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LINEAR CABLE THEORY

In the previous chapter, we briefly met some of the key actors of this book. In particular, we introduced the *RC* model of a patch of neuronal membrane and showed an instance where such a “trivial” model accounts reasonably well for the input-output properties of a neuron, as measured at its cell body (Fig. 1.4). However, almost none of the excitatory synapses are made onto the cell body, contacting instead the very extensive dendritic arbor. As we will discuss in detail in Chap. 3 (see Fig. 3.1), dendritic trees can be quite large, containing up to 98% of the entire neuronal surface area. We therefore need to understand the behavior of these extended systems having a cablelike structure (Fig. 2.1).

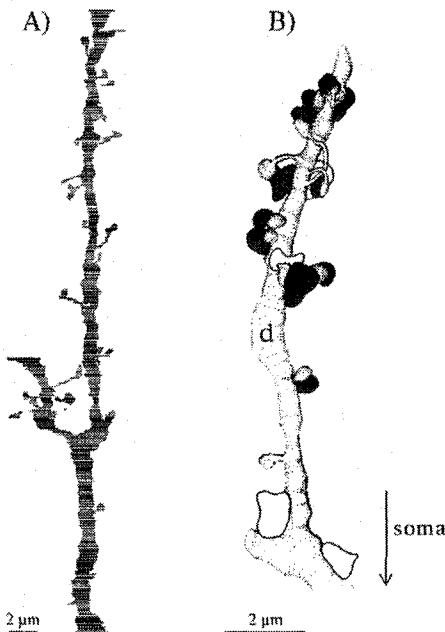


Fig. 2.1 CLOSEUP VIEW OF DENDRITES Two reconstructed dendrites of a spiny stellate cell in the visual cortex of the cat. The reconstructions were carried out by a very laborious serial electron microscopic procedure. Notice the thin elongated, thornlike structures, *dendritic spines*. The vast majority of neuronal processes, whether axons or dendrites, possess such an elongated, cylindrical geometry. Studying the spread of electrical current in these structures is the subject of cable theory. (A) Cross section of a branching dendrite. (B) Three-dimensional view of another dendrite. The black blobs are excitatory synapses and the three clear blobs are inhibitory synapses. Reprinted by permission from Anderson et al. (1994).

The basic equation governing the dynamics of the membrane potential in thin and elongated neuronal processes, such as axons or dendrites, is the *cable equation*. It originated in the middle of the last century in the context of calculations carried out by Lord Kelvin, who described the spread of potential along the submarine telegraph cable linking Great Britain and America. Around the turn of the century, Herman and others formulated the concept of *Kernleitermodel*, or core conductor model, to understand the flow of current in nerve axons. Such a core conductor can be visualized as a thin membrane or sheath surrounding a cylindrical and electrically conducting core of constant cross section placed in a solution of electrolytes (see Fig. 2.2).

The study of the partial differential equations describing the evolution of the electrical potential in these structures gave rise to a body of theoretical knowledge termed *cable theory*. In the 1930s and 1940s concepts from cable theory were being applied to axonal fibers, in particular to the giant axon of the squid (Hodgkin and Rushton, 1946; Davis and Lorente de No, 1947).¹ The application of cable theory to passive, spatially extended dendrites started in the late 1950s and blossomed in the 1960s and 1970s, primarily due to the work of Rall (1989). In an appropriate gesture acknowledging his role in the genesis of quantitative modeling of single neurons, Segev, Rinzel, and Shepherd (1995) edited an annotated collection of his papers, to which we refer the interested reader. It also contains personal recollections from many of Rall's colleagues as well as historical accounts of the early history of this field.

We restrict ourselves in this chapter to studying *linear cable theory*, involving neuronal processes that only contain voltage-independent components. In particular, we assume that the membrane can be adequately described by resistances and capacitances (*passive membrane*). Given the widespread existence of dendritic nonlinearities, it could be argued that studying neurons under such constraints will fail to reveal their true nature. However, it is also true that one cannot run before one can walk, and one cannot walk before one can crawl. In order to understand the subtlety of massive synaptic input in spatially extended passive and active cables, one first needs to study the concepts and limitations of linear cable theory before advancing to nonlinear phenomena.

Cable theory, whether linear or nonlinear, is based on a number of assumptions concerning the nature and geometry of neuronal tissue. Let us discuss these assumptions prior to studying the behavior of the membrane potential in a single, unbranched, passive cable.

2.1 Basic Assumptions Underlying One-Dimensional Cable Theory

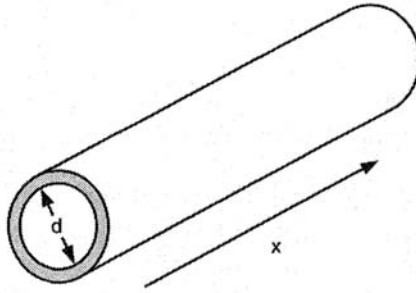
In a standard copper wire, electrons drift along the gradient of the electrical potential. In axons or dendrites the charge carriers are not electrons but, in the main, one of two ionic species, sodium and potassium, and, to a lesser extent, calcium and chloride. How can this current be quantified?

1. Starting point for any complete description of electrical currents and fields must be Maxwell's equations governing the dynamics of the electric field $\mathbf{E}(x, y, z, t)$ and the magnetic field $\mathbf{B}(x, y, z, t)$,² supplemented by the principle of conservation of charge

1. For a detailed account of all the twists and turns of this story, see Cole (1972) and Hodgkin (1976). When reading these down-to-earth monographs, one becomes painfully aware of the very limited amount of real knowledge and insight gained during decades of intensive experimental and theoretical research. Most of one's effort is usually spent on pursuing details that turn out to be irrelevant and in constructing and developing incorrect models.

2. We follow standard convention in using holdface variables for all vector quantities.

A)



B)

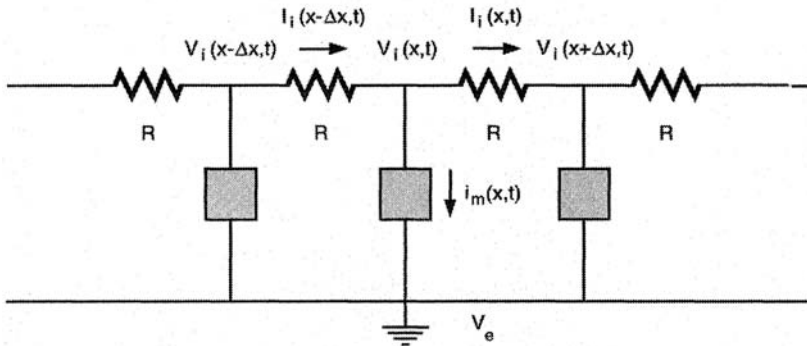


Fig. 2.2 ELECTRICAL STRUCTURE OF A CABLE (A) Idealized cylindrical axon or dendrite at the heart of one-dimensional cable theory. Almost all of the current inside the cylinder is longitudinal due to geometrical (the radius is much smaller than the length of the cable) and electrical factors (the membrane covering the axon or dendrite possesses a very high resistivity compared to the intracellular cytoplasm). As a consequence, the radial and angular components of the current can be neglected, and the problem of determining the potential in these structures can be reduced from three spatial dimensions to a single one. On the basis of the bidomain approximation, gradients in the extracellular potentials are neglected and the cable problem is expressed in terms of the transmembrane potential $V_m(x, t) = V_i(x, t) - V_e$. (B) Equivalent electrical structure of an arbitrary neuronal process. The intracellular cytoplasm is modeled by the purely ohmic resistance R . This tacitly assumes that movement of carriers is exclusively due to drift along the voltage gradient and not to diffusion. Here and in the following the extracellular resistance is assumed to be negligible and V_e is set to zero. The current per unit length across the membrane, whether it is passive or contains voltage-dependent elements, is described by i_m and the system is characterized by the second-order differential equation, Eq. 2.5.

(Feynman, Leighton, and Sands, 1964). As detailed in Rosenfalck's thesis (1969), the magnetic vector potential associated with the movement of charges during an action potential in biological tissues only has a negligible effect (10^{-9}) on the electric field and can therefore safely be neglected. Indeed, it took the technological development of very sensitive quantum devices (SQUIDS) to be able to measure the magnetic field associated with massive electrical activity in the brain. So the first simplification involves neglecting the magnetic field.

2. This leaves us with three fundamental relationships governing electrodynamics in neuronal structures.
 - a. Gauss's law, stating that the divergence of the field \mathbf{E} is identical to the charge density normalized by the electrical permittivity ϵ . Equivalently, Poisson's equation, which links the Laplacian of the electrical potential to the negative charge density normalized by ϵ , serves as well.
 - b. Charge conservation, that is, the sum of the flux of current through any closed surface and the change of the charge over time inside this surface must be zero.
 - c. An equation linking the electrical current to the electric field. In general, charged carriers can move either by drift along an electric field or by diffusion, from a volume of high carrier concentration into one of lower concentration, and the total current flow is the sum of these two independent components. The mathematical expression of this fact constitutes the Nernst-Planck electrodiffusion equation, treated in Sec. 11.3. As discussed there, for almost all cases of interest the changes in concentration of the various ions (Na^+ , K^+ , Ca^{2+} and Cl^-) are too small to measurably contribute to current flow. Only in very thin fibers of less than $1\text{ }\mu\text{m}$ diameter does longitudinal current flow due to concentration differences begin to play any role. In other words, Ohm's law is perfectly adequate to describe the electrical current moving within an axon or dendrite.³
3. This is the starting point for most derivations of cable theory (Lorente de N6, 1947; Clark and Plonsey, 1966, 1968; Plonsey, 1969; Rall, 1969b; Eisenberg and Johnson, 1970).
 - a. The dominant fraction of current inside a neuronal process, such as a dendrite or axon, flows parallel to its longitudinal axis. Only a very small fraction of the current flows across the neuronal membrane. This is true both for geometrical reasons—the diameter of axons and dendrites being much smaller than their longitudinal extent—as well as for electrical ones. As detailed in Appendix A, the neuronal membrane is all but impermeable to current flow. Charged carriers can only cross the membrane through the ionic channels. **The high transmembrane resistivity stands in contrast to the relatively small intracellular resistivity.**

A major implication is that instead of having to solve for the voltage in three dimensions, our problem is reduced to one of describing the voltage along a single spatial dimension. In a careful comparison between the membrane potential derived as the solution of Laplace's equation in a three-dimensional cylindrical coordinate system and the solution of the one-dimensional cable equation, **Rall (1969b) showed that the radial and angular membrane potential terms typically decay 10^4 times faster than the components of the membrane potential along the axis.** Fortuitously, we can safely neglect two out of three dimensions for all of the cases considered in this book.
 - b. Electrical charge in the cytoplasm, no matter whether inside or outside the cell, relaxes in a matter of microseconds or less. In other words, **any capacitive effects of the cytoplasm itself can be totally ignored** on the millisecond or longer time scale (inductive effects can be completely neglected; Scott, 1971). Thus, from an electrical point of view, the extracellular as well as the intracellular cytoplasm can be approximated by ohmic resistances.

3. This is analogous to the situation prevalent in a copper wire, where the current flow due to drift down the gradient of the electrical potential exceeds by many orders of magnitude the current flow due to differences in the local densities of electrons.

- c. The solution of the equation for the electrical potential is still extremely complicated if all the neuronal structures and membranes outside the dendrite or axon under investigation are explicitly included. Fortunately for modelers (but less so for the electrophysiologist, who has to infer the neuronal activity of a cell from its extracellular signature), the extracellular potential (1) usually is small (since the small amount of current making it through the membrane encounters a relatively large extracellular volume), and (2) decays over distances which are usually much larger than the diameters of the fiber itself. **This implies that the extracellular space can be treated as a homogeneous dielectric, averaging over local inhomogeneities.** The problem of computing the membrane potential is therefore reduced to two homogeneous domains, the extracellular and the intracellular ones.

The extracellular resistivity is often defined in the case when the external medium is a shell of conducting cytoplasm surrounding the cable, a shell that can be characterized by a resistance per unit length of cylinder r_e . For large external volumes (think of the case of a single neuronal fiber placed in a bath solution) r_e is assumed to be zero. **In this case, no extracellular voltage gradients exist and the entire extracellular space is isopotential, $V_e(x, t) = \text{const}$, which we set to zero.** Including a uniform extracellular resistivity complicates matters only slightly, and the solution of the cable equation is qualitatively similar to the solution for $r_e = 0$. Therefore, the *membrane potential* $V_m(x, t)$, defined as the intracellular potential minus the extracellular potential (Eq. 1.1), is identical to the intracellular potential. Indeed, throughout the book, we use these two variables interchangeably. Yet it should always be kept in mind that the membrane potential corresponds to the difference in voltage across the membrane separating the inside from the outside.

A timely research topic of considerable interest is a detailed investigation of electrical coupling of realistically modeled neurons via the extracellular potential. Lengthy experimental and theoretical studies have been carried out for the case of two parallel axons. For this geometry, any direct electrical coupling is slight (the extracellular potential due to a spike is in the $10 \mu\text{V}$ range; Clark and Plonsey, 1968, 1971; Marks and Loeb, 1976; Scott and Luzader, 1979; Barr and Plonsey, 1992; Bose and Jones, 1995; Struijk, 1997). However, extracellular potentials recorded close to dendritic trees can be much larger (up to a few mV) than those next to axons. Given the extremely tight packing among neurons, this type of ephaptic⁴ coupling could be of functional relevance, yet almost no theoretical work has been carried out on this subject (Lorente de Nó, 1953; Hubbard, Llinás and Quastel, 1969; Holt, 1998).

At this stage, we represent the neuronal tissue with the help of a series of discrete electrical circuits of the type shown in Fig. 2.2B. Without making any specific assumption concerning the detailed nature of the neuronal membrane, we express the current per unit length flowing through the membrane at location x as $i_m(x, t)$. We can write down Ohm's law for the discrete circuit illustrated in Fig. 2.2B,

$$V_i(x, t) - V_i(x + \Delta x, t) = R I_i(x, t) \quad (2.1)$$

or, in the limit of an infinitesimal small interval Δx , and with $V_m = V_i$,

$$\frac{\partial V_m}{\partial x}(x, t) = -r_a \cdot I_i(x, t), \quad (2.2)$$

4. Greek for "touching onto," rather than *synaptic*, "touching together."

where $r_a = R/\Delta x$ is the intracellular resistance per unit length of cable with dimensions of ohms per centimeter. I_i is the intracellular core current flowing along the cable, assumed to be positive when flowing toward the right, in the direction of increasing values of x . Kirchhoff's law of current conservation stipulates that the sum of all currents flowing into and out of any particular node must equal zero. Applied to the node at x in Fig. 2.2B, we have

$$i_m(x, t)\Delta x + I_i(x, t) - I_i(x - \Delta x, t) = 0 \quad (2.3)$$

or, in differential form in the limit that $\Delta x \rightarrow 0$,

$$i_m(x, t) = -\frac{\partial I_i}{\partial x}(x, t). \quad (2.4)$$

Inserting the spatial derivative of Eq. 2.2 into Eq. 2.4 leads to

$$\frac{1}{r_a} \frac{\partial^2 V_m}{\partial x^2}(x, t) = i_m(x, t). \quad (2.5)$$

This second-order ordinary differential equation, together with appropriate boundary conditions, describes the membrane potential in an extended one-dimensional cable structure with an ohmic intracellular cytoplasm, regardless of the exact nature of the neuronal membrane.

2.1.1 Linear Cable Equation

In Sec. 1.1, we discussed the nature of a patch of passive membrane and assumed that the membrane current includes a capacitive (Eq. 1.3) and a resistive (Eq. 1.4) component (Figs. 1.1 and 1.2). Including an external current term $I_{inj}(x, t)$, the membrane current per unit length of the cable, i_m , is given by

$$i_m(x, t) = \frac{V_m(x, t) - V_{rest}}{r_m} + c_m \frac{\partial V_m(x, t)}{\partial t} - I_{inj}(x, t), \quad (2.6)$$

where r_m is the membrane resistance of a unit length of fiber, measured in units of ohms-centimeter. If the electrical nature of the membrane is constant along the length of the passive fiber under investigation (Fig. 2.3), we can replace $i_m(x, t)$ on the right-hand side of Eq. 2.5 with Eq. 2.6 and multiply both sides with r_m to arrive at

$$\lambda^2 \frac{\partial^2 V_m(x, t)}{\partial x^2} = \tau_m \frac{\partial V_m(x, t)}{\partial t} + (V_m(x, t) - V_{rest}) - r_m I_{inj}(x, t), \quad (2.7)$$

with the membrane time constant $\tau_m = r_m c_m$ and the *steady-state space constant* $\lambda = (r_m/r_a)^{1/2}$. We will discuss their significance forthwith.

Equation 2.7 is the *linear cable equation*, a partial differential equation, first order in time and second order in space. This type of parabolic differential equation is quite similar to the heat and diffusion equations. The behavior of all three is characterized by dissipation and the absence of any wavelike solution with constant velocity. Parabolic differential equations have a well-specified and unique solution if appropriate initial conditions, such as the voltage throughout the cable at $t = 0$ should be zero, or boundary conditions, such as no current should leak out at either end of the cable, are specified. The cable equation is fundamental to understanding the behavior of the membrane potential, the principal state variable used for rapid intracellular communication in neurons. We will discuss its behavior in both this chapter and the next.

As expressed in Eq. 2.7, a simple, unbranched cable has a nonzero resting potential V_{rest} which does not vary with the position along the cable. For a homogeneous cable in the

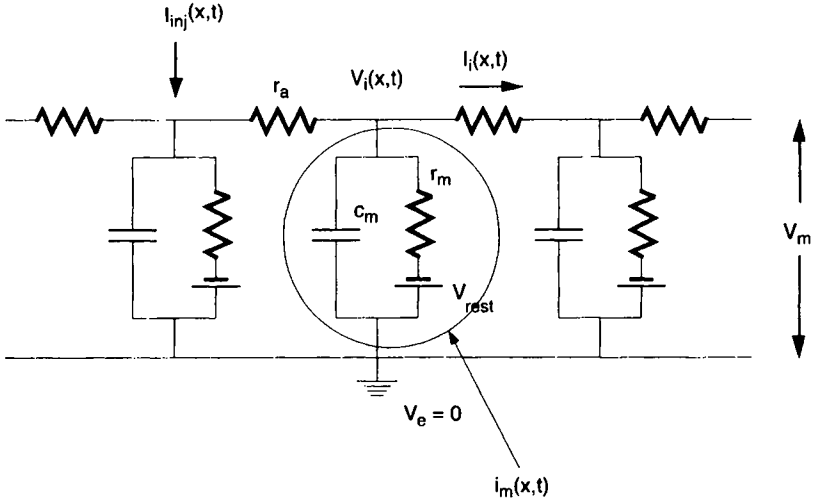


Fig. 2.3 A SINGLE PASSIVE CABLE Equivalent lumped electrical circuit of an elongated neuronal fiber with passive membrane. The intracellular cytoplasm is described by an ohmic resistance per unit length r_a and the membrane by a capacitance C_m in parallel with a passive membrane resistance r_m and a battery V_{rest} . The latter two components are frequently referred to as *leak resistance* and *leak battery*. An external current $I_{inj}(x, t)$ is injected into the cable. The associated linear cable equation (Eq. 2.7) describes the dynamics of the electrical potential $V_m = V_i - V_e$ along the cable.

absence of any input $I_{inj}(x, t)$, the membrane potential throughout the cable will be equal to a constant. The amplitude of V_{rest} varies between -50 and -90 mV, depending on cell type and other circumstances, with the inside of the neuron being at the negative potential. V_{rest} need not always be constant throughout the dendritic tree (see Sec. 18.3.4).

Because the resting potential is simply an offset, it is often set to zero. This can be thought of as defining the membrane potential $V_m(x, t)$ as relative to this resting potential. Very often the equations will be somewhat simplified when the potential is defined as relative to V_{rest} . We use the convention that $V_m(x, t)$ refers to the absolute membrane potential, while $V(x, t)$ refers to the potential relative to V_{rest} .

We should here also allude to the vexing question of units. The three voltage-independent components of a passive cable are commonly specified in one of two ways. If they are expressed as quantities per unit length, they are conventionally labeled

$$r_a = \frac{4R_i}{\pi d^2} \quad (2.8)$$

in units of Ω/cm ,

$$r_m = \frac{R_m}{\pi d} \quad (2.9)$$

in units of $\Omega \cdot \text{cm}$ and

$$C_m = C_m \cdot \pi d \quad (2.10)$$

in units of F/cm . Using these variables has the advantage that the cable equation contains no explicit terms depending on the diameter d of the cable.

The more common way, and the one we adopt throughout the book, is to specify these quantities in units that are independent of the diameter of the fiber, using capital letters: the

intracellular resistivity R_i , the specific membrane resistance R_m and the specific membrane capacitance C_m , with dimensions of $\Omega \cdot \text{cm}$, $\Omega \cdot \text{cm}^2$ and F/cm^2 , respectively. For more details, consult Appendix A.

2.2 Steady-State Solutions

Let us investigate the behavior of the cable equation in response to a current $I_{\text{inj}}(x)$ injected at location x via an intracellular microelectrode or a synapse. We assume that the current is switched on at $t = 0$ and remains on. One frequently encounters this situation in experiments to investigate the cable properties of neurons and axons. After some initial transients, the voltage will reach a steady-state value. To compute the steady-state membrane potential, we set $\partial V / \partial t = 0$ and write the cable equation as

$$\lambda^2 \frac{d^2 V(x)}{dx^2} = V(x) - r_m I_{\text{inj}}(x). \quad (2.11)$$

This reduces the original partial differential Eq. 2.7 to an ordinary second-order differential equation depending solely on space. We now study its solutions for different neuronal geometries.

2.2.1 Infinite Cable

We begin by assuming that a current I_{inj} of constant amplitude is injected at the origin, $x = 0$, of an infinite cable of diameter d . Mathematically, we describe this by setting $I_{\text{inj}}(x)$ to $I_0 \delta(x)$, where $\delta(x)$ is the Dirac delta or impulse distribution in space. As boundary condition we assume that the voltage at the two infinitely distant terminals goes to zero as $|x| \rightarrow \infty$. Using the theory of Fourier transforms (see Appendix B) we arrive at the solution

$$V(x) = V_0 e^{-|x|/\lambda}, \quad (2.12)$$

with $V_0 = I_0 r_m / (2\lambda)$. This solution can easily be verified by placing it into Eq. 2.11. The stationary voltage distribution, sometimes referred to as the *electrotonus*, in the infinite cable decays exponentially away from the site of injection. The parameter controlling this decay is the *space constant* λ . The voltage decreases to e^{-1} , that is, to 37% of its original value, at $x = \lambda$ and to e^{-2} , or 13% of its original value, at $x = 2\lambda$. In the derivation of the cable equation, the *steady-state space constant* is defined as

$$\lambda = \left(\frac{r_m}{r_a} \right)^{1/2} = \left(\frac{R_m}{R_i} \cdot \frac{d}{4} \right)^{1/2}. \quad (2.13)$$

The larger the membrane resistance R_m , the less current leaks across the membrane and the larger the space constant λ . Furthermore, a thick dendrite has a larger space constant than a thin one, reflecting the fact that the spread of current is enhanced by a larger diameter. Another way of deriving λ involves computing the distance l over which the total resistance to current flowing across the membrane is identical to the total longitudinal resistance. Paying careful attention to the relevant units, we have $r_m/l = r_a l$, or $l = \sqrt{r_m/r_a} = \lambda$. For a typical apical dendrite of a cortical cell with a $4 \mu\text{m}$ diameter, $R_i = 200 \Omega \cdot \text{cm}$ and $R_m = 20,000 \Omega \cdot \text{cm}^2$, the space constant λ comes out to be 1 mm. This large distance, compared to the diameter of the dendrite, is the reason why we can neglect the radial components of voltage along these cables.

Given the importance of λ for the electrotonic spread of the potential in a neuron, we frequently normalize the spatial coordinate x with respect to λ , expressing it in dimensionless units: $X = x/\lambda$. Any particular distance ℓ can likewise be expressed in terms of the associated dimensionless *electrotonic distance* $L = \ell/\lambda$.

What is the input resistance of the infinite cable? Operationally, it is measured by inserting an electrode that passes current and, at a distance that is small compared to λ , an electrode to record the voltage. In the limit that this distance shrinks to zero, we can write

$$R_{\text{in}} = \frac{V(x)}{I_i(x)} = \frac{V(x=0)}{I_0}. \quad (2.14)$$

The last equality holds because the input resistance at the location of the injecting electrode is, by definition, equal to the ratio of the evoked potential to the injected current causing this change. It follows that

$$R_{\text{in}} = \frac{r_m}{2\lambda} = \frac{r_a\lambda}{2} = \frac{(r_ar_m)^{1/2}}{2}. \quad (2.15)$$

The input resistance is—as expected—constant throughout the infinite and homogeneous cable. Confirming our intuition, increasing either the membrane resistance or the intracellular resistivity will increase R_{in} .

Conceptually, we can think of an infinite cable as two semi-infinite cables, one going off to the left and one to the right. The input resistance associated with a single semi-infinite cable R_∞ must therefore be twice the resistance associated with the infinite cable (since current can only flow in one direction); or

$$R_\infty = (r_a \cdot r_m)^{1/2} = r_a\lambda = \frac{r_m}{\lambda} = (R_m R_i)^{1/2} \frac{2}{\pi d^{3/2}}. \quad (2.16)$$

This variable, rather than the resistance associated with an infinite cable, is called R_∞ , since it corresponds to the situation of a soma with a single dendrite extending into infinity (Rall, 1959).

The input conductance of a semi-infinite cylinder is given by the inverse of Eq. 2.16,

$$G_\infty = \frac{1}{R_\infty} = \left(\frac{1}{R_m R_i} \right)^{1/2} \frac{\pi d^{3/2}}{2}. \quad (2.17)$$

The input conductance decreases as the square root of the membrane resistance R_m and increases as the $\frac{3}{2}$ power of the diameter of the fiber, a relationship that will be important later on.

The input resistance of a patch of membrane is linearly related to the membrane resistance R_m (with the constant of proportionality given by the total membrane area). In general, as the dimensionality of the space increases, the dependency of the input resistance on R_m lessens. Thus, R_{in} in an infinite cable is proportional to the square root of R_m . For a two-dimensional resistive sheet, $R_{\text{in}} \propto \log(R_m)$. In a three dimensional syncytium (such as muscle tissue) $R_{\text{in}} \propto e^{-1/R_m^{1/2}}$ (see Chap. 3 in Jack, Noble, and Tsien, 1975; Eisenberg and Johnson, 1970). Given the area- or volume-filling geometry of the dendritic tree, the dependency of its input resistance on R_m falls somewhere between that of an infinite cable and that of the resistive sheet.

2.2.2 Finite Cable

Real neurons certainly do not possess infinitely long dendrites, so we need to consider a finite piece of cable of total electrotonic length $L = \ell/\lambda$. The general solution to the

linear second-order ordinary differential cable equation can be expressed in normalized electrotonic units as

$$V(X) = \alpha \cosh(L - X) + \beta \sinh(L - X), \quad (2.18)$$

with $\cosh(x) = (e^x + e^{-x})/2$ and $\sinh(x) = (e^x - e^{-x})/2$. The values of α and β depend on the type of boundary conditions imposed at the two terminals. (What happens at the end of the finite cable influences the voltage throughout the fiber.) We distinguish three different boundary conditions.

Sealed-End Boundary Condition

This is the boundary condition of most relevance to neurons embedded in the living tissue. It assumes that the end of the fiber is covered with neuronal membrane with resistance R_m . It follows that the resistance terminating the equivalent circuit in Fig. 2.3 has the value $4R_m/\pi d^2$. For $d = 2 \mu\text{m}$ and $R_m = 10^5 \Omega \cdot \text{cm}^2$ this is about $3000 \text{ G}\Omega$, a value so high that for all intents and purposes we can consider it to be infinite. If the terminating resistance is infinite, no axial current $I_i(X = L)$ will flow. And since the axial current is given by the derivative of the voltage along the cable, this implies that

$$\left. \frac{dV(X)}{dX} \right|_{X=L} = 0 \quad (2.19)$$

at the terminal. This *zero-slope* or *von Neumann* boundary condition is referred to as a *sealed-end* boundary condition and is the one commonly adopted to model the terminals of dendrites or other neuronal processes. Applying Eq. 2.19 to Eq. 2.18 leads to

$$V(X) = V_0 \frac{\cosh(L - X)}{\cosh(L)}. \quad (2.20)$$

Figure 2.4 illustrates the voltage profile in a short and a long cable with such a sealed-end boundary condition. As expected from Eq. 2.19, the slope of both curves flattens out as the terminal is approached. Furthermore, both curves lie above the voltage decay in a semi-infinite cable. In other words, the voltage in a cable with a sealed end—regardless of its length—decays less rapidly than the voltage in a semi-infinite cable.

We compute the input resistance R_{in} at the origin of the cable, looking into the cable toward its terminal, using the same strategy as in the previous section,

$$R_{\text{in}} = R_\infty \coth(L), \quad (2.21)$$

with $\coth(x) = \cosh(x)/\sinh(x)$. This is plotted in Fig. 2.5 (upper curve). This input resistance is always higher than that of the semi-infinite cable, since the intra-axial current I_i is prevented from leaving the cable at the endpoint of the cable.

Killed-End Boundary Condition

Another type of boundary condition is of relevance when the dendrite or axon is physically cut open or otherwise short-circuited. Under these conditions the intracellular potential at the terminal is identical to the extracellular potential, that is, the effective potential is set to zero,

$$V(X)|_{X=L} = V_L = 0. \quad (2.22)$$

This *Dirichlet* type of boundary condition is also known as *open-* or *killed-end* boundary

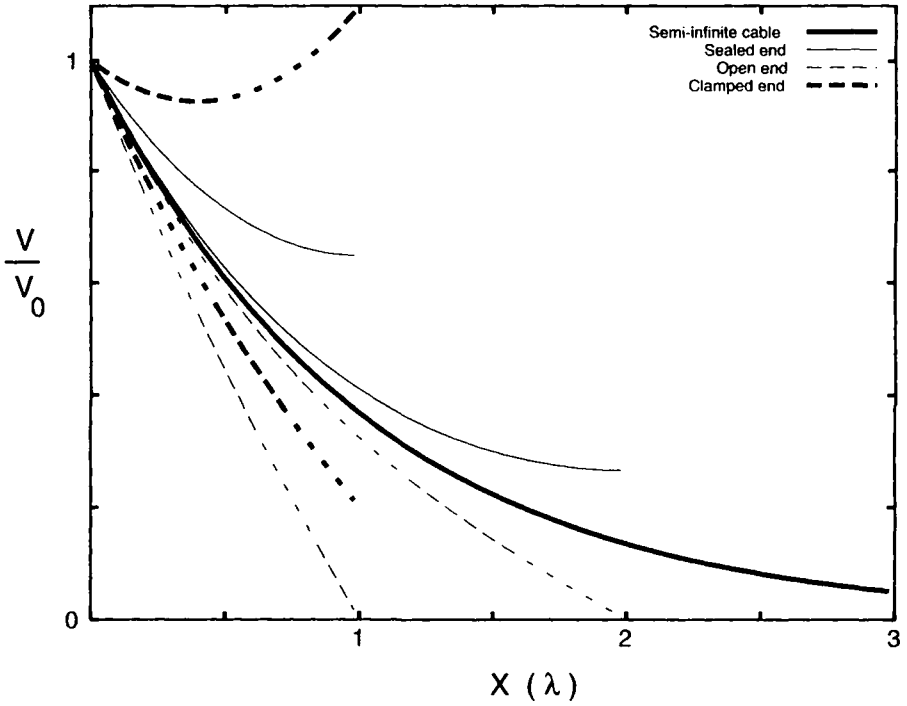


Fig. 2.4 STEADY-STATE VOLTAGE ATTENUATION Steady-state voltage attenuation in a finite piece of cable as a function of the normalized electrotonic distance $X = x/\lambda$ from the left terminal. The potential at the left terminal is always held fixed at $V = V_0$, while the normalized potential throughout the cable varies with the boundary condition at the right terminal. The bold continuous line corresponds to the voltage in a semi-infinite cable, showing a pure exponential decay. The thin continuous lines show the voltage decay for two cables that terminate in a sealed end (Eq. 2.20) at $X = 1$ or $X = 2$. This is the type of boundary condition used most commonly in simulations. The two thin dashed curves show the same two cables, but now terminating in a short circuit (killed-end boundary condition; Eq. 2.23). Note that either the spatial derivative of voltage (sealed-end) or the voltage itself (killed-end) is zero at the rightmost terminal. That the spatial voltage profile can be nonmonotonic in a passive cable is witnessed by the topmost bold dashed curve, where the voltage at $X = 1$ is clamped to 1.1 times the voltage at the origin. For the lower bold dashed curve, the voltage at the terminal is clamped to $0.2V_0$. Reprinted in modified form by permission from Rall (1989).

condition and corresponds to setting the terminating resistance to zero. It follows that the voltage along the cable is

$$V(X) = \frac{V_0 \sinh(L - X)}{\sinh(L)}, \quad (2.23)$$

and the input resistance is

$$R_{in} = R_{\infty} \tanh(L), \quad (2.24)$$

with $\tanh(x) = \sinh(x)/\cosh(x)$. The two thin dashed curves in Fig. 2.4 are the voltage profiles along two cables of electrotonic length $L = 1$ and 2 with a killed-end boundary condition. Their values are always less than the voltage at the corresponding location in a semi-infinite cable. Correspondingly, the input resistance of these cables is always less than that of the semi-infinite cable (Fig. 2.5). The input resistance at the origin $X = 0$ of the

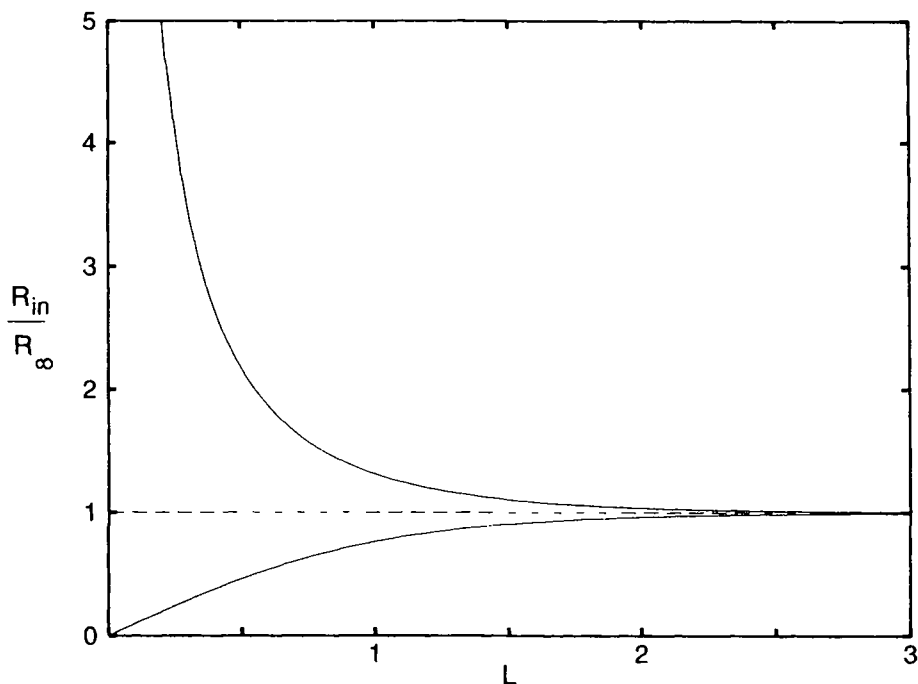


Fig. 2.5 INPUT RESISTANCE OF A FINITE CABLE Input resistance R_{in} looking into a cable of electrotonic length L toward the right terminal. The ordinate is normalized in terms of the input resistance R_{in} of a semi-infinite cylinder (Eq. 2.16). The normalized input resistance for a sealed-end boundary condition (upper curve) is always larger than R_{∞} , while the input resistance of a cable with killed-end boundary condition (lower curve) is always less. In the former case, the current is prevented from leaving the cable at the endpoint, while the voltage is “shorted to ground” in the latter case. For cables longer than two space constants, $R_{in} \approx R_{\infty}$.

cable is inversely proportional (see Eq. 2.2) to the slope of V . The actual input resistance as a function of the electrotonic length of a killed-end cable is shown in Fig. 2.5 (lower curve).

Arbitrary Boundary Condition

In general, the terminal has neither infinite (sealed-end) nor zero (killed-end) resistance, but some finite value R_L . This, for instance, is the case if the cable is connected to some other cable or even to an entire dendritic tree. If we know the value of the voltage at this boundary, that is, V_L , we can express the voltage as

$$V(X) = \frac{V_0 \sinh(L - X) + V_L \sinh(X)}{\sinh(L)}. \quad (2.25)$$

Notice how this expression takes on the value V_0 at $X = 0$ and V_L at $X = L$. In Fig. 2.4 we show two such cases in which V_L is either clamped to $0.2V_0$ or to $1.1V_0$ (causing the non-monotonic appearance). Note that this sagged appearance is a direct consequence of the unusual boundary condition.

The leak current through the terminal follows from Ohm's law and Eq. 2.2 as

$$i_L = \frac{V_L}{R_L} \Big|_{X=L} = \frac{-1}{r_a} \frac{dV(X)}{dX} \Big|_{X=L}. \quad (2.26)$$

We can now rewrite Eq. 2.25 as

$$V(X) = V_0 \cdot \frac{\cosh(L - X) + (R_\infty/R_L) \sinh(L - X)}{\cosh(L) + (R_\infty/R_L) \sinh(L)}, \quad (2.27)$$

resulting in a general expression for the voltage in a finite piece of cable.

With the help of Eq. 2.3 and the above equation, we can derive an expression for the input resistance of a cable of length L with a terminating resistance R_L ,

$$R_{in} = R_\infty \frac{R_L + R_\infty \tanh(L)}{R_\infty + R_L \tanh(L)}. \quad (2.28)$$

The previous two equations allow us to obtain the values for the voltage and the input resistance for the sealed-end and the killed-end boundary conditions by setting R_L to either ∞ or 0. Furthermore we recover $R_{in} = R_\infty$ for an infinite cable (since $\tanh(L)$ goes to 1 as $L \rightarrow \infty$).

2.3 Time-Dependent Solutions

So far, we have only been concerned with the behavior of the voltage in a cable in response to a stationary current injection, a situation where the voltage settles to a constant value. In general though, we need to consider the voltage trajectory in response to some time-varying current input. Since the time-dependent solution of the cable equation is substantially more complex than the steady-state solution treated above, we will only discuss the solution to two special cases. The interested reader is referred to the monographs by Jack, Noble, and Tsien (1975) and by Tuckwell (1988a) for a treatment of many more cases of interest.

Before we do so, we will introduce a normalized version of the cable equation. Recalling the definition of the neuronal time constant from Chap. 1 as

$$\tau_m = r_m c_m = R_m C_m \quad (2.29)$$

allows us to introduce dimensionless variables for both time, $T = t/\tau_m$, and space, $X = x/\lambda$. Written in these units and taking care to properly transform the input current (Sec. 4.4 in Tuckwell, 1988a), the cable equation becomes

$$\frac{\partial^2 V(X, T)}{\partial X^2} = \frac{\partial V(X, T)}{\partial T} + V(X, T) - \frac{I_{inj}(X, T)}{\lambda c_m}, \quad (2.30)$$

with $I_{inj}(X, T) = \lambda \tau_m I_{inj}(x, t)$ and $I_{inj}(x, t)$ corresponds to the stimulus current density.

2.3.1 Infinite Cable

In order to compute the dynamic behavior of the infinite cable in response to current injections we will once again exploit the linearity of Eq. 2.30, that is, the fact that if the response of the membrane to the current $I(X, T)$ is $V(X, T)$, the polarization in response to the current $\alpha I(X, T)$ is $\alpha V(X, T)$.

Voltage Response to a Current Pulse

As discussed in the first chapter (and summarized in Appendix B), we can completely characterize the system by computing the *impulse response* or *Green's function* associated with Eq. 2.30, which we do by transforming to the Fourier domain, assuming that $V(X) \rightarrow 0$ as $|X| \rightarrow \infty$, and transferring back to the time domain (Jack, Noble, and Tsien, 1975).

Assuming that a fixed amount of charge Q_0 is applied at $X = 0$ as an infinitely brief pulse of current $I_0 = Q_0/\tau_m$, the resultant voltage is

$$V_\delta(X, T) = \frac{I_0 r_m}{2\lambda(\pi T)^{1/2}} e^{-\frac{X^2}{4T}} e^{-T}. \tag{2.31}$$

In order to gain a better intuitive understanding of cable theory, let us review various special cases. If we record the voltage at the same location at which we injected the current, corresponding to $X = 0$, the Green's function is proportional to e^{-T}/\sqrt{T} . $V_\delta(0, T)$ diverges at the origin and decays a bit faster than exponentially for large times (Figs. 2.6 and 2.7B). The singularity at the origin comes about due to the infinitesimal amount of capacitance for $X = 0$ between the site of current injection and that of the measuring device. Using L'Hôpital's rule, we can see that the limit of $V_\delta(X, T)$ for any value of X other than the origin is zero. No singularity exists for the membrane patch model, which possesses a simple exponentially decaying Green's function with a fixed amount of capacitance (Fig. 2.6).

If one waits long enough, the voltage decay throughout the cable will be identical, approaching more and more to the decay seen at the spatial origin. This can be observed

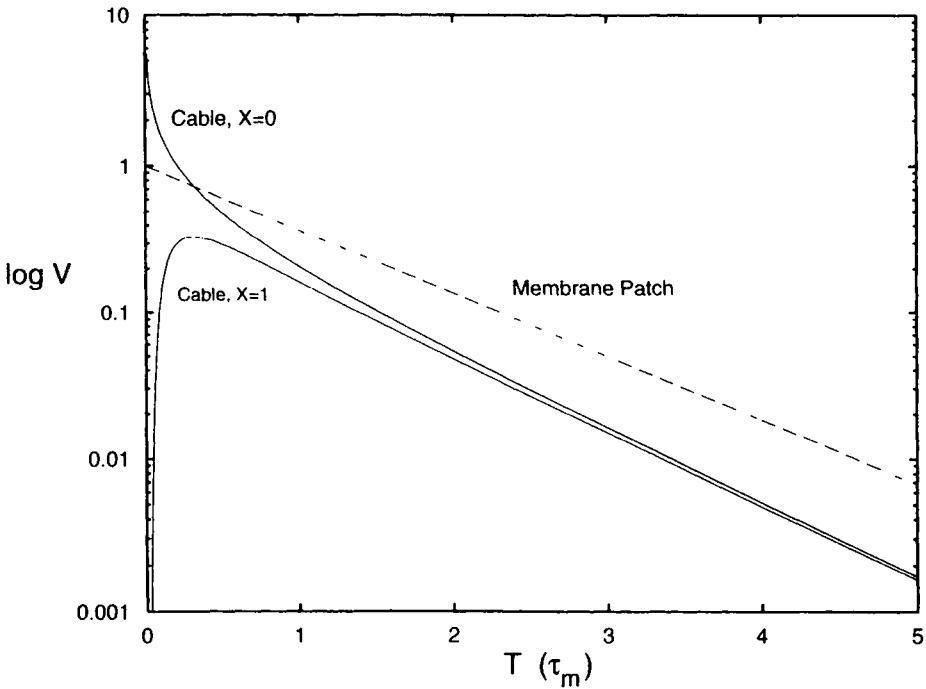


Fig. 2.6 IMPULSE RESPONSE AT THE ORIGIN OF AN INFINITE CABLE Comparison of the impulse response or Green's function for an infinite cable $V_\delta(X, T)$ (Eq. 2.31) for $X = 0$ and $X = 1$ and the normalized Green's function for a patch of passive membrane (e^{-T} ; Eq. 1.17; dashed line) on a logarithmic voltage scale. Time is expressed in units of τ_m . The voltage in the infinite cable (solid lines) is measured at the location where the δ pulse of current is applied or one space constant λ away. The Green's function diverges at $X = 0$, since the amount of membrane capacitance between the current injection and the voltage recording electrode is infinitely small, but has a constant value of C for the membrane patch case.

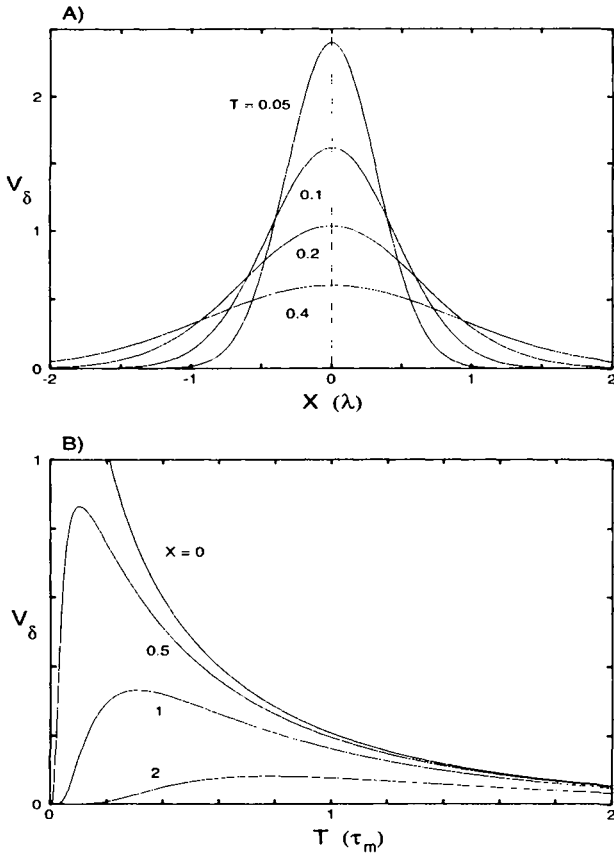


Fig. 2.7 IMPULSE RESPONSE OF THE INFINITE CABLE Impulse response or Green's function $V_\delta(X, T)$ (Eq. 2.31) at $X = 0$ and $T = 0$ as a function of normalized space (A) and time (B) using different linear scales. At any point in time, the spatial profile of the voltage along the cable in the upper panel can be described by a Gaussian. One of the consequences of the low-pass nature of the membrane is evident in the bottom panel: more distant locations respond with a delay.

very well using a logarithmic scale, as in Fig. 2.6, where the decay ultimately scales as e^{-t/τ_m} .

In other words, immediately following the current injection, the voltage is sharply peaked around the injection site. As time goes by, the spatial voltage profile becomes broader, smearing out more and more (Fig. 2.7A). At any particular instant T , the spatial distribution of the voltage along the cable is proportional to e^{-X^2} , corresponding to a Gaussian function centered at the injection site. If the time course of voltage is recorded at increasing distances from the site of the charge application, the voltage response takes longer to reach its peak due to the low-pass nature of the membrane capacitance (Fig. 2.7B).

Since the nature of the filtering carried out by the membrane does not depend on the applied potential across it, the system is a linear one. It follows that the voltage in response to an arbitrary current stimulus $I_{inj}(T)$ injected at the origin is given by the superposition of the impulse response function with the input current. Conceptually, one can think of the input $I_{inj}(T)$ as a series of delta pulses staggered in time. The final voltage is the sum of the

impulse functions associated (and weighted) with the individual pulses. This is concisely expressed by the convolution integral

$$V(X, T) = \frac{\tau_m}{Q_0} V_\delta(X, T) * I_{\text{inj}}(T) = \frac{\tau_m}{Q_0} \int_0^T V_\delta(X, T') I_{\text{inj}}(T - T') dT', \quad (2.32)$$

where $*$ denotes convolution and the τ_m/Q_0 factor is responsible for the correct normalization (converting the voltage V_δ into an impedance).

Voltage Response to a Current Step

If a rectangular step of current is injected into the cable, such that $I_{\text{inj}}(T) = I_0$ for $T \geq 0$ and 0 otherwise, the previous integral evaluates to $I_0(\tau_m/Q_0) \int_0^T V_\delta(X, T') dT'$. Due to the presence of the Gaussian term in Eq. 2.31, this integral has no closed-form solution and must be expressed in terms of the error function $\text{erf}(x) = \frac{2}{\sqrt{\pi}} \int_0^x e^{-y^2} dy$ (as first carried out by Hodgkin and Rushton, 1946). While we will not discuss the full solution in all of its glory (see Eq. 3.24 in Jack, Noble, and Tsien, 1975), we will consider several cases of particular interest to us. The transient voltage response at the site of current injection is

$$V_{\text{Step}}(0, T) = \frac{I_0 R_\infty}{2} \text{erf}(\sqrt{T}). \quad (2.33)$$

Since $\text{erf}(1) = 0.84$, the voltage in the cable at the site of the current step rises to 84% of its steady-state value in one time constant, compared to 63% of its peak value for the exponential charging in the case of a patch of membrane (see Eq. 1.9). Conceptually, this latter case can be thought of as resulting from injecting a current into a cable, only that in the membrane patch case the entire cable has been “space clamped” by introducing an imaginary wire along its length. Let us plot the normalized membrane potential for both cases (Fig. 2.8A), that is, the potential relative to its steady-state value,

$$W(X, T) = \frac{V(X, T)}{\lim_{T \rightarrow \infty} V(X, T)}, \quad (2.34)$$

and plotted in Fig. 2.8A.

When considering why the potential in the cable reaches its steady-state value faster than the potential across a patch of membrane with the same input impedance, it is helpful to consider the closely related problem (for linear cables) of why voltage decays faster in a cable than across a membrane patch. In the former, current can flow longitudinally and therefore escapes more rapidly than when it must all flow across the membrane. The same argument holds for an electrode injecting current into the soma of a neuron with an extended dendritic tree. A significant fraction of the injected current flows onto the extensive dendritic membrane surface, and as a result, the buildup and decay of the somatic voltage is faster compared to the isopotential membrane patch. This effect was first recognized by Rall (1957). Coombs, Eccles, and Fatt (1955) had fitted the experimentally observed membrane transients at the motoneuron soma with a single exponential with $\tau_m = 2$ msec. Rall argued that the cable properties of the dendrites needed to be accounted for and—on the basis of Eq. 2.33—estimated a τ_m of 4 msec.

Frequency-Dependent Space Constant

As expressed by Eq. 2.12, the steady-state space constant λ is defined as the distance in an infinite cable over which a *steady-state* voltage decays by $1/e$. This variable can be generalized to a function depending on frequency f . If a sinusoidal current $I(t) = I_0 \sin(2\pi f t)$ is injected into an infinite cable, the theory of Fourier transforms can be

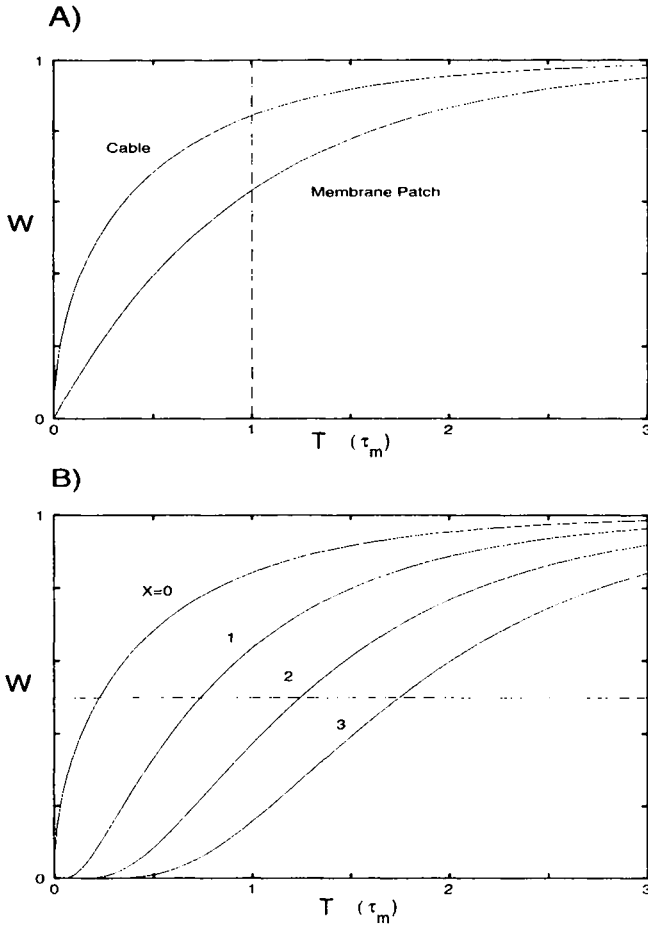


Fig. 2.8 VOLTAGE IN AN INFINITE CABLE IN RESPONSE TO A CURRENT STEP (A) Normalized voltage $W(X, T)$, that is, $V(X, T)$ divided by its steady-state value at location X (Eq. 2.34), in an infinite cable in response to a current step injected at the same location is compared to the voltage increase in response to the same current injected into a patch of membrane. In the cable, the voltage rises faster to its final value than in a patch of membrane. (B) The normalized voltage in response to a current step in an infinite cylinder at different distances X from the site of current injection. As X increases, the response becomes more smeared out. The point at which the voltage at any one location X reaches half of its final value moves—in the limit for long times—with constant velocity $2\lambda/\tau_m$ along the cable (see Sec. 2.4).

used to introduce a generalized *frequency-dependent* or *transient* space constant $\lambda(f)$ (see Appendix B).

It is relatively straightforward to formulate the cable equation in a generalized linear system by representing a finite or an infinite cable as a ladder network with arbitrary intracellular impedance $z_a(f)$ and membrane impedance $z_m(f)$ (Koch and Poggio, 1985a). In this case, the membrane can contain any collection of linear elements, including inductances, capacitances, and resistances. Under certain conditions, explored in more detail in Chap. 10, a nonlinear membrane can be linearized and can be expressed by a combination of these linear circuit elements.

If the current $I_0 \sin(2\pi ft)$ is injected into an infinite cable, the voltage at any point in the cable will be proportional to $\sin(2\pi ft + \phi)$, with a phase shift $\phi(f)$. The constant of proportionality is given by $e^{-\gamma(f)x}$, where x is the distance between the site of current injection and the recording electrode, and the *propagation constant* is

$$\gamma(f) = \sqrt{\frac{z_a(f)}{z_m(f)}}. \quad (2.35)$$

For a passive membrane, $z_a(f) = r_a$ and $z_m(f) = r_m/(1 + i2\pi f\tau_m)$. By extracting the real part of this function, we can define the frequency-dependent space constant $\lambda(f)$ as

$$\lambda(f) = \frac{\lambda(0)}{\text{Re}\{\sqrt{1 + i2\pi f\tau_m}\}}, \quad (2.36)$$

with $\lambda(0)$ the sustained or steady-state space constant (Eisenberg and Johnson, 1970). As seen in Fig. 2.9, $\lambda(f)$ decays steeply with increasing frequency, becoming proportional to $1/\sqrt{f\tau_m}$ in the limit of $2\pi f\tau_m \gg 1$. This decay is due to the distributed membrane capacitance that soaks up more and more of the current as the frequency increases. For instance, at 1000 Hz (roughly corresponding to the inverse of the width of a typical action potential), λ has decreased to 8% of its steady-state value (assuming $\tau_m = 50$ msec). This emphasizes once again the low-pass nature of the passive neuronal membrane: high frequencies are preferentially filtered out.

The frequency-dependent space constant also informs us about the limit of one-dimensional cable theory. It is clear that as $\lambda(f) \approx d$, the diameter of the fiber, one can no longer neglect the radial dimensions of the cable and has to treat the full three-dimensional problem. In general, this is not expected to occur until very high frequencies. For instance, in an apical dendrite of $4\text{-}\mu\text{m}$ diameter with $R_m = 50,000\ 2\pi f\ \text{cm}^2$, $R_i = 200\ 2\pi f\ \text{cm}$, and $C_m = 1\ \mu\text{F}/\text{cm}^2$. The steady-state space constant λ equals 1.581 mm. Under these conditions, one has to go to frequencies close to 1 MHz in order for $\lambda(f) \approx d$. We conclude that under most circumstances, one-dimensional cable theory will hold.

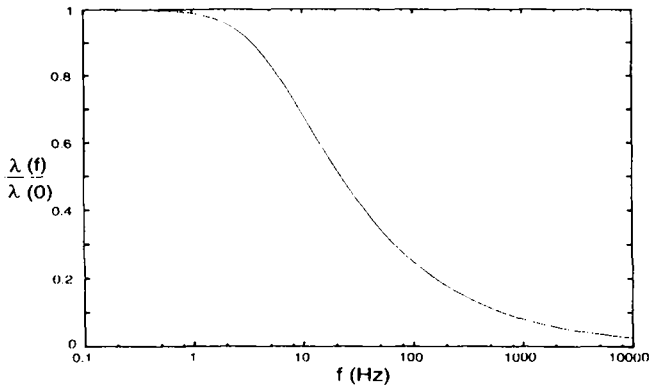


Fig. 2.9 FREQUENCY-DEPENDENT SPACE CONSTANT If a sinusoidal current of frequency f is injected at $x = 0$ into an infinite passive cable, the voltage at location x will also be a sinusoid of frequency f , but attenuated by $e^{-x/\lambda(f)}$ and phase shifted. We here plot $\lambda(f)$, normalized by the steady-state space constant $\lambda(0)$, for $\tau_m = 50$ msec. At 1 kHz, the space constant has decayed to 8% of its original value.

2.3.2 Finite Cable

A number of different techniques are available for computing the Green's function in finite cables (Tuckwell, 1988a). One classical method, known as separation of variables, assumes that the Green's function can be written as the product of two functions, one depending only on X while the other one depends solely on T . Rall (1969a) used this technique to derive the voltage in a finite cable with sealed-end boundary conditions at $X = 0$ and $X = L$. The voltage in response to an arbitrary current input anywhere in the cable can be expressed as an infinite series,

$$V(X, t) = \sum_{n=0}^{\infty} B_n \cos \frac{n\pi X}{L} \cdot e^{-\alpha_n t / \tau_m} . \quad (2.37)$$

The B_n depend on the initial conditions chosen, such as injection of a delta pulse current or a current step. The coefficients α_n are the ratios of the membrane time constant τ_m to the *equalizing time constants* that are associated with the redistribution of charge and with the reduction of voltage differences between different regions of the cable. They are defined as

$$\alpha_n = 1 + \left(\frac{n\pi}{L} \right)^2 . \quad (2.38)$$

The physical intuition behind Eq. 2.37 is that each term results from a “reflection” of the voltage at one of the terminals. Each term becomes progressively smaller as it is reflected back and forth an infinite number of times (Fig. 2.10). Another way to understand Eq. 2.37 is to note that the $n = 0$ term, relating to the slowest decay, is constant throughout the cable and corresponds to an exponential decay away from the average voltage along the finite cable. The $n = 1$ term is associated with decay and rapid equalization of charge between two half-lengths of the cylinder ($V(X, T)$ is positive for $0 \leq X \leq L/2$ and negative for the other half of the cylinder). Higher order terms lead to an even more rapid equalization of charge over shorter lengths of the cable. The sum in Eq. 2.37 can also be expressed as

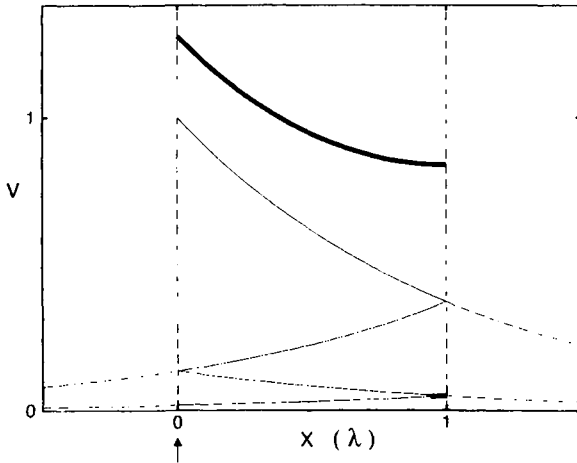


Fig. 2.10 VOLTAGE RESPONSE IN A FINITE CABLE In a finite cable with sealed end boundary conditions at $X = 0$ and 1 , the voltage V in response to any current input can be described as the sum (bold line) of infinitely many “reflection” terms (thin lines), each term becoming progressively smaller. This leads to the convergent series in Eq. 2.41. Here, the current is injected at $X = 0$.

$$V(X, t) = V_{\infty}(X) + C_0 e^{-t/\tau_0} + C_1 e^{-t/\tau_1} + C_2 e^{-t/\tau_2} + \dots, \quad (2.39)$$

where the C_i 's depend both on the initial conditions as well as on X , and V_{∞} captures the steady-state components of the voltage. τ_0 equals the passive membrane time constant τ_m , while all other values of τ_n , called *equalizing time constants*, are smaller than τ_0 , with

$$\tau_n = \frac{\tau_m}{1 + \left(\frac{n\pi}{L}\right)^2}. \quad (2.40)$$

The voltage decay for large t is always dominated by the largest time constant $\tau_0 = \tau_m$. In other words, if the logarithm of the membrane potential in response to, say, a current step, is plotted as a function of time, the linear slope at the tail end of the pulse is identical to the membrane time constant τ_m (see also Fig. 2.6 and the next chapter).

A different way to express the voltage in a finite piece of cable with sealed-end boundary condition at $X = 0$ and $X = L$ in response to a current pulse (with $I_0 = Q/\tau_m$) at $X = 0$ uses the theory of Laplace transforms (Jack, Noble, and Tsien, 1975; Tuckwell, 1988a),

$$V(X, T) = \frac{R_{\infty} I_0}{2} \frac{e^{-T}}{(\pi T)^{1/2}} \sum_{n=-\infty}^{+\infty} e^{-(\frac{x}{2} + nL)^2/T}. \quad (2.41)$$

As $L \rightarrow \infty$, we recover the impulse response function for the infinite cable (Eq. 2.31). This expression has a simple graphical interpretation (as expressed in Fig. 2.10) in terms of ever reflecting and decreasing contributions, corresponding to an infinite number of virtual electrodes that inject charge at $\pm L, \pm 2L, \dots$

While the time constants τ_n depend on L , they are independent of the site of the current pulse, the site of recording, or the initial conditions. Thus, they provide a convenient way to calculate the electrotonic length of a cable. In particular, the ratio of the first two time constants provides a measure of the cable's electrotonic length,

$$L = \frac{\pi}{\sqrt{\frac{\tau_0}{\tau_1} - 1}}. \quad (2.42)$$

This expression has frequently been applied to experimental data from different preparations by measuring the two slowest time constants, obtained by *peeling* the slopes (time constants) of the logarithm of the transient voltage response (see Fig. 3.12). The outcome of this procedure is quite dependent on the neuronal geometry of the cell recorded from and the amount of noise in the measured voltage transient and needs to be used with great care. For an overview of the advantages and limitations of this method see Rall et al. (1992) and Holmes, Segev, and Rall, (1992).

A related, but more complicated, expression for the voltage can be derived if one end of the finite cable is terminated with an equipotential "soma," consisting of a somatic leak and capacitance (Rall, 1962, 1969a). We refer the interested reader to the monograph by Tuckwell (1988a) that lists the Green's functions associated with a host of other neuronal geometries and initial conditions.

2.4 Neuronal Delays and Propagation Velocity

How fast does the potential induced by the current step propagate along the cable? Figure 2.8B shows the relative voltage change along an infinite cable in response to a current

step. The potential is normalized at each location by its steady-state value (Eq. 2.34). This normalization accounts for the effect of the exponential attenuation of V along the cable (Eq. 2.12). Because the membrane capacitance preferentially “soaks” up electrical charge associated with high temporal frequencies, the farther any particular point X is away from the site of current injection, the longer it takes $W(X, T)$ to rise to a particular value, say 0.5 (that is, half of its maximum). Is this delay proportional to the distance or, in other words, can one define a propagation velocity?

The linear cable equation does not admit any wave solution due to the dissipation of energy through the passive membrane. As long as no inductive elements are present in the neuronal membrane across which the current cannot change instantaneously, the voltage will, in principle, respond infinitely fast to a change in the current input an arbitrary distance away. In other words, the answer to the above question is, “No, in general one *cannot* define a velocity in a passive cable.” This can change if voltage-dependent nonlinear components are incorporated in the membrane, as witnessed by the propagation of spikes at constant velocities along axons.

Yet all is not lost. Because one cannot readily define the delay of voltages in passive cables, Agmon-Snir and Segev (1993) used the trick of computing the propagation delay of the *centroid* or the *first moment* of the voltage or the current in a passive cable. Following the nomenclature of Zador, Agmon-Snir, and Segev (1995), we define the centroid of the signal $h(x, t)$ at location x as

$$\hat{t}_x^h = \frac{\int_{-\infty}^{+\infty} t h(x, t) dt}{\int_{-\infty}^{+\infty} h(x, t) dt}. \quad (2.43)$$

Here h can be either a current or a voltage with a single peak or with multiple peaks. This measure is frequently also called the *center of mass* if t is thought of as distance and $h(x, t)$ as the mass distribution, with

$$\int_{-\infty}^{+\infty} (t - \hat{t}_x^h) h(x, t) dt = 0. \quad (2.44)$$

We define the *transfer delay* as the difference between the centroid of the induced voltage measured at location y and the centroid of current that was injected at location x ,

$$D_{x \rightarrow y} = D_{xy} = \hat{t}_y^V - \hat{t}_x^I. \quad (2.45)$$

We define the *input* or the *local delay* in the same spirit as the difference between the centroids of the voltage response and the current that gave rise to it,

$$D_{xx} = \hat{t}_x^V - \hat{t}_x^I. \quad (2.46)$$

It is possible to prove a number of useful properties of these delays by multiplying the cable equation by t and integrating over t . This results in an ordinary linear differential equation, similar to the steady-state cable equation, which can be analyzed by very similar techniques. Most importantly, Agmon-Snir and Segev (1993) prove that the transfer delay D_{xy} is always positive and is independent of the shape of the transient input current. In other words, D_{xy} is a property of the passive cable and not of the input. Furthermore, no matter what the electrical structure of the cable under consideration, the transfer delay is symmetric, that is,

$$D_{xy} = D_{yx}, \quad (2.47)$$

and it does not depend on the direction of travel.

In the simple case of an isopotential neuron,

$$D_{xx} = \tau_m, \tag{2.48}$$

due to the capacitive nature of the neuronal membrane (Fig. 2.11A). In other words, the centroid for a depolarizing potential occurs exactly one time constant later than the centroid for the current underlying this potential.

In an infinite (or semi-infinite) cable, potentials rise and decay faster, as we saw already in Fig. 2.8A. Indeed, because the charge injected into the cable not only flows onto

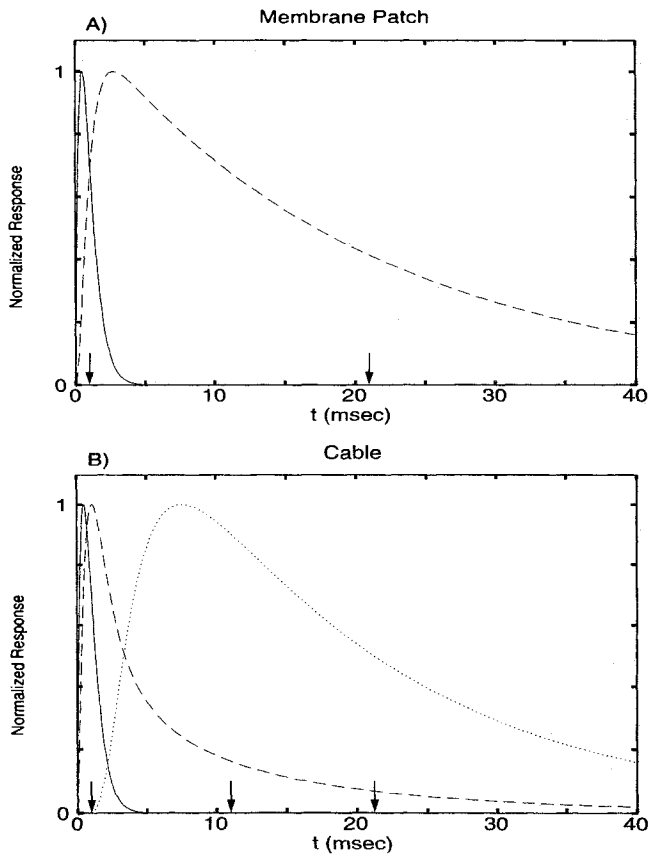


Fig. 2.11 NEURONAL INPUT AND PROPAGATION DELAYS An elegant way to define propagation delays in passive cables involves tracking the *centroid* or *center of mass* of voltages or currents in passive cable (Agmon-Snir and Segev, 1993). This is illustrated in (A) for an isopotential patch of membrane with $\tau_m = 20$ msec. A brief current pulse (solid profile with $t_{\text{peak}} = 0.5$ msec) gives rise to a rapidly rising but very slowly decaying depolarizing potential (shown dashed using normalized units). The centroids of the two signals (see arrows at 1 and 21 msec) are displaced by one time constant. In (B), the same current is injected into a very long cable, and the normalized potential at the same location (dashed) and at a location one space constant displaced (dotted) are plotted. In an infinite cable, the *transfer delay* D_{xy} between the centroid of the current at x and the centroid of the voltage at y is $(1 + |x - y|/\lambda)\tau_m/2$ (see the arrows at 1, 11, and 21 msec). As witnessed already in Fig. 2.8A, the potential decays faster in a cable than in an isopotential patch of membrane.

the capacitance at the location of the electrode but via the intracellular resistance onto neighboring capacitances, the input delay between any current input and the associated potential at the same location is only delayed by half a time constant,

$$D_{xx} = \frac{\tau_m}{2}, \quad (2.49)$$

as compared to τ_m for an isopotential patch of membrane. The faster local response time of an infinite cable compared with that of a patch of membrane is obvious in Fig. 2.8A. If the current is injected at x and the voltage recorded at y , the two centroids are displaced by

$$D_{xy} = \left(1 + \frac{|x - y|}{\lambda}\right) \frac{\tau_m}{2}. \quad (2.50)$$

This is clearly evident in Fig. 2.11B. Again, this delay does not depend on the particular form of the current input but holds for any input. This dependency on distance allows us to define a *propagation delay* P_{xy} as the difference between the centroids of the voltage at x and at y ,

$$P_{xy} = \hat{t}_x^V - \hat{t}_y^V = D_{xy} - D_{xx}. \quad (2.51)$$

For an infinite cable,

$$P_{xy} = \left(\frac{|x - y|}{\lambda}\right) \frac{\tau_m}{2}. \quad (2.52)$$

This linear relationship between space and time is equivalent to the notion of a *propagation velocity* in an infinite cable,

$$v = 2 \frac{\lambda}{\tau_m} = \left(\frac{d}{R_m R_i C_m^2}\right)^{1/2}. \quad (2.53)$$

It is important to emphasize that v is a “pseudovelocity” rather than the physical velocity of a constant wave moving along the cable for which $V(x, t) = V(x - vt)$ should hold. Yet, despite the fact that any potential will decay and become smeared out as it moves along a cable, its center of mass travels with a fixed velocity.

We feel obliged to point out a serious drawback when using D_{xy} or P_{xy} in active structures. The D_{xy} measure of a dendritic input giving rise to a somatic EPSP with an undershoot, that is, a hyperpolarization due to potassium current activation (as in Fig. 18.1B), will seriously underestimate the delay due to the small, but long-lasting negative contribution to the centroid, rendering it less useful for real cells than for purely passive structures (Bernander, 1993). Under these conditions, D_{xy} can be negative.

2.5 Recapitulation

One-dimensional cable theory is based on several approximations. (1) The magnetic field due to the movement of charge can be neglected. (2) Changes in the concentration of the charged carriers, Na^+ , K^+ , and other ions, is slight so that the current can be expressed by Ohm's law, and the intracellular cytoplasm can be mimicked by an ohmic resistance. (3) Due to the wirelike geometry of dendrites and axons and the high resistivity of the neuronal membrane, the radial and angular components of voltage can be neglected, reducing the complexity of the solution from three spatial dimensions to a single one. (4) The extracellular space is reduced to a homogeneous resistive milieu whose resistivity is usually set to zero.

This allows us to solve for the potential $V(x, t)$ across the neuronal membrane on the basis of a single equation.

Linear cable theory further assumes that for a limited range of voltage excursions around the resting potential, the membrane properties are independent of the membrane potential, reducing the electrical description of the membrane to resistances and capacitances, greatly simplifying analysis.

Starting in the late 1950s and early 1960s, the linear cable equation was solved by Rall and others to study the dynamics of the membrane potential in dendritic trees. Several key concepts associated with the linear cable equation for a single finite or infinite cylinder are the *space constant* λ , determining the distance over which a steady-state potential in an infinite cylinder decays e -fold, the neuronal *time constant* τ_m , determining the charging and discharging times of $V(x, t)$ in response to current steps, and the *input resistance* R_{in} , determining the amplitude of the voltage in response to slowly varying current injections.

The voltage in response to a current input, whether delivered by an electrode or by synapses, can be expressed by convolving the input with an appropriate Green's function. For passive cables, this always amounts to filtering the input by a low-pass filter function.

While the class of parabolic differential equations (to which the cable equation belongs) does not admit to any wave solutions but only shows dissipative behavior, one can define input, transfer, and propagation delays by computing and tracking the centroid or center of mass of $V(x, t)$ relative to the centroid of the current input. In the following chapter, we will apply these concepts to realistic dendritic trees.