A STUDY OF CONDUCTION VELOCITY IN NONMYELINATED NERVE FIBERS

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ABSTRACT By treating a nonmyelinated nerve fiber as a continuous cable consisting of three distinct zones (resting, transitional, and excited), the following mathematical expression was derived: $v = \sqrt{[d/(8R^*\rho C^2)]}$, where v is the conduction velocity, d the diameter of the fiber, R^* the resistance of the membrane of unit area at the peak of excitation, ρ the resistivity of the medium inside the fiber, and C the capacity of the membrane per unit area. The validity of this expression was demonstrated by using squid giant nerve fibers intracellularly perfused with dilute salt solutions. The relationship between these results and previous theories and experiments on conduction velocity is discussed.

INTRODUCTION

Attempts to calculate the velocity of nerve conduction based on the cable properties of the nerve fiber are not new. Near the turn of the century Göthlin (1910) discussed the possibility of estimating the conduction velocity by the use of Lord Kelvin's theory of the electric telegraph (Thompson, 1856). Later, Cremer (1924) derived a mathematical expression relating the conduction velocity to the rate of rise of membrane potential in the nerve produced by a propagated impulse. These classical studies were directed toward elucidating the process of nerve conduction in myelinated nerve fibers. It is now known that the conduction velocity in the myelinated fiber is determined primarily by the discontinuous variation in the cable properties at the nodes of Ranvier (Tasaki and Takeuchi, 1941; Hodler et al., 1952; Goldman and Albus, 1968). By use of the cable equation for nonmyelinated nerve fibers, Offner et al. (1940) derived a mathematical expression that relates the conduction velocity to the critical (i.e., threshold) membrane depolarization. Rushton (1951) derived an expression indicating a linear relationship between the square root of the fiber diameter and the conduction velocity in nonmyelinated nerve fibers. Shortly afterward, Hodgkin and Huxley (1952) succeeded in calculating the entire time-course of a propagated action potential based on their sodium theory of nerve excitation.

The objective of this paper is to demonstrate that the calculation of the conduction velocity in nonmyelinated nerve fibers does not require information about the time-dependent process of nerve excitation. We have derived simple equations that directly relate the velocity to the electric parameters of the axon membrane in the resting and

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excited states. To test these equations, we measured the conduction velocity in squid giant axons under a variety of experimental conditions. These data, as well as others found in literature, agree well with the equations described in this paper. From these findings, it is concluded that when nerve conduction is nondecremental, the membrane resistance at the peak of excitation can be estimated from the velocity of nerve conduction.

DERIVATION OF MATHEMATICAL EXPRESSIONS RELATING CONDUCTION VELOCITY WITH MEMBRANE RESISTANCE

A uniform nonmyelinated nerve fiber carrying an impulse is visualized as consisting of three zones: resting, transitional, and active (excited) (see Fig. 1). The membrane resistance is high in the resting and low in the active zone. There is a finite difference in the emf across the membrane in these two zones. The physicochemical processes that maintain these differences are immaterial to the present analysis. The existence of a transitional zone is a reflection of the experimental finding that there is, in the time-course of an intracellularly recorded action potential, a brief period during which the membrane potential rises linearly with time. It follows from this finding that there is, between the resting and active zones of a nerve fiber, a short zone where the gradient of the internal potential is constant. In the present theory, the transitional zone is treated as a short portion of the axon across which the second derivative of the membrane potential (with respect to space) reverses its sign.

The major difference between the previous mathematical theories and the present one lies in how transition from the resting to the active zone is treated. In the theory advanced by Offner et al. (1940), the boundary between the resting and active zones is represented as a point in space where the membrane potential and its first derivative, defined separately in the two zones, are connected without discontinuity. In the theory of Hodgkin and Huxley (1952), a precise knowledge of voltage- and time-dependence of quantities g_K and g_{Na} is required for calculation of conduction velocity. Formally

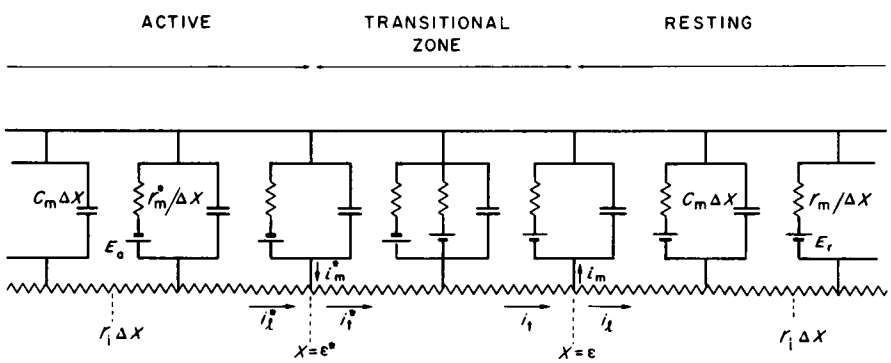

FIGURE 1 Schematic diagram used to describe the electric properties of the squid axon. It consists of three zones: resting, excited (or active), and transitional. The excited zone extends from $X = -\infty$ through ϵ^*; the transitional from ϵ^* to ϵ, and the resting zone from $X = \epsilon$ through $+\infty$. The symbols used here are explained in detail in the text.

this method of calculating the conduction velocity may be applicable to squid axons under intracellular perfusion when empirical formulas required to describe voltage-clamp data are determined. However, in axons internally perfused with (or immersed in) a sodium-free medium, the absolute value of E_{Na} becomes formally infinite and, consequently, some modification of the original formula for E_{Na} is required.

In the following analysis, it is shown that the application of Kirchhoff's law to the transitional zone leads to a simple, compact, analytical expression which directly related the conduction velocity to the membrane resistance in the resting and active zones. A precise knowledge of the length of the transition zone is not required in the following derivative. In spite of several recent reports suggesting a change of the membrane capacity with the membrane potential (Takashima, 1976), it is assumed in the present derivation that this change is negligibly small and that in the squid axon membrane it is 1.0 μF/cm^2 (Cole, 1968). Furthermore, it is assumed that the electric resistance of the medium outside the axon is negligibly small compared with the internal resistance. This assumption (also made by previous investigators) may seem unsafe except in axons internally perfused with dilute salt solutions. However, as long as action potentials recorded with an external electrode placed directly on the axon surface (referred to an electrode far away from the axon) are far smaller than internally recorded action potentials, this assumption should not lead to a significant error.

The following symbols are used to denote the electric properties of the membrane in the resting and active zones and of the axon interior:

r_i: the longitudinal resistance per unit length of the axon interior.
c_m: the membrane capacity per unit length of the axon.
r_m: the membrane resistance for unit length of the axon in the resting state.
r_m^*: the membrane resistance for unit length of the axon in the active state.
E_r: the emf of the membrane in the resting state.
E_a: the emf of the membrane in the active state.
x: the distance along the axon.
t: time.
V: the potential difference across the membrane at point x and time t.
v: the conduction velocity.
X: $(x - vt)$.
ϵ: the value of X at the boundary between the resting and transitional zone.
ϵ^*: the value of X at the boundary between the active and transitional zone.
κ: r_m^*/r_m or R^*/R.
d: the diameter of the axon.
ρ: the resistivity of the medium in the axon interior: $\frac{1}{4}\pi r_i d^2$.
R: the resistance of the membrane of unit area at rest; $\pi r_m d$.
R^*: the resistance of the membrane of unit area in the excited state; $\pi r_m^* d$.
C: the membrane capacity per unit area; $C = c_m/(\pi d)$.

The Cable Equation for the Resting Zone

By applying the standard electric circuit theory, the differential equation staisfied by V, the potential difference between the inside and outside of the membrane in the resting

state, is described as

$$c_m r_m(\partial V/\partial t) - (r_m/r_i)(\partial^2 V/\partial x^2) + (V - E_e) = 0. \tag{1a}$$

The impulse is assumed to travel in the positive direction of x at a constant velocity v. Introducing X according to the definition that $X \equiv (x - vt)$, Eq. 1 can be rewritten as follows:

$$\frac{1}{c_m r_i}\frac{d^2V}{dX^2} + v\frac{dV}{dX} - \frac{1}{c_m r_m}(V - E_r) = 0. \tag{1b}$$

The solution of this equation yielding a finite value of V at $X = +\infty$ is

$$V = E_r + (V_0 - E_r)e^{-\xi(X-\epsilon)}, \tag{2a}$$

where V_0 represents the value of V at $X = \epsilon$, and ξ is a solution of the following quadratic equation

$$(1/c_m r_i)\xi^2 - v\xi - (1/c_m r_m) = 0. \tag{2b}$$

The solution meaningful in the present case is

$$\xi = \frac{+c_m v + \sqrt{(c_m v)^2 + 4/(r_i r_m)}}{2/r_i} \tag{3}$$

Note that the other solution of Eq. 2*b* has a negative value and does not satisfy the condition imposed on Eq. 2*a*.

The Cable Equation for the Active Zone

With the same treatment used for the resting zone, the membrane potential in the active state is found to obey the following differential equation:

$$c_m r_m^* \frac{\partial V}{\partial t} - \frac{r_m^*}{r_i}\frac{\partial^2 V}{\partial x^2} + (V - E_a) = 0, \tag{4a}$$

or

$$\frac{1}{c_m r_i}\frac{d^2V}{dX^2} + v\frac{dV}{dX} - \frac{1}{c_m r_m^*}(V - E_a) = 0. \tag{4b}$$

Again, the solution which gives a finite value of V at $X = -\infty$ is

$$V = E_a + (V_0^* - E_a)e^{+\eta(X-\epsilon^*)}, \tag{5}$$

where V_0^* is the membrane potential at $X = \epsilon^*$ and η is a parameter that satisfies the following quadratic equation

$$\frac{1}{c_m r_i}\eta^2 + v\eta - \frac{1}{c_m r_m^*} = 0.$$

In the present case, η is given by

$$\eta = \frac{-c_m v + \sqrt{(c_m v)^2 + 4/(r_i r_m^*)}}{2/r_i}. \tag{6}$$

Note that this quantity has to be positive on account of the condition imposed in Eq. 5.

Boundary Conditions

The longitudinal current in the transitional zone coming from the active zone is i_t^* is equal to that flowing into the resting zone, i_t, as shown in Fig. 1. These currents, i_t^* and i_t in the figure, can be expressed as follows:

$$i_t^* = \frac{V(\epsilon^*) - V(\epsilon^* + \Delta X)}{r_i \Delta X} = \frac{-1}{r_i} \frac{dV}{dX}_{|\epsilon^*} - 0(\Delta X)^2,$$

and

$$i_t = \frac{V(\epsilon - \Delta X) - V(\epsilon)}{r_i \Delta X} = \frac{-1}{r_i} \left.\frac{dV}{dX}\right|_{\epsilon} - 0(\Delta X)^2. \tag{7a}$$

It should be noted that the terms involving the second derivatives are absent in the above expression because the gradient of the potential is constant in the transition zone. Therefore, apart from the terms of the second order of (ΔX), the following condition should be satisfied:

$$\frac{1}{r_i} \left.\frac{dV}{dX}\right|_{\epsilon^*} = \frac{1}{r_i} \left.\frac{dV}{dX}\right|_{\epsilon}. \tag{7b}$$

Further, by application of Kirchoff's theorem to the vicinity around $X = \epsilon^*$ and ϵ, it is found that $i_t^* = i_m^* + i_l^*$ and $i_t = i_m + i_l$ as shown in Fig. 1. Considering the above condition that $i_t^* = i_t$,

$$i_l^* + i_m^* = i_l + i_m \tag{8}$$

where i_m^* and i_m denote the membrane currents in the active and resting zones and i_l^* and i_l are the longitudinal currents in the active and resting zones, respectively. Eq. 8 immediately yields the following relation:

$$\begin{aligned}
&-\frac{1}{r_i} \left.\frac{dV}{dX}\right|_{\epsilon^*} + \frac{1}{2r_i} \left.\frac{d^2V}{dX^2}\right|_{\epsilon^*} \cdot(\Delta X) - 0(\Delta X)^2 \\
&+\left\{\frac{E_a - V(\epsilon^*)}{r_m^*} + c_m v \left.\frac{dV}{dX}\right|_{\epsilon^*}\right\}\cdot(\Delta X) \\
&= -\frac{1}{r_i} \left.\frac{dV}{dX}\right|_{\epsilon} - \frac{1}{2r_i} \left.\frac{d^2V}{dX^2}\right|_{\epsilon} \cdot(\Delta X) - 0(\Delta X)^2 \\
&+\left\{\frac{V(\epsilon) - E_r}{r_m} - c_m v \left.\frac{dV}{dX}\right|_{\epsilon}\right\}\cdot(\Delta X).
\end{aligned} \tag{9}$$

The initial three terms in Eq. 9 represent the longitudinal current at the end of the active zone, $-\{V(\epsilon^*) - V(\epsilon^* - \Delta X)\}/(r_i \Delta X)$, expanded in a Taylor's series. The next term represents the membrane current through the portion of the axon of length ΔX; note that this term is of the same order of magnitude as the second term in the series above. The terms on the right-hand side of Eq. 9 represent the corresponding quantities at the beginning of the resting zone. The first terms on two sides of Eq. 9 cancel each other on account of Eq. 7*b*. By neglecting the terms of the higher order of ΔX, the condition that holds good in the vicinity of the transition zone can be obtained:

$$\frac{1}{2r_i}\left.\frac{d^2V}{dX^2}\right|_{\epsilon^*} + c_m v \left.\frac{dV}{dX}\right|_{\epsilon^*} + \frac{1}{r_m^*}\{E_a - V(\epsilon^*)\} = -\frac{1}{2r_i}\left.\frac{d^2V}{dX^2}\right|_{\epsilon} - c_m v \left.\frac{dV}{dX}\right|_{\epsilon} + \frac{1}{r_m}\{V(\epsilon) - E_r\}. \quad (10)$$

This equation indicates that the difference between the inward membrane current (at the end of the active zone) and the outward current (at the beginning of the resting zone) is directly related to the difference between the second derivitives of the membrane potential. The two boundary conditions expressed by Eqs. 7*b* and 10 can be rewritten in the following forms by using Eqs. 2*a* and 5:

$$\eta(V_0^* - E_a) = -\xi(V_0 - E_r), \quad (11)$$

and

$$[(\eta^2/2r_i) + c_m \eta v - (1/r_m^*)](V_0^* - E_a) = [-(\xi^2/2r_i) + c_m \xi v + (1/r_m)](V_0 - E_r). \quad (12)$$

Now, a basic equation for the conduction velocity is obtained from these two equations (11 and 12):

$$\frac{1}{2c_m r_i}(\eta - \xi) + 2v - \frac{1}{\eta c_m r_m^*} + \frac{1}{\xi c_m r_m} = 0. \quad (13)$$

Note here that all the quantities denoting the state of the membrane in the transition zone are eliminated from this equation. This equation can be further simplified by substituting ξ and η with the solutions given by Eqs. 3 and 6.

$$v = \frac{1}{c_m \sqrt{2r_i r_m^*}} \sqrt{\frac{(1-\kappa)^2}{1+\kappa}} \quad (14)$$

where κ is defined as r_m^*/r_m. When specific resistances and capacitance, ρ, R, R^*, and C, are introduced, Eq. 14 becomes:

$$v = \frac{1}{2\sqrt{2}} \frac{1}{C} \sqrt{\frac{d}{R^*\rho}} \sqrt{\frac{(1-\kappa)^2}{1+\kappa}}, \quad (15)$$

where $\kappa = R^*/R$. When $\kappa \ll 1$, it becomes:

$$v \cong \frac{1}{2\sqrt{2}} \frac{1}{C} \sqrt{\frac{d}{R^*\rho}}. \tag{16}$$

The conclusion drawn from the present theory may be stated as follows: Apart from the numerical factor, the conduction velocity is inversely proportional to the membrane capacity per unit area C and to the square root of the resistivity of the medium in the axon interior ρ, and is proportional to the square root of the axon diameter d. Moreover, when the resistance of the membrane of unit area in the excited state R^* is negligibly small as compared with the one in the resting state R, the conduction velocity can be expressed in very simple analytical form, as seen in Eq. 16, and is also inversely proportional to the square root of the membrane resistance of unit area in the excited state, R^*.

Eq. 16 is the desired formula by which the conduction velocity can be estimated when the membrane resistance at the peak of an action potential (R^*), the membrane capacity (C), the resistivity of the internal medium (ρ), and the diameter (d) are known. When the velocity is known, this equation can be used to estimate the value of R^* by using the accepted values of C and ρ.

EXPERIMENTAL TEST OF THE EQUATIONS DERIVED

Methods

Giant axons of squid *(Loligo pealei)*, available at the Marine Biological Laboratory, Woods Hole, Mass., were used. The diameter of the axons used was between 400 and 450 μm. The major portion of the adherent tissues surrounding the giant axons was removed under a dissecting microscope. The axon was then transferred to a Lucite chamber filled with artifical sea water (ASW). The internal perfusion of the axon was performed by the technique previously described by Tasaki (1968), which consisted basically in inserting a glass cannula into each end of the axon. The flow rate of the internal perfusion fluid was maintained between 20 and 50 μl/min. The length of the perfusion zone was usually 15 mm. A long glass pipette (approximately 100 μm in diameter and filled with 3 M KCl making contact with a Ag-AgCl wire) was used to record action potentials intracellularly from the perfusion zone in the conduction velocity measurements. A pair of platinized platinum twisted wires were used for monitoring the membrane potential and applying voltage pulses across the membrane in the voltage-clamp experiments. A calomel electrode immersed in the external fluid medium was used as the reference point for potential measurements.

To study the dependence of the conduction velocity on the resistance of the intracellular fluid and the membrane resistances, five different concentrations of the intracellular *K*-fluoride-phosphate solution were prepared; expressed in milliequivalents per liter, these concentrations were 400, 200, 100, 50, and 25. These solutions were prepared by diluting the stock solution containing the 400 meq/liter K-salt (pH 7.2–7.3) with a 12% (by volume) glycerol solution. As the extracellular fluid, ASW was used. The composition of the ASW was 423 mM NaCl, 9 mM KCl, 23 mM $MgCl_2$, 25 mM $MgSO_4$, 10 mM $CaCl_2$, and 5 mM Tris., the pH being adjusted to between 8.0 and 8.1. The extracellular fluid medium was grounded through a large coil of platinized platinum wire. In the present study the major portion of the axoplasm was removed initially by enzymatic digestion, namely, by perfusing the axon intracellularly with a solution containing 400 meq/liter K-fluoride-phosphate and 0.1 mg/ml pronase (Calbiochem, San Diego, Calif.) for about 1 min. After this enzymatic treatment, the internal solution was switched to

one of the prepared K-fluoride-phosphate solutions. When measuring conduction velocity, the action potential was recorded with an oscilloscope connected to an internal glass pipette electrode: the recording electrode could be moved along the longitudinal axis of the axon within a 9-mm portion in the middle of the 15-mm perfusion zone. Stimulating shocks were delivered externally; the electrodes used for this purpose were placed 2 or 3 mm away from one of the ends of the perfusion zone, and the intensity of stimulation was kept at twice that of the threshold.

The resistance of the membrane in the active state was measured by the voltage-clamp technique. In this case, the potential difference across the membrane at the center of the perfusion zone, monitored with a platinized platinum electrode in the middle of the perfusion zone, was controlled by an electronic feedback system connected to a 15-mm-long platinized platinum electrode. The duration of the rectangular clamping voltage pulse was 3 ms. The membrane current was measured as a potential drop across a 7.2-Ω resistor, placed between a coil of platinized platinum electrode and the ground. The coil, 7.5 mm long, was aligned in parallel with the perfused axon and placed alongside the middle of the perfused zone. At each end of this coil, an additional coil of platinized platinum wires was placed in the chamber; the potentials of these two lateral coils were kept at the same level as that of the central coil.

All the experiments described in this paper were carried out at room temperature (17–19°C).

Experimental Results

To determine the conduction velocity, the action potentials were recorded photographically at several positions in the axon. From these records, the conduction

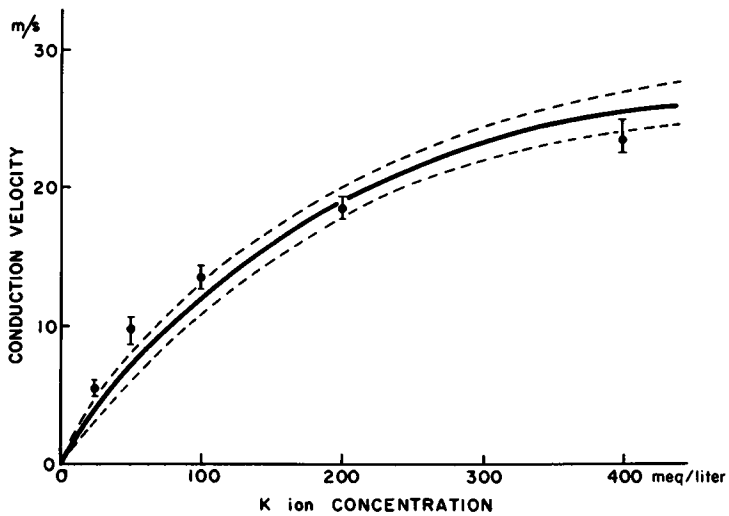

FIGURE 2 Calculated and experimentally obtained conduction velocities. The dots (with vertical bars) stand for the experimentally obtained conduction velocities for the axons with diameters of approximately 400 μm immersed in ASW (pH 8.1). The axons were intracellularly perfused with K-fluoride-phosphate solutions (pH 7.3) of various concentrations. The length of the vertical bars shows the variation of the conduction velocities from axon to axon at a given K-ion salt concentration. Altogether, 14 axons were used. The solid line represents the conduction velocity calculated with the use of Eq. 16, where $C = 1\ \mu F/cm^2$, $d = 0.04$ cm. The values of ρ and R^* were experimentally determined are are shown in Table I. The two thin broken lines drawn on two sides of the solid one show the degree of the variation, which derives mainly from the variation of R^*.

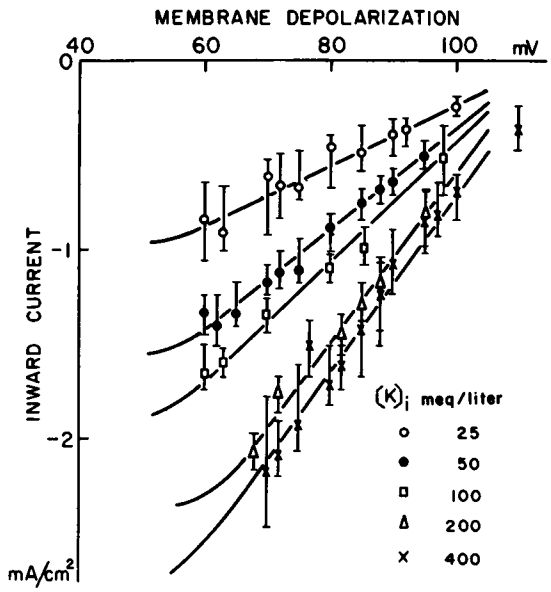

FIGURE 3 The relationship between the clamping voltage and the membrane current at the peak of excitation. The axons were immersed in ASW and intracellularly perfused with K-fluoride-phosphate solution. The K ion concentrations of the internal perfusion fluid are indicated. From the slope of the line passing through the average values of the observed points for each K salt concentration, the membrane resistance R^* at the peak of excitation was determined. A total of 12 axons was used to obtain the data. The vertical bar for each plot represents the variation from axon to axon.

velocity was determined as a function of the K-salt concentration of the internal perfusion solution. The results obtained are shown in Fig. 2. In this figure, the conduction velocity calculated with Eq. 16 is shown by the continuous line. This calculation was carried out by using the experimentally determined values of membrane and internal resistances that will be discussed below.

TABLE I

ρ, R^*, AND CONDUCTION VELOCITIES IN PERFUSED AXONS

$[K^+]$	ρ	R^*	v_{cal}	v_{exp}
meq/liter	$\Omega\ cm$	$\Omega\ cm^2$	*m/s*	*m/s*
400	36.1	21.5 ± 3.5	25.4 ± 2.0	23.5 ± 0.8
200	64.5	22.0 ± 1.0	18.8 ± 0.5	18.5 ± 0.5
100	132	29.5 ± 4.5	11.3 ± 0.8	13.5 ± 1.5
50	257	39.5 ± 3.5	7.0 ± 0.3	9.7 ± 0.8
25	530	91.5 ± 8.5	3.2 ± 0.2	5.5 ± 0.4

The resistivity of the internal perfusion fluid, ρ, the resistance of the axon membrane of unit area in the excited state, R^*, and the calculated and experimentally obtained conduction velocities in the axons intracellularly perfused with K-fluoride-phosphate solution (pH 7.3) and immersed in ASW (pH 8.1). To determine the resistivity, ρ, a standard AC impedance bridge operated at 1 kHz was used. The voltage-clamp technique was used to determine the membrane resistance R^* at the peak of excitation. For the calculated and experimentally obtained conduction velocities, see the caption of Fig. 2.

The membrane resistances, R^* and R, were obtained from the voltage-current relationship determined by the voltage clamp technique. The results of measurements of the peak membrane currents at various levels of voltage pulse are presented in Fig. 3; 12 axons were used to obtain the data shown in this figure. From the slope of the line passing through the average values of the observed points for each K-salt concentration, the membrane resistance at the peak of excitation was determined (see Table I).

A standard AC impedance bridge operated at 1 kHz was used to determine the resistivity, ρ, of each of the internal perfusion solutions used. As the standards, 0.1 and 0.01 demal (7.42 and 0.745 g/liter) solutions of KCl were used (see Robinson and Stokes, 1959). The results of these measurements are presented in the second column of Table I. This table shows a linear relation between the conductivity (reciprocal value of resistivity) and the K-salt concentration in the range below about 250 meq/liter. At 400 meq/liter, the conductivity was found to be roughly 11% less than the value expected from the simple linear relationship.

The results of calculation of the conduction velocities based on these measured values of R^* and ρ are compared with the values observed under the corresponding conditions (see the continuous line in Fig. 2 and the last column in Table 1). In spite of the considerable variation in the measured values, the agreement between the observed and calculated values is good. It should be noted that no adjustable parameters were used in this calculation.

DISCUSSION

Additional experimental data in support of the theory presented in this paper can be found in literature. Pumphrey and Young (1938) measured the conduction velocity of action potentials from intact squid axons (*Loligo*) of various diameters immersed in

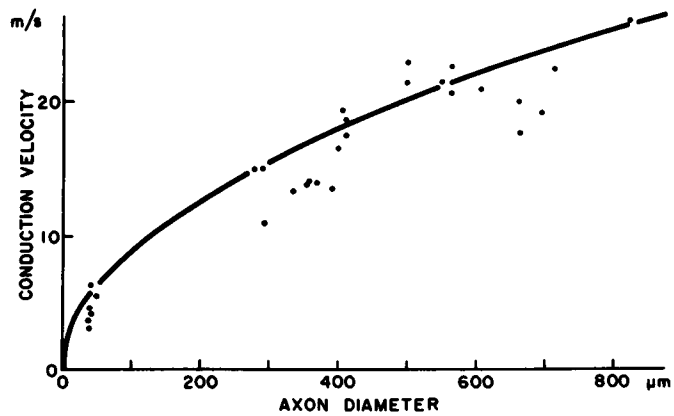

FIGURE 4 Dependence of the conduction velocity on the axon diameter. Experimentally obtained values of the conduction velocity, shown by black circles in the figure, are taken from Pumphrey and Young (1938). The solid represents the calculated results of the conduction velocity of Eq. 16 where C is set at 1 $\mu F/cm^2$. The values of R^* and ρ used here are listed in Table II.

TABLE II

R, R^*, ρ, AND CONDUCTION VELOCITIES

Internal solutions	External medium	R^*	R/R^*	ρ	v_{exp}	v_{cal}
		$\Omega\ cm^2$		$\Omega\ cm$	m/s	m/s
A. Axoplasm	Seawater	45	>100	34	18.8	18.0
B. 30 mM NaF	100 mM $CaCl_2$	700 ~ 1,000	~10		~1	0.8
	100 mM $CaCl_2$ + 100 mM NaCl	200	15	784	~3	1.6
	100 mM $CaCl_2$ + 400 mM NaCl	100	20		~6	2.5

The resistances of the axon membrane of unit area at rest and in the excited state, R and R^*, the resistivity of axoplasm or internal perfusion fluid, ρ, the calculated and experimentally obtained conduction velocities. A. Intact axons immersed in natural sea water. The values of R^* and R were taken from Takashima (1976), and v_{exp} from Cole (1968). The value of v_{cal} was obtained with Eq. 16. B. Axons under bi-ionic conditions. The data R^*, R, and v_{exp} were quoted from Inoue et al. (1974). The value of ρ was measured for 30 mM NaF solution with a standard AC impedance bridge operated at 1 kHz. Eq. 15 was used to calculate the conduction velocity.

natural sea water. By using various branches of axons in the squid mantle, they were able to measure axons whose diameters varied from 20 to 820 μm. The calculation of the conduction velocity in intact axons was performed by introducing the known values R^* and ρ into Eq. 16. The membrane resistance in the excited state, R^*, was obtained from the most recent data (Takashima, unpublished) for large axons, and ρ was from Cole's data (1968) (see Table II). The result of this calculation is shown in Fig. 4. The observed values in this figure are quoted from Pumphrey and Young (1938). Again, there is good agreement between the calculated and experimental result.

Inoue et al. (1974) measured the conduction velocity and the membrane resistance in resting and excited states under bi-ionic conditions. Table II shows these experimental results compared to the values calculated for axons under these conditions. The reproducibility of conduction velocity measurements is quite limited in these axons. Some discrepancy seen in the table between the experimental and calculated values may be due to the difficulty of performing reliable velocity measurements. However, this comparison appears to lend additional support to the theory of conduction velocity presented in this paper.

We have also compared the results obtained in the present study with those of previous investigators. The conclusion that the velocity depends on the square root of the axon diameter is not surprising, for all of the previous theories and the known experimental data are in line with this conclusion. Rushton's theory used a linear wave equation (instead of cable equations) to describe the process of nerve conduction which is not a wave. (Note, for example, that two nerve impulses vanish after head-on collision.) This theory does not give any information about the relationship between the velocity and the membrane properties of the axon. In the theory advanced by Offner

TABLE III

SPACE PARAMETERS

$[K^+]$	η^{-1}	$\eta^{-1}/(d/2)$	ξ^{-1}	$\xi^{-1}/(d/2)$
meq/liter	*mm*		*mm*	
400	1.1	5.52	1.03	5.2
200	0.84	4.2	0.75	3.8
100	0.68	3.4	0.63	3.2
50	0.56	2.8	0.52	2.6
25	0.61	3.0	0.52	2.6

The "space parameters," η^{-1} and ξ^{-1}, in the excited and resting states for the axon intracellularly perfused with K-fluoride-phosphate and immersed in ASW. The calculation was based on Eqs. 3 and 6.

et al. (1940), the critical membrane potential, which corresponds to V_0^* or V_0 in the present theory, plays a decisive role; only by a proper choice of this potential can one obtain an agreement between the calculated and observed velocities. Since the critical membrane potential is not the same as the readily determinable threshold membrane potential, the value of this theory is limited.

In the theory of Hodgkin and Huxley, a large number of parameters required to describe the empirical formulae for the conductances must be determined before numerical calculation of the velocity is possible. The velocity is given in this theory by $v = \sqrt{Kd/(4\rho C)}$, where k is considered to be a constant for an unperfused axon and to depend only on properties of the membrane. By comparing this formula with Eq. 16, it is found that K corresponds to $1/(2R^*C)$ in the present theory. Since Eq. 16 is shown to describe the velocity in axons under intracellular perfusion fairly accurately, K has to be considered as a variable which depends on C and R^* under these conditions. In normal (i.e., internally unperfused) axons immersed in normal sea water, the value of K estimated by Hodgkin and Huxley (1.05×10^4 s^{-1}) is very close to that calculated by $K = 1/(2R^*C) = 1.1 \times 10^4$ s^{-1}, from the data shown in Table II.

In the present theory, the length of the excited zone is treated as being infinite. This treatment is equivalent to assuming that the flow of electricity at and around the transition zone plays a decisive role in determining the conduction velocity. This assumption is justifiable because of the finding that the "space parameter" in the excited zone, namely, $1/\eta$ in Eq. 6, is far shorter than the length of the region of the axon occupied by an action potential at one instance. The values of $1/\eta$ and $1/\xi$ for axons under internal perfusion with various K-salt solutions are listed in Table III.

It might be added that the present theory deals with a relationship between the membrane resistance and the conduction velocity under the condition that the axon can carry a nerve impulse that travels at a constant velocity. In the form presented in this paper, this theory does not give any information about the requirements that have to be satisfied by E_a and E_r to sustain uniform (i.e., decrementless) conduction.

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