Part II -- Single Neuron Computation

Chapter 2

Neurons as Cables

INTRODUCTION

Chapter 1 introduced some concepts of how neurons might be involved in executing computations that underlie behavior. One concept, that of an "Eccles neuron", was based upon the ideas of synaptic interactions that were developed in the 1950's and 1960's. Reviewing briefly, activation of synapses causes currents to flow either into or out of neurons. Synaptic currents cause changes in the potential difference that exists across neuronal membranes and result in the activation of proteins (voltage-gated channels) that, in turn, generate currents of their own. These channels can cause a neuron to generate action potentials. The crux of understanding how groups of neurons execute computations that determine behaviors, then, quickly becomes a matter of understanding current flow in neurons. Currents generated by synapses and voltage-gated channels are considered in detail in later chapters. However, we will reduce the complexity of the problem in this chapter by temporarily ignoring these two sources of currents and focusing on current flow within the neuron itself. We will also simplify the problem by assuming that the neuron is geometrically simple. This will allow us to bring an existing mathematical framework called cable theory to bear on the problem.

The pattern of current flow in a simple, cable-like, neuron is shown in a diagrammatic way in Figure 2-1. The neuron is a cylinder, or cable, and an

excitatory synapse is shown as current flowing into the dendrite of the neuron. Currents occur when the neurotransmitter causes channels in the cell's membrane to open, allowing ions to flow transiently into the cell. The current generated by a synapse flows along the inside of the dendrite. Current also exits the cell along the way by leaking through the membrane. Current then flows

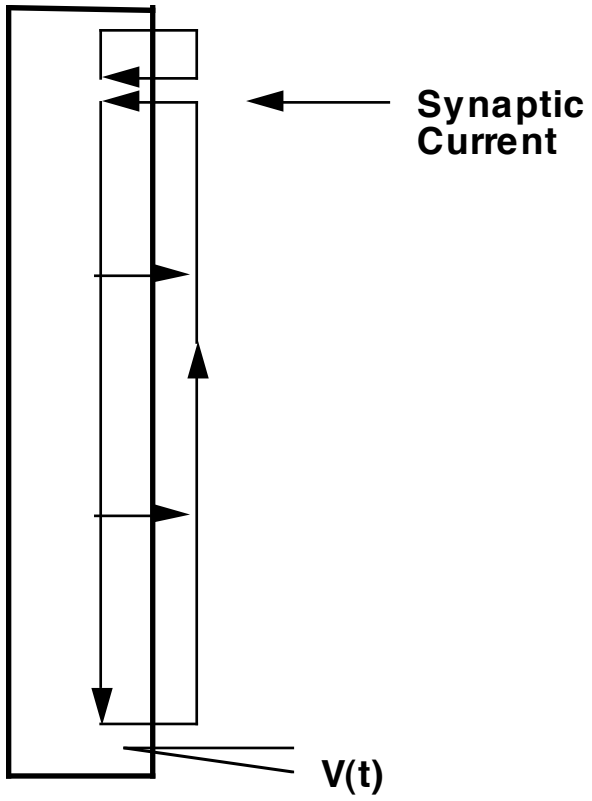


Figure 2-1. Current flow in a neuron. This diagram illustrates how a synapse produces a current flow within an idealized neuron. The neuron is represented as a cable with a finite length. The ends of the cable are sealed so that current cannot exit the two ends. A synapse situated near the top of the cable produces a current that flows into the neuron when it is activated. The current flows in both directions. In particular, current flows down the core of the cable towards the recording electrode. As current leaks through the membrane of the cell near the electrode, it produces a voltage transient, V(t), which is recorded by the electrode. Current which has gained access to the extracellular space surrounding the cable flows back towards the synapse, completing the electrical circuit.

through the extracellular space towards the current sink created by the synapse. Activation of the synapse produces a series of lines of current flow beginning and ending at the synapse. Since current can flow in both directions when it enters the cell, lines are centered around the site of the synapse. This much is common to the current flow produced by synaptic activation in any cell. However, the details of current flow vary from cell to cell and depend explicitly upon its anatomy -- the size and shape of the neuron's soma and dendrites and the sites of active synapses.

To get a feel for the significance of these differences, consider the cases of the CA3 pyramidal cell and a CA1 pyramidal cell. Activation of the mossy fiber system produces current that flows into a CA3 pyramidal cell close to its soma. Some current flows from the proximal dendrite into the apical dendrite while the rest flows into the soma and basal dendrites. Current flowing into the soma has special significance because it activates the voltage-gated sodium channels situated on the soma and axon hillock region and results in an action potential. The density of current flowing out of the membrane decreases along the apical and basal dendrites because less and less current remains in the more distal regions of the dendrites. However, the soma and axon hillock are close enough to the synaptic site to be subjected to relatively dense current flows. The current flowing though the resistance of the soma membrane produces a voltage change, which opens voltage-gated sodium channels.

The pattern of current flow in CA1 pyramidal cells resulting from activation of the Schaffer collateral system is similar, but the synaptic site is more distant from the soma. The density of current per synapse flowing through the somatic membrane is, thus, less than that flowing through the

somata of CA3 pyramidal cells when the mossy fibers are activated. The intuitive prediction is that Schaffer collateral synapses should be less effective in firing the CA1 pyramidal cells than are the mossy fibers in firing the CA3 pyramidal cells.

The problem is to understand how currents -- such as those generated by synaptic activity -- flow through a branched neuron like a pyramidal cell.

STUDYING CURRENT FLOW IN NEURONS

One approach would be to measure the current lines produced around the neuron when synapses become active. This can be done using a method called *current source density analysis* in special cases in which the geometry of the neuron is favorable (see Johnston and Wu, 1995). Pyramidal cells in the isocortex, Purkinje cells in the cerebellar cortex or mitral and granule cells in the olfactory bulb have been studied with current source density analysis. However, current source density analysis is difficult for neurons in which the dendrites do not establish a regular geometric pattern. A second direct approach, which is just now becoming possible, is to visualize the voltage of the neuron's membrane (Zecevíc, 1996). This can be accomplished by injecting a voltage-sensitive dye into a living neuron. These dyes change their optical properties as the voltage of the cell's membrane changes. A current can be injected into the neuron and the resulting changes in membrane voltage visualized directly.

Most work on current flow in neurons has been carried out in a more controlled situation that involves measuring the voltage response of the neuron

to the injection of a known current. Figure 2-2B shows the results of an experiment in which a square current pulse 1 sec in duration was injected into the soma of a neuron. The bottom trace shows the time course of the injected current. The top trace shows the resulting voltage trace recorded from the cell. Notice that the waveform of the voltage response differs from the waveform of the input current. Studies of current flow in neurons attempt to deduce the electrical properties of the neuron from such current traces. Before discussing how they are interpreted, let's first consider how they are obtained.

Early studies were carried out with *in vivo* ("in life") preparations such as the cat spinal cord preparation. However, most contemporary work is done *in vitro* ("in glass") in more reduced preparations. One way to study the electrotonic structure of neurons *in vitro* is to prepare a slice of some region of the nervous system that allows it to be maintained alive in a chamber through which oxygenated Ringer's solution is perfused (Fig. 2-3). The slice is relatively thin to allow oxygen to diffuse into the neurons situated within the slice. Slice preparations are the most common way to study elements of mammalian nervous systems *in vitro* because of the high demand of mammalian nervous tissue for oxygen. They give the investigator precise control of the environment of individual neurons and work particularly well in cortical regions such as the hippocampus in which the neurons are

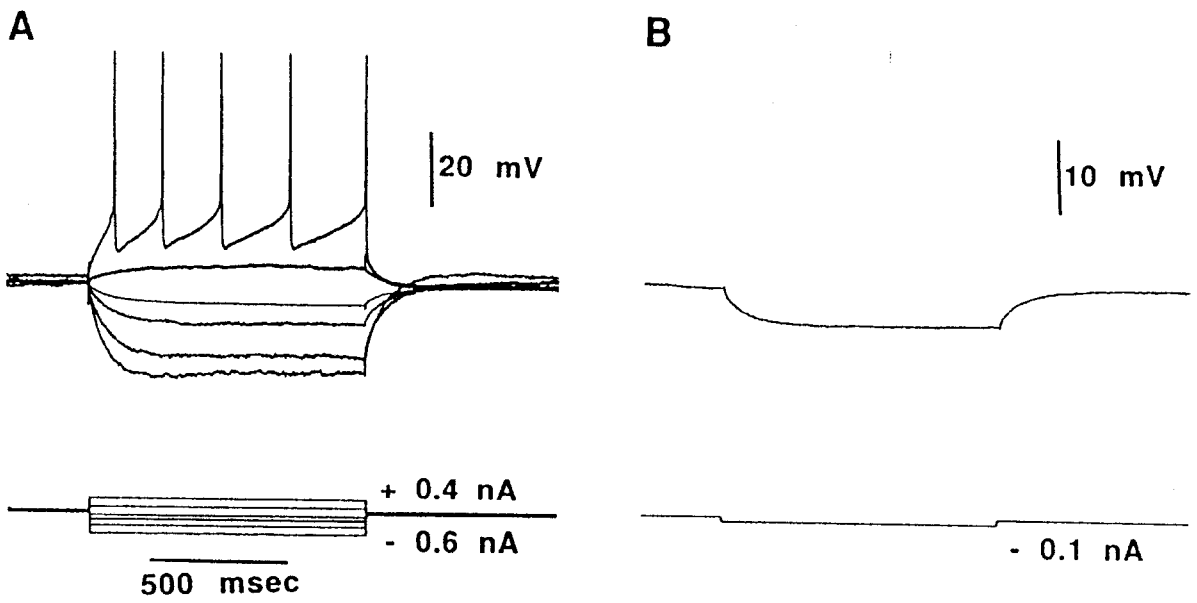


Figure 2-2. Response of a neuron to intrasomatic current injection. This figure illustrates the voltage responses produced by injecting currents into the soma of a pyramidal cell from the visual cortex of a turtle in an *in vitro*. A. The top series of traces show the voltage responses produced by current injections. Six voltage traces are superimposed to facilitate comparison. The top trace contains five action potentials. The lower five traces do not produce action potentials. Notice that the vertical scale bar situated near the top traces represents a voltage deflection of 20 mV. The bottom traces, again superimposed, show the six current traces used to produce the voltage transients shown above. The top current trace has an amplitude of +0.4 nanoamperes (nA); the bottom current trace has an amplitude of -0.6 nA. The horizontal scale at the bottom of the figure represents 500 msec. B. The voltage transient produced by a - 0.1 nA current trace has been isolated and shown at a high gain. A trace like this one would be used to study the current flow within the neuron.

arranged in a regular geometric pattern. The layers of the hippocampus can be visualized in hippocampal slices and the electrode introduced into a particular layer such as the *stratum pyramidale*. If it is desirable to activate a specific fiber system, such as the mossy fibers or the Schaffer collaterals, a stimulating electrode can be placed in the *stratum lucidum* or *stratum lacunosum*. Slices are less advantageous for regions of the nervous system that lack a layered organization or when axon systems run through the slice and are interrupted when the slice is made. The nervous systems of invertebrates and some non-

mammalian vertebrates such as lampreys, frogs or turtles can be maintained *in vitro* in a more intact preparation because of the less stringent dependence on oxygen (Jahnsen, 1990). Axon systems can often be preserved in such preparations and some elements of behavior, such as rhythmic bursts of action potentials, that resemble those present in the intact animal can be obtained in so-called *fictive preparations*.

The first measurements of electrotonic structure were carried out by impaling a neuron with two electrodes. One electrode was used to pass an electrical current into the neuron and the second electrode was used to record the voltage changes induced in the neuron by the current pulse. The problem with this method is that the need to impale a neuron with two electrodes limits the use of the technique to relatively large neurons and makes it difficult to use either *in vivo* or slice preparations in which the neuron to be studied cannot be directly visualized. This limitation can be overcome with electronic switching circuits that allow a single electrode to be used in alternation for passing an electrical current into the cell and then recording the resulting voltage changes.

The introduction of even a single electrode into the cell damages its membrane and raises the possibility that some of the current injected into the cell leaks out around the electrode. A way of circumventing this difficulty is to use *patch clamp electrodes* on whole cells (Fig. 2-4). Patch-

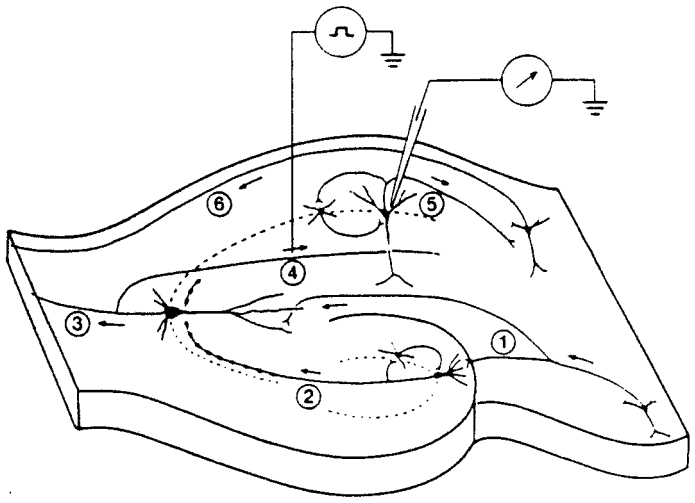


Figure 2-3. Slice preparation. This is a diagram of a slice from the hippocampal formation of a rat. The geometric arrangement of cells within the hippocampus is such that some of the basic features of the hippocampal neural circuits are preserved when making the slice. The axon labeled "2" is a mossy fiber that originates from a granule cell in the dentate gyrus and intersects the apical dendrites of a CA3 pyramidal cell. The axon of this cell is a Schaffer collateral and is labeled "3". It courses within the slice and intersects the apical dendrite of a CA1 pyramidal cells. A stimulating electrode has been placed on the Schaffer collateral at the point indicated "4". The CA1 pyramidal cell has been impaled with a sharp recording electrode. A ground wire is placed in the bath that surrounds the slice. From Bliss and Lømo (1973).

clamp electrodes have large tips that are polished so they adhere to the membrane of the cell when a gentle suction is applied to the electrode (Sakman and Neher, 1983). They were initially used to isolate a patch of the cell's membrane for studies of voltage-gated channels. This will obviously not work for studies of current flow in nelurons because the entire cell must be maintained intact. A variant of the patch-clamp technology is the *whole cell patch-clamp* which applies a patch-clamp electrode to the surface of an intact cell (Blanton et al., 1989; Edwards et al., 1989). Measurements of the electrical properties of neurons can be conducted on isolated cells, cells in slice

preparations or, with more difficulty, *in vivo* and are generally considered to be more accurate than those obtained by impalements with

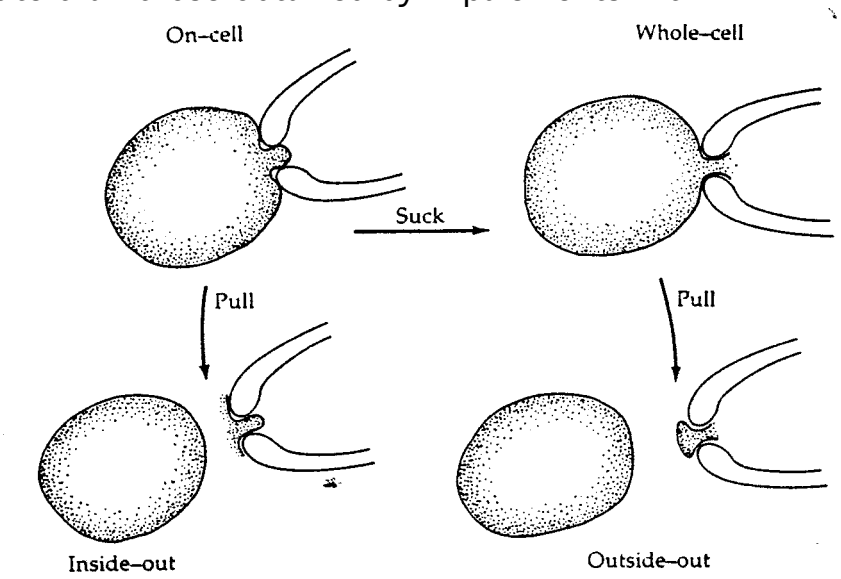


Figure 2-4. Patch clamp recording. Patch clamp recording methods involve attaching either an entire cell or a piece of the cell's membrane to a recording electrode fabricated from a polished glass pipette. The electrode is pressed against the cell and a gentle suction applied (top left) in all cases. For whole cell patch clamp methods, the membrane is ruptured but the cell stays attached to the electrode (top right). Alternatively, patches of membranes can be pulled from the cell in either an inside-out (lower left) or outside-out (lower right) configuration. From Hille (1992).

traditional or "*sharp*" electrodes.

A limitation to whole-cell patch methods is that, although the electrodes form a secure seal with the cell's membrane, they do rupture the membrane so the contents of the cell can diffuse into the electrode. This can be avoided by using *perforated patch clamp methods* in which only small holes are formed in the cell's membrane by exposing the neuron to an antibiotic such as *nystatin* or *amphotericin* (Rae et al., 1991). The biochemical systems inside the neuron are maintained relatively intact in this way. A second limitation is that some isolation or clearing of the soma of the cell is necessary to apply the patch

electrode and this inevitably interrupts synapses that terminate in the vicinity of the soma.

Regardless of how they are achieved, records of the responses of neurons to injected current provide only a limited view of the electrical properties of the cell unless they are accompanied by information on the actual geometry of the cell. One way to obtain the needed information is to compare populations of neurons impregnated via one of the Golgi methods to other populations of neurons characterized in physiological studies. This establishes some correlation between the anatomy and electrical properties of populations of neurons, but does not permit direct correlations of anatomical and physiological properties of individual neurons. It is usually preferable to fill individual neurons with a substance that enables a characterization of their morphology after they have been studied physiologically. Early studies used fluorescent labels such as Lucifer yellow or procion yellow (Kater and Nicholson, 1973). These labels provide a good image of the morphology of the neuron, but are difficult to study in detail because the fluorescence often fades with time. Most workers now use a substance such as horseradish peroxidase or neurobiotin which can be visualized histochemicaly and which does not fade (Horikawa and Armstrong, 1988).

CABLE MODELS OF NEURONS

Having obtained the voltage response of a neuron with known anatomic structure to an injected current, the next step is to relate the voltage response of the cell to its structure. This general problem has been studied extensively over the past several decades. Much of the resulting work is summarized by

Julian Jack, Dennis Noble and Richard Tsien (1975) in a book that should be consulted by readers interested in a complete and mathematically rigorous account of the subject. The treatment here is limited to those results of most interest to the integrative biology of neurons. The central concept is an equation called the *cable equation*, which looks like this:

(2-1) $$\lambda^2 \frac{\partial^2 V}{\partial x^2} - \tau \frac{\partial V}{\partial t} - V = 0$$

It contains partial derivatives and is, therefore, a partial differential equation or "PDE".

Deriving the cable equation

A satisfactory account of current flow in neurons must ultimately include the details of their geometry. However, it is useful to begin with the idealized case of a neuron that has a finite diameter but is infinitely long, or has a length very much greater than its diameter. The axons of neurons meet this requirement and were the initial focus of studies of current flow in neurons. The appeal of the approach is that it allows the application of an equation introduced in the 19th century to describe the voltage changes in a trans-Atlantic telephone cable as a result of current being injected at some point along its length. Several assumptions are needed for the derivation of the cable equation. Some can be relaxed (see Rall, 1977) with the consequence of more complex equations. One assumption is that the neuron is maintained in a solution that is *isopotential* or has the same voltage throughout. This will generally be the case if the neuron is isolated in an *in vitro* preparation, but will

usually not be the case if it is in an intact nervous system surrounded by other neurons. A second assumption is that the resistance of the membrane of the neuron and the resistance of its cytoplasm are the same at all points along its length. This is seldom the case, and it will be necessary to deal with the issue of variable membrane properties later. Finally, all of the ligand-gated and voltage-gated conductances present on the neuron are being ignored for the time being. Using these assumptions, it is possible to derive an equation that describes the flow of current in a cable. We begin by establishing a coordinate system in which to work and defining the quantities that can be measured experimentally.

Establishing a spatial coordinate system. The anatomic structure of a neuron is important because it determines the pattern of connections that the neuron has with other neurons. The pyramidal cells in the CA1 region of the hippocampus, for example, receive synaptic inputs from the Schaffer collaterals because their apical dendrites extend into the *stratum lucidem*. Spinal motoneurons receive particular patterns of synapses from the collaterals of Ia afferents because their dendrites extend in columnar arrangements in the ventral horn of the spinal cord. The three dimensional arrangement of dendrites, however, has no bearing on the flow of current through the neuron, which is determined only by the sizes and branching patterns of the dendrites and the dimensions and shape of the soma. We will deal shortly with the complexities that result from variations in the sizes of somata and dendrites. However, we are considering for the moment a neuron that is infinitely long and has a constant diameter. A coordinate system can be established by aligning this neuron along the x-axis and designating an origin at $x = 0$ (Fig. 2-5). Distance from the origin can then be measured in positive and negative

directions from the origin. The cable is a cylinder with length l, diameter d and radius r. It has a surface area given by $A = \pi dl = 2\pi rl$. By convention, properties of the cable are given in terms of centimeters (cm) or centimeters squared (cm^2). This is actually not a convenient choice because most neuronal parts are only a fraction of a centimeter in length and it would be more reasonable to express these in terms of microns (μm) or microns squared (μm^2). Nonetheless, it is the convention to use centimeters and useful to remember that 1 μm = 10^{-4} cm. Since it will be necessary to define the derivatives in the cable equation, we divide the cable into pieces of finite lengths, $\Delta x = x_2 - x_1$, where x_1 and x_2 are two points along the cable, and then take the limit as $\Delta x \to 0$.

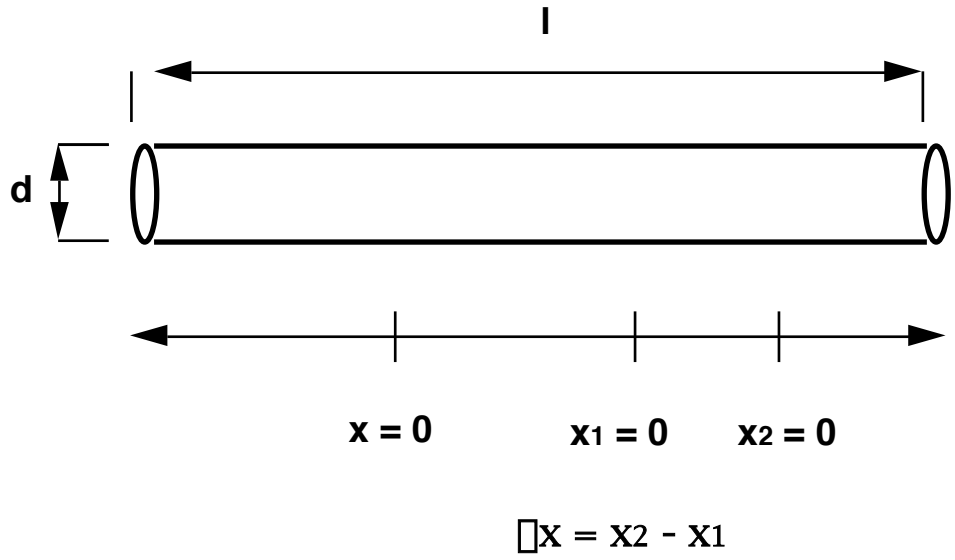


Figure 2-5. Spatial coordinate system. This figure shows a spatial coordinate system established to study a cable with diameter, d, and length, l.

Voltage. One quantity measured experimentally is the voltage or *potential difference* between the inside and outside of the neuron at some

particular point in the neuron, typically the soma (Fig. 2 – 6). A fundamental property of neurons is that they have a resting membrane potential, E_r, which results from a balance of the forces causing ions to diffuse across the membrane and the electrostatic forces causing charge to be equalized on both sides of the membrane. The value of E_r is determined by the *Goldmann-Hodgkin-Katz equation*

(2-2) $$E_r = \frac{RT}{F} \ln \frac{P_{K+}\left[K^+\right]_o + P_{Na+}\left[Na^+\right]_o + P_{Cl-}\left[Cl^-\right]_i}{P_{K+}\left[K^+\right]_i + P_{Na+}\left[Na^+\right]_i + P_{Cl-}\left[Cl^-\right]_o}$$

which expresses the resting membrane potential of a cell in terms of the interior (e.g. $\left[K^+\right]_i$) and exterior (e.g. $\left[K^+\right]_o$) concentrations of sodium, potassium and chloride ions and their respective permeabilities (e.g. P_{K+}). T is the temperature in degrees Kelvin, R is the natural gas constant and F is Faraday's constant. This equation is derived and discussed in all textbooks on cellular neurobiology (e.g. Johnston and Wu, 1995). Resting membrane potentials vary, with values of - 40 to - 80 mV being typical. An experimental measurement of the electrotonic properties of a neuron involves injecting a current into the neuron and measuring the change in the membrane potential. The value of interest is the difference between the membrane potential and resting membrane potential. This quantity is given by $V = V_i - V_e - E_r$. V_i is the electrical potential of the interior of the neuron, measured in mV, and V_e is the electrical potential of the solution bathing the neuron. Prior to the current injection, the potential difference between the exterior and interior of the neuron is equal to the resting membrane potential. Thus, $V_i - V_e = E_r$ and $V = 0$. The membrane potential, V, deviates from E_r following the current injection and will have non-zero values that vary along the length of the neuron. The value of V also varies

with time during the course of the experiment. Thus, $V = V(x,t)$. If the time at which the current injection begins is defined as $t = 0$, then time, t, during the experiment is usually measured in msec.

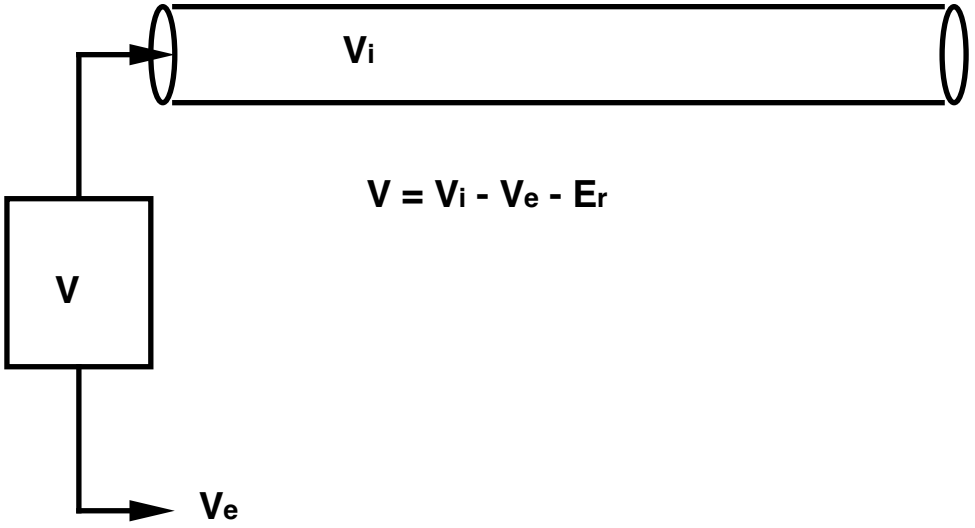


Figure 2-6. Membrane voltage. A voltmeter is used to record the potential difference between the interior of the cable and the bath fluid in which the cable is immersed.

Since the membrane potential is a function of both distance along the cable and time, we can define two derivatives of $V(x,t)$. The partial derivative $\partial V / \partial x$ is obtained by measuring the value of $V(x,t)$ at two points, x_1 and x_2 along the cable at time t. The ratio $\Delta V / \Delta x$ expresses the difference of membrane potential at the two points and the partial derivative is obtained by taking the limit of the ratio as $\Delta x \to 0$. Alternatively, we can measure the value of $V(x,t)$ at the same point along the cable at two different times, t_1 and t_2 and obtain the partial derivative $\partial V / \partial t$ by taking the limit of the ratio $\Delta V / \Delta t$ when $\Delta t \to 0$.

Resistances and conductances. Before we can relate $V(x,t)$ and the partial derivatives $\partial V/\partial x$ and $\partial V/\partial t$ to current flows within the cable, we need to discuss three other quantities. The first two are resistance and conductance, which are reciprocals of each other. Resistance is a measurement of impedance, or the ability of substances to reduce the magnitude of currents flowing through them. A structure with infinite resistance allows no current to flow through it; a structure with zero resistance provides no impediment to current flow. The resistance of a structure is measured in *ohms*. Conductance is the inverse of resistance. A structure with infinite resistance has zero conductance, and *vice versa*. Conductance used to be measured in reciprocal ohms or ohms^{-1}, but is now measured in units of *Siemens*. One Siemen is equal to one reciprocal ohm: 1 S = □$^{-1}$.

Resistances and conductances determine the relationship between voltage and current for many structures. Such structures conform to Ohm's law and are said to be *ohmic*. It is important to understand that many (most, actually) structures do not conform to Ohm's law and are *non-ohmic*. The voltage-gated channels universally present on neurons give neurons non-ohmic properties. Since we are ignoring these channels for the moment, the cable we are describing can be considered an ohmic structure that conforms to Ohm's law. This law can be expressed in two equivalent forms. The most familiar is that the difference in voltage between the two ends of a cylinder of length, Δx, is given by $V = IR$ where I is the current flowing through the cylinder in *amperes* or amps (A) and R is the resistance in ohms. If g is the conductance of the cylinder, Ohm's law can easily be rewritten as $I = gV$, where $g = 1/R$. Both forms of Ohm's law are in common use and it is important to be able to switch between them.

Two resistances are associated with neuronal structures. One is the *core* or *axial resistance*, which is the resistance of the cytoplasm inside the neuron. The second is the *membrane resistance*, which is the resistance of the membrane bounding the neuron. The two resistances are quite different and the axial resistance is always much smaller than the membrane resistance. Thus, a current entering the neuron will tend to flow easily throughout the neuron. It is possible, but more difficult, for current to leak through the membrane into the extracellular space. The convention adopted in modeling cables is to define resistances in terms of a cable of uniform diameter, d, and express axial and membrane resistances per unit length of the cable. Resistances with a unit length of the cable are designated by lower case letters: r_a and r_m. These are the resistances of the core (axial resistance) and membrane (membrane resistance) of a segment of the cable one unit in length, respectively. The resistances associated with unit areas are called *specific resistances* and are designated by upper case letters: R_a and R_m. R_a is the resistance across a unit cross-sectional area of the internal medium. R_m is the resistance across a unit area of membrane. R_a and R_m are more useful for general biophysical treatments of neurons because they do not require assumptions about the geometry of the neuron.

Looking first at the axial resistance, imagine that the cable is made up of several segments hooked up end-to-end. Each volume of the cable has a certain resistance and current flows in *series* through the sequence of segments. The resistance associated with any two of the elements is the sum of the two individual segments, or $2r_a$, and the resistance associated with the entire length of the cable is the sum of all of the individual resistances. Thus,

we obtain the axial resistance of a cable with length, Δx, by multiplying the axial resistance per unit length by Δx: $r_a \Delta x$. To relate R_a to r_a, divide R_a by the surface area of the end of the cable to obtain r_a. If the cable has a diameter of d, its radius is $d/2$, the surface area of the end of the cable is $\pi d^2/4$ and

(2-3) $$r_a = \frac{4R_a}{\pi d^2} \quad .$$

r_a has units of Ω/cm and R_a has units of Ω cm. A specific axial resistance of R_a = 100 Ω cm is typical for many neurons.

Turning to the membrane resistance, notice that we can think of the surface of the cable as made up of a number of patches of membrane, each with a unit area. Any current inside of the cell can leak out of all of the patches, so a fraction of current inside of the cell is leaking through each patch of membrane. The membrane resistance is, thus, composed of individual resistors which are in *parallel*. The rule for adding together resistors arranged in parallel is to add the reciprocals of the resistors. If the N resistors have resistances of $R_1, R_2, ..., R_N$, then the total resistance, R_T, is given by

(2-4) $$\frac{1}{R_T} = \sum_{ik=1}^{N} \frac{1}{R_k} \quad .$$

Because of the rule for adding parallel resistors, we obtain the total resistance of the membrane by dividing (rather than multiplying) the specific membrane resistance by the surface area. We can find the membrane resistance per unit length, r_m, by dividing the specific membrane resistance per unit area, R_m, by the circumference (πd) of the cylinder:

(2-5) $$r_m = \frac{R_m}{\pi d} \quad .$$

r_m has units of Ω cm and R_m has units of Ω cm^2. A typical value for R_m is 100,000 Ω cm^2 or 100 kiloohms·cm^2 (100 kΩ cm^2). A useful relationship is that the ratio $r_m / r_a = (R_m / R_a)(d/4).$

Capacitance. The last concept we need before considering the cable equation is that of *capacitance*. Capacitance is the tendency for a structure to store electrical charge. In our case, the membrane of the neuron has a capacitance due to its chemical composition. Capacitance is the charge across the membrane divided by the voltage across the membrane, $C = Q/V$, where Q is charge measured in coulombs and V is potential measured in volts. The unit of capacitance is the Farad, F, which has dimensions of coulombs per volt. The capacitance per unit length, c_m, of the membrane of the cable is expressed in units of F/cm. The specific capacitance, C_m, is the capacitance per unit area and has units of F/cm^2. The relationship between c_m and C_m is $c_m = C_m \pi d$. The total capacitance of two or more capacitors arranged in parallel is calculated by adding together the individual capacitances

(2-6) $$C_T = \sum_{k=1}^{N} C_k$$

A typical value for the specific capacitance per unit area of a biological membrane is 1 μF/cm^2.

Like resistance and conductance, the concept of capacitance expresses a relationship between voltage and current. The relationship is obtained by rewriting the definition of capacitance as $CV = Q$ and taking the derivative of both sides of the equation with respect to time

(2-7) $$\frac{d}{dt}[CV] = C\frac{dV}{dt} = \frac{dQ}{dt}.$$

Since we can consider the capacitance of the membrane to be a constant, it was removed from the brackets. Also, notice that the derivative of charge is the rate at which charge is changing, which is the definition of *current*. Thus, $dQ/dt = i_c$, where i_c is the *capacitive current*. Rewriting Equation (2-7) gives

(2-8) $$C\frac{dV}{dt} = i_c$$

This equation establishes a relationship between the capacitive current and the rate at which voltage is changing. The current flowing across the capacitor is small if the voltage is changing slowly, but large if the voltage is changing rapidly. For a cable of unit length

(2-9) $$i_c = c_m\frac{dV}{dt}$$

Currents. Injecting a current into a cable produces two currents (Fig. 2-7). The first is the *axial* or *core* current, which flows within the neuron, and the second is the *membrane current,* which flows through the membrane. A quantitative description of current flow in the neuron must proceed in three steps. The first is to describe the axial current, the

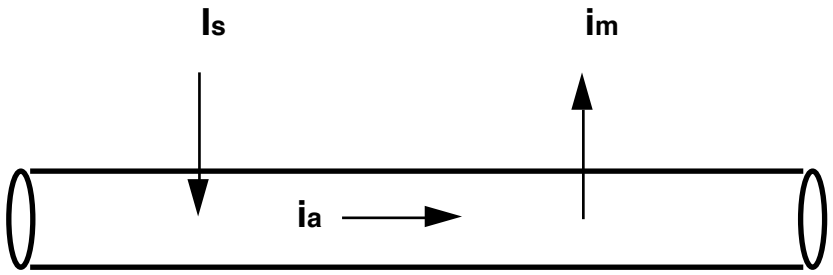


Figure 2-7. Currents in a cylinder. A stimulating current, I_s, produces an axial current, i_a, and a membrane current, i_m, in the cylinder.

second is to describe the membrane current and the third step is to relate the axial current to the membrane current. Let's consider each of these steps in sequence.

The axial current, i_a, is determined using Ohm's law and the rules for calculating series resistance. What we need is the current flowing through a cylinder of length Δx and axial resistance, r_a. If the potential difference between the two ends of the cylinder is $V_2 - V_1 = \Delta V$, then

(2-10) $$\Delta V = -i_a r_a \Delta x \quad .$$

(Notice that a minus sign has appeared because we defined ΔV as $V_2 - V_1$ but expressed the potential difference as $V_1 - V_2$). Dividing both sides of the equation by Δx gives

(2-11) $$\frac{\Delta V}{\Delta x} = -i_a r_a \quad .$$

The axial current can then be expressed in terms of a partial derivative of the voltage by taking the limit as $\Delta x \to 0$ and rearranging the equation

(2-12) $$i_a = \frac{-1}{r_a}\frac{\partial V}{\partial x} \quad .$$

The membrane current, i_m, is the current flowing through the membrane of the cylinder. It has two separate components, a resistive component and a capacitive component. Thus, there are two routes by which a current can flow. One is a conductor with a membrane conductance of $g_m = 1/r_m$, and the other is a capacitor with membrane capacitance, c_m. If we express the current flowing through the conductor in terms of resistance and use Ohm's law we obtain

(2-13) $$i_r = \frac{V}{r_m} \quad .$$

We already know that the capacitive current is given by

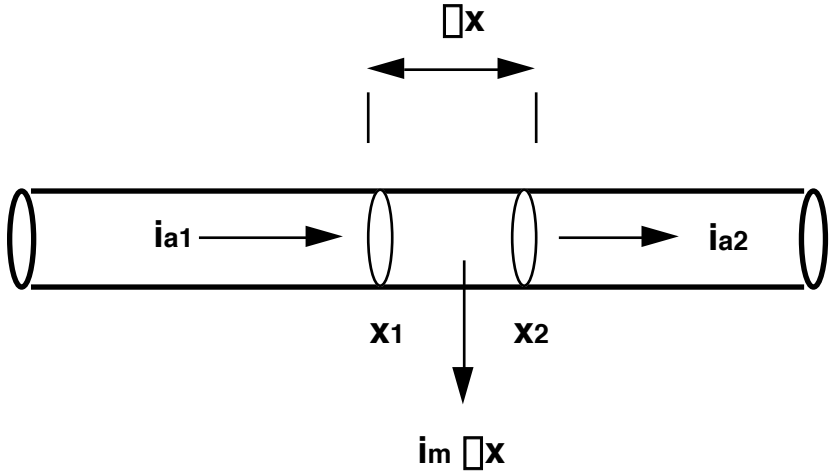
(2-14) $$i_c = c_m \frac{\partial V}{\partial t} \quad .$$

The total current flowing through the membrane is the current flowing through the conductive (resistive) component of the membrane plus the current flowing across the capacitive component of the membrane

(2-15) $$i_m = i_r + i_c = \frac{V}{r_m} + c_m \frac{\partial V}{\partial t} \quad .$$

The final step in deriving the cable equation is to determine the relationship between the axial current and the membrane current (Fig. 2-8). To do this, we take advantage of the principle that *current is conserved*: it can neither be created nor destroyed. If current is flowing through the cable from left to right, then the amount of current that enters the cable through its left side must equal the current that leaves the interior of the cylinder by passing through the membrane bounding the cylinder (the membrane current) plus the current that proceeds through the cylinder and exits through its right side. In a hypothetical case in which the membrane had infinite resistance, no current would leak through the membrane and the amount of current that enters from the left would be exactly equal to the amount of current that exits from the right. If the resistance of the membrane is finite, then some current will leak out of the membrane as it passes through the cylinder. The amount of current exiting the cylinder from its right side will be less than the amount that enters from its left side.

This idea can be expressed in quantitative terms by defining *current density* or the amount of current passing through a unit area. The current



$$i_m \Delta x = i_{a1} - i_{a2} = -\Delta i_a$$

Figure 2-8. Relationship between membrane and axial current. The density of current entering the left side of the small cylindrical segment of the cable is given by i_{a1}. The density of current exiting the right side of the cylinder is given by i_{a2}. The difference between these two quantities is equal to the current lost due to leakage of current through the membrane.

density at the left side of the cylinder is obtained by dividing the axial current at point x_1 by the cross-sectional area of the opening of the cylinder: i_{a1}. Similarly, the current density at the exit of the cylinder is i_{a2}. Since we assumed at the outset that the diameter of the cylinder is constant, the difference between the amount of current entering the cylinder at the left and exiting the cylinder at the right is $\Delta i_a = i_{a2} - i_{a1}$. This difference would be zero were the membrane resistance infinite, but it actually decreases along the length of the cylinder because current leaks out of the cylinder at each point on the membrane. We obtain the rate at which the axial current is decreasing for each increment, Δx, of cylinder by dividing Δi_a by Δx and converting this into a spatial derivative by taking the limit of $\Delta i_a / \Delta x$ as $\Delta x \to 0$.

(2-16) $$\lim_{\Delta x \to 0} \frac{\Delta i_a}{\Delta x} = \frac{\partial i_a}{\partial x} \quad .$$

The principle of continuity requires that the rate at which the axial current decreases within each increment of the cylinder equals the amount of current leaking through the membrane surrounding that increment of cylinder. Thus, $-\partial i_a / \partial x = i_m$, and

(2-17) $$\frac{\partial i_a}{\partial x} + \frac{V}{r_m} + c_m \frac{\partial V}{\partial t} = 0 \quad .$$

If we then substitute the relationship between axial current and the spatial derivative for voltage (Equation 2-12) into Equation (2-14), we obtain

(2-18) $$\frac{\partial i_a}{\partial x} = \frac{\partial}{\partial x}\left(-\frac{1}{r_a}\frac{\partial V}{\partial x}\right) = -\frac{1}{r_a}\frac{\partial^2 V}{\partial x^2}$$

and, finally, have a form of the cable equation

(2-19) $$\frac{1}{r_a}\frac{\partial^2 V}{\partial x^2} - c_m\frac{\partial V}{\partial t} - \frac{1}{r_m}V = 0 \quad .$$

This is a second order, partial differential equation that expresses the rate at which membrane potential, $V(x,t)$, is changing as a function of distance along the cable, time and the geometric and electrical properties of the cable.

Alternative forms of the cable equation. The cable equation is seldom used in this form and is typically expressed in one of two more compact forms. The first is obtained by defining parameters called the *space constant* or *characteristic length*, $\lambda = \sqrt{r_m / r_a}$, and the *time constant*, $\tau = c_m r_m$. Notice that the space constant is the ratio of the membrane and axial resistances and reflects how much current leaks out of the cable as current flows through the interior of the cylinder. If r_m is zero, current leaks quickly out of the cylinder and $\lambda = 0$. If r_m is infinite, no current can leak out of the cylinder and λ is also infinite. Real neurons, of course, have values of λ somewhere between zero and infinity. The time constant depends entirely upon the two electrical properties of the membrane, the membrane resistance and membrane capacitance.

The dimensions of the two constants are important. λ is expressed in units of length (centimeters or microns). To see this, note that

$$\lambda = \sqrt{\frac{r_m}{r_a}} = \sqrt{\frac{R_m}{R_a}\frac{d}{4}} \quad . \tag{2-20}$$

$$\left(\frac{(\Omega\, cm^2)(cm)}{(\Omega\, cm)}\right)^{1/2} = cm$$

τ is expressed in units of time (sec or msec). To see this, note that

$$\tau_m = c_m r_m = (C_m \pi d)\left(\frac{R_m}{\pi d}\right) = C_m R_m \tag{2-21}$$

$$\left(\frac{F}{cm^2}\right)(\Omega\, cm^2) = (F)(\Omega) = \left(\frac{Coulomb}{V}\right)\left(\frac{V}{A}\right) = (Coulomb)\left(\frac{Coulomb}{\sec}\right)^{-1} = \sec \quad .$$

The cable equation can be rewritten in terms of the space and time constants as

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} = \tau \frac{\partial V}{\partial t} + V = 0 \quad . \tag{2-22}$$

You should verify that each term in the equation has units of volts.

A second alternative expression of the cable equation is obtained by eliminating dimensions of space and time from the equation altogether. We do this by defining *electrotonic distance,* X, and *normalized time,* T. The membrane potential, $V(x,t)$, at point, x, along the cylinder at time, t, is expressed in terms of electrotonic distance and normalized time by substituting

$x = \lambda X$ and $t = \tau T$ into Equation (2-22) and obtaining a function, $V(X,T)$, of X and T. Equation (2-22) can then be written as

(2-23) $$\frac{\partial^2 V}{\partial X^2} - \frac{\partial V}{\partial T} - V = 0 \quad .$$

Again, each term in the equation has units of volts.

Solving the Cable Equation

The three versions of the cable equation express the membrane potential at each point on the cable in terms of the geometry of the cable (specified by its diameter) and its electrical properties (specified by λ and τ). Solutions to the equations allow us to predict the voltage response of the cable to an arbitrary current input at some point along its length. The ideal situation would be if we could use the cable equation to interpret experiments in which currents are injected into neurons of known geometry by solving the cable equation. That is, finding a function $V(x,t)$ or $V(X,T)$, that satisfies the equation for a particular neuron. Finding a solution in a *closed* or *analytic form* is prohibitively difficult for most real neurons, but analytic solutions can be obtained for instructive, simple cases. We will discuss four cases here; others are considered by Jack et al. (1975) and by Rall (1977). Our discussion proceeds from a relatively unrealistic example through progressively more realistic cases and concludes with a method of studying the electrotonic properties of real neurons. The analysis of the simpler cases introduces the important concept of electrotonic length.

Infinite cable,space-clamped case. The simplest case involves an infinitely long cable of constant diameter, $d = 2r$, with the origin defined at $x = X = 0$ (Fig. 2-9A). We place a charge, Q_o, instantaneously and evenly along the length of the cable (Fig. 2-9B). The charge causes a current to flow through the resistance of the membrane, resulting in a membrane potential of V_o at time $T = 0$. Since the membrane potential is the same at all points along the cable, the first and second partial derivatives of $V(X,T)$ with respect to X are zero because the membrane potential does not vary as a function of X. $V(X,T)$ is then effectively a function, $V(T)$, of only T and the partial derivative $\partial V(T)/\partial T$ is equivalent to the ordinary derivative, $dV(T)/dT$. The cable equation (Equation 2-19) simplifies to the ordinary differential equation (or "ODE").

(2-24) $$-\frac{dV(T)}{dT} - V(T) = 0 \quad \text{or} \quad \frac{dV(T)}{dT} = -V(T) \ .$$

The task is to find a function of T that satisfies this equation. Begin by multiplying both sides of the equation by dT, divide both sides by $V(T)$ and then rearrange

(2-25) $$\frac{dV(T)}{V(T)} = -dT \ .$$

Both sides of the equation can now be integrated. The integrals will be definite integrals and the limits of the integration must be specified. A natural choice is to integrate the right hand side of the equation from 0 to T. The equivalent limits for the left hand side of the equation will then be the value of the membrane potential at time $T = 0$, which is V_o, and the value of the membrane potential at time T, which is $V(T)$:

(2-26) $$\int_{V_o}^{V(T)} \frac{dV(T)}{V(T)} = \int_0^T dT \quad .$$

The integral on the right is simple; the integral on the left can be evaluated by remembering that the integral of dy/y is $\ln(y)$ or the natural logarithm of y. Thus,

(2-27) $$\int_{V_o}^{V(T)} \frac{dV(T)}{V(T)} = \ln[V(T)]\Big|_{V_o}^{V(T)} = \ln[V(T)] - \ln[V_o] \quad .$$

Using the rule for subtracting logarithms

(2-28) $$\ln\left[\frac{V(T)}{V_o}\right] = \int_0^T dT = T\Big|_0^T = T + 0 = T \quad .$$

If we take the antilogarithm of both sides of Equation (2-28), we finally obtain

(2-29) $$V(T) = V_o e^{T} \quad \text{or} \quad V(t) = V_o e^{t/} \quad .$$

It is easy to verify this is a solution to Equation (2-25) by calculating the derivative of $V(T)$ with respect to dT and substituting the result into Equation (2-25)

$$\frac{dV(T)}{dT} = V(T)$$

(2-30) $$\frac{d}{dT}\left[V_o e^{T}\right] = V(T)$$

$$\Delta V_o e^{-T} = \Delta V_o e^{-T} \quad .$$

This solution predicts the membrane potential of the cable at each point in time following the application of a charge, Q_o, along the length of the cable. It shows that the time dependence of the membrane potential is determined entirely by the electrical properties of the membrane, r_m and c_m. Figure 2-17C is a plot of $V(t)$ as a function of t; Figure 2-17D is a plot of the same relationship, except that $\ln[V(t)/V_o]$ has been plotted as a function of t, so that the plot is now a straight line with slope equal to $-1/$. Larger values of r_m or c_m lead to a larger value of the membrane time constant and a slower decline in the value of the membrane potential. This relationship can

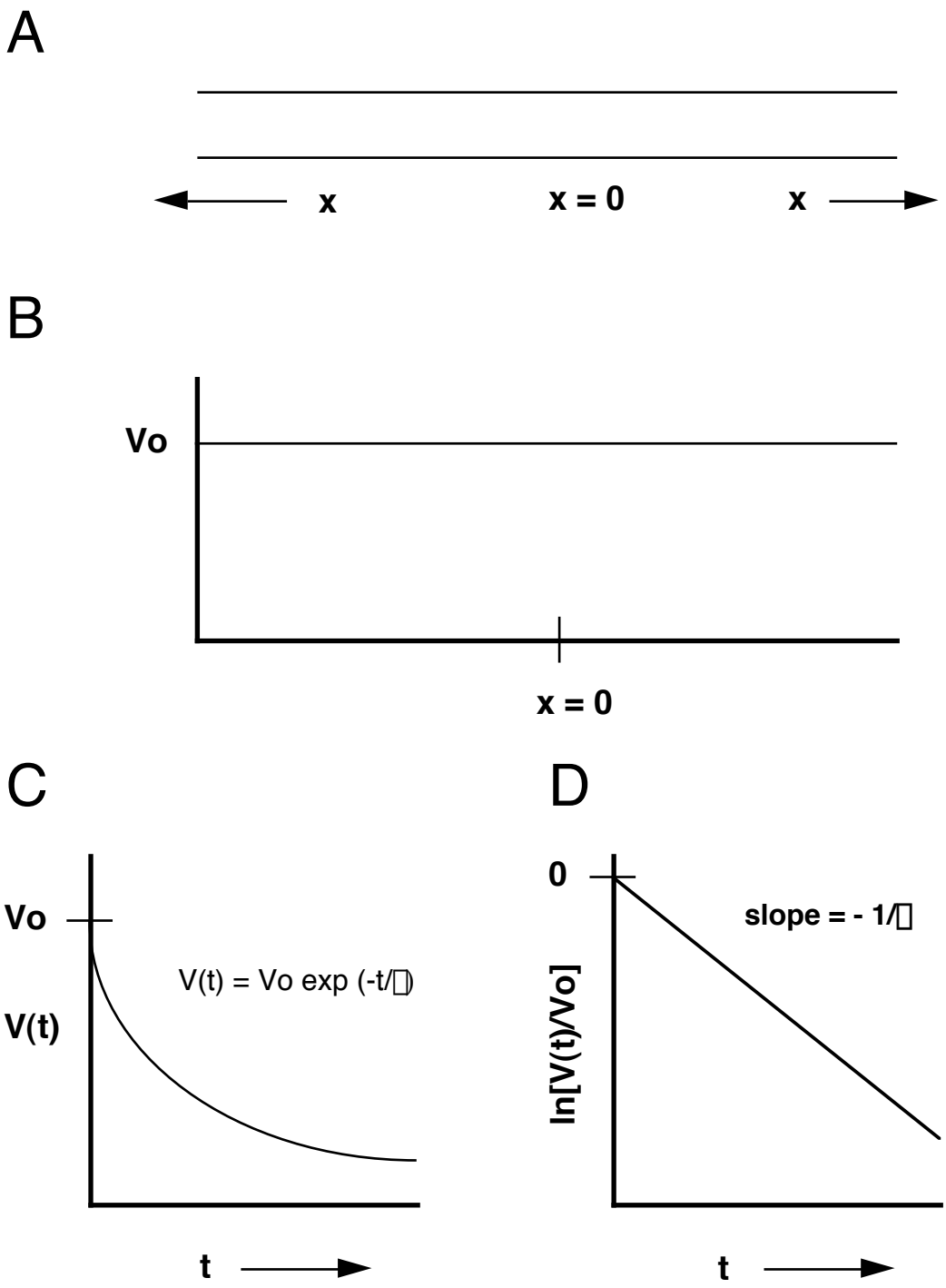


Figure 2-9. Solution of the cable equation for the infinite cable, space clamped case. A. An infinite cable centered on the origin. B. The initial voltage across the membrane of the cable plotted as a function of distance along the cable. C. The membrane potential plotted as a function of time. D. Semi-logarithmic plot of the membrane voltage.

be used to measure the membrane time constant in experimental situations. For example, an approximately uniform charge can be applied to a large axon such as that found in squid by placing a wire along the length of the axon in a bath of saline solution. The membrane potential is then measured at a series of time intervals and the value obtained at each time divided by V_o. The data are transformed by calculating $V(t)/V_o$ for each time interval and then plotting $\ln\left[V(t)/V_o\right]$ as a function of time. The slope of this plot is the reciprocal of the time constant.

Semi-infinite cable, steady state case. Now let's consider a situation in which some device is delivering a constant current at a point $X = 0$ on a cable that is semi-infinite. That is, the cable is defined only to the right of the origin. The cable develops a constant voltage, V_o, at $X = 0:\ V(0) = V_o$ (Fig. 2-10B). Current flows to the right along the cable. It leaks out of the membrane at each point, producing a voltage, $V(T)$. We expect that $V(X)$ decreases along the cable because current is being lost as it flows along the cable, so a smaller amount of current flows through each successive patch of membrane and produces a smaller voltage. How fast is this decline ? To answer the question, we return to the cable equation (Equation 2-23) and assume $V(X,T)$ can be expressed as the product of two functions $V(X,T) = u(X)v(T)$. This method is called *separation of variables*. $v(T)$ is a constant in this case because the current is being constantly applied to the cable at $X = 0$ to maintain a steady voltage and we can simply set $v(T) = 1$. The calculus exercise of evaluating the partial derivatives of $V(X,T)$ gives

$$\frac{\partial V(X,T)}{\partial X} = \frac{\partial}{\partial X}u(X)v(T) = \frac{du(X)}{dX}$$

(2-31) $$\frac{\partial^2 V(X,T)}{\partial X^2} = \frac{d^2 u(X)}{dX^2}$$

$$\frac{\partial V(X,T)}{\partial T} = \frac{\partial}{\partial T} u(X)v(T) = u(X)\frac{dv(T)}{dT} = 0$$

Substituting these derivatives into the cable equation gives

(2-32) $$\frac{d^2 u(X)}{dX} - u(X) = 0 \quad .$$

We approach the solution of Equation (2-32) by introducing the concept of an *operator*. An operator is a mathematical entity that changes (or "operates" on) a function. An operator designated as O, for example, would change one function of x, $y(x)$, to a new function of x, $z(x)$. This is written $Oy(x) = z(x)$ and is actually a familiar concept because taking the derivative of a function changes it into a new function. We define an operator $D = d/dx$ and write $Du(X) = du(X)/dX$. Operators can often be treated as algebraic entities, so Equation (2-32) can now be expressed in the compact form

(2-33) $$D^2 u(X) - u(X) = 0 \quad .$$

where $D^2 = d^2/dx^2$. Written in a slightly different way, this is

(2-34) $$(D^2 - 1)u(X) = 0$$

where it is understood that the terms on the left must be multiplied together before working with them. We use the rule for factoring a difference of squares from algebra and write

(2-35) $$(D-1)(D+1)u(X)=0 \ .$$

Equation (2-35) has three solutions. The first is that $u(X)=0,$ which is a valid solution from a mathematical viewpoint, but is uninteresting from a biological viewpoint because it corresponds to the case in which there is no potential and no current passing into the cable. We choose to discard this solution. The other two solutions are

(2-36) $$(D-1)u(X)=Du(X)-u(X)=0 \quad \text{and} \quad (D+1)u(X)=Du(X)+u(X)=0$$

which correspond to

(2-37) $$\frac{du(X)}{dX}=-u(X) \quad \text{and} \quad \frac{du(X)}{dX}=+u(X) \ .$$

Notice that this equation is the same as Equation (2-26) except that it contains $u(X)$ rather than $V(T)$, so we can simply write down that the solutions are

(2-38) $$u(X)=ae^{+X} \quad \text{and} \quad u(X)=be^{-X} \ .$$

where a and b are constants of integration. We can use them both and construct a *general solution* to the equation:

(2-39) $$u(X) = ae^{+X} + be^{-X}$$

You should check that this is actually a solution to Equation (2-32) by differentiating $u(x)$ and substituting it into Equation (2-32). However, it is necessary to evaluate the two constants in the equation to obtain a specific solution that fits the details of our particular case. First, note that $u(X)$ becomes infinite, or unbounded, as X tends towards infinity. This is acceptable mathematically, but makes no intuitive sense. We remedy this by setting $a = 0$. Next, recall that $u(X)$ should equal V_o when $X = 0$. Thus,

(2-40) $$V(0) = u(0) = be^0 = V_o \quad \text{and} \quad b = V_o \ .$$

Recalling that $X = x/\lambda$, the final solution to the equation for an infinite cable with a steady-state voltage of V_o at $X = 0$ is

(2-41) $$V(x) = V_o e^{-x/\lambda} \ .$$

The solution is shown in graphical form in Figure 2-10C. The rate at which the voltage declines along the cable is specified by the space constant, λ. The larger the value of λ, the more slowly the voltage falls off. We can calculate λ by measuring $V(X)$ along the cable and plotting $\ln[V(X)/V_o]$ as a function of X (Fig. 2-10D).

Finite cable with sealed ends, steady state case. To make the situation more realistic, let's now consider the problem of understanding current flow in a cable of constant diameter, d, and *finite* length, l, (Fig. 2-

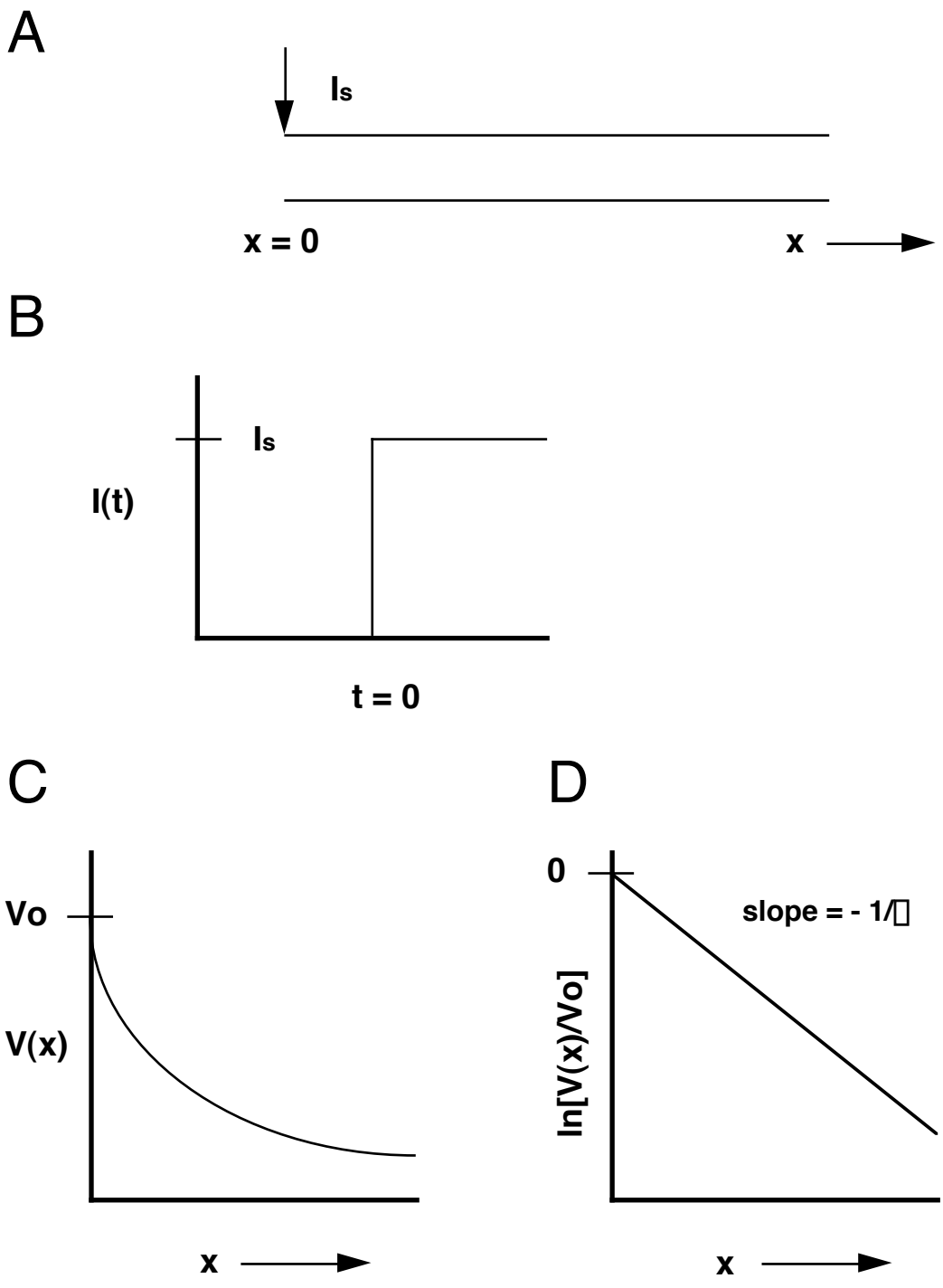


Figure 2-10. Solution of the cable equation for the semi-infinite cable, steady-state case. A. Semi-infinite cable with its left end at the origin. B. Stimulating current plotted as a function of time. C. Membrane potential as a function of distance along the cable. D. Semi-logarithmic plot of membrane potential.

11A). We specify that $X = 0$ at the left end of the cable. A new entity, the *electrotonic length* of the cable is defined to be $L = l / \lambda$ and the anatomic length of the cable is then $l = \lambda L$. Apply a constant current at the left end of

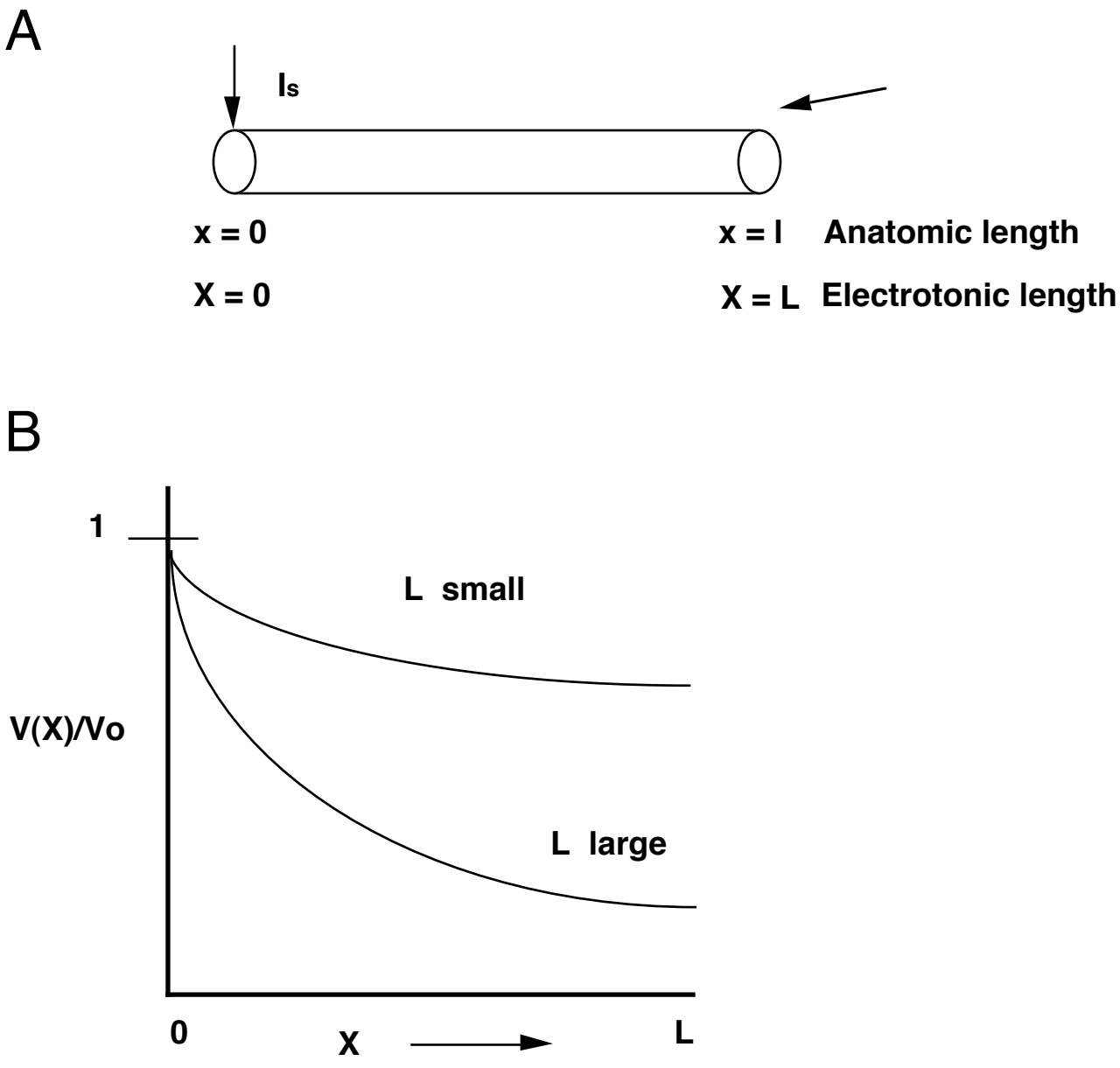


Figure 2-11 Finite cable with sealed ends, steady state case. A. finite cable with sealed ends. The left end of the cable is at the origin; the right end is at an anatomic length, l and an electrotnic length, L, from the origin. B. Membrane potential plotted as a function of distance along the cable for two different values of electrotonic length.

the cable, which produces a constant voltage of $V(0) = V_o$

This is similar to the problem we just solved, so we can again use the general solution to the cable equation given in Equation (2-39). An important difference is that we now want the cable to have a finite length and it is necessary to express this idea in mathematical terms. We do this by imposing what is known as a *sealed end boundary condition*. That is, the end of the cylinder located at $X = L$ is sealed and no current can flow either into or out of the cylinder. The axial current flowing along the cylinder at any point, X, is

(2-40) $$i_a = -\frac{1}{r_a}\frac{\partial u(X)}{\partial X}\Big|_X \quad .$$

Since the axial resistance, r_a , must be finite (or else no current will flow through the cylinder), the fact that the end is sealed means that $\partial u(X)/\partial X = 0$ and $i_a = 0$ at $X = L$. The mathematical expression of the sealed end boundary condition is, thus,

(2-41) $$\frac{\partial u(X)}{\partial X}\Big|_L = 0$$

Since $u(X) = ae^{+X} + be^{-X}$,

(2-42) $$\frac{\partial u(X)}{\partial X} = ae^{X} + be^{-X} \ ,$$

(2-43) $$\frac{\partial u(X)}{\partial X}\Big|_L = ae^{L} - be^{-L} = 0 \quad \text{and} \quad a = be^{-2L} \quad .$$

The current injected at the origin of the cable produces a steady-state voltage of $u(0) = V_o$, so Equation (2-39) becomes $u(0) = ae^0 + be^0 = a + b = V_o$.
Substituting the value of a from Equation 2-43 and rearranging gives

(2-44) $$b = \frac{V_o}{e^{-2L} + 1} = \frac{V_o}{e^{-2L} + e^L e^{-L}} = \frac{\frac{1}{2} e^L V_o}{\frac{1}{2}[e^{-L} + e^L]} \quad .$$

Using the definition of the *hyperbolic cosine function*

(2-45) $$\cosh(X) = \frac{1}{2}\left[e^X + e^{-X}\right] \quad ,$$

we can simplify Equation (2-44) and obtain

(2-46) $$b = \frac{\frac{1}{2} e^L V_o}{\cosh(L)} \quad .$$

Thus,

$$u(X) = ae^X + be^{-X} = be^{-2L} e^X + be^{-X} = \frac{\frac{1}{2} e^L V_o}{\cosh(L)} [e^{-2L} e^X + e^{-X}]$$

(2-46)

$$u(X) = \frac{\frac{1}{2} V_o}{\cosh(L)} [e^{(L-X)} + e^{-(L-X)}] \quad .$$

The solution for the cable equation with a steady state voltage V_o at $X = 0$, anatomic length l and space constant λ is

(2-47) $$V(X) = \frac{V_o \cosh(L - X)}{\cosh L} \quad .$$

Figure 2-11B shows plots of Equation (2-47) for two values of electrotonic length, L . The general form of the plot is the same for each value of L. It has a maximal value of L at $X = 0$ and then declines monotonically towards the end of the cable. The rate of decline is determined by the value of L. Small values of L produce curves that decline slowly so that voltage at the right end of the cable is not much smaller than V_o. This means that a current flowing into the left end of the cylinder can produce a relatively large voltage at the right end of the cable. The cable is then said to be *electrotonically compact*. By contrast, large values of L produce curves that decline more rapidly so that voltage at the right end of the cable is much smaller than V_o. A current flowing into the left end of the cable will have relatively little effect at the right end of the cylinder and the cable is said to be *electrotonically elongate*.

It is important to notice that the electrotonic length is determined by the resistive properties of the membrane and core of the cable as well as its size. The space constant, λ, is given by $\lambda = \sqrt{r_a / r_m} = \sqrt{(R_m / R_a)(d/4)}$ and the electrotonic length of the cable is given by the ratio l/λ. Using Equations (2-3) and (2-5), we calculate

(2-48) $$L = \frac{l}{\lambda} = l\left(\frac{4R_a}{dR_m}\right)^{1/2} = \frac{2l}{\sqrt{d}}\left(\frac{R_a}{R_m}\right)^{1/2} \quad .$$

The electrotonic length, thus, expresses the relationship between the biophysical parameters, R_a, and, R_m, and the size of the cable. It can be viewed as a product of an "anatomical" factor and a "biophysical" factor.

Our discussion of neuronal organization early in this chapter stressed the importance of anatomy in determining the spatial distribution of synapses from neighboring neurons upon the soma and dendrites of a neuron under study. The general significance of the concept of electrotonic length, however, is that the anatomic position of a synapse on a neuron is only one determinant of the functional properties of the synapse. The electrical properties of the neuron also play a role in determining how synaptic currents flow through a neuron. It is reasonable, then, to think of the neuron as represented in *electrotonic coordinates* that depict the functional distances between different regions of the neuron. Figure 2-12A shows two neurons in anatomic coordinates while Figure 2-12B shows how the same two neurons can appear significantly different in electrotonic coordinates if the electrical properties of the soma and dendrites of the neuron vary. The translation from anatomical to electrotonic coordinates has been called a *morphoelectrotonic transformation* (e.g. Zador et al., 1995).

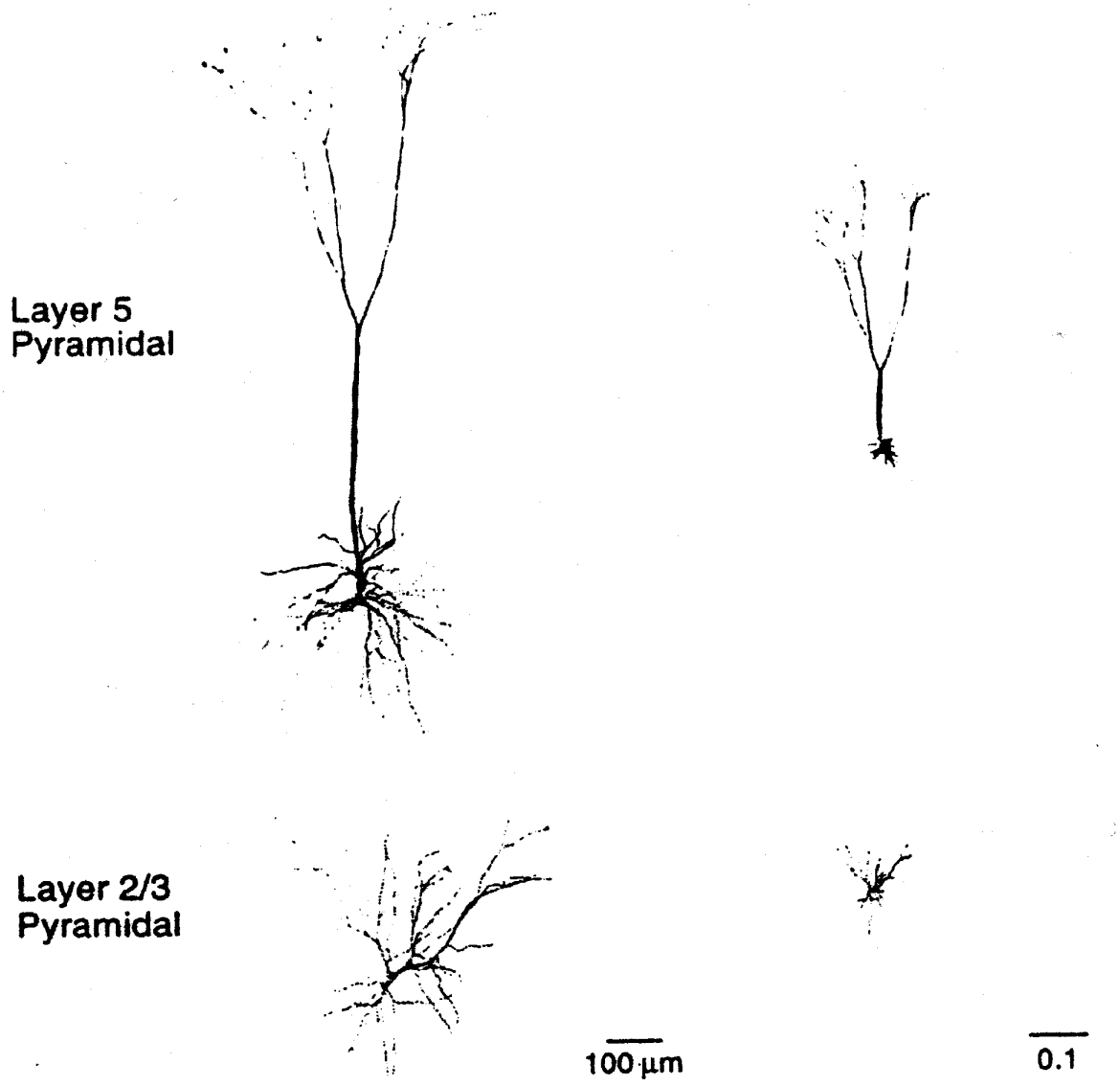


Figure 2 – 12. Morphotonic transformations. This figures shows a layer 5 pyramidal cell and a layer 2/3 pyramidal cell from neocortex in anatomical coordinates (on the left) and in electrotonic coordinates (on the right).

Equivalent cylinder and Equivalent cable models of branched neurons

Wilfrid Rall (Rall, 1959) suggested a way to extend analysis of finite cables to certain kinds of branched cables (Fig. 2-13). He showed that branched cables can be reduced or collapsed into equivalent unbranched, finite cylinders if the diameters of the parent and daughter branches conform to a rule known as the *3/2 power law*. The 3/2-power law places a number of requirements on the neuron, the first of which is that the diameter of the parent branch raised to the 3/2 power must equal the sum of the diameters of each of the daughter branches raised to the 3/2 power. This rule is a variant of a general feature of branching structures such as neurons, vascular systems like arterial or venous plexuses, trees and river beds. These structures often follow a power law in which the parent branch equals the sum of the daughter branches raised to a fractional power. It is the 3/2 power for neurons but the 5/2 power in other cases. Relationships of this form result from impedance matching or continuity relations that require that fluid flowing from the parent branch must be conserved as it flows into the daughter branches. Other requirements are that the individual branches must be of constant diameter (they cannot taper) and that each of the daughter branches originating from a given parent branch must be of the same electronic length. The derivation of the 3/2 power relation is relatively involved (Rall, 1962) and not particularly instructive, but interested readers are referred to the original article.

If a particular neuron meets the requirements of the 3/2 power law, the branches can be collapsed into a single cylinder so the entire neuron is

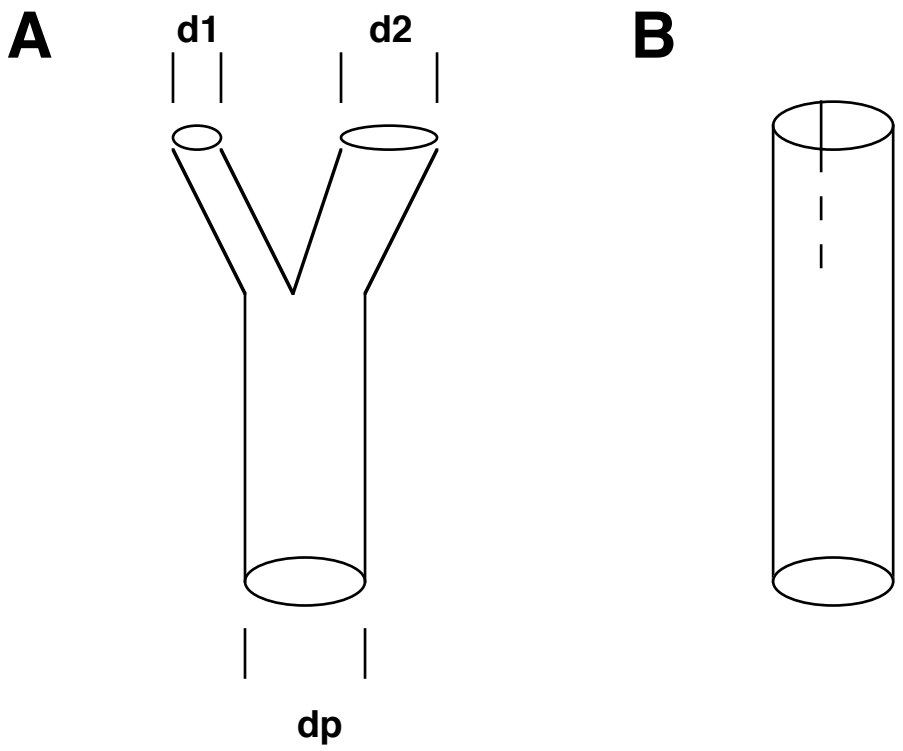


Figure 2-13. 3/2 power law. A. Branched dendritic tree with one parent branch (dp) and two daughter branches (d1 and d2). B. Equivalent cylinder formed by collapsing the two daughther branches.

represented by an unbranched structure known as an equivalent cylinder. The suitability of applying the 3/2 power law to a neuron can be assessed from morphological preparations by measuring the diameters of dendrites along their lengths to look for tapering, and plotting the ratio of the parent branch raised to the 3/2 power to the sum of the daughter branches raised to the 3/2 power. Some neurons conform to the requirements of the 3/2 power law, but others do not. Larkman (1991), for example, examined the dendritic branching pattern of pyramidal cells from the neocortex of rats and found that the preterminal branches (those small branches near the tip of the dendritic tree) followed the 3/2 power law, but the other branches showed significant

variations in the ratio of their parent and sums of daughter branches raised to the 3/2 power (Fig. 2-14). These pyramidal cells cannot be modeled accurately as equivalent cylinders.

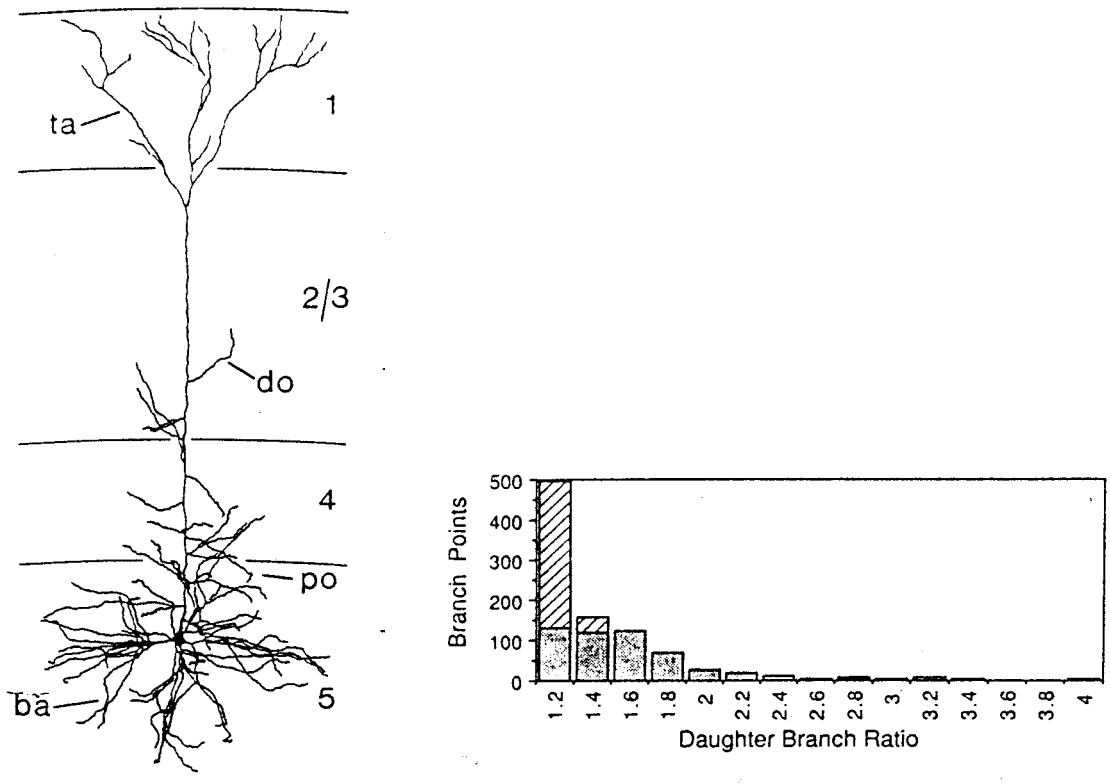


Figure 2-14. Branching in a neocortical pyramidal cell. A. Neocortical pyramidal cell from layer 2/3 of rat visual cortex. The cell was filled with horseradish peroxidase. The apical dendrites (ta) and basal dendrites (ba) are indicated. B. Histogram showing number of branch points with a given daughter branch ratio. A ratio of 1.0 indicates the branches follow the 3/2 power law. Preterminal branches are indicated by shaded bars and have low branch ratios. Other branches have a range of larger ratios. From Larkman (1991).

A less restrictive procedure can be used to model neurons that do not satisfy the requirements for the 3/2-power law (e.g. Stratford, 1989). This involves dividing the neuron into a number of segments so that there is no significant taper along their lengths. The characteristic lengths of the individual segments are calculated and used to estimate their electrotonic lengths

assuming particular values of R_m and R_a. Segments situated at equal electrotonic distances from the soma are then combined using the 3/2 power law. Like equivalent cylinders, these *equivalent cables* are linear structures. They differ from equivalent cylinders in that they do not have uniform diameters and consist, instead, of a chain of cables with different diameters. Although equivalent cable models can be applied to any neuron and are useful for many kinds of studies, they do not adequately portray the full geometry of the neuron and cannot be used when the details of the branching patterns of neurons are important. Unlike equivalent cylinder models, they do not require that the specific membrane and specific internal resistances of the individual segments be the same. Differences in specific resistances can be incorporated in the calculations of the characteristic lengths. However, the membranes must be passive and voltage- or ligand-gated conductances cannot be included in the model. None of these restrictions hold for *compartmental models* which are now being used with increasing frequency for computational studies. Compartmental models will be discussed in the next chapter.