PASSIVE MEMBRANE POTENTIALS

A GENERALIZATION OF THE THEORY OF ELECTROTONUS

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ABSTRACT The theory of electrotonus, which has been well developed for small cylinders, is extended: the fundamental potential equations for a membrane of arbitrary shape are derived, and solutions are found for cylindrical and spherical geometries. If two purely conductive media are separated by a resistance-capacitance membrane, then Laplace's equation describes the potential in either medium, and two boundary equations relate the transmembrane potential to applied currents and to currents flowing into the membrane from each medium. The core conductor model, on which most previous work on cylindrical electrotonus has been based, gives rise to a one dimensional diffusion equation, the *cable* equation, for the transmembrane potential in a small cylinder. Under the assumptions of the core conductor model the more general equations developed here are shown to reduce to the cable equation. The two theories agree well in predicting the transmembrane potential in a small cylinder owing to an applied current step, and the extracellular potential for this cylinder is estimated numerically from the general theory. A detailed proof is given for the isopotentiality of a spherical soma membrane.

INTRODUCTION

Electrotonus, the spread of potential along a passive neural membrane, is of fundamental importance in neurophysiology. It mediates spatial and temporal summation of the postsynaptic potentials which trigger active membrane processes, and it generates electrical events which can be measured by macroelectrodes in large neural populations. Extracellular fields arising from these potentials may affect the behavior of cells located within the fields (Nelson, 1966).

The mathematical theory of electrotonus traces its origin to the late nineteenth century (Hermann, 1879). Since then, the transient and steady-state characteristics of cylindrical membrane potentials have been well explored (see Rall, 1959 *a*, for history). Results of these investigations have proved of value in understanding and evaluating the electrical response of the cell membrane to intracellular current injections, and have provided insight into the effect of dendritic synapses on soma potentials and spike initiation (Davis and Lorente de Nó, 1947; Rall, 1959 through 1967; Ito and Oshima, 1965; Lux and Pollen, 1966). These studies are based upon the core conductor model for potential in a small cylinder, which gives rise to a one dimensional "cable" equation, closely related to the diffusion equation, for the transmembrane potential. The core conductor model requires strong assumptions on the off-membrane distribution. The model has been extended to describe extracellular potentials (Lorente de Nó, 1947; Rall, 1962), but Rall notes the difficulty implicit in computing these potentials from a theory in which the extracellular distribution is prescribed. Clark and Plonsey (1966), in a study of the core conductor model, conclude that it is adequate for approximating intracellular distributions, but inaccurate for extracellular derivations.

Weinberg (1941) has derived a formal solution for extracellular electrotonic potentials *in the steady state* based on Weber's theory of stationary currents in cylinders (Weber, 1873), which is considerably more general than the core conductor model. Weinberg also developed a Green's function analysis for the steady-state distribution of off-membrane electrotonic potential given the potential and normal current on one side of a membrane of arbitrary shape (Weinberg, 1942). Recently interest has focused on more general integral kernels which produce the off-membrane distributions given arbitrary membrane shape and electrical characteristics, but for which all transmembrane currents or potentials must usually be specified (Plonsey, 1964, 1965; Geselowitz, 1967). Barnard et al. (1967) have introduced time dependence into these formulations.

The theory presented here retains the generality of Weber's approach, and extends it to include time-dependent potentials. The specific boundary conditions applicable to a resistance-capacitance membrane are invoked, and as a result only stimulating or active driving currents need be specified. We obtain a set of equations describing the distribution of extracellular, intracellular, and transmembrane potential for a membrane of arbitrary shape. We solve these equations for the special cases of a cylinder and of a sphere, in each case driving the cell with a step current introduced over a small patch of membrane. We show how these fundamental equations may be reduced to the cable equation for the transmembrane potential of a small cylinder, and also provide details for the proof of soma isopotentiality.

Derivation of the Fundamental Equations of Electrotonus

Assumptions. 1. *The membrane.* We assume that the passive nerve membrane may be characterized electrically as a distributed capacitance, C (capacity/unit area), with a shunting resistance, R (resistance × unit area). Such a resistance-capacitance (RC) model is not complete, but other processes involved are of second order, and have time constants quite different from that of the RC processes considered here (Ito and Oshima, 1965). The validity of the RC assumption may be weakened by the presence of synaptic endfeet which densely cover the somadendritic membrane of many classes of nerve cells, and are separated from the membrane by a gap of some 0.02 μ. However, there is evidence from squid ganglia that the transmembrane current flows through this cleft into the extracellular fluid with little resistive or capacitive flow into the presynaptic fiber, at least over a frequency range characteristic of neural potentials (Hagiwara and Tasaki, 1958). Synaptic endfeet in the central nervous system are small, about 1 μ or less in diameter (Eccles, 1964). If we examine an area of membrane that contains many such knobs, we would therefore expect only the apparent resistivity of the membrane to be affected, and the assumption of an *RC* membrane may still have approximate validity.

2. *The media.* We assume that the intracellular and extracellular media are homogeneous, isotropic, and purely conducting; i.e., the electrical behavior of each medium is entirely characterized by its conductivity, σ, which is a real scalar constant. (*a*) Reactance: We neglect the reactive component of the conductivity in the media. In mammalian cerebral cortex, for example, the phase angle is only 4° at 1 kHZ (Van Harreveld, 1966). Since the membrane time constant for pyramidal cells in the cortex is 8.4 msec (Lux and Pollen, 1966), the capacitive effects of the medium over times characteristic of the decay of membrane potentials will be assumed small. There are electrical membrane events with higher frequency components, such as the rising phase of the potential during active spiking, and for accurate analysis of such components the reactive impedance of the media may have to be included. Even for such rapid events, however, this assumption has frequently (Lorente de Nó, 1947; Rosenthal et al., 1966; Clark and Plonsey, 1966) although not always been made (Hendrix, 1965). (*b*) Homogeneity: The effect of the membranes of neighboring cells on the *conductivity* is neglected. The extracellular space in the cortex is considerable, about 20% of total volume (van Harreveld, 1966). Moreover, since the presynaptic fibers are much smaller (about 0.1 μ in diameter—Eccles, 1964) than their endfeet, we may expect the volume immediately behind the synaptic feet to contain a relatively high proportion of extracellular space. Most of the extracellular current flow will take place near the membrane since the membrane is generally convex outward; hence it will not meet with much interference from neighboring membranes. We therefore assume that currents flow only in *homogeneous* regions of pure conductivity. This brings up the interesting point that in the analyses below, the appropriate extracellular resistivity is probably closer to that of cerebrospinal fluid (about 50 ohm-cm) than to that of a volume of CNS tissue (about 300 ohm-cm).

ANALYSIS

Consider an *RC* membrane forming a closed surface that separates an interior region, *i*, from an exterior region, *e* (quantities with subscripts *i*, *e* or *m*, refer to the interior region, the exterior region, and the membrane surface, respectively). The surface membrane is shown schematically in Fig. 1.

Let *V* be the potential due to charges which have distributed themselves as a result of electrotonic currents; i.e., let us *exclude* from *V* the stimulating potentials due to electrodes or to active membrane processes (we include them later as known

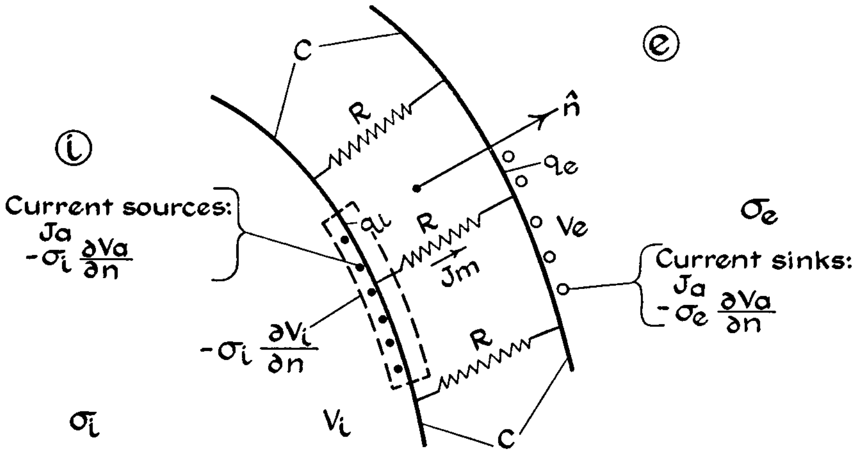

FIGURE 1 Membrane model for the fundamental electrotonic equations. The external medium (e), characterized by a conductivity, σ_e, is separated from the internal medium (i), of conductivity, σ_i, by a membrane with a distributed resistance × unit area, R, and capacitance/unit area, C. $\hat{n}$ is the unit normal to the membrane directed into the external medium. The surface charge density, q_i, on the inner membrane surface builds up as a result of currents from the internal medium, $-\sigma_i \partial V_i/\partial n$, currents due to applied potentials, $-\sigma_i \partial V_a/\partial n$, and applied current sources, J_a. This charge density is depleted by the transmembrane current density, J_m, which builds up the charge density on the external surface, q_e; q_e is in turn depleted by currents into the external medium, $-\sigma_e \partial V_e/\partial n$ (not shown), currents due to applied potentials, $-\sigma_e \partial V_a/\partial n$, and applied current sinks, J_a.

driving functions). We note that this step is the mathematical equivalent of using a bridge to balance out the stimulating potential when driving a cell membrane with stimulating current from the same electrode that is used to measure the resulting potential. If there is no membrane present, the potential in the medium is entirely that used to drive the current, and the use of a bridge or our mathematical exclusion causes V, the measured response to the stimulation, to be zero.

We begin by proving that Laplace's equation holds in both media. The potential everywhere obeys the Poisson equation (Barnard et al., 1967)[1]:

$$\nabla^2 V = -\rho/\epsilon_0 \tag{1}$$

where ρ (charge per unit volume) is the charge density, and where assumption 2 a allows us to use ϵ_0, the permitivity of free space. The current density, $\vec{J}$ (charge/(area × time)), is related to the potential in each medium by

$$\vec{J} = -\sigma \nabla V. \tag{2}$$

The charge and current everywhere obey the equation of continuity

$$\nabla \cdot \vec{J} + \frac{\partial \rho}{\partial t} = 0 \tag{3}$$

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[1] MKS units are used throughout, unless otherwise specified.

In the internal and external media, the relaxation time for charge concentration, ϵ_0/σ (Abraham and Becker, 1950), is less than 10^{-11} sec, so no charge density will be able to build up. Hence anywhere in the internal and external media Laplace's equation is obeyed.

$$\nabla^2 V = 0. \tag{4}$$

We cannot ignore the charge density on the membrane itself, however, and we must return to the Poisson equation (1) to determine the boundary conditions imposed by the membrane (Agin, 1967). Let q_i be the charge density (charge/unit area) on the inner surface of the membrane, and let q_e be the charge density on the outer surface. Let J_m be the transmembrane current density, flowing from the inner to the outer surface of the membrane, and let $\hat{n}$ be the unit normal to the membrane, directed into the exterior medium. We introduce stimulating currents and potentials: J_a, the applied current density, may be due to a local current generator, such as an active membrane event; V_a, the applied voltage, may be due to a potential generator, such as a stimulating electrode. V_a produces a current density $-\sigma_i \partial V_a/\partial n$ and $-\sigma_e \partial V_a/\partial n$, normal to the inner and outer membrane surfaces, respectively.

Laplace's equation for V is still obeyed in the media, since the applied potential is excluded from V. However, the applied potential, V_a, or the applied current density, J_a, results in the collection of charge densities, q_i and q_e, on the membrane. Hence, if we surround the inner surface of the membrane with a gaussian surface (dotted line in Fig. 1), integrate equation 3 over this surface (assuming the stimulating currents result from charges created within the gaussian surface), and choose a region sufficiently small that the charge and potential are constant over the region, we have

$$\frac{\partial q_i}{\partial t} = -\sigma_i \frac{\partial V_i}{\partial n} - J_m + J_a - \sigma_i \frac{\partial V_a}{\partial n}. \tag{5}$$

Similarly, we may show that at the outer surface,

$$\frac{\partial q_e}{\partial t} = +\sigma_e \frac{\partial V_e}{\partial n} + J_m - J_a + \sigma_e \frac{\partial V_a}{\partial n}. \tag{6}$$

If we integrate over a gaussian surface containing both inner and outer membrane surfaces, we obtain from Gauss's law

$$\frac{\partial V_e}{\partial n} - \frac{\partial V_i}{\partial n} = -\frac{q_e + q_i}{\epsilon_0} \tag{7}$$

since J_a and V_a are not generated by the membrane charge density.

If we differentiate equation 7 with respect to time, and eliminate the charge densities with equations 5 and 6, we find

$$\epsilon_0 \frac{\partial}{\partial t}\left(\frac{\partial V_e}{\partial n} - \frac{\partial V_i}{\partial n}\right) = -\sigma_e\left(\frac{\partial V_e}{\partial n} + \frac{\partial V_a}{\partial n}\right) + \sigma_i\left(\frac{\partial V_i}{\partial n} + \frac{\partial V_a}{\partial n}\right). \tag{8}$$

We note as we did with the volume charge density that the relaxation time, ϵ_0/σ, is of the order of 10^{-11} sec, hence the left-hand side of equation 8 is essentially zero over time intervals of interest (msec), which implies that *the normal current density is continuous across the membrane*:

$$\sigma_i\left(\frac{\partial V_i}{\partial n} + \frac{\partial V_a}{\partial n}\right) = \sigma_e\left(\frac{\partial V_e}{\partial n} + \frac{\partial V_a}{\partial n}\right). \tag{9}$$

This result is basic to the core conductor model (Clark and Plonsey, 1966). It does not require that the net charge density on the membrane be zero. Indeed, if the internal and external conductivities are unequal, then in the absence of stimulating current the continuity of normal current (equation 9) together with equation 7 require the existence of a small charge density.

If we subtract equation 5 from 6, we have

$$\frac{\partial}{\partial t}(q_e - q_i) = 2J_m + \sigma_e\left(\frac{\partial V_e}{\partial n} + \frac{\partial V_a}{\partial n}\right) + \sigma_i\left(\frac{\partial V_i}{\partial n} + \frac{\partial V_a}{\partial n}\right) - 2J_a. \tag{10}$$

But the membrane charge and current may be related through the equations of potential for an *RC* membrane (see Fig. 1)

$$J_m = -\frac{V_e - V_i}{R} \tag{11}$$

and

$$\frac{q_e - q_i}{2} = C(V_e - V_i). \tag{12}$$

Hence, they may be eliminated from equation 10. We define the membrane time constant, $\tau \equiv RC$, and using equation 9, we get:

$$R\left(\sigma_i\left(\frac{\partial V_i}{\partial n} + \frac{\partial V_a}{\partial n}\right) - J_a\right) = \tau\frac{\partial}{\partial t}(V_e - V_i) + (V_e - V_i) \tag{13}$$

$$R\left(\sigma_e\left(\frac{\partial V_e}{\partial n} + \frac{\partial V_a}{\partial n}\right) - J_a\right) = \tau\frac{\partial}{\partial t}(V_e - V_i) + (V_e - V_i) \tag{14}$$

which with Laplace's equation:

$$\nabla^2 V_i = 0 \tag{15}$$

$$\nabla^2 V_e = 0 \tag{16}$$

are the final form of the equations for electrotonic potentials.

These are two partial differential equations (15, 16) coupled to each other by the boundary equations (13, 14). There is a simple interpretation for the boundary equations, which can be seen by dividing both sides of the equation by $-R$:

$$-\sigma_i \frac{\partial V_i}{\partial n} - \sigma_i \frac{\partial V_a}{\partial n} + J_a = C \frac{\partial}{\partial t} (V_i - V_e) + \frac{(V_i - V_e)}{R} \tag{17}$$

$$-\sigma_e \frac{\partial V_e}{\partial n} - \sigma_e \frac{\partial V_a}{\partial n} + J_a = C \frac{\partial}{\partial t} (V_i - V_e) + \frac{(V_i - V_e)}{R}. \tag{18}$$

We recognize the right side of the equation as the potential of a parallel *RC* circuit in response to a driving current, and the left side as a driving current composed of three terms: $-\sigma \partial V / \partial n$, the current due to the electrotonic potential, $-\sigma \partial V_a / \partial n$, the current due to the applied potential, and J_a, the applied current.

Reduction to Cable Equation

The derivation of the electrotonic cable equation for a small *RC* cylinder is based upon a model introduced by Hermann (1879), the core conductor model. Clark and Plonsey (1966) have investigated the assumptions underlying the model, and have shown that a necessary and sufficient condition for the general electrostatic equations (i.e., Laplace's equation) to reduce to those of the core conductor model is that the total internal and total external axial current flowing across any plane normal to the cylinder axis be proportional to the axial voltage gradient at the internal and external membrane surface, respectively. This is essentially a form of Ohm's law, requiring that the total current, internal or external, be proportional to the electric field evaluated at the membrane surface, with the proportionality constant acting as the inverse of the resistance per unit length. Consider an infinite cylinder of radius a, centered on the origin, whose axis lies along the z-axis. The core conductor assumptions can now be written:

$$I_i^l = -\frac{1}{r_i} \frac{\partial V_i}{\partial z} \bigg]_{r=a} \tag{19}$$

$$I_e^l = -\frac{1}{r_e} \frac{\partial V_e}{\partial z} \bigg]_{r=a} \tag{20}$$

where I_i^l and I_e^l are the total longitudinal currents in the interior and exterior regions:

$$I_i^l = \int_0^a 2\pi r J_z \, dr, \qquad I_e^l = \int_a^\infty 2\pi r J_z \, dr \tag{21}$$

and r_i and r_e are the corresponding effective resistances per unit length. Since the cable equation is based on the core conductor model, these assumptions are sufficient to reduce the fundamental electrotonic equations (13–16) to the cable equation, as we prove below for the case of no sources.

If we express the current in terms of the potential gradient we may write equation 21 as

$$I_i^l = -2\pi\sigma_i \int_0^a r \frac{\partial V_i}{\partial z} dr \tag{22}$$

$$I_e^l = -2\pi\sigma_e \int_a^\infty r \frac{\partial V_e}{\partial z} dr \tag{23}$$

and differentiating with respect to z yields

$$\frac{\partial I_i^l}{\partial z} = -2\pi\sigma_i \int_0^a r \frac{\partial^2 V_i}{\partial z^2} dr \tag{24}$$

$$\frac{\partial I_e^l}{\partial z} = -2\pi\sigma_e \int_a^\infty r \frac{\partial^2 V_e}{\partial z^2} dr. \tag{25}$$

From Laplace's equation we know that for a cylindrically symmetrical potential

$$\frac{\partial}{\partial r}\left(r \frac{\partial V}{\partial r}\right) = -r \frac{\partial^2 V}{\partial z^2} \tag{26}$$

which implies

$$\frac{\partial I_i^l}{\partial z} = 2\pi\sigma_i \left[r \frac{\partial V_i}{\partial r}\right]_0^a \tag{27}$$

and

$$\frac{\partial I_e^l}{\partial z} = 2\pi\sigma_e \left[r \frac{\partial V_e}{\partial r}\right]_a^\infty. \tag{28}$$

Equation 27 is easily evaluated

$$\frac{\partial I_i^l}{\partial z} = 2\pi\sigma_i \, a \left.\frac{\partial V_i}{\partial r}\right]_a. \tag{29}$$

The upper limit in the right hand side of equation 28 must be zero, provided that the source is bounded in space. This is because, if we are sufficiently far from this region, any source within it will appear to fall off as a point source, i.e. as $1/r$, or faster. Hence dV/dr will fall off at least as fast as $1/r^2$, and equation 28, evaluated at its upper limit, must be zero. Strictly speaking this does not apply to our cylinder, which we have assumed to be infinite. However, if the cylinder is several miles long its termination will have no detectable effect on the shape of potentials which are nonzero for the order of millimeters, yet the convergence of the integral is still assured and equation 28 becomes

$$\frac{\partial I_e^l}{\partial z} = -2\pi\sigma_e a \frac{\partial V_e}{\partial r}\bigg]_a. \tag{30}$$

Solving equations 19 and 20 for the axial gradient, differentiating with respect to z, and subtracting gives:

$$\left(\frac{\partial^2 V_e}{\partial z^2} - \frac{\partial^2 V_i}{\partial z^2}\right) = 2\pi a\left(r_e \sigma_e \frac{\partial V_e}{\partial r} + r_i \sigma_i \frac{\partial V_i}{\partial r}\right), \quad r = a. \tag{31}$$

From the continuity of transmembrane current (equation 9) we know that if there are no sources

$$\sigma_e \frac{\partial V_e}{\partial n} = \sigma_i \frac{\partial V_i}{\partial n} \tag{32}$$

implying

$$\frac{\partial^2 V_e}{\partial z^2} - \frac{\partial^2 V_i}{\partial z^2} = 2\pi a(r_e + r_i)\sigma_e \frac{\partial V_e}{\partial r}, \quad r = a. \tag{33}$$

Substituting equation 33 for $\sigma_e \partial V_e/\partial r$ in the boundary equation (14) and assuming no sources, gives

$$\left(\frac{R}{2\pi a}\right)\frac{1}{r_e + r_i}\frac{\partial^2(V_e - V_i)}{\partial z^2} = \tau \frac{\partial}{\partial t}(V_e - V_i) + (V_e - V_i), \quad r = a. \tag{34}$$

Since $V_e - V_i$ is the transmembrane potential, and $R/(2\pi a)$ is the membrane resistance of a unit length of cylinder, this equation is the cable equation for electrotonic spread in a small cylinder, in the form presented by Davis and Lorente de Nó (1947).[2]

Solutions for Cylinder

Let us apply the fundamental equations of electrotonus to the potential distribution in a cylinder. If we assume that $V_a = 0$ and that the stimulating current exhibits cylindrical symmetry, these equations may be written:

$$\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial V_i}{\partial r}\right) + \frac{\partial^2 V_i}{\partial z^2} = 0 \tag{35}$$

$$\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial V_e}{\partial r}\right) + \frac{\partial^2 V_e}{\partial z^2} = 0 \tag{36}$$

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[2] To establish this identity, we note that in equation 18 (p. 449) of Davis and Lorente de Nó we must set $i_p = 0$, since there are no sources, and $E = 0$, since the membrane is passive.

$$R\left(\sigma_i\left(\frac{\partial V_i}{\partial r}\right) - J_a\right) = \tau\frac{\partial}{\partial t}(V_e - V_i) + (V_e - V_i) \tag{37}$$

$$R\left(\sigma_e\left(\frac{\partial V_e}{\partial r}\right) - J_a\right) = \tau\frac{\partial}{\partial t}(V_e - V_i) + (V_e - V_i). \tag{38}$$

We solve equations 35, 36 by separation of variables, requiring that the solutions be finite at the center of the cylinder, and zero as r approaches infinity. If, as below, we restrict ourselves to stimulating functions which are even in z, our solutions will be symmetric about the $z = 0$ plane. Any solution of the form

$$A(\eta, t)I_0(\eta r)\cos(\eta z) \tag{39}$$

satisfies equation 35 and these conditions inside the cylinder, and any solution of the form

$$B(\eta, t)K_0(\eta r)\cos(\eta z) \tag{40}$$

satisfies equation 36 and these conditions in the extracellular space, where η is an arbitrary parameter. Since equations 35, 36 and our conditions are homogeneous the sum of two solutions is a solution, so we may write the potential in integral form:

$$V_i = \int_0^\infty A(\eta, t)I_0(\eta r)\cos(\eta z)\,d\eta \tag{41}$$

$$V_e = \int_0^\infty B(\eta, t)K_0(\eta r)\cos(\eta z)\,d\eta. \tag{42}$$

$A(\eta, t)$ and $B(\eta, t)$ are determined by the boundary equations (37, 38). If we define the Fourier cosine transform, $\mathfrak{F}_c$, such that

$$\mathfrak{F}_c\{f(\eta)\} \equiv \int_0^\infty f(\eta)\cos(\eta z)\,d\eta, \tag{43}$$

then

$$V_i = \mathfrak{F}_c\{A(\eta, t)I_0(\eta r)\} \tag{44}$$

$$V_e = \mathfrak{F}_c\{B(\eta, t)K_0(\eta r)\}. \tag{45}$$

Let us cosine transform the boundary equations (37, 38) with the transform

$$\mathfrak{F}_{c'}\{g(z)\} \equiv \int_0^\infty g(z)\cos(\eta z)\,dz. \tag{46}$$

The derivatives in equations 37, 38 may be brought outside the transform integral, so that

$$R\left(\sigma_i \frac{\partial}{\partial r}\left(\mathfrak{F}_{c'}(V_i)\right) - \mathfrak{F}_{c'}(J_a)\right) = \tau \frac{\partial}{\partial t}\left(\mathfrak{F}_{c'}(V_e - V_i)\right) + \mathfrak{F}_{c'}(V_e - V_i) \quad (47)$$

$$R\left(\sigma_e \frac{\partial}{\partial r}\left(\mathfrak{F}_{c'}(V_e)\right) - \mathfrak{F}_{c'}(J_a)\right) = \tau \frac{\partial}{\partial t}\left(\mathfrak{F}_{c'}(V_e - V_i)\right) + \mathfrak{F}_{c'}(V_e - V_i). \quad (48)$$

The cosine transform is self reciprocal (Erdélyi et al., 1954).

$$\mathfrak{F}_{c'}\{\mathfrak{F}_c\{f(\eta)\}\} = \frac{\pi}{2} f(\eta). \quad (49)$$

Substituting equations 44, 45 into 47, 48 therefore reduces to

$$\left.\begin{aligned} R\left(\sigma_i \frac{\partial}{\partial r}\left(A(\eta, t)I_0(\eta r)\right) - \frac{2}{\pi} J_c\right) &= \tau \frac{\partial}{\partial t}\left(B(\eta, t)K_0(\eta r)\right. \\ &\quad \left. - A(\eta, t)I_0(\eta r)\right) + \left(B(\eta, t)K_0(\eta r) - A(\eta, t)I_0(\eta r)\right) \quad (50) \\ R\left(\sigma_e \frac{\partial}{\partial r}\left(B(\eta, t)K_0(\eta r)\right) - \frac{2}{\pi} J_c\right) &= \tau \frac{\partial}{\partial t}\left(B(\eta, t)K_0(\eta r)\right. \\ &\quad \left. - A(\eta, t)I_0(\eta r)\right) + \left(B(\eta, t)K_0(\eta r) - A(\eta, t)I_0(\eta r)\right) \quad (51) \end{aligned}\right\} r = a$$

where we have used

$$J_c \equiv \mathfrak{F}_{c'}\{J_a\}. \quad (52)$$

Let us assume that $J_a = 0$ for $t \leq 0$, and Laplace transform (50, 51) with respect to time. We represent the Laplace transform by a tilde:

$$\tilde{f} \equiv \int_0^{\infty} e^{-st} f(t)\, dt. \quad (53)$$

Then

$$\left.\begin{aligned} R\left(\sigma_i \tilde{A} \frac{\partial}{\partial r}\left(I_0(\eta r)\right) - \frac{2}{\pi} \tilde{J}_c\right) &= (\tau s + 1)\left(\tilde{B} K_0(\eta r) - \tilde{A} I_0(\eta r)\right) \quad (54) \\ R\left(\sigma_e \tilde{B} \frac{\partial}{\partial r}\left(K_0(\eta r)\right) - \frac{2}{\pi} \tilde{J}_c\right) &= (\tau s + 1)\left(\tilde{B} K_0(\eta r) - \tilde{A} I_0(\eta r)\right) \quad (55) \end{aligned}\right\} r = a$$

Taking the derivative with respect to r, and setting $r = a$ as it must be on the membrane where these equations are valid, we are left with two algebraic equations

$$R\left(\sigma_i \eta \tilde{A} I_1(\eta a) - \frac{2}{\pi} \tilde{J}_c\right) = (\tau s + 1)\left(\tilde{B} K_0(\eta a) - \tilde{A} I_0(\eta a)\right) \quad (56)$$

$$R\left(-\sigma_e \eta \tilde{B} K_1(\eta a) - \frac{2}{\pi} \tilde{J}_c\right) = (\tau s + 1)\left(\tilde{B} K_0(\eta a) - \tilde{A} I_0(\eta a)\right) \quad (57)$$

which may be solved for $\tilde{A}$ and $\tilde{B}$

$$\tilde{A} = \frac{2\tilde{J}_c}{\pi} \frac{R\sigma_e K_1(\eta a)}{\tau(\sigma_i I_1(\eta a)K_0(\eta a) + \sigma_e I_0(\eta a)K_1(\eta a))\left(s + \frac{1}{\tau}(1 + (\eta\delta)^2)\right)} \tag{58}$$

$$\tilde{B} = -\frac{2\tilde{J}_c}{\pi} \frac{R\sigma_i I_1(\eta a)}{\tau(\sigma_i I_1(\eta a)K_0(\eta a) + \sigma_e I_0(\eta a)K_1(\eta a))\left(s + \frac{1}{\tau}(1 + (\eta\delta)^2)\right)} \tag{59}$$

where

$$\delta^2 \equiv \frac{1}{\eta} \frac{R\sigma_e\sigma_i I_1(\eta a)K_1(\eta a)}{(\sigma_i I_1(\eta a)K_0(\eta a) + \sigma_e I_0(\eta a)K_1(\eta a))}. \tag{60}$$

If we wish to find the transmembrane potential these expressions may be somewhat simplified. Substituting equations 58 and 59 into the Laplace transforms of equations 41, 42

$$[\tilde{V}_e - \tilde{V}_i]_{r=a} = -\int_0^\infty \frac{2\tilde{J}_c}{\pi} \frac{R\cos(\eta z)}{\tau\left(s + \frac{1}{\tau}(1 + (\eta\delta)^2)\right)}\, d\eta. \tag{61}$$

Let us solve equation 61 for the transmembrane potential in response to a constant current applied across the membrane at $t = 0$ to a thin ring of cylinder at $z = 0$. Such a current supplying positive charge to the inner membrane surface and negative charge to the outer surface at a rate, I, may be represented by the density:

$$J_a = \begin{cases} 0 & t \leq 0, r = a \\ \dfrac{I\delta(z)}{2\pi a} & t > 0, r = a \\ 0 & \text{elsewhere} \end{cases} \tag{62}$$

since

$$\int_{0-\epsilon}^{0+\epsilon} J_a \cdot 2\pi a\, dz = I \quad \text{for all} \quad \epsilon > 0. \tag{63}$$

The Fourier cosine and Laplace transform of this current is

$$\tilde{J}_c = \frac{I}{4\pi a s}. \tag{64}$$

Substituting into equation 61 and inverting the Laplace transform gives

$$[V_e - V_i]_a = -\frac{IR}{2\pi^2 a}\int_0^\infty \frac{\left(1 - \exp\left(-\frac{t}{\tau}(1 + (\eta\delta)^2)\right)\right)\cos(\eta z)}{1 + (\eta\delta)^2}\, d\eta. \tag{65}$$

This is the final form of the transmembrane potential, and the integral may be evaluated numerically. However, the integral may be very closely approximated in closed form. Let us choose the length constant, λ, identified by Rall (1959 *a*):

$$\lambda \equiv \left(\frac{R\sigma_i a}{2}\right)^{1/2}. \tag{66}$$

If we change variables in equation 65

$$\eta \leftarrow \xi \quad \text{where} \quad \xi \equiv \lambda\eta \tag{67}$$

we get

$$[V_e - V_i]_a = -\frac{IR}{2\pi^2 a\lambda}\int_0^\infty \frac{1 - \exp\left(-\frac{t}{\tau}\left(1 + \left(\xi\frac{\delta}{\lambda}\right)^2\right)\right)}{1 + \left(\xi\frac{\delta}{\lambda}\right)^2}\cos\left(\xi\frac{z}{\lambda}\right) d\xi. \tag{68}$$

In terms of ξ

$$\left(\frac{\delta}{\lambda}\right)^2 = \frac{1}{\lambda\xi}\,\frac{R\sigma_e\sigma_i I_1\left(\xi\frac{a}{\lambda}\right)K_1\left(\xi\frac{a}{\lambda}\right)}{\left(\sigma_i I_1\left(\xi\frac{a}{\lambda}\right)K_0\left(\xi\frac{a}{\lambda}\right) + \sigma_e I_0\left(\xi\frac{a}{\lambda}\right)K_1\left(\xi\frac{a}{\lambda}\right)\right)}. \tag{69}$$

If the internal and external conductivities are equal, this simplifies considerably, since (Abramowitz and Stegun, 1964)

$$I_1(x)K_0(x) + I_0(x)K_1(x) = \frac{1}{x} \tag{70}$$

which implies, noting the definition of λ (equation 66)

$$\left(\frac{\delta}{\lambda}\right)^2 = 2I_1\left(\xi\frac{a}{\lambda}\right)K_1\left(\xi\frac{a}{\lambda}\right). \tag{71}$$

Even if the conductivities are not exactly equal, equation 71 is a very good approximation provided the order of magnitudes of the conductivities are about equal.[8] This is because the argument of the Bessel functions, $\xi a/\lambda$, is much less than unity

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[8] This is true of invertebrate nerve cells (Katz, 1966) and in all probability is true of the mammalian CNS, although no accurate estimates of intracellular resistivities are available.

for values of the integrand which are significantly greater than zero. For example, for a typical dendrite $a = 2.5\ \mu$, $R = 4{,}000$ ohm-cm^2, and $\sigma = 0.02$ mho/cm (i.e. cerebrospinal fluid). Then

$$\lambda = 1 \text{ mm} \quad \text{and} \quad a/\lambda = 2.5 \times 10^{-3}. \tag{72}$$

If $\xi = 30$, the argument $\xi a/\lambda = 0.075 \ll 1$ and the Bessel functions may be approximated (Abramowitz and Stegun, 1964)

$$I_1\left(\xi \frac{a}{\lambda}\right) K_0\left(\xi \frac{a}{\lambda}\right) \simeq -\frac{1}{2}\left(\xi \frac{a}{\lambda}\right) \ln\left(\xi \frac{a}{\lambda}\right) < 0.1$$

$$I_0\left(\xi \frac{a}{\lambda}\right) K_1\left(\xi \frac{a}{\lambda}\right) \simeq 1 \Big/ \left(\xi \frac{a}{\lambda}\right) = 13.3 \tag{73}$$

By ignoring the I_1K_0 term in the denominator of equation 69 and using the approximation in equation 73 for I_0K_1, we would expect to introduce an error of about 1% into $(\delta/\lambda)^2$, but at $\xi = 30$ the integrand is very small, down 10^{-3} from its original value, hence the error is negligible. For smaller ξ the integrand is large, but the per cent error drops to zero and the approximation remains very good. If we insert this approximation for the Bessel functions into equation 69, we get equation 71 again, indicating that the errors in setting

$$I_1\left(\xi \frac{a}{\lambda}\right) K_0\left(\xi \frac{a}{\lambda}\right) = 0 \tag{74}$$

and using equation 73 for I_0K_1 tend to cancel, and that for $\sigma_e \simeq \sigma_i$ the approximation is even better than our error analysis suggests.

For $\xi \leq 1$,

$$K_1\left(\xi \frac{a}{\lambda}\right) I_1\left(\xi \frac{a}{\lambda}\right) \simeq \frac{1}{2} \tag{75}$$

implying

$$\left(\frac{\delta}{\lambda}\right)^2 \simeq 1 \tag{76}$$

and we approximate

$$[V_e - V_i]_a = -\frac{IR}{2\pi^2 a\lambda} \int_0^\infty \frac{\left(1 - \exp\left(-\frac{t}{\tau}(1 + \xi^2)\right)\right)}{1 + \xi^2} \cos\left(\xi \frac{z}{\lambda}\right) d\xi. \tag{77}$$

As ξ becomes large, the integrand goes to zero as $1/\xi^2$, hence we may use the substitution in equation 77 over the entire range of integration. How good is *this* approximation? The integral in equation 77 is of the order of magnitude of unity over times and positions of interest (a maximum of $\pi/2$ in the steady state). Now over the range of a significantly nonzero integrand ($t/\tau > 0.001$, $\xi < 10^3$) an upper bound on the magnitude of the integrand error is

$$\left| \frac{1 - \exp\left(-\frac{t}{\tau}(1 + \xi^2)\right)}{1 + \xi^2} - \frac{1 - \exp\left(-\frac{t}{\tau}\left(1 + \xi^2 2K_1\left(\xi\frac{a}{\lambda}\right)I_1\left(\xi\frac{a}{\lambda}\right)\right)\right)}{1 + \xi^2 2K_1\left(\xi\frac{a}{\lambda}\right)I_1\left(\xi\frac{a}{\lambda}\right)} \right| \tag{78}$$

since $\cos(\theta) \leq 1$. We have estimated this error numerically and found it to be less than 2×10^{-5}. At $\xi = 10^2$ the error $\simeq 10^{-6}$, and the error goes to zero as $\xi \rightarrow \infty$. Hence we may approximate an upper bound for the error in the integral from

$$\text{error} \leq \int_0^{100} |\text{upper bound on error}|\, d\xi = 2 \times 10^{-3} \tag{79}$$

Since the integral is of the order of unity over the domain of interest, we are justified in using equation 77 as an approximation to equation 68 for the transmembrane potential. Equation 77 may be evaluated in closed form (Erdélyi et al., 1954)

$$[V_e - V_i]_a = -I\frac{\lambda}{4\pi a^2\sigma_i}\left(\exp(-z/\lambda)\, erfc\left(\frac{z}{2\lambda}\left(\frac{t}{\tau}\right)^{-1/2} - \left(\frac{t}{\tau}\right)^{1/2}\right) - \exp(z/\lambda)\, erfc\left(\frac{z}{2\lambda}\left(\frac{t}{\tau}\right)^{-1/2} + \left(\frac{t}{\tau}\right)^{1/2}\right)\right). \tag{80}$$

This is exactly the result that is predicted by the cable equation for this type of stimulation (Davis and Lorente de Nó, 1947).[4] We can therefore reaffirm that the core conductor model provides an accurate representation for the transmembrane potential distribution.

Extracellular Potential

If we choose J_a according to equation 62, combine with equation 59, substitute into equation 42, and change variables to ξ as above (equation 67), we may represent

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[4] There is one apparent difference in the formulation of Davis and Lorente de Nó (1947); where their formula (34, p. 452) has r_e, the *external* resistance per unit length, ours has $1/(\pi a^2\sigma_i)$, the *internal* resistance per unit length. The difference comes about in the nature of the stimulating current; in the model of Davis and Lorente de Nó, the stimulating current, i_p, is applied *outside* the membrane only, whereas in our model we apply a current, $+i_p$, inside the membrane, and an equal and opposite current, $-i_p$, outside the membrane in the same plane. With this type of stimulation, their equation 9, p. 447, would be modified to $\partial I_i/\partial x = i_m + i_p$, and their net axial current, I, becomes zero. Using these modified equations we must replace r_e in their solution with $-(r_e + r_i)$, and since the internal resistance per unit length is much higher than the effective external resistance per unit length (Rall, 1959 *a*) this is approximately $-r_i$, and their solution (with the source, I_0, at p_2 and the corresponding sink at infinity) is identical to ours.

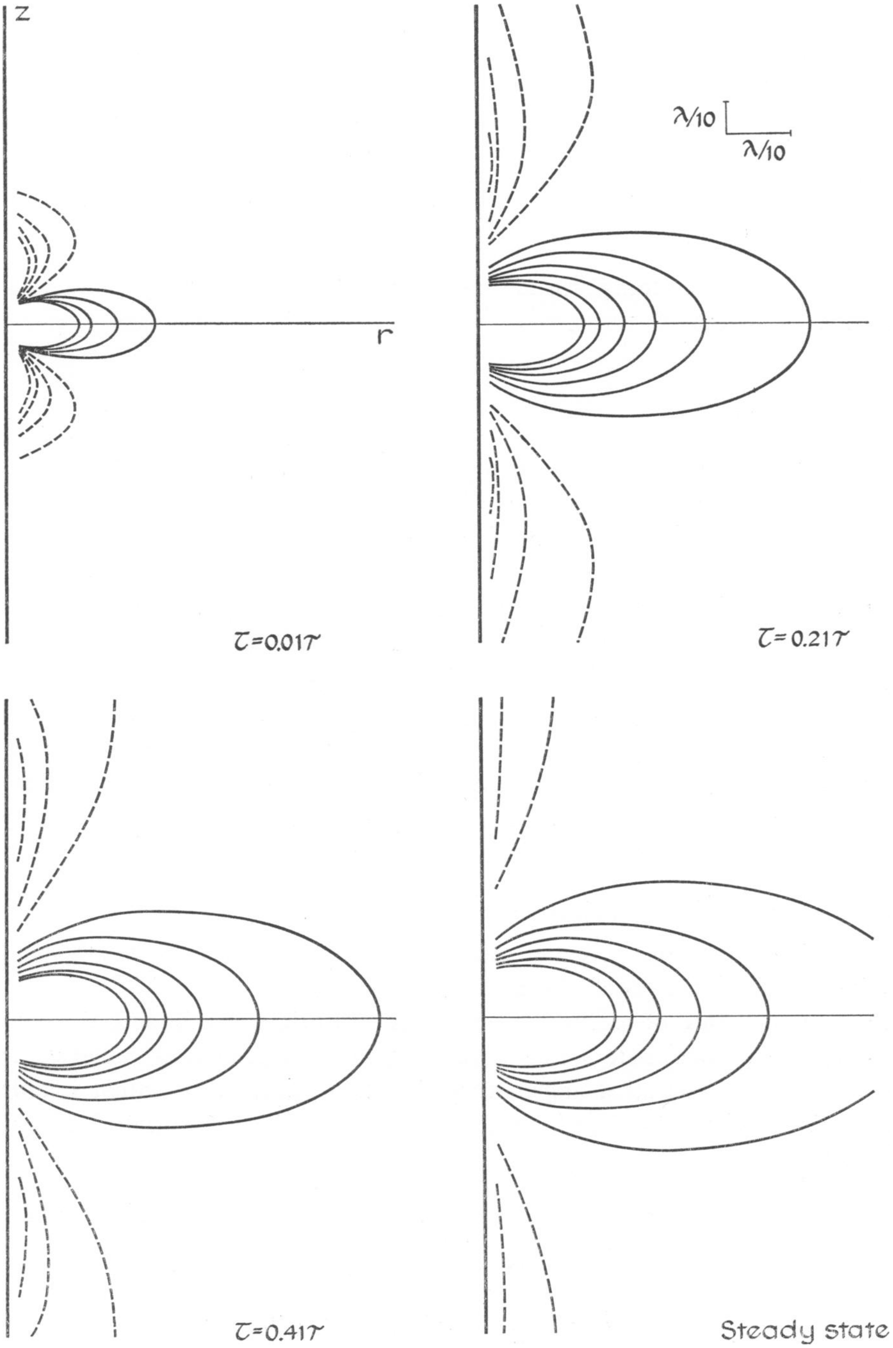

FIGURE 2 The extracellular potential distribution surrounding an infinite cylinder lying parallel to the z axis, of length constant, λ, diameter, 0.005 λ, and membrane time constant, τ. From time $t = 0$ a current of strength I is applied outward across an infinitesimal ring of the cylindrical membrane at $z = 0$. Solid lines represent negative equipotentials; broken lines represent positive equipotentials. Contour interval is 0.04 $I/(\sigma_e\lambda)$ volts. Diameter of the cylinder is drawn to scale.

the extracellular potential

$$\tilde{V}_e = -\int_0^\infty \frac{2}{\pi}\left(\frac{I}{4\pi a s}\right)$$

$$\cdot \frac{R\sigma_i I_1\left(\xi\frac{a}{\lambda}\right) K_0\left(\xi\frac{r}{\lambda}\right)\cos\left(\xi\frac{z}{\lambda}\right)}{\tau\lambda\left(\sigma_i I_1\left(\xi\frac{a}{\lambda}\right)K_0\left(\xi\frac{a}{\lambda}\right) + \sigma_e I_0\left(\xi\frac{a}{\lambda}\right)K_1\left(\xi\frac{a}{\lambda}\right)\right)\left(s + \frac{1}{\tau}\left(1 + \left(\xi\frac{\delta}{\lambda}\right)^2\right)\right)}\, d\xi. \quad (81)$$

Inverting the Laplace transform and assuming that the internal and external conductivities are equal[5]

$$V_e = -\frac{I}{\pi^2 a\sigma_e}\int_0^\infty$$

$$\cdot \frac{\xi I_1\left(\xi\frac{a}{\lambda}\right)K_0\left(\xi\frac{r}{\lambda}\right)\left(1 - \exp\left(-\frac{t}{\tau}\left(1 + \xi^2 2K_1\left(\xi\frac{a}{\lambda}\right)I_1\left(\xi\frac{a}{\lambda}\right)\right)\right)\right)}{1 + \xi^2 2K_1\left(\xi\frac{a}{\lambda}\right)I_1\left(\xi\frac{a}{\lambda}\right)}$$

$$\cdot \cos\left(\xi\frac{z}{\lambda}\right) d\xi. \quad (82)$$

We have approximated this integral numerically, and Fig. 2 shows a plot of the equipotentials at several instants of time following the onset of the stimulating current. We see from the figure that shortly after stimulation, the current sources (as viewed extracellularly) are found close to the sink of stimulating current, but that as time passes and charge from the stimulating sink distributes itself along the cylinder the current sources move down the cylinder.

Isopotentiality of a Spherical Soma

We now investigate the potential distribution across a spherical membrane, and provide details for the proof of soma isopotentiality.

Consider a sphere of radius a, centered on the origin. We choose the conventional spherical coordinate system, with r, θ, and φ representing radial distance, polar angle, and azimuthal angle, respectively. We assume azimuthal symmetry, and require that $\lim_{r\to\infty} V_e = 0$ and that the potential be finite at the origin. Under these assumptions we may solve Laplace's equation (15, 16)

$$V_i = \sum_{n=0}^{\infty} A_n(t) r^n P_n(\cos\theta)$$

$$V_e = \sum_{n=0}^{\infty} B_n(t) r^{-(n+1)} P_n(\cos\theta). \quad (83)$$

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[5] Or, equivalently, as shown above, that over the domain of ξ where the integrand is significantly nonzero $\sigma_i I_1(\xi a/\lambda)K_0(\xi a/\lambda) + \sigma_e I_0(\xi a/\lambda)K_1(\xi a/\lambda) \simeq \sigma_e\lambda/\xi a$.

Since the $P_n(\cos(\theta))$ form a complete set we may expand J_a in terms of them (Courant and Hilbert, 1953)

$$J_a(t, \theta) = \sum_{n=0}^{\infty} J_n(t) P_n(\cos\theta) \tag{84}$$

where J_n is defined:

$$J_n = \frac{2n+1}{2} \int_0^{\pi} J_a(t, \theta) P_n(\cos\theta) \sin\theta \, d\theta. \tag{85}$$

Because the P_n are orthogonal, we may write the boundary equations (13, 14) separately for each value of n:

$$\left.\begin{aligned} R\left(\sigma_i \frac{\partial}{\partial r}(A_n r^n) - J_n\right) &= \tau \frac{\partial}{\partial t}\left(\frac{B_n}{r^{n+1}} - A_n r^n\right) + \left(\frac{B_n}{r^{n+1}} - A_n r^n\right) & (86)\\ R\left(\sigma_e \frac{\partial}{\partial r}\left(\frac{B_n}{r^{n+1}}\right) - J_n\right) &= \tau \frac{\partial}{\partial t}\left(\frac{B_n}{r^{n+1}} - A_n r^n\right) + \left(\frac{B_n}{r^{n+1}} - A_n r^n\right) & (87)\end{aligned}\right\} r = a$$

Taking the radial derivatives, Laplace transforming in time, and evaluating at $r = a$ (i.e., on the boundary)

$$\tilde{A}_n(R\sigma_i n a^{n-1} + a^n(\tau s + 1)) - \tilde{B}_n((\tau s + 1)a^{-n-1}) = RJ_n \tag{88}$$

$$\tilde{A}_n((\tau s + 1)a^n) - \tilde{B}_n(R\sigma_e(n + 1)a^{-n-2} + (\tau s + 1)a^{-n-1}) = R\tilde{J}_n \tag{89}$$

which can be solved algebraically for $\tilde{A}_n$

$$\tilde{A}_n = \frac{\tilde{J}_n R\sigma_e(n + 1)}{a^n \tau(n\sigma_i + (n + 1)\sigma_e)\left(s + \frac{1}{\tau}(1 + \alpha_n)\right)} \tag{90}$$

where α_n is defined

$$\alpha_n \equiv \frac{Rn(n + 1)}{a(n/\sigma_e + (n + 1)/\sigma_i)}. \tag{91}$$

Let us apply a constant current, I, at $t = 0$, across the membrane at $\theta = 0$.

$$J_a = \begin{cases} 0 & t \leq 0, r = a \\ \dfrac{I\delta(\theta)}{\pi a^2 \sin\theta} & t > 0, r = a \\ 0 & \text{elsewhere} \end{cases} \tag{92}$$

so that

$$\int_0^{0+\epsilon} J_a \, 2\pi a \sin(\theta) a \, d\theta = I \text{ for all } \epsilon > 0 \tag{93}$$

using the convention for the delta function

$$\int_0^{0+\epsilon} f(\theta)\delta(\theta)\, d\theta = f(0)/2. \tag{94}$$

From equation 85 and the fact that $P_n(1) = 1$ for $n = 0, 1, 2, 3 \cdots$ we find

$$J_n = \frac{I}{4\pi a^2}(2n + 1) \qquad t > 0, \quad r = a \tag{95}$$

and Laplace transforming

$$\tilde{J}_n = \frac{I}{4\pi a^2}\frac{(2n + 1)}{s}. \tag{96}$$

We combine this stimulation with equations 83 and 90 to find the Laplace transform of the potential inside the sphere

$$\tilde{V}_i = \frac{IR}{4\pi a^2}\sum_{n=0}^{\infty}\frac{(2n + 1)}{s}\left(\frac{r}{a}\right)^n \frac{(n + 1)\sigma_e P_n(\cos\theta)}{(n\sigma_i + (n + 1)\sigma_e)\tau\left(s + \frac{1}{\tau}(1 + \alpha_n)\right)}. \tag{97}$$

Inverting the transform

$$V_i = \frac{IR}{4\pi a^2}\sum_{n=0}^{\infty}(2n + 1)\left(\frac{r}{a}\right)^n \frac{(n + 1)\sigma_e P_n(\cos\theta)\left(1 - \exp\left(-\frac{t}{\tau}(1 + \alpha_n)\right)\right)}{(n\sigma_i + (n + 1)\sigma_e)(1 + \alpha_n)} \tag{98}$$

which is the final form for the potential inside a spherical membrane subject to a transmembrane current step at $\theta = 0$. To get an idea of the relative magnitude of the different terms in the sum, we consider the maximum for each term, which occurs at $\theta = 0$, in the steady state. The ratio of the maximum of the first to the zero order term, V_{i1}/V_{i0}, is

$$\frac{V_{i1}}{V_{i0}} = \frac{3\left(\frac{r}{a}\right)}{(1 + \sigma_i/2\sigma_e)\left(1 + 2R\Big/\left(a\left(\frac{1}{\sigma_e} + \frac{2}{\sigma_i}\right)\right)\right)}. \tag{99}$$

For a typical cortical neuron $a = 2.5 \times 10^{-3}$ cm, σ_i, $\sigma_e \simeq 0.02$ mho/cm, and $R = 4 \times 10^8$ ohm-cm. Hence

$$\frac{2R}{a\left(\frac{1}{\sigma_e} + \frac{2}{\sigma_i}\right)} = 2 \times 10^4 \gg 1 \tag{100}$$

and

$$\frac{V_{i1}}{V_{i0}} \simeq \frac{3r\left(\frac{1}{\sigma_e} + \frac{2}{\sigma_i}\right)}{2R(1 + \sigma_i/2\sigma_e)}. \tag{101}$$

This ratio will be largest on the membrane ($r = a$); if we replace the conductivities with their reciprocals, the resistivities R_e and R_i, and assume that these are approximately equal so that in the denominator $1 + R_e/2R_i$ becomes $\frac{3}{2}$, we get

$$\frac{V_{i1}}{V_{i0}} \simeq \frac{a(R_e + 2R_i)}{R} \tag{102}$$

which is the result that Rall (1959 *b*) has published for the order of magnitude of this ratio. However, equation 101 may be evaluated without this assumption, and on the membrane

$$\frac{V_{i1}}{V_{i0}} \simeq \frac{3a}{R\sigma_i} = \frac{3aR_i}{R}. \tag{103}$$

Plugging in the typical values above we find the ratio of the terms to be about 10^{-4}. Higher order terms are even smaller, and we conclude that all terms besides the zero order term are negligible. Since $P_0(\cos\theta) = 1$ for all θ, the interior potential is

$$V_i = \frac{IR}{4\pi a^2}(1 - \exp(-t/\tau)) \quad \text{for all} \quad \theta \quad \text{and} \quad r \leq a \tag{104}$$

and the cell soma is isopotential. From equation 103 it is clear that provided equation 100 is valid, the isopotentiality of the soma does not depend upon the resistivity of the exterior medium, but rather on the ratio of the interior resistivity and the membrane resistance; this is intuitively satisfying, since regardless of what is going on outside the cell, if the soma is sufficiently well insulated from the outside by a highly resistive membrane and is itself a good conductor, we would expect it to be isopotential.

A similar analysis for the *transmembrane* potential shows it to be isopotential provided equation 100 is valid and

$$\frac{V_{e1} - V_{i1}}{V_{e0} - V_{i0}} = \frac{3}{2}\frac{a(R_e + 2R_i)}{R} \ll 1 \tag{105}$$

which agrees with equation 102 (and with Rall's result) up to a factor of $\frac{3}{2}$. The resulting transmembrane potential is

$$[V_e - V_i]_a = -\frac{IR}{4\pi a^2}(1 - \exp(-t/\tau)) \quad \text{for all} \quad \theta. \tag{106}$$

SUMMARY

The core conductor model has recently been shown to be inadequate for evaluating extracellular potentials generated by passive (electrotonic) membrane processes. We have presented a more general theory to describe electrotonic potentials—the theory is embodied in a set of partial differential equations: Laplace's equation, in the intra- and extracellular media describes the *potential* there as electrostatic, and without sources. The media are coupled at the membrane surface by two boundary equations which relate the *currents* normal to the membrane to the transmembrane potential.

These equations reduce to those of the core conductor model, under the necessary and sufficient conditions for this model described by Clark and Plonsey (Clark and Plonsey, 1966). The generalized equations are solved for a cylinder, and the transmembrane potential is in very good agreement with the results of the core conductor model. The extracellular response to a current step applied across a thin ring of membrane is evaluated numerically (Fig. 2). For the case of a spherical soma, we prove that in an expansion in Legendre polynomials of the potential distribution in response to a current step injected at some point on the membrane, only the zero order term does not vanish; this results in an isopotential soma, whose potential is everywhere equal to the potential drop across any point on the membrane.

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