

**THE MAXIMUM FREQUENCY OF REFLEX RESPONSE
IN THE SPINAL CAT.** BY SYBIL COOPER (*Yarrow
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THE experiments described in this paper form an extension of the attempt made by Adrian and Olmsted⁽¹⁾ to measure the refractory period in the central part of a reflex arc, the object being to obtain some of the numerical data needed for an understanding of central conduction. We have found that the conclusions drawn by Adrian and Olmsted have to be modified in one important particular and this has involved a re-examination of several related points. One of their methods consisted in stimulating a sensory nerve with a rapid series of break shocks and recording the electric responses of the muscle contracting reflexly. They found that in the spinal cat the tibialis anticus would give a regular sequence of electric responses as rapidly as 160 a second in response to stimuli of the same frequency applied to the popliteal nerve; with stimuli at 200 a second the response of the muscle became irregular after a few hundredths of a second and with higher rates it was always irregular. Since the same muscle stimulated by its motor nerve would respond as rapidly as 320–400 a second, they concluded that the maximum frequency of reflex response was determined by some factor in the central part of the reflex arc which limited the frequency of activation of the motor neurones to 160 a second.

Last summer Beritoff⁽²⁾ announced that in the semitendinosus of a spinal or decerebrate cat he had found regular responses at a frequency as high as 250 and often 300 a second produced by reflex stimuli of the same frequency. We have therefore re-examined the response of the tibialis anticus and other muscles with various changes in technique, and we find that the value given by Beritoff must be accepted as correct, the lower value given by Adrian and Olmsted depending partly on a different method of assessing the "maximum frequency" and partly on a faulty method of recording the electric response.

Method. Our experiments have been made on spinal cats decapitated by Sherrington's method. Shielded stimulating electrodes are applied

to the popliteal branch of the sciatic and shocks are delivered at the requisite frequency by a rotating contact breaker connected with a coreless induction coil. Strengths of stimuli are expressed as reciprocals of the resistance in the primary circuit, unit strength corresponding to 1500 ohms, and also as multiples of the threshold stimulus. The nerves to the hamstring muscles are cut unless the response of the semitendinosus is to be investigated, but other nerves are left intact and the tendon of the muscle is left attached to its insertion. The temperature of the muscle under investigation is measured by a needle thermojunction of the form described by Adrian and Watts(3). The chief points in which our methods differ from those of Adrian and Olmsted are concerned with the recording of the electric response of the muscle. The string tension used by them was such that .001 volt through the string (2500 ohms resistance) gave a deflection of $7\frac{1}{2}$ to 10 mm. at a magnification of 440. This tension appeared to be great enough for accurate recording, since the string would give a regular series of oscillations at frequencies as high as 400 a second when a series of break shocks were sent through it from the stimulating apparatus. But a string might be able to follow a simple periodic oscillation of high frequency and yet be unable to give a true rendering of the more complex action currents in a reflex. In the response of the tibialis anticus there are irregular variations in amplitude as soon as the stimulation frequency reaches 160–200 a second, and we now find that a string at 10 mm. tension will give the impression of an irregular frequency of response when a tighter string will show a regular sequence of small waves superimposed on a slower, irregular series. In the present work we have used a tension of 5 mm. or 2.5 mm. for .001 volt. Condenser damping was sometimes used at the higher tension to make the string aperiodic. Since an increase of tension above 5 mm. does not lead to the appearance of any greater frequencies in the record but merely produces a reduction in size, we conclude that this tension gives a faithful record of the highest frequencies in a reflex response. It must be admitted that the frequencies involved are only just within the accurate range of the instrument according to Fahr's analysis(4).

The action currents are led from the muscle by electrodes of stout silver wire thrust into its substance. Before use the surface of the wire is roughened with a file and silver chloride is deposited on it electrolytically. Some of this is rubbed off when the wire is introduced into the muscle, but enough remains to prevent very rapid polarisation when a constant current is passed (see calibration curve, Fig. 1).

Maximum frequency of response to reflex stimulation. Fig. 2 shows typical records of the response of the tibialis anticus to high frequencies

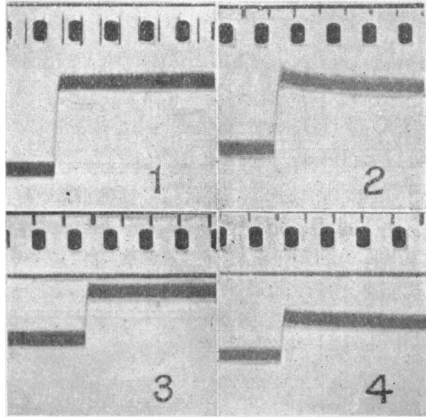


Fig. 1. Calibration curves of string galvanometer. Silvered glass string
4 microns diam., resistance 2500 ohms.

1. Tension 5.5 mm. per millivolt. 2 mv. through string alone.
2. Ditto with electrodes and muscle in circuit.
3. Tension 3 mm. per millivolt. 2 mv. through string alone.
4. Ditto with electrodes and muscle in circuit.

Time marker (vertical lines at top of film) gives .02 sec. intervals in all records.

of reflex stimulation. It will be seen that irregularities of amplitude are present with frequencies of 200 a second but that the intervals between the oscillations are still regular with stimuli at 240 a second. When the reflex excitability of the preparation is good, a regular sequence of responses at 240 a second may last for $\frac{1}{2}$ second or more, but with continued stimulation the response eventually becomes irregular. With stimulation at 280 and at 320 a second the irregularity appears much sooner and there may be small groups of responses at 280 or 320 a second separated by groups with no definite rhythm. To produce these high frequencies of response we have used stimuli from 5 to 10 times the threshold strength. A further increase in strength up to 50 or 100 times the threshold does not increase the frequency which can be attained, though a reduction below 5 may diminish it. We have not examined the relation between strength and frequency in any detail, but it seems to be in general agreement with what we should expect from the form of the recovery curve for mammalian nerve.

The only difference between these results and those of Beritoff is

that in the tibialis anticus we find as a rule a greater irregularity in the amplitude of successive responses than there is in his records of the

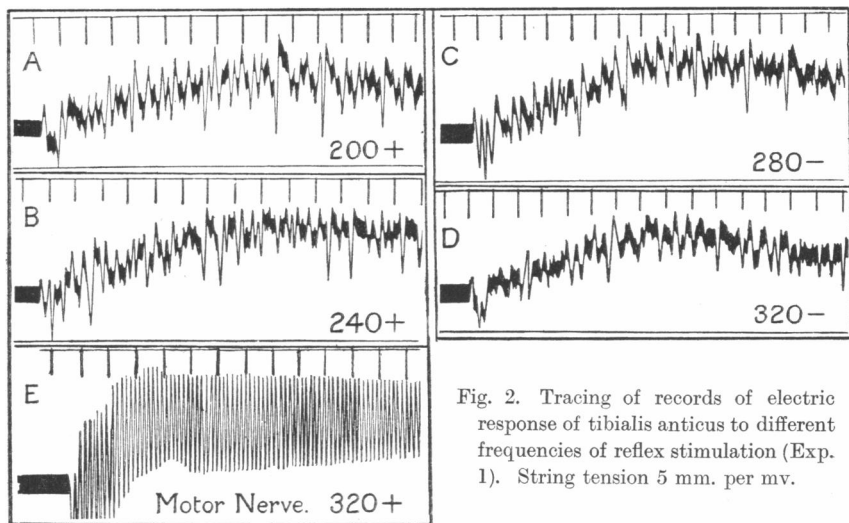


Fig. 2. Tracing of records of electric response of tibialis anticus to different frequencies of reflex stimulation (Exp. 1). String tension 5 mm. per mv.

- A. Stim. 200 per sec. Strength 27 units (18 times threshold). Response regular.
 B. " 240 " " 27 " (18 " "). " "
 C. " 280 " " 27 " (18 " "). " irregular.
 D. " 320 " " 27 " (18 " "). " "

(Same results given with stimuli 108 units and string at 2.5 mm. tension.)

- E. Stim. to motor nerve 320 per sec. 14 units (18 times threshold). Response regular.

semitendinosus. The difference appears to depend on the muscle, for we have found a much greater uniformity in the size of response in the semitendinosus; we have not made much use of this muscle, however, as we have found it difficult to eliminate current spread from the stimulating electrodes.

Table I records the maximum frequency at which a regular series of responses to reflex stimulation can occur in the tibialis anticus. The criterion of maximum frequency we have chosen is one at which at least twenty successive oscillations can occur at regular intervals during some part of the response. Thus a frequency of 250 a second would be included even though the muscle only responded at this rate for the initial $\frac{1}{2}$ sec. of the response. As Adrian and Olmsted used a much more severe criterion (regular oscillations lasting for at least $\frac{1}{2}$ sec.) their figures would naturally have been lower, quite apart from the possible errors introduced by a slacker string. We have changed to the present standard because we wished to eliminate the effects of fatigue as far as possible.

The table gives the maximum frequency defined in this way in seven experiments. The results give a value for the maximum reflex frequency somewhere between 240 and 320¹ per second and this agrees closely with the value 250–300 given by Beritoff.

TABLE I.

Exp.	Temperature	<i>Reflex response.</i>		
		Maximum regular frequency (per sec.)		
1	37.5°		240 +	280 -
3	38.5		320 +	
5	37		240 +	320 -
6	39	280 +	320 ±	360 -
7	38		320 +	360 -
9	39		280 +	320 -
10	38	280 +	320 ±	360 -

These figures give the frequency of stimulation. The + sign indicates that the response is regular and has the same frequency as the stimulus. The - indicates that the response to this frequency of stimulation is irregular. The sign ± is only used when one test gave a regular response and another an irregular.

When the sensory nerve is stimulated so rapidly that the responses of the muscle are irregular in frequency, the number in one second is usually not greater than about 200–250, but there may be small groups at 300.

Maximum frequency of response to stimulation of motor nerve. Adrian and Olmsted found that the tibialis anticus would give regular responses at 320 a second for half a second or longer when stimulated by its motor nerve and they concluded that the limiting frequency of 160, which they found for the reflex, must be determined by something in the central part of the reflex arc. If we accept the higher value of 240–320 a second for the reflex frequency we can no longer be certain that this is determined by the spinal centres rather than by the muscle itself, and as long as this is in doubt we must remain in ignorance of the upper limit of frequency of the discharge from the cord. This has been urged by Beritoff in his recent paper.

There are, however, several facts which throw doubt on the ability of the cord to give a regular series of motor impulses at a higher frequency than 240–320 a second. We have redetermined the maximum frequency of response in the tibialis anticus stimulated by its motor

¹ The least interval between successive responses in a series (.004–.003 sec.) is somewhat shorter than the least interval between two isolated responses determined by Adrian and Olmsted with the capillary electrometer. This was .0046 sec. in the most complete experiment and longer in two others. The present records seem to show that with rapid stimulation the interval between the first two responses of a series is generally greater than that between subsequent responses, but this may be due to instrumental distortion.

nerve and we find that at 37–38° C. the muscle will usually follow a rhythm of 400 a second and occasionally one of 480. These frequencies are rarely maintained for more than $\frac{1}{4}$ to $\frac{1}{2}$ sec. and sooner or later the responses drop to half the original frequency, usually passing through a stage where alternate responses are large and small. But with stimuli at 360 or 320 the muscle will continue to follow the rhythm for several seconds at least. With reflex stimulation, on the other hand, the same muscle at the same temperature will rarely follow a rhythm of 320 a second except for occasional short periods at the beginning of a contraction, and even at 240 the responses become irregular after one or two seconds. The point is illustrated in Fig. 2, which gives the response of the same muscle to reflex and motor nerve stimulation.

Again, if the muscle is stimulated by its motor nerve at a frequency too great for it to follow (500 a second or more) or if it has been stimulated at a lower rate until fatigue has set in, the response will generally consist of a regular series of action currents occurring at half the frequency of the stimuli. In a reflex we have never observed responses at half the frequency of stimulation; when the frequency is not followed the responses occur irregularly at a rate slightly less than the maximum regular frequency. If the motor side of the reflex arc is transmitting impulses at the frequency of stimulation and the failure is due to the muscle, it is difficult to see why the frequency of response is never halved as it is when the motor nerve is stimulated directly.

These arguments are both of some value, but further proof is needed before we can be certain that the failure lies in the central paths and not in the muscle.

Frequency of response in motor nerve with reflex stimulation. The most direct way of investigating the question would be to record the electric responses of the motor nerve during reflex stimulation instead of recording those of the muscle. We have made several attempts to do this but the technical difficulties have been too great. It is a relatively simple matter to record single reflex electric response in the motor nerve with a string at 10–20 mm. tension, but difficulties begin to arise when the responses follow one another at very short intervals. The chief problem is to eliminate the slight spread of the stimulating current into the high resistance circuit of the nerve and galvanometer. If the string is tight enough for accurate recording, the reflex responses are very small, and at high frequencies we have found it almost impossible to disentangle the true action currents from the small artefact due to current spread (or capacity effect) from the stimulating circuit. We have therefore aban-

done the attempt in favour of a less direct, but technically simpler method.

Effects of change of temperature in the spinal cord. The foregoing results suggest that the motor neurones concerned in the flexion reflex cannot be made to send out a regular series of impulses at a frequency greater than 250–300 a second. If this is so when both spinal cord and muscle are at 38° C., a fall of temperature limited to the cord ought to reduce this frequency. If, on the other hand, the cord at 38° can give a regular series of discharges as often as, say, 500 a second, then cooling the cord will not begin to affect the maximum frequency of response in the muscle until a much lower temperature has been reached. To test this point we have made a series of experiments with the tibialis anticus kept throughout at 38° and the spinal cord cooled to various temperatures between 38° and 28°.

A spinal preparation in good condition will usually give a fairly strong reflex although its rectal temperature has been allowed to fall to 28° C. In the earlier experiments the heating of the table was turned off and the whole body of the cat was allowed to cool, the leg being kept warm by a hot-water bottle or a lamp. The temperature of the muscle was measured by a needle thermo-junction and that of the cord was assumed to be equal to the rectal temperature. As the temperature of the body falls very slowly, we changed the method in the later experiments and cooled the cord more rapidly by shaving the skin over the lumbar region and covering it with small lumps of ice. A needle thermo-junction was thrust into the back muscles by the side of the vertebral column so that the junction was at the same depth below the surface as the spinal cord. The temperature measured by this method was found to agree within one degree with that given by a junction in the cord itself. When the cord had reached the required temperature the sensory nerve was stimulated at various frequencies and the response of the muscle was recorded in the usual way. Five experiments were made and their results are given in Table II. In the last two, after the reflex observations had been made with the cord at its lowest temperature, the stimulating electrodes were transferred to the motor nerve and the maximum frequency of response was determined with the muscle at 38° and then at lower temperatures.

All the experiments agree in showing a fall in the maximum frequency of response when the cord is cooled, and the actual values agree very well with one another. With the cord at 28–30° the maximum frequency lies between 160 and 200 in all the experiments and at 32–35°

TABLE II.

Exp.	Temperature		Reflex response. Maximum regular frequency			Stimulus to motor nerve.			
	Muscle	Cord				Temperature of muscle	Maximum regular frequency		
6	39°	39°	280 +	320 ±	360 -				
	—	32		200 +	240 -				
7	41	33		240 +	280 -				
	40	38		320 +	360 -				
8	39	32		200 +	240 -				
9	38	39	160 +	280 +	320 -	37.5°	400 +		
	—	31		200 ±	240 -	28	320 +	360 ±	
10	38	38	280 +	320 ±	360 -	38	400 +	480 ±	
	—	35		240 +	280 -	30	320 +	360 ±	
	—	32		240 +	280 -	27.5	240 +	280 +	320 ±
	—	30.5		200 +	240 -				
	—	27.5		160 +	200 -				

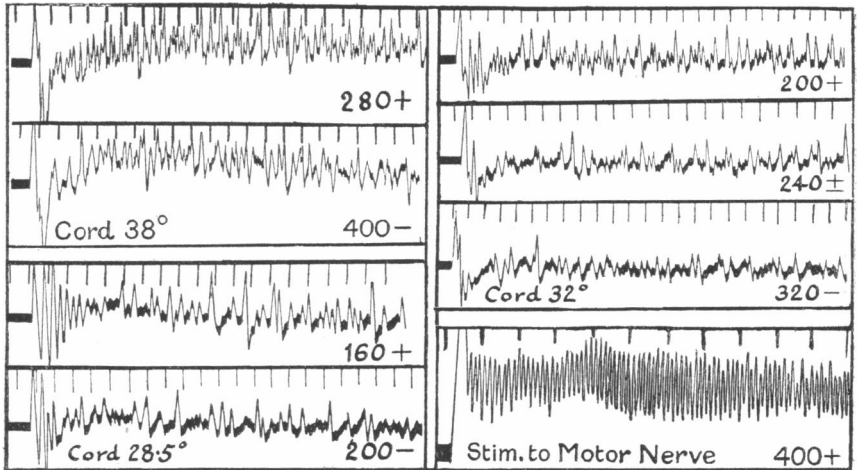


Fig. 3. Maximum frequency of reflex response with spinal cord at different temperatures, muscle at 38° C. throughout. String tension 5 mm. per mv.

Cord 38°, stim. 15 units (17 times threshold).

280 per sec. regular.

400 per sec. irregular.

Cord 28.5°, stim. 30 units (13 times threshold).

160 per sec. regular.

200 per sec. irregular.

Cord 32°, stim. 15 units (9 times threshold).

200 per sec. regular.

240 per sec. doubtful.

320 per sec. irregular.

Stimulus to motor nerve. 15 units (12 times threshold).

400 per sec. regular.

it lies between 200 and 240. Records from the last and most complete experiment are shown in Fig. 3, together with a record obtained subsequently by stimulating the motor nerve. This has been enlarged to show the very high frequency which can be followed by the muscle.

These experiments show that cooling limited to the spinal cord

causes a reduction in the maximum frequency of reflex response in the muscle, but caution is needed before we draw more detailed conclusions. In the first place the reduction may have been due to the lengthening of the refractory period of the motor and sensory fibres in the spinal roots. This possibility may be dismissed at once. When the muscle itself is cooled to 27.5° C. and stimulated by way of the motor nerve, the maximum frequency of response is still as high as 240 a second. That of the nerve cannot well be less than this and will be almost certainly greater, so that the maximum reflex frequency of 160–200 with the cord at 28° cannot be due to the cooling of peripheral nerve fibres. Neither can it be due to the inability of the muscle to respond at a higher frequency, for the muscle is kept at 38° and is able to respond at 400 a second to motor nerve stimulation. Evidently the limit of 160 a second is imposed by the central nervous system when the cord has been cooled. When the cord is at its normal temperature, however, the maximum frequency of discharge will naturally be greater than 160 a second and it may then surpass the ability of the muscle to respond. We have therefore to decide what will be the maximum frequency of discharge when the cord is at 38°, granting that the frequency at 28° is 160 a second. We are handicapped by the lack of exact knowledge of the temperature coefficient of the recovery process in the spinal centres, but direct measurements of the coefficient can be made in the case of the muscle and it is probably safe to assume that much the same value will hold good for the cord. Table III gives the results of a series of experiments in which the motor nerve is stimulated and the maximum

TABLE III.

Exp.	Temperature of muscle	<i>Stimulus to motor nerve.</i>			
		Maximum regular response			
2	40°	360 +	400 ±		
9	34.5	360 +	400 ±		
	28		320 +	360 -	
10	38	400 +	480 ±	640 -	
	30	320 +	360 ±	640 -	
	27.5	240 +	280 ±	320 ±	
11	39		400 +		
	29		320 +	360 -	
12	33.5		400 +	440 -	
	40		560 +		
13	30.5		320 +	360 -	
	38		400 +	440 -	
	29.5		320 +	360 -	
	35		360 +	400 -	
	40		440 +	480 -	
	30		320 +	360 -	
	25	240 +	280 ±	320 -	

frequency of regular response (defined as before) is measured at different temperatures. Fig. 4 shows the measurements in Exp. 13 and it will be seen that a rise of temperature from 30–40° increases the maximum

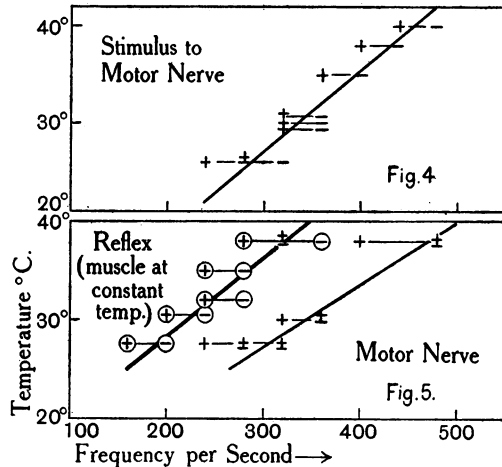


Fig. 4. Effect of change of temperature on maximal frequency of response in tibialis anticus to stimuli applied to motor nerve. Stimuli 27 units strength (7.3 times threshold). Exp. 13.

Fig. 5. Effect of change of temperature of spinal cord on maximal frequency of reflex response, the muscle remaining at 38° throughout (Exp. 10). The curve on the right gives the maximum frequency for the muscle at different temperatures with motor nerve stimulation.

frequency from about 320 to 440. This gives a coefficient of about 1.4 for a ten degree rise between 30 and 40°. If we take this as applying to the maximum frequency of discharge from the cord, and if the frequency at 28° is 160–200 a second, the frequency at 38° should be 220–280 a second—and this agrees fairly well with the observed maximum frequency of reflex response in the muscle when the cord is at 38°.

Suppose, however, that the low temperature imposes an abnormally slow rate of discharge because it interferes with the function of the cord in some way over and above that due to the slowing of the recovery processes. The temperature coefficient might then be considerably higher than 1.4 and the cord at 38° might really be able to discharge as rapidly as *e.g.* 500 a second, though the muscle would be unable to follow this rate. If so, we ought to find that cooling the cord from 38° will cause no change in the maximum frequency of the muscle response until the temperature has fallen to such an extent that the cord can no longer discharge too rapidly for the muscle to follow, and further cooling below

this temperature will produce a sudden reduction in frequency. The curve relating the temperature of the cord to the maximum frequency of response ought therefore to show a discontinuity somewhere between 28° and 38°. In Fig. 5 the results of Exp. 10 are shown graphically and there is evidently no such discontinuity. The maximum frequency of the reflex response increases in a perfectly regular way with the temperature of the cord. The rate of increase is slightly greater than in the case of the muscle at different temperatures stimulated by the motor nerve, but the difference is not outside the range of error. It seems clear, therefore, that the value of 240–320 a second for the maximum frequency of reflex response with the cord at 38° represents the maximum frequency of discharge from the cord and not the maximum frequency which the muscle can follow.

A comparison of the two curves in Fig. 5 shows that if the temperature of the whole animal is reduced, the maximum frequency in the reflex is always slightly less than the frequency which the muscle can follow at that temperature. The difference is not great, and if the muscle alone were cooled it might cease to be able to respond to the highest frequency which the cord can send to it. In a cat which has just been anaesthetised the temperature in the substance of the tibialis anticus has been as low as 34° C. although the rectal temperature was 38.5°, but even with this difference the muscle should still be able to follow the highest rate of discharge from the cord.

Frequency of response with other reflex arcs. Beritoff has shown that the maximum reflex frequency is about 300 a second in the flexors and in the extensors of the thigh and our own experiments now give the same value for the tibialis anticus. We have also tried the effect of stimulating the internal saphenous instead of the popliteal and have found the same maximum frequency in the tibialis anticus. In four experiments we have stimulated the descending tracts of the spinal cord by small bipolar electrodes thrust into the exposed cross section of the cord in the cervical region. The effect of stimulation is to produce sometimes flexion and sometimes extension in the legs and the galvanometer leads are placed on whichever muscle is most active. With frequencies of stimulation below about 80 a second the contractions are often feeble and the responses of the muscle may be irregular. With higher frequencies (80–160 a second) the rhythm of the stimulus generally appears on the muscle response, though a complete lack of any regular frequency is not uncommon. The highest regular frequency we have recorded is 280 for occasional short periods and 240 for $\frac{1}{2}$ sec. or more,

the muscle being the gastrocnemius. Destruction of the cord in the cervical region put a stop to the responses, so that the stimuli presumably took effect on the descending tracts in the cervical region and did not spread down the cord. These experiments are too few to generalise from, but they suggest that the motor centres for the hind limb muscles, through whatever paths they are activated, will not send out a regular succession of impulses to the muscles at a frequency greater than 240–320 a second. There is, of course, the alternative possibility that 320 a second is all that the muscles can do, but in one muscle at least, namely, the tibialis anticus, our results show that motor nerve stimulation will give definitely higher rhythm.

“Repetitive Discharge” from the spinal cord. Forbes, Ray and Griffith⁽⁵⁾ have raised the possibility that in response to a single afferent stimulus each neurone of the motor centre may discharge, not a single impulse, but a succession of impulses occurring at so high a frequency that the muscle can only respond to the first of the series. If each stimulus produces a group of these high frequency discharges, the response to reflex stimulation in the motor nerve and in the muscle might be represented graphically as in Fig. 6.

If this suggestion is correct the maximum frequency of regular response in the muscle may depend, not on the maximum frequency with which the cord can discharge impulses, but on the duration of each group which it discharges—for the muscle response will become irregular (if it does not cease altogether) as soon as the successive groups coalesce.

There is no doubt that under certain conditions a single impulse in the afferent nerve may produce a multiple discharge in the efferent, for the electric response of the muscle may be multiple. In this case, however, the impulses in the motor nerve are obviously spaced in such a way that the muscle gives a succession of responses, and we have no

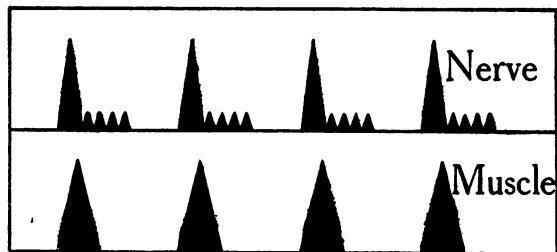


Fig. 6. For description see text.

direct evidence of a discharge of impulses from the cord at so high a frequency that the muscle only responds to the first of the series. That such a grouping of impulses determines the maximum frequency of reflex response seems to be ruled out by the experiments in Table II, where the cord was cooled. If the maximum frequency is fixed by the length of each group of impulses, as in Fig. 6, a reduction in frequency must be due to a greater duration of each group. The interval between the successive impulses in the group cannot be increased to any considerable extent or the muscle will give a multiple instead of a single response; thus the number of impulses in each repetitive discharge should increase when the cord is cooled. But cooling the cord does, in fact, reduce the tendency to repetitive discharge, or at any rate to that form of discharge which gives a multiple response in the muscle. This may be seen from Fig. 7, which gives the response of the muscle in

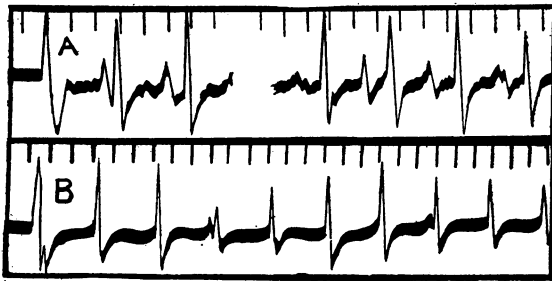


Fig. 7. Disappearance of "repetitive response" when cord is cooled.

Exp. 10. A. Spinal cord and muscle at 38° . Reflex response to stimuli at 17 per sec., 3 units strength.

B. Cord at 35° and muscle at 38° . Stimuli 17 per sec., 3 units.

Exp. 10 to reflex stimulation at 16 a second with the cord at 38° and at 35° . With the cord at 38° and stimuli 3.5 times the threshold strength (3 units) the response consists of large "primary" waves at the frequency of stimulation with many small secondary waves between them. At the lower temperature with the same stimulus no secondary waves appear. The same disappearance of repetitive response in the muscle was observed in other experiments in which the cord was cooled.

Again, if we compare the flexion reflex in a number of spinal preparations we find that the duration of the repetitive response in the muscle with low frequencies of stimulation varies within wide limits. Adrian and Olmsted stated that very strong stimuli were necessary to produce repetitive responses, but later work has shown that this is

only true of preparations observed fairly soon after decapitation when the effects of shock and of the anæsthetic are probably still considerable. A preparation with brisk reflexes, observed some hours after decapitation will generally give a record like that of Fig. 7A, with stimuli only 5-10 times the threshold strength, but another, less active, may need much stronger stimuli before any secondary waves appear. Yet both will give the same maximum frequency of reflex response, and the length of time after decapitation makes no difference to the result. In the same way we find a much greater tendency to repetitive response in decerebrate as compared with spinal animals(6), but the maximum regular frequency in the reflex is the same in both. It is, therefore, highly improbable that this frequency depends on a particular grouping of repetitive discharges from the spinal cord.

Frequency of discharge with other forms of reflex stimulation. When a spinal cat carries out the flexion reflex in response to a mechanical stimulus such as pinching the skin of the foot, the electric response of the tibialis anticus consists of a series of oscillations, irregular in frequency and amplitude and occurring at an average rate of 150-200 a second. A response of this kind in the muscle might be produced by impulses discharged from the spinal centres at the same frequency as that appearing in the electromyogram, or at a frequency much too rapid for the muscle to follow. In the latter case the frequency of discharge from the cord would have to be well over 500 a second, for with lower frequencies the muscle would be likely to show a regular 2 : 1 response. The experiments already described suggest that the former explanation is correct, for the spinal centres appear to be unable to discharge at a frequency too great for the muscle.

The question needs further investigation, however, for it has been the subject of considerable discussion and it is vital to the interpretation of the electromyogram. In some recent work on the frog we have given a brief account of the main arguments involved(7). In this work we concluded that the frequency shown in the electromyogram was generally identical with the frequency of discharge from the cord, since there was little or no change in rate when the temperature of the muscle was altered within limits, provided that the temperature of the spinal cord remained unchanged. In these experiments the muscle was generally warmed above the general body temperature, since there was some danger that cooling would make it unable to keep pace with the discharge from the cord although it had been able to do so at normal temperature. In mammalian experiments the muscle cannot be warmed above 38° without

danger of damage from heat rigor, but if the rate of discharge from the cord is not higher than about 200 a second it ought to be possible to cool the muscle through 10° or more without interfering with its ability to respond to every impulse from the cord.

We have made three experiments in which reflex contractions were provoked by pinching the foot, the temperature of the tibialis anticus being varied from 22° to 40° C. Typical records of the electric response at different temperatures are given in Fig. 8. Evidently a change of 10° in

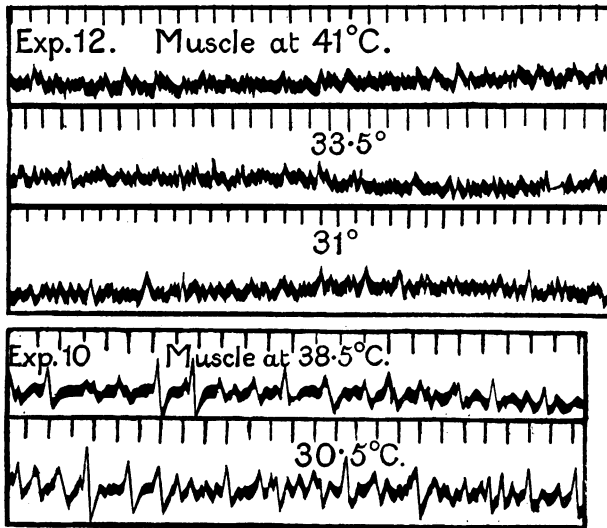


Fig. 8. Flexion reflex produced by pinching foot. Response of tibialis anticus. Temperature of cord remains constant and temperature of muscle is changed. The frequency of the responses remains unaltered. Tension 5 mm. in both experiments.

the muscle makes no obvious difference to the frequency of the reflex electromyogram, though the response is so irregular that the oscillations have to be counted over considerable periods before we can be certain. In Table IV the actual frequencies are given, the total number of oscillations being counted in periods of $\frac{1}{10}$ second taken at random from different parts of the record. There is no evidence that the frequency is altered by a change of temperature of 10° in the muscle, though the total number of oscillations in a second is reduced slightly when the muscle is cooled as low as 22° C.

To determine how great a change in frequency should occur if the muscle were responding to a series of excitations too rapid for it to follow, we have taken records from the cat's tibialis anticus, at different

TABLE IV.

Exp.	Temperature		Reflex response to pinching.					Average
	Rectal	Muscle	Frequency per sec. in periods of $\frac{1}{17}$ sec.					
10	38°	32°	150	140	130	140	140	140
	—	38.5	100	130	110	90	120	110
	—	38	120	140	120	130	100	122
	—	30.5	140	100	110	130	140	124
	—	31.5	120	130	120	90	140	120
12	38.8	40	190	180	210	180	180	188
	—	33.5	200	190	200	180	170	188
	—	41	190	150	180	170	210	180
	—	31	170	180	190	180	190	182
	—	40	160	200	180	170	180	178
14	38.5	39	190	230	190	200	210	204
	—	40.5	200	210	200	190	240	208
	—	32	270	220	260	240	220	242
	—	29	240	220	240	200	210	222
	—	22	200	200	210	220	190	204
	—	38	200	200	210	270	230	222

temperatures, stimulated by the motor nerve at a frequency of 640–800 a second. The results are shown in Table V. The response of the muscle

TABLE V. Exp 13. Motor nerve stimulated at 640–800 a second.

Temperature of muscle	Irregular response in muscle. Frequency per second (average)
25°	220
29.5	220
30.5	200
35	270
38	300
40	320

was irregular in each case and the figures give the average frequency. This increases from 220 at 25° to 320 at 40°, giving a temperature coefficient of at least 1.3 for a change of 10°. A slightly higher coefficient is shown in Garten's results (8). Stimulating a rabbit's muscle nerve preparation with a constant current applied to the nerve, he found that the frequency of response in the nerve or muscle was about 100 a second at 25° and 180–400 a second at 37°. These results are not strictly comparable to those in Table V as a different type of stimulus is used, but it is probably safe to assume that a change from 28 to 38° would increase the frequency of the irregular response by at least 1.3 times. Table IV shows that in the reflex there is no such increase in frequency.

These records do not show that the spinal cord never discharges at a higher rate than that shown in the electromyogram, but merely that it does not do so as a rule. It is not uncommon to find small groups of four or five oscillations at a high frequency and these occur so irregularly that it is difficult to make sure whether their frequency is or is not

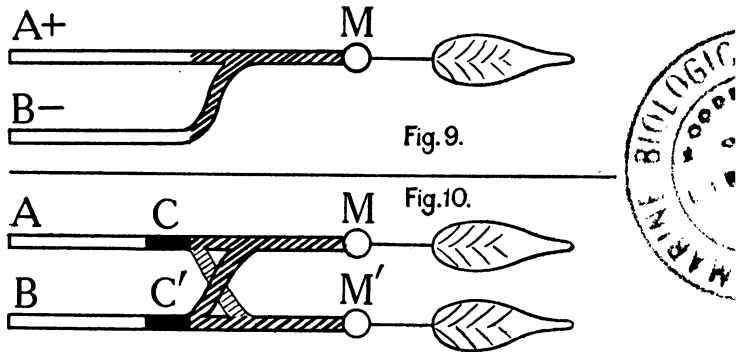
affected by a change of temperature of the muscle. Since the total number of oscillations in a second does not change appreciably, it is unlikely that there can be a change of frequency lasting for any appreciable fraction of the response. It is possible, therefore, that the frequency of discharge from the cord may occasionally become too fast for the muscle to follow, but by far the greater part of the reflex discharge must be composed of impulses with a frequency identical with that shown in the electromyogram.

DISCUSSION.

The chief interest of these results lies in the fact that the highest frequency of discharge from the cord is considerably smaller than the highest frequency of response in a motor or sensory nerve. The smallest interval between successive impulses leaving the cord lies between .004 and .003 second, whereas the smallest interval between successive impulses set up in a nerve by direct stimulation lies between .001 and .002 second. Presumably there exists somewhere in the grey matter of the cord a region which will only transmit impulses at 250-300 a second, although impulses at a higher frequency may be reaching it from the afferent part of the arc. The result will be that on the motor side of this limiting region the impulses will be so spaced out that each travels in a fibre which is well on the way to complete recovery after the passage of the previous impulse.

This conclusion has a bearing on the suggestion that the mechanism of central inhibition is comparable to that of Wedensky inhibition in a muscle nerve preparation. The basis of the Wedensky phenomena is that impulses recurring at a high frequency may fail to pass a region of decrement because the tissue will have no time for complete recovery between successive impulses and so each will be of small size and unable to travel far without extinction. A region so occupied by a rapid series of small impulses will be unable to transmit any other impulses which may reach it in addition to the inhibiting series. Fig. 9 shows how this type of inhibition might occur in the central nervous system. *A* is an excitatory nerve and *B* an inhibitory, *M* is the group of motor neurones on which they take effect. The shaded region conducts imperfectly and part of it is common to both arcs. Assume that the decrement is so adjusted that impulses from *B* can never reach *M* whatever their frequency, whereas impulses from *A* can do so provided that the region is given time for complete or almost complete recovery between each impulse. If we stimulate *A* at a fairly low frequency, the impulses set up

will be able to pass through to *M*. If we stimulate *B* simultaneously, the impulses from *B* will not reach *M* but they will travel for some



Figs. 9 and 10. Scheme of central connections for excitatory and inhibitory arcs. The shaded areas conduct with a decrement and the black areas limit the frequency of impulses to 250-300 a second.

distance over the same path as the impulses from *A* and the overcrowding which results will reduce the size of the impulses from *A* and make them no longer able to reach *M*. Thus the stimulus at *B* will give rise to inhibition.

The likelihood of some such process actually taking place when an inhibitory nerve is stimulated has been greatly strengthened by the important work of Brücke (9) and of Beritoff (10). Brücke has shown that an impulse in the inhibiting afferent nerve has a maximum effect when it bears a definite phase relation to the impulse in the exciting afferent nerve, and Beritoff has shown that the inhibitory effect of each of a series of impulses lasts for about $\cdot 004$ second, so that there is a definite rhythm of inhibition corresponding to the rate of stimulation of the inhibitory nerve. Both lines of work suggest that the inhibitory effect of an impulse is closely connected with the refractory phase (absolute and relative) which accompanies it. If we assume that the inhibitory effect is due to the delay of recovery which the impulse will produce in the decremental region, we can calculate the recovery time of this region as follows. Since Beritoff finds the effect of each impulse lasting for $\cdot 004$ second it follows that the decremental region cannot take less than this time for complete recovery. Adrian and Olmsted found that the part of the arc upon which anaesthetics take effect cannot take more than $\cdot 006$ second for complete recovery, and in view of the present results this time should probably be shorter. A region which conducts imperfectly

under normal conditions is likely to be affected by anæsthetics in preference to any other part of the arc and we may therefore conclude that in the decremental region the time for complete recovery after the passage of an impulse is not less than $\cdot004$ or more than $\cdot006$ second.

Now it is clear that the simple mechanism shown in Fig. 9 is not enough. It accounts for the fact that stimuli at *B* always inhibit, but not for the fact that stimuli at *A* always excite. Since the impulses are extinguished in the region of decrement if they follow one another too closely, we ought to find that a rapid succession of impulses from *A* would fail just as much as a slower succession from *A* combined with impulses from *B*. Actually we find that in a normal preparation very rapid stimulation of an excitatory nerve is as effective as slow stimulation. To account for this we must add to the scheme a region somewhere on the afferent side of the region of decrement which will prevent the passage of impulses from *A* at too high a frequency. Suppose, for instance, that the region marked *C* (Fig. 10) will only allow impulses to pass through at such a frequency that the decremental region has time for complete recovery between each impulse; then stimulation at *A* can never lead to inhibition although combined stimulation of *A* and *B* may still lead to overcrowding and extinction.

It will be seen that the experimental results agree in a remarkable way with the requirements of this scheme. Our results show that somewhere in the reflex arc there is a region which limits the number of impulses passing to 250–300 a second. We may reasonably locate this at *C* in the figure. The least interval between successive impulses entering the decremental region from *A* must therefore be $\cdot004$ – $\cdot0033$ second. We have calculated the time for complete recovery in the decremental region as somewhere between $\cdot004$ – $\cdot006$ second. Thus the least interval between successive impulses from *A* is long enough to admit complete or almost complete recovery in the decremental region, and it follows that stimulation of the excitatory nerve is never likely to produce inhibition whatever the frequency of the stimuli.

In the diagram the inhibitory impulses from *B* are represented as having to pass through a similar filter *C'* before they join the path from *A* to *M*. It will make little difference to the result whether such a filter is or is not present, for the only essential is that the impulses from *B* should always be extinguished before they reach *M* and that for the final part of their career they should travel over the same path as that of the impulses from *A*. With such an arrangement a single impulse travelling from *C'* towards *M* should produce inhibition for $\cdot004$ second.

To account for the more lasting inhibitory effect which may follow a strong single stimulus at *B* or a series of stimuli at low frequency, we have only to suppose that these produce a repetitive discharge of impulses in the inhibitory path from *C'* to *M* just as they do in the motor centres (*M'*) to which they lead. In fact the exact coincidence in the duration of the inhibitory and excitatory effects which result from stimulating an afferent nerve is readily explained if we suppose that the train of impulses passing from *C'* towards *M* is exactly similar to that passing from *C'* to *M'*.

The scheme of inhibitory and excitatory arcs shown in the figure differs in several respects from that given in Keith Lucas's book⁽¹¹⁾ and from the amplified form of this discussed by Forbes⁽¹²⁾; it has a closer resemblance to that given by Brücke. Our excuse for putting forward another modification with the same underlying principles is that we have now some of the numerical data which are needed to bring the scheme into closer relation with the facts of experiment.

SUMMARY.

Adrian and Olmsted stated that if the popliteal nerve of a spinal cat is stimulated rhythmically, the reflex response of the tibialis anticus shows rhythmic oscillations of the same frequency as the stimuli up to 160 a second. Beritoff has recorded a higher maximum frequency for the semitendinosus, namely, 250–300 a second, and we now find that this value applies also to the tibialis anticus, the lower figure depending partly on a different criterion of "maximum frequency" and partly on faulty galvanometric technique. The maximum frequency in our experiments ranges from 240 to 320 a second, though the latter value is only maintained for very short periods.

We have attempted to decide whether this maximum frequency is determined by some factor in the central part of the reflex arc or by the inability of the muscle to respond at a higher rate. We find that the muscle stimulated by its motor nerve will give a regular response at a frequency appreciably higher than that in the reflex, but the most conclusive evidence is given by experiments in which the temperature of the spinal cord is reduced whilst that of the muscle remains constant. This has the effect of reducing the maximum frequency of reflex response, though the ability of the muscle to respond at a higher frequency remains, of course, unchanged. We conclude that the maximum frequency of 240 to 320 a second represents the maximum rate at which the motor centre can discharge a regular succession of impulses.

The electromyogram of the flexion reflex evoked by pinching the foot shows irregular oscillations of an average frequency of 100–250 a second. These might be due to a discharge of identical frequency from the cord, or to one much too rapid for the muscle to follow (over 500 a second). If the latter interpretation is correct, a change of temperature in the muscle ought to change the frequency of the electromyogram, but we find that cooling the muscle through 10° C. makes no appreciable change in frequency. We have, therefore, no evidence that the rate of discharge from each motor neurone can exceed 240–320 a second. This conclusion, taken in conjunction with Beritoff's work on inhibition, leads to a simple explanation of the difference between excitatory and inhibitory arcs.

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On p. 464, line 5 from the top, omit "this." The passage should read "a retention of the testicle was caused without spermatogenesis (as we see) being necessarily inhibited."