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Lecture 4
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Exercise 4.1: Basic model circuit

Membranes can be modelled as electrical circuits. Each ion type that the cell membrane is permeable to can be modelled as a resistor and a battery connected in series. The resistance depends on the permeability of the membrane to that given ion: the higher the permeability, the lower the resistance for that ion. The ion species also generates an electrical potential across the membrane as expressed by its Nernst potential, and is represented by a battery in the model circuit. This simple representation for each given ion can be integrated into a full equivalent circuit for the cell membrane by connecting the circuit for each ion in parallel. The full model can then be analyzed using basic circuit theory so that the voltage across the membrane and current for a particular ion can be determined. Some useful relationships for this analysis are Ohm's law and Kirchhoff's laws:

Ohm's Law:	$V = I \cdot R$ (voltage equals current times resistance)
Kirchhoff's Current Law (KCL):	The sum of all currents entering and leaving any node in a circuit is zero.
Kirchhoff's Voltage Law (KVL):	The sum of all voltages around a closed loop is equal to zero.

Using the equivalent circuit representation of nerve membrane given in Fig. **??** and the data listed in the following table, calculate the unknown quantities. Assume steady state conditions (*i.e.*, sum of currents is zero). Note that in steady state condition, we can neglect the cell capacitance C_{mem}, depicted in gray.

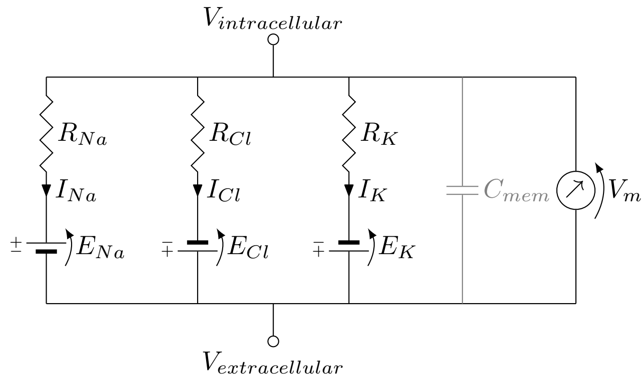

Figure 1: A membrane modelled as an electrical circuit. The arrows for currents and voltages indicate the direction of the measurement, also known as the 'reference direction'. By convention, the directionality of the electric current is defined as positive from the intracellular to extracellular node. (However, for *electrode currents*, a current *into* a cell (depolarizing current) is treated as positive.)
For the voltage, the direction can be specified in several ways (passive sign convention, active sign convention, generator convention, load convention). A number of neuroscience textbooks avoid this problem by displaying bidirectional arrows for the voltage. In these exercise sheets we consistently draw the voltage arrows from the reference electrode to the measurement electrode. We never use plus or minus signs to indicate the reference direction. Of course, the variables can be negative. Note that (almost) no current flows through the voltmeter.

Given	**Find**
$V_m = -30$mV; $E_{Na} = +50$mV; $E_K = -70$mV; $R_{Na} = 1$MΩ; $R_{Cl} = \infty$	R_K
$E_{Na} = +55$mV; $E_K = -90$mV; $E_{Cl} = -70$mV; $R_{Na} = 45$MΩ; $R_K = 18$MΩ; $R_{Cl} = 85$MΩ	V_m
$V_m = -45$mV; $E_{Na} = +60$mV; $E_K = -85$mV; $R_K = 7$MΩ; $R_{Cl} = \infty$	R_{Na}, I_{Na} (is I_{Na} inward or outward?)

Exercise 4.2: The Membrane Capacitance

Typically, there is an excess of negative charge on the inside surface of the cell membrane, and a balancing positive charge on its outside surface. In this arrangement, the cell membrane creates a capacitance C_m. The voltage across the membrane V_m and the excess charge Q are related by the standard equation for capacitors: $C_m V_m = Q$.

1. For a neuron with a total membrane capacitance of 1nF, how many Coulombs are required to produce a resting potential of -70mV? If a single charged ion (=‘*monovalent ion*’) has a charge of $1.6 \cdot 10^{-19}$C, how many ions does this represent?

2. The time derivative of the above equation gives $C_m \cdot (dV_m/dt) = dQ/dt$. Recall that $dQ/dt = I$, the current passing the membrane. What current (in nA) will change the membrane potential of a neuron with a capacitance of 1nF at a rate of 1mV/ms?

3. Plot V_m as a function of t, if a constant current is injected with an electrode into a cell with a membrane whose resistance is infinite (no leaking current).

4. In fact, the situation is a little more complicated, since some charges will always leak through the membrane. Sketch the circuit you use to model these characteristics, with a membrane resistance R and membrane capacitance C. Did you put them in series or in parallel?

5. The timecourse of the change in voltage for a given step injection of current is described by the equation: $\Delta V_m(t) = R \cdot I_{in} \cdot (1 - e^{-t/\tau})$, where I_{in} is the injected current and $\tau = R \cdot C$ (membrane resistance times membrane capacitance). The charging curve for an Aplysia neuron is shown in Fig. **??**. The cell is at its resting potential of -45mV in the beginning. Then a constant current of 9.2nA was injected. An exponential function can be fitted to that curve. This yields a time constant τ of 0.124 sec (time to reach $1/e = 37\%$ of the original difference between resting potential and asymptotic value). The asymptotic value of the depolarization is -38.3mV. Determine (i) the total membrane resistance R and (ii) the membrane capacitance C.

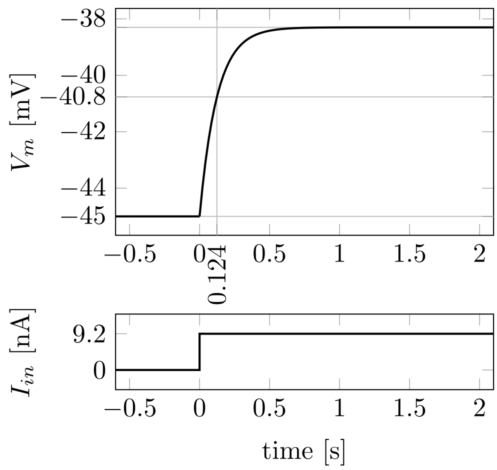

Figure 2: Charging curve of a neuron when a constant current is injected

Exercise 4.3: Cable Equation

For this exercise, nomenclature corresponds to the one used in Peter Dayan and L. F. Abbott, Theoretical Neuroscience, The MIT Press.
For a passive membrane, the membrane potential $V(x,t)$ is determined by solving the following partial differential equation (linear cable equation):

$$\tau_m \left(\frac{\partial v}{\partial t}\right) = \lambda^2 \left(\frac{\partial^2 v}{\partial x^2}\right) - v + r_m i_e$$

where: $\tau_m = (r_m c_m)$ sets the scale for the temporal variation in the membrane potential

$\lambda = \sqrt{\dfrac{a r_m}{2 r_L}}$ sets the scale for the spatial variation in the membrane potential

(λ is called the *electrotonic length)*

with:
- c_m = specific membrane capacitance
- a = radius of the axon (= 2 μm)
- $v = V - V_{rest}$
- r_m = specific membrane resistance (= 1 MΩ·mm^2)
- r_L = longitudinal resistance (= 1kΩ·mm)
- i_e = the current injected into a cell

We now assume an infinite cable and inject a constant current i_e locally at $x = 0$. The steady-state solution (so that $\frac{\partial v}{\partial t} = 0$) of the cable equation then is:

$$v(x) = \left(\frac{i_e R_\lambda}{2}\right) e^{-|x|/\lambda} \text{ , where } R_\lambda = \frac{r_L \lambda}{\pi a^2}$$

1. The ratio of the change in membrane potential at the injection site to the magnitude of the injected current is called the *input resistance* of the cable. Can you express this value with the help of the last formula?

2. We consider an infinitely long axon, which can be assumed passive, apart from two nodes where there are sodium channels. These nodes are at $x = 0$ and $x = 2\lambda$. Let the resting potential be -70mV and the threshold for action potential generation at the nodes be -50mV. Artificially we generate a prolonged 'action potential' at $x = 0$ (sufficiently long to assume constant current injection) of peak voltage 30mV. Will this procedure trigger an action potential at the second node?

3. If we double the radius of the axon (without changing the absolute position of the two nodes), does this change the answer to question 2? Note that the situation in questions 2, 3, and 4 is a voltage-clamp experiment, so we inject whatever current is necessary to bring the membrane potential from -70mV to 30mV.

4. In a second axon extra membrane tightly surrounds the axon between the nodes. As a consequence the membrane resistance increases by a factor of 4, while the capacitance decreases by a factor of 4. In all other respects the axon is similar to the first one, with the same absolute position of the two nodes and the radius of $a = 2$ μm. Again, does this change the answer to question 2?

Exercise 4.4: Circuit Elements

Match these cellular elements to their equivalent circuit elements:

Resistor	Lipid bilayer
Capacitor	Ionic concentration gradient
Battery	Ion channels