physically what electricity really was. For example Benjamin Franklin's famous demonstration in 1752 that lightning was just a very big electrical spark led to much speculation and experimentation on electricity in general. Lacking sophisticated measurement devices, it was natural for the scientists of the day to focus on the role of electricity in living organisms, in effect using them as their instruments. The physicians Albrecht von Haller and Luigi Galvani found that electricity, generated by physical means and stored in a capacitor, could stimulate strong contraction in animal muscles. Galvani published his observations in 1791, and speculated that muscles were also a *source* of electricity. After all, he reasoned, even without the capacitor he could evoke muscle twitches just by inserting electrodes between two points.

Alessandro Volta did not accept this last conclusion. He regarded muscles as electrically passive, receiving electrical signals but not generating any electricity themselves. He explained Galvani's no-capacitor experiment by suggesting that an electrical potential could develop between two dissimilar metals in any electrolyte, alive or not. To prove his point, in 1800 he invented a purely nonliving source of electricity, merely placing two metal plates in an acid bath. Volta's device—the "Voltaic cell"—led to decisive advances in our understanding of physics and chemistry. As technology, Volta's device also wins the longevity award: The batteries in your car, flashlight, and so on are Voltaic cells.

But Volta was too quick to dismiss Galvani's idea that life processes could also generate electricity directly. Sections 11.1.2–11.2.3 will show how this can happen. Our discussion will rest upon many hard-won experimental facts. For example, after Galvani decades would pass before E. DuBois Reymond, another physician, showed in the 1850s that living frog skin maintained a potential difference of up to 100 mV between its sides. And the concept of the cell membrane as an electrical insulator only a few nanometers thick remained a speculation until 1927, when H. Fricke measured quantitatively the capacitance of a cell membrane and thus estimated its thickness, essentially using Equation 7.26 on page 236.

To understand the origin of resting membrane potentials, we first return to the topic of ions permeating membranes, a story begun in Chapter 4.

11.1.2 Ion concentration differences create Nernst potentials

Figure 4.14 on page 125 shows a container of solution with two charged plates outside supplying a fixed external electric field. Section 4.6.3 calculated the concentration profile in equilibrium, and from this the change in concentration of charged ions between the two ends of the container (Equation 4.25). We then noted that the potential drop needed to get a significant concentration jump across the container was roughly comparable to the difference in electrical potential across the membrane of most living cells. We're now in a position to see *why* the results of Section 4.6.3 should have anything to do with cells, starting with some ideas from Section 7.4.

Figure 11.1 shows the physical situation of interest. An uncharged membrane, shown as a long cylinder, separates the world into two compartments, #1 and #2. Two electrodes, one inside and one outside, measure the electrical potential across the membrane. The figure is meant to evoke the long, thin tube, or axon, emerging from the body of a nerve cell. Indeed experimentally one can literally insert a thin needle-like electrode into living nerve axons, essentially as sketched here, and connect them to an amplifier. Historically the systematic study of nerve impulses opened up only when a class of organisms was found with large enough axons for this delicate procedure (the cephalopods). For example, the **"giant" axon** of the squid *Loligo forbesi* has a diameter of about a

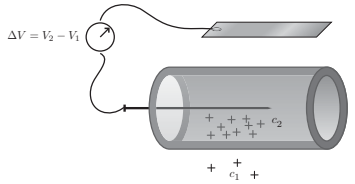

Figure 11.1: (Schematic.) Measurement of membrane potential. The bulk concentration c_2 of interior cations is greater than the exterior concentration, c_1, as shown; the corresponding bulk concentrations of negative charges follow the same pattern (not shown), as required by charge neutrality. The symbol on the left represents a voltmeter.

millimeter, much bigger than the typical axon diameter in your body, about 5–20 μm.

Each compartment contains a salt solution, which for simplicity we'll take to be monovalent—say potassium chloride. Imagine that the membrane is slightly permeable to K^+ ions, but not at all to Cl^- (actually, squid axon membranes are only about twice as permeable to K^+ as they are to Cl^-). For now we will also ignore the osmotic flow of water (see Section 11.2.1). We imagine initially preparing different salt solutions on the inside and outside of the cell: Far from the membrane, the salt concentration in each compartment is uniform and equals c_2 on the inside, and c_1 on the outside. Suppose that $c_2 > c_1$ as shown in Figure 11.1.

After the system reaches equilibrium, the concentration $c_+(r)$ of potassium ions will not be uniform near the membrane, and neither will be the chloride concentration, $c_-(r)$ (see Figure 11.2a). To understand the origin of membrane potential, we must first explain these equilibrium concentration profiles.

The permeant K^+ ions face a dilemma: They could increase their entropy by crossing the membrane to erase the imposed concentration difference. Indeed they will do this, up to a point. But their impermeant partners, the Cl^- ions, keep calling them back by electrostatic attraction. Thus, far from the membrane on both sides the concentrations of K^+ and Cl^- will be equal, as required by overall charge neutrality. Only a few K^+ ions will actually cross the membrane, and even these won't travel far: They deplete a thin layer just inside the membrane, and cling in a thin layer just outside (see the c_+ curve in Figure 11.2a).

The behavior shown in Figure 11.2 is just what we could have expected from our study of electrostatic interactions in Section 7.4.3 on page 233. To see the connection, first consider the region to the right of point C in Figure 11.2. This region is a salt solution in contact with an "object" of net negative charge. The "object" consists of the membrane plus the interior of the cylinder in Figure 11.1; it's negatively charged because some of its positive ions have permeated the membrane and escaped. But a solution in contact with a negatively charged object develops a neutralizing positive layer, just as in Figure 7.8a on page 233. This layer is shown in Figure 11.2 as the region between points C and D. Its thickness λ is roughly analogous to x_0 in our discussion

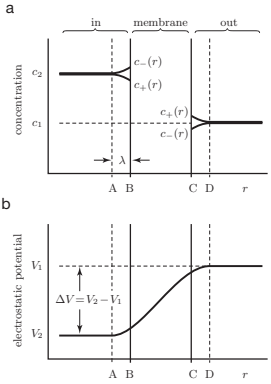

Figure 11.2: (Sketch graphs.) (a) Concentration profiles near a membrane, for the situation sketched in Figure 11.1. Far outside the membrane the concentrations $c_\pm$ of positive and negative ions must be equal, by charge neutrality; their common value c_1 is just the exterior salt concentration. Similarly, deep inside the cell $c_+ = c_- = c_2$. The situation shown assumes that only the positive ions are permeant. Thus some positive ions leak out, enhancing c_+ in a layer of thickness λ just outside the membrane and depleting it just inside. c_- drops just outside the membrane, because negative ions move away from the negatively charged cell. The concentrations in the membrane's hydrophobic interior (the region between B and C) are nearly zero. (b) The corresponding electrical potential V created by the charge distribution in (a). In equilibrium, ΔV equals the Nernst potential of the permeant species (in this case the positive ions).

of the electrical double layer (Equation 7.25 on page 236).[1] Unlike Figure 7.8a, however, we now have both positive and negative mobile charges in the solution. Hence, the layer of enhanced K^+ concentration is also *depleted* of Cl^-, since the negative region to the left of point C in the figure *repels* anions. The effect of both these disturbances is to create a layer of net positive charge just outside the membrane.

Just inside the membrane the situation is reversed. Here we have a salt solution facing a *positive* object, namely everything to the right of point B in the figure. Thus there is a region relatively depleted of K^+, and enriched in Cl^-, a layer of net negative charge just inside the membrane.

We can now turn to the question of finding the electrical potential jump across the membrane. One way to find it would be to solve the Gauss Law (Equation 7.20 on page 232) for the electric field $\mathcal{E}(x)$ given the charge density shown in Figure 11.2a, then integrate to find $V(x)$. Let's instead think physically (see Figure 11.2b). Suppose we bring a positively charged test object in from

[1] **T2** Or more appropriately, to the Debye length λ_D (Equation 7.34 on page 250).

outside (from the right of the figure). At first, everything to the left of our test object has net charge zero, and so the net force on it is also zero and its potential energy is a constant. Once the test object enters the outer charge cloud, at point D, however, it starts to feel and be attracted to the net negative object to the left of point C. Its potential thus begins to decrease. The deeper it gets into the cloud, the more charge it sees: The slope of its potential curve increases.

The membrane itself was assumed to be uncharged. There will be a few permeant ions inside it, in transit, but typically very few. Thus while traversing the membrane the test charge feels a *constant* force attracting it toward the interior, from the charge of the region to the left of point B. Its potential thus falls linearly until it crosses point B, then levels off in the neutral interior of the cylinder.

The potential curve $V(r)$ sketched in Figure 11.2b summarizes the narrative in the preceding two paragraphs.

Your Turn 11a

Arrive at the same conclusion for the potential $V(r)$ by describing qualitatively the solution to the Gauss law with the charge density $\rho_q(r) = e(c_+(r) - c_-(r))$, where $c_\pm(r)$ are as shown in Figure 11.2a.

Your Turn 11b

Repeat the discussion, again assuming that $c_2 > c_1$, but this time considering a fictitious membrane permeable to Cl^- but not to K^+. What changes?

To determine the potential drop $\Delta V = V_2 - V_1$ quantitatively, imagine replacing the voltmeter in Figure 11.1 by a battery of adjustable voltage, and cranking the voltage until the current through the system just stops. The permeant ion species is then in equilibrium throughout the system. Writing its charge q as the proton charge e times an integer z (the ion's valence), its concentration must obey the Boltzmann distribution: $c(x) = \text{const} \times e^{-zeV(x)/k_BT}$. Taking the logarithm and evaluating on the inside and outside reproduces the Nernst relation:

$$\Delta V = \mathcal{V}^{\text{Nernst}} \text{ in equilibrium, where}$$
$$\Delta V \equiv V_2 - V_1 \text{ and } \mathcal{V}^{\text{Nernst}} \equiv -\frac{k_BT}{ze} \ln \frac{c_2}{c_1}. \tag{11.1}$$

In the language of Section 8.1.1, the Nernst relation says that in equilibrium the electrochemical potential of any permeant ion species must be everywhere the same.

Notice that z in Equation 11.1 is the valence of the permeant species only (in our case it's +1). In fact the other, impermeant species in the problem doesn't obey the Nernst relation at all, nor should it, since it's not at all in equilibrium. If we suddenly punched a hole through the membrane, the impermeant Cl^- would begin to rush out, while K^+ would not, since we adjusted the battery to exactly balance its electric force (to the left) against its entropic, diffusive force (to the right). Similarly, you just found in Your Turn 11b that switching the roles of the two species actually *reverses* the sign of the membrane's equilibrium potential drop.

T2 *Section 11.1.2′ on page 437 gives some further comments involving ion permeation through membranes.*