

Wilfrid Rall

(G.H1)

ABSTRACT A theoretical basis is provided for the estimation of the electrotonic length of a membrane cylinder, or the effective electrotonic length of a whole neuron, from electrophysiological experiments. It depends upon the several time constants present in passive decay of membrane potential from an initially nonuniform distribution over the length. In addition to the well known passive membrane time constant, $\tau_m = R_m C_m$, observed in the decay of a uniform membrane potential, there exist many smaller time constants that govern rapid equalization of membrane potential over the length. These time constants are present also in the transient response to a current step applied across the membrane at one location, such as the neuron soma. Similar time constants are derived when a lumped soma is coupled to one or more cylinders representing one or more dendritic trees. Different time constants are derived when a voltage clamp is applied at one location; the effects of both leaky and short-circuited termination are also derived. All of these time constants are demonstrated as consequences of mathematical boundary value problems. These results not only provide a basis for estimating electrotonic length, $L = l/\lambda$, but also provide a new basis for estimating the steady-state ratio, ρ , of cylinder input conductance to soma membrane conductance.

INTRODUCTION

When membrane depolarization or hyperpolarization is distributed uniformly over the entire surface of a neuron, and the membrane potential is then allowed to decay passively to its resting value, the time course of this decay is the same at every point of the membrane and consists of a single exponential decay having a time constant known as the passive membrane time constant, $\tau_m = R_m C_m$. However, for a nonuniform distribution of membrane polarization over the neuron surface, the time course of passive decay to the resting state is not the same at all points of the membrane. In those regions where the membrane potential has been displaced farthest from the resting value, the rate of decay will be initially more rapid than elsewhere and more rapid than for the case of uniform decay; this is because there is an equalizing

(passive electrotonic) spread from more polarized regions to less (or oppositely) polarized regions of the membrane surface.¹ The different decay transients expected at different membrane locations can all be expressed as different linear combinations of several specific exponential decays (Rall, 1962; also 1964).

The tendency for membrane polarization to equalize over the neuron surface during passive decay is analogous to the tendency for temperature to equalize over an unevenly heated metal surface as it cools. This analogy is helpful to physical intuition; also, the mathematical treatment of these problems is essentially the same. All of the time constants of exponential decay, namely both the passive membrane time constant and the many shorter equalizing time constants, correspond to characteristic roots (eigenvalues) of the mathematical boundary value problem.

Both the statement and solution of several boundary value problems for nerve cylinders of finite length and for a certain class of dendritic neurons were presented several years ago (Rall, 1962). That paper, however, was concerned with a problem more general than passive decay of nonuniform membrane potential; it was concerned also with the effects of nonuniform synaptic membrane conductance. Here, my purpose is to focus attention upon the equalizing time constants, and to point out their importance for an experimental estimation of effective electrotonic length in nerve cylinders and in dendritic neurons.

Application to Motoneurons

Explicit focus upon these theoretical relations is now timely because my suggestions to Drs. P. G. Nelson, H. D. Lux, and R. E. Burke have led them to seek and obtain experimental results specifically intended for such estimation of effective electrotonic length. Their experimental results (Nelson and Lux, 1969; Burke²) are consistent with interpreting the dendritic trees of cat motoneurons as being electrotonically equivalent to membrane cylinders of lengths in the range from about one to about two characteristic lengths. It is both interesting and gratifying that this estimated range of lengths agrees with that I obtained several years ago from entirely different calculations based upon the anatomical measurements of Aitken and Bridger (1961); although the details of these calculations have not been published, the resulting estimates have been explicitly stated (Rall, 1964, p. 83–84). Also, this same range of electrotonic lengths was found to be consistent with the range of synaptic potential shapes (monosynaptic EPSP) found in motoneurons (Burke, 1967; Rall et al. 1967, p. 1180–1181).

The fact that membrane potential transients in dendritic neurons should not be viewed as single exponential decays was recognized (Rall, 1957, 1960) in dealing with the problem of estimating the passive membrane time constant. The fact that a

¹ See, for example, Fig. 4 of Rall, (1960) and Figs. 6 and 7 of Rall (1962).

² Personal communications with R. E. Burke; this forms part of a larger study that has not yet been submitted for publication.

synaptic potential may decay in two stages was demonstrated by Fadiga and Brookhart (1960); they also noted that such two stage decay is observed at the soma when the synaptic input is delivered to the soma, but not when the input is delivered to the dendrites. Time constants for finite dendritic length were provided by (Rall, 1962; see p. 1083 and 1088). Ito and Oshima (1965) found that they could represent certain membrane potential transients as a linear combination of three exponential decays having time constants of about 25, 5, and 1 msec, respectively. With regard to shortest time constant, they discussed the possible role of dendrites, and of the endoplasmic reticulum. Their slowest time constant corresponds to some still incompletely understood slow process that underlies the over- and under-shoots they studied, and possibly also the anomalous rectification studied by Nelson and Frank (1967). Whatever this underlying slow process may be, it is important to emphasize that it cannot be accounted for by the passive membrane potential theory of the present paper. Fortunately, these complications appear to be significant only in some motoneurons, and negligible in others (Nelson and Lux, 1969). Also, different neurons, such as those studied by Tsukahara, Toyama, and Kosaka (1967), appear to be free of complication by this slow process.

With regard to variety in the shapes of miniature monosynaptic EPSPs in motoneurons, the observations of Burke (1967) have been essentially confirmed in several other laboratories (Jack et al., 1967; Mendell and Henneman, 1968; Letbetter et al., 1968; and also personal communications from these groups). Essentially all of this observed variety in EPSP shape has been accounted for theoretically (except for the slow process mentioned in the previous paragraph) by means of computations (Rall, 1967; Rall et al., 1967) which imply the validity of the equalizing time constants to be explained and discussed below.

Definitions of Symbols

- $V_m = V_i - V_e$ membrane potential, as intracellular minus extracellular electric potential.
 $V = V_m - E_r$ deviation of membrane potential from its resting value; electrotonic potential.
 r_i intracellular (core) resistance per unit length of cylinder; (ohm/cm).
 r_e extracellular resistance per unit length of cylinder, if defined; otherwise set equal to zero; (ohm/cm).
 r_m membrane resistance across a unit length of cylindrical membrane; (ohm cm).
 c_m membrane capacity per unit length of cylindrical membrane; (farad/cm).
 $\tau_m = r_m c_m$ passive membrane time constant; (sec).
 $T = t/\tau_m$ time in terms of τ_m ; dimensionless time variable.
 $\lambda = [r_m/(r_i + r_e)]^{1/2}$ characteristic length of nerve cylinder, with r_e usually set equal to zero; (cm).
 $X = x/\lambda$ distance along axis of cylinder in terms of λ ; dimensionless electrotonic distance variable.
 $L = l/\lambda$ length of cylinder in terms of λ ; dimensionless electrotonic length.
 $C_0, C_1, C_2, \dots, C_n$ coefficients (independent of t) used to form a linear combination of exponential decays; (volt).
 $\tau_0 = \tau_m$ passive membrane time constant; (sec).

$\tau_1, \tau_2, \dots, \tau_n$ equalizing time constants, in parts I and II below, where n can be any positive integer; different time constants in part III below; (sec).

α^2 separation constant, for separation of variables.

α_n^2 eigenvalues of boundary value problem.

$\alpha_n = +\sqrt{\alpha_n^2}$ roots in form most used.

B_n constant coefficients in infinite series solutions; sometimes Fourier coefficients; (volt).

I_A current applied outward across membrane at $X = 0$; (amp).

V_A voltage (V) applied at $X = 0$; (volt).

I_S soma membrane current; (amp).

I_C current flowing into cylinder at $X = 0$; (amp).

G_S soma membrane conductance, being steady-state value of I_S/V_A ; (mho).

$G_\infty = [\lambda r_i]^{-1} = \lambda/r_m = [r_i r_m]^{-1/2}$ input conductance of a cylinder of infinite length; (mho)

$G_C = G_\infty \tanh(L)$ input conductance (at $X = 0$) of a cylinder with a sealed end at $X = L$, being steady-state value of I_C/V_A ; (mho)

$\rho = G_C/G_S = \rho_\infty \tanh(L)$ ratio of cylinder input conductance to soma membrane conductance, being steady-state value of I_C/I_S .

$\rho_\infty = G_\infty/G_S$ ratio, ρ , for limiting case when cylinder has infinite length.

$\rho_j = G_{C_j}/G_S$ ratio of cylinder input conductance (for j^{th} of several cylinders) to the membrane conductance of a common soma.

RESULTS

I. General Statement for Users

This section attempts to summarize in usable form the results judged to be of most direct importance to an experimental neurophysiologist. More detailed definitions, derivations and special cases are presented in the later sections of this paper.

The passive decay transients can be expressed as a sum of exponential decays

$$V = C_0 e^{-t/\tau_0} + C_1 e^{-t/\tau_1} + C_2 e^{-t/\tau_2} + \dots + C_n e^{-t/\tau_n} + \dots \quad (1)$$

where $\tau_0 \equiv \tau_m$ represents the passive membrane time constant, and $\tau_1, \tau_2, \dots, \tau_n, \dots$ represent infinitely many equalizing time constants which are smaller than τ_0 . Usually only the first one or two equalizing time constants are important to the interpretation of experimental results. The coefficients, C_n , are constants.³

The values of the equalizing time constants, relative to τ_0 , depend upon the effective electrotonic length of the cylinder or neuron; they do not depend upon a specification of the initial non-uniform distribution of membrane potential from which the passive decay takes place. For a cylinder with both ends sealed and of electrotonic length, $L = \ell/\lambda$, the values of the equalizing time constants are given by the expression

$$\tau_n = \frac{\tau_0}{1 + (n\pi/L)^2} \quad (2)$$

³ These coefficients are independent of t . They generally have different values at each point of observation (i.e. value of x); they are also different for different initial conditions.

This implies, of course, that

$$L = \frac{\pi\tau}{\sqrt{\tau_0/\tau_n - 1}}. \quad (3)$$

Although these equations can be used to calculate the value of L corresponding to any given value of the ratio, τ_0/τ_n , it is helpful to have a few sets of illustrative values; this is provided by Table I.

The relative values of the coefficients, $C_0, C_1, C_2, \dots, C_n, \dots$ depend upon the nonuniform initial condition, upon the effective electrotonic length and, for a dendritic neuron, also upon the dendritic-to-soma conductance ratio, ρ . A completely uniform initial condition would cause all of the coefficients except C_0 to be zero. A nonuniformity that is distributed symmetrically about the mid-point of the cylinder would cause all of the odd numbered coefficients to be zero; in this case, the most important equalizing time constant would be τ_2 . Usually, however, with asymmetric initial nonuniformity, the most important equalizing time constant is τ_1 .

The feasibility of estimating the first one or two equalizing time constants in equation 1 from an observed decay transient depends upon three considerations: (1) C_1 and/or C_2 must not be too small relative to C_0 , this is enhanced by having the initial polarization concentrated near the point of observation, and, for a dendritic neuron, also upon the dendritic-to-soma conductance ratio, ρ , not too small; (2) the effective electrotonic length must not be too long, because this would make successive time constants too close together to permit their resolution; increased length leads, in the limit, to expressions involving error functions as on p. 528 of (Rall, 1960); (3) the effective electrotonic length must not be too short, and the transient must be recorded with sufficiently high fidelity that at least one of the faster decaying components is preserved.

Although the above has all been stated for passive decay to the resting state, the same applies also to the transient approach to a nonresting steady state of passive membrane, such as when a constant current step is applied to one end of a cylinder, or to the soma of a dendritic neuron. It should be emphasized that this holds for

TABLE I
RATIO OF τ_0 TO EQUALIZING TIME CONSTANTS*

Ratio	$L = 1$	$L = \tau/2$	$L = 2$	$L = 3$	$L = 4$
τ_0/τ_1	10.9	5.0	3.5	2.1	1.6
τ_0/τ_2	40.5	17.0	10.9	5.4	4.5
τ_0/τ_3	89.8	37.0	23.2	10.9	6.6
τ_0/τ_4	159.0	65.0	40.5	18.5	10.9

* $\tau_0 = \tau_n = R_m C_m$. Ratios based on equation 16.

constant current, but not for a voltage clamp;⁴ also the membrane must remain passive.

Given the favorable conditions specified above, the procedure is to “peel” the slowest exponential decay from the faster decaying portion of the transient. This procedure, long known to physicists studying multiple radioactive decays, can be carried out quite simply with the help of semilogarithmic plotting; nevertheless, it is sometimes misunderstood and done incorrectly. If we plot $\log V$ vs. t , the result (from equation 1) is a straight line only for values of t sufficiently large that faster decaying terms of equation 1 are negligibly small compared with the first (zero index) term; for such values of t , the transient has a single exponential “tail”; in other words

$$[\text{tail } V] = C_0 e^{-t/\tau_0} \quad (4 a)$$

implying that

$$\log_e [\text{tail } V] = -t/\tau_0 + \text{const.} \quad (4 b)$$

and that

$$\tau_0 = \frac{-0.4343}{\text{slope of } \log_{10} [\text{tail } V]} \quad (4 c)$$

where “slope of” means (d/dt) , or slope with respect to t . In the semilog plot, we can extrapolate the straight line tail back to earlier values of the time; when these extrapolated values are subtracted from the observed values, the resulting difference is the “peeled” transient; in other words

$$[\text{peeled } V] = V - [\text{tail } V] \quad (5 a)$$

$$= V - C_0 e^{-t/\tau_0}. \quad (5 b)$$

When τ_1 and τ_2 are not too close together, and C_1 is not too small, we can find a range of values of t for which all faster decaying terms (corresponding to $n > 1$) are negligibly small compared with the term for $n = 1$; then we can write

$$[\text{peeled } V] = C_1 e^{-t/\tau_1} \quad (6 a)$$

implying that

$$\log_e [\text{peeled } V] = -t/\tau_1 + \text{const.} \quad (6 b)$$

and that

$$\tau_1 = \frac{-0.4343}{\text{slope of } \log_{10} [\text{peeled } V]} \quad (6 c)$$

for this intermediate range of t .

⁴ See part III below for the effect of voltage clamping.

It is important to note that, over this intermediate range of t , it is not the observed V , but "peeled V ," whose log has a constant slope with respect to t . When someone inadvertently fits a straight line to $\log V$ vs. t , for this intermediate range of t , the slope of that straight line is not the same as in equations 6 and will not yield a correct estimate of τ_1 .

From the results above, it can be seen that

$$\tau_0/\tau_1 = \frac{\text{slope of log [peeled } V]}{\text{slope of log [tail } V]}. \quad (7)$$

Also, from equation 3 for a cylinder of finite length, with sealed ends, it can be seen that

$$L = \pi[\tau_0/\tau_1 - 1]^{-1/2}. \quad (8)$$

Thus, when they have been correctly applied to experimental data,⁵ equations 7 and 8 provide an estimate of the electrotonic length of the cylinder most nearly equivalent to the whole neuron in question. Part II below also provides results for a lumped soma coupled to one or more dendritic cylinders; there it is shown to what extent the electrotonic length of the dendrites can differ from the L defined by equation 8. Results for voltage clamping are in part III.

Although it is sometimes possible to peel a sum of exponential decays in several successive steps, it is usually best to use a well tested computer program to obtain the most reliable decomposition of a linear combination of several exponential decays.

II. DERIVATION OF EQUALIZING TIME CONSTANTS

Equalization over Length or Circumference?

Because this paper is concerned with membrane cylinders (and dendritic neurons) whose lengths are much greater than their diameters, it can be shown that equalization of membrane potential over the length is of primary importance. However, it is important to note that additional time constants govern equalization of membrane potential over the circumference of the cylindrical cross section. Expressions for such circumferential equalizing time constants are derived in a companion paper (Rall, 1969). There it is estimated (for typical neuronal values) that circumferential equalization should be around a thousand times more rapid than equalization over the length of the cylinder. This provides a justification for considering only the one spatial variable, X , in the derivation that follows.

⁵ It should be noted that such peeling can be applied also to the slope, dV/dt , because this is a differently weighted sum of the same exponential decays. This is useful in situations where the level but not the direction of the baseline is uncertain. Also, peeling this sum of exponentials is aided by the greater weight of the equalizing terms relative to the uniform decay term.

Statement of Boundary Value Problem, for Cylinder with Sealed Ends

The partial differential equation for passive membrane potential distributions in a nerve cylinder is well established; it can be expressed

$$\frac{\partial^2 V}{\partial X^2} = V + \frac{\partial V}{\partial T} \quad (9)$$

for all values of X and T . For a cylinder of finite electrotonic length, L , we restrict consideration of this differential equation to the range $0 \leq X \leq L$. We assume a "sealed end" (Rall, 1959, p. 497) at both ends of this cylinder; this corresponds to the mathematical boundary conditions

$$\frac{\partial V}{\partial X} = 0, \quad \text{at } X = 0, \quad \text{for } T > 0, \quad (10)$$

and

$$\frac{\partial V}{\partial X} = 0, \quad \text{at } X = L, \quad \text{for } T > 0. \quad (11)$$

The initial condition can be expressed

$$V(X, 0) = F(X), \quad \text{for } 0 \leq X \leq L. \quad (12)$$

Taken together, equations 9–12 define a boundary value problem which has a unique mathematical solution obtainable by classical methods (Churchill, 1941; Carslaw and Jaeger, 1959; and Weinberger, 1965).

Equalizing Time Constants, for Cylinder with Sealed Ends

Because of present interest in these time constants, we wish to pay particular attention to the way in which they are determined by the differential equation and the boundary conditions. First, we note that a solution of the partial differential equation 9 can be expressed

$$V(X, T) = (A \sin \alpha X + B \cos \alpha X) e^{-(1+\alpha^2)T} \quad (13)$$

This solution, obtained by the classical method of separation of variables,⁶ represents $V(X, T)$ as the product of two functions, one of which is a function of X only, the other being a function of T only; the constant, α^2 , is known as the separation constant. The fact that this is a solution can be verified by differentiation and substitution in equation 9; it should be noted that equation 9 is satisfied for any arbitrary combination of values for the constants A , B and α .

⁶ See, for example, Chapter IV in Weinberger (1965), or pages 25–27 in Churchill (1941).

In order to apply the boundary conditions (equations 10 and 11), we must consider the partial derivative with respect to X ,

$$\frac{\partial V}{\partial X} = (\alpha A \cos \alpha X - \alpha B \sin \alpha X) e^{-(1+\alpha^2)\tau}.$$

At $X = 0$, $\sin \alpha X = 0$ and $\cos \alpha X = 1$; therefore the boundary condition (equation 10) at $X = 0$ requires that $\alpha A = 0$, and this, in fact, requires that we set $A = 0$; (A could differ from zero only in the special case when $\alpha = 0$; then $\sin \alpha X = 0$, and again $A \sin \alpha X$ vanishes in equation 13). With $A = 0$, the other boundary condition (equation 11) at $X = L$ then requires that

$$\alpha B \sin \alpha L = 0. \quad (14)$$

This condition is satisfied when $\alpha = 0$, and also by every value of α for which αL is equal to some integral multiple of π , because then $\sin \alpha L = 0$. Thus, the infinitely many roots of equation 14 can be expressed

$$\alpha_n = n\pi/L \quad (15)$$

where n is any positive integer,⁷ or zero. It may be noted that the numbers, α_n^2 , correspond to the "eigenvalues" or the "characteristic numbers" of classical boundary value problems.

For $n = 0$, $\alpha = 0$, and it follows that the time dependent part of equation 13 becomes simply

$$e^{-t} \equiv e^{-t/\tau_m} \equiv e^{-t/\tau_0}$$

which represents exponential decay with the passive membrane time constant, $\tau_m = r_m c_m$, which we here identify also as τ_0 .

When n is any positive integer, the corresponding α_n of equation 15 implies that the exponent in equation 13 has the value

$$-[1 + (n\pi/L)^2]t/\tau_0 \equiv -t/\tau_n$$

from which it follows that

$$\tau_0/\tau_n = 1 + (n\pi/L)^2 \quad (16)$$

This result defines the equalizing time constants, τ_n , for n equal to any positive integer. This provides the basis for equations 2 and 3 and the illustrative values of Table I, in part I above.

⁷ For all of these values of n , the functions (equation 13) are linearly independent of each other; negative integer values of n also satisfy equations 14 and 15, but their use in equation 13 would not provide any additional independent eigenfunctions.

Comment on Solution as a Sum of Exponentials

The preceding section has shown that the two boundary conditions (equations 10 and 11) constrain two of the arbitrary constants in equation 13, which defines a class of solutions of the partial differential equation 9. The resulting class of solutions can be expressed

$$V(X, T) = B \cos (\alpha_n X) e^{-(1+\alpha_n^2)T}$$

where B is still an arbitrary constant, and each solution corresponds to a particular value of α_n , as defined by equation 15.

Because equation 9 is linear, any linear combination of these distinct solutions is also a solution. The class of all such linear combinations can be expressed as the following infinite series

$$V(X, T) = \sum_{n=0}^{\infty} B_n \cos (n\pi X/L) e^{-[1+(n\pi/L)^2]T} \quad (17)$$

where the B_n are still arbitrary constants. Only when we impose the constraint provided by the initial condition (equation 12) of the complete boundary value problem, do the coefficients, B_n , become constrained to particular values. These particular values can be defined as the Fourier coefficients,

$$B_0 = (1/L) \int_0^L F(X) dX$$

and, for $n > 0$,

$$B_n = (2/L) \int_0^L F(X) \cos (n\pi X/L) dX.$$

Then equation 17 expresses a unique solution of the boundary value problem originally defined by equations 9–12; see Churchill (1941), or Weinberger (1965). Explicit solutions for particular choices of $F(X)$ will be presented in a separate paper.

This solution obviously represents a sum of exponentials like equation 1 in part I, above. Any particular point of observation corresponds to a particular value of X ; then the coefficients of equation 1 are related to those of equation 17 by the expression

$$C_n = B_n \cos (n\pi X/L).$$

Coupling of Single Cylinder to Lumped Soma

The point, $X = 0$, is taken as the point where a lumped soma membrane is coupled with the origin of the membrane cylinder (Rall, 1959). This cylinder may be thought of as a single cylinder of finite length, with a sealed end at $X = L$; it may also be

thought of as an “equivalent cylinder” representing an entire dendritic tree, or even several dendritic trees which have the same electrotonic length (Rall, 1962, 1964).

The boundary condition at $X = 0$ is more complicated than before. The current flowing outward across the lumped soma membrane can be expressed

$$I_s = G_s(V + \partial V/\partial T)$$

where G_s represents soma membrane conductance. The current flowing into the cylinder at $X = 0$ can be expressed

$$\begin{aligned} I_c &= (1/r_i)[- \partial V/\partial x]_{x=0} \\ &= (1/\lambda r_i)[- \partial V/\partial X]_{x=0}. \end{aligned}$$

If there is a current, I_A , applied outward across the membrane at $X = 0$, continuity requires that

$$I_A = I_s + I_c.$$

Hence, the boundary condition at $X = 0$ can be expressed

$$[\partial V/\partial X]_{x=0} = \lambda r_i[-I_A + G_s(V + \partial V/\partial T)]. \quad (18)$$

The symbol, ρ , has previously (Rall, 1959) been used to represent the ratio of cylinder input conductance to soma membrane conductance; this ratio equals the ratio of the steady-state values of I_c and I_s , above; thus

$$\begin{aligned} \rho &= \frac{(1/\lambda r_i)V_0 \tanh L}{G_s V_0} \\ &= \frac{\tanh L}{\lambda r_i G_s} \end{aligned}$$

where V_0 is the steady-state value at $X = 0$ and

$$V = V_0 \cosh [L - X]/\cosh L$$

is the steady-state solution in the cylinder.

Using the above expression for ρ , and setting $I_A = 0$ in equation 18, we obtain the expression

$$\rho \partial V/\partial X = (V + \partial V/\partial T) \tanh L, \quad \text{at } X = 0 \quad (19)$$

as the boundary condition expressing cylinder-to-soma coupling during passive membrane potential decay.

The mathematical boundary value problem to be solved differs from that defined

by equations 9–12 only in that the previous boundary condition (equation 10) at $X = 0$ is now replaced by equation 19 above. This difference, however, results in a changed set of equalizing time constants and in a solution that involves a generalized Fourier expansion in which special attention is required to obtain correct values of the coefficients.⁸

Equalizing Time Constants for Cylinder with Soma

Because the differential equation is the same as before, we again use a solution of the same general form as equation 13, above, except that we replace the argument, αX , by the argument, $\alpha(L - X)$, to take advantage of the fact that the simpler boundary condition is at $X = L$. Thus, we consider the solution

$$V(X, T) = [A \sin \alpha(L - X) + B \cos \alpha(L - X)]e^{-(1+\alpha^2)\tau}. \quad (20)$$

The boundary condition (equation 11) at $X = L$ requires that $A = 0$, and the boundary condition (equation 19) at $X = 0$ then requires that

$$\rho\alpha B \sin \alpha L = (-\alpha^2 B \cos \alpha L) \tanh L.$$

This requirement is satisfied by $\alpha = 0$, and by values of α which are roots of the transcendental equation

$$\alpha L \cot \alpha L = -\rho L / \tanh L = -C \quad (21)$$

where C is a positive constant; the roots of this equation have been tabulated.⁹ The equalizing time constants can be expressed

$$\tau_n = \frac{\tau_0}{1 + (\alpha_n)^2} \quad (22)$$

where each α_n is a root of equation 21. The consequences of equations 21 and 22 are summarized in Fig. 1, which shows the dependence of τ_0/τ_1 upon L for several different values of ρ . It is apparent that any given value of τ_0/τ_1 corresponds to many possible combinations of values for ρ and L . For example, a value of 6 for the ratio, τ_0/τ_1 , corresponds approximately to $L = 1.1$ for $\rho = 2$, or to $L = 1.25$ for $\rho = 5$, or $L = 1.4$ for $\rho = \infty$; of course, ρ need not be an integer, and many other combinations are possible.

Some intuitive grasp of the possible values of the roots, α_n , can be obtained by considering briefly the limiting cases for ρ very large and ρ very small.

The limiting case, $\rho = \infty$, corresponds to *complete dendritic dominance* (Rall,

⁸ This has been done for several cases, but the results have not yet been submitted for publication.

⁹ See Table II of Appendix IV in Carslaw and Jaeger (1959); note that their α corresponds to αL here.

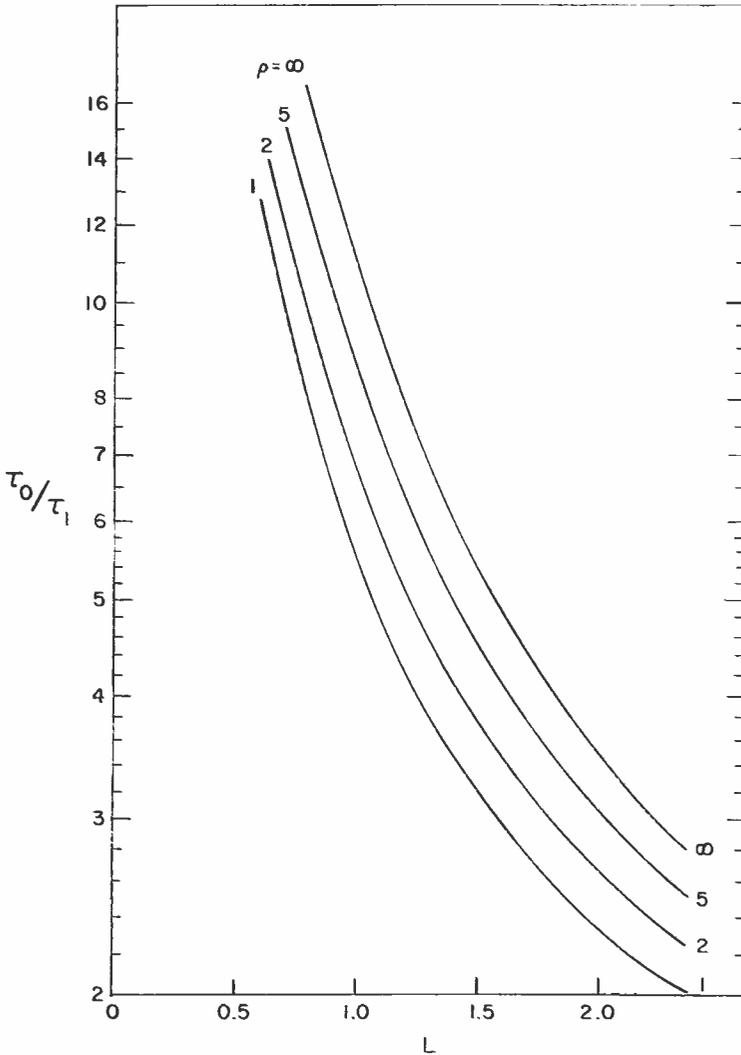


FIGURE 1 Dependence of the time constant ratio, τ_0/τ_1 , upon the value of L , for several values of ρ . Calculations based upon equations 21 and 22.

1959) or to a *vanishing soma admittance* at $X = 0$; it is equivalent to the zero slope boundary condition at $X = 0$, and implies that

$$\alpha_n = n\pi/L \quad (\text{for } \rho = \infty)$$

where n may be zero or any positive integer; (cf. earlier equations 14–16).

The other limiting case, $\rho = 0$, corresponds to *vanishing dendritic admittance*, or to an *infinite soma admittance* at $X = 0$; it is equivalent to a voltage clamp at $X = 0$,

Copyrighted Material

and implies that

$$\alpha_n = (2n - 1)\pi/2L, \quad (\text{for } \rho = 0)$$

where n may be any positive integer; (cf. equations 27 and 29, below).

Illustrative Example For any finite value of ρL , $\alpha_0 = 0$, and $\pi/2 < \alpha_1 L < \pi$. For example, if $L = 1.5$ and $\rho = 4.82$, then $\rho L/\tanh L = 8.0$, and the first nonzero root of the transcendental equation 21 is $\alpha_1 L = 2.80$, or, since $L = 1.5$, $\alpha_1 = 1.87$; it follows that $\tau_0/\tau_1 = 4.5$ for this particular case. This time constant ratio for the cylinder-coupled-to-soma may be compared with two related cases of a cylinder alone, with sealed ends at both $X = 0$ and $X = L$, where equation 16 applies. First consider the cylinder alone with $L = 1.5$; then $\tau_0/\tau_1 = 5.4$ is implied. However, this cylinder alone has an electrotonic length that is less than that of the previous combination of soma with cylinder. Therefore, we consider a longer cylinder, lengthened by the factor, $(\rho + 1)/\rho$, to allow for the soma membrane surface as an extension of the cylinder instead of as a lump; for this length

$$\tau_0/\tau_1 = 1 + \left[\frac{\pi}{L(\rho + 1)/\rho} \right]^2$$

which equals 4.0 in the case of this particular example. It may be noted that the correct τ_0/τ_1 value of 4.5, found above for the soma coupled to the cylinder, lies between the two values 5.4 and 4.0, found for the two different lengths of a cylinder alone just considered.

From the foregoing, it can be seen that when the inverse problem of estimating L from a τ_0/τ_1 value is considered, simple use of equation 8 yields an L value for that cylinder which best approximates the whole neuron or cylinder being studied. If we know at least an approximate value of ρ and wish to estimate the L value for the equivalent *dendritic* cylinder, the value provided by equation 8 would be too large by a factor, f , where $1 < f < (\rho + 1)/\rho$. A reasonable approximation is provided by either $f \simeq (1 + 0.5/\rho)$, or $f \simeq \sqrt{1 + 1/\rho}$. Thus, we can write the approximate expression

$$L \simeq \pi \left[\frac{\rho/(\rho + 1)}{\tau_0/\tau_1 - 1} \right]^{1/2} \quad (23)$$

for an estimate of L (of the equivalent dendritic cylinder) when the values of ρ and τ_0/τ_1 are known. This expression gives results in agreement with Fig. 1.

Several Dendrites Coupled to Single Soma

When the several dendritic trees of a neuron correspond to equivalent cylinders of significantly different electrotonic length, it is not correct to represent them all together as one cylinder. Here we show that it is possible to obtain correct equalizing

time constants even for such more complicated problems. The previous analysis shows that the current flowing into one cylinder could be expressed

$$I_c = \frac{\rho G_s}{\tanh L} \left[-\frac{\partial V}{\partial X} \right]_{x=0}.$$

Now, if we have several cylinders, k in number, and the j^{th} cylinder has a length, L_j , and a cylinder input conductance to soma membrane conductance ratio, ρ_j , the total dendritic input current can be expressed

$$I_D = G_s \sum_{j=1}^k \frac{\rho_j}{\tanh L_j} \left[-\frac{\partial V_j}{\partial X_j} \right]_{x=0}. \quad (24)$$

In each cylinder, there is a solution of the form (equation 20), with $A = 0$ and with α_n required to satisfy the following generalization of equation 21

$$\alpha = -\sum_{j=1}^k \frac{\rho_j \tan \alpha L_j}{\tanh L_j}. \quad (25)$$

Consider, for example, $k = 2$, $L_1 = 1$, with $\rho_1/\tanh L_1 = 3$ and $L_2 = 2$, with $\rho_2/\tanh L_2 = 5$; then the transcendental equation is

$$\alpha = -3 \tan \alpha - 5 \tan 2\alpha.$$

Obviously, $\alpha = 0$ is a root. Seeking, by trial and error, a root between 0 and $\pi/2$, we find $\alpha_1 \simeq 1.10$, because then $\tan \alpha \simeq 1.96$ and $\tan 2\alpha \simeq -1.37$, which values nearly satisfy the above equation. Between $\pi/2$ and π , we find $\alpha_2 \simeq 1.97$, because then $\tan \alpha \simeq -2.37$ and $\tan 2\alpha \simeq 1.03$, which values also nearly satisfy the above equation. Notice, for α_1 and α_2 , $\tan \alpha$ and $\tan 2\alpha$ have opposite signs. However, near π , we find the root, $\alpha_3 \simeq 2.92$, because then $\tan \alpha \simeq -0.22$ and $\tan 2\alpha \simeq -0.47$, which values have the same sign and nearly satisfy the above equation. For $n > 3$, it can be shown that $\alpha_n \simeq n\pi/3$, which is rather interesting because this is the same as equation 15, where the denominator here represents $L_1 + L_2$, the sum of the lengths of the two cylinders. In fact, this simple rule provides first approximations to the smaller roots as well. On reflection, it is obvious that this simple result would hold best when both ρ are large and approximately equal; then the whole neuron can be approximated as an equivalent cylinder of length, $L_1 + L_2$, with the soma located not at $X = 0$ but at a point L_1 from one end.

Although the roots of equation 25 can also be found for any particular case of three or more cylinders coupled to a single soma, little purpose would be served by another illustrative example. It will be clear to anyone who has carefully considered the example above, that the addition of a third cylinder of a different length must increase the number of roots between 0 and π , because of the greater number of possibilities of positive and negative contributions to the summation in equation 25.

III. VOLTAGE CLAMP AND RELATED PROBLEMS

Drastic Effect of Voltage Clamp

When the membrane potential is held to a constant value at one end of the cylinder, or at the point ($X = 0$) of soma-to-cylinder coupling, the boundary value problem becomes very significantly changed: the time constants are changed and should not be called "equalizing" time constants; furthermore these new time constants are independent of ρ ; in fact, after the initial instantaneous charging of the soma to its clamped value, the soma membrane draws a constant current from the voltage clamp, while the transient component of the clamping current flows entirely into the cylinder (cf. Rall, 1960, p. 514–515 and 529–530 for the case of a cylinder of infinite length).

Before demonstrating it mathematically, it can be understood physiologically, that simple passive decay and simple equalizing decay cannot take place when there is a voltage clamp placed across the cell membrane at any point. The voltage clamp has much in common with a short circuit; whereas passive membrane decay requires that the membrane have its normal membrane conductance (also capacitance and EMF) everywhere. A short circuit, or a voltage clamp, must make the decay to a steady state be more rapid than a simple passive decay. Nevertheless, these faster time constants may also be useful for estimation of L by means of equation 33 below.

Time Constants for Voltage Clamp at $X = 0$

The boundary value problem differs from that stated earlier with equations 9–12 in that the previous condition (equation 10) at $X = 0$ is replaced by

$$V(0, T) = V_0. \quad (26)$$

It is simplest to show the effect of voltage clamping upon the time constants by considering first the particular case of $V_0 = 0$. Thus, the boundary condition

$$V(0, T) = 0 \quad (27)$$

requires that the coefficient, B , in the solution (equation 13) be set equal to zero. Then the zero slope boundary condition (equation 11) at $X = L$ requires that

$$\alpha A \cos \alpha L = 0. \quad (28)$$

Although this equation is satisfied by $\alpha = 0$, this root is trivial because it makes $\sin \alpha X = 0$ for all X . However, equation 28 is satisfied by $\alpha L = \pi/2$, and by every value of α for which αL is equal to $\pi/2$ plus $(n - 1)\pi$, because then $\cos \alpha L = 0$. Thus, the infinitely many roots of equation 28 can be expressed

$$\alpha_n = (2n - 1)\pi/2L \quad (29)$$

Copyrighted Material

where n may be any positive integer. In this case, the infinite series solution to the boundary value problem can be expressed

$$V(X, T) = \sum_{n=1}^{\infty} A_n \sin(\alpha_n X) e^{-(1+\alpha_n^2)T} \quad (30)$$

where the α_n are defined by equation 29 and the A_n are the Fourier coefficients defined by

$$A_n = \frac{2}{L} \int_0^L F(X) \sin(\alpha_n X) dX. \quad (31)$$

Here, the time constants implied by equations 29 and 30 are quite different from those considered earlier; here

$$\tau_n = \frac{\tau_m}{1 + (2n - 1)^2(\pi/2L)^2} \quad (32)$$

where n may be any positive integer. We note again that $\alpha_0 = 0$, which would have given a $\tau_0 = \tau_m$, has been excluded because such an α_0 would make $\sin(\alpha_0 X)$ in equation 30 vanish for all X . Thus, even the largest time constant, τ_1 , is smaller than τ_m . For example, if $L = \pi/2$, $\tau_1 = 0.5 \tau_m$ and $\tau_2 = 0.1 \tau_m$; see also Table II.

These time constants are obviously different from the equalizing time constants discussed in parts I and II above. Nevertheless, if both τ_1 and τ_2 can be measured reliably, the following expression, obtained from equation 32 above, permits an estimate of L ,

$$L = (\pi/2)(9\tau_2 - \tau_1)^{1/2}(\tau_1 - \tau_2)^{-1/2}. \quad (33)$$

When the clamped value, V_0 , is different from zero, the time constants are the same, but solution becomes

$$V(X, T) = V_0 \frac{\cosh(L - X)}{\cosh L} + \sum_{n=1}^{\infty} A_n \sin(\alpha_n X) e^{-(1+\alpha_n^2)T}$$

TABLE II
RATIO OF τ_m TO TIME CONSTANTS* UNDER VOLTAGE CLAMP†

Ratio	$L = 1$	$L = \pi/2$	$L = 2$	$L = 3$	$L = 4$
τ_m/τ_1	3.5	2.0	1.6	1.27	1.15
τ_m/τ_2	23.2	10.0	6.5	3.5	2.4
τ_m/τ_3	62.6	26.0	16.4	7.9	4.9
τ_m/τ_4	121.9	50.0	31.2	14.4	8.5

* Ratios based on equation 32. Note that these time constants need not be referred to τ_m ; they can be referred to each other, as in equation 33.

† Voltage clamp applied at one end.

where the A_n are obtained from equation 31 provided that $F(X)$ is replaced by the difference, $F(X) - V_0 \cosh(L - X)/\cosh L$, in equation 31.

At $X = 0$, this transient simply gives $V = V_0$, as it should. However, referring back to equation 18, we can express the voltage clamping current, minus the constant current to the soma, as proportional to $[-\partial V/\partial X]$ at $X = 0$, as follows,

$$[I_A - I_B] \propto \left[V_0 \tanh L - \sum_{n=1}^{\infty} \alpha_n A_n e^{-(1+\alpha_n^2)T} \right] \quad (34)$$

where the A_n are the same as those of the preceding paragraph, and the α_n and the resulting time constants are the same as equations 29, 32, and 33 above.

Special Case of Voltage Clamps at $X = 0$ and $X = L$.

This special case merits brief mention because the time constants turn out to be the same as the equalizing time constants found earlier for the cylinder with both ends sealed, except that here there is no $\tau_0 = \tau_m$. The boundary conditions can be expressed,

$$V(0, T) = V_0, \quad \text{and} \quad V(L, T) = V_L$$

where V_0 and V_L are both constants. The steady-state solution can be expressed

$$V(X, \infty) = [V_0 \sinh(L - X) + V_L \sinh X]/\sinh L. \quad (35)$$

Now, if we consider the function

$$U(X, T) = V(X, T) - V(X, \infty) \quad (36)$$

we obtain a boundary value problem in which the partial differential equation for $U(X, T)$ has the same form as equation 9, and the boundary conditions become simplified to

$$U(0, T) = 0 = U(L, T).$$

When a general solution of the form (equation 13) is subjected to the boundary condition at $X = 0$, we find that $B = 0$, and then the boundary condition at $X = L$ requires that

$$A \sin \alpha L = 0$$

which has the roots

$$\alpha_n = n\pi/L. \quad (37)$$

The solution for $U(X, T)$ can thus be expressed

$$U(X, T) = \sum_{n=1}^{\infty} A_n \sin(n\pi X/L) e^{-[1+(n\pi/L)^2]T}. \quad (38)$$

Although the α_n are the same as in equation 17, equation 38 differs significantly both by being a sine series instead of a cosine series, and by summing from $n = 1$ instead of $n = 0$.

This solution would be of practical value in those axons, dendrites or muscle fibers where it may be possible to voltage clamp at two points and observe the time course of the transient at a location between the two clamped points. This would have the merit of being completely undisturbed by any activity outside the region between the two voltage clamps.

Killed-End at $X = L$

The killed-end boundary condition corresponds to a short circuit between interior and exterior media; this means that $V_m = 0$, at $X = L$, and since $V = V_m - E_r$, we have the boundary condition,

$$V(L, T) = -E_r = V_L$$

which is equivalent to a voltage clamp at $X = L$.

If the boundary condition at $X = 0$ is a voltage clamp, the problem becomes the same as that of the preceding section. However, if the boundary condition at $X = 0$ is a zero slope, then the problem becomes the same as that of equations 26–33 with the ends reversed.¹⁰ These results would be relevant to experiments in which one would apply a voltage clamp to a neuron soma, and measure time constants both before and after severing or killing the dendritic terminals.

For a current clamp at $X = 0$ with cylinder-to-soma coupling, it would be necessary to use a modification of the analysis previously used (equations 18–22). First, we define $G(X)$ as the steady state (equation 35) for $I_A = 0$ and $V = V_r = -E_r$ at $X = L$. Then, for the function

$$W(X, T) = V(X, T) - G(X)$$

we have the boundary conditions

$$W(X, T) = 0 \quad \text{at} \quad X = L$$

¹⁰ Very recently, I learned that Lux (1967), treated the problem of constant current at $X = 0$, with a differently defined short circuit at $X = L$. By using Laplace transform methods, he obtained time constants that agree with those obtained here (equation 32). These same time constants have also been obtained by Jack and Redman (personal communication) using still another method.

and

$$\gamma \partial W / \partial X = (W + \partial W / \partial T) \coth L, \quad \text{at } X = 0.$$

This second boundary condition differs from previous equation 19 because

$$\gamma = \frac{(1/\lambda r_i) W_0 \coth L}{G_s W_0}$$

is a steady-state (conductance) ratio with respect to W , whereas the true ρ would be

$$\rho = \frac{(1/\lambda r_i)(W_0 \coth L - [dG/dX]_0)}{G_s (W_0 + G_0)}$$

where the zero subscript designates values at the point, $X = 0$. When these boundary conditions are applied (cf. equations 20 and 21 above) we set $B = 0$ and find that

$$-\gamma \alpha A \cos \alpha L = (-\alpha^2 A \sin \alpha L) \coth L$$

which can be rewritten as the transcendental equation

$$\alpha L \tan \alpha L = \gamma L \tanh L \quad (39)$$

where $\gamma L \tanh L$ is a positive constant. The roots of this equation have been tabulated by Carslaw and Jaeger (1959, Appendix IV, Table I). The solution for $W(X, T)$ is thus of the form (equation 30), where here each α_n is a root of equation 39.

Case of Leaky End at $X = L$

Instead of a short circuit by an infinite conductance at $X = L$, consider a leaky end having a finite conductance, G_L , between interior and exterior media at $X = L$. At this end, the leakage current must equal the core current

$$G_L V_m = (1/\lambda r_i) [-\partial V_m / \partial X], \quad \text{at } X = L.$$

This can be expressed more simply as the boundary condition

$$\partial V_m / \partial X = -h V_m, \quad \text{at } X = L \quad (40)$$

where $h = G_L \lambda r_i$. Let the other boundary condition be

$$\partial V_m / \partial X = 0, \quad \text{at } X = 0. \quad (41)$$

Then the solution takes the form

$$V_m(X, T) = \sum_{n=1}^{\infty} B_n \cos(\alpha_n X) e^{-(1+\alpha_n^2)T} \quad (42)$$

where the roots, α_n , must satisfy the transcendental equation

$$\alpha L \tan \alpha L = hL \quad (43)$$

where hL is a positive constant. The roots of this equation have been tabulated by Carslaw and Jaeger (1959, Appendix IV, Table I).

If instead of the boundary condition (equation 41), the value of V_m were clamped to zero at $X = 0$, but still satisfied equation 40 at $X = L$, then the solution takes the form (equation 30) where the roots, α_n , must satisfy the transcendental equation

$$\alpha L \cot \alpha L = -hL. \quad (44)$$

These roots have also been tabulated by Carslaw and Jaeger (1959, Appendix IV, Table II).

Effect of Series Resistance with Voltage Clamp

In actual experimental situations, it may be difficult to prevent the presence of a series resistance between the clamped voltage, V_A , and the voltage at $X = 0$. This means that the soma-dendritic system is not truly voltage clamped at $X = 0$. Instead, the apparatus provides an applied current,

$$I_A = G_*(V_A - V), \quad \text{at } X = 0$$

where G_* is the reciprocal of the series resistance,¹¹ V_A is the applied constant voltage, and V is the transient voltage at $X = 0$. Then, previous equation 18 can be used to obtain the boundary condition

$$\partial V / \partial X = \lambda r_i [G_*(V - V_A) + G_s(V + \partial V / \partial T)], \quad \text{at } X = 0$$

for G_* finite. If we take the other boundary condition as $\partial V / \partial X = 0$ at $X = L$, and if we consider the function

$$U(X, T) = V(X, T) - V(X, \infty)$$

then, the boundary value problem for U has the boundary condition

$$\rho \partial U / \partial X = kU + (U + \partial U / \partial T) \tanh L, \quad \text{at } X = 0$$

where $k = (G_*/G_s) \tanh L$ is a positive constant of finite magnitude; this result may be compared with equations 19 and 40. The other boundary condition is $\partial U / \partial X = 0$

¹¹ In this section G_* is finite, and V at $X = 0$ differs from V_A when there is current, I_A , flowing. In the limit, as $G_* \rightarrow \infty$, $V \rightarrow V_A$, and perfect voltage clamping is restored; then the boundary condition of the present section is replaced by one like equation 26, and the transcendental equation 45 is replaced by equation 28, which implies the roots given by equation 29.

at $X = L$. Then, using a solution of the form (equation 20), the boundary conditions require that

$$\rho\alpha B \sin \alpha L = kB \cos \alpha L - \alpha^2 B \cos \alpha L \tanh L$$

which is not satisfied by $\alpha = 0$. In this case, the α_n are roots of the transcendental equation

$$\alpha L \tan \alpha L = [G_*/G_s - \alpha^2](L/\rho) \tanh L \quad (45)$$

which differs from all previous examples. It may be noted that for large G_*/G_s the right hand side is approximately independent of α for small α_n ; then equation 45 can be treated almost like equation 39; as G_*/G_s becomes very large the voltage clamp condition is approached.¹² At the other limit, as $G_* \rightarrow 0$, equation 45 reduces to equation 21. Intermediate cases must be treated individually.

Illustrative Example Suppose that the whole neuron steady state conductance is 6×10^{-7} mho, and that $\rho = 5$; then the soma membrane conductance, $G_s = 10^{-7}$ mho. Suppose also that $L = 1.5$ and $G_* = 2 \times 10^{-5}$ mho. Then the equation for the α becomes

$$\alpha L \tan \alpha L = (200 - \alpha^2)(0.272).$$

Because G_*/G_s is large, we know that $\alpha_1 L$ is close to $\pi/2$; then $\sin \alpha_1 L \simeq 1.0$ and $\cos \alpha_1 L \simeq \pi/2 - \alpha_1 L$. Thus, we have

$$\alpha_1 L \simeq (\pi/2)C/(C + 1)$$

where

$$C = [G_*/G_s - (\pi/2L)^2](L/\rho) \tanh L.$$

In the above example, $C \simeq 54$, giving $\alpha_1 L \simeq 1.54$, $\alpha_1 \simeq 1.03$, and a value of about 2.06 for τ_m/τ_1 .

Experimental values obtained in voltage clamping experiments on cat motoneurons can be found in papers by Frank, Fuortes and Nelson (1959), Araki and Terzuolo (1962), and Nelson and Frank (1963).

DISCUSSION AND CONCLUSIONS

This paper presents solutions to a number of mathematical boundary value problems which characterize transient distributions of membrane potential in passive membrane cylinders and in neurons whose dendritic trees can be represented as equivalent

¹² See footnote 11.

lent cylinders.¹³ These solutions can all be expressed as the sum of a steady state component plus several transient components which decay to zero; together these transient components represent a linear combination of exponential decays. This linear combination is actually an infinite series, whose coefficients (in the simpler cases) are Fourier coefficients determined by the initial condition of the boundary value problem; more complicated cases involve coefficients of generalized Fourier expansions; these will be presented explicitly in a separate publication.

Solutions have been obtained for a variety of boundary conditions. All of the cases in parts I and II of the Results have in common that the membrane is nowhere short-circuited in any way; the ends of the cylinders are either sealed or coupled to a soma; constant current electrodes are also permitted. However, voltage clamping electrodes, and killed-end or leaky-end boundary conditions are excluded from parts I and II, and are dealt with separately in part III.

The essential difference between these two classes of solutions is that uniform passive decay with the passive membrane time constant, τ_m , can occur and usually does occur¹⁴ under the conditions of parts I and II; it cannot occur under the conditions of part III. Also, the time constants, $\tau_1, \tau_2, \tau_3, \dots$ etc. in parts I and II have meaning as equalizing time constants; the time constants in part III are usually quite different,¹⁵ and should be thought of not as equalizing, but as governing the transient approach to the steady state associated with the given voltage clamp or leak.¹⁶

Special attention has been given to explaining how the equalizing time constants arise from the boundary conditions, and how the effective electrotonic length can be estimated from time constant ratios, especially the ratio, τ_0/τ_1 , of the passive membrane time constant, $\tau_0 = \tau_m$, to the first equalizing time constant, τ_1 ; see equations 8 and 23 in parts I and II above. In contrast, for voltage clamp conditions, the effective electrotonic length can be estimated from a different relation; see equation 33 in part III above.

For those cases which include the coupling of a cylinder to a lumped soma membrane, the ratio, ρ , of cylinder input conductance to soma membrane conductance,

¹³ The class of dendritic trees that can be represented as equivalent cylinders has been defined (Rall, 1962) and discussed (Rall, 1964); this class has the property, $dA/dx \propto dZ/dx$, which means that the rate of increase of dendritic surface area, with respect to x , remains proportional to the rate of increase of electrotonic distance, with respect to x . A larger class of dendritic trees has the more general property, $dA/dZ \propto e^{KZ}$, where K is a constant that may be positive or negative (Rall, 1962). Mathematical solutions have been obtained for this larger class, and will be presented in a separate publication in collaboration with Steven Goldstein.

¹⁴ It does not occur when the initial condition does not contain a uniformly distributed component; then $C_0 = 0$, in equation 1.

¹⁵ Compare Table II with Table I. However, for voltage clamping at both ends, see equation 37.

¹⁶ Although it is true that $[V(X, T) - V(X, \infty)]$ decays to zero everywhere in all of these cases, uniform decay is possible only in parts I and II, where the boundary conditions at $X = 0$ and $X = L$ are either $\partial V/\partial X = 0$ or coupling to an intact soma. Uniform decay is not possible in part III, because a point of short-circuit or of voltage clamp imposes nonzero $\partial V/\partial X$ at that point.

effects the value of L (for the cylinder) estimated from a given τ_0/τ_1 value; this is displayed in Fig. 1 above. By using $\rho = \infty$ (which is equivalent to cylinder without soma) we obtain the value of L for that cylinder which best approximates the whole neuron. However, to estimate the value of L for the cylinder which best approximates a dendritic tree as distinct from the soma, it is necessary to have an estimate of ρ , when working with the equalizing time constants and Fig. 1.

In contrast to the above, it is significant that the different time constants obtained with voltage clamping at the soma do not depend upon ρ at all, for ideal clamping, and the effect of ρ is very small even when there is a moderate amount of series resistance in the system; see illustrative example following equation 45 in part III above. This means that the value of L for the cylinder can be estimated without knowing ρ ; this can be done either with τ_1 and τ_2 in equation 33, or by using τ_1 from voltage clamp together with τ_m obtained either with current clamp or unclamped passive decay, and using equation 32 with $n = 1$.

It is noteworthy that using both current clamping and voltage clamping at the soma could thus provide a new method of estimating ρ . Obtain τ_m from current clamp; also obtain τ_1 and, if possible, τ_2 with voltage clamp; these provide an estimate of L for the cylinder (from equations 32 and 33). Now using this L and the equalizing time constants obtained with current clamping, one can estimate ρ from Fig. 1, or from equations 21 and 22.

There are two other electrophysiological methods of estimating ρ . One is based upon sinusoidal stimulation applied to the soma (Rall, 1960; Nelson and Lux, 1969). Because the original theory was based upon the assumption of a cylinder of infinite length, it should be remarked that finite length has less effect upon the steady-state AC input admittance of the cylinder than upon the steady-state DC input conductance of the cylinder.¹⁷ The other method is based upon equations 6 and 12 of (Rall, 1960) for the slope, dV/dt , of the response to an applied current step. This method was used by Lux and Pollen (1966). It also is based upon the assumption of a cylinder of infinite length; however, the early part of the transient should be little changed by finite length. The amount of error can be evaluated by adding to the transient, $V(0, T)$, the transient, $V(2L, T)$. This is because a matched current step applied at $X = 2L$ would result, by symmetry, in making $\partial V/\partial X = 0$ at the point, $X = L$, halfway between the two current sources; this $\partial V/\partial X = 0$ at $X = L$ is equivalent to the sealed-end boundary condition used in the present paper. For longer times, it becomes necessary to consider more terms, corresponding to $X = 4L$, $X = 6L$, etc.;¹⁸ however, these additional terms are not needed for the early portion of the slope.

¹⁷ An explicit solution for sinusoidal steady states in cylinders of finite length (with sealed ends) has been worked out and will be published separately; see also Lux (1967) for a case of finite length with a different terminal boundary condition.

¹⁸ These additional terms are more complicated. They have been derived and computed by Jack and Redman (personal communication), as part of an extensive program of theory, computations and ex-

In conclusion, it can be seen that it is now appropriate to explore various procedures for estimating the most consistent set of the parameters, ρ , L , R_m and $\tau_m = R_m C_m$ which determine the electrical properties of a passive neuron, for particular neurons and neuron types. Such exploration has now begun.¹⁹ At present, it is too early to say which of the several possible combinations of theory and experiment will provide the best simultaneous estimate of the values of these parameters; this will be determined largely by the limitations of experimental precision.

Notes Added in Response to Referee Comments. I thank one referee for drawing my attention to the recent work of Koike, Okada, Oshima, and Takahashi (*Exp. Brain Res.* 1968. 5:173–188 and 189–201. Following Ito and Oshima (1965), the authors have applied a “triple exponential analysis” to pyramidal tract cells of cat’s cerebral cortex.

One referee expressed reservations about assuming the same passive dendritic membrane properties for the soma and the dendrites. This is a simplifying assumption that has been discussed earlier (Rall, 1959, p. 494 and 523–524; Rall, 1960, p. 514–515, 519, and 529). Fortunately, careful experiments with voltage clamping at the soma, compared with current clamping at the soma, can provide a test of this simplifying assumption for each neuron type.

One referee questioned the assumption that the membrane itself should have only one passive membrane time constant; he asks why I did not include another membrane time constant corresponding to the tubular system of muscle fibers; see Ito and Oshima (1965). My approach has been to investigate how much can be accounted for by a consideration of finite dendritic length without the addition of more complicated membrane models. If electron microscopy should reveal similar tubular systems in certain neuron membranes, this question would merit further study in those neurons. In the case of cat motoneurons, the EPSP shape analysis (Rall et al., 1967) supports the notion that the faster time constant depends upon finite length, and that the weight of its contribution to the observed transient depends upon the nonuniformity (over dendritic length) of the membrane depolarization.

I am grateful to Dr. J. Z. Heaton and to Drs. P. G. Nelson and R. E. Burke for helpful comments on an earlier draft of this manuscript.

periments that they and their collaborators have carried out. They have used Laplace transform methods to obtain the terms of their mathematical series; these terms are expressed in terms of parabolic cylinder functions (or, alternatively, in terms of error functions). This mathematical series is quite different from the sums of exponential decays presented here. It is interesting that these different mathematical approaches are not contradictory; they are complementary.

Jack and Redman have recently read a draft of this paper, and I have recently read drafts of two of their unpublished manuscripts. Although we have not yet had the opportunity to make detailed quantitative comparisons, we do find our results to be in substantial agreement. Also, we know that the sums of exponentials converge most poorly for small values of t , while the sums of terms involving error functions converge most poorly for large values of t .

¹⁹ For example, Nelson and Lux (1969), and Burke (earlier footnote 2); also, Jack and Redman (earlier footnote 18) have devised a particular set of procedures for estimating values of these parameters. Furthermore, the parameter, K (see earlier footnote 13), as well as the long time constant of Ito and Oshima (1965) need to be taken into account for some neurons.

REFERENCES

- AITKEN, J. and J. BRIDGER. 1961. *J. Anat.* **95**:38.
- ARAKI, T. and C. A. TERZUOLO. 1962. *J. Neurophysiol.* **25**:772.
- BURKE, R. E. 1967. *J. Neurophysiol.* **30**:1114.
- CARSLAW, H. S. and J. C. JAEGER. 1959. *Conduction of Heat in Solids*. Oxford Press, London. 510.
- CHURCHILL, R. V. 1941. *Fourier Series and Boundary Value Problems*. McGraw-Hill, New York. 206.
- CLARK, J. and R. PLONSEY. 1966. *Biophys. J.* **6**:95.
- FADIGA, E. and J. M. BROOKHART. 1960. *Amer. J. Physiol.* **198**:693.
- FRANK, K., M. G. F. FUORTES, and P. G. NELSON. 1959. *Science*. **130**:38.
- ITO, M. and T. OSHIMA. 1965. *J. Physiol. (London)*. **180**:607.
- JACK, J. J. B., S. MILLER, and R. PORTER. 1967. *J. Physiol. (London)*. **191**:112.
- LETBETTER, W. D., W. D. WILLIS, JR., and W. M. THOMPSON. 1968. *Fed. Proc.* **27**:749.
- LUX, H. D. 1967. *Pflügers Archiv*. **297**:238.
- MENDELL, L. and E. HENNEMAN. 1968. *Fed. Proc.* **27**:452.
- NELSON, P. G. and K. FRANK. 1963. *Actual. Neurophysiol.* **15**:15.
- NELSON, P. G. and K. FRANK. 1967. *J. Neurophysiol.* **30**:1097.
- NELSON, P. G. and H. D. LUX. 1969. *Biophys. J.* In Press.
- RALL, W. 1957. *Science*. **126**:454.
- RALL, W. 1959. *Exp. Neurol.* **1**:491.
- RALL, W. 1960. *Exp. Neurol.* **2**:503.
- RALL, W. 1962. *Ann. N. Y. Acad. Sci.* **96**:1071.
- RALL, W. 1964. In *Neural Theory and Modeling*. R. F. Reiss, editor. Stanford University Press, Stanford, Calif. p. 73-97.
- RALL, W. 1967. *J. Neurophysiol.* **30**:1138.
- RALL, W. 1969. *Biophys. J.* **9**:1509.
- RALL, W., R. E. BURKE, T. G. SMITH, P. G. NELSON, and K. FRANK. 1967. *J. Neurophysiol.* **30**:1169.
- TSUKAHARA, N., K. TOYAMA, and K. KOSAKA. 1967. *Exp. Brain Res.* **4**:18.
- WEINBERGER, H. F. 1965. *Partial differential equations*. Blaisdell, Waltham, Mass. 446.