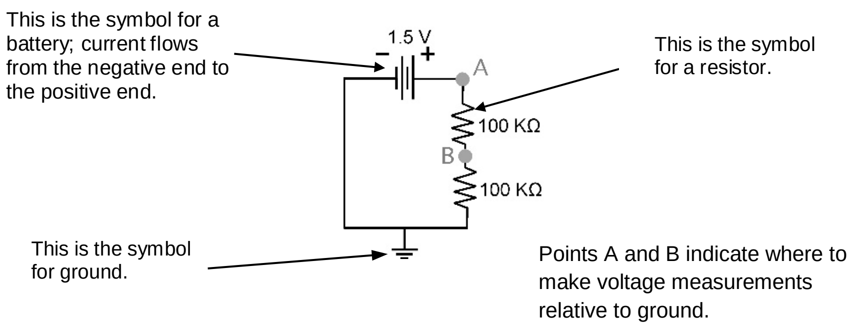
Circuitry #1: Ion channels in a membrane.

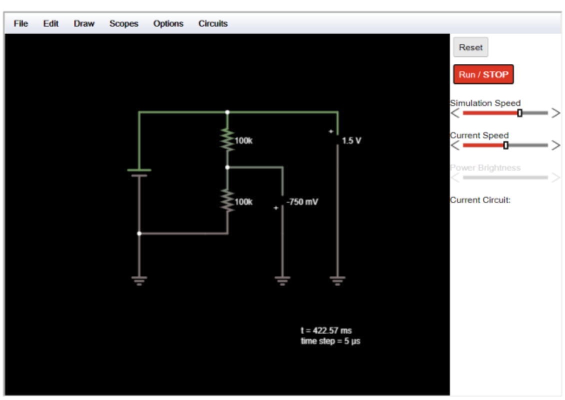
Every cell – neurons included – has different concentrations of ions on either side of its outer membrane that set up a relatively stable "resting potential". The concentration gradients of these ions can be modeled as batteries. The voltage and direction of these batteries depend on the amplitude and direction of the concentration gradient, the charge on the ions, and the conductance (1/R) of the channels specific for each ion.

To get an intuition for how this occurs electrically, you will review some properties of resistors arranged in series and in parallel.

Start with building the circuit below.
Battery with two 100 KΩ resistors in series.



We will simulate this circuit on http://www.falstad.com/circuit/
First, select all and delete the existing circuit.
We will build a circuit like this one



In the "Draw" menu:

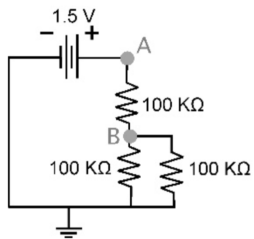
- Add voltage sources, make it 1.5V
- Add 2 resistors, make them 100KΩ
- Add wires to connect the battery to the resistors
- Add ground to the battery
- Add 2 voltmeters
- Add wires and grounds to connect the voltmeters to the appropriate locations.
- Run/Stop to measure the voltage.

Here are a few questions you need to answer:

- What is the voltage across one resistor (B relative to ground)?
- What is the voltage across both resistors (A relative to ground)?
- Calculate the voltage across the second resistor. $R_{total} = R_1 + R_2$ for two resistors in series.
- Calculate the current, I, across each resistor. To verify your calculation, you can add an ammeter.

Modify the circuit as indicated below.

Add an 100 KΩ resistor in parallel with one of the resistors.

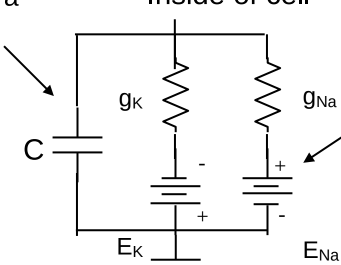


- Measure point A relative to ground and point B relative to ground. Are they the same voltages as you measured in Circuit 1?
- Explain, remembering that $1/R_{total} = 1/R_1 + 1/R_2$ for resistors in parallel.
- Calculate I through each resistor. To verify your calculation, you can add an ammeter.

We now build a circuit that resembles the membrane, but without the capacitative elements

This is the symbol for a capacitor

‘Inside of cell’



‘Outside of cell’

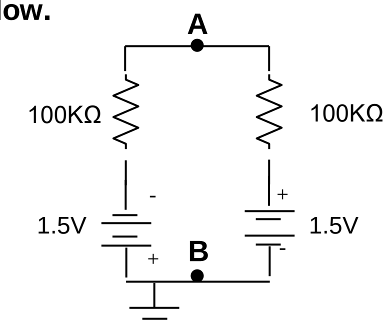
Each battery represents the gradient of an ion (e.g., Na or K) in series with its resistance causing that ion to flow through the membrane.

Note: biophysicists usually refer to the conductance (g) rather than the resistance (R). Remember, g = 1/R and is measured in Siemens (S).

The balance between the concentration gradients and their associated conductances is what leads to a resting membrane potential. [Leaving out the capacitor does not change measurements at equilibrium, i.e. after we have not changed any of the resistances or voltages for a while.]

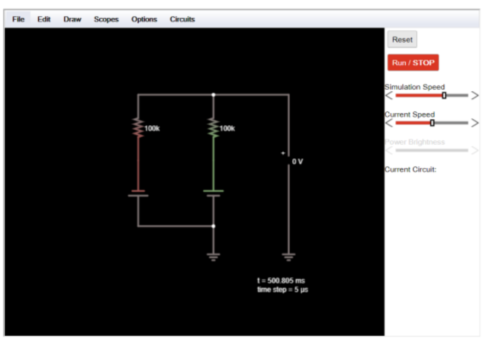
Modify the circuit as indicated below.

Notice that the battery on the left is inverted (has the opposite polarity) relative to the one on the right.



Q: If you measured the voltage between **A** and **B**, what would you get?

A: Since there's an equal and opposite voltage gain and voltage drop going in each direction, you should measure zero resting membrane potential. (We've left out the capacitor for simplicity; it won't change the results here).



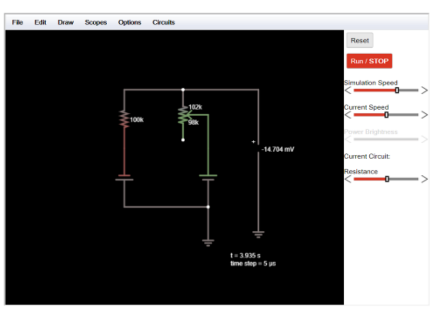
Q: Does this mean that no current is flowing?

A: Negative. A lot of current is flowing (15 μA), but the voltage between A and B is 0.

Q: So, how can we get a non-zero resting membrane potential?

A: We could either have non-equal batteries (i.e. different concentration gradients) or non-equal conductances (i.e. different permeabilities for different ions).

Now replace one of the resistors with a potentiometer.



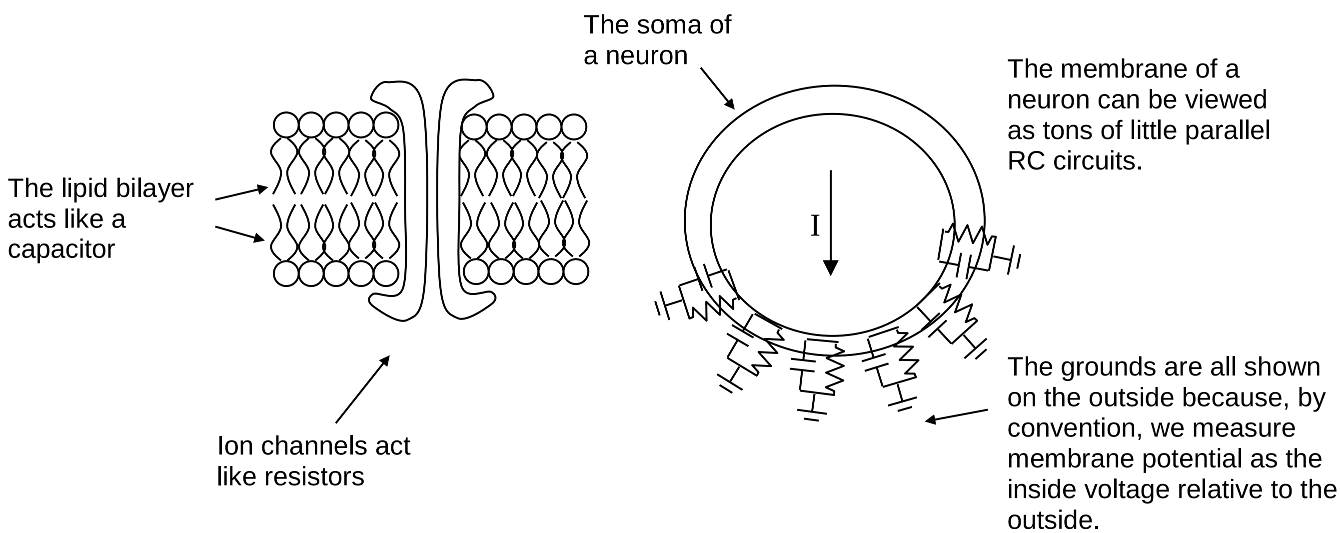
In this exercise, you'll test the effect of changing one of the conductances. To get a non-zero resting potential, <u>dial the potentiometer on the resistance slider:</u>

Bonus question: What resistance do you need to set the pot to in order to get a resting membrane potential of –50 mV? (Hint: figure out how much current needs to flow through one branch to get a potential of –50 mV and then how much resistance you need to get this current.)

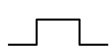
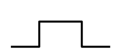
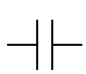
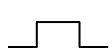
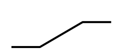
Circuitry #2: Cell membrane

So far, how fast the voltage changes take place has been omitted from all the measurements. If membranes and electrodes were purely resistors, all voltage changes would take place instantaneously. In fact, the changes always have a delay because the membranes also have properties of capacitors.

The next RC circuit of interest is the cell membrane of a neuron. Here's a picture of a membrane:

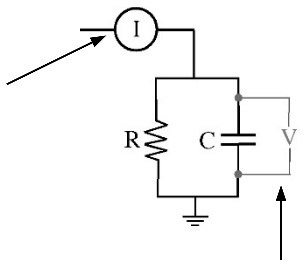


All of the tiny parallel RC circuits around the membrane can be lumped into one big RC circuit; this is what we'll consider next.

Symbol	**A current step (I) like this…**	**… produces this voltage (V) response.**	**Equation**
			V = IR R is measured in ohms (Ω)
			I = C dV/dt C is measured in farads (F)

When you connect a resistor in parallel with a capacitor, it's a *parallel RC circuit:*

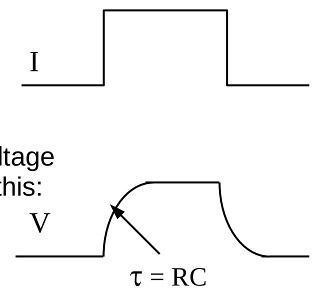
This means current is going into the circuit



This means that voltage is being measured across the capacitor.
(NB: The voltage is the same across every element of a parallel circuit, so the same voltage drops across the resistor.)

In this circuit, a current step like this:

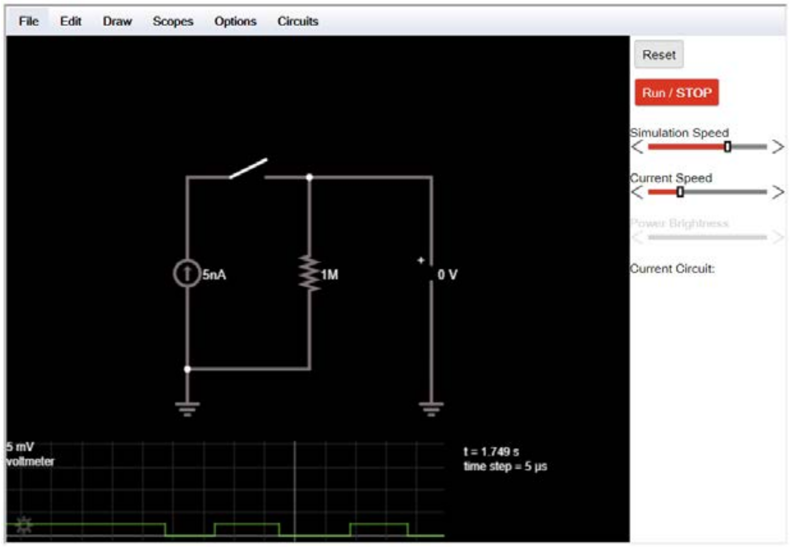
produces a voltage response like this:



The exponential increase in the voltage measurement up to the steady state is called the **RC time constant (τ)**. Why does this happen? When you increase the current, it flows through both branches of the circuit. The current flowing into the capacitor is stored; this is called "charging up the capacitor". Since the capacitor can store only so much charge (the bigger the capacitance, the greater the charge stored), current eventually stops flowing in this branch and all of it then flows through the resistor; at steady-state the voltage level is the same as it would be across the resistor by itself.

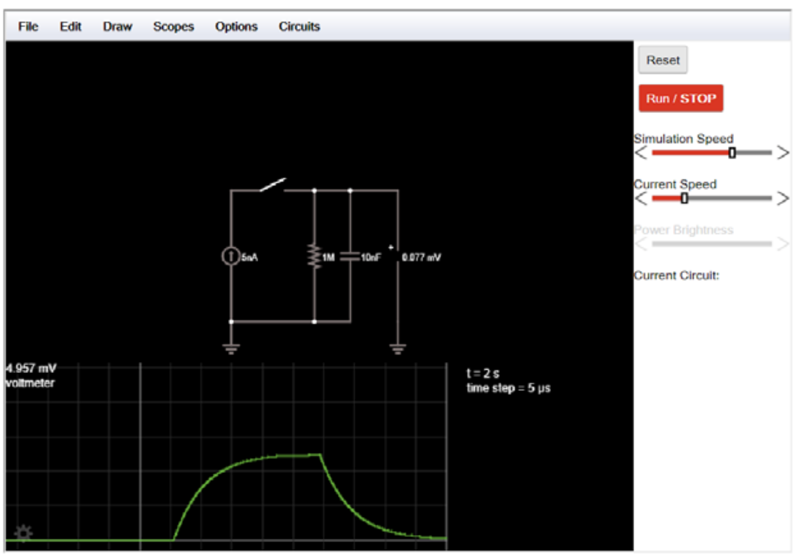
Why is the rise in voltage exponential? You can solve the equations for a resistor and capacitor in parallel to see why. Intuitively, it's because the accumulated charge creates an opposing voltage to stop the addition of charge; this kind of physical process always produces an exponential change over time. τ is the time the voltage takes to reach 0.63 (~2/3) of its steady-state level. Also, τ equals the resistance (in ohms) times the capacitance (in farads). In units: 1 second = 1 ohm x 1 farad. The following exercises are intended to help you understand the effects of capacitance on membrane properties.

Now let's build a circuit with a current source of 5nA, a switch and a 1.0MΩ resistance. In the scope display the voltage across the resistor. Flip on the switch, you should see the voltage change.



What is the maximum voltage change?

Next, add a capacitor in parallel with the resistor. Observe the maximum voltage change and the speed of the change.



You can add another capacitor of the same size in parallel or in series to observe how the time constant changes. Hint: capacitors in parallel $C = C_1 + C_2$. In series, $1/C = 1/C_1 + 1/C_2$.