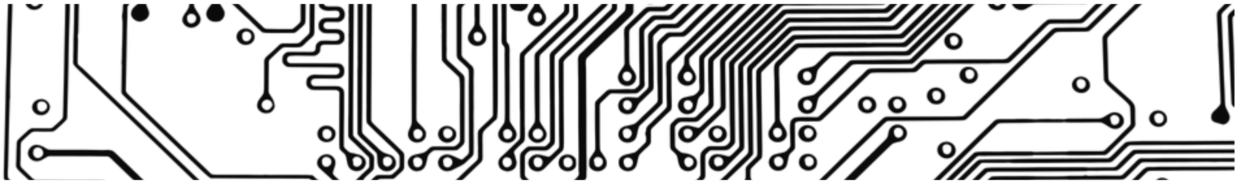
The neuron as an RC circuit



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This lab is largely based on "Electric Circuits for Electrophysiology", adapted by Daniel Wagenaar, originally by Kevin Briggman et al. as well as Dabrowski et al., *JUNE*, 2013.

Background & Goals

The brain as a circuit board

We often describe the brain in terms of circuits, which is a useful and pretty accurate metaphor. This lab focuses on RC circuits. RC stands for **resistance** & **capacitance**. Building on these fundamental concepts we will build and manipulate a basic working circuit representation of the biophysical properties of a neuron.

Modeling resistance

A resistor converts electrical energy into heat when current flows through it. A current flowing through a resistance creates a voltage drop across that resistor, described by Ohm's law:

$$V = IR$$

V = voltage (Volts)
I = current (Amps)
R = resistance (Ohms, Ω)

In a neuron, the **resistance** is determined by the opening and closing of ion channels, which allow current to flow in and out of the cell. When more ion channels are open, more ions are able to flow. Ion channels can be represented with resistors in an RC circuit, since they resist the flow of electricity.

It's important to note the units in the equation above: **1 Amp** flowing through a **1 Ohm** resistor produces **1 Volt** across the resistor. In electrophysiology, we typically work with different scales of numbers:

millivolts (mV) = 10^{-3} V
nanoamps (nA) = 10^{-9} A
megaohms (MΩ) = 10^{6} Ω

Sometimes you'll see Ohm's Law with **conductance** instead of resistance. Conductance (measured in siemens and often denoted by *g*) is the *inverse* of resistance. In other words, it's equal to 1/R.

Kirchhoff's circuit laws

Kirchhoff's laws state two relatively intuitive facts:

1. The voltage at a given point in a circuit is uniquely defined. Thus:
   a. If there are two (or more) paths to go from point A in a circuit to point B, the voltage drop along each of those paths is the same.
   b. The voltage drops around a closed loop must sum to zero.
2. The sum of all currents going into a point equals the sum of all currents going out of it.

Modeling capacitance

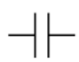
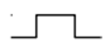
Capacitors are defined by two conducting substances separated by a non-conducting substance in the middle. Capacitors accumulate electric charge on the insulator. The accumulated charge creates an electric field between the conductors and stores electrical energy. Salty fluids that make up the intra- and extracellular solutions of the cell are conductive, the lipid bilayer is not. Therefore, the neural membrane acts as a capacitor.

When one conducting region of the capacitor accumulates a charge, an electric field is created, which pushes the charge off of the next conducting region. This phenomenon only lasts a short amount of time, producing a brief current which is expressed as:

$$I = C * dV/dt$$

I = current (amperes)
C = capacitance (farads)
dv/dt = rate of voltage change with time

To summarize and add a couple useful symbols:

Circuit component	Symbol	A current step (I) like this...	... produces this voltage (V) response.	Equation
Resistor				$V = I R$ R is measured in ohms (Ω)
Capacitor				$I = C\, dV/dt$ C is measured in farads (F)

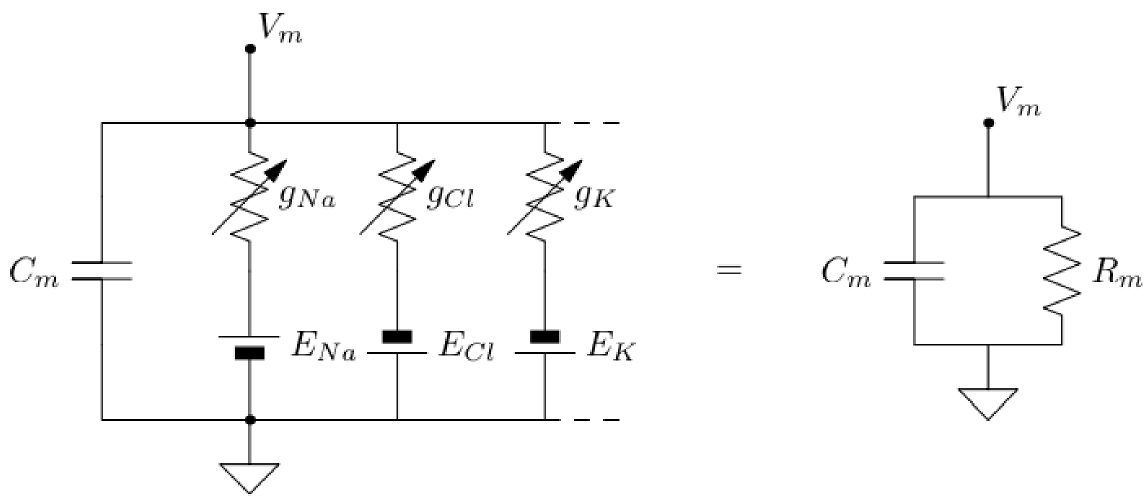
Modeling concentration gradients

In a neuron, there's also a steep concentration gradient due to the different concentrations of ion on either side of its membrane. This is the basis of the neuron's **resting potential**. The inside of the cell is more negative than the extracellular cell space -- typically by about -60 mV, depending on the cell type. We'll use batteries to model this offset of voltage.

Putting it all together

With these components – resistors, capacitors, and a battery – current flow in a neuron can be modeled. In reality, there are many different ion channels, and multiple different ion conductances (left in the figure below). We'll simplify each of these into one membrane resistance, and we'll model the membrane of the cell with one capacitor (right, below).

When we send current into the circuit on the right, the capacitor will charge. In both a neuron and an electrical circuit, voltage rises to a steady state level asymptotically in the response to an external current (e.g., from an action potential or passively passing charge). Once the external current is shut off, the voltage drops in a similar asymptotic way. As you'll discover today, this charging time course depends on a few different factors.



From Barbour, 2014, "Electronics for Electrophysiologists"

These characteristics of the membrane voltage can be measured with a simple voltmeter in the RC circuit. Opening more ion channels (or resistors, as in this RC circuit), which decreases resistance and increases conductance, will express a more rapid increase in voltage on the voltmeter, visually demonstrating the properties of resistance in a neuron.

We can calculate a **time constant**, which represents the time it takes to reach a steady state after a change in voltage across the membrane:

$$\tau = RC$$

τ =time constant (seconds)
R = resistance (ohms)
C = capacitance (farads)

Today you will:

- Learn how to interpret circuit diagrams
- Demonstrate an understanding of Ohm's Law and its applications to resistance in a neuron
- Describe the properties of resistance and capacitance in terms of both an electrical circuit and a neuron
- Show how changing the conductance of ions creates a resting membrane potential
- Observe how the capacitor generates an asymptotic rise in voltage rise
- Describe how the membrane resistance affects the time constant

Protocol

For this lab, we'll rely on an online applet, which will simulate circuits. You can access the applet here: http://www.falstad.com/circuit/ (full screen version here)

When the applet starts up you will see an animated schematic of a circuit with an inductor, resistor, and capacitor. The green color indicates positive voltage. The gray color indicates ground. A red color indicates negative voltage. The moving yellow dots indicate current, showing you both the direction and speed of the current.

Useful tips for using the applet:

- You can easily undo and redo changes using command/ctrl-z.
- You can click and drag to select multiple items.

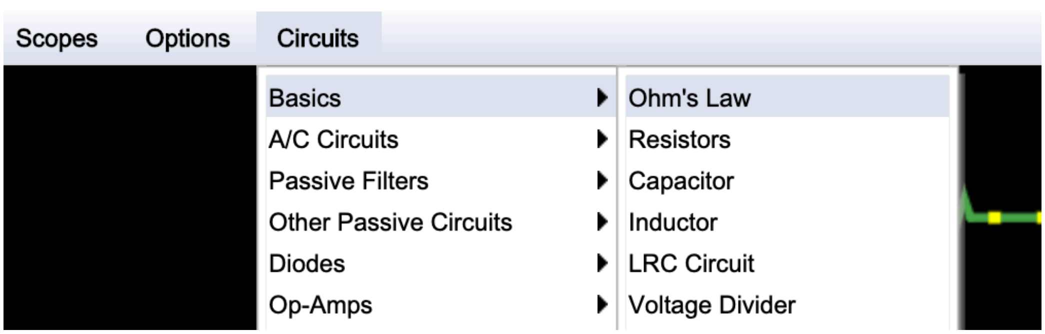
Group Roles for this Activity

In your lab group, designate the following roles:

- **Teammate #1: Circuit wrangler.** You'll set up the circuit on your screen, and share your screen with the group so that they can see what you're doing.
- **Teammate #2: Instructor**: You'll read the instructions so that the circuit wrangler knows what to do.
- **Teammate #3**: **Scribe**: You'll guide the team through the questions on the assignment, taking notes as necessary (but each group member needs to submit the Quiz on Canvas).

Circuit #1: Demonstration of Ohm's Law

At the top, go to Circuits > Basics > Ohm's Law. This will open an example circuit, which is a clever demonstration of **Ohm's** Law.



Note: Throughout this protocol, you'll see questions. These should be answered on the "Quiz" on Canvas. You're welcome to discuss these questions with your lab team.

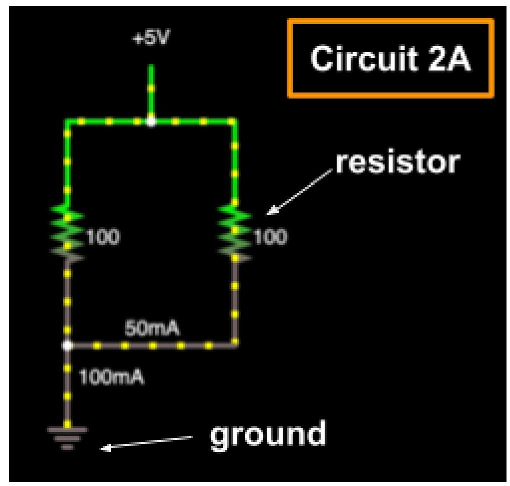
Q1: Why are the dots moving faster on the left than on the right?

Circuit #2: A model of ion channels in a membrane

Next, we'll set up a simple circuit with a battery (representing the concentration gradient) and resistors (representing ion channels). We'll put two 100 Ω resistors in **parallel** (side-by-side). This is similar to the situation in a neural membrane, where many ion channels pass ions in parallel.

Follow these steps to convert your Ohm's Law demonstration into this circuit:

1. Remove the right ground by clicking on it and pressing "Delete" on your keyboard while it is still blue.
2. Connect the open right wire to the left wire, just above the left ground.
3. Double click the right resistor to change the value to 100 Ω.

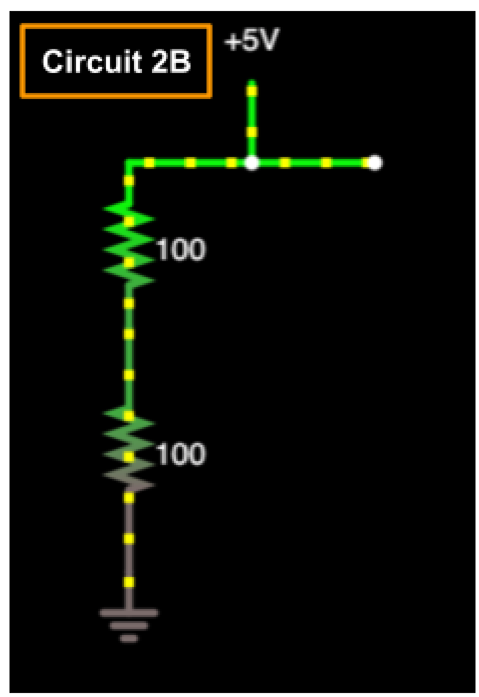


Q2: Resistance in parallel can be calculated with the equation $1/R_{total} = 1/R_1 + 1/R_2$. What is the total resistance in this circuit (in Ohms)?

Q3: What is the total current in this circuit?

Let's see what happens if we put our resistors in **series** (head-to-tail), instead. To change your circuit so that you have resistors in series, follow these steps:

1. Delete the bottom of the circuit (the wire connecting your right resistor to the left wire). *(you might need to play with the wires a bit here to get them to connect properly, or even drag the right wire away entirely so that it doesn't interrupt the flow)*
2. Delete the wire connecting the left resistor to the ground.
3. Move the ground down, to make room for the right resistor.
4. Drag the right resistor into the space between the left resistor and the ground (you may need to shorten the wires around the resistors).



Q4: Resistance in series can be calculated as

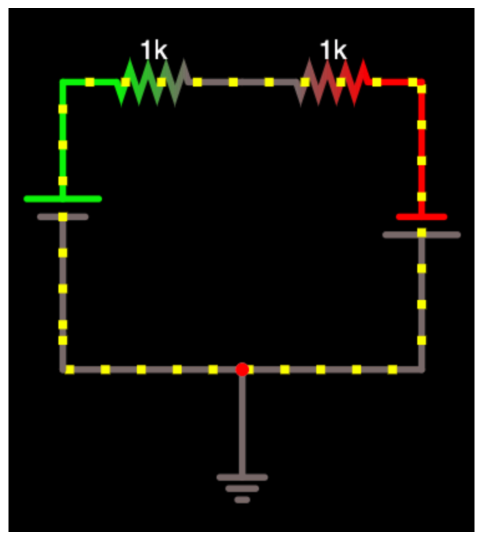
$R_{total} = R_1 + R_2$. What is the total resistance (in Ohms)?

Q5: Using V = IR, calculate the total current (in Amps) in this circuit.

Q6: What is the voltage between the two resistors? Why is it that value?

Circuit #3: A circuit with two concentration gradients

Now, we'll take our circuit up a notch with two batteries that represent the gradient of different ions (e.g., Na+ and K+). We'll also define our circuit in terms of conductances, since that makes more sense when we're talking about ion channels. The balance between the two concentration gradients (batteries) and conductances (resistors) is what leads to a resting membrane potential.

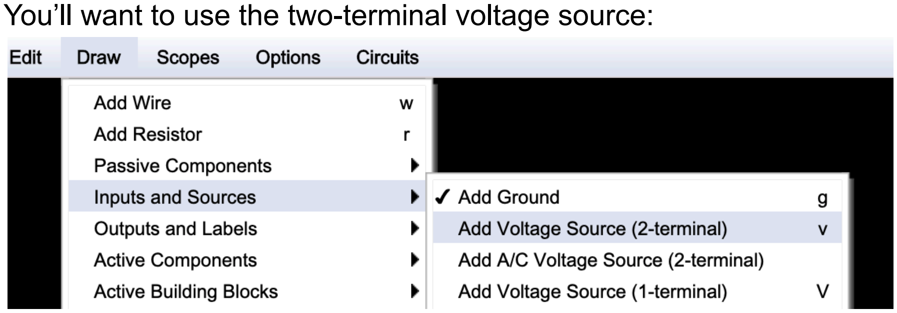


Build the following circuit on the applet.
Note the orientation of the two batteries, and that the two resistors are both 1**kilo**Ohm. The batteries are each **5V**. You can double click on components to check their values.

It'll be easiest to build this circuit from scratch. On the menu, go to **Circuits > Blank Circuit** to create a blank page.

Tips for drawing your circuit:

- You can use the Draw menu to add each component.
- The components have useful keyboard shortcuts too (e.g., **r** for resistor, **w** for wire).
- Go to Draw > Select/Drag Sel or hold down the space bar if you'd like to select items instead of create new ones.
- You'll want to use the two-terminal voltage source:



- This is a pretty unconventional circuit, from an electronics perspective. So, the applet will tell you it's "bad." It'll still illustrate our point, though!
- Since this isn't a conventional circuit, the way the circuit functions in the applet is a little fickle and depends on the order in which you add components. Move things around until

it looks like the above, with a positive (green) current on the left, and a negative (red) current on the right.

Questions for your own comprehension
What is the voltage between the resistors at the top (make sure you choose the point connecting the two resistors)? Does that mean no current is flowing?

Using V = IR, what is the total current in this circuit (you can add the *absolute* voltage of the two batteries)?

Q7: In your own words, how does this circuit model what is happening in the membrane of the neuron?

Adjusting the resistance to create a non-zero membrane potential

How then can we get a non-zero resting membrane potential? There are two ways: We could either have non-equal batteries (i.e. different concentration gradients) or non-equal conductances (i.e. different permeabilities for different ions).So, let's test the effect of changing conductances.

Double click the left resistor to change its resistance.

Q8: What happens to the voltage between the resistors if you lower the resistance of the left resistor, and briefly, why?

Circuit #4: A rather complicated resistor circuit

Let's look at a circuit that has resistors in both parallel and in series. On the top menu, go to **Circuits > Basics > Resistors** to open up a rather fun example. You can click the switches to open and close them.

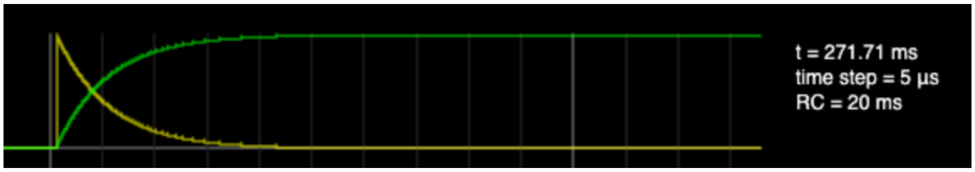
Q9: With all of the resistors in the circuit (in other words, all of the switches closed), why is the current primarily flowing through the wire on the bottom right?

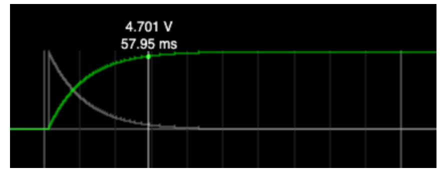
Circuit #5: RC circuit

Finally, what we came here for: an RC circuit. So far, all the measurements have ignored how fast the voltage changes take place. Indeed, if membranes and electrodes were purely resistors, all voltage changes would take place instantaneously. However, the changes always have a delay because the membranes also have properties of **capacitors**.

Open up the sample RC circuit in Circuits > Basic > Capacitor. This sample circuit has two loops, with a switch that enables you to choose which loop to go through. With the left loop connected, the capacitor will charge.

On the bottom of the screen, you can see the capacitor charging. Voltage is shown in green, and current is shown in yellow. You can hover over the traces to get a precise idea of the time and measurements.





After the capacitor has charged fully (the voltage goes to 5 V), discharge it by moving the switch to the right. You should notice that the shape of the discharge mirrors the shape of the charge.

Q10: The time constant should equal τ = RC. What *should* the time constant be (in seconds), given the resistors and capacitor in the circuit here?

We can also measure the time constant by measuring how long it takes the curve to rise or decay. One time constant (τ) is defined by when the circuit rises to **63.2%** of its total charge (alternatively, we could see how long it takes to decay 1/e, about 37%).

To *empirically* measure your time constant, we'll need a clean measurement of the capacitor charging.

1. Restart the stimulation by clicking the "Reset" button on the right hand side.
2. Hit the RUN / Stop button on the side once the voltage gets close to 5 V.
3. Hover over the trace to figure out the time constant for this circuit.

Note your recorded time constant with 5 V stimulation, a 100Ω resistor, and a 200 μF capacitor? (This should be pretty close to the theoretical time constant, assuming someone built a reasonable simulator!)

In engineering, 5τ is considered the time it takes for a capacitor to fully charge (technically, it's at ~99% of its full charge). The time constant is symmetrical for charging as well as losing charge.

Q11: How long would it take this patch of membrane to return to baseline, then?

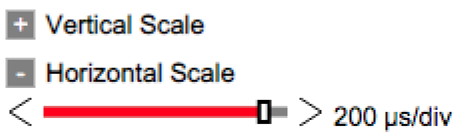
Q12: What are the implications for a long time constant for any integration (in other words, the summation of inputs over time) happening in this membrane?

Record & plot your time constant with different resistors

Next, we'll see how the time constant of the circuit changes in response to the resistance strength. Use the following resistors in your circuit, and determine the time constant for each one.

Tips:

- You may need to change the scroll speed to be able to accurately judge the time constant! You can do this by clicking on the little gear on the bottom left corner of the screen. Try 500 μS/div for the lower resistances.



- The voltage will appear to jump for some of the higher resistances; this is just the plot readjusting the scale.
- In your shared Google drive folder, create a new spreadsheet titled "RC Circuit Lab." On that spreadsheet, create the following table:

Resistance (in Ω)	Time Constant
3	
15	
33	
100	
220	
470	
600	

Q13: Plot the time constant against the resistance. The link for your data & plot needs to be uploaded to the RC Circuit quiz on Canvas.

Your plot should have

- A line fit to it, with a description of what the trendline is (you can *either* show the equation or say in the figure caption what kind of trendline is plotted, with the R^2 value).
- Labeled axes & units
- Seven data points

Plotting Tips:

- Insert your plot as a scatterplot so that you can see the individual points without lines between them.
- Add a trendline under Customize > Series > Trendline. You should add a trendline *for the trend you're expecting given what we know about how these variables interact*.
- Make sure none of the markers for your points are cut off. If they are, change your axes so that they fit.

Q14: Write a 1-2 sentence figure caption for your plot. This figure caption should describe the axes as well as any different lines on your plot, including the type of trendline you included.

~~Check your time constants against the literature~~

~~Let's circle back to biology. Are the time constants you measured similar to what you'd find in a real neuron? Check this website to look at a collection of examples from the literature: https://www.neuroelectro.org/ephys_prop/4/~~

~~**Q15: Choose a paper from the example above and look for the reported time constant. Is the time constant in your circuit similar? If not, why might it be different? You are welcome to find a time constant that is similar (to any of the recorded time constants above), or one that is very different. Regardless, you should explain what contributes to this time constant, and what the time constant tells us about the composition of the membrane.**~~

~~**Note:** *Input resistance* here can be treated as membrane resistance. Don't overthink this question — *I'm not looking for a specific answer*. Just looking to see that you're thinking about what these values look like in real neurons, and how they relate to one another.~~

~~**Note #2**: It is fine for group members to cite the same paper!~~