# THE PROPAGATION OF THE NERVE IMPULSE

NIKOLA JURISIC
*Departamento de Fisica, Facultad de Ciencias, Universidad Central de Venezuela, and Department of Physiology, University of California, Los Angeles, California 90024*

ABSTRACT A partial differential equation for the propagated action potential is derived using symmetry, charge conservation, and Ohm's law. Charge conservation analysis explicitly includes the gating charge when applied in the laboratory frame. When applied in the system of reference in which capacitive currents are zero, it yields a relation between orthogonal components of the ionic current allowing us to express the nonlinear ionic current in terms of the voltage-dependent membrane capacitance $C(V)$ and the axial current that satisfies Ohm's law. The ionic current is shown to behave as $C(V)V[C(V)V^2]'$ at the foot of the action potential while the gating current behaves as $C(V)V[C_g(V)V]'$ where $C_g(V)$ is the capacitance associated with gating. Improved knowledge of the nonlinear current makes it possible to describe the propagated action potential in an approximated way with quasilinear partial differential equations. These equations have analytical solutions that travel with constant velocity, retain their shape, and account for other properties of the action potential. Furthermore, the quasilinear approximation is shown to be equivalent to the FitzHugh–Nagumo equation without recovery making apparent its physical content.

## INTRODUCTION

The study of the propagated action potential has a long history culminating with the work of Hodgkin and Huxley (1952*a–d*). They described the functioning axon with a nonlinear diffusion equation in which the ionic current term is an empirical expression representing data obtained with the voltage-clamp technique (Cole, 1949; Hodgkin et al., 1952). The Hodgkin–Huxley equations have been successful in predicting a wide range of effects such as repetitive firing, effects of toxins, threshold behavior, etc. Because of their mathematical intractability, it has been fruitful to formulate simpler models that provide qualitative descriptions of the excitable membrane even if experimental results are described less accurately. The most instructive of these was developed from the van der Pol's oscillator (FitzHugh, 1961, 1969; Nagumo et al., 1962). This model, known as the FitzHugh–Nagumo model, preserves the essential characteristics of the Hodgkin–Huxley equations and can be used to illustrate many of the physiological properties of the axon. Many relevant references that deal with these topics can be found in books and reviews by Katz (1966), Cole (1968), FitzHugh (1969), Khodorov (1974), Scott (1975), Cronin (1981), Davydov (1982), Meves (1984), and others.

In their 1952 work, Hodgkin and Huxley proposed that the membrane conductance is coupled to the potential by a motion of charges confined to the membrane. In other words, the membrane bound motion of charges is responsible for the opening and closing of the ionic channels. This capacitive current, detected for the first time by Armstrong and Bezanilla (1973), was named as the gating current. Its voltage and time dependence are now well known, but it has not been possible to use this knowledge to reconstruct the voltage and time dependence of the ionic current without specific physical models.

In the present work, we derive a partial differential equation for the propagated action potential using symmetry, charge conservation, and Ohm's law. Charge conservation analysis explicitly includes the gating charge when applied in the laboratory frame. When applied in the frame in which the capacitive currents are zero, it yields a relation between orthogonal components of the ionic current allowing us to express the nonlinear ionic current across the membrane in terms of the voltage-dependent capacitance, $C(V)$, and the axial current that satisfies Ohm's law. The ionic current is shown to behave as $C(V)V[C(V)V^2]'$ at the foot of the action potential while the gating current behaves as $C(V)V[C_g(V)V]'$, where $C_g(V)$ is the capacitance associated with gating. The present formulation predicts a number of features of the propagating action potential. In particular, we predict the value of the capacitance associated with gating at the voltage corresponding to the steepest rate of rise.

Improved knowledge of the nonlinear term behavior makes it possible to describe the propagated action potential in an approximated way with quasilinear partial differential equations. These equations have analytical solutions that travel with constant velocity, retain their shape, and account for other properties of the action potential. Furthermore, we show that the quasilinear approximation is equivalent to the FitzHugh–Nagumo

Address correspondence to Dr. Nikola Jurisic, c/o Dr. Francisco Bezanilla, Department of Physiology, Center for the Health Sciences, University of California, Los Angeles, CA 90024.

model without recovery, making apparent the physical content of this model.

## CHARGE CONSERVATION

Closed loops of current are present in a conductive medium as long as energy is supplied to maintain the potential distribution. In the case of the propagating action potential, the energy is provided by the chemical potential of sodium and the axial symmetry of the axon restricts the closed loop current flow to two possible circulations corresponding to the two directions along the axis. In what follows, for the sake of simplicity, we neglect the undershot of the action potential. Directional asymmetry of the propagating action potential is best exhibited by the current flow in the frame of reference in which the action potential is at rest. In this frame, which we call the action potential frame, the capacity charges responsible for the potential are at rest and there is a steady ionic current flow with a definitive circulation. See Fig. 1 for a schematic picture. In the laboratory, in addition to the ionic current, which is invariant under Galilean transformation, there is a capacity current loop coming from the displacement current and the motion of the double layer of capacity charges. The total axial current in the axoplasm satisfies Ohm's law; therefore, the ionic current and capacity current loops circulate in opposite directions. The capacity component of the axial current predominates during the rising phase of the action potential, while the ionic component predominates during recovery. The net result is two loops of total current circulating in opposite directions (Fig. 2). The impulse depicted in Fig. 1, at rest in the action potential frame, is seen in the laboratory to propagate toward the left. Positive ions enter the axon at the front of the impulse and exit at the back.

Charge conservation requires that the surface charge

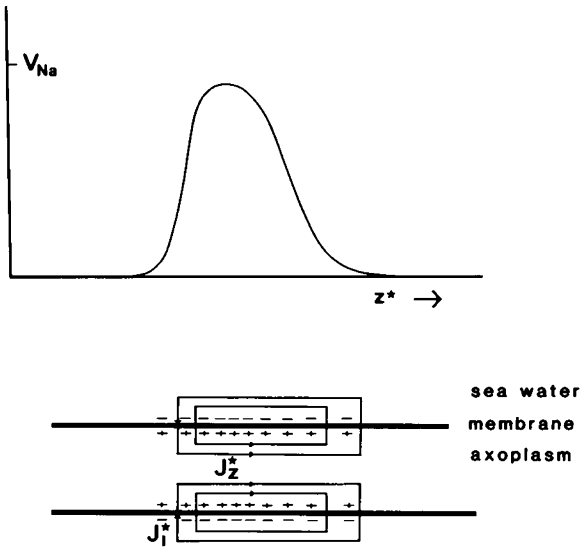


FIGURE 1 Action potential (*top*) and schematic ionic current flow (*bottom*) in the action potential frame.

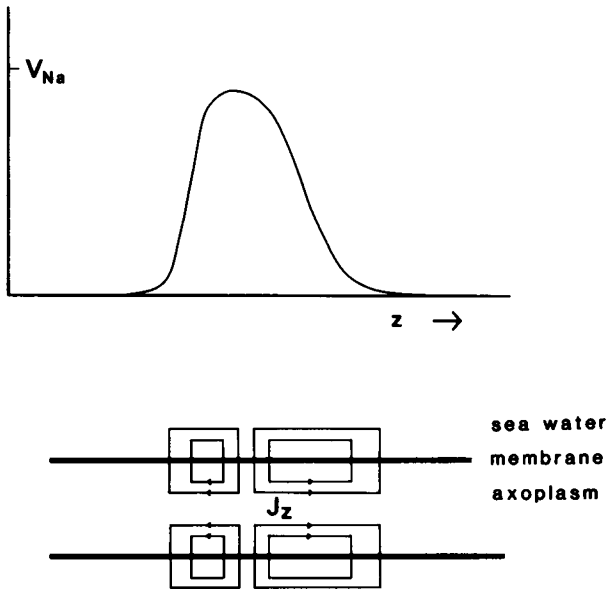


FIGURE 2 Action potential (*top*) and schematic total current flow (*bottom*) in the laboratory frame. The action potential propagates to the left.

integral of the current, **J**, over a closed surface plus a change of the charge, $q$, per unit time inside the surface add to zero,

$$\int_s \mathbf{J} \cdot \mathrm{d}\mathbf{a} + \frac{\mathrm{d}}{\mathrm{d}t} \int_v \rho \, \mathrm{d}^3x = 0. \tag{1}$$

$\int \mathbf{J} \cdot \mathrm{d}\mathbf{a}$ is the instantaneous rate at which charge is leaving the enclosed volume, while $\int \rho \, \mathrm{d}^3x$ is the total charge, $q$, inside the volume at any instant. Applying this identity to a cylindrical volume element of length $\Delta z$ and radius $R$ (see Fig. 3) gives

$$\pi R^2 [J_z(z + \Delta z) - J_z(z)] + 2\pi R \Delta z J_1(z) + \frac{\Delta q}{\Delta t} = 0, \tag{2}$$

where $J_1(z)$ is the radial or the ionic current density flowing across the membrane and $J_z(z)$ is the total axial current density in the axoplasm. $J_1$ is positive for outward current and $J_z$ is independent of the radial variable if the spatial extension of the action potential is much larger than the axon's radius. The net charge, $q$, crossing the surface of the volume element includes the gating charge, $q_g$, whose movement is confined to the membrane. The motion of the gating charge is a nonlinear function of the potential and therefore the membrane capacity per unit surface $C$, in addition to the voltage-independent part $C_m$, has a contribution $C_g(V)$ associated with gating,

$$C(V) = C_m + C_g(V) \tag{3a}$$

and

$$q = 2\pi R \Delta z C(V) V. \tag{3b}$$

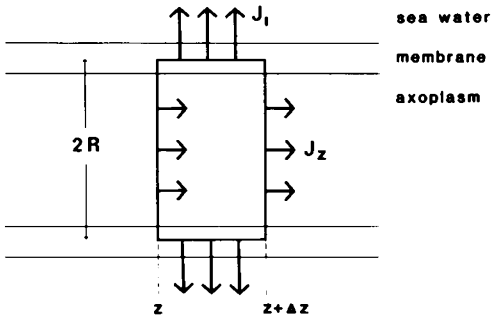


FIGURE 3 Schematic cross section of the axon, current densities, and the volume element of radius $R$ and length $\Delta z$.

The different voltage dependences of $C_m$ and $C_g$ constitutes the basis for detection of gating currents (Armstrong and Bezanilla, 1973; Keynes and Rojas, 1973).

Using Eq. 3b in Eq. 2 and taking the limit $\Delta z \to 0$, the charge conservation expression valid in the laboratory is obtained,

$$\frac{\partial C(V)V}{\partial t} + J_l + \frac{R}{2}\frac{\partial J_z}{\partial z} = 0. \tag{4}$$

With Ohm's law, $R_i J_z = -\partial V/\partial z$, Eq. 4 becomes

$$\frac{\partial C(V)V}{\partial t} + J_l = \frac{R}{2R_i}\frac{\partial^2 V}{\partial z^2}, \tag{5}$$

where $R_i$ is the resistivity of the axoplasm. If $C(V)$ and $J_l(V)$ were known, Eq. 5 would be a full description of the propagated action potential. Hodgkin–Huxley (H–H) equations are obtained by neglecting $C_g(V)$ and taking for $J_l$ the empirical expressions representing data obtained with the voltage clamp.

Charge conservation also holds in the frame of reference in which the action potential is at rest. The quantities in this frame have asterisks, the currents are steady, no charge accrues inside the cylindrical volume element, and the expression equivalent to Eq. 4 is

$$J_l^* + \frac{R}{2}\frac{\partial J_z^*}{\partial z^*} = 0. \tag{6}$$

There is no time dependence in Eq. 6 and the partial derivative is equal to the total derivative. The ionic axial current $J_z^*$ is a function of the potential $V^*$ since without $V^*$ no current exists. Therefore, Eq. 6 may become

$$J_l^* + \frac{R}{2}\frac{dJ_z^*}{dV^*}\frac{dV^*}{dz^*} = 0. \tag{7}$$

For the pulse traveling to the left, the laboratory frame and the action potential frame are related through a Galilean transformation along the $z$ axis: $z^* = z + vt$, $t^* = t$, where $v$ is the velocity of the laboratory frame as seen from the action potential frame. Scalar functions, all vectors perpendicular to the $z$ axis and the electrical field, are the same in the two frames when they coincide at some instant of time,

$$V^* = V, \qquad J_l^* = J_l, \qquad \frac{dV^*}{dz^*} = \frac{\partial V}{\partial z} \tag{8}$$

The axial current transforms as follows:

$$J_z^* = J_z + 2vC(V)V/R \tag{9}$$

and

$$\frac{dJ_z^*}{dz^*} = \frac{\partial}{\partial z}[J_z + 2vC(V)V/R] \tag{10}$$

$$\frac{dJ_z^*}{dV^*} = \frac{d}{dV}[J_z + 2vC(V)V/R]. \tag{11}$$

The axial current $J_z$ is an instantaneous function of the potential $V$. With Eq. 8 in Eq. 7, the membrane ionic current is

$$J_l = -\frac{R}{2}\frac{dJ_z^*}{dV}\frac{\partial V}{\partial z} \tag{12}$$

and the cable equation, Eq. 5, becomes

$$\frac{\partial C(V)V}{\partial t} - \frac{R}{2}\frac{dJ_z^*}{dV}\frac{\partial V}{\partial z} = \frac{R}{2R_i}\frac{\partial^2 V}{\partial z^2}, \tag{13}$$

where $J_z^*$ is given by Eq. 9. The ionic current is invariant under Galilean transformation and therefore $J_z^*$ in Eqs. 12 and 13 can be interpreted as the ionic component of the axial current in the laboratory. Eq. 13 is quite general and in principle it could describe a number of physical phenomena with propagating excited domains. The unknown functions $C(V)$ and $J_z^*$ are determined by a particular physical situation. In the case of the nerve impulse, the first function includes the capacitance associated with gating and the second, in addition, depends on other properties of the membrane. If $C(V)$ is a constant and if $J_z$ is a quadratic function of potential, Eq. 13 reduces to the quasilinear Burgers equation.

## IMPULSE PROPAGATION

The nonlinear membrane current density $J_l$ is an instantaneous function of the potential. Eq. 12 exhibits $J_l$ in terms of physically explicit factors: the velocity of propagation, $v$; the action potential, $V$; the voltage-dependent capacitance, $C(V)$; and the axial current $J_z$, which is also an instantaneous function of the potential. We shall construct a phenomenological expression for $J_z$ taking into account the following facts: (*a*) At the peak of the action potential, where $V = V_p$ and $\partial V_p/\partial t = \partial V_p/\partial z = 0$, it follows from Eqs. 9 and 5 and from Ohm's law that

$$J_z(V_p) = 0 \tag{14a}$$

$$J_l(V_p) = \frac{R}{2R_i}\frac{\partial^2 V_p}{\partial z^2} \tag{14b}$$

$$J_z^*(V_p) = 2vC(V_p)V_p/R. \tag{14c}$$

(*b*) The axial current flows from high potential to low potential; therefore, for the rising phase of the action potential propagating to the left, $J_z \leq 0$ and taking Eq. 9 into account,

$$J_z^*(V) \leq 2vC(V)V/R. \tag{15}$$

Furthermore, as $V \rightarrow 0$, $J_z^*$ must go to zero faster than $C(V)V$, otherwise incorrect behavior for $J_I$ is obtained. Therefore, $J_z = -2vC(V)V/R$ for small $V$ at the foot of the action potential. (*c*) The ionic current, $J_I$, is proportional to the driving force, $(V_{Na} - V)$, where $V_{Na}$ is the reversal potential of sodium. Behaviors described in *a*, *b*, and *c* are incorporated in the following phenomenological expressions for the axial currents:

$$J_z(V) = -2vC(V)V[V_{Na} - V - b(V)V^2]/RV_{Na} \tag{16a}$$

$$J_z^*(V) = 2vC(V)V^2[1 + b(V)V]/RV_{Na}, \tag{16b}$$

where, because of Eq. 14a, $b(V_p) = (V_{Na} - V_p)/(V_p)^2$. Using Eq. 16 in Eq. 12, the corresponding $J_I(V)$ during the rising phase is obtained,

$$J_I(V) = -GC(V)V[V_{Na} - V - b(V)V^2] \cdot \frac{d}{dV}\{C(V)V^2[1 + b(V)V]\}, \tag{17}$$

where

$$G = 2R_i v^2/R(V_{Na})^2.$$

The current density, $J_I$, cannot depend on $R$ and $R_i$. Therefore, the velocity of propagation must be proportional to $(R/R_i)^{0.5}$, which is a well known result (see the work of Hodgkin, 1954). Also, it is known that at the foot of the action potential, $J_I$, is proportional to the driving force, $(V_{Na} - V)$. Therefore, the function $G$ does not depend on $V_{Na}$ and the velocity of propagation is proportional to sodium's reversal potential,

$$v = V_{Na}(GR/2R_i)^{0.5}. \tag{18}$$

The function $G$ depends on the local membrane properties such as the number of channels per unit surface.

The total membrane current during action potential is proportional to the second derivative of potential respect to time; it is zero when the first derivative is at a maximum or a minimum. The following relations apply at voltage for which the total membrane current is zero,

$$J_I(V) = -\frac{\partial C(V)V}{\partial t} \tag{19}$$

$$\frac{dJ_z(V)}{dV} = 0, \tag{20}$$

and with Eq. 9,

$$\frac{dJ_z^*(V)}{dV} = \frac{2v}{R}\frac{dC(V)V}{dV}. \tag{21}$$

Our phenomenological currents Eqs. 16a and b and 17 for the rising phase of the action potential satisfy the general relations Eq. 19, 20, and 21 if the following identity holds:

$$[V_{Na} - 2V - 3b(V)V^2 - b'(V)V^3]C(V) + V[V_{Na} - V - b(V)V^2]C'(V) = 0 \tag{22}$$

at the point $V = V_s$ at which the total membrane current is zero. According to Eq. 22, propagation requires a coupling between the capacitance, $C(V)$, and the function, $b(V)$. For the case when $C'(V_s) = 0$ and $b = 0$, the relation Eq. 22 yields $V_s = V_{Na}/2$. For the case when $V_{Na}C'(V_s)/2C(V_s) = x \ll 1$, and $3V_{Na}b(V_s)/2 = y \ll 1$ and neglecting $b'(V_s)$,

$$V_s \simeq (V_{Na}/2)(1 - x)^{-1}[1 - (x + y)(1 - x)^{-2}] \simeq (V_{Na}/2)(1 - y). \tag{23}$$

Using Eq. 16a and Ohm's law, the steepest rate of rise in the action potential in the approximation Eq. 23 is

$$\frac{\partial V_s}{\partial t} = R_i C(V_s)v^2 V_{Na}(1 - y/3)/2R, \tag{24a}$$

or with Eq. 18,

$$\frac{\partial V_s}{\partial t} = G(V_{Na})^3 C(V_s)(1 - y/3)/4. \tag{24b}$$

Hodgkin and Huxley (1952*d*) compared the predictions of their equations with experimental records from a particular axon which is now called the H–H axon. It is appropriate to formulate our predictions for the same axon. For the H–H axon [Hodgkin and Huxley, 1952*d*; Fig. 15 *C*, $V_{Na}$ = 115 mV, $R_i$ = 35.4 ohm · cm, $R = 238 \times 10^{-4}$ cm, $v$ = 21.2 m/s, $C_m$ = 1 $\mu$F/cm$^2$ was measured on the fiber on which the record 15 *C* was made; and reading from Fig. 15 *C*, $V_p = (105 \pm 3)$ mV, $dV/dt|_{max} = (506 \pm 30)$ mV/ms] the relation Eq. 24a predicts the maximum value of the voltage-dependent capacitance to be

$$C(V_s) = 1.33 \pm 0.10\ \mu\text{F/cm}^2, \qquad V_s = 57.5\ \text{mV if } b(V_s) = 0$$

or

$$C_g(V_s) = 0.33 \pm 0.10\ \mu\text{F/cm}^2, \tag{25a}$$

and

$$C(V_s) = 1.40 \pm 0.10\ \mu\text{F/cm}^2,$$

$$V_s = 48\ \text{mV if } b(V_s) = b(V_p)$$

or

$$C_g(V_s) = 0.40 \pm 0.10\ \mu\text{F/cm}^2 \tag{25b}$$

The experimental data presented as charge shifted vs. potential $(Q_g - V)$ curves yield capacitances that fall within the range of values predicted by Eq 25. The $Q_g - V$ curves are sigmoids rising steadily from $\sim -160$ mV and

saturating at 50 mV (Bezanilla et al., 1982; Figs. 3, 7, and 8; holding potential, −70 mV). The region of interest for comparison is from −65 mV–40 mV (0–105 mV when measuring the potential as a deviation from the resting potential). Approximating this region of the curves with straight lines, gating capacitance $C_g(V_s)$ of 0.45, 0.34, and 0.29 $\mu F/cm^2$ are obtained.

Also, Hodgkin and Katz (1949) have measured the dependence of the maximum rate of rise of the action potential on the external sodium concentration. Fig. 4 shows experimental ratios of these rates of rise and the ratios predicted by Eq. 24b with $b = 0$. The error introduced by neglecting $b$ is negligible. The predicted rectification at low and high concentration ratios is exhibited by the experimental data. Also, according to Eq. 24b, the maximum rate of rise does not depend on the axon's radius $R$ and the resistivity $R_i$. Numerical calculations carried out by the author using H–H equations yield the same lack of dependence.

## QUASILINEAR APPROXIMATION

The substitution of $C(V)$ for $C(V_s)$ in Eq. 13 introduces errors at the foot and the peak of the action potential. However, in these regions the derivatives of the action potential are small when compared with the derivatives in the $V_s$ region, making the error relatively less important. In addition, to obtain the quasilinear simplification, we set $b = 0$. With these approximations, and using Eq. 16b, the general equation for propagation, Eq. 13, reduces to the quasilinear Burgers equation,

$$C(V_s)\frac{\partial V}{\partial t} - \frac{2vC(V_s)}{V_{Na}}V\frac{\partial V}{\partial z} = \frac{R}{2R_i}\frac{\partial^2 V}{\partial z^2}. \quad (26)$$

The Burgers equation, first introduced by Bateman (1915), was specifically stressed by Burgers (1948) as being the simplest one to combine typical nonlinearity with typical heat diffusion. The Cole–Hopf transformation (Cole, 1951; Hopf, 1950) eliminates the nonlinear term and the resulting heat equation has a known solution that satisfies arbitrary initial conditions. The Burgers equation, Eq. 26, has a particular wave front solution that propagates to the left without changing its shape (Toda, 1975; p. 23),

$$V = V_{Na}/2 + A\tanh\{[2AC(V_s)vR_i/RV_{Na}](z + vt)\} \quad (27)$$

In general, the velocity, $v$, and the amplitude, $A$, are arbitrary constants. In our case, these constants are determined by physical requirements of the propagation. The potential, $V$, is always positive, so $A = V_{Na}/2$. The velocity, $v$, appears as a factor in the ionic current, $J_I$. As before, the requirement that ionic current $J_I$ be independent of $R$, $R_i$ and be proportional to $(V_{Na} - V)$ yields again the expression Eq. 18 for the velocity. Furthermore, the solution, Eq. 27, satisfies the relations Eqs. 24a and b with $b = 0$.

Using the same quasilinear approximation to write $\partial V/\partial z$ as a function of the potential, Eq. 26 becomes

$$C(V_s)\frac{\partial V}{\partial t} - 2G[C(V_s)]^2V^2(V_{Na} - V) = \frac{R}{2R_i}\frac{\partial^2 V}{\partial z^2}. \quad (28)$$

Many years ago, A. F. Huxley proved that if the ionic current density is an instantaneous function of the potential proportional to $V^2(V_{Na} - V)$ as in Eq. 28, the cable equation has a wave front solution that propagates with constant velocity (see Hodgkin, 1975). Eq. 28 admits

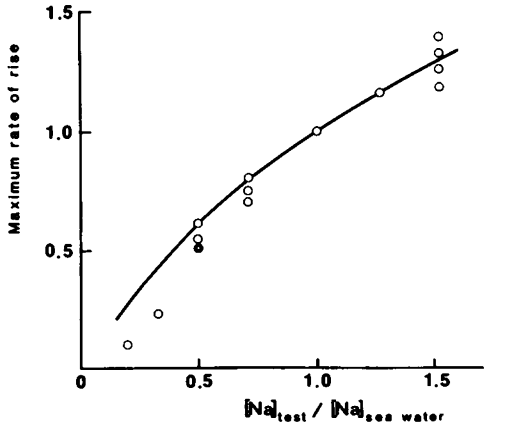


FIGURE 4 *Ordinate*, maximum rate of rise of spike in test solution/maximum rate of rise in sea water. *Abcissa*, sodium concentration of test solution/sodium concentration in sea water. *Circles*, experimental points. Redrawn from Fig. 11 of Hodgkin and Katz (1949). *Curve*, $(V_{Na})^3_{\text{test solution}}/(V_{Na})^3_{\text{sea water}}$ against sodium's concentration ratios.

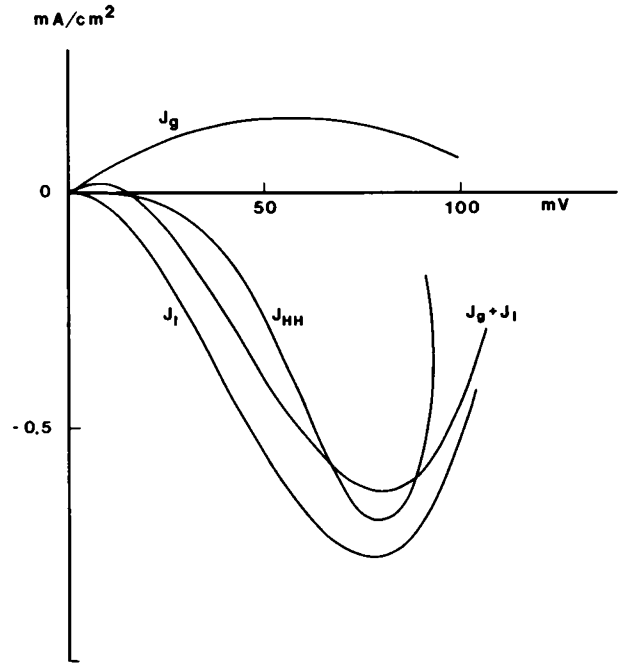


FIGURE 5 Currents vs. voltage for the propagated action potential. Gating current $J_g$, ionic current $J_I$, and their sum in the quasilinear approximation. $J_{HH}$ is the ionic current computed numerically using Hodgkin and Huxley equations.

following solutions, which propagate to left/right:

$$V = (V_{Na}/2)\{1 \pm \tanh[vC(V_s)R_i/R](z \pm vt)\}, \quad (29)$$

where $v$ is given by Eq. 18.

Combining the gating current $J_g = C_g(V_s)\partial V/\partial t$ with the ionic current $J_I$ turns Eq. 28 into the FitzHugh–Nagumo equation without recovery,

$$C_m \frac{\partial V}{\partial t} + G^* V(V_{Na} - V)(V_{th} - V) = \frac{R}{2R_i}\frac{\partial^2 V}{\partial z^2}, \quad (30)$$

where

$$G^* = 2G[C(V_s)]^2 \quad \text{and} \quad V_{th} = V_{Na}C_g(V_s)/2C(V_s).$$

The physical content of the FitzHugh–Nagumo model is now apparent. In particular, the early outward current and the threshold properties of the FitzHugh–Nagumo model come from gating. With $C_g(V_s) = 0.33\ \mu F/cm^2$ and $V_{Na} = 115$ mV we obtain $V_{th} = 14$ mV. This prediction compares well with the fit of the experimental current–voltage relations taken from Hodgkin et al., (1952) with a cubic equation with zeros at 0, 11, and 110 mV (Hunter et al., 1975).

In Fig. 5, we plot the gating current, $J_g$, the ionic current, $J_I$, their sum, $G^*V(V_{Na} - V)(V_{th} - V)$, and the current $J_{HH}$. The current $J_{HH}$ is computed numerically from the empirical expression for the ionic current during propagation given by Hodgkin–Huxley equations. In the quasilinear approximation, both the gating and the ionic current are overestimated at the foot of the action potential. However, the errors tend to cancel each other when the two currents are added. The comparison of $J_g + J_I$ with $J_{HH}$ suggests that the bulk of the gating current is included in the empirical expressions for the ionic current constructed by Hodgkin and Huxley.

## RECOVERY

For simplicity we neglect the potential undershot during recovery. In this approximation, the axial current goes from zero at the peak value $V_p$ of the action potential through a maximum down to zero when the resting potential is reached,

$$J_z = f2vC(V)V(V_{Na} - V - bV^2)/RV_{Na}. \quad (31)$$

In the recovery region, we do not have an argument about the behavior of the axial current at small $V$ as we have at the foot of the action potential, hence the dimensionless factor $f$. The function $f$ must include physical properties of the recovery region.

In the quasilinear approximation, the outgoing ionic current is

$$J_I(V) = 2f^2G[C(V_I)]^2V(V_{Na} - V)[V_{Na}(1 + f)/(2f) - V], \quad (32)$$

where $V_I$ is the potential at which the total membrane current is zero. The wave solution equivalent to Eq. 30 is

$$V = (V_{Na}/2)\{1 \mp \tanh[fvC(V_I)R_i/R](z \pm vt)\}, \quad (33)$$

where the velocity $v$ is given by Eq. 18.

The steepest rate of descent is

$$\frac{\partial V_I}{\partial t} = -fG(V_{Na})^3C(V_I)/4. \quad (34)$$

The measured steepest rate of descent is rather insensitive to the variation of the external sodium concentration, while Eq. 34 would seem to predict a cubic dependence in $V_{Na}$. According to the independence principle, which says that the ions traverse the membrane without interfering with each other, one expects that the ratio of the steepest rate of descent to the steepest rate of rise is proportional to the ratio of the internal potassium concentration, $[K]_i$, to the external sodium concentration, $[Na]_o$. Furthermore, the axial current Eq. 31 should be proportional to the concentration of potassium $[K]_i$, which is the predominant ion in the axoplasm. Both of these physical requirements are satisfied to a first order approximation, while leaving the amplitude unchanged, if

$$f = f^*[K]_i/[Na]_o \quad (35)$$

Then

$$\frac{\partial V_I}{\partial t} = -f^*GC(V_I)[K]_i(V_{Na})^3/4[Na]_o. \quad (36)$$

The experimental results exhibited in Fig. 4 show that at least for small variation in sodium concentration $(V_{Na})^3/[Na]_o$ is a constant and therefore Eq. 36 is insensitive to changes in sodium concentration.

## CONCLUSION

We have shown that symmetry, Ohm's law, and charge conservation allow us to describe the propagated action potential with a partial differential equation in which the gating current is explicitly included and the nonlinear ionic current across the membrane is given as a function of the axial current and the voltage-dependent capacitance.

In the frame in which the action potential is at rest, the charge conservation yields a relation between radial and axial components of the ionic current. This relation allows us to write the membrane ionic current in terms of physically explicit factors: the velocity of propagation, the action potential, the voltage-dependent capacitance, and the axial current. The physical makeup of the nonlinear current is now apparent and its construction is greatly simplified since the axial current satisfies Ohm's law and is proportional to the spatial derivative of the action potential. Thus, only the main features of the action potential (peak value and $b$) and the voltage-dependent capacitance are needed to predict the voltage dependence of the ionic current. The voltage-dependent capacitance fully describes

the gating current during propagation and the main features of the action potential (steepest rate of rise and the velocity of propagation) allow us to predict the value of the capacitance and hence the gating current for the steepest rate of rise voltage. The value of the gating capacitance predicted for the H–H axon agrees well with values obtained from direct measurements of gating currents. The predicted dependence of the maximum rate of rise on sodium's reversal potential agrees with experimental data. Also, the maximum rate of rise is predicted to be independent of the diffusion constant. A numerical computation shows the same lack of dependence for the H–H equations.

At the foot of the action potential, the axial current behaves as its capacitive contribution and its magnitude is equal to $2vC(V)V/R$, where $C(V)V$ is the surface charge density, $Q(V)$, of the double layer responsible for the potential difference across the membrane. The construction of the axial current is completed by including a factor that goes to zero at the crest of the action potential. The corresponding behavior of the ionic current is then completely determined. At the foot of the action potential it is proportional to $Q(V)[Q(V)V]'$, while the gating current is proportional to $V_{Na}Q(V)[Q_g(V)]'$. The velocity of propagation is obtained by imposing simple physical conditions that must be satisfied by the ionic current.

Neglecting recovery and approximating the capacitance with a constant reduces the differential equation for propagation into a quasilinear Burgers equation that admits analytical solutions traveling with constant velocity. By combining the gating current with the ionic current, the quasilinear approximation is shown to be equivalent to the FitzHugh–Nagumo model without recovery. The physical content of this model is now apparent. The early outward current and the threshold behavior of this model come from gating.

Comparison of the combined gating and ionic current from the quasilinear approximation with the ionic current computed from the H–H equations suggests that, although Hodgkin and Huxley were unable to detect the gating current by itself, the bulk of it is included in their empirical expression for the ionic current.

I want to thank Dr. F. Bezanilla for the hospitality at his laboratory that allowed me to write the last version of this work. I am also indebted to Dr. J. Vergara and Dr. R. E. Taylor for fruitful discussions and generous help.

*Received for publication 4 August 1986 and in final form 29 December 1986.*

## REFERENCES

Armstrong, C. M., and F. Bezanilla. 1973. Currents related to movement of gating particles of the sodium channels. *Nature (Lond.).* 242:459–461.

Bateman, H. 1915. Some recent researches on the motion of fluids. *Monthly Weather Rev.* 343:163–170.

Bezanilla, F., R. E. Taylor, and J. M. Fernandez. 1982. Distribution and kinetics of membrane dielectric polarization. *J. Gen. Physiol.* 79:21–40.

Burgers, J. M. 1948. A mathematical model illustrating the theory of turbulence. *Adv. Appl. Mech.* 1:171–199.

Cole, J. D. 1951. On a quasilinear parabolic equation occurring in aerodynamics. *Q. Appl. Math.* 9:225–236.

Cole, K. S. 1949. Dynamic electrical characteristics of the squid axon membrane. *Arch. Sci. Physiol.* 3:253–258.

Cole, K. S. 1968. Membranes, Ions and Impulses. University of California Press, Berkeley and Los Angeles. 1–369.

Cronin, J. 1981. Mathematics of Cell Electrophysiology. Marcel Dekker, Inc., New York.

Davydov, A. S. 1982. Biology and Quantum Mechanics. Pergamon Press Ltd., Oxford.

FitzHugh, R. 1961. Impulses and physiological states in theoretical models of nerve membrane. *Biophys. J.* 1:445–466.

FitzHugh, R. 1969. Mathematical models of excitation and propagation in nerve. In Biological Engineering. H. P. Schwan, editor. McGraw-Hill Book Co., New York. 1–85.

Hodgkin, A. L. 1954. A note on conduction velocity. *J. Physiol. (Lond.).* 125:221–224.

Hodgkin. A. L. 1975. The optimum density of sodium channels in an unmyelinated nerve. *Phil. Trans. R. Soc. Lond. B. Biol. Sci.* 270:297–300.

Hodgkin, A. L., and A. F. Huxley. 1952*a*. Currents carried by sodium and potassium ion through the membrane of the giant axon of Loligo. *J. Physiol. (Lond.).* 116:449–472.

Hodgkin, A. L., and A. F. Huxley. 1952*b*. The components of membrane conductance in the giant axon of Loligo. *J. Physiol. (Lond.).* 116:473–496.

Hodgkin, A. L., and A. F. Huxley. 1952*c*. The dual effect of membrane potential on sodium conductance in the giant axon of Loligo. *J. Physiol. (Lond.).* 116:497–506.

Hodgkin, A. L., and A. F. Huxley. 1952*d*. A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol. (Lond.).* 117:500–544.

Hodgkin, A. L., and B. Katz. 1949. The effect of sodium ions on the electrical activity of the giant axon of the squid. *J. Physiol. (Lond.).* 108:37–77.

Hodgkin, A. L., A. F. Huxley, and B. Katz. 1952. Measurements of current–voltage relations in the membrane of the giant axon of Loligo. *J. Physiol. (Lond.).* 116:424–448.

Hopf, E. 1950. The partial differential equation $U_t + UU_x = \nu U_{xx}$. *Commun. Pure Appl. Math.* 3:201–230.

Hunter, P. J., P. A. McNaughton, and D. Noble. 1975. Analytical models of propagation in excitable cells. *Prog. Biophys. Mol. Biol.* 30:99–144.

Katz, B. 1966. Nerve, Muscle and Synapse. McGraw-Hill Book Co., New York. 1–96.

Keynes, R. D., and E. Rojas. 1973. Characteristics of the sodium gating current in the squid giant axon. *J. Physiol. (Lond.).* 233:28–30P.

Khodorov, B. I. 1974. The Problem of Excitability. Plenum Publishing Corp., New York.

Meves, H. 1984. Hodgkin-Huxley: thirty years after. *Curr. Top. Membr. Transp.* 22:279–329.

Nagumo, J., S. Arimoto, and S. Yoshigawa. 1962. An active pulse transmission line simulating nerve axon. *Proc. IRE.* 50:2061–2070.

Scott, A. C. 1975. The electrophysics of a nerve fiber. *Rev. Mod. Phys.* 47:487–533.

Toda, M. 1975. Studies of a non-linear lattice. *Phys. Rep. (Sec. C Phys. Let.).* 18 (No. 1):1–124.