THE RÔLE PLAYED BY THE SIZES OF THE CONSTITUENT FIBERS OF A NERVE TRUNK IN DETERMINING THE FORM OF ITS ACTION POTENTIAL WAVE

H. S. GASSER AND JOSEPH ERLANGER

From the Laboratories of Pharmacology and Physiology of the Washington University
School of Medicine, St. Louis

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Numerous experiments, performed in this laboratory during the last few years, upon the form of the action potential wave of nerve, have established the fact that the wave is built up of units, which we have designated as axon potential waves. The form of the potential-time curve, as led off from a point on the nerve, depends in part upon the distance of this point from the point stimulated, and in part upon the composition of the nerve. Some nerves, as for instance the phrenic or motor spinal roots, always give simple waves (Erlanger, Gasser and Bishop, 1924, 1926); others, as for example the sciatic or the sensory spinal roots, show definite secondary waves which for convenience we have called α, β, γ and δ. The particular action potential pattern which is characteristic for each nerve, depends upon the velocities of the constituent axon action potentials involved.

When many fibers of low velocity are present, as occurs in the posterior roots, the action potential becomes much elongated on conduction; in the absence of such fibers, as is the case in the anterior roots, the action potential is much shorter.

In the nerves and roots whose action potential curves show secondary waves, these waves are not themselves definite entities, but also change their form as they are propagated. They are made up of axon action potentials of varying velocities; in fact the slowest fibers of the α group are about as slow as the fastest fibers of the β group, and the slowest fibers of the β group show the same relationship to the fastest fibers of the γ group. The nerve thus seems to be composed of fibers whose velocities of conduction form practically a continuous series from the fastest to the slowest. The continuity of the series is indicated by the growth of the area of the recorded wave as the stimulus is increased in size. The growth is continuous, but at varying rates, as the stimulus is increased, taking place either without gaps or with gaps corresponding to a very short range of stimuli (1926). The appearance of secondary waves cannot therefore
be produced merely by the presence of fibers of widely different velocities
of conduction but there must be variations in the numbers of the fibers at
each velocity.

The purpose of this paper is to investigate the morphology of the differ-
ent nerves, to see if any relationship can be ascertained between their
structure and their action potential curves.

Before proceeding further with this question we must point out collateral
lines of evidence focusing upon the solution of the problem. Some of
these were reviewed in our previous communication (1924) in the dis-
ussion of the possible explanations of the wave form. It was stated by
us at that time that "it is not at all surprising, in view of the varied histo-
logical composition of mixed nerve, that the action current of such a nerve
as the sciatic is compound."

In 1913 Lapicque and Legendre established experimentally the relation
between the chronaxie of nerve and its morphology. While they con-
sidered the possibility of chemical or colloidal factors as variables in the
nerve’s composition, they felt that the first series of observations should
be directed along simpler lines, and they compared the time constants of
different nerves with their gross histological aspects. The research led
very definitely to the conclusion that the factor relating chronaxie to
nerve structure was the size of fiber, and that this operated in such a way
that the larger the fiber the shorter the chronaxie. Knowing that the
chronaxie has a relation to the velocity of conduction they say, "... les
fibres nerveuses sont d’autant plus rapides qu’elles sont plus grosses."
The exact function of the size of fiber was not determined, though it was
suggested that it might be the area. More recently Langley as the result
of some histological studies on nerve constitution, expressed the opinion
that one of the main factors accounting for the extraordinary variations
in the size of the myelinated fibers is the nature of the tissue in which they
end. This opinion, taken with the older observation by Carlson that the
velocity of propagation in a motor nerve depends upon the speed of the
muscle innervated, again brings an association between velocity and size.
Also, from a theoretical consideration of how a cable with the dimensions
and constants of nerve would conduct, Göthlin has pointed out that a
large strand would conduct faster than a small one. Such a calculation
does not, however, establish any relationship between nerve size and
velocity unless a cable like conduction can be demonstrated. As will be
seen later, there is no evidence that such a relation obtains.

When Professor Lapicque was shown the cathode ray oscillograph records
of the action potential wave in nerve, during a visit of one of us to the
Sorbonne, he expressed an opinion very strongly in favor of the possibility
that the form of the wave would depend upon the sizes of the fibers in
the nerve. The two most striking cases known at that time in mammalian
nerve were the phrenic wave, which is simple, and the saphenous, which is compound. On investigating these nerves histologically (Lapicque, Gasser and Desoille) it was found that their microscopic appearances were as notably different as their electrical signs. The phrenic nerve presented a relatively homogeneous appearance; the saphenous was composed of fibers of widely varying sizes.

Such an observation was very encouraging and a further effort was made to find more exactly the relationship between the distribution of fibers and the action potential wave. After various trials the function of the size which seemed the most probable in determining their propagation velocity was found to be the diameter of the fibers. At this point the researches at the Sorbonne were interrupted, and after a year the problem was again taken up in the Washington University laboratory where it was possible to make electrical observations upon the same nerves that were to be examined histologically.

The analyses have necessitated three procedures: the measurement of the nerve fibers, the recording of their action potential waves and the theoretical reconstructions of the potential wave forms, on the basis of the fiber distribution in the nerves, for comparison with the actual waves as recorded.

The measurement of the nerve fibers. After the action wave was recorded the nerve was removed from the moist chamber, tied to a piece of glass so as to maintain as nearly as possible its natural length, then fixed in 1 percent osmic acid. Paraffin sections 4μ thick were prepared,1 care being taken that the section was at right angles to the nerve. These were photographed, and the negatives then enlarged so that finally a print was obtained at 1000 or more diameters. During the process of experimentation and fixation some distortion of the fibers took place so that they had a tendency to appear ellipsoidal. On account of the nature of the problem it was impossible to prepare large numbers of nerves and select the best ones; it was necessary to make the best utilization possible of those nerves whose potential waves had been recorded. The routine procedure was, therefore, to make two measurements of each fiber, one through the long axis and the other through the diameter at right angles to this. The mean diameter of the fiber was then obtained by extracting the square root of the product of the measurements. The product itself was a figure representative of the cross-sectional area. The outside diameter only was measured in the case of most nerves, because it was shown by Lapicque and Legendre (1922) that in injured nerves the myelin swells at the expense of the axis cylinder. If, as Donaldson and Hoke

1 We are indebted to Professor Ranson for permission to have the histological sections prepared in his laboratory.
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claim, the ratio of the thickness of the myelin to the fiber diameter be a constant for all sizes of fibers, then for comparative purposes the outside diameters are as good as the inside diameters with the advantage that there is less danger of pathological distortion. We have not made a rigid investigation of Donaldson and Hoke's observation, but measurements of our material do show some deviation from the constancy of this ratio. Such a deviation in so far as it occurs is a source of error, but where it occurs in very small fibers, it is of little importance as it will be seen that the small fibers contribute very little to the total area of the potential-time curve obtained from the nerve. In the small number of cases where both the total diameters and the diameters of the axis cylinders were measured the resulting size-distribution curves showed no significant deviation one from the other. In some nerves all the fibers were measured, in others only a number such that further additions would be of no important statistical significance.

Due to distortion of fibers or proximity to a node of Ranvier a single measurement of a fiber might deviate somewhat from the mean diameter. To gain some idea of this error a number of fibers were followed through five sections. As the result of this it was found that the probable error of a single result, as determined by comparison with the mean of the five measurements, varied between 2 and 8 per cent. This error would not be sufficient to interfere with any conclusion that is drawn from the investigation.

In order that an analysis of a nerve on the basis of fiber size can be made at all there must be sufficient constancy of diameter throughout its course. Sherrington quotes Schwalbe to the effect that the diameters of the motor nerve fibers remain unaltered throughout their course except when branching occurs, and branching does not occur, according to Mays, either in the nerve trunks or the sciatic plexus of a frog, a fact confirmed by Sherrington. Schwalbe on the other hand states that the sensory fibers across the dorsal lymph sacs of frogs decrease in size in their course. If tapering occurred in our nerves to any considerable extent, then the number of large fibers in the peripheral nerves should be smaller than one would expect from the large fiber content of the spinal roots, and this is not obviously the case as can be seen by comparison of figures 2, 4, 8 and 9 of spinal roots, with figures 6 and 10 of peripheral nerve; so here again we may infer that tapering of the fibers within the nerve trunk is not of a disturbing magnitude.

The unit action potential wave. In the reconstruction of nerve trunk potentials it is necessary to define the dimensions of the unit axon potential both as to magnitude and duration.

The magnitude of the unit wave was selected as constant for all sizes of fibers. This arbitrary assumption was necessitated by the complete absence of any data indicating its value, and whatever justification it may
have lies in the *a posteriori* reflection that a group of fibers, which in the analyses seems to produce a secondary wave, would not produce one of the proper magnitude if the individual potentials were assigned any other value.

Although we have assumed the potentials developed in the different fibers to be the same, this does not mean that they will have equal effects upon the recording mechanism, in fact there is reason to believe that their values would correspond more closely to their cross-sectional areas, which determine the electrical resistances per unit length.

The potential drops across a recording instrument produced by two sources of potential having the same E.M.F. but different resistances will be to each other inversely as the resistances, only when the resistance of the recording instrument is low compared with that of the source. A vacuum tube properly adjusted releases power according to the potential of the grid; and the resistance in the grid circuit is very large so that the tube acts as a potentiometer with considerable independence of the resistance of the source. But, on the other hand, the resistance of the axon of a single nerve fiber must also be a very large quantity. Its value can only be calculated; but if one take as the specific value of the resistance of the axon protoplasm that of blood serum, in round numbers 98 ohms (Bugarsky and Tangl), the resistance of a nerve fiber turns out to be between $10^8$ and $10^9$ ohms per centimeter depending upon the size of the axon. These figures accord very well with the value, given by Gothlin, of $10^9$ ohms for a small fiber, using the specific resistance of cerebrospinal fluid which he determined for the purpose. If we assign to the grid circuit a value of $2,000,000^\circ$, then the resistance of a single fiber is so much higher, that the potential drop across $2,000,000^\circ$ would be determined mainly by the nerve’s resistance.

As will be seen in the actual analyses, there is reason to believe that it is possible to reveal in the action potential wave the effect of only a few large fibers, so that a consideration of the effect of a single fiber on the potentiometer is of some practical interest. In addition to the resistances considered above there is a third factor of considerable importance in determining the effect of a fiber. An active fiber or a group of active fibers of the same size is shunted by the inactive fibers and the other structures in the nerve. We may picture the situation as is indicated in the accompanying diagram (fig. 1). The active fiber developing a constant potential, $E$, but having a resistance, $r$, depending upon its cross section, is shunted by the remaining parts of the nerve, $R_1$, and is recorded on a potentiometer with a resistance $R_2$. The potential drop across $R_2$ will then be

$$\frac{R_1 R_2 E}{r (R_1 + R_2) + R_1 R_2}$$
This expression is symmetrical with respect to $R_1$ and $R_2$; therefore the effect of the inactive portions of the nerve is the same as that of a low resistance potentiometer in making the recorded E.M.F. a function of the resistance of the source. If one assume 100 fibers each of the $10^8$ and the $10^9$ ohm sizes to be active in a nerve whose total resistance is around 50,000$^\circ$ per centimeter, and that their potentials are recorded on a potentiometer having 2,000,000$^\circ$ internal resistance, using leading off electrodes two centimeters apart, then the ratio of the potentials recorded will only vary 4 per cent from the ratio of the resistances. In view of these considerations it was routinely assumed in making reconstructions that the potentials recorded were a linear function of the areas of the fiber cross-sections.

The duration of the unit wave. For the sake of convenience the shape of the axon potential curve has been assumed to be triangular and the duration the same for all fibers of the nerve trunk. The potential curve may be simplified to a triangle of nearly equivalent area, which can be much more easily manipulated in the analyses. The durations were chosen as the same in all fibers because they seem to be constant in actual measurements made at the stimulating cathode (1926).

The values for the duration of the rising phase of the potential wave and for the total duration are taken from actual data. When leads are made from the stimulating cathode on the phrenic nerve of the dog at 37$^\circ$ C., rising phases of about 0.3 $\sigma$ and less are found, which include whatever utilization periods there may exist, and total durations of about 1.0 $\sigma$, measured to the point where the potential has practically returned to the base line (1926). The start of the action potential even at the stimulating cathode has an initial upward concavity, and similarly and to a very much more marked extent the potential dies away asymptotically. Triangles drawn with the crest, the start and the end of the action wave, as apices, would include an area much larger than the actual wave, a deviation which would be theoretically undesirable; on the other hand triangles drawn with their legs having the principal slopes of the rising and falling phases would have areas differing but slightly from the actual ones. Accordingly the latter procedure was adopted and when this was done, 0.2 $\sigma$ seemed a good value to take for the rising phase and 0.6 $\sigma$ for the total duration. For cold blooded nerve similar considerations led to the adoption of 0.3 $\sigma$ and 0.9 $\sigma$ as the proper values.

The velocities of the unit waves in terms of fiber diameters. In searching for the connection between these two values the cable-like construction of the nerve was taken into consideration. The existence of protoplasmic
strands surrounded by a sheath having some insulating value has from
time to time led physiologists to consider nerve conduction in the light of
the physics of submarine cables. While it has been calculated that in a
cable of strands having the dimensions of nerve fibers, the velocity of
conduction would be of the same order of magnitude as in a nerve fiber,
provided the length be suitably chosen, the analogy seems to end here.
The conduction time in nerve is a linear function of the length and not a
function of the square of the length as in a cable; contrary to what takes
place in a cable, the size of the wave in an axon is independent of the shape
and size of the impressed potential; decremental conduction present in a
cable is absent in nerve (Kato; Davis, Forbes, Brunswick and Hopkins);
and, whereas high frequency unidirectional currents applied to a cable
cause it to deliver a constant current, the nerve responds repetitively
according to its intrinsic properties (Eigenperiode).

Most theories of nerve conduction postulate that some of the energy
liberated in an active portion of a nerve is responsible for the activation of
the adjacent inactive portion, the process thus being carried on without
decrement due to the energy added to the disturbance at each successive
point in its progress. The particular form of this type of theory which
has the most adherents is the one which considers that the action current
is the agent of excitation, especially as this theory has been elaborated by
Lillie. It might be argued that while propagation in nerve is quite differ-
ent from what occurs in a cable, that in so far as propagation is brought
about by the action current it could be modified by the nerve's cable-like
structure. This seems to be essentially the attitude taken by Göthlin
(1907).

According to the telegraph equation of Lord Kelvin, the time of arrival
of the wave front at the end of a cable, after the closure of a key at the
sending station, is \( CR^2 \) times a constant, where \( C \) and \( R \) denote respectively
the total capacity and resistance of the circuit, and \( l \) is its length (Fleming,
p. 154). The capacity per unit length of a cylindrical conductor of radius
\( R_1 \), placed concentrically in the interior of a conducting cylinder of inner
radius \( R_2 \) and separated from it by a substance having a dielectric con-
stant \( K \), is \( \frac{K}{2 \ln \frac{R_2}{R_1}} \). According to Donaldson and Hoke, the ratio of the
myelin to the total diameter of the fiber is constant. In so far as this is
true, the ratio \( \frac{R_2}{R_1} \) would be constant for all fibers and their capacities would
be constant except for variations in the composition in the myelin. In
any case, then, the capacity factor could alter the propagation rate only
as the myelin sheaths might be of different qualities. Actually it will
be seen that the action potential waves can be satisfactorily reconstructed
without supposing that the myelin sheath enters in as a controlling factor at all.

The other factor determining rate of propagation in a cable is the resistance, that is, the smaller the resistance the faster the conduction. The operation of this factor in the case of nerve would lead one to infer that the velocities of conduction would vary as the cross-sectional areas of the fibers, but reconstructions made on this basis yielded results differing widely from the facts. On the other hand velocities varying among one another as the diameters of the fibers were found empirically to lead to the synthesis of action potential waves very much like those recorded. This relationship was therefore used in all the reconstructions in the following section. As far as cable conduction is concerned, its consideration yielded no clues useful in the theoretical analysis of the potential curves.

The analyses. These involved the measurement and tabulation of 10,500 fibers in various nerves.

![Distribution curve of all the fibers (875) in the IXth motor root of a bullfrog. Each dot is a fiber. Solid lines: total area of the underlying fibers. The ordinate in this and similar figures is on an arbitrary scale which is not the same in the different figures.](http://ajplegacy.physiology.org/)

The first group of nerves which will be reported consists of the IXth pair of roots of a bullfrog (*Rana catesbiana*) together with the peroneal from the same animal. The roots were studied after the peroneal nerve, and the frog had been in the refrigerator at 2°C during the interval of two hours. This may explain the velocity of conduction which was found to be 35 m.p.s., somewhat less than usual. When the nerve and roots had been dissected they were mounted in the moist chamber at room temperature. A stimulating electrode was placed 48 mm. from the central end, this being the longest distance usable before important branching took place. Stimulation of practically all the fibers was thus assured. A long series of records was taken from each root in turn at graded strengths of stimulation, after which the roots were fixed for histological examination.

The motor root. As is well known, the motor root has a rather homogeneous histological appearance compared with the sensory. This is
due to the large mass of fibers which centers about 14 μ, as seen in figure 2. In this figure and in others of the same kind each dot represents a nerve fiber. It is located along the abscissa at its proper mean diameter and by counting in the direction of the ordinate, the number of the fibers at the size may be determined; the figures therefore serve as a form of tabulation. The solid lines in steps represent the total areas of successive groups made up of fibers within a range of 0.5 μ. In this motor root all the fibers (893) were measured except the very small ones beyond the left end of the series,

Fig. 3. Reconstruction of motor root action potential at 48 mm. of conduction. The triangles are plotted on twice the scale of the summation line. Inset: action potential of the motor root as recorded (10/27/25). 1 mf., 4020", X = 87 mm.

which are presumably the preganglionic fibers to the sympathetic system. The striking point about this chart is a single peak at 14 μ, with the number of fibers decreasing to either side. The largest fibers are just over 20 μ in diameter. These were considered to have the maximum velocity of 35 m.p.s. The other velocities were calculated according to the diameters of the groups, and then the lag of each group was determined when the 20.25 μ group had reached a point 48 mm. from the start, which was the distance at which the records were taken.
In figure 3, the action potential corresponding to each group was plotted at its proper delay, marked out along the abscissa, with triangles whose height was determined by the total area of the group. The sum of these then made the reconstructed composite action potential, for comparison with its real counterpart. As would be expected from the regular fiber distribution, the curve is perfectly smooth. The real action potential is inserted for comparison. The correspondence is quite satisfactory. The crest time of 0.84 s in the reconstruction compares well with 0.76 s measured on the record; also the endings are in accord, the potential having returned nearly to zero in both at 3 s.

The sensory root. When we turn now to the sensory root (fig. 4), all of whose fibers were measured, we find a very different picture. The range of sizes is about the same, the largest being just over 20 μ, but there is a relatively much smaller number of fibers above 15 μ than in the motor root. The peak in the number comes at 7 μ, but on the basis of area the maximum comes at 8.5 μ. Furthermore, a mere glance at the figure reveals that the area of the fibers smaller than 11.5 μ is greater than that of those larger. The effect of this appears quite clearly in the action potential which is recorded in figure 5. Upon the reconstructed action potential is redrawn in linear coördinates a maximal action potential from the root. It can be seen that the smaller fibers are definitely responsible for the β wave. Attention should be drawn to the fact that in figure 4 the peak of the area of the smaller fibers is higher than the peak of the larger fibers, while in the reconstruction and in the actual action potential, the β wave is lower than the α. The reason for this is that according to the hypothesis the axon potentials of the smaller fibers separate out more rapidly than those of the larger ones, therefore fewer of them are summed at any one time.
One source of error occurs in the posterior root which is absent in the anterior, that is, the delay which has been found in the ganglion, amounting to an average of 0.14 s (1926). Whether or not it is the same for all fibers is not known. In any case no correction could be made for it. But in spite of the fact that the conduction time in the fibers of the same size in the two roots has been taken to be the same, the agreement between the real action potential and the reconstruction is sufficiently satisfactory both as to shape and time constants. The differences are best described by the figure itself.

Fig. 5. Reconstruction of action potentials in posterior root of bullfrog at 48 mm.

Inset: maximal action potential of nerve as recorded (10/27/25). × 0.7, 1 mf., 4020W, X = 87 mm.

Starting with the larger fibers, the area of the first 15 groups in figure 4, as subtended by the rectangles, is 38.8 per cent of the area of all the fibers. The reconstructed action potential of these fibers alone has been added to figure 5. From the series of action potentials made from this nerve, the strengths of stimuli were plotted against the areas of the curves, the areas being measured with the aid of a planimeter on large scale redrawings of the originals, in rectangular linear coördinates. The area curve showed an acceleration at the point at which the β fibers began to respond. It happened that the last potential curve before this acceleration had an area
38.3 per cent of the maximum; accordingly, it has also been inserted in figure 5 to show its agreement with its reconstructed counterpart. In the introduction the reason for considering that a fiber affects the galvanometer as its area was presented. The agreement between theory and fact in this experiment may be taken as experimental evidence of the correctness of the assumption. It also shows that the fibers larger than 11.5 μ are responsible for the α wave and that the area of the β group also corresponds with the fibers belonging to the second peak in the analysis (fig. 4).

The peroneal nerve. The fibers in the preparation of this nerve turned out to be quite wrinkled, thus making the measurements less accurate. However, there appear definitely three groups (fig. 6), the first two corresponding to the α and β groups which were analysed in the roots and the third corresponding presumably to the γ fibers. As this nerve had the fastest velocity of conduction of the three (43.2 m.p.s.), because it was studied under the most favorable conditions, its largest fiber was credited with this velocity instead of the value taken for a fiber of the same size in the roots. The forms of the action potential and of the reconstruction have a superficial resemblance. The deviation (fig. 7) consists in an earlier appearance of every point on the reconstruction as compared with the corresponding real point. This means that the small fibers are conducting relatively more slowly than that calculated on a diameter basis. The peroneal is a fine nerve and it is possible that it received some injury in dissection. While we know very little about the relative susceptibilities of fibers of different sizes to injury, and while we have had little experience with peroneal nerves, we do know that the spread of fibers as indicated by the crest time is greater than appears in the sciatic data published in 1924. The potential wave was recorded at 146 mm. of conduction; but at 80 mm. of conduction the crest time was 1.1 σ, which may be compared with 0.8 σ, an average of the published values in the sciatic at that distance. The supposition that tapering occurs in the fibers would not aid in the explanation and the sizes recorded in figure 6 are not in favor of its existence.

In figure 7, there is an instance of the dependence of the wave form on the distribution curve. There is an extra hump on the rising phase and this also appears in the recorded potential.

In the distribution curve every size is represented. When the action potential was built up in 18 successive steps by increasing the strength of stimulation, no point could be found in which additional fibers could not be added to the total. While injury of fibers might tend to fill a gap in the electrical picture, and the error in measuring diameters one in the distribution curve, the results clearly indicate that there is no marked free interval in either. Also addition of the fibers in the two roots does not
indicate that there would be free spaces in the distribution curves of a mixed nerve.

In order to prove that the analysis of the IXth pair of roots may be taken as typical of roots in the bullfrog, partial analyses were made of the seventh and eighth pairs of another frog. These analyses, which are put on record in figures 8 and 9, indicate that essentially the same conditions obtain in the other roots. In a previous paper on the spinal roots (1926) it was stated that the velocities of conduction in the motor and sensory roots are essentially alike and that if there be any difference, the sensory root contains fibers of lower threshold and higher velocity, the roots however differing somewhat with respect to one another. The similarity of the maximum velocities is borne out by the fact that the largest fibers are usually about 20 μ in diameter. On the other hand no regular morphological evidence for faster fibers in the sensory root appears. The larger fibers in the eighth pair arc sensory but the reverse is true in the seventh. But, masmuch as there is a variation in the relationship as recorded in the series of experiments quoted, these few analyses cannot be considered out of accord with the earlier observations. Among the observations in the same paper is an estimation of the range of fiber velocities in the motor root, derived from experimental data. The range was stated to be between 42 and 20 m.p.s. These values are in accord with the distribution curves if we assume that what was recorded in the experiments was the beginning and end of the main mass of the fibers, the actual total range must be larger.

Sciatic nerve. The nerve which has been most studied by us in the last few years and about which the most data have been collected, is the sciatic nerve of the bullfrog. More comparisons can, therefore, be made between reconstructions of this nerve and various characteristics of the action potential wave than are possible for any other nerve. An analysis of a part of the nerve for fibers above 5 μ gives the distribution curve recorded in figure 10, which shows again the three groups of fibers seen in the peroneal nerve. Reconstructions were made at 82 and 31 mm. of conduction (fig. 11) which may be compared with the potentials published in figure 2, 1924. The agreement is amazingly excellent, the differences being hardly greater than those between the two nerves of figures 2 and 3 in the same paper. The positions of the α and β crests coincide.

Fig. 6. Distribution curve of all the fibers (377) in the peroneal nerve of the bullfrog.
Fig. 7. Reconstruction of peroneal action potential at 146 mm. Corresponding recorded potential.
Fig. 8. Distribution curve of the VIIIth pair of spinal roots of the bullfrog, (partial analysis). a. motor root (350 fibers, about ½ total). b. sensory root (396 fibers).
Fig. 9. VIIth pair of roots (partial analysis). a. motor (194 fibers). b. sensory (287 fibers).

Fig. 10. Distribution curve for the sciatic nerve of the bullfrog (partial analysis, 514 fibers).

Fig. 11. Reconstruction of the action potential of the sciatic nerve of the bullfrog. • • • • •, at 82 mm. of conduction. xxxxxx, at 31 mm. of conduction.
Inset: duration of the rising phases at the distances indicated on abscissae. xxxxxxx, from reconstructions. • • • • •, experimental data from table 2, 1925, lxxiii, 620, this Journal.

Fig. 12. Reconstruction of the maximum potentials at various distances of conduction. xxxxxxx, whole nerve active. ○ ○ ○ ○ ○, activity only in the α group. • • • • •, recorded maximum potentials taken from an experiment especially performed for the purpose. + + + + +, points on a curve of maximum potentials of the α fibers only (6/19/24).
Also a trace of the $\gamma$ wave shows in the reconstruction. It begins about 0.5 $\sigma$ later than the one in figure 2b, but a reference to the original figure in 2a shows that the position of this point in the line is not one to give accurate readings.

In addition to the reconstructions reproduced, others were made at various distances of conduction, so that the behavior of the predicted curves could be compared with the real ones. Taking first the duration of the phase of rising potential (inset, fig. 11), the theoretical upper curve has the same general shape as the lower curve obtained by experiment. They both start with a steep slope. The theoretical durations however are around 0.07 $\sigma$ longer than the real ones and at 8 cm. the slope of the reconstructed curve is slightly greater. The reason for this will appear after we examine the maximum potentials at the various distances. These are recorded in figure 12. The upper solid line is the reconstruction for the whole nerve; it should be compared with the dotted line experimentally determined. The agreement is good enough to pass without comment. At the longer distances the slope of the real curve is less steep so that it comes to lie above the theoretical. This relationship corresponds with the slightly longer rising phases found at these distances in the reconstructions, and must be attributed to a slightly slower mutual separation of fibers than that postulated. The lower solid line is the reconstructed maximum potentials of the $\alpha$ fibers only. On this curve are placed as $+$ signs data from an experiment in which these values were determined. The coincidence of the potentials with the theoretical, when plotted on the same scale as the latter, is exact. The two theoretical curves of the maximal potentials obtained when the whole nerve is active and when the $\alpha$ fibers only are active, deviate in figure 12, at about 4 cm. This is the position of deviation in fact; it merely means that beyond this point the large mass of fibers which makes up the $\beta$ group is so far behind, that it does not enter into the maximum value at all; therefore, beyond 4 cm. the maximum is the same in the two cases.

Green frog nerve (Rana pipiens). The only green frog nerve that has been examined is the peroneal. Its analysis (fig. 13) gives a distribution which on reconstruction gives a $\beta$ wave somewhat earlier than the real one, just as occurred in the bullfrog. The principal interest in this curve lies in the range of fiber sizes. The largest fiber is 13.9 $\mu$ in size, while the largest
fiber in the bullfrog nerve (fig. 6) was 19.2 µ. Ever since we have been working on bullfrogs we have known that its fastest fibers are much faster than those in the green frog, without having any explanation of why this should be so. It now appears that this is connected with the size of fibers. The recorded velocities were 31.8 m.p.s. and 43.2 m.p.s. respectively; 19.2/13.9 of 31.8 is 43.9, therefore size for size the nerve fibers in the two species seem to have the same velocity.

Mammalian Nerve. The phrenic and saphenous nerves of the dog may be taken as two good examples of mammalian nerves giving action potentials of different forms. Three phrenic nerves have been analysed and two saphenous nerves. Of the former two are reproduced (figs. 14 and 15) and of the latter, one (fig. 15). The phrenic nerves have a single peak at 8 µ with the number of fibers dropping off to either side as occurs in a motor root, the total range being between 5 and 12 µ, the very small sympathetic fibers in the nerves not having been measured.

While the figure 14 analysis is more complete, it does not deviate from that in figure 15. As the latter was the first one made, it happens that the data have been examined in more detail. In the first place the data, as would be expected, give a perfectly smooth reconstruction which corresponds to the smooth action potential. Reconstructions were made up to distances of 10 cm., and the decrease in the maximal potential and the increase in the time to maximum were compared with experimental data in figure 16. Small size redrawings of the large size originals appear in the inset of figure 15. The curve of maximal potentials from the reconstructions is plotted to the scale of the recorded potentials so that the curves will coincide at the start; the durations of the rising phases are absolute values and are plotted as determined. The general slopes of the curves are alike. The deviation of the curves of maximal potentials is in such a direction that the reconstructed curve falls off more rapidly than the one from the nerve. Corresponding to this the time to maximum tends to increase slightly more rapidly in the former than in the latter. The explanation of this may be again that the axon potentials actually become mutually separated at a slightly slower rate than that postulated, though other factors can enter. Times to maximum differing less from the theoretical curve have been recorded, for instance in the experiment of 5/16/23, published in 1924, points from which are inserted into the figure as black dots.

The saphenous nerve differs from the phrenic in the large number of fibers below 6 µ, and in the possession of a few larger fibers. As the saphenous is purely sensory it follows that many of its functions are subserved by small fibers, such as do not go to a muscle at all. The muscle sense must therefore, as has been suggested by Sherrington, be carried by relatively large fibers.
Fig. 16. Analysis of reconstructions of the action potential in the phrenic nerve of the dog made from the data in figure 15. XXXX, reconstructions. O O O O, data from recorded action potentials of the phrenic of 2/14/24. • • • •, data from recorded action potentials of the phrenic of 5/16/23 (published 1924).

Fig. 17. Reconstruction of the saphenous action potential at 95 mm., for comparison with that of experiment 12/16/22 (1924, p. 653, fig. 13).
In an experiment of 12/16/22, the velocity of conduction in the saphenous nerve was found to be 83 m.p.s. In the reconstruction of the saphenous action potential this velocity was assigned to the 15 μ group. This ignored the two fastest fibers and it must be admitted that this was done to obtain a better result. The two fibers omitted, however, were larger than any appearing in the other saphenous nerve examined. The resulting curve (fig. 17) bears a definite resemblance to the real action potential. The β wave is perhaps somewhat less prominent but it is definitely present, a point which is not so obvious at a first glance at the distribution curve.

The chorda-tympani and the lingual nerve of the dog. A statement of Heidenhain's that the chorda-tympani is made up almost entirely of 4 μ fibers led us to try to identify the velocity of fibers of this size, which could be observed both before and after entrance into the lingual. The lingual was dissected out and followed back to the point where the chorda-tympani entered it from the facial. The chorda was then traced to its point of emergence from the Glaserian fissure, excised and mounted in a moist chamber at 37°. By distal stimulation a lead could be taken from the chorda-lingual just before the chorda branch, then by a three millimeter shift the lead could be moved to the latter; when this procedure was followed a small wave appeared on the falling phase of the chorda-lingual action potential which was identified because it turned off into the chorda to become its action potential (fig. 18). A secondary wave was thus associated with a definite group of fibers, but the histological picture showed that, while 4 μ is the maximum of the distribution curve of the chorda fibers, there are many fibers on each side of this position extending from 1.5 μ up to 7 or 8 μ. The recorded velocities of the lingual fibers and the chorda fibers were respectively 69.1 and 36.4 m.p.s.; 13.5/8.2 × 36.4 is 60.0, a value considerably smaller than 69.1, which would indicate faster conduction in the slow fibers than that predicted from a strictly linear relationship. However, if the assumption be made that the potential effect of the two largest fibers of the chorda would be missed in an action potential as small as that of the chorda, then 13.5/7.25 × 36.4 = 67.8, which is in much better accord with the actual lingual velocity. While this experiment is in accord with the general thesis, it did not yield the decisive data which were hoped for.

Comparison of frog and mammalian nerve. We have seen that the difference between the velocities of the sciatic nerve fibers of the bullfrog and of the green frog can be explained by the difference in the sizes of the fibers. This is an incentive to examine what data are available on mammalian nerve to see if, when allowance is made for the difference in temperature, the velocity in mammalian fibers may not be calculated from
that in the frog fibers. In making the comparison, fibers of the same size must be considered. The present state of the knowledge of the effect of temperature upon nerve is not sufficiently good for one to employ the temperature coefficient with any feeling of security. In general the coefficients are found to lie between 1.5 and 2.0. Lucas found for frog nerve an average of 1.79, Ganter 1.75, Broemser 1.79 for nerves kept a short period at the temperatures examined. Snyder reports higher values, but his average between 20° and 30° is 1.5. He gives a value of 2.6 between 10° and 20°; however, there are much lower coefficients to be calculated from his data. As Broemser has pointed out, the coefficient depends on

![Figure 18](http://ajplegacy.physiology.org/)

**Fig. 18.** Distribution curves of the chorda-lingual of the dog (upper) and the chorda-tympani (lower); partial analyses.

Inset: action potentials of chorda-lingual (upper) and chorda-tympani (lower); reproduction X 0.7. Movement of the chorda-lingual figure on the screen has caused it to make three impressions.

the previous condition of the nerve, and after conservation in Ringer's solution for 40 minutes before the determinations, he obtained values as low as 1.15 thus recalling the contention of Weiss that temperature is without effect. With the coefficient in frogs depending upon the temperatures from which it is calculated, upon the duration at those temperatures and upon the previous temperatures, selection of one for comparison with mammalian nerve is bound to be a purely arbitrary procedure. What is really done is to see what would happen in a mammalian nerve if the local reaction velocity in the latter can be compared with frog nerve by such a constant.
A start was made by comparing the green-frog sciatic and the phrenic nerve of the dog. The velocities of three frog nerves, whose temperatures at the time of observation were known, were selected from table 1, 1924. In figure 13 of this paper, which is the only analysis we have of a green frog nerve trunk, the largest fiber is \(13.75\ \mu\). In three phrenic nerves of the dog the largest fibers were found to be respectively 12.1, 12.3 and 12.7 \(\mu\) (ave. 12.4 \(\mu\)). From the velocities of the fastest fibers of a green frog the velocity of a 12.4 \(\mu\) fiber was computed by the ratio of the diameters; then this velocity was recalculated for 37\(^\circ\). In order to cover the possibilities this was done for three values of \(Q_{10}\): 2, 1.7 and 1.5. The calculation was easily made graphically with sufficient accuracy. The averages for the three fibers at the three coefficients were then determined and recorded in table 1.

### Table 1

<table>
<thead>
<tr>
<th>NERVE SIZE ((\mu))</th>
<th>VELOCITY M.P.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Q_{10} = 2)</td>
</tr>
<tr>
<td>11/18/22 (35.5 m.p.s. at 24.5(^\circ))</td>
<td>76.5</td>
</tr>
<tr>
<td>11/20/22 (29.8 m.p.s. at 21.6(^\circ))</td>
<td>77.0</td>
</tr>
<tr>
<td>11/22/22 (33.3 m.p.s. at 23.3(^\circ))</td>
<td>76.5</td>
</tr>
<tr>
<td>Average..................</td>
<td>76.7</td>
</tr>
</tbody>
</table>

| If 17 | 105 | 84 | 71 |
| If 14.4 | 89 | 71 | 60 |
| At 13.5 | 84 | 67 | 50 |
| At 8.2 | 31 | 40.6 | 34 |

In general the phrenic nerve has given quite variable velocities of conduction. One source of error, not realized in the earlier determinations, is that the nerve has a tendency to curl up in its sheath so that the measurements of the length may be inaccurate. In table 1, 1924, values of 50, 52.9 and 73.5 m.p.s. are given. A recent determination gave 61.5 m.p.s. (1/7/26). An average of the former, or the latter, agrees very well with the calculated velocity at 37\(^\circ\) for the green frog using \(Q_{10} = 1.7\). This value happens to be close to the average values of \(Q_{10}\) cited above.

In two saphenous nerves of the dog (1924) the velocities were respectively 83.3 and 71.5 m.p.s. In the two saphenous nerves which have been analysed for size of fibers the largest fibers were found to be 17 \(\mu\) and 14.4 \(\mu\) respectively. Accordingly, the velocities green frog fibers of these sizes would have, were calculated for 37\(^\circ\) (table 1). If \(Q_{10} = 2\) the velocities would be too high to accord with those observed. At \(Q_{10} = 1.7\)
however the two velocities accord very well with the two nerves on which we have data. At 1.5 the calculated velocities become too slow.

The other mammalian nerves on which we have the necessary information are the lingual of the dog and the chorda tympani, whose largest fibers are 13.5 μ and 8.2 μ respectively, with velocities of 69.1 and 36.4 m.p.s. These are comparable to the values in the \( Q_{10} = 1.7 \) column of Table 1, which gives for these sizes 67 and 40.6 m.p.s. One experiment was made directly on the conduction rates in mammalian nerve at room and body temperature. The nerve employed was the popliteal division of the sciatic of the rabbit. At 24° the velocity was 44.2 m.p.s.; at 38.7°, 87.6 m.p.s., which would give a \( Q_{10} \) of about 1.6. An examination of the rabbit nerve showed that the largest fibers were about 18 to 19 μ in size which must be compared with 20 to 21 μ in bullfrog nerve. Forty-four m.p.s. is an average rate in bullfrog nerve at room temperature. It is therefore somewhat faster than the average velocity in frog 18 to 19 μ fibers. However, it is not an impossible figure for the latter, as in exceptional cases we have obtained velocities which would indicate rates as fast as 44 m.p.s. in such fibers.

The analyses as far as they go are compatible with the generalization that conduction in nerve fibers from different species depends primarily upon the size of fiber and the temperature. To establish this point will require a more extensive and detailed study necessitating the proof of lack of exceptions.

DISCUSSION. The foregoing data are believed to show that the important variable in nerve fiber construction, determining the velocity of conduction, is the size. The shape of the action potential wave, the appearance of secondary waves, the increase in time to maximum potential and the decrease in its value can be satisfactorily explained at least to a first order approximation by conduction velocities differing from one another as the ratio of the diameters of the fibers. Deviations from this assumption are not constant, the small fibers conducting more slowly than thus postulated in the two peroneal nerves recorded at their distal ends, and slightly less slowly than postulated in some other nerves examined. In general the evidence indicates that, if the small fibers deviate from the rule, their conduction is slightly faster than that predicted from the ratios of their diameters to the maximum diameter in the trunk.

SUMMARY

In this paper the relation between the activity of nerve, as revealed by its electrical sign, and its morphology is studied.

In various nerves the fibers were measured and the results plotted so as to reveal graphically the number and area of the fibers at each size.

Theoretical reconstructions were made of the action potential waves
making use of the following observations and assumptions which are explained in the text.

a. In a given nerve trunk the duration of the axon action potential is the same in fibers of all velocities.

b. The wave form is assumed to be triangular but its dimensions are chosen so as to subtend an area equal to the recorded axon potential area, as near as this can be determined. For this purpose, in mammalian nerve the rising phase is taken as 0.2 $\sigma$ and the duration as 0.6 $\sigma$. For frog nerve the corresponding values are 0.3 $\sigma$ and 0.9 $\sigma$.

c. The rate of propagation is uniform throughout the fiber.

d. The maximum potential developed is the same in all fibers. The fiber would then affect the recording instrument as the internal resistance (cross-section) of the fiber.

The reconstructions closely resemble the actually recorded potential waves, if the velocities of conduction in the axons are assumed to vary directly as the diameters of the axons. We therefore conclude that at least to a first approximation the velocity in a fiber is determined by the diameter.

It is possible by a histological examination of a nerve trunk to predict with some accuracy the form of the action potential it will yield. The reconstructed action potential wave behaves with regard to form, changes of form with conduction (such as increase in the time to maximal potential and decrease of the size of this maximal potential), and appearance of secondary waves, in the same manner as does the corresponding action potential as recorded.

The distribution curves of the spinal roots are just as different as the action potential waves. The total range of fiber sizes in the two roots is nearly the same, but the peak of the area of the fibers comes at about 15 $\mu$ in the motor root, while in the sensory root the peak comes at 8 to 9 $\mu$, with a secondary peak at 14 to 15 $\mu$. The single peak in the motor root corresponds with its simple action potential curve. The two peaks in the sensory root on the other hand correspond with the two waves in its compound action potential. The second or $\beta$ wave is due to fibers below about 12 $\mu$ in size. The area of this group is larger than that of the group of $\alpha$ fibers and corresponding to this, the area of the $\beta$ group in the recorded potential is also larger; but the height is lower than that of the $\alpha$ wave due to the greater mutual spread of the smaller fibers on conduction.

In the sciatic and peroneal nerves the fibers appear in three groups. It is this unequal distribution which is responsible for the $\alpha$, $\beta$ and $\gamma$ waves.

The velocity of conduction in the green frog sciatic is less than in that of the bullfrog at the same temperature; corresponding to this, the fibers in the former are smaller.

The distribution curves of the phrenic and saphenous nerves of the dog correspond to their widely different action potentials. As in the sensory
root the β wave in the latter nerve is due to the large mass of small fibers in its composition.

The chorda-tymanini fibers in the chorda-lingual nerve, producing a secondary potential wave, may be identified by tracing them into the chorda before its union with the lingual. Their size is then found to correspond with the velocity of the wave.

The available data are analysed for the degree of relationship which may be inferred between mammalian and frog fibers of the same size, when the temperature coefficient is taken into consideration.

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