

So far, this section has been concerned with steady-state situations, where the membrane potential is constant in time. Equation 12.5 shows that in such situations the left-hand side equals zero. The following sections, however, will discuss transient phenomena such as the action potential; here, capacitive effects will play a crucial role.

Two identical capacitors in parallel will have the same ΔV as one when connected across a given battery because the electrostatic potential is the same among any set of joined lines (see point (3) in the list on page 509). Thus they will store twice as much charge as one capacitor (adding two copies of Equation 12.4). That is, they act as a single capacitor with *twice* the capacitance of either one. Applying this observation to a membrane, we see that a small patch of membrane will have capacitance proportional to its area. Thus $C = AC$, where A is the area of the membrane patch and C is a constant characteristic of the membrane material. We will regard the capacitance per area C as a measured phenomenological parameter. A typical value for cell membranes is $C \approx 10^{-2} \text{ F m}^{-2}$, more easily remembered as $1 \mu\text{F cm}^{-2}$.

In summary, we now have a simplified model for the electrical behavior of an individual small patch of membrane, pictorially represented by Figure 12.3b. Our model rests on the Ohmic hypothesis. The phrase *small patch* reminds us that we have been implicitly assuming that ΔV is uniform across our membrane, as implied by the horizontal wires in our idealized circuit diagram, Figure 12.3b. Our model involves several phenomenological parameters describing the membrane (g_i and C) as well as the Nernst potentials (V_i^{Nernst}) describing the interior and exterior ion concentrations.

12.1.3 Membranes with Ohmic conductance lead to a linear cable equation with no traveling wave solutions

Although the membrane model developed in the previous section rests on some solid pillars (like the Nernst relation), nevertheless it contains other assumptions that are mere working hypotheses (like the Ohmic hypothesis, Equation 11.8). In addition, the analysis was restricted to either a small patch of membrane or a larger membrane maintained at a potential that was uniform along its length. This section will focus on lifting the last of these restrictions, to let us explore the behavior of an Ohmic membrane with a *nonuniform* potential. We'll find that in such a membrane, external stimuli spread passively, giving behavior like that sketched in Figure 12.1b. Later sections will show that to understand nerve impulses (Figure 12.2b), we'll need to reexamine the Ohmic hypothesis.

When the potential is not uniform along the length of the axon, then current will flow axially (in the x direction, parallel to the axon). So far, we have neglected this possibility, considering only radial flow (in the r direction, through the membrane). In the language of Figure 12.3, axial flow corresponds to a current I_x flowing through the ends of the top and bottom horizontal wires. We will adopt the convention that I_x is called positive when positive ions flow in the $+\hat{x}$ direction. If I_x is not zero, then the net radial current flow need not be zero, as assumed when deriving the chord conductance formula, Equation 12.3. Accordingly, we first need to generalize that result.

**Your
Turn
12A**

Show that the three resistor–battery pairs in Figure 12.3b can equivalently be replaced by a *single* such pair, with effective conductance $g_{\text{tot}}A$ and battery potential V^0 given by Equation 12.3.

We can now represent the axon as a *chain* of identical modules of the form you just found, each representing a cylindrical slice of the membrane (Figure 12.4). Current can flow axially through the interior fluid (representing the axon's cytoplasm, or **axoplasm**, represented by the upper horizontal line) or through the surround-

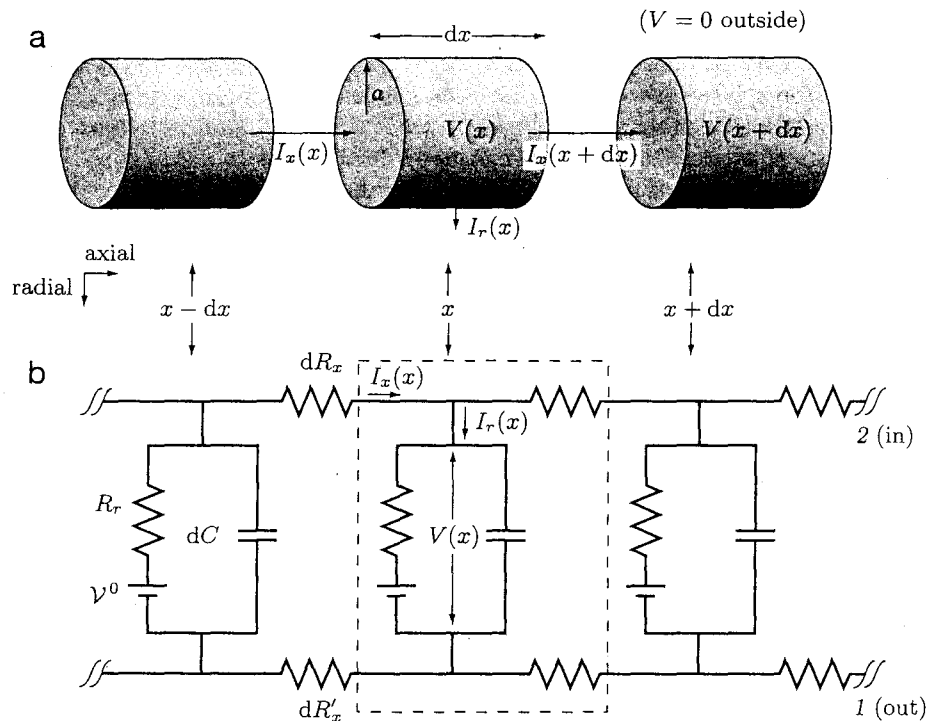


Figure 12.4: (Schematic; circuit diagram.) Distributed-element model of an axon. The axon is viewed as a chain of identical modules, labeled by their position x along the axon. (a) Modules viewed as cylindrical segments of length dx and radius a . Each one's surface area is thus $dA = 2\pi a dx$. (b) Modules viewed as electrical networks, each containing a battery of voltage V^0 (recall that this quasi-steady state potential is negative). The "radial" resistor, with resistance $R_r = 1/(g_{\text{tot}}dA)$, represents passive ion permeation through the axon membrane; the associated capacitor has $dC = CdA$. The "axial" resistors dR_x and dR'_x represent the fluid inside and outside the axon, respectively. We will make the approximation that $dR'_x = 0$, so the entire lower horizontal wire is at a common potential, which we define to be zero. The "radial" current, $I_r(x) \equiv j_{q,r}(x) \times dA$, reflects the net charge of all the ions leaving the axoplasm (that is, downward in (b)) at x ; the axial current I_x represents the total current flowing to the right inside the axoplasm (that is, in the upper horizontal wire of (b)). $V(x)$ represents the potential inside the axon (and hence also the potential difference across the membrane, because we took the potential to be zero outside).

ing extracellular fluid (represented by the lower horizontal line). The limit $dx \rightarrow 0$ amounts to describing the membrane as a chain of infinitesimal elements, a **distributed network** of resistors, capacitors, and batteries.

To explore the behavior of such a network under the sort of stimuli sketched in Figure 12.1, we now take four steps:

- Find numerical values for all the circuit elements in Figure 12.4, then
- Translate the figure into an equation;
- Solve the equation; and
- Interpret the solution.

a. Values To find the interior axial resistance dR_x , recall that the resistance of a cylinder of fluid to axial current flow is proportional to the cylinder's length divided by its cross-sectional area, or $dR_x = dx/(\kappa\pi a^2)$, where κ is the fluid's electrical conductivity (see Section 4.6.4 on page 142). The conductivity of axoplasm can be measured in the lab. For squid axon, its numerical value is $\kappa \approx 3 \Omega^{-1}\text{m}^{-1}$, roughly what we would expect for the corresponding salt solution (see Problem 12.5).

To simplify the math, we will set the electrical resistance of the exterior fluid equal to zero: $dR'_x = 0$. This approximation is reasonable because the cross-sectional area available for carrying current outside the cylindrical axon is much larger than the area πa^2 of the interior. Thus we have the very convenient feature that the entire exterior of the axon is "short-circuited" and therefore is at a uniform potential, which we take to be zero: $V_1(x) \equiv 0$. The membrane potential difference is then $\Delta V(x) = V_2(x)$; to simplify the notation, we will abbreviate this quantity as $V(x)$.

The resistance R_r of the membrane surrounding the axon slice is just the reciprocal of its total conductance; according to Your Turn 12A, it equals $(g_{\text{tot}} \times 2\pi a dx)^{-1}$, where g_{tot} is the sum of the g_i 's. As mentioned in Section 11.2.2, a typical value for g_{tot} in squid axon is $\approx 5 \text{ m}^{-2} \Omega^{-1}$.

Finally, Section 12.1.2 says that the membrane capacitance is $dC = (2\pi a dx) \times C$ and quoted a typical value of $C \approx 10^{-2} \text{ F m}^{-2}$.

b. Equation To get the equation for the spread of an external stimulus, we write down the condition of charge neutrality for one cylindrical slice of the axon (Figure 12.4a). This condition says that the net current into the ends of the slice, $I_x(x) - I_x(x + dx)$, must balance the total rate at which charge flows radially out of the axoplasm. The radial current equals the sum of the charge permeating *through* the membrane, or $2\pi a dx \times j_{q,r}$, plus the rate at which charge *piles up* at the membrane, $(2\pi a dx) \times C \frac{dV}{dt}$ (see Equation 12.5). Thus

$$I_x(x) - I_x(x + dx) = -\frac{dI_x}{dx} \times dx = 2\pi a \left(j_{q,r}(x) + C \frac{dV}{dt} \right) dx. \quad (12.6)$$

This equation is a good start, but we can't solve it yet: It's one differential equation in three unknown functions, namely, $V(x, t)$, $I_x(x, t)$, and $j_{q,r}(x, t)$. First let's eliminate I_x .

The axial current at a point x of our axon just equals the potential drop along a short distance, divided by the axial resistance dR_x :

$$I_x(x) = -\frac{V(x + \frac{1}{2}dx) - V(x - \frac{1}{2}dx)}{dx/(\pi a^2 \kappa)} = -\pi a^2 \kappa \frac{dV}{dx}.$$

To understand the minus sign, note that if V increases as we move to the right, then positive ions will be driven to the left. Substituting this result into Equation 12.6 yields our key formula:

$$\pi a^2 \kappa \frac{d^2 V}{dx^2} = 2\pi a \left(j_{q,r} + C \frac{dV}{dt} \right). \quad \text{cable equation} \quad (12.7)$$

(The cable equation also describes the propagation of signals along a wire, or "cable," partially short-circuited by a surrounding bath of salt water.)

Next, we write the membrane current in terms of the potential, using Your Turn 12A: $j_{q,r} = (V - V^0)g_{\text{tot}}$. We can also tidy up the cable equation some more by letting v be the difference between the interior potential and its quasi-steady value:

$$v(x, t) \equiv V(x, t) - V^0.$$

Also define the axon's **space constant** and **time constant** as

$$\lambda_{\text{axon}} \equiv \sqrt{a\kappa/2g_{\text{tot}}}; \quad \tau \equiv C/g_{\text{tot}}. \quad (12.8)$$

(Check that these expressions have the units of length and of time, respectively.) These abbreviations yield

$$(\lambda_{\text{axon}})^2 \frac{d^2 v}{dx^2} - \tau \frac{dv}{dt} = v. \quad \text{linear cable equation} \quad (12.9)$$

Equation 12.9 is a special form of the cable equation, embodying the extra assumption of the Ohmic hypothesis (see Your Turn 12A). As desired, it's one equation in one unknown, namely, $v(x)$. It has the pleasant feature of being a *linear* differential equation (every term is linear in v). And there's something very, very familiar about it: It's almost, but not quite, the diffusion equation (Equation 4.20 on page 131)!

c. Solution In fact, we can make the link to the diffusion equation complete by one last change of variables. Letting $w(x, t) \equiv e^{t/\tau} v(x, t)$, the linear cable equation becomes

$$\frac{(\lambda_{\text{axon}})^2}{\tau} \frac{d^2 w}{dx^2} = \frac{dw}{dt}.$$

We already know some solutions to this equation. Adapting the result of Section 4.6.5, we find that the response of our cable to a localized impulse is

$$v(x, t) = \text{const} \times e^{-t/\tau} t^{-1/2} e^{-x^2/(4t(\lambda_{\text{axon}})^2/\tau)}. \quad (\text{passive-spread solution}) \quad (12.10)$$

In fact, *the linear cable equation has no traveling wave solutions* because the diffusion equation has no such solutions.

Some numerical values are revealing: Taking our illustrative values of $a = 0.5 \text{ mm}$, $g_{\text{tot}} \approx 5 \text{ m}^{-2} \Omega^{-1}$, $C \approx 10^{-2} \text{ F m}^{-2}$, and $\kappa \approx 3 \Omega^{-1} \text{ m}^{-1}$ (see step (a)) yields

$$\lambda_{\text{axon}} \approx 12 \text{ mm}, \quad \tau \approx 2 \text{ ms}. \quad (12.11)$$

d. Interpretation Our model axon is terrible at transmitting pulses! Besides the fact that it has no traveling wave solutions, we see that there is no threshold behavior, and stimuli die out after a distance of about 12 mm. Certainly a giraffe would have trouble moving its feet with neurons like this. Actually, though, these conclusions are not a complete disaster. Our model *has* yielded a reasonable account of electrotonus (passive spread, Section 12.1.1). Equation 12.10 does reproduce the behavior sketched in Figure 12.1; moreover, like the solution to any linear equation, ours gives a graded response to the stimulus. What our model lacks so far is any hint of the more spectacular action-potential response (Figure 12.2b).

12.2 SIMPLIFIED MECHANISM OF THE ACTION POTENTIAL

12.2.1 The puzzle

Following the Roadmap at the start of Section 12.1, this section will motivate and introduce the physics of voltage gating, in a simplified form, then show how it provides a way out of the impasse we just reached. The introduction to this chapter mentioned a key question whose answer will lead us to the mechanism we seek: The cellular world is highly dissipative, in the sense of electrical resistance (Equation 11.8) just as in the sense of mechanical friction (Chapter 5). How, then, can signals travel without diminution?

We found the beginning of an answer to this puzzle in Section 11.1. The ion concentrations inside a living cell are far from equilibrium (Section 11.2.1). When a system is not in equilibrium, its free energy is not at a minimum. When a system's free energy is not at a minimum, the system is in a position to do useful work. "Useful work" can refer to the activity of a molecular machine, but more generally, it can include the manipulation of information, as in nerve impulses. Either way, the resting cell membrane is poised to *do* something, like a beaker containing nonequilibrium concentrations of ATP and ADP.

In short, we'd like to see how a system with a continuous distribution of excess free energy can support traveling waves despite dissipation. The linear cable equation did not give this behavior, but in retrospect, it's not hard to see why: The value of V^0 dropped out of the equation altogether, once we defined v as $V - V^0$! This behavior is typical of any linear differential equation (it's called the superposition property of