ON THE RELATION BETWEEN THE EXTERNAL STIMULUS APPLIED TO A NERVE AND THE RESULTING NERVE IMPULSE AS MEASURED BY THE ACTION CURRENT.

By C. W. Greene.

Instructor in Physiology, Stanford University.

[From the Physiological Laboratory of the Johns Hopkins University.]

The experiments described in this paper were undertaken with the idea of ascertaining the quantitative relation between the strength of the external stimulus applied to the nerve, and the strength of the resulting nerve impulse. The nature of the nerve impulse is as yet undetermined. We may recognize its presence in the nerve, however, in two ways: by the change in the electrical condition of the nerve fibres which accompanies the nerve impulse, or by the changes produced in the peripheral organ in connection with the nerve. In the latter case the quantitative changes in the peripheral organ obey laws peculiar to the organ itself, and cannot, therefore, be used directly as an index to the quantitative changes in the nerve fibres.

On the other hand, the changes in the electrical condition of the nerve are immediately associated with and are presumably the direct result of the changes constituting the nerve impulse. The intensity of the electrical change is measurable in the form of the action current. In the experiments described in this paper the action current is taken throughout as a measure of the intensity of the nerve impulse, it being assumed, in accordance with recent authors,¹ that the action current varies proportionately with the change constituting the nerve impulse.

In support of this assumption we may refer especially to the work of Waller, who has made extensive use of the action current in the study of the reactions of nerve fibres to anaesthetics and to many of

¹ A. D. Waller: Brain, xviii and xix; and Journal of physiology, xviii, p. xxxviii.

the chemical reagents used in experimental physiology and in medicine. His work offers strong presumptive evidence in favor of the view that there is a direct relation between the action current and the nerve impulse.

Waller also made observations on the relation between the strength of the external stimulus and the resulting electrical change in the nerve. He reached conclusions which will be discussed later in the paper.

**METHODS AND APPARATUS.**

Determinations of the quantitative relation between the strength of the external stimulus applied to a nerve and the strength of the resulting nerve impulse were made on isolated nerves from the frog (Rana virescens), the terrapin (Pseudemys, two species), the cat, and the dog. The particular nerves used were the sciatic, ulnar, and vagus. Isolated pieces of nerve five to six centimetres in length were used for experimentation. During an experiment the nerve was laid across two pairs of nonpolarizable electrodes in a moist chamber, one pair of the electrodes being used to stimulate one end of the nerve, the other pair to lead off the action current from the other end of the nerve to a very sensitive aperiodic galvanometer.

The form of stimulus used throughout the experiment was the induced current produced by a du Bois-Reymond induction coil. The secondary circuit included an automatic short-circuiting key, the stimulating electrodes, and an electrodynamometer. The short-circuiting key consisted of a small clock placed horizontally and carrying on its second-hand a platinum connector which revolved in two parallel circular mercury troughs. One of these troughs was interrupted for a definite proportion of its circumference.

The intensity of the stimulus was varied by moving the secondary coil of the induction apparatus toward or away from the primary coil, according to the maker's scale of proportional currents, the intensity of the resulting current being measured by the electrodynamometer in the circuit. The primary circuit was fed by a large storage cell with sufficient resistance in the circuit to give a current of the desired intensity. This arrangement gave a practically constant current during the time limits of an experiment. The current was interrupted by the Neeff's hammer attached to the induction coil. Helmholtz's modification was used for equalizing the make and the break inductions.
The electrical measuring instruments used in these experiments are new and especially adapted to physiological work. They may, therefore, be given special mention. Both instruments were devised by Professor H. A. Rowland of the Johns Hopkins University.

The galvanometer is of the d'Arsonval type. It consists of a small coil of fine wire suspended between the closely approximated poles of a powerful horse-shoe magnet. The coil is suspended by a phosphor-bronze filament and the circuit is completed by a spiral spring of the same material at the bottom of the coil. The instrument is rendered aperiodic by a mica vane attached to the suspended coil and swinging in an enclosed box. The deflections of this movable coil are determined by means of a telescope reading the divisions of a scale reflected from a mirror attached to the coil. The reading telescope is attached to the instrument by means of a horizontal arm which can be raised or lowered.

The galvanometer is independent of the earth's magnetism and can therefore be placed upon any convenient supporting surface without reference to the magnetic meridian. When the instrument is once adjusted it is always ready for immediate use, and its sensitiveness, the ease and accuracy with which its deflections may be read, and its freedom from vibrations, make it very convenient in physiological experimentation.

The particular instrument used in these experiments has a resistance of 671 ohms, and gives a current value of 49 ten-millionths of a milli-ampere (49 × 10⁻¹⁰ amperes) per millimetre of scale deflection.

The electrodynamometer consists of a small high resistance coil of fine wire suspended within and at right angles to a fixed coil of high resistance. The free coil is suspended in precisely the same manner as in the galvanometer just described. The instrument is rendered aperiodic by a mica vane, and the deflections are read by means of a telescope and scale, as in the galvanometer. The magnetic field in this instrument is produced by passing the current to be measured through the fixed coil. A current sent through both coils gives a deflection in a constant direction, whether the current be direct or rapidly reversed. It is therefore especially adapted to the measurement of alternating induction currents, such as are used in physiological experiments.

The deflection of the suspended coil in this instrument represents the mean squares of the series of waves of induced current, hence the mean current varies directly as the square root of the deflection.
The resistance of the electrodynamometer used is 3371 ohms. Measured by direct current methods it gives a standard value of 158 ten-thousandths of a milli-ampere \((158 \times 10^{-7} \text{ amperes})\) for the unit obtained by taking the square root of the scale deflection measured in millimetres. It must be remembered, however, that this value represents only the mean value of the series of waves of induced current as stated above.

To those accustomed to use induction currents for physiological stimulation, it will be of additional value to know that 2.5 units of current as measured on this electrodynamometer can just be detected by the sensory effect on the tip of the tongue, that 6 to 8 units become sharp, and 12 units painful.

The range of stimulation strength ordinarily used in the laboratory varies between 5 and 10 units of current as defined above. The range of the dynamometer extends from 0.5 to 15 units. This range just about covers the working range of stimulating currents, though scarcely delicate enough to measure minimal stimuli for very sensitive nerves, such as those of winter frogs.

In each experiment the nerve was stimulated for 12 seconds, once every minute, until the desired variation of strength of stimulation was obtained. The resulting action currents were led from the nerve to the galvanometer for measurement. The time of the stimulation was regulated by the automatic short-circuiting clock key already described. The strength of the stimulus was varied by moving the secondary coil toward or away from the primary in the interval between stimulations.

In some control experiments records of the muscular contractions were also taken. In these experiments the gastrocnemius muscle was left in connection with the sciatic nerve and arranged in the usual way in the moist chamber, the muscle lever recording on a slowly moving drum. The sciatic nerve was stimulated near the muscle and the resulting action current was led off from the central end of the nerve to the galvanometer. Experiments of this kind were made on preparations from the frog and the turtle, but not on the nerves from mammals. However, in most experiments the isolated nerve alone was used.

**The Results of Experiments.**

The quantitative relation between the strength of the external stimulus applied to the nerve and the strength of the action current
produced by it, is shown in the curves constructed from the experiments. In these curves I have plotted units of increase of stimulating current along the abscissae and the associated change in the strength of the action current along the ordinates.

One millimetre of scale deflection of the galvanometer by the action current has a value of 49 ten-millionths of a milli-ampere, as previously stated. There is a great difference in the absolute values of the action currents obtained from different nerves, but as we are concerned here only with the relative variations in values I have reduced all curves to a uniform magnification in order to facilitate comparisons.

**Nerves of the Frog.** — The plotted curve expressing the relation between stimuli of different strengths applied to a frog nerve and the strengths of the resulting action currents shows three characteristic parts (Fig. 1): (1) an abruptly ascending straight limb, including the range from minimal nerve stimuli to stimuli above the strength that calls forth maximal muscular contractions; (2) a middle portion, in which the curve is still ascending but strongly concave to the abscissae; (3) a supra-maximal straight portion parallel to or more often slightly diverging from the abscissa.

These regions I shall now describe in greater detail. The first record of a current of action in a frog nerve was obtained when the nerve was stimulated with an induced current just strong enough to produce a minimal muscular contraction. This was the usual result in test experiments, although sometimes the minimal muscular contraction was obtained with a stimulus slightly weaker than that causing a readable action current in the nerve. In every case the minimal action current produced in the galvanometer a deflection of only a fraction of a millimetre.

A series of stimuli applied to the nerve, increasing above the minimal stimulus by very small but equal increments up to a strength about twice that necessary to call forth a maximal muscular effect, produced a relatively strong and rapid increase in the action current. This increase in the action current was by increments proportional to the increase in stimulus, giving in the plotted curve a straight line. Such slight variations as occurred in successful experiments were apparently within the limits of error of determination. The strength of a minimal stimulating current for the nerve varied from 0.02 to 0.2 units. The increase in stimulus that was necessary in order to call forth maximal muscular contractions in test experiments, was approxi-
mately 0.2 of a unit. The upper limit of the first straight portion of the curve is not sharply bounded.

**FIG. 1. SCIATIC OF THE FROG. EXPERIMENT 39.**

Curve representing the quantitative relation between the strength of an external stimulus applied to the frog's sciatic and the strength of the resulting action current. The abscissae represent units of stimulating current (1 unit = 158 × 10⁻⁷ amperes). The ordinates represent units of action current (1 unit = 49 × 10⁻⁸ amperes). The dots on the plot represent the individual readings. The mean for this series of readings was drawn after a comparison of several typical experiments.

Ml. Minimal muscular effects. Ma. Maximal muscular effects.

A further increase in the strength of the stimulus above that just described produced an increase in the action current of the nerve, but the added increments of action current accompanying the increase in stimulus were successively smaller. At this point the plotted curve is strongly concave to the abscissa. This middle portion of the curve of relation between the strength of the stimulus and the strength of the action current varies in extent and in degree of concavity, and its limits can be determined only very roughly.

A further increase in the strength of the stimulus produced only a slight additional increase of the action current, even though the strength of the stimulus was increased tenfold and more. This slight
increase in the action current was by increments proportional to the
increase in stimulus. When plotted, the results give a straight line
slightly diverging from the abscissa. Occasionally there is no in-
crease in the amount of the action current, and the line is then par-
allel to the abscissa.

The nerves of winter frogs are sometimes very irritable and the
relations of minimal stimuli to the corresponding action currents are
accordingly difficult to determine. The strength of minimal stimuli
for many frog nerves was too slight to be measured by the electro-
dynamometer, and in such experiments it was determined indirectly
by the corrected scale of the induction coil. In these very irritable
nerves the abruptness in the increase in action current with small
increase above minimal stimuli is most marked. Variations and
irregularities were frequently obtained also in the response of frog
nerves to stronger stimuli.

Nerves of the Terrapin. — Nerves of the terrapin (Pseudemys),
are much less irritable than those of the frog, but the curve of rela-
tion between stimulus and action current response, plotted from
experiments on the sciatic of the terrapin, exhibits the general charac-
ters just described for that of the sciatic of the frog. That is, it shows
a beginning straight limb of rapidly increasing action current pro-
duced by slight increase in the energy of the stimulus, a middle
portion concave to the abscissa in which the action current still
increases, but by diminishing increments, and a long supra-maximal
straight limb slightly diverging from the abscissa.

The first straight part of the curve usually ascends less abruptly
from the abscissa and the second curved portion is usually longer
and less concave than in the curve from the frog's sciatic. The
series of tests as a whole was more regular and constant than in the
experiments on the frog's sciatic.

The total action current obtained from the nerves of the terrapin
was relatively much less than that obtained from the frog's sciatic.
A minimal stimulus for the sciatic of the terrapin varied from 0.7 to
2 units of stimulus; an increase above this by 0.3 to 0.7 units pro-
duced a maximal stimulus for the muscle attached to the nerve in
test experiments.

1 By a new arrangement of the dynamometer, suggested by Professor Rowland,
this difficulty has been obviated, the sensitiveness of the dynamometer being so
greatly increased that minimal or sub-minimal stimulating currents, even for very
irritable nerves, can probably be determined without difficulty.
External Stimulus and Nerve Impulse.

The results of experiments on the vagus of the terrapin have been quite variable. In eight experiments no action current was obtained from the vagus, even with excessively strong stimuli. In other experiments, especially after the nerves were kept in the moist chamber for from one to three hours, an action current of relatively slight intensity was obtained. The results of experiments which yielded the most pronounced action currents, when plotted, exhibit in a degree the relations shown by the curve from the sciatic of the terrapin. However, the first straight portion of the curve is obscure in experiments on the vagus in that it merges at once into the second or strongly concave portion. The upper straight limb of the curve is quite closely comparable to that in curves from the sciatic nerve.

Nerves of the Cat and the Dog. — Nerves of the cat and the dog were used under precisely the same conditions as those of the frog and the terrapin. The curve expressing the relation between the strength of the external stimulus and the strength of the action current in nerves of the cat and the dog (Figs. 3 and 4) is very like that obtained from the frog or the terrapin. Beginning with minimal stimuli applied to the nerve and increasing by small but equal increments of stimulation there is a rapid increase in the amount of the action current also by equal proportional increments.

![Graph](http://ajplegacy.physiology.org/DownloadedFrom)
This ascending straight limb of the curve is followed by a middle portion increasing by diminishing increments and thus concave to the abscissa, and this, finally, by a long supra-maximal straight portion diverging slightly from the abscissa. The middle portion of the curve is usually longer and less concave (Fig. 4, ah) than in the curves from the nerves of the frog or the terrapin, but sometimes this difference is not apparent. In a small percentage of experiments on the sciatic of the dog I have obtained an initial short curve convex to the abscissa. That is, with an increase by equal increments above a minimal stimulus for the nerve there is for one or two readings an increase in the action current by successively increasing increments. This short initial part of the curve is always followed by the first straight portion as described above. It should be stated here that the long and tedious precautions for cooling the animal to room temperature before its death, as described by Bernard, Schiff, and Israel, seemed unnecessary and were not observed. The animals used were such as had been killed in the laboratory at the end of other experiments. The nerves were taken soon after the animal was killed in some instances, and in others not until the animal had cooled to near the room temperature. In one case, one sciatic of a dog was removed at once after the animal was killed, the other after it had cooled to near the room temperature. No difference was observed between the character of the results in experiments made on the two nerves immediately thereafter. However, after being kept over night on clean filter paper moistened with physiological saline solution, the

---

warm nerve gave no response even to the strongest stimuli, while the cooled nerve was still alive as shown by the strong action current. A nerve taken from the body of a dog after 15 hours, was dead, while nerves from the same dog removed immediately and kept on filter paper for 15 hours were still alive and very irritable, as shown by the marked action current caused by stimulation.

FIG. 4. SCIATIC OF THE DOG. EXPERIMENTS 91, 95, AND 118.

Curves expressing the relation between the strength of stimulating current and the resulting action current. No. 91, ab, from the nerve immediately after its removal from the body. No. 95, cd, from the same nerve after 17 hours in a moist chamber at room temperature. The curve cd shows in comparison with the curve ab the increase in irritability and decrease in the amount of the action current which occurs when nerves are kept for some time. No. 118, ef, the beginning of a curve introduced here to show the initial minimal portion convex to the abscissa. Curve cd also shows the phenomenon. The values of the stimulating current and the action current are not given in curve ef, but the magnification is about twice that of the curves ab and cd.

Nerves from dogs and cats remain alive in the moist chamber at room temperature a surprisingly long time. Nerves from the dog have been frequently kept alive over night and experimented on the next day 15 to 20 hours after removal from the body of the animal. In one case two sciatics and an ulnar of the dog were alive and hyper-irritable after 25 hours, and the following morning, after an isolation of 41 hours at room temperature, the ulnar still gave a small action current; the two sciatics gave no action current, i.e., were no longer

1 L. Fredericq obtained an action current after 24 hours. Archiv. f. Anat. u. Physiol., 1880, p. 70.
capable of responding to stimuli. Even in these sciatics, however, very strong currents of rest were present.

I have uniformly obtained a strong action current from isolated nerves of the dog. The action current decreases after 12 hours (see Table), but a current may still be obtained after at least 41 hours. The action current varied from 20 to 30 per cent of the demarcation current in fresh nerves. The strongest action current Grützner obtained from rabbit nerves did not exceed 4 per cent of the demarcation current. As the nerves were kept, the demarcation current increased for some time, becoming two to three times the original value after 15 hours, the measurement being made after a fresh section of the nerve. This increase in the value of the demarcation current was true also for the nerves of the terrapin, and has been described before in the nerves of frogs.  

TABLE  
Showing data from successive experiments on the same nerve, to illustrate the increase in irritability and the decrease in maximal action current, which occur when the nerve is kept alive on filter paper wet with physiological saline solution.

FROM THE ULNAR NERVE OF THE DOG.

<table>
<thead>
<tr>
<th>Ulnar of Dog.</th>
<th>Strength of Stimulating Current giving rise to a minimal action current.</th>
<th>Strength of Action Current with a supra-maximal stimulus, 10 units.</th>
</tr>
</thead>
<tbody>
<tr>
<td>After 20 minutes.</td>
<td>1.94 units.</td>
<td>33 2 mm. of deflection.</td>
</tr>
<tr>
<td>&quot; 18 hours.</td>
<td>.54 &quot;</td>
<td>17 4 &quot; &quot;</td>
</tr>
<tr>
<td>&quot; 24 &quot;</td>
<td>.25 &quot;</td>
<td>9.8 &quot; &quot;</td>
</tr>
<tr>
<td>&quot; 41 &quot;</td>
<td>.55 &quot;</td>
<td>0.9 &quot; &quot;</td>
</tr>
</tbody>
</table>

The irritability of isolated nerves from the cat and the dog increased for several hours, 24 hours at least, and then decreased until its final disappearance. The test on which this statement is based is the strength of a minimal stimulus necessary to produce an action current in the nerve.

COMPARISON OF RESULTS.

From about one hundred and twenty experiments I am unable to deduce any general law applicable to the entire curve of relation

1 Grützner: Pflüger's Archiv., 188, xxv, p. 278.
2 Howell: Journal of physiology, 1894, xvi, p. 476.
between the external stimulus applied to a nerve and the strength of the action current produced. There is a close similarity in the form of the curves expressing the results of experiments on nerves from the three classes of animals used. In every case the entire curve shows three distinct parts as described above. Each of these parts varies according to its own laws. The first part and the last portion vary according to arithmetical ratios, but the ratios are different in the two portions.

Waller, from his experiments, describes the relation of the strength of the external stimulus and the action current response as an S-shaped curve consisting of three portions: (1) an initial "short subminimal portion convex to the abscissa, increasing by increasing increments; (2) a long straight middle portion, inclusive of and beyond the functional range of nerve measured by maximal muscular effects, increasing by equal increments; (3) an ultra-maximal portion far above the values of maximal functional effects concave to the abscissa, increasing by diminishing increments."

The first sub-minimal portion of the curve that he describes I have been unable to obtain on the nerves of the frog. But on the sciatic of the dog I have obtained a short initial curve similar to that described by Waller for the nerves of the frog, although I cannot say what relation it bears to minimal muscular contractions. This initial curve in the nerves of the dog, when present, is much more strongly marked than in the single curve which Waller shows. In fact, the particular experiment that he has plotted exhibits a variation scarcely greater than might be accounted for by the limits of error in determination. However, some of his tables, if plotted, show the phenomenon much more strongly, while others do not exhibit it at all.

My results on all nerves confirm Waller's statements with reference to the second part of the curve which he describes. That is, I have found that variations in the strength of the stimulus between the limits of strength that call forth minimal and maximal muscular contractions are accompanied by proportionately increasing increments of action current. In experiments in which I have used the nerve alone, this region is a straight line in the plotted results. Waller's supra-maximal portion of the curve seems to correspond with the

1 Waller: Brain, xviii, p. 200.
2 Waller: Journal of physiology, 1895, xviii, p. xxvii, Exps. 103, 130a, 130b.
middle portion of my curves, which, following his description, I have spoken of as concave to the abscissa.

The third or supra-maximal straight portion, which I have described and figured, he does not describe, although the data for it is contained in one of his protocols (No. 106). Throughout this portion of the curve a wide variation in the strength of the stimulating current occasions but little and in some cases practically no variation in the strength of the action current. We have here a phenomenon which at first sight suggests a comparison with the maximal contraction of a muscle. This maximum is reached, in the nerve, at a point far beyond the strength necessary to cause a maximal muscular contraction. It lies, therefore, beyond the probable range of normal functional activity. As between the muscle and the motor nerve, however, it may be said that the latter is capable of imparting a stimulus far in excess of that necessary for the production of a maximal shortening in the muscle. How completely this relation may hold when the nerve fibre is stimulated from its cell instead of directly by artificial means, cannot be determined.

Finally, I wish to express my deep obligation to Professor W. H. Howell, at whose instigation this work was undertaken. To his many helpful directions and suggestions given while prosecuting the investigation, and especially to his kindly criticism during the preparation of the manuscript, are chiefly due whatever of value attaches to this paper.