A POSSIBLE MECHANISM INVOLVED IN THE CONDUCTION PROCESS OF THIN SHEATHED NERVE FIBERS[1]

WILLIAM J. FRY AND RUTH BAUMANN FRY

University of Illinois, Urbana, Illinois

FOUR FIGURES

INTRODUCTION

The relationship between the speed of the conduction process and the diameter of an invertebrate nerve is well known. However, no satisfactory theory yet exists which correlates this experimentally observed relation (Prosser, '46). To this end a theoretical investigation of localized propagated mechanical disturbances in the fibers appears worthwhile. In part, this consideration is prompted by the order of magnitude of the velocities in the nerves. The velocities of propagation of the nerve impulses compare in magnitude to the velocities of propagation of localized mechanical disturbances in various structures. Geometrically, the nerve fiber approximates a cylinder consisting of a medium enclosed by a membrane. We consider, therefore, the propagation of small ampltitude transverse disturbances on a cylindrical membrane embedded in a fluid. A possible role of shear waves in the nerve conduction process has been discussed by Sutherland ('05, '06-'07, '08-'09).

Results reported in the literature indicate the possibility of mechanical motion in nerve. For example, investigators (Curtis, and Cole, '42; Hodgkin and Huxley, '45; Hodgkin and Rushton, '46) have postulated the existence of a membrane inductance in order to correlate certain aspects of the observed

electrical characteristics of nerve on a passive electrical network basis. The magnitude of the required inductance, of the order of 0.2 H cm², is extremely large to accept as a pure electrical element manifested in nerve tissue. However, if mechanical motion coexists with electrical activity in nerve, this movement would manifest itself in the equivalent electrical circuit of the tissue as an inductive element. If this is the case, then values for the inductance of 0.2 H cm² are not unreasonable.

Tobias and Solomon ('50), Solomon and Tobias ('50) and Tobias ('50a) have observed dimensional and opacity changes which occur in the region of electrodes supplying polarizing current. Tobias ('50b) has discussed possible implications of these observations. Their results when considered in conjunction with the work of Hill and Keynes ('49) on the opacity changes accompanying propagated electrcial activity suggest the possibility of mechanical motion during such activity.

The presence of a mechanical disturbance during activity is also suggested by the ease of stimulation of a nerve by mechanical means (Blair, '36). The extreme sensitivity of mechano-receptors may be considered as additional support for such a picture.

Any theory of nerve conduction which involves dimensional changes must include a mechanism for coupling the electrical and mechanical activity. Suitable coupling mechanisms might involve piezoelectric or electrostrictive materials. The theory discussed herein does not depend critically on any one particular coupling scheme.

In this and another paper (Fry and Fry, '50), which includes the detailed mathematical development, an expression is presented which relates the velocity of propagation of a transverse disturbance along a tubular membrane to the diameter of the tube. The identification of this velocity with the velocity of propagation of the spike potential of thin sheathed nerves requires not unreasonable values of the associated parameters. The experimentally observed relation between conduction velocity and fiber size for such nerves can then be

realized theoretically. The picture developed can also be reconciled with other aspects of the nerve conduction process.

In the following discussion no attempt has been made to consider critically all available experimental data since concomitant electrical and chemical phenomena have not yet been incorporated into this theory. Therefore, at this stage, the development is to be regarded as suggestive.

THEORY AND DISCUSSION

We consider the propagation of a mechanical disturbance of the transverse type along a tubular membrane, as illustrated in figure 1. The interior of the tube is filled with a liquid of density ρ_i and the system is immersed in a fluid of density ρ_e. The membrane is under tension, perhaps the result of a difference in hydrostatic pressure between the interior
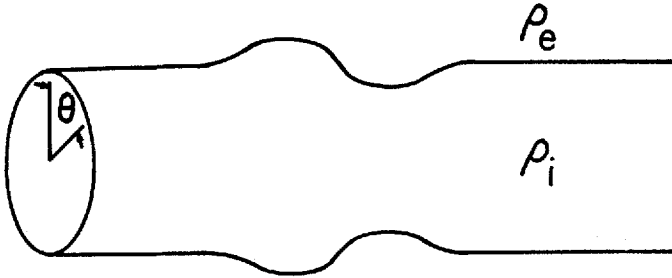

Fig. 1 A transverse disturbance on a tubular membrane. The amplitude of the displacement is shown in an exaggerated form.

liquid and the exterior medium. Let T denote this tension in units of force per unit length. If we assume that the disturbance is symmetrical, i.e., independent of θ, (fig. 1) and that its amplitude is small, the following approximate expression is obtained for the velocity of propagation of a sinusoidal disturbance guided along the membrane

$$V_\omega^4 = \frac{\omega^2 T r_0}{2\rho_i}$$ (1)

where $\omega = 2\pi f$, f is the frequency of the sinusoidal disturbance, V_ω is the velocity, T is the tension in the membrane in units of

force per unit length, r_o is the radius of the tube and ρ_i is the density of the internal fluid. This expression is applicable only if ω is not larger than about $(10)^5$. The effect of viscosity has been neglected in deriving expression (1). Ordinarily, the viscosity term affects the expression for velocity only slightly and introduces an amplitude damping factor. An indication of the amount of damping introduced by viscosity for small amplitude disturbances, such as those discussed here, might be given by the damping factor of an acoustic disturbance of the same frequency. On the basis of measurements made at high acoustic frequencies, it appears that the damping factor for the frequencies and path lengths involved herein would be small.

An immediate consequence of (1) is that the velocity is independent of the density of the external fluid. An exact analysis shows that the velocity varies less than 10% for values of the parameters appropriate for a giant squid axon if the density of the external fluid is changed from that corresponding to water to a zero value for an $\omega = (10)^5$ (representing a frequency of 16,000 cycles per sec.). It is assumed that the tension does not change.

If we postulate that the tension T is determined solely by a difference in hydrostatic pressures, P_o, we can derive the formula $T = r_o P_o$. The relation (1) then becomes

$$V_\omega{}^4 = \frac{\omega^2 r_o{}^2 P_o}{2\rho_i}. \tag{2}$$

If we further assume that the pressure difference P_o is independent of fiber size, i.e., the quantity P_o in (2) is constant, we obtain the result that the phase velocity varies as $r_o{}^{\frac{1}{2}}$. If the tension arises through some mechanism other than a difference in hydrostatic pressure, it appears necessary to take $T \propto r_o$ in order to obtain agreement with experiment.

The disturbance which is propagated along a nerve fiber is not an infinite sine wave train of some fixed frequency but is rather one which is localized spatially. However, further

analysis shows that the velocity, V_s, of propagation of a localized disturbance varies in exactly the same fashion, i.e.,

$$V_s \propto r_o^{\frac{1}{2}} (\frac{P_o}{\rho_1})^{\frac{1}{4}} \qquad (3)$$

or with the tension T as $V_s \propto T^{\frac{1}{4}}$.

If one plots experimentally determined conduction velocities as a function of fiber diameter for invertebrate nerves with thin sheaths, for which data are tabulated by Prosser ('46), the graph of figure 2 is obtained. All of the data available in Prosser's article for crustacea and cephalopod molluses are included on the graph. The straight line is plotted for a
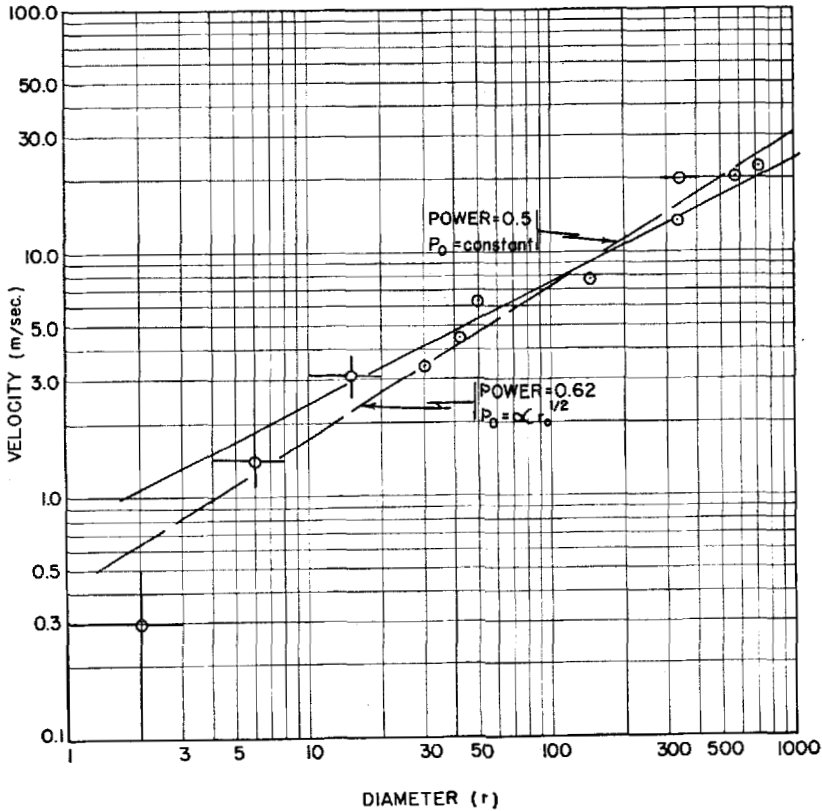

Fig. 2 Logarithmic plot of experimental data: conduction velocity versus fiber diameter.

power dependence relation of 0.5. Good agreement with the experimental observations is obtained over the entire range of fiber diameters from $1\,\mu$ to about $800\,\mu$. Pumphrey and Young ('38) indicate that their data although not excluding a 0.5 relationship might be fitted somewhat better by about a 0.62 power dependence. If such is the case, agreement with the theory developed herein can be obtained by assuming that the pressure difference P_o in (3) is proportional to the square root of the radius, r_o, of the fiber. However, for the subsequent discussion, we will consider P_o constant since this appears to us to be the most natural choice with regard to existing experimental observation. The value of P_o may vary with the animal classification and the type of fiber system.

We would like to obtain some idea of the required pressure difference if this is the mechanism which gives rise to the tension, in order to realize velocities in agreement with experiment. Therefore, we have carried out the following approximate analysis.

From an examination of the shape of the spike potential and the shape of the membrane conductance change with time, it is clear that frequencies of the order of $(10)^4$ are present with reasonable amplitudes (Cole and Curtis, '39). This implies values of ω of the order of $(10)^5$. If we assume that a steep wavefront is necessary in order to insure propagation (possibly to trigger an energy release process which is necessary to compensate for both electrical and mechanical losses), we may calculate a value for the required pressure by assuming that the velocity of propagation of a spike is of the order of the phase velocity of the high frequency components of the pulse. A graphical analysis for an exciting pulse of the form indicated in figure 3a yields the results indicated in figure 3b. The exciting function is repetitive in time with a period of approximately 5 times the width of the individual pulses. This was convenient for the purposes of the graphical analysis. It should be noted that the exciting function is symmetrical. When this exciting function for displacement is applied to the tube at the position $z = 0$, a disturbance will spread out in

both directions. At points removed from $z = 0$, the pulse will
arrive at some later time. If we observe the displacement of
the tube at such points, the curves of figure 3b result. The
curve labeled (c) is obtained for a point twice as far from
$z = 0$ as the curve labeled (b). These curves show that the
disturbance maintains a sharp wavefront at least initially and
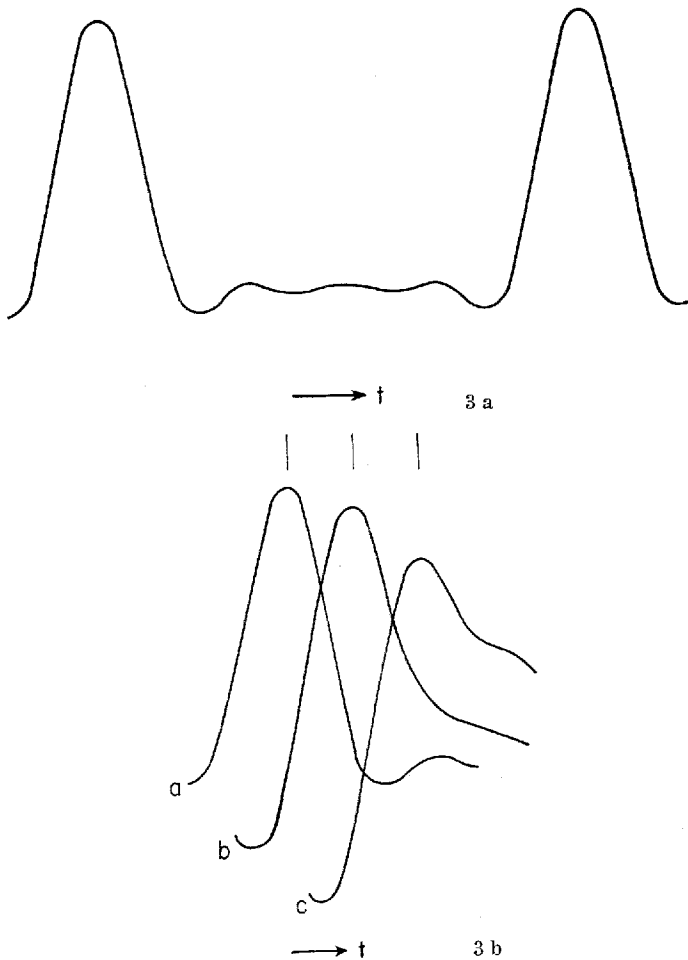that a relatively slow drop-off develops as evidenced by the

Fig. 3   (a) Periodic excitation function plotted against time; (b) the propa-
gated disturbance; a, the exciting pulse, b, and c, the propagated pulse observed
at two points along the tube.

non-symmetrical shapes of the curves (b) and (c). At points further removed from the source of disturbance, the shape is drastically changed. This is partially a consequence of the choice of a periodic excitation function. Since the phase velocity is proportional to the square root of the frequency, it is not possible for a pulse to retain its initial shape identically as it progresses along the tube. However, this does not appear to be a serious difficulty since in any case an energy release mechanism must be included in a complete theory to account for energy losses, both electrical and mechanical. Observed electrical activity (nonpassive) could then correspond to an energy release process triggered by the mechanical disturbance. The steepness of the wavefront of the mechanical motion might, for example, be the important factor for such triggering action. The resultant electrical activity would then initiate further mechanical activity because of the mutual coupling action.

If we insert into equation (2) values appropriate for a giant squid axon, a value of $\omega = (10)^5$ sec.$^{-1}$, $r_0 = 2.5(10)^{-2}$ cm, $\rho_i = 1$ gm/cm^3, $V_\omega = 2(10)^3$ cm/sec., we obtain $P_0 \sim 0.5(10)^7$ dynes/cm^2 or about 5 atmospheres. The choice of a value for ω is somewhat arbitrary. From formula (2), we see that a doubling of the value of ω decreases the value of the required pressure by a factor of 4. The calculated value of the pressure is very sensitive to the value of the velocity. A reduction of 30% in the velocity changes the required pressure to about $1\frac{1}{4}$ atmospheres. Pressure differences of this order of magnitude appear not unreasonable from the point of view of the strength of the materials involved.

In addition to the above results, it is possible to obtain correlation of other aspects of the nerve conduction process. For example, the effects of longitudinal tension and transverse pressure might be elucidated. Experimentally, the conduction velocity is observed to increase when a nerve is pulled along its length (Bullock, '45). Such a pulling would have the effect of increasing the tension, T, in formula (1) and would thus increase the conduction velocity. Quantitative results on

single fibers might permit a determination of internal pressure. The experimental evidence that lateral squeezing reduces the conduction velocity (Gasser and Erlanger, '29) might also be reconciled with this theory since such lateral compression would reduce the tension, T, and thus reduce the conduction velocity as shown by relation (1).

Application of hydrostatic pressure to the whole system would have no direct effect on the conduction velocity if it is not applied too rapidly, that is, if equilibrium were maintained, the pressure difference between inside and outside could remain constant. It is assumed, of course, that no changes in structure or shifts of equilibria occur under application of the pressure. This conclusion is consistent with the fact that experimentally rather high hydrostatic pressures are required to affect the conduction process appreciably (Grundfest, '36). However, sudden changes in pressure or mechanical motion might give rise to a disturbance.

As one moves radially away from the surface of the tube, the amplitude of the disturbance in the external medium falls off rapidly for the higher frequency components of the propagated pulse. For example, if we consider the numerical case discussed above, which is appropriate for the giant squid axon, we obtain for the frequency component corresponding to an ω of $(10)^5$, the result that at one diameter distance from the surface of the tube, the amplitude of the disturbance is less than $1/10$ the value at the membrane.

Electrical activity can be associated with mechanical movement in a variety of ways. For the present, perhaps the most natural postulate is that a piezoelectric or electrostrictive mechanism is operative as indicated above. The dependence of the velocity of propagation on the resistivity of the external medium might then follow from the influence which the electrical characteristics exert on the mechanical quantities because of strong mutual coupling. The detailed development of such a picture awaits further consideration.

SUMMARY

The possibility of mechanical motion as a contributing factor in the conduction process of thin sheathed invertebrate nerve fibers is discussed. However, it is not implied that such activity in nerve is the only important factor in conduction.

It is shown that the experimentally observed relation between the velocity of conduction and the fiber diameter can be explained on such a basis. The effect of lateral squeezing and longitudinal stretching can also be correlated.

ACKNOWLEDGMENT

LITERATURE CITED

BLAIR, H. A. 1936 The time-intensity curve and latent addition in the mechanical stimulation of nerve. Am. J. Physiol., *114:* 586–593.

BULLOCK, T. H. 1945 Functional organization of the giant fiber system of lumbricus. J. Neurophysiol., *8:* 55–72.

COLE, K. S., AND H. J. CURTIS 1939 Electrical impedance of the squid giant axon during activity. J. Gen. Physiol., *22:* 649–670.

CURTIS, H. J., AND K. S. COLE 1942 Membrane resting and action potentials from the squid giant axon. J. Cell. and Comp. Physiol., *19:* 135–144.

FRY, W. J., AND R. B. FRY 1950 Theoretical consideration of a possible mechanism in the conduction process of thin sheathed nerve fibers. Bull. Math. Biophys., *12.* (In press.)

GASSER, H. S., AND J. ERLANGER 1929 The role of fiber size in the establishment of a nerve block by pressure or cocaine. Am. J. Physiol., *88:* 581–591.

GRUNDFEST, H. 1936 Effects of hydrostatic pressure on the excitability, the recovery and the potential sequence of frog nerve. Cold Spring Harbor Symposia on Quantitative Biology, *4:* 179–187.

HILL, D. K., AND R. D. KEYNES 1949 Opacity changes in stimulated nerve. J. Physiol., *108:* 278–281.

HODGKIN, A. L., AND A. F. HUXLEY 1945 Resting and action potentials in single nerve fibers. J. Physiol., *104:* 176–195.

HODGKIN, A. L., AND W. A. H. RUSHTON 1946 The electrical constants of a crustacean nerve fibre. Proc. Royal Soc., Series B, *133:* 444–479.

PROSSER, C. L. 1946 The physiology of nervous systems of invertebrate animals. Physiol. Rev., *26:* 337–382.

PUMPHREY, R. J., AND J. Z. YOUNG 1938 The rates of conduction of nerve fibers of various diameters in cephalopods. J. Exp. Biol., *15:* 453–466.

SOLOMON, S., AND J. M. TOBIAS 1950 Further observations on electrically induced transparency changes in nerve. Anodal rigidity, cathodal softening and the effects of several ions. (In preparation.)

SUTHERLAND, W. 1905 The nature of the propagation of nerve impulse. Am. J. Physiol., *14*: 112–119.

———— 1906–07 A molecular theory of the electric properties of nerve. Am. J. Physiol., *17*: 297–311.

———— 1908–09 The nature of the conduction of nerve impulse. Am. J. Physiol., *23*: 115–130.

TOBIAS, J. M. 1950a Qualitative observations on electrically induced transparency and dimensional changes and quick movements in single frog axones. Implications for excitation, propagation and the transport of materials along nerve. (In preparation.)

———— 1950b A possible contribution to the general theory of excitation. (In preparation.)

TOBIAS, J. M., AND S. SOLOMON 1950 Opacity and diameter changes in polarized nerve. J. Cell. and Comp. Physiol., *35*: 25–37.