AXON DIAMETERS IN RELATION TO THE SPIKE DIMENSIONS AND THE CONDUCTION VELOCITY IN MAMMALIAN A FIBERS

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The problem of the relationship between the diameters of nerve fibers and the velocity at which the fibers conduct impulses cannot be considered solved until it is possible, within the range of a homogeneous group of fibers, to predict correctly the form of the action potential on the basis of the histological picture. Of all the methods as yet proposed, the reconstruction method is the most sensitive. As the method was first employed (11) it appeared to work satisfactorily on the basis of direct proportionality between conduction velocity and the diameter of the fibers. But the full range of the fiber velocities was then unknown and later attempts to apply the procedure to the complete series failed to give an acceptable result, or involved an assumption the validity of which can no longer be maintained (10).

Recent developments have been made with other methods. Blair and Erlanger observed that in frog nerves the size of single-fiber spikes varies directly as the velocity of conduction, and they argued that if the size of the spike is proportional to the cross-section of the fiber, the velocity must vary as the square of the diameter. And Zotterman came to the same conclusion after confirming their results on mammalian fibers. Reconstructions, however, in accord with the power relationship fail to match the recorded potentials (Erlanger, 1937, fig. 14).

A different conclusion was reached by Hursh (1939a), who compared the maximal velocities in a series of mammalian nerves with the respective sizes of the largest fibers. All the points relating the two properties fell about a straight line. A still different relationship was found by Pumphrey and Young for squid fibers. The diameters of the large axons in the fresh state were measured and compared with the individually determined velocities; those of the small axons were measured after fixation and compared with the maximal velocity for the group. The result was a distribution of points best connected by a curve describing the velocity as varying with the 0.6 power of the diameter.

The fact that the relationship of velocity and fiber diameter has been
set forth in the several descriptions in terms of functions as different as the square, the first power, and the square root indicates the existence of steps in the derivation of the formulations that need re-evaluation. In view of this need the present investigation was undertaken. Extensive use was made of the reconstruction method for two reasons. In the first place, the potentialities of the method as they would appear if advantage were taken of the current knowledge of the constants of mammalian fibers were unknown. And in the second place it was realized that the prevalent theories would be subjected to rigorous test. If the method failed to produce anything constructive, it could at least be expected that it would reveal which of the considerations forming the basis of the theories should be retained and which rejected.

Homogeneity of material. If the effect of the dimensions of nerve fibers upon the velocity of conduction is to be delimited, size must be the only variable, or the effect of all the variables other than size must be known. The duration of the spike has long been thought to be a factor entering into the determination of the velocity, but precise information about the nature of the relationship is lacking. Until this information is supplied, any system of fibers brought under examination for the purpose of ascertaining the effect of size upon velocity must have action potentials characterized by spikes of the same duration.

The saphenous nerve has been used for most of the observations, because the prominence of the elevations in the conducted action potential makes the nerve a favorable one for the identification of the position of the potentials belonging to given fiber groups. The elevations are best seen in the nerve of the rabbit (fig. 11). For convenience the groups are labelled $\alpha$, $\beta$, $\gamma$, $\delta$. In the cat's nerve the alpha and beta elevations are fused, and the alpha and delta groups headed by velocities of about 90 and 20 m.p.s. supply the prominent features.

The specific question must be asked: Do the spikes entering into the delta elevation have the same duration as those entering into alpha? One of the first procedures that was devised for the determination of spike duration was to extrapolate the duration of an elevation back to zero distance (9). Great accuracy cannot be claimed for the method, but the procedure has in its favor the fact that it orients the experimenter forthwith concerning the relative durations of the alpha and delta spikes, and gives at one time and under the best of experimental conditions information about all the five hundred or more fibers in the delta pile. Figure 1, which shows the application of the procedure, is in a large measure self-explanatory. The action potentials as recorded at five distances of conduction are drawn with

1 For the history of the names of the groups and of the ideas about them, the following references may be consulted: Bishop and Heinbecker, 1930; Bishop, Heinbecker and O'Leary, 1932; and Erlanger, 1937.
their base lines at ordinate positions corresponding to the distances. Pro-
jections on the base lines of the starts and ends of the alpha and delta eleva-
tions and of the start of a small predelta wave mark the times of these
events. And lines drawn through the projection points give at their inter-
section with the line of zero distance, the time of the event in the uncon-
ducted action.

Proof of the expediency of determining the times by extrapolation is
found in the fact that the lines marking the starts of the elevations pass
through the origin. The first two lines, marking respectively the start and
the end of the alpha elevation, subtend at the zero line a time of about 0.4
msec.,—a time which corresponds very closely with that obtained from
the best single fiber records of alpha spikes. The third and fourth lines
marking the starts of the predelta and delta groups again pass through the
origin. The fifth line at the end of the delta elevation cuts the zero line
at between 0.4 and 0.5 msec. Thus it is clearly shown that the spikes in
the delta elevation must have a duration the same as, or very close to,
those in the alpha elevation. Any possibility of the duration being pro-
portional to the velocity is completely eliminated. The potential of the
whole group has a duration of only 0.9 msec. at 5 cm. of conduction.
Another line could have been drawn from the delta crests. It would cut
the zero line at 0.15 msec., again a time which is in close correspondence
to that for alpha fibers.

The opportunity for error, which the method shares with all methods in-
volving extrapolations, is in this instance reduced by the fact that the ex-
trapolation is effected with the aid of a straight line passing through five
real points. One could not draw conclusions from small differences, but
on the other hand, the indication that the alpha and delta spikes are closely
similar in duration must be taken as being valid. It will be shown later
that the finding is in accord with the body of evidence obtained from the
measurements of single-fiber spikes.

Figure 1 contains another feature that has orienting significance. After
9 cm. of conduction, temporal dispersion has brought the delta elevation
from an initial value of < 0.5 msec. to a total of 1.3 msec. As the potentials
in slow fibers disperse rapidly, it follows that the elevation must represent
a very narrow band of fibers. A brief calculation indicates how wide a
band is to be looked for. If the spikes last 0.5 msec., the last of the im-
ulses will be 0.8 msec. behind the first. With an initial velocity of 23
m.p.s., the final velocity, therefore, must be 19 m.p.s. If the wave starts
at 4 μ and the velocity is in a linear relationship to the diameter, it will
end at 3.3 μ. Thus the elevation will be produced by a band much less
than 1 μ wide.

In the saphenous nerve of the rabbit the delta fibers conduct more slowly
than in the cat (12.5 m.p.s. as compared with 22 m.p.s.). Extrapolations
were, therefore, made to see whether these fibers also have spikes with an alpha duration. The experiments were not as satisfactory as in the cat,

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

**Fig. 1.** Action potential in the saphenous nerve of the cat recorded at the distances indicated on the ordinates. Because of crowding in the figure, only the projections of the events on the base line are shown at 2 cm. of conduction. The distance subtended by the converging lines at the axis of abscissas measures the duration of the alpha and delta spikes. The delta elevation in the tracings rises from the negative after-potential of alpha. Between alpha and delta a well defined gamma elevation is visible. It will be seen later in the reconstructions that there is always a group of fibers corresponding to it.

**Fig. 2.** Durations of the beta and delta elevations in the action potential of the saphenous nerve of the rabbit as recorded at four distances of conduction, and the extrapolation of these durations to zero distance. The experiment parallels the one shown in figure 1. The action potentials are omitted and only the projections of the elevations on the base lines are shown. The velocity in the fastest alpha fibers in this nerve was 70 m.p.s.

but they sufficed to show that the spikes in the two groups of fibers are similar (fig. 2). Part of the interest in the experiment lies in the fact that
the rabbit delta fibers have a velocity equivalent to the fastest B fibers in visceral nerves, but a much shorter spike duration, as the duration in the latter is about 1.2 msec. (Grundfest). The data, therefore, favor the view of Bishop and Heinbecker that there is a break in the properties of the fibers sharp enough to justify their classification into separate groups (A and B), rather than the idea that the fiber types form a continuous series. Single fiber records of rabbit delta spikes confirm the fact that these spikes have an alpha duration (fig. 3). That beta spikes also resemble alpha is shown in figure 2.

The constancy of the duration of the spikes of all fibers of the A group, regardless of the conduction velocity, also appears in series of single axon action potentials. Spikes in fibers with slow and intermediate velocities of conduction were obtained from nerves in which these velocities were at the maximum of those present. The nerves were stimulated at threshold, and the singularity of the potentials was insured by watching for indivisible constant-sized responses playing in the manner described by Blair and Erlanger (1933). Many of the nerves containing only slow fibers are short, and for that reason are unfavorable for velocity determinations, as the shock-response time is the only measurement from which the velocity can be calculated. Measurements of the shock-response time at threshold are valueless, but if the strength of stimulus is increased, a point can be found at which the time does not change with the strength of the shock. From this time it is possible to calculate a velocity that is sufficiently accurate for the present purposes.

Single delta spikes can be obtained from the saphenous nerve by using small branches and conduction distances long enough to permit clearance of the preceding groups. For these preparations, Hodgkin’s method of transferring the nerve from saline into a layer of liquid paraffin was employed, after making the changes in the method necessary for its adaptation to mammalian fibers.

The recording of mammalian spikes which last but little over 0.4 msec. requires a fast amplifier, particularly if the recording is from a small strand of nerve with a high resistance. Our amplifiers have now been rebuilt by Doctor Toennies to a speed which is more than adequate for the purpose. A rectangular impulse applied through an input resistance of 100,000 ohms reaches 90 per cent of its final value in 0.015 msec. At 10 Kc the loss of amplification is only 0 to 10 per cent (as compared with 60 per cent with the former amplifiers), and at 15 Kc it is only 5 to 15 per cent, depending upon how the amplification control dials are set. An impulse with spike dimensions would have its crest delayed about 25 per cent by the old amplifiers as compared with the new,—which means that a 0.14 msec. crest time would appear to be 0.17 msec. The fidelity at high frequencies, however, brings with it one disadvantage,—the ability to record noise is also augmented, and the noise level is raised from ±5 μV to ±10 12 μV.
Samples of single axon spikes obtained from fibers conducting at different velocities have been collected in figure 3. They all appear alike in duration and the measurements all fall between 0.4 and 0.5 msec., without a systematic difference with respect to velocity. It would be difficult to measure them closer than to 0.1 msec.

Fig. 3. Single axon spikes arranged according to velocity (simultaneous responses in 2 fibers in record i). Record h shows two sweeps. Owing to the play the spike is missing in one of them. The velocities are marked at the left in meters per sec. All records have the same time scale. a and b, from rabbit cervical sympathetic; c, d, e, g, h, from cat hypogastric; f, from rabbit depressor; i, from rabbit saphenous.

Fig. 4. a and b, after-potential record and excitability cycle curve for the same nerve. c, excitability cycle curve for the delta fibers of the saphenous nerve of the cat.

After-potentials as evidence of homogeneity. The configurations of the after-potentials of the three groups of fibers, A, B, and C, are so distinctive that classification of any set of fibers under examination with one or the other group would be impossible if the after-potentials did not conform. If the delta fibers are to be included among the A fibers, their after-potentials must be the same as the alpha after-potentials, which have been taken as representative of the A group.
The after-potentials in fibers of delta velocity can be directly recorded in the cervical sympathetic nerve of the cat, as these fibers are the largest in the nerve. The potentials have an A configuration (fig. 4 a).

In the delta group of the saphenous nerve of the cat the after-potentials cannot be recorded directly, and they are even too small to have their form determined by difference in comparisons of the action potentials of the whole nerve, with and without the inclusion of the delta group in the activity. There is, however, a good indirect method for determining their form, derivative from the parallelism that exists between the after-potential and the excitability cycle. Below the action potential of the cervical sympathetic nerve shown in figure 4 a there is drawn for comparison with it (fig. 4 b) the curve of excitability as determined on the nerve by the method of size of response to a near-threshold stimulus. That the curve follows the form of the potential is readily apparent. In the saphenous nerve at long distances of conduction the separation of the delta elevation is sufficiently great to permit an examination of the excitability. A good deal of random variation occurs in the responses to near-threshold stimuli, but the variation is not so great as to prevent the form of the curve from emerging (fig. 4 c). It is like that in the cervical sympathetic nerve. Both curves have the form known to hold for alpha fibers (12) and they differ widely from the curves for B fibers (13), although the velocity in the fibers approaches a B value.

The velocities in the delta elevation of the saphenous nerve of the rabbit actually fall in the B range, and the delta fibers are so numerous in this nerve that the form of the after-potential can be directly observed. It has an A configuration.

Additional evidence that the after-potentials in all A fibers are alike is contributed by Hursh's observation that the after-potentials in immature alpha fibers, at the stage in which their impulses are conducted at delta velocity, have the form of those in adult fibers.

The medullated fibers in the saphenous nerve are within the limits of measurement homogeneous with respect to the spike and after-potentials. They differ with respect to their velocities and periods of absolute refractoriness. We have not examined the refractory period extensively, but we have had enough experience with it to know that it varies in a continuous manner, as described for frog fibers by Blair and Erlanger. The delta fibers have a refractory period of 0.6 to 0.7 msec. in the cat and 0.9 to 1.0 msec. in the rabbit, as opposed to 0.4 to 0.45 msec. for the fastest alpha fibers. In view of the constancy of the spike, the variation of the refractory period is surprising, as no previous examples have been known of exceptions to Adrian's finding that the absolutely refractory period ends at the base of the spike. The reason for the progressive divergence between the spike duration and the refractory period as the velocities de-
crease is not clear. The properties of the after-potentials cannot be called upon, as they are constant throughout. Size, however, may enter into the determination of the duration of the absolutely refractory period, just as it does into the determination of the resting threshold of excitation. The prolongation of the absolutely refractory period of immature alpha fibers found by Hursh affords another example of a modification of this property by the size of the fibers.

Preparation and measurement of fibers. The obtaining of good histological preparations depends in large measure upon having the nerve in good condition at the time of fixation. In order to make the technique as conservative as possible, the action potential was recorded as soon after isolation of the nerve from the body as enough time had elapsed to permit the preparation to come to 38°C. and into equilibrium with the gas mixture (95 per cent O₂ + 5 per cent CO₂). Immediately thereafter the nerve was fixed in 1 per cent osmic acid. The outside diameters of the fibers were measured with an ocular micrometer, and as each measurement was made the fiber was checked on a microphotograph of the section enlarged to 2000 diameters. The fibers were then catalogued according to size and the distribution was plotted to the nearest 0.1 or 0.25 μ, as seen in the charts (figs. 5, 8, 10, 12, 15).

The first question to be asked about the measured diameters is: how faithfully do they represent the diameters of fresh fibers? There can be little doubt that shrinkage occurs in the course of preparation. Hursh found that the dehydration process used during embedding shrunk the fibers 10 per cent (8.2–12.9), and Arnell had previously found a similar amount of shrinkage produced by another method. A corrective factor, however, would permit calculation of the size in the fresh state with a fair degree of accuracy, and shrinkage could only cause difficulty if it were differential. Hursh found that it was not differential for fibers larger than 10 μ. Smaller fibers were not examined.

A more serious difficulty is found in the random variation of the diameter in the course of the fibers. In 100 serial sections from 0.6 mm. of nerve Hursh found the standard deviation of a single measurement of a 6.5 μ fiber to be ±0.47 μ. Of this amount not more than ±0.1 to 0.2 μ could be attributed to fortuitous error in reading. Duncan found a still greater irregularity in the outline of fibers fixed in osmic acid. In parts of the distribution curves, where the number of fibers is changing slowly with the diameter, the differences between the measured diameters and the true mean diameters would tend to cancel out, as erroneously large measurements would compensate erroneously small measurements of adjacent fibers. But, as will be seen later, in positions where there is a rapid transition in the sizes of the fibers, it is possible for a deviation of the above magnitude to cause considerable difficulty in the preparation of reconstructions through making a band of fibers appear too wide.
The distribution of fibers according to size in the saphenous nerve of the cat can be seen in figures 5 and 8. The charts are similar. Both show the fibers grouped in two piles. Many indications of how the fibers will enter into the compound action potential appear straightaway on inspection of the distribution curves. Enumeration of the indications will be made, using the information contained in figure 5; but figure 8 would have served as well. It is obvious at the outset that the first pile will form the first elevation, and the second pile the second elevation. The minimum in the fibers comes at about 5 \( \mu \), and the minimum in the potential just after the first elevation; therefore, the fibers between 5 and 6 \( \mu \) should form the end of the elevation. Following the minimum in the potential, the potential builds up again, slowly at first and then more rapidly to form the delta peak. According to an expectation from an observation previously cited, the delta peak should be produced by a narrow band of fibers. Of all the fibers available, the group that is found in such great numbers around 3 \( \mu \) appears to be the most likely one for the purpose. The elevation should start with fibers between 3 and 4 \( \mu \) in diameter. As the fibers at the start of the first elevation are 14 \( \mu \) in diameter, they are four times as large. Four is approximately the factor that relates the velocities of the fastest alpha fibers to those of the fastest delta fibers. Therefore, the most favorable basis for starting the reconstructions is one which considers the relationship between fiber diameter and velocity to be linear.

*The method of making reconstructions* is the following. After a velocity
has been assigned to a fiber of a given size, the conduction time is calculated from that velocity and the distance of conduction at which the action potential in the nerve had been recorded. A triangle imitating the dimensions of a spike and having a height proportional to the number of fibers of the size in question present in the nerve is then drawn above the baseline, with its front touching the abscissa corresponding to the conduction time. After all the triangles are in place, they are added together and the resulting curve is compared with the form of the recorded action potential.

The assumptions on which the original reconstructions were made were that the axon spike height is proportional to the cross-sectional area of the fiber and that the velocity is proportional to the diameter. That there is a fallacy in these assumptions soon became apparent when reconstructions were attempted on the same basis with the present data. Of the defects in the result one of the most outstanding was the fact that the second elevation was much too small as compared with the first. There could only be one explanation for the discrepancy; namely, that the assumption that the spike height varies as the cross-section of the fiber was incorrect.

At the basis of the assumption was the sound physical fact that the potential drop across a resistance, through which a current is flowing from a source that would yield the potential, \( E \), on open circuit, depends upon the internal resistance of the source. As the resistance of the nerve fibers would vary as their cross-section, this dimension was taken to be the controlling one in the calculation of the spike heights used for the first reconstructions. At the time there was no reason for questioning the calculation, because of the apparent success with which the then known part of the compound action potential was reproduced. Nor has the calculation been questioned up to the present time.

One factor, however, was neglected. The resistance of a nerve fiber depends not only upon its cross-section, but also upon its length. Neglect of this factor is equivalent to the assumption, either that the factor is not important, or that the length is constant. The second alternative reveals the source of the difficulty. Data have just been presented showing that the spike duration is constant; and the view that the wave length varies with the velocity is, therefore, reaffirmed. If one work on the hypothesis that the velocity varies as the diameter, one must at the same time recognize that the length of the source of the potential must vary as the diameter. Thus the proper statement about the internal resistance controlling the height of the spike would be that the resistance varies directly as the diameter—because of the wave length—and inversely as the square of the diameter, on account of the effect of the cross-sectional area. The net variation, therefore, is inversely as the first power of the diameter.

Spike height and fiber size. Introduction of the internal resistance into
the calculation of the spike height as the first power rather than as the second makes a large difference in the values obtained. The expression connecting the spike potential, \( e \), and the diameter, \( D \), would have the form

\[
e = \frac{R}{A/D + R} E
\]

where \( R \) is the external resistance, \( A/D \) is a term representing the internal resistance, and \( E \) is the e.m.f. generated by the fiber. If the membrane resistance were included it would be in series with the internal resistance; and as it too varies inversely as the diameter, the two terms representing resistance could be combined and the form of the above expression would be unchanged. The expression is in the second degree and represents a hyperbola. However, if \( R \) is small compared with \( A \), the graph approaches a straight line.

An idea of the relative magnitudes of \( R \) and \( A \) can be gained from the recorded potential of a single axon spike. Large axons in the saphenous nerve give potentials of about 0.1 mv. If the e.m.f. generated by the fiber is 50 mv, \( e/E \) would have a value of 0.002; and if the diameter of the axon is 10 \( \mu \), it can readily be shown by the substitution of these values in the above expression that \( A \) is about 5000 times as large as \( R \). With a ratio of this magnitude \( e \) would come closely into linear relation with \( D \). That the spike heights actually vary linearly with the diameters of the fibers may be concluded from the existing data on the relationship of the spike size to conduction velocity. Blair and Erlanger observed that the two properties are in linear relationship in frog fibers, and Zotterman later made a similar observation in mammalian fibers.

A few observations of our own confirm their findings. Some of them are shown in figure 6 and in figure 3 d. In the latter, two axon spikes are shown in the same record, one with a velocity of 40 m.p.s., the other with a velocity of 20 m.p.s. One spike is twice the other in size.

Blair and Erlanger, and Zotterman concluded, on the ground that the spike size would vary as the cross-section of the axon, that the velocity of conduction must vary as the square of the diameter. Another interpretation, however, is possible. If the velocity varies as the diameter, the size of the spike must also vary in this manner. With Hursh’s recent data at hand it would be impossible to postulate a velocity-diameter relationship far from linear; therefore, the best working hypothesis appeared to be that the spike-size diameter relationship is linear.

When reconstructions were made with the use of linearly varying spikes, it was found that the needed area had been supplied for the potentials of the slow fibers. But the reconstructions had other faults. The delta elevation was too close to the alpha elevation. Analysis of the cause of
the proximity brought out the finding that it was attributable not only to the fact that the delta crest came a little too early, but also to the fact that the alpha crest came a little too late. It was somewhat surprising to find that temporal dispersion in accord with linear variation of the velocity with the diameter made the first elevation too broad. Not only was all possibility that the velocity might vary as the square of the diameter thereby removed, but linear variation was also called into question.

Fig. 6

Fig. 6. Comparison of the durations and heights of spikes in single axons conducting at different velocities in a branch of the saphenous nerve of the cat. The two groups are from different preparations. Upper, Velocity₁/Velocity₂ = 1.2; height₁/height₂ = 4.3. Lower, Velocity₁/Velocity₂ = 3.3; height₁/height₂ = 3.8.

Fig. 7. Reconstruction of the action potential of the saphenous nerve of the cat from the data contained in figure 5. Conduction distance 4 cm. ---, recorded potential. --------, reconstructed potential at the places at which it does not coincide with the recorded potential. The fibers larger than 12 μ are grouped with the 12 μ fibers. Inset, Size-velocity curve. Each dot in the curve represents a triangle.

At this point the statement of the problem was changed. The form of the action potential was so close to emerging in the reconstructions and so good an idea had been gained about the part of the action potential to which given groups of fibers should contribute, that it was decided to locate the fibers in the reconstruction in the proper place to make the contribution, and then to calculate the velocity which would give them that position. The result would be an empirical velocity-diameter curve, which could be studied for further clues to the mechanism of velocity control.
Reconstructions. The procedure was in every case the same. The fibers were grouped according to the amount of dispersion that would take place in their potentials. For the large fibers the dispersion is small and the fibers could be taken in groups up to 1 \( \mu \) wide. But for the small fibers the dispersion is very large (vid. figs. 9 and 14) and bands of 0.25 to 0.1 \( \mu \) had to be used. The smallest unit was necessary, in order to prevent the appearance of a saw-tooth contour in the summation curve. The height of the triangles used in the plotting was obtained by multiplying the mean diameter of the group represented by the number of fibers. The base of the triangle was in accord with a spike duration of 0.4 msec. (0.44 msec. in figs. 7 and 16), and the crest time was set at one-third of the duration.

After the reconstruction had been completed, the velocities of conduction that would put the potentials in the positions occupied by the triangles were calculated from the conduction times. These velocities were then plotted against the fiber diameters, as is seen in the insets of the figures.

The excellence of the reconstructions could be judged by comparison with the action potential that had previously been recorded from the nerve. Certain precautions are necessary with respect to obtaining the action potential form. As is well-known, when a weak shock is used, the response appears after a latency. And when a strong shock is used, excitation spreads along the nerve away from the cathode. The ordinary saphenous nerve picture obtained with a shock strong enough to stimulate the delta fibers is distorted by the fact that the alpha elevation has been brought too far forward by the spreading shock; and the distortion is sufficiently great to be a disturbance in an analysis in which tenths of milliseconds are of significance. In order to obtain the form of the potential without distortion, the stimulus was increased with the development of the alpha elevation under observation, and a record was taken at a strength of stimulation at which the latency effect had disappeared and spread of excitation had not begun. The strength of the stimulus was then increased above the point of any latency effect in the delta fibers, and a second record was taken. The final potential form used was a composite of the two records, in which the first elevation was located from the first record and the second elevation added from the second record. The alpha elevation was adjusted in height to the height of the alpha elevation in the reconstruction and the other points were put in accordingly.

Size-velocity curves. As may be seen in a survey of the figures, all the matches between the reconstructions and the recorded potentials are good. The size-velocity curves obtained from them must, therefore, give a reliable picture of what the velocities of conduction in the several fiber groups must be. A survey of the size-velocity curves in turn brings out the fact that they have similar forms. Roughly they follow a straight line, but they
deviate from linearity in a systematic manner. The curves are all serpentine. They start with an upward concavity in the region of the small fibers and pass through a point of inflection at about 6 μ, to continue from there on with a downward concavity.

When the form of the empirical velocity-diameter curves was established, the next step was to account for their features. The first question asked was whether any part of the curve was traceable to the fact that the outside diameter instead of the axon diameter had been used in the reconstructions. Use of the outside diameter is valid only in so far as its ratio to the axon diameter is a constant. If there is variation of the ratio with respect to fiber size, a correction for it should bring the curve one step nearer to the true form.

**Ratio of axon diameter to outside diameter.** A constant ratio was claimed by Donaldson and Hoke, but the more recent measurements of Schmitt and Bear and of Arnell are not in accord with their description. Arnell's data show that the myelin is relatively thicker on mammalian fibers smaller than 9 μ,—which means smaller than 8 μ in fixed preparations. As the slopes of the velocity diameter curves are greater below 8 μ, the observation appeared to be significant to our problem. If the fibers below that diameter have relatively thicker myelin sheaths, they will have relatively thinner axons and slower velocities. Therefore, when the velocities are plotted against the diameters, the line through them will not pass through the points representing the larger fibers.
A further investigation of the relationship was easily possible because suitable data were already present in our files. Doctor Ranson had given us a section of an osmic acid preparation of the saphenous nerve of the cat in which the fibers were in a nicely rounded state. In a fasciculus of this nerve containing 675 fibers, measurements of the inside and the outside diameters had been made upon a photographic enlargement; and calculation of the ratios was a simple matter. The ratios of the axon diameter to

Fig. 9. Reconstruction of the action potential of the saphenous nerve of the cat from the data comprised in figure 8. Conduction distance 6 cm. ————, recorded potential. Heavy dots, summation of triangles. Note that the recorded action potential is diphasic. It undercuts the reconstruction following the first elevation, and the second elevation is so diphasic that the potential passes below the base line at the position of the 15 m.p.s. fibers. The latter, therefore, are visible in the reconstruction, but not in the potential. The fibers larger than 16 \( \mu \) are grouped with the 16 \( \mu \) fibers.

the total diameter are plotted in figure 12, along with the distribution curves of the fibers. Each point represents the average ratio for all the fibers of the size in the bundle. There is some scatter of the points, but it will be noted that the places at which it is greatest are those at which there are few fibers, and therefore at which there is less opportunity for the random error of individual readings to be compensated. As in Arnell's data, the myelin begins to get relatively thicker on fibers below 8 \( \mu \). Below 3 \( \mu \) the scatter of the points is too great to permit drawing a curve,
and Arnell's statement that the relative thickness begins to decrease again at that point cannot be tested. Above 8 μ the ratio is practically constant at 0.69, a value corresponding with Donaldson and Hoke's figure of 0.71.

![Distribution of fibers according to size in a bundle of the saphenous nerve of the rabbit (597 fibers)](image)

Fig. 10

![Reconstruction of the action potential of the saphenous nerve of the rabbit from the data comprised in figure 10. Conduction distance 4 cm. ---, recorded potential. -----------, reconstructed potential at the places at which it does not coincide with the recorded potential. Although every column of fibers in the distribution chart recording fibers smaller than 5 μ was plotted individually, the dispersion is so great that gaps appear between the triangles. The addition is done in a way allowing an area below the summation line equivalent to the projections above it. Two fibers, one at 11 μ and one at 10.3 μ, are included with the pile at 9.6 μ.](image)

Fig. 11. Reconstruction of the action potential of the saphenous nerve of the rabbit from the data comprised in figure 10. Conduction distance 4 cm. ---, recorded potential. -----------, reconstructed potential at the places at which it does not coincide with the recorded potential. Although every column of fibers in the distribution chart recording fibers smaller than 5 μ was plotted individually, the dispersion is so great that gaps appear between the triangles. The addition is done in a way allowing an area below the summation line equivalent to the projections above it. Two fibers, one at 11 μ and one at 10.3 μ, are included with the pile at 9.6 μ.

The data contained in the ratio curve make it possible to calculate what the size-velocity curves would be like in terms of the axon diameter; and the calculation has been made for the three graphs found in the insets of figures 7, 9 and 11. The result is striking (fig. 13 A). In two of the derivative curves there is none of the initial upward concavity that made the
Fig. 12. Distribution of the fiber sizes in a fasciculus of the saphenous nerve containing 675 fibers, plotted for both the axon diameter and the outside diameter. In the uppermost graph the axon-diameter outside-diameter ratio is plotted against the outside diameter.

Fig. 13. A, size-velocity curves from figures 7, 9, and 11, calculated in terms of the axon diameter and presented respectively in curves 1, 2, and 3. B, curves in A brought together by multipliers. Points representing curve 2 may be identified as they fall at 3, 3.5, 4, etc. μ. Those for curve 3 occur at the same intervals, but 0.15 μ later; for curve 1 they fall 0.3 μ later.

original curves serpentine, and in the third the concavity is nearly obliterated. This residual flattening at the end of the curve may have another cause. Wherever in the distribution of the fibers there is a sharply sep-
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arate band, the error of measurement will tend to make the band appear too wide; and moving the fibers back from their registered position to their proper position, in order to obtain a fit with the action potential, will flatten the size-velocity curve.

If the conclusion drawn from the adjusted curves is correct, it should be possible to construct the action potential from the axon-size distribution curve and obtain the elevations in their proper positions, when a constant multiplier is used to obtain the several axon velocities. The action potential had not been taken from the nerve analyzed in figure 12, but saphenous action potentials are so much alike that the merits of a reconstruction can be judged without having the individual potential available. The form that the potential would have after the impulses have been con-

Fig. 14. Action potential which would be obtained at 4 cm. of conduction from the branch of the saphenous nerve shown in figure 12, if the conduction velocities in meters per second were 7.4 times the diameters of the axons in micra. The entries into the reconstruction in the delta region were at 0.1 \( \mu \) intervals. The lower scale shows the positions of the potentials according to fiber size.

ducted 4 cm., if the velocities of the impulses in meters per second are 7.4 times the axon diameter, is shown in figure 14. The late elevations are in exactly the right place with respect to the start of the first elevation and their size is usual, except that the gamma group is a little too prominent. The principal fault is that the first elevation is too broad and has its crest too late; but this part of the potential is determined by fibers larger than 8 \( \mu \), and therefore is subject to the same difficulties that attend constructions on a linear basis when outside diameters are used.

The sum of the evidence is so greatly in favor of the conclusion that the initial upward concavity of the outside-diameter velocity curves is a consequence of using the outside diameter as representative of the axon diameter, that further investigation of the size-velocity relationship will be
confined to the derived curves. There still remains to be considered the downward concavity of that portion of the curve representing the large fibers.

Before it can be concluded that the function relating size and velocity has a curved graph, the possible objections to that interpretation must be considered. The principal objection arises from an uncertainty in the data,—the possibility that the diameter measurements may not represent the true fiber sizes. In addition to the irregularity in the outline of the fibers previously mentioned, attention must now be called to the fact reported by Arnell and evident to a lesser degree in our data, that there is variation in the thickness of the myelin on fibers of all sizes. Both of these modes of variation in the dimensions of the fibers will influence the outcome of the reconstructions in the same manner.

Suppose that there are no fibers corresponding to the stray entries ahead of the main pile of fibers in the distribution charts and that the entries are there only because of fortuitous variation in smaller fibers. If one of these entries be placed at the head of the potential and the calculation of the velocities in the other fibers be based upon it, the crest of the potential would obviously come too late. If, on the other hand, one put the crest where it should be and the proper fibers under it to produce it—as was actually done—then one would have to set back these advanced fibers from their registered positions in order to bring them within the front of the wave. The location of the fibers in the size-velocity curve would then be such that the large-fiber end of the curve would be flattened. Despite the fact that the largest fibers plotted in the graphs in figure 13 A are not the largest fibers encountered in the measurement of the nerve, but are fibers having sizes closer to those of the fibers at the start of the main pile, there is definite evidence of a terminal decrease of slope in two of the curves. The slope near the ends is different from that of the part of the adjacent curve which records fibers of the same size but which is not near the end of the curve, and it can hardly be taken to have significance as far as the size-velocity relationship is concerned.

In the same manner that fibers with fictitiously large values ahead of the crest would have to be assigned a velocity slower than their apparent size would indicate, in order to bring them under the elevation, fibers with fictitiously small values behind the crest would have to be assigned faster values. This movement again would tend to create a spurious curvature to the graph. In the saphenous nerve of the rabbit, where the first elevation is divided into two parts, the situation would be particularly aggravated. The secondary humps in the size-velocity curve of this nerve (fig. 11, inset) could also be attributed to lack of precision in the size measurements.

Whether or not there is a residual curvature in the size-velocity curve,
after allowance is made for the adventitious disturbances, cannot be stated. Against the idea that there is one is the fact that a curvature is not always

Fig. 15. Distribution of fibers according to size in the phrenic nerve of the cat. Total number of fibers - 879

Fig. 16. Reconstruction of the action potential of the phrenic nerve of the cat from the data comprised in figure 15. Calculated for 4 cm. of conduction and on the basis that the velocity is 6 times the diameter. ---, recorded action potential. --------, reconstructed potential at the places at which it does not coincide with the recorded potential. Inset. The dots give the positions of the triangles in the reconstruction, the bars through the dots the width of the band of fibers represented. xxxxxx, fibers not plotted. Their potentials were visible at high amplification. As the strength of stimulus was raised they appeared on the crest of the negative after-potential in the region between 2 and 5 msec., which is the right place for their size.

in evidence. Figure 16 shows a perfect reconstruction of the action potential in the phrenic nerve on a strictly linear basis, and graphs 1 and 3 in
figure 13 have very little curvature that cannot be accounted for along the above lines.

The three curves in figure 13 A were brought together by multipliers, in order to visualize, as well as can be done with present data, the form of the axon-diameter velocity curve when freed from the idiosyncrasies of the individual curves. The points are plotted in figure 13 B. The result is as close to a straight line as are Hursh’s data with another method. It describes the velocity as being 8.7 times the axon diameter. This is the factor used for the reconstruction of the phrenic nerve in figure 16. The significant features of the curve are all produced by fibers larger than 8 μ, and consequently the ratio 0.69 would apply. The factor 6 for the outside diameter is converted by it to 8.7 for the axon diameter.

A close examination of figure 13 A, however, reveals that the points fall along a line having a slight curvature. The line is not straightened by plotting it on logarithmic coordinates, and therefore it is not exponential. Its form is unknown. All that can be concluded at the present time is that in so far as the velocity is not a linear function of the diameter, it does not vary from linearity in the direction of being a power greater than one. It has been seen that empirically the relationship of the spike height to axon size is linear, although theoretically it is a function with a curved graph. And the velocity relationship may similarly be represented by a curve approaching a straight line.

The region in which the myelin sheath begins to increase in thickness relative to the axon is the one in which its composition according to the birefringence data of Schmitt and Bear begins to change. The spike duration and the after-potential configuration remain constant and the velocity follows the axon diameter. Therefore the properties that may be related to the characteristics of the sheath as such remain to be determined.

SUMMARY

From charts showing the distribution of fibers according to size in the saphenous nerve of the cat and the rabbit, reconstructions of the form of the conducted action potentials were made. Good fits were obtained with the recorded action potentials from the same nerves, and the medullated fibers of all sizes were accounted for. From these reconstructions empirical size-velocity curves were prepared.

The following evidence was obtained that the medullated fibers of these nerves constitute a homogeneous system and therefore are suitable for study of the variations dependent upon size.

a. The spikes all have the same duration within the limits, 0.4 to 0.5 msec.

b. The fibers all have the same after-potential system.

Success in the reconstructions depended upon the determination of the
fact that the spike size varies as the axon radius, and not as the square of the radius, as previously held.

Measurements were made of the axon diameters and the outside diameters of the 675 fibers in a fasciculus of the saphenous nerve, and the ratios of the two diameters were plotted against the outside diameters. For fibers larger than 8 μ the mean ratio was found to be approximately constant. Below 8 μ it decreased progressively. With the aid of these data axon-diameter velocity curves were calculated from the outside-diameter velocity curves.

The velocity of conduction was found to be approximately proportional to the axon diameter, but a slight curvature in the graph connecting the two variables indicated that the velocity may change somewhat less rapidly than it would if the relationship were strictly linear.

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