Notes for Electrophysiology

J.M. Colacino

An **electric field** is a place in which a charged particle experiences a force. The **electric field intensity** $\vec{E}$ is the force felt by a unit charge and is obtained by dividing the force $\vec{F}$ exerted on a charge by the charge magnitude q.

$$\vec{E} = \frac{\vec{F}}{q} \quad \text{newtons coulomb}^{-1} \text{ or volts meter}^{-1}$$

This is in direct analogy to a gravitational field of intensity $\vec{g}$ in which a test mass m experiences a force $\vec{F}$.

$$\vec{g} = \frac{\vec{F}}{m} \quad \text{newtons kilogram}^{-1}$$

The **electric work** W_{AB} required to move a charge q from point A to point B is:

$$W_{AB} = -q\int_A^B \vec{E}\,d\vec{l} \quad = -\int_A^B \vec{F}\,d\vec{l} \quad \text{joules}$$

The **electric potential difference** or **voltage** V_{AB} between points A and B is the work required per unit charge to move a charge q from point A to point B:

$$V_{AB} = \frac{W_{AB}}{q} \quad = -\int_A^B \vec{E}\,d\vec{l} \quad = -\int_A^B \frac{\vec{F}}{q}\,d\vec{l} \quad \text{joules coulomb}^{-1} \text{ or volts}$$

We can now see that the work W_{AB} required to move a charge q across a membrane with a **membrane potential** difference V_{AB} is:

$$W_{AB} = -q\int_A^B \vec{E}\,d\vec{l} \quad = -qV_{AB} \quad = -nz\mathrm{F}\,V_{AB} \quad \text{joules,}$$

where n is number of moles, z is ion charge and F is the Faraday (coulombs mole^{-1}).

NOTES ON ELECTRICAL RESISTANCE

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Resistance, R, to current flow through an object is measured by taking the ratio of voltage across the object to the current through it: R = V/I. Resistance is a property of an object and depends on the intrinsic resistance (resistivity) of the material from which it is made and on the object's size and shape. These are related as follows:

$$R = \frac{V}{I} = \frac{El}{jA} = \rho \frac{l}{A}$$

where R is the resistance of the object (ohms), V is the voltage across the object (volts), I is the current through the object (amperes), E is the electric field strength (volts per unit length), j is the current density (amperes per unit area), ρ is the resistivity of the material (ohm cm), l is length in the direction of current flow and A is the area through which the current flows.

Resistivity is a property of a material and does not depend on size or shape. It is determined by measuring the current flow, I, through a 1 x 1 x 1 cm cube of the material when a voltage, V, is applied to opposite faces of the cube. The resistance, R, of such a cube is numerically equal to the resistivity, ρ, because l and A both have the numerical value of 1.0. The unit of resistivity (usually called volume resistivity) is the ohm cm. Look at the equation above to make sense of the unit.

The simple equation above can be used to calculate the resistance of any object whose cross-sectional area in the direction of current flow is constant (e.g. rectangular parallelopipeds, right circular cylinders etc.). For more complicated objects in which the cross-sectional area changes (e.g. spheres, tetrahedrons etc.), advanced mathematics must be employed.

Volume resistivities for several materials are listed below:

Lipid bilayer	3.3×10^{16} ohm cm
Squid axon membrane	1.3×10^{9}
Squid axon axoplasm	60
Sea water	20.5
Deionized water	1×10^{7}
Glass	9×10^{13}
Copper	1.7×10^{-6}
Aluminum	2.8×10^{-6}

We will be interested in current flow, and hence resistance, in nerve cell membranes, axoplasm and external (extracellular) fluid. Resistance to current flow in the extracellular fluid is usually so low in comparison to resistance in the other regions that it is neglected (set equal to zero) in computations.

The axoplasm resistance of an axon of constant radius, r, and length, l, is: $R = \rho \frac{l}{\pi r^2}$.

The longitudinal resistance of a unit length, r_i, of axoplasm is: $r_i = \frac{R}{l} = \frac{\rho}{\pi r^2}$.

r_i is constant if ρ and r are constant. ($\rho = 60$ ohm cm for axoplasm.)

In an axon membrane of thickness d and resistivity, ρ, resistance is given by: $R = \rho \frac{d}{2\pi r l}$.

($\rho = 1.3 \times 10^9$ ohm cm for axon membrane.)

The specific resistance of a unit area of membrane, R_m, is: $R_m = \rho d = 2\pi r l R$.

This form is useful for comparing different membranes.

The specific resistance of a unit length of axon membrane, r_m, is : $r_m = Rl = \frac{\rho d}{2\pi r} = \frac{R_m}{2\pi r}$.

The values r_m and r_i are important in the electrical behavior of nerve cells in time (time constant) and space (space constant).

(These notes are an expanded and modified version of similar notes originally prepared by Dr. A.P. Wheeler.)

NOTES ON CAPACITANCE

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The capacitance, C, of an object is a measure of its ability to store charge and is equal to the ratio of charge on either "side" of the object to the voltage across the object, C = Q/V. Capacitance is a property of an object and depends on the intrinsic capacity (permittivity) of the material from which it is made and on the object's size and shape. These are related as follows:

$$C = \frac{Q}{V} = \frac{\sigma A}{El} = \varepsilon \frac{A}{l}$$

where C is the capacitance of the object (farads or coulombs^2/joule), Q is the charge (coulombs), V is the voltage across the object (volts), E is the electric field strength (volts per meter), σ is the charge density (coulombs/meter^2), ε is the permittivity of the material (coulombs^2/(Newton meter^2)), l is length (meters) in the direction of potential difference and A is the area (meters^2) of the charged region. The equation can be used to calculate the capacitance of cell and axon membranes.

Permittivity is a property of a material and does not depend on size or shape. Biologists and chemists are more used to seeing this property expressed as the dielectric constant K. The dielectric constant for a material is the dimensionless ratio of the permittivity of the material to the permittivity of a vacuum: K = $\varepsilon/\varepsilon_o$. ($\varepsilon_o = 8.85 \times 10^{-12}$ coulombs^2/(Newton meter^2))
The dielectric constant of lipids ranges from 2 to about 10. The dielectric constant of water is 80 at 20C. (This is what makes water a good solvent.) The cell membrane has parts with a high K (polar head groups) and low K (hydrophobic interior).

Physiologists use C_m , the capacitance per unit area as their basic quantity, rather than K or ε , because it can be measured directly and avoids the requirement of measuring the membrane thickness. C_m = C/A (= ε/l) is remarkably constant in cell and nerve membranes at about 1 uF/cm^2. With radius and length explicit, C_m = C/A = C/(2π r l).

One other form, c_m , the capacitance per unit length of axon, is very useful in computations of time constants and conduction velocity. c_m = C/l = 2π r C_m.

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Notes on Equilibrium and Diffusion Potentials

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Ions are under the influence of two forces, electrical and chemical, which tend to push them in one direction or the other across cell membranes.

The chemical "push" arises from concentration differences across the membrane and can be expressed as a chemical potential difference, $RT \ln (X_o / X_i)$, where Xo and Xi are the outside and inside concentrations, respectively, ln is the natural logarithm, R is the universal gas constant and T is the Kelvin temperature. The chemical potential difference has the units of energy per mole and is the amount of work necessary to carry one mole of ions across the membrane against the concentration gradient.

The electrical "push" arises from separation of charge across the membrane and is given by the electrical potential difference, V, across the membrane. The potential difference has the units of energy per unit charge and is the amount of work necessary to carry one coulomb of ions across the membrane against the potential difference. Multiplying V by z, the ion charge, and F, the Faraday, gives zFV, which has the same units, energy per mole, as the chemical potential.

Nernst reckoned that for an ion to be in equilibrium, the chemical and electrical work would have to be equal in amplitude and opposite in direction. Thus, $zFV = RT \ln (X_o / X_i)$. Solving for V gives the Nernst equation: $V_x = (RT/zF) \ln (X_o / X_i)$. V is usually subscripted to indicate the ion in question. The Nernst equation computes the equilibrium electrical potential for a single ion; the electrical potential necessary to exactly offset the chemical potential for that ion. Because there is no net ion flux, no energy is required to maintain this potential.

When more than one kind of permeable ion is present, each with a different equilibrium potential, there is no single membrane potential that can simultaneously satisfy all of them and so they cannot all be in equilibrium. There is a net force on unbalanced ions which results in a net movement of those ions from one side of the membrane to the other. A net movement of any ion implies a continuing charge separation and a changing membrane potential. Yet we know that under such conditions the membrane potential can be constant, and if that is so there can be no continuing separation of charge.

The paradox is easily resolved: net movement of ions in one direction can be balanced by net movement of other ions of the same charge in the opposite direction, or by net movement of other ions of the opposite charge in the same direction. This condition can be formalized as $\sum I_j = 0$, where the I_j's are the individual ion currents. Each ion current can be computed from the membrane potential (Vm), the equilibrium potential, and the ion permeability, Px. Adding the currents together, setting the result equal to zero, and solving the resulting equation for Vm gives the Goldman, Hodgkin, Katz (GHK) equation:

$$V_m = (RT/F) \ln \frac{P_K K_o + P_{Na} Na_o + P_{Cl} Cl_i}{P_K K_i + P_{Na} Na_i + P_{Cl} Cl_o}$$

Vm is the potential that keeps the sum of the individual ion currents equal to zero. Individual net ion currents persist, however, and the membrane potential, a diffusion potential, will eventually run down as concentration gradients disappear. Under normal conditions, ion pumps maintain the concentration gradients and, thus, energy is required to maintain this potential.

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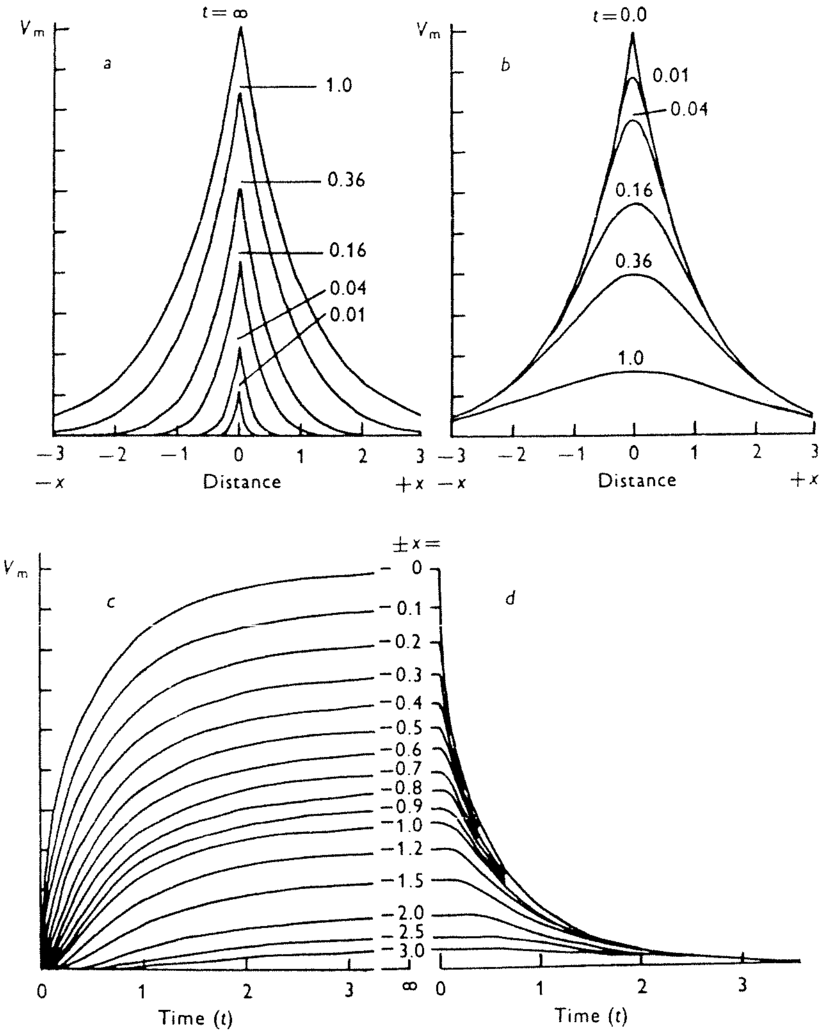

Fig. 4.13. Theoretical distribution of potential difference across a passive nerve membrane in response to onset (*a* and *c*) and cessation (*b* and *d*) of a constant current applied at the point $x = 0$. *a* and *b* show the spatial distribution of potential difference at different times, and *c* and *d* show the time courses of the potential change at different distances along the axon. Time (t) is expressed in units equal to the time constant, τ, and distance (x) is expressed in units equal to the space constant, λ. (From Hodgkin and Rushton, 1946, by permission of the Royal Society.)

REPRESENTATIVE EQUATIONS:

a & b - $V_x = V_0 e^{-x/\lambda}$

c - $Q_t = Q_\infty (1 - e^{-t/\tau})$

d - $Q_t = Q_0 e^{-t/\tau}$

WHERE:

$\lambda = \sqrt{\frac{r_m}{r_o + r_i}}$

$\tau = r_m C_m$

r_m = transverse memb. resistance

r_o = long. res. ext. medium

r_i = long. res. axoplasm

C_m = transverse capacitance

Problems in electrophysiology
2006

1. A nerve cell has the following (fictitious) ion distribution and permeabilities:

	Inside	Outside	Permeability
K^+	350 mM	20 mM	$P_K = 8 \times 10^{-6}$ cm/sec
Na^+	50	400	$P_{Na} = 8 \times 10^{-8}$
Cl	100	560	$P_{Cl} = 4 \times 10^{-6}$

a. Compute the membrane potential.
b. Which ion(s) are in electrochemical equilibrium?

($R = 8.314$ J mol^{-1} K^{-1}, $T = 20°C$, $F = 96500$ coulombs/mol)

2. It is often stated that the numbers of positive and negative ions on either side of a resting nerve or muscle membrane are "approximately" equal. It is interesting and important to know what is meant by "approximately".

Assume that you have a cylindrical axon of 1 mm diameter (negligible wall thickness) with an inside $[K^+] = 400$ mM, an outside $[K^+] = 20$ mM, and a specific membrane capacitance $C = 1 \times 10^{-6}$ farads/cm^2.

a. Find the membrane potential. Assume that the membrane potential is due solely to K^+, the membrane being impermeable to all other ions.

b. Find the number of moles of K^+ that must move across 1 cm^2 of the membrane to set up this potential. (Use the formula for the charge on a parallel plate capacitor. Modify the equation so that the charge is in moles rather than coulombs.)

c. In order to see whether the amount of K^+ that moves is large or small, it must be compared to the amount that was present before the charge separation. You have made the calculation in part (b.) on the basis of 1 cm^2 of membrane. Find the number of moles of K^+ enclosed by 1 cm^2 of membrane, assuming that the inside concentration is 400 mM.

d. What percent of the K^+ ions had to move to set up the potential? Is "approximately" a reasonable term to use?

e. The squid axon is so large that it is not representative of most nerve cells. A more typical neuron might have a spherical cell body with a diameter of 50 um. What percent of the K^+ ions would have to move to set up the membrane potential in this case? (Assume that the inside and outside potassium concentrations and the specific membrane capacitance are the same as above.)