Nerve Conduction in the Pre-Medical Physics Course

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The steady state electrical behavior of a nerve subjected to small signals provides an example of voltage attenuation in a resistance ladder. If capacitive effects are included, the nerve is similar to a cable with capacitance but without inductance. Discussion of the steady state problem is within the scope of a noncalculus general physics course, and students going into medicine or the life sciences would benefit from such a treatment. This paper introduces physics teachers to the basic properties of a nerve axon, the networks analogous to it, and the regenerative changes in the electrical properties of the nerve membrane which accompany the propagation of the action potential. These have been known to physiologists for over twenty years but are rarely discussed in physics courses.

INTRODUCTION

During the last two years I have been auditing courses in the University of Minnesota Medical School in order to learn what areas of physics are most useful to medical students. I was somewhat surprised in the first neurophysiology lecture to hear the professor tell the students, "You will remember the telegrapher's equation from your physics course." Fortunately, I was able to resuscitate and comfort my near neighbors. Although this equation is seldom covered in today's general physics course, a discussion with or without calculus is possible when circuits are being treated. Such a discussion is unavailable in most physics texts, although experiments on nerve conduction are now done in some introductory physics laboratories.[1,2] This paper will review for physicists some of the properties of nerves and will show the form which both a noncalculus and a calculus discussion of the analogous network might take. It will then review the currently accepted modifications to this equation which allow it to describe the regenerative action accompanying the propagation of a nerve impulse.

PROPERTIES OF NERVES[3]

A nerve consists of many parallel, independent signal paths made up of nerve cells. Each nerve is capable of transmitting a signal in only one direction; separate nerves carry signals to or from the brain. Each nerve cell contains an input end, a long conducting portion or axon, and an output end. It is these ends, rather than the axon, which give the nerve its unidirectional property. The input end may be a transducer (stretch receptor, temperature receptor, etc.) or a junction (synapse) with other nerve fibers. A threshold mechanism is built into the input end. When an input signal exceeding a certain level is received, this mechanism causes the nerve to fire and generate an impulse, of fixed size and duration, which travels along the axon. The axon is a long tail on the nerve cell and transmits the impulse without change of shape. The axon may be more than a meter in length, extending in a human, for example, from the brain to low in the spinal cord, or from the spinal cord to a finger or toe. Bundles of axons constitute what we usually think of as a nerve. The far end of the axon branches out into fine nerve endings, which appear to be separated by a gap from the next nerve cell or muscle cell which they drive. Transmission of the signal across the gap is discussed below.

The long, cylindrical axon has properties similar to those of an electric cable. Its diameter may range from less than a micron up to 500μ for the giant axon of a squid; in humans the upper limit is about 20μ. Pulses propagate along it with speeds from 0.6 m/sec to 100 m/sec, depending, among other things, on the diameter of the axon. The

TABLE I. Properties of typical axons.

Property	Nonmyelinated	Myelinated
Axon radius, a	5×10^{-6} m	5×10^{-6} m
Resistivity of axoplasm, ρ_i	0.5 Ω-m	0.5 Ω-m
Resistance per unit length of axoplasm, $r_i=\rho_i/\pi a^2$	6.37×10^{9} Ω/m	6.37×10^{9} Ω/m
Thickness of membrane or myelin, t	5×10^{-9} m	2000×10^{-9} m
Dielectric constant, κ	5.7	5.7
Capacitance per unit area, $\kappa\epsilon_0/t$	10^{-2} F/m²	25×10^{-5} F/m²
Capacitance per unit length, $2\pi\kappa\epsilon_0 a/t$	3×10^{-7} F/m	8×10^{-10} F/m
Resistivity of membrane or myelin, ρ_m	5×10^{7} Ω-m	5×10^{7} Ω-m
Resistance times length of membrane, $\rho_m t/2\pi a$	8000 Ω-m	3×10^{6} Ω-m
Conductivity per unit length of membrane, $2\pi a/\rho_m t$	1.25×10^{-4} mho/m	3×10^{-7} mho/m
Resting potential inside, V	−70 mV	−70 mV
Electric field across membrane or myelin, V/t	1.4×10^{7} V/m	3.5×10^{4} V/m
Charge per unit area, $\sigma=\kappa\epsilon_0 V/t$	7×10^{-4} C/m²	1.75×10^{-6} C/m²
Number of univalent ions/unit area	4.4×10^{15}/m²	1.1×10^{13}/m²
Number of univalent ions/unit length	1.4×10^{11}/m	3.4×10^{8}/m
Distance between nodes		2×10^{-3} m
Total capacitance between nodes		5×10^{-9} F
Capacitance of node		10^{-12} F
Resistance across myelin between nodes		1.5×10^{9} Ω
Resistance across node		50×10^{6} Ω
Resistance along axon between nodes		12.7×10^{6} Ω

core of the axon may be surrounded either by a membrane of thickness about 7–10 nm (an *unmyelinated* fiber) or by a much thicker sheath of fatty material (*myelin*), wound on like electrical tape. A myelinated fiber has its fatty sheath interrupted at intervals of about a millimeter and replaced by a short segment of membrane similar to that on an unmyelinated fiber. These

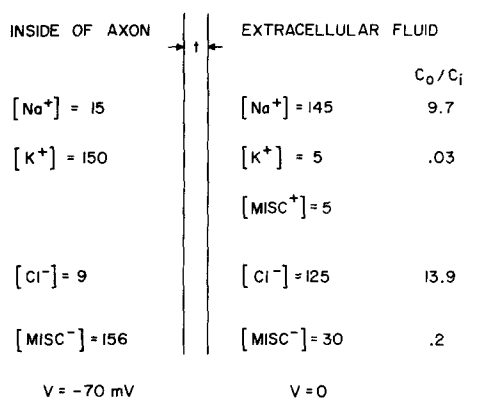

FIG. 1. Ion concentrations in a typical mammalian nerve and in the extracellular fluid surrounding the nerve. Concentrations are in millimoles/liter. C_0/C_i is the ratio of concentrations.

interruptions in the myelin sheath are called the *nodes of Ranvier*. The axon may be detached from the remainder of the cell, but it will still conduct impulses. Its conduction properties depend on the membrane; the interior protoplasm (axoplasm) has in fact been squeezed out of squid giant axons and replaced by an electrolyte solution without altering appreciably the propagation of the impulses. (However, the axoplasm contains elements essential to the long-term metabolic requirements of the cell. A discussion of these or of the Schwann cells which surround each axon must be left to the physiology literature.[4]) Comparison of the axoplasm with the interstitial fluid surrounding the cells shows an excess of potassium ions and a deficit of sodium and chloride ions, as shown in Fig. 1. Table I shows values for the resistance of the axoplasm and the resistance and capacitance of the membrane or myelin sheath. These are typical values, drawn from Refs. 3 and 4, and should not be identified with a specific species. The resistivity of the membrane is about 10^8 times that of the axoplasm. Also shown in Table I are values for resistance and capacitance at and between the nodes of Ranvier for a typical myelinated fiber.[5]

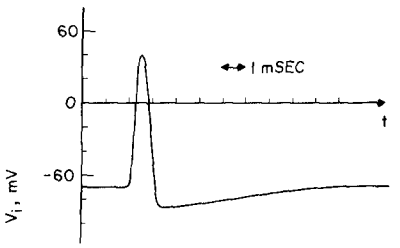

FIG. 2. A typical nerve impulse, also called the action potential, viewed at one position on the axon as a function of time.

The Nernst equation[6] can be used to determine whether, for the existing potential of −70 mV inside the cell, any of the ion species are near equilibrium. For a temperature of 310°K, the equilibrium ration C_0/C_i would be 0.07 for univalent positive ions and 13.7 for univalent negative ions. If the ions were free to equilibrate under these circumstances, sodium would move in, potassium would move out, chloride would already be in equilibrium, and the miscellaneous anions would move out. However, most of these miscellaneous anions in the axoplasm are large protein molecules which cannot penetrate the membrane. An interior potential of −90 mV would just support the observed concentration difference of potassium ions but would cause sodium ions to move further from equilibrium. Tracer studies show that potassium leaks out and sodium leaks in slowly, but that this is balanced by a process in which energy is expended to pump sodium back out and potassium back in.[7] If the permeability of the membrane to sodium were suddenly to increase, sodium would enter because of the concentration gradient, raising the interior potential. It is this process which appears to be responsible for the generation of the nerve impulse (action potential); the rising interior potential is accompanied by a further increase in the sodium permeability.

A typical impulse is shown in Fig. 2. The potential inside the axon rises abruptly, then falls towards −90 mV, and then slowly recovers to −70 mV. The membrane is said to depolarize and then to repolarize. The regenerative action which creates this pulse is due to the changing permeability of the membrane for sodium and potassium ions as the voltage changes. This will be discussed below in the section on Hodgkin–Huxley theory; the next section will discuss the response of the membrane to smaller signals for which changes in permeability can be neglected.

We now turn to the question of what happens at the end of the nerve fiber, where the signal must pass on to a muscle or to another nerve across a junction called a synapse: Is the transmission electrical or chemical?[8] There are gaps of 10–20 nm between presynaptic and postsynaptic nerve cells, and 50–100 nm at a neuromuscular junction. There are instances, such as in the heart, in which the transmission appears to be electrical[8]; yet in many cases chemicals are the carrier. Katz[9] provides convincing evidence of the chemical nature of the transmission at the usual neuromuscular junction, including a calculation of the small size of any electrical effect present. At most vertebrate neuromuscular junctions, the nerve impulse is followed by an electrical pulse which propagates throughout the muscle fiber and initiates contraction. There is good experimental evidence that in this case the chemical acetylcholine is released by the nerve endings when the nerve fires. The acetylcholine increases the permeability of the nearby muscle membrane to sodium, allowing sodium to leak in so that the muscle depolarizes. This process is quantized: packets of acetylcholine of definite size are liberated. This provides an excellent example of the Poisson distribution which can be discussed in class.[10] Other chemical mediators are important elsewhere in the nervous system.[11]

Now consider the input end of a nerve cell. The response of a nerve to chemical packets from a synapse with a preceding nerve is a change of membrane permeability which increases the interior potential. If the potential becomes high enough, the regenerative action of the membrane takes over and the nerve fires.[12] If the input portion of the cell is acting as a transducer, the interior potential rises as the transducer is stimulated. If the input is from another nerve or nerves at a synapse, a signal from a preceding nerve may cause it to fire, or the signal may cause a subthreshold increase or decrease of the internal potential. In this way, two or more input signals may be required simultaneously for the nerve to fire, or one input signal may inhibit the effect of another. This makes possible the Boolean network

of which the central nervous system is believed to consist.[13]

SMALL ELECTRICAL DISTURBANCES: ELECTROTONUS

The propagation of an electrical signal in an axon is similar to the propagation of a signal in a cable, as long as variation of membrane resistance with voltage can be neglected. This similarity was noted by workers in the field in the last century.[14] Physiologists call this small-signal spread of a change in potential along the axon *electrotonus*.

Consider charge flowing from the axoplasm to the inner wall of the membrane. There will be two components to the current, one charging the membrane capacitance, the other passing through the membrane:

$$i = C(dv/dt) + Gv,$$

where G is the membrane conductance. Now assume that for a length of axon dx, the resistance along the axoplasm is $R_i = r_i dx$, the exterior resistance is $R_0 = r_0 dx$, and the capacitance and conductance of the membrane are $C_m = c_m dx$ and $G_m = 1/R_m = dx/r_m$, respectively. Voltages, v, are measured as departures from the resting value (-70 mv). In the resting state, i must be zero. Then the axon has the equivalent circuit shown in Fig. 3.

The simplest approximation to this is an infinite resistive ladder network. Since this ignores capacitive effects, it can show only the spatial dependence of a steady-state signal, but it is

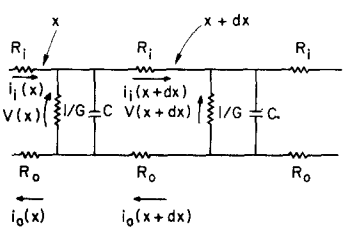

FIG. 3. Resistance–capacitance model for a segment of axon of length dx. R_i is the resistance inside the axon; R_0 is the resistance outside; G and C are the conductance and capacitance of the membrane. The departure of the transmembrane potential from equilibrium is v.

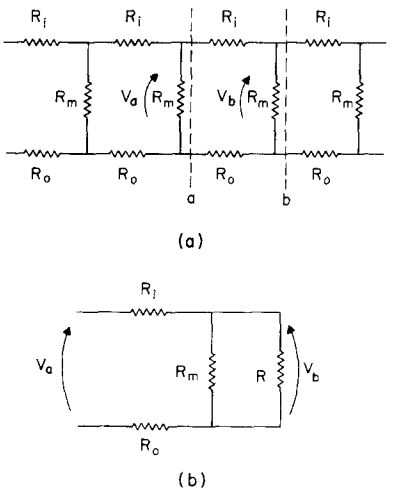

FIG. 4. (a) Approximation to the network of Fig. 3 with capacitance ignored. (b) Consideration of the circuit elements between points a and b, with the infinite network to the right of b replaced by a single resistance R.

easily within the scope of a noncalculus physics course. Such a ladder is shown in Fig. 4(a). Finding the relation between v_a and v_b can be considerably simplified by using the following trick. Cut the ladder at point b. Everything to the right of this point has resistance R. Then cut the ladder at a and replace everything to the right by the network shown in Fig. 4(b). Since the ladder is infinite, this must also have resistance R. Hence,

$$R = (R_0 + R_i) + RR_m/(R + R_m). \qquad (1)$$

This may be solved for R:

$$2R = (R_0 + R_i) + [(R_0 + R_i)^2 + 4(R_0 + R_i)R_m]^{1/2}. \qquad (2)$$

(Only the positive square root gives a positive value for R.) The ratio v_b/v_a may be obtained from the circuit of Fig. 4(b):

$$v_b = \frac{v_a}{[(R_0 + R_i)(R + R_m)/RR_m] + 1} = \frac{v_a}{1 + \beta}. \qquad (3)$$

Then one can write

$$\Delta v = v_b - v_a = -\beta v_a/(1 + \beta). \qquad (4a)$$

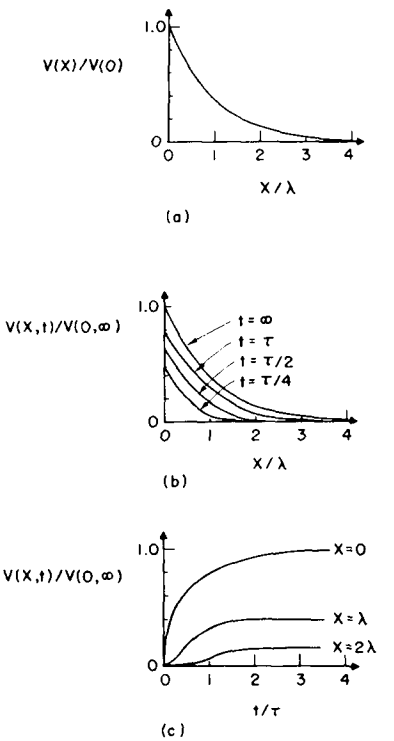

FIG. 5. (a) The voltage along the axon when $v=v_0$ at $x=0$. This is the solution of Eq. (4b), for which capacitance has been neglected. (b) The voltage along the axon at different times after the application of a constant current at $x=0$. For $t=\infty$ this is identical to (a). (c) Voltage at a fixed point on the axon as a function of time, for the same excitation as in (b).

The voltage change between rungs of the ladder is thus proportional to the voltage across a rung, and the voltage decays exponentially[15] down the ladder. If $\beta \ll 1$, then Eq. (4) takes the form

$$\Delta v = -\beta v. \tag{4b}$$

To apply this model to the unmyelinated axon of Table I, take

$$R_0 \approx R_i = r_i \Delta x = 6.37 \times 10^9 \Delta x,$$
$$R_m = r_m/\Delta x = 8000/\Delta x.$$

Then, from Eq. (2) we obtain

$$R = r_i \Delta x + [r_i^2 \Delta x^2 + (2r_i \Delta x)(r_m/\Delta x)]^{1/2}.$$

As $x \to 0$, this gives $R = (2r_i r_m)^{1/2}$. From Eq. (3), taking the same limit, we get $\beta = (2r_i/r_m)^{1/2}\Delta x = 1200\Delta x$. This means that if the voltage at some point is held at v_0, the voltage to the right will decay exponentially:

$$v(x) = v_0 \exp(-x/\lambda), \tag{5}$$

where the decay length or space constant, $\lambda = (2r_i/r_m)^{-1/2}$, is 0.8 mm. By symmetry, the voltage will decay in the same way to the left of that point. If the voltage at $x=0$ is held at v_0, while it is zero at $\pm\infty$, the voltage will be as plotted in Fig. 5.

To consider the temporal behavior of small signals, we must include the capacitance of the membrane. The simplest model which does this is that of Fig. 3, for which we can write the following equations:

$$i_i(x,t) = G_m v(x,t) + C_m(\partial v/\partial t) + i_i(x+dx,t), \tag{6a}$$

$$v(x,t) = v(x+dx,t) + R_i i_i(x+dx,t) + R_0 i_0(x+dx,t). \tag{6b}$$

The symmetry of the ladder requires that $i_i = i_0$. If we call these currents i, we obtain from Eqs. (6) the equations

$$\partial v/\partial x = -(r_i+r_0)i, \tag{7a}$$
$$\partial i/\partial x = -v/r_m - c_m(\partial v/\partial t). \tag{7b}$$

These can be combined to give

$$(\partial^2 v/\partial x^2) - (r_i+r_0)(v/r_m) - (r_i+r_0)c_m(\partial v/\partial t) = 0,$$

or

$$\lambda^2(\partial^2 v/\partial x^2) - v - \tau(\partial v/\partial t) = 0, \tag{8}$$

where $\lambda = [r_m/(r_i+r_0)]^{1/2}$ and $\tau = r_m c_m$. This is the homogeneous equation in the absence of external stimulation. The inhomogeneous equation has been considered in detail by Davis and Lorente de Nó,[16] and by Hodgkin and Rushton[17]; their work is summarized by Plonsey.[18]

This equation was once familiar to physicists as the differential equation for a submarine cable with negligible inductance per unit length[19]; hence the name telegrapher's equation. It can be transformed into the heat conduction equation by the

substitution $v=ue^{-t/\tau}$. When there is no time dependence, the equation reduces to Eq. (4). If the potential is made uniform along the axon (as with a fine wire inserted longitudinally), the voltage changes exponentially with time constant τ. The general solution is discussed in the references. The exact analytic form will not be repeated here, but the behavior of $v(x)$ at various times after an excitation is applied is shown in Fig. 5(b). The solution shown there is for a constant current injected at $x=0$ for all positive time. For $t=\infty$, the curve is identical to that for the earlier model, as the cable capacitance is charged and only the membrane leakage current attenuates the signal. For earlier times the shape is not quite exponential (the solution involves error functions). The rise of the voltage at fixed positions along the cable is shown in Fig. 5(c), which displays both the finite propagation time and the spatial attenuation of the signal.

More complicated models for the membrane with two time constants have also been used and are discussed in the references.

PROPAGATION OF THE ACTION POTENTIAL: HODGKIN-HUXLEY THEORY

Considerable work on this problem was done in the late 1940s, culminating in a set of equations relating impulse propagation to permeability changes measured in other experiments, which were presented by Hodgkin and Huxley in 1952.[20] Most of the experiments were carried out on the giant axon from the squid, which provides a single axon several centimeters long and 0.5 mm or more in diameter. The removal of the axoplasm from this preparation and its replacement by electrolytes had shown that the critical phenomena take place in the membrane. We will not review all the experiments which were done; the important ones are discussed in Refs. 3 and 18. We will mention only one type that is particularly illuminating. These were voltage clamp experiments which were reported by several workers in 1949.[21] Two long electrodes were inserted in the axon. One, paired with an electrode in the surrounding medium, sampled the potential across the membrane. The other injected whatever current was necessary to keep the membrane potential constant. If the membrane potential was abruptly increased from the resting value, the resulting current was found to have three components: (1) a current lasting a few μsec which changed the surface charge on the membrane (i.e., charged the membrane capacitance); (2) an inward current which lasted for 1 or 2 msec (various experiments showed that this was due to the inward flow of sodium ions; if the membrane potential were not clamped, of course, this flow would raise the potential further); (3) an outward current which rose for about 4 msec and which then remained steady for as long as the voltage was maintained at this value (tracer studies proved this to be due to a flow of potassium).

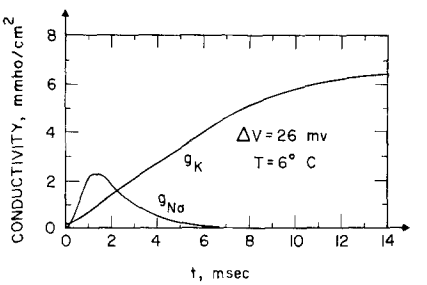

FIG. 6. Sodium and potassium conductivity as a function of time, for squid giant axon at 6°C subjected to a voltage step $\Delta V=26$ mv at $t=0$. The values are calculated from the equations in Ref. 20.

Hodgkin and Huxley used these results to define sodium and potassium conductivities. For example, the sodium conductivity, g_{Na}, is defined in terms of the sodium current density, j_{Na}, the transmembrane potential, V, and the sodium Nernst potential, V_{Na}, by the equation

$$j_{Na}=(V-V_{Na})g_{Na}. \tag{9}$$

A similar equation is written for the potassium conductivity. The conductivity at any time is a function of both the potential at that instant and its past history, so the definition is quite arbitrary. Nonetheless, it is useful to extract the term $(V-V_{Na})$, because we expect the sodium current to be zero when $V=V_{Na}$ since the ions inside and outside will then be in equilibrium. Factoring this term eliminates the need for g_{Na} to become zero when $V=V_{Na}$.

Hodgkin and Huxley found that if a voltage step was applied, the sodium and potassium currents behaved as shown in Fig. 6. The behavior

of the potassium conductivity is similar to $g_K(t) = \bar{g}_K(1-e^{-t/\tau})$, except that it has zero slope near $t=0$, while $(1-e^{-t/\tau})$ rises linearly from zero ($\bar{g}_K$ is the maximum potassium conductance). They chose to fit the conductivity by raising this expression to the fourth power. That is, they wrote

$$g_K = \bar{g}_K n^4,$$
$$dn/dt = \alpha_n(1-n) - \beta_n n. \tag{10}$$

The functions α_n and β_n are empirical functions of V.[20] It is postulated that a changing voltage affects g_K only through the behavior of this differential equation for n. For constant values of α_n, β_n, and $n(0)=0$, $n=n_\infty(1-e^{-t/\tau})$.

The sodium conductivity is described by

$$g_{Na} = m^3 h \bar{g}_{Na},$$
$$dm/dt = \alpha_m(1-m) - \beta_m m,$$
$$dh/dt = \alpha_h(1-h) - \beta_h h. \tag{11}$$

In this case, the growth of m describes the increase in sodium conductance, while a decrease of h describes its subsequent decay. Typical behavior of the conductivities for a voltage step is shown in Fig. 6. Although the authors give some arguments to justify the form of Eqs. (10) and (11), the equations must be regarded as phenomenological fits to the time-dependent permeabilities in response to a sequence of voltage steps. Alternative descriptions of the conductivity have been given which also fit the data but which suggest a different microscopic interpretation.[22]

The question we wish to consider here is whether this description, which describes the voltage clamp experiments well, is also consistent with the observed shape of the propagated nerve impulse. For $G_m v(x,t)$ in Eq. (6a), Hodgkin and Huxley substituted the following term:

$$G_m v = 2\pi a dx[\bar{g}_K n^4(V-V_K) + \bar{g}_{Na} m^3 h(V-V_{Na}) + \bar{g}_l(V-V_l)]. \tag{12}$$

The last term is a leakage term representing the migration of other ions. The leakage conductivity (0.3 mmho/cm^2) is smaller than the others; V_l is set so that the total current is zero in a resting membrane. Note that we have switched to the membrane potential V, instead of $v = V+70$ mV, which was used earlier. This shift has no effect on the derivatives. With this substitution, Eq. (7b) becomes

$$\partial i/\partial x = -2\pi a[\bar{g}_K n^4(V-V_K) + \bar{g}_{Na} m^3 h(V-V_{Na}) + \bar{g}_l(V-V_l)] - c_m(\partial V/\partial t).$$

If this is combined with Eq. (7a), one has

$$(r_i+r_0)^{-1}(\partial^2 V/\partial x^2) = c_m(\partial V/\partial t) + 2\pi a[\bar{g}_K n^4(V-V_K) + \bar{g}_{Na} m^3 h(V-V_{Na}) + \bar{g}_l(V-V_l)]. \tag{13}$$

Hodgkin and Huxley observed that the signal propagated without change of shape,

$$V = V(x-ut),$$

so that

$$\partial^2 V/\partial x^2 = (1/u^2)\partial^2 V/\partial t^2.$$

This is inserted in Eq. (13) to give

$$[2\pi a u^2(r_i+r_0)]^{-1}(\partial^2 V/\partial t^2) = (c_m/2\pi a)(\partial V/\partial t) + \bar{g}_K n^4(V-V_K) + \bar{g}_{Na} m^3 h(V-V_{Na}) + \bar{g}_l(V-V_l). \tag{14}$$

The quantity $c_m/2\pi a$ is the membrane capacitance per unit area, $\kappa\epsilon_0/t$ of Table I. If we assume $r_0 \ll r_i$, we can identify $r_i = \rho_i/\pi a^2$ and write the constant on the left side of Eq. (14) as $a/2\rho_i u^2$. Hodgkin and Huxley solved this equation by guessing a value for u and numerically integrating Eqs. (10), (11), and (14) from the foot of an action potential obtained by solving Eq. (8). The conduction velocity was an eigenvalue: For incorrect values of u, $V(t)$ diverged. For one value, in fairly good agreement with experiment, a pulse like that in Fig. 2 was reproduced. The experimental shape of the action potential was reproduced well, showing that the action potential is completely consistent with the conductance changes observed in the voltage clamp experiments. The more difficult question, asking what model for the membrane can explain these conductivity changes, is still being actively pursued.[22]

In the case of a myelinated fiber, the extra layer decreases both c_m and g_m, the mechanism of Eq. (8) allowing the signal to propagate more

rapidly and with less attenuation. At the nodes of Ranvier, the regenerative process reshapes the impulse. This process has been calculated in detail by a method analogous to the Hodgkin–Huxley equation.[23]

An anesthetic which is injected to block signals travelling along a nerve does so by preventing the membrane permeability from increasing. Thus, no regenerative restoration of the signal takes place, and the signal decays exponentially. The nerve must be blocked for several space constants, λ, to assure that the signal cannot get through.[24]

CONCLUSION

An introduction to nerve conduction for physicists has been presented. A time-independent network model of the nerve is given, suitable for the introductory physics course. A model including membrane capacitance which leads to the telegrapher's equation is also shown. The regenerative propagation of the signal due to changes of membrane permeability, which was first described quantitatively by Hodgkin and Huxley, is also reviewed.

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[2] P. Strong, *Biophysical Measurements* (Tektronix, Beaverton, OR, 1970), p. 189.

[3] B. Katz, *Nerve, Muscle, and Synapse* (McGraw-Hill, New York, 1966).

[4] A. L. Hodgkin, *The Conduction of the Nervous Impulse* (Charles C. Thomas, Springfield, IL, 1964).

[5] Reference 4, p. 53.

[6] T. C. Ruch and H. D. Patton, *Physiology and Biophysics* (Saunders, Philadelphia, PA, 1965), 19th ed., Chaps. 1, 43. It should be pointed out that some physiology books describe the concentration difference as giving rise to the potential difference. It seems better to say that a double layer of charge on the membrane gives rise to the potential difference, which then causes a concentration difference if the ions are free to move. Note that the Nernst equation is simply an expression of the Boltzmann factor for the potential energy difference across the membrane.

[7] Reference 4, Chap. VI.

[8] Reference 3, Chap. 7.

[9] Reference 3, Chap. 8; A. R. Martin, Physiol. Rev. **46**, 51 (1966).

[10] Reference 3, Chap. 9.

[11] F. O. Schmitt, "Molecular Neurobiology in the Context of the Neurosciences," in *The Neurosciences*, edited by G. C. Quarton, T. Melnechuk, and F. O. Schmitt (Rockefeller U. P., New York, 1967), p. 209.

[12] Reference 6, Chap. 4.

[13] Reference 11, Chap. 6.

[14] Reference 4, p. 30.

[15] R. K. Hobbie, Am. J. Phys. **41**, 389 (1973).

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