7 Action Potentials - Cole's Impedance Measurements

The singular feature of neuronal communication is the presence of the action potential, which allows robust signaling over large distances. The generation of the action potential further performs a threshold behavior on the inputs - essentially a binary logic in the simplest form.

Cole and others spent considerable effort studying the impedance of the cell membranes. The experiments are pretty out of date, but have useful lessons associated with them. The greatest lesson is to focus on the science, not the technique. Anyway the naive view of the impedance across a membrane is that it is just a capacitor in parallel with a resistor. The impedance is just

$$Z(f) = \frac{R\frac{1}{i2\pi fC}}{R + \frac{1}{i2\pi fC}} = R\frac{(1 - i2\pi fRC)}{1 + (2\pi fRC)^2} \tag{7.1}$$

The magnitude falls off at high frequency as

$$|Z(f)| = \frac{R}{\sqrt{1 + (2\pi fRC)^2}} \rightarrow \frac{1}{f} \tag{7.2}$$

and the phase varies as

$$\phi(f) = -arctangent(2\pi fRC) \rightarrow -\frac{\pi}{2} \tag{7.3}$$

The minus sign means that the current lags the voltage step.

FIGURE - chapt-7-cole-1.eps

Cole studied the giant squid axon and, as a first step toward understanding the possible dynamics of the membrane, plotted the impedance as a function of frequency (on a polar plot) with low excitation voltages in his bridge. Low and behold, the system looked like a parallel resistor and capacitor.

FIGURE - chapt-7-cole-2.eps

When the potentials were raised, however, Cole found that the phase actually reversed! Which is to say, that current flowed against the potentials drop. This is the kind of behavior on would imagine if you had an inductor in series with the resistor, for which our circuit becomes

$$Z(f) = \frac{(R + i2\pi fL)\frac{1}{i2\pi fC}}{R + i2\pi fL\frac{1}{i2\pi fC}} = R\frac{(1 - 4\pi^2 f^2 LC - i2\pi fRC)}{(1 - 4\pi^2 f^2 LC)^2 + (2\pi fRC)^2} \tag{7.4}$$

$$|Z(f)| = \frac{R}{\sqrt{(1-4\pi^2 f^2 LC)^2 + (2\pi f RC)^2}} \rightarrow \frac{1}{f} \rightarrow \frac{1}{f^2} \tag{7.5}$$

and the phase varies as

$$\phi(f) = arctangent\left(\frac{2\pi f RC}{1-4\pi^2 f^2 LC}\right) \rightarrow ? \ \rightarrow 0 \tag{7.6}$$

The phase comes in with the opposite sign. Of course, one gets something close to this with a "negative resistance", which is the transient phenomena we eluded to in the very first lecture. The change in phase was really a warning that Cole was opening up an active current so that the current flowed against the initial potential. Another way to say this is that there is a region of negative resistance (with an unstable equilibrium point). This should only happen transiently (and why did the good Dr. Cole not consider transient behavior early on?). In fact, Cole later recorded the first intracellular action potential, both as a change in conductance as well as a change in membrane voltage.

FIGURE - chapt-7-cole-3.eps

What Cole failed to do was to consider the underlying basis for the action potential. This program began with Katz and Hodgkin, who found evidence that the voltage change had an ionic basis.

FIGURE - chapt-7-hodgkin-katz.eps

With the advent of the voltage clamp, the ionic basis of the action potential (and any cellular process) could be explored. The idea is that the premeabilities, $P \equiv \frac{D}{L}$, depend on voltage, so that these need to be explored under conditions of constant potential. Self-consistency then implies that the voltage changes associated with the action potential may be calculated in terms of these voltage dependent conductances. This self-consistency is the basis of the Hodgkin-Huxley model of the neuronal action potential.

We now take a look at a key technological innovation, the voltage clamp, that is due to Cole. This is essentially the same device that chemists call a potentiostat (in which they sweep the voltage). The idea is that we measure the voltage at a point, compare the measured value against a target value, and then pass whatever current is necessary for the cell to achieve this potential. A simple way to make such a device, in the age of integrated circuits, is to use an op-amp. This is a dual-input, high gain device that, for linear operation, is only useful when used as an element in a feedback circuit.

FIGURE - chapt-7-voltage-clamp.eps

$$V_{out} = A\left(V_{+in} - V_{-in}\right) \tag{7.7}$$

The V_{+in} input is set to the desired holding potential, and the V_{-in} input records the potential of the cell. The possible difference between these values leads to a

current $AG_{cell}\,(V_{+in} - V_{-in})$ to flow that negates the difference. This is a negative feedback loop. Often, for various technical reasons, the clamps are more complicated than this simple description. In particular, the open loop gain A is strongly frequency dependent, i.e., $A = A(f)$. But the basic idea holds.

FIGURE - chapt-6-electrodes-1.eps

FIGURE - chapt-6-electrodes-3.eps

FIGURE - chapt-6-electrodes-2.eps

The same op-amp device can be wired as a high impedance amplifier, for use in a current clamp experiment, and as a current-to-voltage converter, for use with optical detections.