetical mean 2.75. These measurements are from different experiments representing all kinds of artificial synapses: fresh sections, old sections, rhythmic and non-rhythmic ones, etc.

The synaptic delay was found by subtracting from the total latent period of the 'reflex' response the conduction times in the A group of motor and sensory fibres, as measured by a faster sweep. In such experiments it was found best to use the response relayed from the cut end of the hamstring nerve and keep the recording electrodes for measuring conduction velocity on the intact sciatic at the point where the hamstring was severed. Values of the order of 0.1–0.3 msec. were found for the synaptic delay. These are just at the limits of accuracy of the experiment, considering that the exact position of the synapse is unknown. It is concluded that the synaptic delay is so brief as to necessitate an electrical mechanism of excitation, comparable with the one responsible for the propagation of the action potential along the nerve. The same conclusion is suggested by Renshaw & Therman's (1941) interesting analysis of a response relayed into the sensory roots from a cross-section in the spinal cord.

3. Rhythmic synapse and nerve compared

The method of applying a test stimulus immediately after a conditioning stimulus has, of course, repeatedly been used with nerve (see especially Graham & Lorente de Nó, 1938, for work with blood-perfused mammalian nerve) and certain facts have become firmly established. Less is known about periodic changes of excitability following a conditioning shock and studied, e.g. by Erlanger & Blair (1936) and Lehmann (1937), though the available literature suggests that the rhythmic tendency is greatly favoured

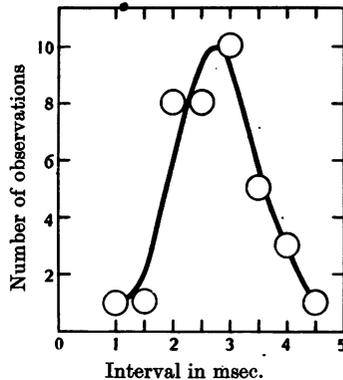


Fig. 4. Distribution of absolute refractoriness of artificial synapse over thirty-seven experiments. Ordinates: number of experiments at the different refractory periods grouped together for each 0.5 msec. Abscissae absolute refractory periods in msec.

by diminished accommodation. v. Brücke, Early & Forbes (1941) speak of the recovery of 'responsiveness' when conditioning and test shock are strong; when the second shock is weaker the method measures 'excitability'. These terms will be used below in comparing a pure nerve experiment dealing with both 'responsiveness' and 'excitability' with a similar synapse experiment utilizing the same stimulating electrodes. In the nerve experiment the leads were at the cut end of the sciatic, in the synapse experiment on the sensory root L7 in the usual manner. The stimulating electrodes were on the motor L7.

Some records from the nerve experiment on *responsiveness* are found in Fig. 5 and the whole experiment is graphically summarized by curve 2 of Fig. 6. It gave for nerve the brief absolute refractory period of 0.4 msec. The second stimulus was uninfluenced by the first as long as the interval between the stimuli was greater than 2.5 msec. The recording electrodes were next shifted to the sensory root in order to repeat the same experiment with the artificial reflex. The stimuli were unchanged and just supramaximal. The relayed effects of conditioning and test stimulus alone are shown as 1 and 2 of Fig. 7. The interval between the stimuli was then systematically shortened, as shown in records 3-12 of the same figure. It is seen that, as the interval shortened, the second response passed through periodic maxima and minima of excitability. This experiment is reproduced as curve 1 of Fig. 6. At an interval of about 4 msec. the second volley actually was facilitated above its normal level, found in record 2.

On returning the recording electrodes once more to the cut end of the nerve, but with the effect of the test shock diminished to 75% of the conditioning shock, the recovery curve numbered 3 of Fig. 6 was obtained. In this case excitability was measured, though merely graded in terms of 'size of the response relative to normal' in order to have the same ordinates as in the measurement of the 'reflex'.

Curve 3 should be compared with curves 1 and 2 in order to show that the introduction of an artificial synapse in the conducting nerve path, despite the use of supramaximal stimuli (curves 1 and 2), changes an experiment on responsiveness (curve 2) into one dealing with excitability. Curve 3 shows that similar curves are obtained with a pure nerve preparation by appropriate

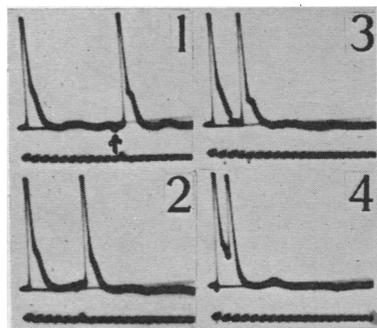


Fig. 5. Recovery of 'responsiveness' in motor L7. Conditioning stimulus, elicits sweep movement to the extreme left, test stimulus at the moment marked by small shock artefact (see arrow in record 1). Both stimuli supramaximal. The ensuing waves, as recorded at the cut end of the nerve (the 'synapse'), approach each other from 1 to 4. Recovery curve plotted as curve 2 of Fig. 6. Time in msec.

adjustment of the experimental conditions for determination of excitability. There is (in curve 3) the long 'least interval' between the stimuli, previously

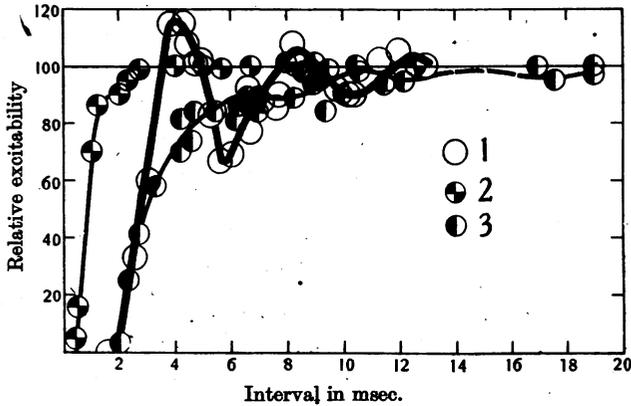


Fig. 6. Comparison of recovery in nerve and synapse. Abscissae: interval between conditioning shock and test shock in msec. Ordinates: relative size of test shock in percentage of normal control. (line marked 100). 1, relayed response, recorded at sensory root; 2, direct response recorded at cut end, with supramaximal stimuli; 3, same, but with test shock 75% of conditioning shock. See text.

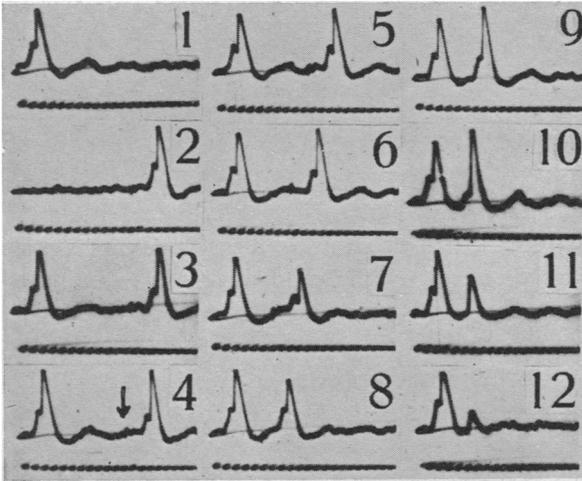


Fig. 7. Artificial synapse. 1, effect of conditioning stimulus alone; 2; test stimulus control, preceded by small artefact (see arrow in record 4); 3-12, shortening of interval between conditioning and test stimulus. Note, inhibition in 7, facilitation at shorter interval in 10, disappearance of secondary volleys during depression at still shorter interval in 12. The same results are plotted in Fig. 6, curve 1. Time in msec.

encountered as the 'absolute refractory period' of the 'reflex' arc. There are some oscillations of excitability (cf. also Graham & Lorente de N6, 1938)

though in this case, of course, located at the region under the stimulating electrode and not at the cut end. The changes of excitability in the artificial synapse similarly determine the number of fibres that is available for cross-excitation at the cut end.

4. Depression at the synapse

It is common to find that the states of absolute and relative refractoriness in the reflex arc are followed by a depression which by no means signifies a dying synapse. Fig. 8 illustrates an experiment of this kind.

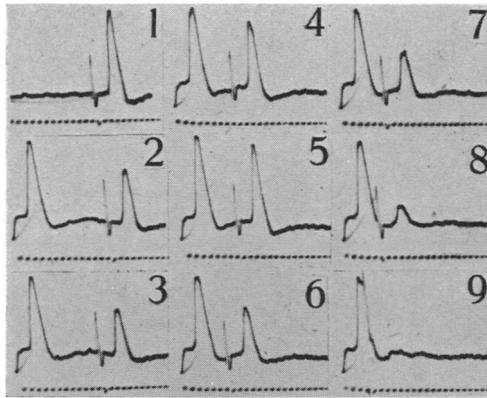


Fig. 8. Artificial synapse with marked depression. 1, test stimulus control preceded by large shock artefact; 2-9, shortening of interval between conditioning and test stimulus. Time in msec.

Record 1 is a control of the test stimulus alone. No increase of stimulus strength increased the relayed response which thus was maximal. In record 2 this stimulus was preceded by the conditioning stimulus. From 2 to 9 the interval was shortened. It is seen that throughout the illustrated intervals (from about 3 to 13 msec.) the test volley is below the level of its control (record 1) and thus depressed in size, even though within this depression there is a peak of relative facilitation in record 5, as compared with the records on either side of it.

In Fig. 9 some graphs of experiments with marked depression have been drawn for comparison. At the critical interval of 4-6 msec. there has been facilitation in the Exps. 1 and 2. In Exp. 2 the depression below the normal level of 100 lasted for about 32 msec., in Exp. 2 for 65 msec. In Exp. 3 of Fig. 9 the depression was unusually heavy. The test volley was at 40% of its normal size at an interval of 15 msec., and the depression lasted for 44 msec. There was no facilitation so that the synapse may be said to have belonged to the non-rhythmic type. But in the beginning of the experiment, as long

as the section was fresh, there had been an initial facilitatory peak around 4 msec. Curve 3 is of especial interest also because in this case the stimulating electrodes were on different motor roots, the conditioning shock being delivered to L7, the test shock to S1. The recording leads were on the sensory L7 in the usual manner.

It is concluded from these facts that neither the early facilitation nor the depression require that the impulse volleys should pass along identical 'afferent' fibres. The stimulating volleys for the synapse can also 'converge' towards the cut end in different fibres. In several experiments 'converging afferents' were used in order to exclude processes under the electrodes.

Depression is certainly common in ageing synapses but this is not the whole explanation of the phenomenon. It must also depend upon other factors as yet unknown.

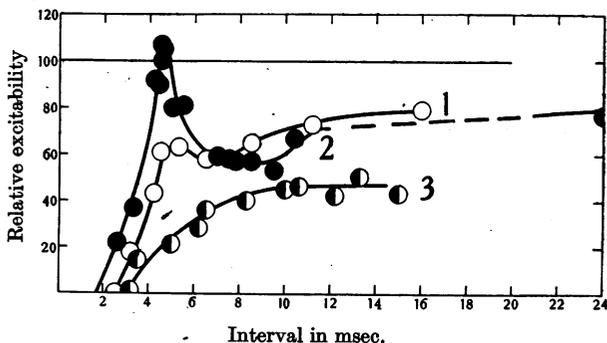


Fig. 9. Measurements of excitability in three different artificial synapses with marked depression. Abscissae: interval between conditioning and test shock as in Fig. 6. See text.

There is evidence to show that the states of depression are additive. Thus depression can easily be augmented by repetition of the stimulation at faster rates than 1-2 per sec., the rates which were used in most experiments. If the relayed volleys consisted of primary and secondary waves (Fig. 7) those with the longest latent periods disappeared first so that, under the influence of a gradually increasing frequency of stimulation, the relayed discharge was cut down from its tail end. At higher frequencies the reflex discharge was completely blocked at a frequency which did not very much affect the primary 'afferent' volley conducted to the synapse.

5. *Some properties of the periodic changes of excitability*

In some experiments the periodic changes of excitability of the artificial synapse have been followed for several periods. This was the case in the experiment of Fig. 10. The lower curve illustrates a combination of depression with the characteristic periodic facilitation and inhibition superimposed. The rhythm is gradually damping out in the typical manner. The upper curve 2

is from the same experiment but the test shock has now been made somewhat weaker so that the reflex response elicited by this shock was 84% of the one

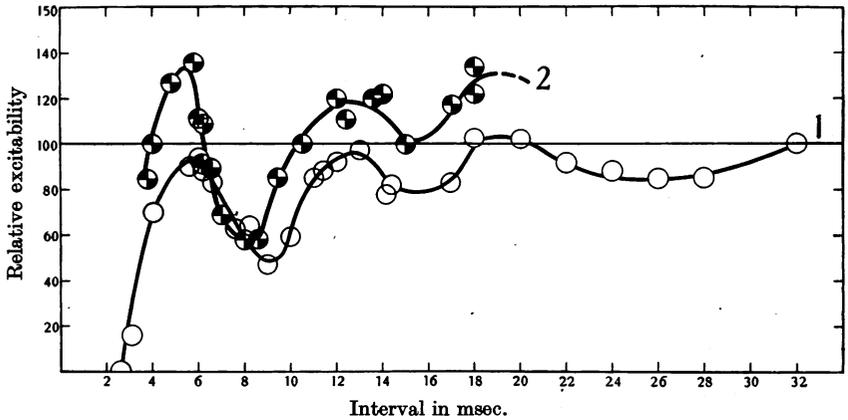


Fig. 10. Measurements of excitability in rhythmic artificial synapse with the method of conditioning shock and test shock as in Fig. 6. Fully explained in text.

caused by the conditioning shock. This increased the crests of facilitation and the troughs of inhibition. Now a synapse is a gradually changing focus of cross-excitation so that comparative experiments of this kind cannot refer to exactly identical conditions, for it takes some time to complete a set of observations. However, this gradual change is in the direction of a diminution of amplitude of all periodic variations and an augmentation of depression. In this case, however, the experiment with the weaker test shock (curve 2) succeeded the one with less facilitation and more depression (curve 1). It is therefore held to be fully reliable and probably representing a phenomenon, which in the terminology of Sherrington and his collaborators (Creed, Denny Brown, Eccles & Sherrington, 1932), may be called 'occlusion'. It means that with maximal relayed volleys (curve 1) so many fibres of the 'neurone pool' have been engaged by the test volley that a smaller margin of fibres is left for facilitation. If the test shock is weakened the changes of excitability at the synapse have a greater chance of adding to or subtracting

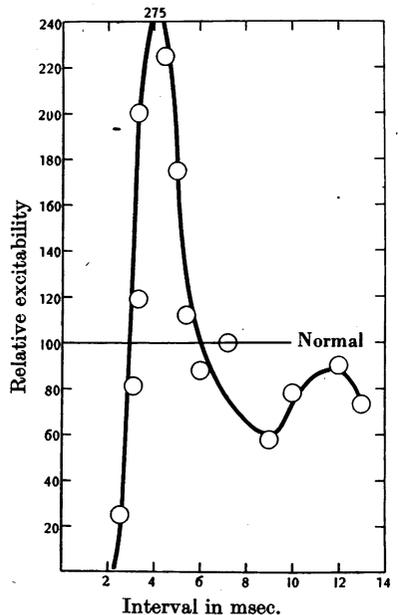


Fig. 11. Peak of increased excitability after conditioning shock in a single experiment. See text.

from the artificial reflex. Very weak test shocks have not been used on account of the irregularities that tend to complicate such measurements.

The greatest facilitation ever seen in one of these experiments is illustrated in Fig. 11. It reached 275% of the normal level of the isolated control. There, as in so many other cases, the peak of facilitation was exceedingly sharp. It is seen at an interval of about 4-5 msec. in Fig. 11.

The first facilitation maximum is the most constant in these experiments. It is generally at some interval between 4 and 6 msec. The second varies from 8 to 12 msec., and the third fluctuates still more. In some good experiments there have been three peaks of facilitation at 4, 8 and 12 msec. Between them there have been the typical troughs of inhibition. This corresponds to a frequency of 250 oscillations per sec. As pointed out above, the fluctuations of excitability are often large enough for the conditioning shock alone to cause a similarly fluctuating discharge to emanate from the synapse, and in many nerves the fresh cross-section discharges spontaneously at the same rate for several seconds, in some even for minutes. The maximal frequencies observed for the fluctuations in excitability have been around 300 per sec. It is impossible to note such facts without questioning whether or not the normal repetitive discharge of neurones is an expression of similar rhythmic fluctuations.

6. *Overlapping shocks to different roots*

It was expected that the use of different adjacent roots, or division of L7 into two halves, for conditioning and test shocks would make it possible to have the two shocks approaching each other with only moderate signs of interference, but this was not found to be the case. On the contrary, the results in this arrangement differed relatively little from those obtained when the shocks were delivered to the same electrodes. Both general depression and the periodic changes in excitability were again found (cf. § 4). Depending upon the preparation used and upon stimulus strength, the refractoriness became 'absolute' or merely 'relative' at short intervals. Precise summation of the reflex volleys was seen for coinciding stimuli but never a 'reflex' overshooting the sum of the volleys caused by conditioning shock and test shock controls. It is possible that facilitation at coincidence would have been obtained if weak stimuli had been used. However, since the artificial reflex was unstable with weak stimuli, all experiments in which the effects from an undivided root were compared with those, obtained when its components were separated into two halves, were carried out with strong stimuli.

Especially interesting is the experiment illustrated in Fig. 12. The stimuli were applied to the motor L7 and S1, and the relayed response was recorded from the sensory L7. The reflex effects were maximal but this meant that S1 elicited a response 67% of that initiated from L7. To the left of zero in the

diagram, L7 received the conditioning shock, to the right of it the stimuli had overlapped and S1 received the conditioning shock.

The following points should be noted: whichever shock went first, it always left a period of absolute refractoriness for the other, as shown by the figure to either side of zero. Both curves indicate a generalized depression, which was most evident with S1 leading; with 'L7 leading' the depression was interrupted by a fairly large peak of facilitation. At coincidence the relayed volley had the size of the larger response (from L7). They did not sum.

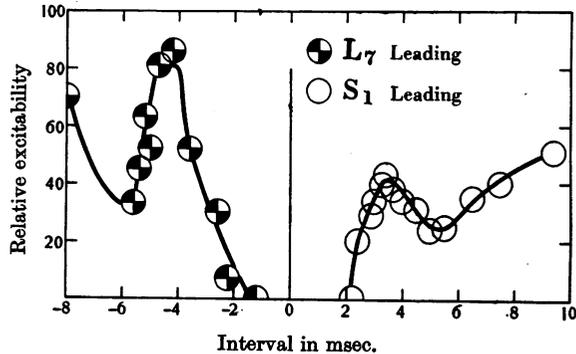


Fig. 12. Effect of successive stimuli applied to L7 and S1 on the excitability of the synapse. See text.

The experiment raises the question: how could S1, which only activated 67% of the number of fibres engaged by L7, leave the reflex path absolutely refractory for L7. The answer can only be that S1 has caused such a large generalized depression in the synapse, that the remaining 33% of the fibres of the 'final common path' were also affected. The peak of facilitation suggests that the two reflexes have had a final common path, but, as long as the fibres have not been identified and the mechanism of excitation is not fully understood, it is also best not to overemphasize the parallels with well-known results from the work on the spinal cord. How depression spreads in the artificial synapse is as yet unknown.

DISCUSSION

When Hering (1882) first found cross-excitation at a cut end of the sciatic plexus of frogs, it had the character of an exceptional phenomenon, present only in animals showing signs of increased irritability. In cats this situation appears to be the normal state of affairs, probably on account of the low accommodation of the sensory fibres in this animal (Skoglund, 1942). Jasper & Monnier (1938) found cross-excitation in crab nerve, and Arvanitaki (1940 *b, c*) showed that the impulse passed across two parallel, adjacent and partly overlapping crab nerves, provided that the 'efferent' contact point of the artificial

synapse had been treated with citrate. From this work one might conclude—and it seems to have been concluded—that cross-excitation easily takes place in crab nerves. Later, however, Katz & Schmitt (1940) have shown that in such nerves also there is a large safety margin provided for isolated conduction. This paper and that of Granit *et al.* (1944) emphasize that the correct explanation of the results of Jasper & Monnier must be that in their cases too the effect was localized to the cut ends of the nerves tested. This would explain their long ‘synaptic delay’.

In her crab nerve synapse, treated with citrate, Arvanitaki (1940-*a, c*) has found a series of oscillating ‘local potentials’. The first effect of the ‘efferent’ impulse is a negative ‘local response’, called the ‘pre-potential’, identical with the local response of Arvanitaki (1936) and Hodgkin (1938). In synapses of the rhythmic type it is succeeded by further oscillations, ‘consecutive potentials’, gradually damping out. The impulses are generated on top of these local changes. With leads at the artificial synapse, formed by the cut end of the cat sciatic, we have also found similar oscillating potentials which in some cases have not been conducted away to the sensory root. The excitability changes have varied in parallel with those potentials. We hope to return to this aspect of the problem with a detailed investigation of the phenomena at the synapse itself.

It would seem to be justifiable to regard the processes at the artificial synapse as something not very far removed from probable events at a real synapse. Bernhard (1944) has recently studied the interaction of a conditioning stimulus to the popliteal nerve with a test stimulus placed in the spinal cord itself (cats). The effect was recorded in the ipsilateral peroneal nerve. The stimulus to the popliteal nerve was found to be succeeded by a fast periodic variation of excitability strongly reminiscent of the effects described in this paper. Quite often a single shock to the spinal cord is seen to elicit a series of rhythmic oscillations of grouped impulses in the efferent nerve (cf. Lloyd, 1941). Bernhard & Granit (1942) have shown that this complex relayed response is cut down from the tail end when stimulus frequency is increased, just as is the case with the volleys relayed from the artificial synapse under similar circumstances.

To sum up, without stressing the analogies, we may say that the work with artificial synapses in peripheral nerve provides an encouraging approach to the physiology of the central nervous system.

SUMMARY

1. The cut end of the cat's sciatic nerve forms an artificial synapse in which a volley passing in the motor fibres is relayed across to the sensory fibres. The effect, established by Granit *et al.* (1944), is here analysed from

the point of view of the changes of excitability which transmission of a volley across the 'synapse' elicits in the latter.

2. Most artificial synapses respond to a single shock to the motor roots by setting up a *periodic variation of excitability*, always preceded by a state of refractoriness. The periodic variation in excitability and the preceding refractoriness have been analysed with the aid of a second test shock. The relayed response of the test shock is *facilitated or inhibited*, depending upon whether it falls in the crest or trough of the periodic change of excitability left by the conditioning shock. It is immaterial whether the two shocks are given to the same root, to separate branches of the same root, or to adjacent roots sending fibres to the cut end which is acting as synapse.

3. In some synapses the periodic changes are superimposed upon a *generalized depression of excitability*, left by the conditioning shock.

4. The artificial synapse does not transmit impulses unless the anaesthesia is light and the animal is reflexly active.

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