

STUDIES ON THE INNERVATION OF SMOOTH  
MUSCLE. II. On the Frequency of Nerve Impulses Entering  
and Leaving the Superior Cervical Ganglion.

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INHIBITION of the smooth muscle of parts of the alimentary canal of the cat, by stimulation of the vagus nerve, resembles Wedensky inhibition so closely<sup>(1)</sup> that the relation of the frequency of discharge from peripheral nerve cells to the frequency of stimulation of the pre-ganglionic fibres assumes a special interest. The reactions of the alimentary tract indicate that this relation is a direct proportion. To obtain further evidence on the question, the present investigation was undertaken. It concerns the frequency of discharge from cells of the superior cervical ganglion of the cat in response to different frequencies of stimulation of the cervical sympathetic nerve, contraction of the nictitating membrane serving as indicator.

*Methods.* Seven experiments were performed, the results being uniform in all. Induction shocks, yielded by coils whose primaries were supplied with iron cores, were used for stimulation, the primary circuit being made and broken by rotary interrupters. A mercury-copper switch was placed also in this circuit. One of its arms was used to govern the duration of stimulation and to yield single makes and breaks, and the other was used to close the signal magnet circuit. In the first three experiments, the lower frequencies were supplied by an interrupter designed by Keith Lucas and described by Adrian<sup>(2)</sup>, and the higher frequencies were given by a contact breaker described by Adrian and Olmsted<sup>(3)</sup>. In the case of the latter, the duration of closure of the primary circuit was about 50 p.c. The former gave interruptions ranging from 1.03 to 31 per second when the circuit was made and broken through a contact operated by the cam wheel,  $D_2$ , in Adrian's figure, the interval between the make and the succeeding break shock being about  $15\sigma$ . As a rule, however, the series of cam wheels,  $E$ , was used to interrupt the current. This yielded frequencies from 1.03 to 15.5 per second, the interval between make and break being about  $30\sigma$ . In the last four experiments a new contact breaker similar to that described

by Adrian and Olmsted was employed. It differed from the latter, however, in this respect. One of the 16 conducting brass segments was extended laterally, beyond its fellows, in the surface of the fibre cylinder, so that with the proper position of the contact brush on the cylinder surface, only one contact per revolution was given. Its duration was about  $\cdot 032$  of that of a revolution. For interruptions from 2.5 to 32 per second, the single contact only was used, but for higher frequencies, the series of segments was employed. For the latter, the duration of closure of the primary circuit was about 48 p.c. The primary current was supplied by a 2-volt accumulator. For the purpose of obtaining thresholds, in the four experiments for which they are given, the same inductorium was used exclusively. This coil was used throughout in the last three of these, the primary current being adjusted to  $\cdot 09$  ampère. The number of interruptions of the primary current per second was taken as the frequency of stimulation, though both make and break shocks affected the nerve. The estimation was not considered accurate beyond the second figure. No extra resistance, other than that of the tissue stimulated, was placed in the secondary circuit.

Each cat received subcutaneously 0.75 to 1 grm. urethane per kilogram of body weight, and about one hour later, the anæsthesia was completed by chloroform. A tracheal cannula was inserted and the anæsthesia was maintained by a mixture of chloroform and ether when required. The animal's head was so adjusted that the nictitating membrane could be attached to the writing lever without friction of the connecting thread with the eye or the apparatus. Regularly the eyelids were cut off, and occasionally the contents of the eyeball were removed, to allow free movement of the membrane. A silk thread connected the middle of the free margin of the membrane with a small metal bar, cemented vertically and at right angles to a delicate lever near its fulcrum. This lever, to which a fire-polished glass writing point was attached by a flexible strip of paper, recorded the movements of the membrane on the kymograph paper. The magnification varied from 6 to 9.5 fold, and the load varied probably between the limits of 2 and 5 grm.

The cervical sympathetic was tied, cut, and isolated low in the neck for 3 to 4 cm. of its peripheral course. For stimulation, it was placed between two silver wire electrodes about 0.5 mm. in diameter and occasionally a glass shield<sup>(4)</sup> was used. The nerve remained in better condition, however, when it was kept covered with the tissues, being removed and placed on the electrodes only at times of stimulation.

After observations with the pre-ganglionic fibres had been completed, the post-ganglionic fibres, in all experiments except the first, were isolated and stimulated. The cervical sympathetic, for this purpose, was isolated up to the superior cervical ganglion; this ganglion was separated from the ganglion nodosum, and the post-ganglionic fibres were freed from their surroundings for several mm. A silk ligature was tied tightly about the nerve bundle at the cephalic end of the ganglion to cut off any possible effects of the ganglion cells. On one occasion, the pre-ganglionic fibres were faradized after this ligation, and there was no trace of contraction. The vagus was removed then from a point several mm. cephalad of the ganglion nodosum to a point several cm. caudad of it. To stimulate the post-ganglionic fibres, the electrodes were held peripheral to this ligature by the hand, and the nerve bundle was drawn between them. As a rule, the cathode for the break shocks was peripheral to the anode for both pre- and post-ganglionic fibres. In the case of the former, the electrodes were probably not more than 3 mm. apart, and for the latter, this distance was probably less than 2 mm.

The usual procedure of stimulation was the following. The threshold was first determined, the smallest contraction of the muscle detectable by the lever method being used as indicator. The usual frequency chosen for this purpose was 165 per second, though others were used at times, and the faradization was prolonged for 15 seconds unless contraction appeared sooner. The secondary coil was approximated then several centimetres from the threshold position toward the primary, to insure stimulation of all of the nerve fibres. The distance of approximation was usually about the same for both pre- and post-ganglionic fibres, and it was so chosen, as a rule, that the single break of the primary circuit caused distinct contraction. The nerves were then subjected to periods of faradization, usually about one second in duration, but occasionally considerably longer, and the corresponding contractions were recorded. Intervals of one to several minutes, depending on the time required for relaxation, separated the periods of faradization.

Special procedures involved in cooling the interior of the eyeball and the nictitating membrane, and in stimulating the nerve of the nerve-muscle preparation will be described in connection with the results obtained.

#### *Results.*

All the data obtained on thresholds are given in the following table. In every instance, the threshold for the post-ganglionic fibres was decidedly higher than that for the pre-ganglionic. In Exps. 3 and 4,

moreover, a greater approximation of the secondary was required, in the case of the former, for the low frequencies of 10.6 and 11.8 than for 165. Single makes and breaks, from closing and opening the mercury-copper switch, also caused contraction, the latter being more efficient for both pre- and post-ganglionic fibres. Little effort was made to determine the minimal intensity of stimulus required for this effect, but in Exp. 2, distinct contraction occurred with a secondary position of 13 cm. for the right pre-ganglionic fibres, in response to the break, and at 7.5 cm. for the right post-ganglionic. The shocks became perceptible to the tongue with a position near 8 cm.

Exp.	Primary current (amp.)	Side stimulated	Frequency (per sec.)	Threshold (cm. distance of secondary)	
				Pre-ganglionic	Post-ganglionic
1	.14	Right	90	12.9	11.8
			136	—	11.5
2	.09	Right	165	13.9	11.5
		Left	165	13.0	10.6
3	.09	Right	165	13.6	12.2
		Left	165	13.0	12.2
			10.6	—	10.8
4	.09	Right	11.8	13.0	6.6
			165	13.3	7.5

The contractions evoked by stimulation of both pre- and post-ganglionic fibres with a given frequency are of quite the same character, provided that due account is taken of the difference in threshold. Thus as the stimulus interval is diminished in brief periods of faradization, either centrally or peripherally of the ganglion, the magnitude of the contractions increases, within limits, progressively (Figs. 1 and 2). The maximum, with periods of about one second duration, is usually reached at 140 per second. In the production of this steady augmentation, the following factors are involved. The latent period tends to decrease, and the rate of development of contraction to increase, as the frequency becomes greater (Figs. 1 and 2). The extent of the shortening during stimulation, therefore, is augmented. The excessive rise in the curve in Fig. 1, *F*, is probably due to the fact that the corresponding period of stimulation was somewhat longer than that immediately preceding and succeeding it. The continuation of the process of shortening on cessation of stimulation, furthermore, increases both in extent and duration with elevation in frequency. This after-action is a striking feature of the progressive augmentation in contraction (Figs. 1 and 2).

The similarity in the character of the response to stimulation of the pre- and post-ganglionic fibres with the same frequencies was illustrated

also in the few observations made with more prolonged periods of faradization. The duration of stimulation was usually about 30 or 60 seconds. For the low frequencies, viz., 1, 1.03 and 3 per sec., the contraction develops relatively slowly, and for the first two, slight elevations

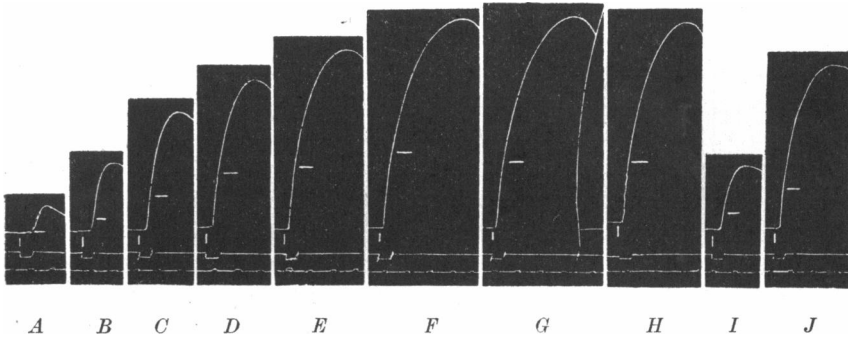


Fig. 1. *Exp. 4.* About  $\frac{1}{2}$  the original size. Right cervical sympathetic (pre-ganglionic fibres) and nictitating membrane. Position of secondary for observations, A to H, inclusive = 8.5 cm.; for I and J = 11.0 cm. Frequencies (interruptions per second): A = 2.95; B = 5.9; C = 11.8; D = 23.6; E = 47.2; F = 94.4; G = 142; H = 755; I = 472; J = 94.4. For this and Fig. 2: primary current = .09 ampère; magnification = 9.5; time is in 2 second intervals, and vertical and horizontal lines next to contraction curves indicate points on the latter corresponding to beginning and end of stimulation respectively.

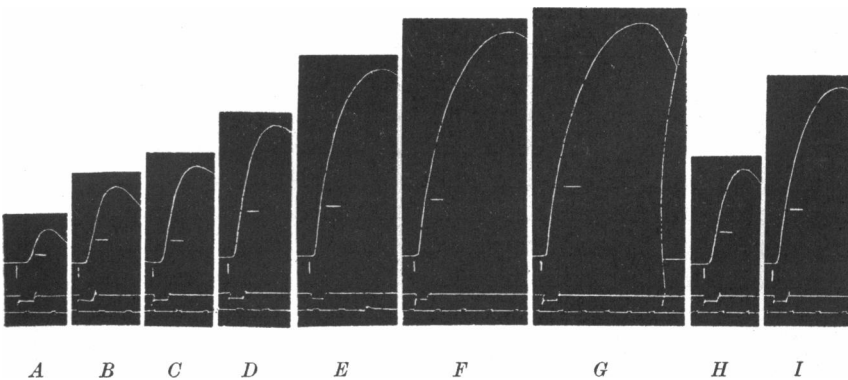


Fig. 2. *Exp. 4.* About  $\frac{1}{2}$  the original size. Right post-ganglionic fibres and nictitating membrane. Position of secondary for observations, A to H, inclusive = 3.0 cm.; for observation, I = 0.0 cm. Frequencies: A = 2.95; B = 5.9; C = 11.8; D = 23.6; E = 47.2; F = 94.4; G = 142; H = 755; I = 755. Otherwise as for Fig. 1.

appear on the contraction curve, corresponding to each interruption. The shortening increases more rapidly during the first 5 to 10 seconds of

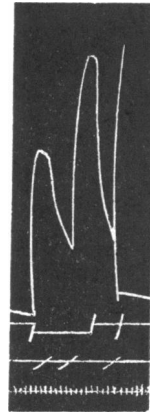
faradization, however, than later, when the curve tends to flatten. For the higher frequencies of 90 and 140, the contraction develops at first more rapidly, and it usually reaches a greater height than that produced by the lower. As faradization proceeds, however, the curve becomes much flatter, usually rising much more slowly in the later part of its course than that in response to the more widely separated stimuli. On cessation of stimulation with the different frequencies, the curve continues to rise or the muscle remains contracted, as a rule, for 1 to 2 seconds before relaxation begins. No pronounced difference in the contractions obtained thus, by stimulation of the pre- and post-ganglionic fibres with corresponding frequencies, was observed.

A further diminution in the interval between stimuli beyond that which suffices to yield the maximum contraction, in a series of brief periods of faradization, has one of two effects: the contractions are not much changed in magnitude, or a diminution occurs, becoming more marked the higher the frequency. If the strength of the stimuli is sufficiently great, the first result is obtained. It is a common occurrence, then, for frequencies up to 755 per second (the highest employed) to produce strong contractions on faradization of either pre- or post-ganglionic fibres (Figs. 1, *H*, and 2, *I*). In one experiment, the position of the secondary coil during a series of periods of stimulation of the post-ganglionic fibres remained unchanged, and the contraction in response to 595 per second was almost as great as that for 142. If the secondary is sufficiently far removed from the primary, however, the diminishing effect is well pronounced, as illustrated for the pre- and post-ganglionic fibres in Figs. 1, *I*, and 2, *H*, respectively. Thus in Exp. 3, a frequency of 94 produced pronounced contraction when applied to the left pre-ganglionic fibres. The shortening evoked by 380, however, was only about 0.7 as great, and 755 failed to produce a response. The position of the secondary for the three observations was 11.5 cm. A succeeding diminution in frequency, for either pre- or post-ganglionic fibres, under such conditions, evokes a stronger contraction. This effect is illustrated for the former in Fig. 1, *J*, and it was well marked for the latter, in Exp. 3, with a decrease from 189 to 142.

A striking difference occurs, when the diminution is pronounced, if the secondary is pushed toward the primary several centimetres and the nerve is faradized. The frequency which was formerly too high to produce strong contraction then causes a shortening of relatively great magnitude. The effect is illustrated in Fig. 2, *I*, the contraction often being relatively greater than that there shown. In Exp. 2, for example,

the contraction in response to a frequency of 575, and a secondary position of 5.0 cm., for the right post-ganglionic fibres, was greater than that produced by either 94 or 188 with a position of 7.5 cm. Likewise, in the same experiment, faradization of the right pre-ganglionic fibres at 377 per second and a secondary position of 6.0 cm., evoked a stronger contraction than 94 or 188 with a position of 9 cm. Similarly by weakening the intensity of stimulus, the effectiveness of a high frequency in evoking contraction is diminished for both pre- (Fig. 1, *I*) and post-ganglionic fibres. The diminishing effects, described in this and the preceding paragraph, involve a diminution in the after-action and in the rate of development of contraction, and usually an increase in the latent period. The augmentor effects, produced by increasing the intensity or decreasing the frequency of faradization, involve a reverse change in these factors.

In accordance with these results, alternately decreasing and increasing the interval between stimuli, in a single period of faradization, results in alternate diminution and augmentation in the extent of contraction respectively. For this reaction, however, the secondary coil must be sufficiently far separated from the primary, and the frequency must be sufficiently high. Furthermore, when partial relaxation has taken place as a result of the increase in frequency, strengthening the stimuli results at once in pronounced and well maintained contraction, as illustrated in Fig. 3. These procedures were carried out only with the post-ganglionic fibres.



In two experiments, an attempt was made to detect any modifying effect of the ganglion on the frequency of impulses passing through it by cooling the muscle of the membrane and its supplying nerve fibres. In the first of these, the pre-ganglionic fibres only were stimulated, but in the other, the pre-ganglionic of the right side and the post-ganglionic of the left were subjected to faradization. A wide transverse incision was made into the eyeball and its contents were removed. In the first experiment, a stream of cold

Fig. 3. *Exp. 2.* Right post-ganglionic fibres and nictitating membrane. Primary current = .09 ampère. Beginning with down-stroke of uppermost signal line, secondary position = 9.8 cm., and frequency = 142 per second. At first stroke on middle signal line, frequency increased to 283, and at second stroke, secondary pushed in to 8.5 cm. Time in 2.9 second intervals. Magnification = 6.

Ringer, from a supply surrounded with an ice-water bath was directed against the medial part of the interior of the eyeball and allowed to flow out over the membrane for several minutes. The contraction in response to stimulation of the pre-ganglionic fibres, with frequencies of 11.8 and 188, was only diminished thus and not abolished. The interior of the eyeball was filled, therefore, with ice, which was allowed to remain for several minutes, with the same results. The characteristics of the diminished contractions, for both procedures, were much the same as those for the second experiment. In the latter, ice-water was substituted for the Ringer solution, and the contraction in response to stimulation of both pre- and post-ganglionic fibres, for periods of about one second, was greatly reduced. The latent period was much prolonged, contraction often appearing only after stimulation had ceased, and its rate of development was much diminished. For the pre-ganglionic fibres, cooling for five minutes reduced the contraction in response to 142 per second to about 5 p.c. of its preceding value. Interruption of the cooling for five minutes resulted in a marked increase in the height of contraction, and it was resumed, therefore, for seven minutes longer. The contraction in response to 142 was reduced about the same as before, and that for an immediately succeeding period at 11.8 per second was still smaller. This condition, however, was followed by gradual recovery. In the series of observations on the post-ganglionic fibres, moreover, 142 produced a weak contraction, immediately after cooling for five minutes, but a succeeding period at 11.8 per second caused no perceptible mechanical change. This observation was of interest in connection with the fact that the latter frequency had produced a contraction only about one half as great as the former before cooling was begun, the duration of stimulation in all instances being about one second. Gradual recovery was evident, however, on interruption of the cooling. Faradization of both pre- and post-ganglionic fibres, on the whole, gave much the same results.

*The cause of the diminished effectiveness of relatively high frequencies.* The increase in the effectiveness of faradization with relatively high frequencies, produced by approximation of the secondary to the primary coil, suggested at once that overlapping of induction shocks was the cause of the diminished mechanical response. To test the probability that the shocks were reduced thus to sub-threshold magnitude for the nerve fibres, two experiments were performed on the nerve-muscle preparation of *Rana temporaria* by the following method. It was placed in a moist chamber at room temperature, and the muscle was attached



to a recording lever. The nerve was drawn between silver wire electrodes, the cathode for the break shocks, in most of the observations, being placed peripheral to the anode. The new rotary interrupter was employed together with the inductorium used exclusively in the last five experiments on the nictitating membrane. The primary current, supplied by a 2-volt accumulator, was kept constant at .09 ampère. No extra resistance, other than that of the sciatic, was placed in the secondary circuit. At the beginning of a series of observations, the threshold of the nerve was tested with a frequency of 5.9 per second, minimal contraction of the muscle being used as indicator. The nerve was then subjected to periods of faradization of progressively increasing frequency, and the threshold was tested for each. Succeeding the determination for each of these frequencies, however, the threshold was again determined for 5.9 in order that variations in excitability might be followed. In each observation, stimulation was continued for ten seconds unless contraction appeared sooner.

The excitability of the nerves gradually rose, during a period of about two hours after excision of the preparations, to a more or less

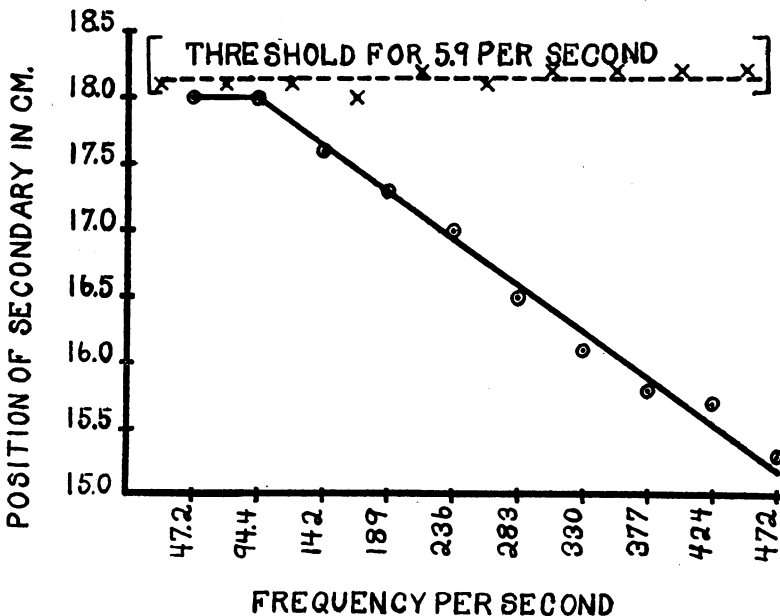


Fig. 4. Graphs illustrating the decrease in stimulating efficiency of the induction shocks as the frequency of interruption is increased above 94 per second. Stimulation of the sciatic of the nerve-muscle preparation of *Rana temp.* Cathode for breaks peripheral to anode.

constant value. Both during the rise and the relative constancy, however, as the frequency was increased progressively above 94 per second, the effectiveness of the shocks diminished. It was necessary to approximate the secondary progressively nearer the primary, from the threshold position for 5.9, to obtain contraction. The results of a series of observations, during which the excitability remained quite constant, are plotted in Fig. 4.

This procedure has since been carried out with two other preparations, by one of us (V.), the duration of the shocks being shortened by removal of the iron core from the primary (10, pp. 412 and 413). The threshold position for frequencies up to 565 per second remained practically the same, under these conditions, as in the intercalated observations at 5.9. For the latter, however, a slightly greater approximation of the coils was usually required. Definite data for frequencies above 565 were not obtained. As an example of the constancy in the ability of the different frequencies to excite, the following table is given.

Frequency per sec.	...	5.9	189	5.9	283	5.9	377	5.9	472	5.9	566	5.9
Threshold (cm. distance of secondary)	...	11.1	11.3	11.0	11.3	10.8	11.3	11.0	11.3	11.2	11.3	11.1
Time (p.m.)	...	4.00	4.04	4.05	4.07	4.10	4.14	4.18	4.21	4.24	4.28	4.32

The ineffectiveness of a relatively high frequency, in contrast to the excitatory action of a lower frequency, is further illustrated in Fig. 5.

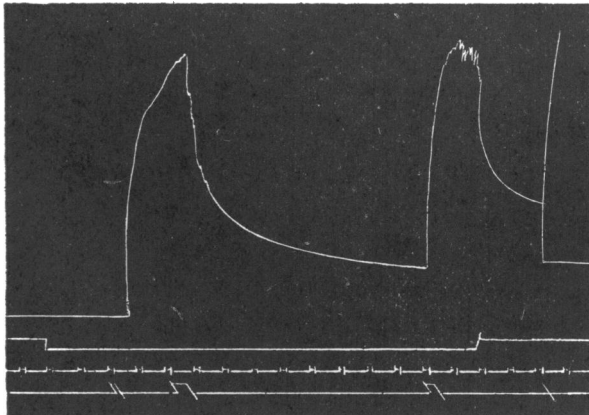


Fig. 5. Nerve-muscle preparation of *Rana temp.* Stimulation of sciatic with cathode for break shocks peripheral to anode. Intensity of primary current = .09 ampere. At beginning of faradization (uppermost signal line), position of secondary = 17 cm., and frequency = 472 per second. At first signal on lowermost signal line, frequency lowered to 47.2; at second signal frequency increased to 472, and at third, secondary pushed in to 13.5 cm. Time in 2 second intervals.

The arrangement of the apparatus was the same as that described above. No trace of contraction of the gastrocnemius was produced by 472 at the beginning of the period of faradization, but lowering the frequency to 47.2 sufficed to cause strong tetanus. The relaxation, which took place with the succeeding elevation to 472, furthermore, was changed to pronounced contraction by pushing the secondary towards the primary.

In these experiments, moreover, it was found that the shocks might be slightly too weak to cause contraction at the beginning of a period, and yet produce weak twitches at irregular intervals, if the faradization was continued. With sufficiently weak shocks, these twitches were often separated by intervals of two seconds or more, though the frequency of interruption was quite high.

*Discussion.* It is obvious from the results of these experiments that the frequency of discharge from the cells of the superior cervical ganglion is proportional to the frequency of disturbances delivered to them from the pre-ganglionic fibres. The similarity of the contractions for the same frequencies of stimulation of the pre- and post-ganglionic fibres, furthermore, would indicate that the propagated disturbances in passing through the ganglion are not altered decidedly in frequency. A definite statement in regard to the ratio of frequency of reception to that of discharge, however, is probably not warranted, for single stimuli might have evoked more than one response in either pre- or post-ganglionic fibres (5), (6), (7). Irregularities in contact, moreover, might have produced at times a larger number of shocks than that indicated by the frequency of interruption. This possibility of contact irregularities must be taken into consideration also with the observations on the single make and break of the primary circuit, which confirm those of Lewandowsky (8).

It is also evident that Wedensky inhibition does not occur to a marked degree on faradizing the pre- or post-ganglionic fibres with frequencies up to 755 per second (the highest employed). The diminished effectiveness of the relatively high frequencies is chiefly the result of reduction of the induction shocks by overlapping to sub-threshold magnitude for the nerve fibres. That this is the case is shown not only by the experiments on the nerve-muscle preparation, but also by the fact that increasing the strength of the high frequency stimuli produces strong and well-maintained contraction. The relaxation of the nictitating membrane obtained recently by Querido (9), on increasing the frequency of faradization of the post-ganglionic fibres, probably has the same

explanation. It appears from the work of Erlanger and Garrey<sup>(10)</sup> that overlapping may begin in the inductorium of the design used by Querido at frequencies as low as 54 per second. The occurrence of the effect more readily for the post-ganglionic than for the pre-ganglionic fibres, in Querido's experiments, probably has its explanation in the higher threshold of the former to induction shocks (cp. (11)).

The character of the diminished contraction obtained, when the frequency of faradization is sufficiently increased, is probably the resultant of two factors: (1) stimulation of only part of the nerve fibres, and (2) stimulation of at least some of these at a relatively low frequency. That the latter factor is involved is indicated by the similarity of such contractions to those produced with stimuli relatively widely separated. Irregularities in the magnitude of the induction shocks, with the higher frequencies of faradization, might lead to the occurrence of infrequent effective stimuli, which would produce a shortening of this sort. Evidence for this statement is given by the occurrence of separate twitches of the gastrocnemius in response to weak faradization of the sciatic with quite high frequencies.

The continuation of contraction of the nictitating membrane, on cessation of stimulation, is probably the result of the slow subsidence of a process set up within the muscle cells. The cells of the superior cervical ganglion are apparently not concerned in this after-action, for it occurs without decided change on stimulation of the post-ganglionic fibres. Experiments with nicotine<sup>(12)</sup>, (8, p. 353, footnote), especially those of Langley, show quite conclusively, furthermore, that the pre-ganglionic fibres end about these cells. Inasmuch as the after-shortening is directly proportional in extent to the frequency of stimulation of the nerve fibres, within limits, and with brief periods of faradization, it is probably similarly related to the frequency of propagated disturbances delivered to the smooth muscle cells.

#### SUMMARY AND CONCLUSIONS.

1. The frequency of discharge from the cells of the superior cervical sympathetic ganglion of the cat is directly proportional to the frequency of reception from the pre-ganglionic fibres. It is probable, furthermore, that the propagated disturbances in passing through the ganglion are not altered decidedly in frequency (Figs. 1 and 2).

2. An erroneous impression of Wedensky inhibition may be derived from the diminished effectiveness of relatively high frequencies of faradization, when applied to either the pre- or post-ganglionic fibres

(Figs. 1, *I*; 2, *H*, and 3). The weak contraction is more readily obtained with the latter, however, because of their higher threshold to induction shocks. The cause of the diminution is shown to be the reduction of the shocks by overlapping to sub-threshold magnitude for the nerve fibres (Figs. 1, *H*; 2, *I*; 3, 4, and 5).

3. A continuation of shortening on cessation of brief periods of faradization is described, and its extent is shown to be directly proportional, within limits, to the frequency of stimulation (Figs. 1 and 2). It is probably the result of a process established within the smooth muscle cells, which is directly dependent, in the extent of its action, on the frequency of propagated disturbances delivered to them.

## REFERENCES.

1. Veach. *Amer. Journ. Physiol.* 71. p. 229. 1925.
2. Adrian. *This Journ.* 54; *Proc. Physiol. Soc.* p. xxvi. 1920.
3. Adrian and Olmsted. *This Journ.* 56. pp. 432 and 433. 1922.
4. Sherrington. *Ibid.* 38. p. 382. 1909.
5. Garten. *Ztschr. f. Biol.* 52. p. 552. 1909.
6. Forbes and Gregg. *Amer. Journ. Physiol.* 39. p. 203. 1915.
7. Adrian and Forbes. *This Journ.* 56. p. 316. 1922.
8. Lewandowsky. *Arch. f. Physiol.* 1899, p. 352.
9. Querido. *Amer. Journ. Physiol.* 70. p. 29. 1924.
10. Erlanger and Garrey. *Ibid.* 35. p. 460. 1914.
11. Lapique and Legendre. *C. R. Acad. Sci.* 157. p. 1165. 1913.
12. Langley. *This Journ.* 27. pp. 226 and 227 (1901); 22. p. 221 (1897); 23. p. 240 (1898).  
Langley. Schäfer's *Text-book of Physiology*, 2. pp. 621 and 622. 1900. Langley and Dickenson. *This Journ.* 11. p. 510. 1890.