A short summary of biophysics

Peter Latham, January 8, 2024

In biophysics the main thing we're interested in is the membrane potential, $V(t)$, which is the voltage difference between the inside and outside of a neuron. Neurons, though, are big objects – they consist of a soma (cell body), as well as dendrites, axons and synapses (Fig. 1). The membrane potential could refer to any of these.

The primary equation we use to describe the membrane potential is $Q = CV$ (charge = capacitance $\times$ voltage). Taking a time derivative (and noting that dQ/dt = current) gives us

$$C\,\frac{dV}{dt} = -I\,. \tag{1}$$

Here I is, by convention, the outward current – the current flowing out of the cell. The sign should make sense: if I is positive, current flows out and the voltage goes down; if I is negative, current flows in and the voltage goes up.

Equation (1) is absolutely fundamental. OK, sort of absolutely fundamental: it ignores magnetic fields, and assumes that the voltage is the same everywhere inside the cell, which isn't always the case. But here we'll assume that Eq. (1) holds.

So what's the current? If charge were carried by electrons, the current would be computed from $V = IR$ where R is resistance, and if R were constant, we would have a classic RC circuit,

$$C\,\frac{dV}{dt} = -V/R \tag{2}$$

which has the solution $V(t) = V(0)e^{-t/RC}$. However, neurons are not nearly this simple, so the equations are a bit more complicated. For several reasons.

First, charge is not carried by electrons, it's carried by ions. And, because neurons have ion pumps, the ions have different concentrations on the inside and outside of the cell. In particular, the concentrations of sodium and chloride (abbreviated Na and Cl) are high on the outside of the cell, while the concentration of potassium (abbreviated K) is high on the inside. (If you ever become a neuroscientist you should memorize that; but if not I wouldn't bother; it's one of those facts you can always look up.) What's important is the effect of an ion imbalance: even when the membrane potential, V, is zero, an ion imbalance will cause a current to flow (for example, an inward Na current). That rules out $V = IR$, and it means we need something more complicated. The thing we use is

$$I_x = g_x(V - \mathcal{E}_x) \tag{3}$$

where x refers to the ion, so it could be Na, Cl or K (other common ions used by neurons are Ca, for calcium, and Mg, for magnesium, but we won't worry about either). The parameter g_x is the conductance of a channel that allows ion x to pass through (it's the inverse of the resistance, R_x: $g_x = 1/R_x$), and $\mathcal{E}_x$ is the reversal potential. The reversal potential needs to be included because of the concentration imbalance. For example, the reversal potential for Na is about 20 mV, which means the voltage on the inside of the cell has to be about 20 mV higher than the voltage on the outside to keep the sodium current from flowing.

Notice that the conductance depends on the ion. That's because channels, which are holes in the cell that ions can flow through, can be ion specific. For example, a channel may allow only Na, or only Cl, to flow through it. But because this is biology, which is inherently complicated, some channels aren't ion specific, and they let any ion flow through them (although often with different conductances). And, of course, there's the in-between case: channels that let a few ions through, like Na and K but nothing else.

The main reason we use conductance rather than resistance is that conductances add: adding more channels gives you more current (remember parallel circuits?). Thus, the total current is

$$I = \sum_x g_x (V - \mathcal{E}_x) \,. \tag{4}$$

It is useful to combine Eqs. (1) and (4), which gives us

$$C \frac{dV}{dt} = - \sum_x g_x (V - \mathcal{E}_x) \,. \tag{5}$$

This is the starting point for pretty much all of biophysics.

All the interesting behavior that we see in the brain is due to the behavior of the conductances, g_x. They can – and do – depend on just about anything. In the simplest case, they're constant, which gives us a passive neuron. Passive neurons are simple, but not very useful as computing devices. Consequently, evolution invented voltage-dependent conductances. As we saw in class, this led to the Hodgkin-Huxley equation,

$$C \frac{dV}{dt} = -g_L (V - \mathcal{E}_L) - g_{Na} m^3 h (V - \mathcal{E}_{Na}) - g_K n^4 (V - \mathcal{E}_K) \tag{6}$$

where g_L is the leak (meaning passive) conductance and m, h and n are the probability of channels being open. These variables obey the equation

$$\tau_x(V) \frac{dx}{dt} = x_\infty(V) - x \tag{7}$$

where $x = m, h$ or n. The time constants, $\tau_x(V)$, the shapes of the curve $x_\infty(V)$, and the relative values of g_L, g_{Na} and g_K tell you everything about the channel. For the latter, the active conductances are quite large: $g_{Na}/g_L \approx 400$ and $g_K/g_L \approx 120$.

As a bit of an aside, the equations for the channels were derived from the opening/closing probabilities,

$$\begin{aligned} \alpha_x(V) &= \text{probability per unit time that channel } x \text{ goes from closed to open} \\ \beta_x(V) &= \text{probability per unit time that channel } x \text{ goes from open to closed.} \end{aligned} \tag{8}$$

From these, you should be able to show that

$$\tau_x(V) = \frac{1}{\alpha_x(V) + \beta_x(V)} \tag{9a}$$

$$x_\infty(V) = \frac{\alpha_x(V)}{\alpha_x(V) + \beta_x(V)} \,. \tag{9b}$$

The conductances can also depend on the concentration of a neurotransmitter in the synaptic cleft (the area between the red presynaptic terminal and the green spine in Fig. 1). In that case the channels are on the spine, and we have

$$I_s = g_s(V - \mathcal{E}_s) \tag{10a}$$

$$g_s = \overline{g}_s s \tag{10b}$$

where s (which stands for "synaptic"), lies between 0 and 1. It obeys the equation

$$\frac{ds}{dt} = c(1-s) - \beta s\,. \tag{11}$$

Here c is the neurotransmitter concentration in the synaptic cleft (which is generally near zero, but goes up when a spike arrives at the presynaptic terminal), and β tells us how fast the synaptic conductance decays when the concentration drops back to near zero.

There is a bit of a subtlety associated with Eq. (10). The voltage should really refer to the voltage in the spine, not at the soma. However, to model networks, we often pretend that it's the voltage at the soma; basically, we pretend that dendrites don't exist (this is the point neuron approximation). In that case, the current, $I_s = \overline{g}_s(V - \mathcal{E}_s)s$, is the current that flows into the soma.

With this approximation, we can combine Eq. (10) with the Hodgkin-Huxley equation, Eq. (6), to give us a set of equations describing a network of neurons. Using the subscript i to label neurons, and letting $\mathcal{E}_s \to \mathcal{E}_j$, $s(t) \to s_j(t)$ and $\overline{g}_s \to W_{ij}$ (and summing over j), we have a set of equations that looks like

$$C\,\frac{dV_i}{dt} = -g_L(V_i - \mathcal{E}_L) - g_{Na}m_i^3 h_i(V_i - \mathcal{E}_{Na}) - g_K n_i^4(V_i - \mathcal{E}_K) - \sum_j W_{ij}(V_i - \mathcal{E}_j)s_j(t)\,. \tag{12}$$

There are several things to note about this equation. First, the reversal potential, $\mathcal{E}_j$, depends on the presynaptic neuron – something that evolution gave us. Second, we should be aware that the weights, W_{ij}, are very sparse: each neuron makes only about 1,000 connections, and a brain the size of, say, a human, contains 100 billion neurons, so most of the weights are zero. Third the very last term, $s_j(t)$, determines the shape of the PSP (postsynaptic potential) associated with neuron j. It obeys something like Eq. (11), but we often assume it has a stereotyped shape, and write

$$s_j(t) = \sum_k f_j(t - t_j^k) \tag{13}$$

where t_j^k is the time of the k^{th} spike on neuron j and $f_j(t)$ is a function that rises rapidly and decays slightly more slowly than it rises. It is sometimes modeled as a double exponential,

$$f_j(t) = \frac{e^{-t/\tau_j^s} - e^{-t/\tau_j^f}}{\tau_j^s - \tau_j^f}\,\Theta(t)\,. \tag{14}$$

Here τ_j^s and τ_s^f are fast and slow time constants; for fast synapses, τ_f^f is in the range 1-5 ms and τ_j^s is in the range 3-10 ms (and they can be many 10s of ms for slow synapses), and $\Theta(t)$ is the Heaviside step function: $\Theta(t) = 1$ if $t > 0$ and 0 otherwise. However, we could swap in just about any function and that wouldn't have much effect on the network dynamics.

As you can see, things are relatively complicated. But just keep in mind two things:

1. All of biophysics comes from Eq. (5).

2. Conductances, g_x, are the interesting part of Eq. (5). So far we have seen that they can depend on voltage and the concentration of a neurotransmitter. (They can, of course, depend on both – this being biology, evolution has thought of just about anything we can imagine, within reason.) But that's not all. For instance, for very early sensory processing, conductances can depend on the outside world: photoreceptors in the retina have conductances that respond to light; hair cells in the ear have conductances that respond to mechanical vibration; the olfactory receptor neurons in the nose have conductances that respond to chemicals, and so on. So, if we want to know the fundamental equations describing the brain, we need to focus on conductances!

So far we have focused on the soma. But neurons also have axons and dendrites. The equations that describe those structures follow, as for the soma, from Eq. (5). But it takes a bit of thinking to derive them.

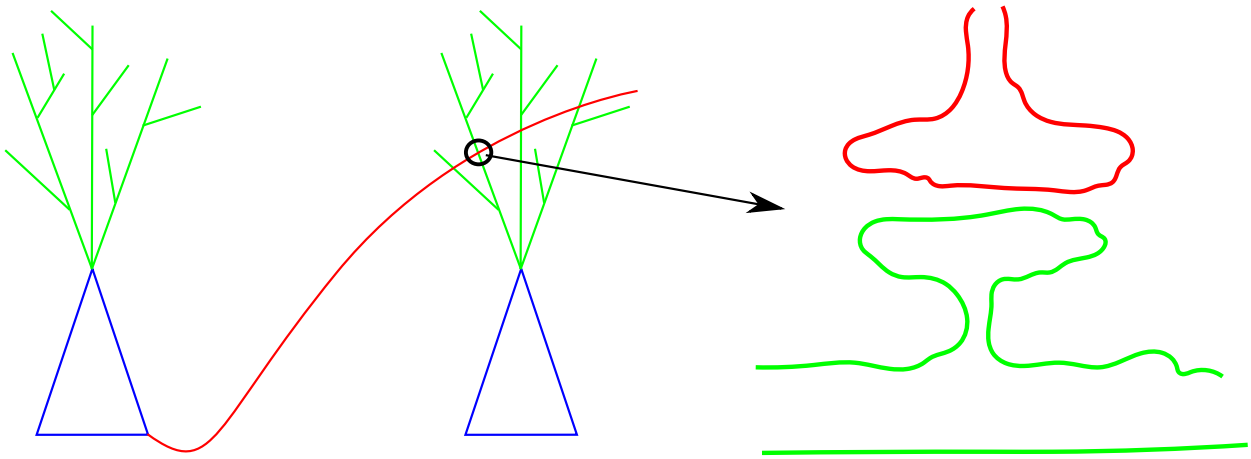

Figure 1: Coupled neurons. The two objects on the left are neurons (which don't really all look alike; I was just too lazy to make them different). The neurons have three main parts: soma (blue), dendrites (green) and axons (red). The dendrites are much, much bigger than shown (50-100 times the size of the soma, which is on the order of 10-20 microns), and so are the axons, which branch (because they connect to about 1,000 other neurons), and can travel long distances (up to a meter). Neurons communicate via synapses, which connect axons to dendrites (usually; axons can also connect directly to the soma). A typical synapse is shown on the right: the presynaptic terminal (red) connects to a spine (green), which is a small structure that sticks out of the dendrites. This being biology, a spine is not always present; the conventional wisdom is that excitatory neurons connect to spines and inhibitory neurons connect directly to dendrites or to the soma. But, this being biology, that conventional wisdom is often violated.