8

Local Signaling: Passive Electrical Properties of the Neuron

WHILE ALL CELLS OF THE body have a membrane potential, only neurons (and muscle cells) generate electrical signals that can be conducted rapidly over long distances. In the last chapter we saw how these electrical signals are generated by the flux of ions across the cell membrane through specialized ion channels, and how to calculate the expected membrane potential for any set of ionic concentration gradients and membrane permeabilities using the Goldman equation.

This description does not, however, provide any information about *changes* in the membrane potential in response to a stimulus, since the Goldman equation applies only to the steady state when the voltage does not change. During signaling, when the neuron generates action potentials, synaptic potentials, or sensory generator potentials in response to a stimulus, the membrane voltage changes constantly. What determines the rate of change in potential? Will a brief synaptic current always produce a similar potential change, regardless of the size of the postsynaptic cell? What determines whether a stimulus will or will not produce an action potential?

Here we consider how a neuron's passive electrical properties and geometry, which are relatively constant, affect the cell's electrical signaling. In the next chapter we shall consider how the properties of the ion channels that generate the active ionic currents also help determine changes in membrane potential.

Neurons have three passive electrical properties that are important to electrical signaling: the resting membrane resistance, the membrane capacitance, and the intracellular axial resistance along axons and dendrites. Because these elements provide the return pathway to complete the electrical circuit when active currents flow into or out of the cell, they determine the time course and amplitude of the synaptic potential change generated by the synaptic current. They also determine whether a synaptic potential generated in a dendrite will result in a suprathreshold depolarization at the trigger zone on the axon hillock. Still further, the passive properties influence the speed at which an action potential is conducted.

Input Resistance Determines the Magnitude of Passive Changes in Membrane Potential

The difference between the effects of passive and active properties of neurons can be demonstrated by injecting

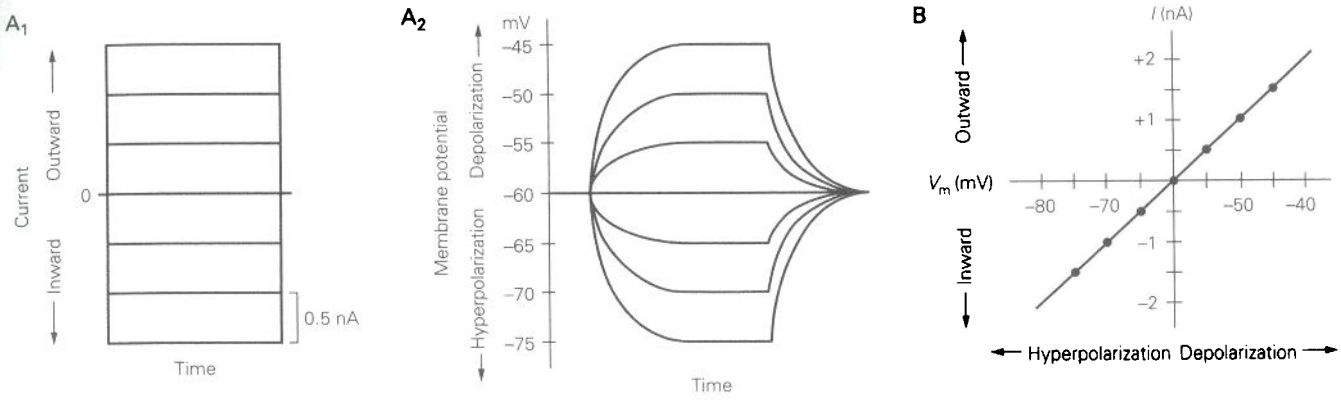

Figure 8-1 Current-voltage relationships. By passing subthreshold, graded, inward and outward current pulses into a cell, one can determine the relationship between current injected into the cell and the resulting changes in membrane potential, V_m.

A. Increases in outward or inward current pulses (A_1) produce proportional and symmetrical changes in V_m (A_2). Note that the potential changes more slowly than the step current pulses.

B. An *I-V* curve is obtained by plotting the steady state voltage against the injected current. The slope of the *I-V* curve defines the input resistance of the neuron. The *I-V* curve shown here is linear; V_m changes by 10 mV for every 1 nA change in current, yielding a resistance of 10 mV/1 nA, or $10 \times 10^6\ \Omega$ (10 MΩ).

current pulses into the cell body (see Box 7-1). Injecting a negative charge through an electrode increases the charge separation across the membrane, making the membrane potential more negative, or hyperpolarized. The larger the negative current, the greater is the hyperpolarization. In most neurons there is a linear relation between the size of the negative current and the steady-state hyperpolarization (Figure 8-1). The relation between current and voltage defines a resistance, R_{in}, the neuron's *input resistance*.

Likewise, when a positive charge is injected into the cell, producing depolarization, the neuron behaves as a simple resistor, but only over a limited voltage range. A large enough positive current will produce a depolarization that exceeds threshold, at which point the neuron generates an action potential. When this happens the neuron no longer behaves as a simple resistor because of the special properties of its voltage-gated channels considered in Chapter 9. Still, much of a neuron's behavior in the hyperpolarizing and subthreshold depolarizing range of voltages can be explained by simple equivalent circuits made up of resistors, capacitors, and batteries.

The input resistance of the cell determines how much the cell will depolarize in response to a steady current. The magnitude of the depolarization, ΔV, is given by Ohm's law:

$$\Delta V = I \times R_{in}.$$

Thus, of two neurons receiving identical synaptic current inputs, the cell with the higher input resistance will show a greater change in membrane voltage. For an idealized spherical neuron with no processes, the input resistance depends on both the density of the resting ion channels in the membrane (that is, the number of channels per unit area of membrane) and the size of the cell. The larger the neuron, the greater will be its membrane surface area and the lower the input resistance, since there will be more resting channels to conduct ions.

To compare the membrane properties of neurons of differing sizes, electrophysiologists often use the resistance of a unit area of membrane, the *specific membrane resistance*, R_m, measured in units of $\Omega \cdot cm^2$. The specific membrane resistance depends only on the density of the resting ion channels (the number of channels per square centimeter) and their conductance.

To obtain the total input resistance of the cell we *divide* the specific membrane resistance by the membrane area of the cell because the greater the area of a cell, the lower its resistance. For the spherical neuron we obtain

$$R_{in} = R_m/4\pi a^2,$$

where a is the radius of the neuron. Thus, for a spherical cell the input resistance is inversely proportional to the square of the radius. For a real neuron with extensive dendrites and axons, the input resistance also depends

on the membrane resistance of its processes as well as on the intracellular cytoplasmic resistance between the cell body and those processes (discussed below).

Membrane Capacitance Prolongs the Time Course of Electrical Signals

In Figure 8-1 the magnitude of the steady state changes in the cell's voltage in response to subthreshold current resembles the behavior of a simple resistor, but the *time course* of the changes does not. A true resistor responds to a step change in current with a similar step change in voltage, but the cell in Figure 8-1 shows a voltage response that rises and decays more slowly than the step change in current. This property of the membrane is due to its *capacitance*.

To understand how the capacitance slows down the voltage response we need to recall that the voltage across a capacitor is proportional to the charge stored on the capacitor:

$$V = Q/C,$$

where Q is the charge in coulombs and C is the capacitance in farads. To alter the voltage, charge must either be added or removed from the capacitor:

$$\Delta V = \Delta Q/C.$$

The change in charge (ΔQ) is the result of the flow of current across the capacitor (I_c). Since current is the flow of charge per unit time ($I_c = \Delta Q/\Delta t$), we can calculate the change in voltage across a capacitor as a function of current and the time that the current flows (Δt):

$$\Delta V = I_c \cdot \Delta t/C. \qquad \textbf{(8-1)}$$

The magnitude of the change in voltage across a capacitor in response to a current pulse depends on the duration of the current, as time is required to deposit and remove charge on the plates of the capacitor.

Capacitance is directly proportional to the area of the plates of the capacitor. The larger the area of a capacitor, the more charge it will store for a given potential difference. The value of the capacitance also depends on the insulation medium and the distance between the two plates of the capacitor. Since all biological membranes are composed of lipid bilayers with similar insulating properties that provide a similar separation between the two plates (4 nm), the specific capacitance per unit area of all biological membranes, C_m, has the same value, approximately 1 $\mu F/cm^2$ of membrane. The total input capacitance of a spherical cell, C_{in}, is therefore given by the capacitance per unit area multiplied by the area of the cell:

$$C_{in} = C_m(4\pi a^2).$$

Because capacitance increases with the size of the cell, more charge, and therefore current, is required to produce the same change in membrane potential in a larger neuron than in a smaller one.

According to Equation 8-1 the voltage across a capacitor continues to increase with time as long as a current pulse is applied. But in neurons the voltage levels off after some time (Figure 8-1) because the membrane of a neuron acts as a resistor (owing to its ion-conducting channels) and a capacitor (owing to the phospholipid bilayer) in parallel.

In the equivalent circuit developed in Chapter 7 to model current flow in the neuron, we placed the resistance and capacitance in parallel, since current crossing the membrane can flow either through ion channels (the resistive pathway) or across the capacitor (Figure 8-2). The resistive current carried by ions flowing across the membrane through ion channels—for example, Na^+ ions moving through Na^+ channels from outside to inside the cell—is called the *ionic membrane current*. The current carried by ions that change the net charge stored on the membrane is called the *capacitive membrane current*. An outward capacitive current, for example, adds positive charges to the inside of the membrane and re-

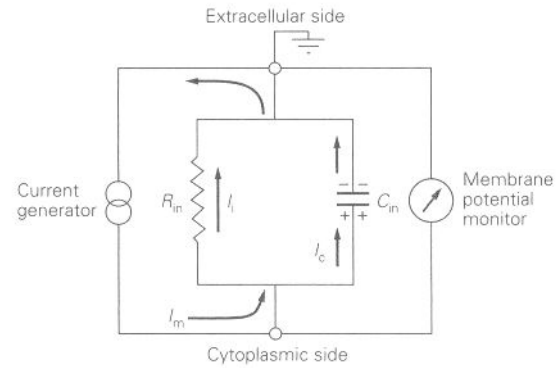

Figure 8-2 A simplified electrical equivalent circuit is used to examine the effects of membrane capacitance (C_{in}) on the rate of change of membrane potential in response to current flow. All resting ion channels are lumped into a single element (R_{in}). Batteries representing the electromotive forces generated by ion diffusion are not included because they affect only the absolute value of membrane potential, not the rate of change. This equivalent circuit represents the experimental setup shown in Box 7-1 (Figure 7-2C), in which pairs of electrodes are connected to the current generator and the membrane potential monitor.

moves an equal number of positive charges from the outside of the membrane. The total current crossing the membrane, I_m, is given by the sum of the ionic current (I_i) and the capacitive current:

$$I_m = I_i + I_c. \quad \textbf{(8-2)}$$

The capacitance of the membrane has the effect of reducing the rate at which the membrane potential changes in response to a current pulse. If the membrane had only resistive properties, a step pulse of outward current passed across it would change the membrane potential instantaneously. On the other hand, if the membrane had only capacitive properties, the membrane potential would change linearly with time in response to the same step pulse of current. Because the membrane has *both* capacitive and resistive properties in parallel, the actual change in membrane potential combines features of the two pure responses. The initial slope of the relation between V_m and time reflects a purely capacitive element, whereas the final slope and amplitude reflect a purely resistive element (Figure 8-3).

It is now easy to explain why a step change in current produces the slowly rising voltage waveform seen in Figure 8-3. Since the resistance and capacitance of the membrane are in parallel, the voltage across each element must always be the same and equal to the membrane potential. Assume that the membrane potential starts off at 0 mV and that at time $t = 0$ a depolarizing current step is applied from a current generator with magnitude I_m. Initially the voltage across the resistor and capacitor are both equal to 0 mV. Since the ionic current through the resistor is given by Ohm's law ($I_i = V/R_{in}$), initially no current will flow through the resistor (since V starts off at 0 mV) and all the current will flow through the capacitor (ie, $I_c = I_m$). As a result of the large initial capacitive current, the potential across the capacitor, and hence the membrane potential, will rapidly become more positive.

As V_m increases, the voltage difference across the membrane begins to drive current across the membrane resistance. As the voltage across the membrane becomes more positive, more current flows through the resistor and less flows across the capacitor, since I_c plus I_i is constant (and equal to I_m). As a result, the membrane potential begins to rise more slowly. Eventually, the membrane potential reaches a value where all the membrane current flows through the resistor ($I_i = I_m$). From Ohm's law this voltage is given by $V_m = I_m \cdot R_{in}$. At this point the capacitative current is zero and, following Equation 8-1, the membrane potential no longer changes. Once the step of current is turned off, the total membrane current I_m equals zero, so that the positive ionic current flowing through the resistor must flow back into the cell

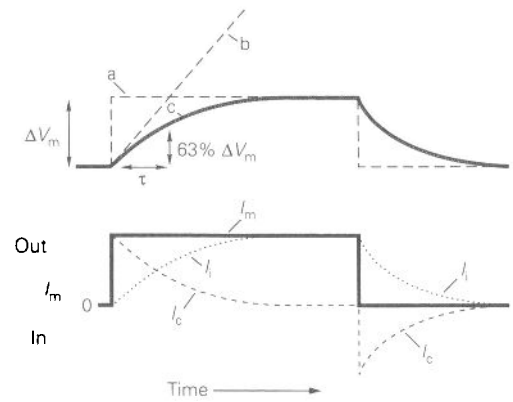

Figure 8-3 The rate of change in the membrane potential is slowed by the membrane capacitance. The response of the membrane potential (ΔV_m) to a step current pulse is shown in the **upper plot.** The actual shape of the response (**red line c**) combines the properties of a purely resistive element (**dashed line a**) and a purely capacitive element (**dashed line b**). The **lower plot** shows the total membrane current (I_m) and its ionic (I_i) and capacitive (I_c) components ($I_m = I_i + I_c$) in relation to the current pulse. The time taken to reach 63% of the final voltage defines the membrane time constant, τ. The time constants of different neurons typically range from 20 to 50 ms.

as an equal and opposite capacitive current, ie, $I_i = -I_c$. With no applied current, the charge on the capacitor dissipates by flowing in a loop around the circuit through the resistive pathway, and the membrane potential returns to zero.

The rising phase of the potential change can be described by the following equation:

$$\Delta V_m(t) = I_m R_{in}(1 - e^{-t/\tau}), \quad \textbf{(8-3)}$$

where e, which has a value of around 2.72, is the base of the system of natural logarithms, and τ is the *membrane time constant*, the product of the input resistance and capacitance of the membrane ($R_{in}C_{in}$). The time constant can be measured experimentally (Figure 8-3). It is the time it takes the membrane potential to rise to $(1 - 1/e)$, about 63% of its steady state value. We shall return to the time constant when we consider the temporal summation of synaptic inputs in a cell in Chapter 12.

Membrane and Axoplasmic Resistance Affect the Efficiency of Signal Conduction

So far we have considered the effects of the passive properties of neurons on signaling only within the cell body. Because the neuron's soma can be approximated

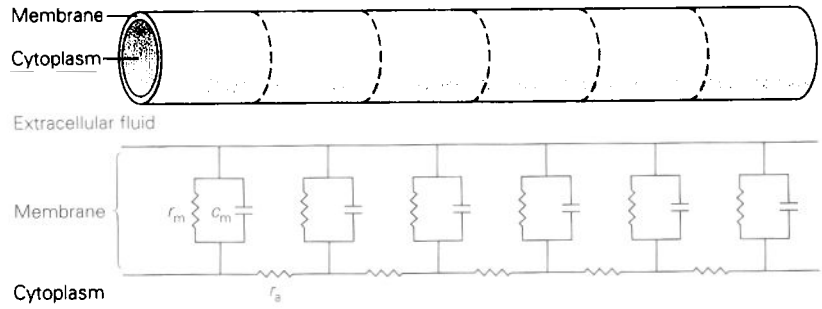

Figure 8-4 A neuronal process can be represented by an electrical equivalent circuit. The process is divided into unit lengths. Each unit length of the process is a circuit with its own membrane resistance (r_m) and capacitance (c_m). All the circuits are connected by resistors (r_a), which represent the axial resistance of segments of cytoplasm, and a short circuit, which represents the extracellular fluid.

as a simple sphere, the effect of distance on the propagation of a signal does not matter. However, in electrical signaling along dendrites, axons, and muscle fibers, a subthreshold voltage signal decreases in amplitude with distance from its site of initiation. To understand how this attenuation occurs we will again have need of an equivalent circuit, one that shows how the geometry of a neuron influences the distribution of current flow.

Synaptic potentials that originate in dendrites are conducted along the dendrite toward the cell body and the trigger zone. The cytoplasmic core of a dendrite offers significant resistance to the longitudinal flow of current, because it has a relatively small cross-sectional area, and ions flowing down the dendrite collide with other molecules. The greater the length of the cytoplasmic core, the greater the resistance, since the ions experience more collisions the further they travel. Conversely, the larger the diameter of the cytoplasmic core, the lower will be the resistance in a given length, since the number of charge carriers at any cross section of dendrite increases with the diameter of the core.

To represent the incremental increase in resistance along the length of the dendritic core, the dendrite can be divided into unit lengths, each of which is a circuit with its own measurable membrane resistance and capacitance as well as an axial resistance within the cytoplasmic core. Because of its large volume, the extracellular fluid has only negligible resistance and therefore can be ignored. The equivalent circuit for this simplified model is shown in Figure 8-4.

If current is injected into the dendrite at one point, how will the membrane potential change with distance along the dendrite? For simplicity, consider the variation of membrane potential with distance after a constant-amplitude current pulse has been on for some time ($t \ggg \tau$). Under these conditions the membrane potential will have reached a steady value, so capacitive current will be zero. When $I_c = 0$, all of the membrane current is ionic ($I_m = I_i$). The variation of the potential with distance thus depends solely on the relative values of the *membrane resistance*, r_m (units of $\Omega \cdot$cm), and the *axial resistance*, r_a (units of Ω/cm), per unit length of dendrite.

The injected current flows out through several parallel pathways across successive membrane cylinders along the length of the process (Figure 8-5). Each of these current pathways is made up of two resistive components in series: the total axial resistance, r_x, and the membrane resistance, r_m, of the unit membrane cylinder. For each outflow pathway the total axial resistance is the resistance between the site of current injection and the site of the outflow pathway. Since resistors in series are added, $r_x = r_a x$, where x is the distance along the dendrite from the site of current injection. The membrane resistance, r_m, has the same value at each outflow pathway along the cell process.

More current flows across a membrane cylinder near the site of injection than at more distant regions because current always tends to follow the path of least resistance, and the total axial resistance, r_x, increases with distance from the site of injection (Figure 8-5). Because $V_m = I_m r_m$, the change in membrane potential produced by the current across a membrane cylinder at position x, $\Delta V_m(x)$, becomes smaller with distance down the dendrite away from the current electrode. This decay with distance is exponential (Figure 8-5) and expressed by

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

where λ is the membrane *length constant*, x is the distance from the site of current injection, and ΔV_0 is the change in membrane potential produced by the current flow at the site of injection ($x = 0$). The length constant λ is defined as the distance along the dendrite to the site where ΔV_m has decayed to $1/e$, or 37% of its initial value (Figure 8-5), and it is determined as follows:

$$\lambda = \sqrt{(r_m/r_a)}.$$

The better the insulation of the membrane (that is, the greater r_m) and the better the conducting properties of the inner core (the lower r_a), the greater the length constant of the dendrite. That is, current is able to spread

farther along the inner conductive core of the dendrite before leaking across the membrane.

To consider how neuronal geometry affects signaling, it will be helpful first to consider how the diameter of a process affects r_m and r_a. Both r_m and r_a are measures of resistance that apply to a 1 cm segment of an individual neuronal process with a certain radius α. The axial resistance of a neuronal process depends on the intrinsic resistive properties of the cytoplasm, expressed as the specific resistance, ρ, of a 1 cm^3 cube of cytoplasm (in units of $\Omega \cdot cm$), and the cross-sectional area of the process, which determines the total volume in a unit length of the process and hence the number of charge carriers. Thus, r_a is given by

$$r_a = \rho/\pi a^2, \qquad \textbf{(8-4)}$$

and r_a has the required units of Ω/cm. The diameter of the process also affects r_m since the total number of channels in a unit length of membrane is directly proportional to both the channel density (number of channels per unit area) and the membrane area. Since r_m is inversely related to the total number of channels in a unit length of membrane and the area in a unit length of cylinder depends on the circumference, r_m is given by

$$r_m = R_m/2\pi a, \qquad \textbf{(8-5)}$$

where R_m is the specific resistance of a unit area of membrane (units of $\Omega \cdot cm^2$) and r_m has the units of $\Omega \cdot cm$.

Neuronal processes vary greatly in diameter, from as much as 1 mm for the giant axon of the squid down to 1 μm for fine dendritic branches in the mammalian brain. These variations in diameter control the efficiency of neuronal signaling because the diameter determines the length constant. For processes with similar intrinsic properties (that is with similar values of R_m and ρ), the larger the diameter of the process (dendrite or axon), the longer the length constant, because r_m/r_a is directly related to the radius (Equations 8-4 and 8-5). Thus, the length constant is expressed in terms of the intrinsic (size invariant) properties R_m and ρ as follows:

$$\lambda = \sqrt{\frac{R_m}{\rho} \cdot \frac{a}{2}}.$$

That is, the length constant is proportional to the square root of the radius (or diameter) of a process. Thus, thicker axons and dendrites will have longer length constants than do narrower processes and hence will transmit electrotonic signals for greater distances. Typical values for neuronal length constants range from 0.1 to 1.0 mm.

The length constant is a measure of the efficiency of the passive spread of voltage changes along the neuron, or *electrotonic conduction*. The efficiency of electrotonic conduction has two important effects on neuronal function. First, it influences *spatial summation*, the process by which synaptic potentials generated in different regions of the neuron are added together at the trigger zone, the decision-making component of the neuron (see Chapter 12).

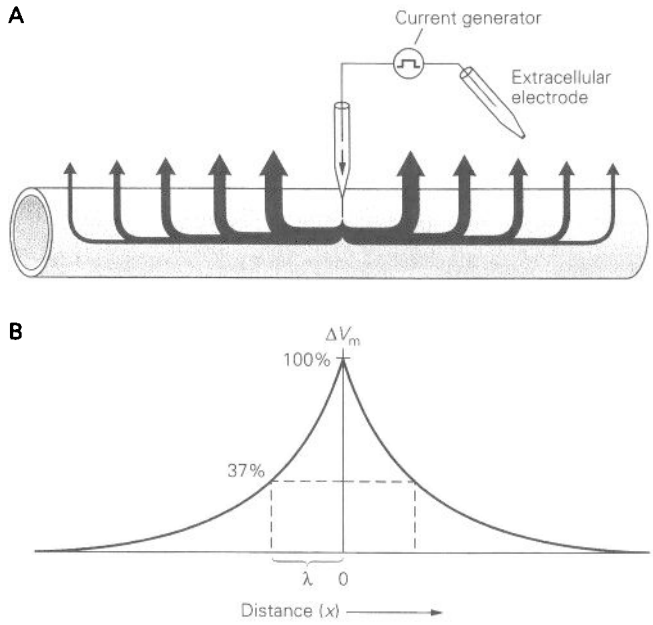

Figure 8-5 The voltage response in a passive neuronal process decays with distance due to electronic conduction. Current injected into a neuronal process by a microelectrode follows the path of least resistance to the return electrode in the extracellular fluid (**A**). The thickness of the arrows represents membrane current density at any point along the process. Under these conditions the change in V_m decays exponentially with distance from the site of current injection (**B**). The distance at which ΔV_m has decayed to 37% of its value at the point of current injection defines the length constant, λ.

Second, electrotonic conduction is a factor in the *propagation* of the action potential. Once the membrane at any point along an axon has been depolarized beyond threshold, an action potential is generated in that region in response to the opening of voltage-gated Na^+ channels (see Chapter 9). This local depolarization spreads electrotonically down the axon, causing the adjacent region of the membrane to reach the threshold for generating an action potential (Figure 8-6). Thus the depolarization spreads along the length of the axon by "local-circuit" current flow resulting from the potential difference between active and inactive regions of the axon membrane. In cells with longer length constants the local-circuit current has a greater spread and therefore the action potential propagates more rapidly.

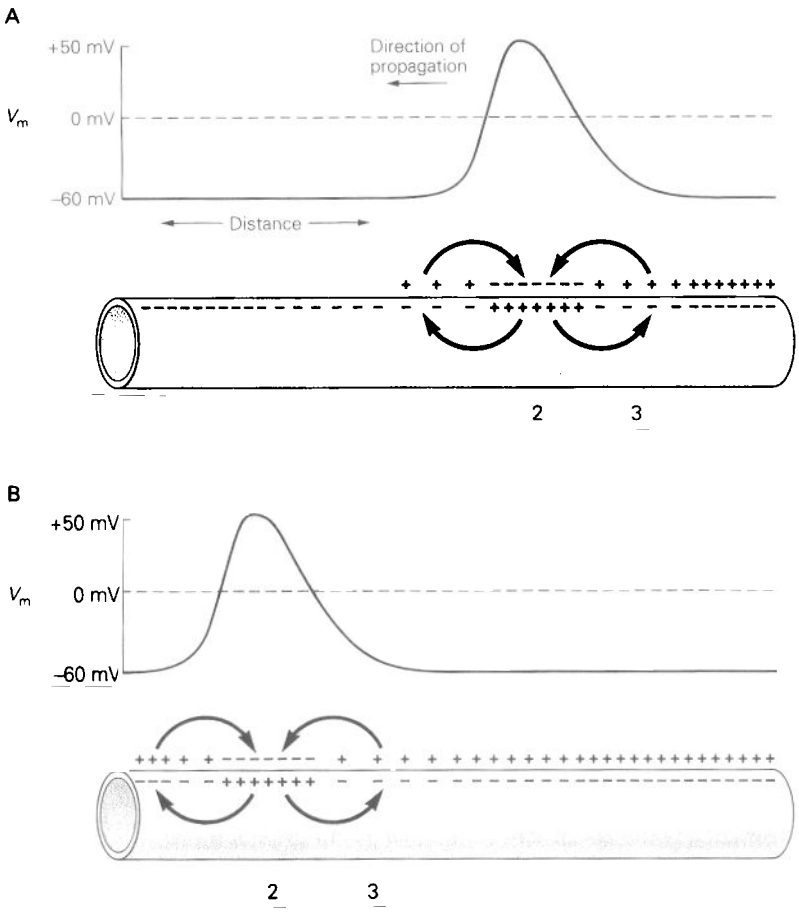

Figure 8-6 Passive conduction of depolarization along the axon contributes to propagation of the action potential.

A. The waveform of an action potential propagating from right to left. The difference in potential along the length of the axon creates a local-circuit current flow that causes the depolarization to spread passively from the active region (**2**) to the inactive region *ahead* of the action potential (**1**), as well as to the area *behind* the action potential (**3**). However, because there is also an increase in g_K in the wake of the action potential (see Chapter 9), the buildup of positive charge along the inner side of the membrane in area **3** is more than balanced by the local efflux of K^+, allowing this region of membrane to repolarize.

B. A short time later the voltage waveform and the current distributions have shifted down the axon and the process is repeated.

Large Axons Are More Easily Excited Than Small Axons by Extracellular Current Stimuli

In examination of a neurological patient for diseases of peripheral nerves the nerve often is stimulated by passing current between a pair of extracellular electrodes placed over the nerve, and the population of resulting action potentials (the *compound action potential*) is recorded farther along the nerve by a second pair of voltage-recording electrodes. In this situation the total number of axons that generate action potentials varies with the amplitude of the current pulse.

To drive a cell to threshold, the current must pass through the cell membrane. In the vicinity of the positive electrode, current flows across the membrane into the axon. It then flows along the axoplasmic core, eventually flowing out through more distant regions of axonal membrane to the second (negative) electrode in the extracellular fluid. For any given axon, most of the stimulating current bypasses the fiber, moving instead through other axons or through the low-resistance pathway provided by the extracellular fluid. The axons into which current can enter most easily are the most excitable.

In general, axons with the largest diameter have the lowest threshold for extracellular current. The larger the diameter of the axon, the lower the axial resistance to the flow of longitudinal current because of the greater number of intracellular charge carriers (ions) per unit length of the axon. Therefore a greater fraction of total current enters the larger axon, so it is depolarized more efficiently than a smaller axon. For these reasons, larger axons are recruited at low values of current; smaller-diameter axons are recruited only at relatively greater current strengths.

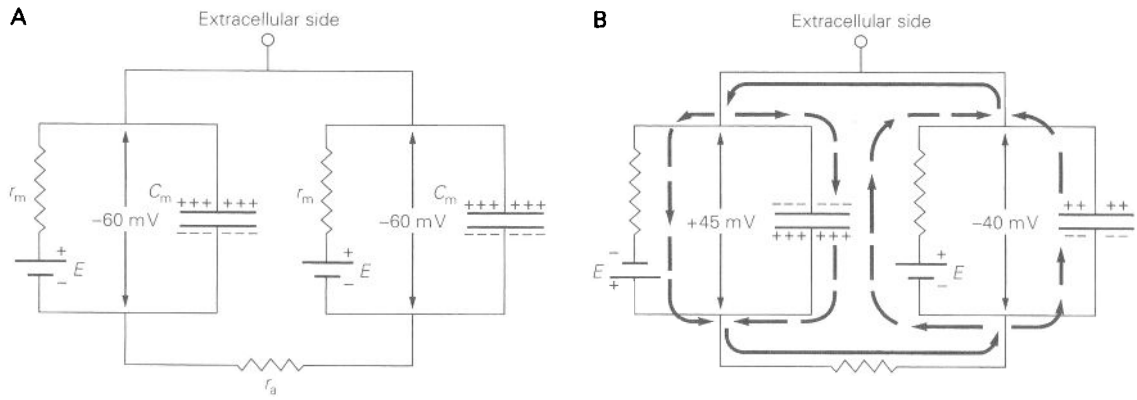

Figure 8-7 Axial resistance and membrane capacitance limit the rate of spread of depolarization during the action potential.

A. The electrical equivalent circuit represents two adjacent segments of the resting membrane of an axon connected by a segment of axoplasm (r_a).

B. An action potential is spreading from the membrane segment on the **left** to the segment on the **right.** Purple lines indicate pathways of current flow.

Passive Membrane Properties and Axon Diameter Affect the Velocity of Action Potential Propagation

The passive spread of depolarization during conduction of the action potential is not instantaneous. In fact, the electrotonic conduction is a rate-limiting factor in the propagation of the action potential. We can understand this limitation by considering a simplified equivalent circuit of two adjacent membrane segments connected by a segment of axoplasm (Figure 8-7). As described above, an action potential generated in one segment of membrane supplies depolarizing current to the adjacent membrane, causing it to depolarize gradually toward threshold. According to Ohm's law, the larger the axoplasmic resistance, the smaller the current flow around the loop ($I = V/R$) and the longer it takes to change the charge on the membrane of the adjacent segment.

Recall that since $\Delta V = \Delta Q/C$, the membrane potential changes slowly if the current is small because ΔQ changes slowly. Similarly, the larger the membrane capacitance, the more charge must be deposited on the membrane to change the potential across the membrane, so the current must flow for a longer time to produce a given depolarization. Therefore, the time it takes for depolarization to spread along the axon is determined by both the axial resistance, r_a, and the capacitance per unit length of the axon c_m (units F/cm). The rate of passive spread varies inversely with the product $r_a c_m$. If this product is reduced, the rate of passive spread increases and the action potential propagates faster.

Rapid propagation of the action potential is functionally important, and two distinct mechanisms have evolved to increase it. One adaptive strategy is to increase conduction velocity by increasing the diameter of the axon core. Because r_a decreases in proportion to the square of axon diameter, while c_m increases in direct proportion to diameter, the net effect of an increase in diameter is a decrease in $r_a c_m$. This adaptation has been carried to an extreme in the giant axon of the squid, which can reach a diameter of 1 mm. No larger axons have evolved, presumably because of the opposing need to keep neuronal size small so that many cells can be packed into a limited space.

A second mechanism for increasing conduction velocity is myelination of the axon, the wrapping of glial cell membranes around an axon (see Chapter 4). This process is functionally equivalent to increasing the thickness of the axonal membrane by as much as 100 times. Because the capacitance of a parallel-plate capacitor such as the membrane is inversely proportional to the thickness of the insulation material, myelination decreases c_m and thus $r_a c_m$. Myelination results in a proportionately much greater decrease in $r_a c_m$ than does the same increase in the diameter of the axon core. For this reason, conduction in myelinated axons is typically faster than in nonmyelinated axons of the same diameter.

In a neuron with a myelinated axon the action potential is triggered at the nonmyelinated segment of membrane at the axon hillock. The inward current that flows through this region of membrane is then available to discharge the capacitance of the myelinated axon ahead of it. Even though the thickness of myelin makes the capacitance of the axon quite small, the amount of current flowing down the core of the axon from the trigger zone is not enough to discharge the capacitance along the *entire* length of the myelinated axon.

To prevent the action potential from dying out, the myelin sheath is interrupted every 1–2 mm by bare patches of axon membrane about 2 μm in length, the nodes of Ranvier (see Chapter 4). Although the area of membrane at each node is quite small, the nodal membrane is rich in voltage-gated Na^+ channels and thus can generate an intense depolarizing inward Na^+ current in response to the passive spread of depolarization down the axon. These regularly distributed nodes thus boost the amplitude of the action potential periodically, preventing it from dying out.

The action potential, which spreads quite rapidly along the internode because of the low capacitance of the myelin sheath, slows down as it crosses the high-capacitance region of each bare node. Consequently, as the action potential moves down the axon it jumps quickly from node to node (Figure 8-8A). For this reason, the action potential in a myelinated axon is said to move by *saltatory conduction* (from the Latin *saltare*, to jump). Because ionic membrane current flows only at the nodes in myelinated fibers, saltatory conduction is also favorable from a metabolic standpoint. Less energy must be expended by the Na^+-K^+ pump in restoring the Na^+ and K^+ concentration gradients, which tend to run down as a result of action-potential activity.

Various diseases of the nervous system, such as multiple sclerosis and Guillain-Barre syndrome, cause demyelination (see Box 4-1). Because the lack of myelin slows down the conduction of the action potential, these diseases can have devastating effects on behavior (Chapter 35). As an action potential goes from a myelinated region to a bare stretch of axon, it encounters a region of relatively high c_m and low r_m. The inward current generated at the node just before the demyelinated segment may be too small to provide the capacitive current required to depolarize the demyelinated membrane to threshold. In addition, this local-circuit current does not spread as far as it normally would because it is flowing into a segment of axon that, because of its low r_m, has a short length constant (Figure 8-8B). These two factors can combine to slow, and in some cases actually block, the conduction of action potentials.

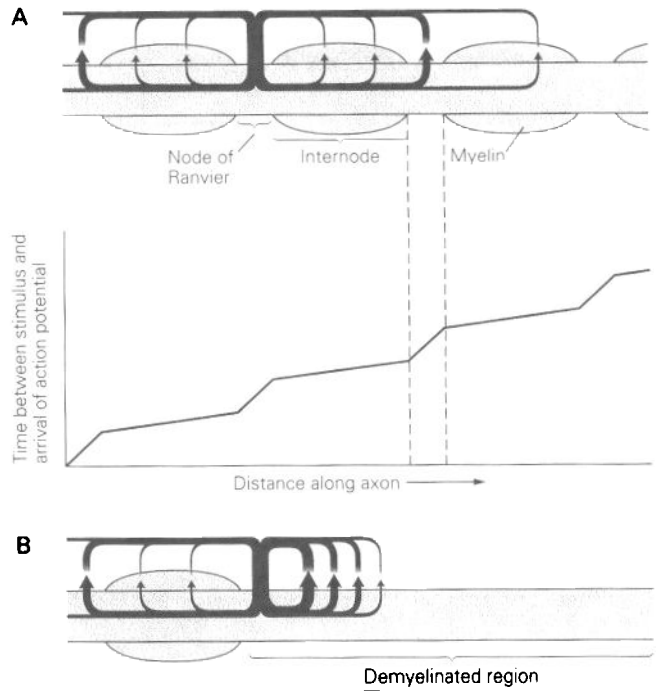

Figure 8-8 Action potentials in myelinated nerves are regenerated at the nodes of Ranvier.

A. In the axon capacitive and ionic membrane current densities (membrane current per unit area of membrane) are much higher at the nodes of Ranvier than in the internodal regions. The density of membrane current at any point along the axon is represented by the thickness of the **arrows**. Because of the higher capacitance of the axon membrane at the unmyelinated nodes, the action potential slows down as it approaches each node and thus appears to skip rapidly from node to node.

B. In regions of the axon that have lost their myelin, the spread of the action potential is slowed down or blocked. The local-circuit currents must charge a larger membrane capacitance and, because of the low r_m, they do not spread well down the axon.

An Overall View

Two competing needs determine the functional design of neurons. First, to maximize the computing power of the nervous system, neurons must be small so that large numbers of them can fit into the brain and spinal cord. Second, to maximize the ability of the animal to respond to changes in its environment, neurons must conduct signals rapidly. These two design objectives are constrained by the materials from which neurons are made.

Because the nerve cell membrane is very thin and is surrounded by a conducting medium, it has a very high capacitance, which slows down the conduction of volt-

age signals. In addition, the currents that change the charge on the membrane capacitance must flow through a relatively poor conductor—a thin column of cytoplasm. The ion channels that give rise to the resting potential also degrade the signaling function of the neuron. They make the cell leaky and, together with the high membrane capacitance, they limit the distance that a signal can travel passively.

As we shall see in the next chapter, neurons use voltage-gated channels to compensate for these physical constraints when generating all-or-none action potentials, which are continually regenerated and conducted without attenuation. For pathways in which rapid signaling is particularly important, the conduction velocity of the action potential is enhanced either by myelination or by an increase in axon diameter, or by both.

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