PEER-LED TEAM LEARNING
ANATOMY & PHYSIOLOGY

MODULE 8: THE (RESTING) MEMBRANE POTENTIAL

NICHOLE MCDANIEL, PH.D.

I. Introduction

One of the most important things that membrane proteins accomplish is the generation of the resting membrane potential (RMP). The RMP is essentially a gradient resulting partly from a difference in concentration (high/low) across the membrane, and partly from a difference in charge (+/-) from one side of the membrane to another. The two gradients combined are called an electrochemical gradient. This gradient drives all sorts of important cell functions that you'll be learning about—from every-day transport to muscle contraction (and therefore the beating heart) and nerve conduction. Today you will focus on how the electrochemical gradient of the RMP is generated.

Prepare for your workshop by reading in your textbook (Chapter 3: 98-102, 106-115) and completing the Pre-Workshop Activities below. Also it's a good idea to review the previous workshop module (membrane transport) before you tackle this one. Show your work in these pages.

II. Pre-Workshop Activities

Define the following terms. Use your own words where possible.

ATPase

channel

chemical gradient

depolarized

electrical gradient

electrochemical gradient

gated channel

gradient

hyperpolarized

ion

ligand

membrane potential

polarized

potential

pump

receptor

resting membrane potential

threshold

voltage

III. Workshop Activities

Divide each group into pairs or groups of three. Each pair/group should receive a bag containing 2 types of beans—40 of each different color, a piece of masking tape, several sticky-notes, a marker, and 5 pennies. All of the activities are linked together and build on one another, so make sure that you don't disturb your beans at the

end of each exercise! At the end of the activity, share your answers and any observations that you made with the larger group.

Activity A. The Na^+K^+-ATPase (otherwise known as the Na^+ pump).

1. Place the piece of masking tape on a flat, level surface. This will be the plasma membrane. For effect, you can draw in the phospholipid bilayer if you wish. The beans will represent sodium (Na^+) and potassium (K^+). Decide which color bean you want to represent each ion and write it down in the table to the right.

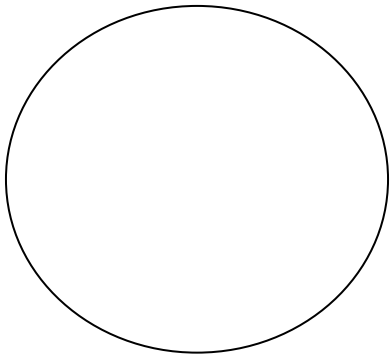
bean color	ion

2. Separate the beans, and put 20 Na^+ ions and 20 K^+ ions on each side of the membrane.
3. We'll assume that the volume of fluid is the same on both sides of the membrane, so we can estimate the concentration of each ion by simply counting the number of ions that are on either side. Record the numbers of Na^+ and K^+ on each side of the membrane in the chart below. Also, count the number of positive charges on each side and record that number in the chart under TPC (total positive charges). Since both ions are positive, all you have to do is add the Na^+ and K^+ from the same side of the membrane together. To determine what we will call the "membrane potential," subtract the positive charges on the outside from the positive charges inside the cell. This calculation is vastly simplified since the true membrane potential is much more than just a separation of charge across the membrane, but the calculation is still useful in understanding how the resting membrane potential is generated.

Event		start	pump 1X	pump 2X	pump 3X	pump 4X	pump 5X	leaky K^+	pump 1X	L-G Na^+	L-G Na^+	V-G Na^+	V-G K^+
IN	Na^+												
	K^+												
	TPC												
OUT	Na^+												
	K^+												
	TPC												
Membrane Potential													

4. Now create a Na^+K^+-ATPase out of a sticky-note. (This is usually represented by a circle with "ATP" written inside it). Somewhere on the ATPase indicate that it moves 3 Na^+ out of the cell and $2K^+$ into the cell each time that it goes through one cycle.
5. The pennies will represent the ATP that is available in the cell. Put all five pennies inside the cell with "heads" facing up. This will symbolize ATP; when is it hydrolyzed (used) you'll turn the pennies over so that "tails" faces up symbolizing ADP.
6. Use one of the ATPs to make the Na^+ pump rotate once. This means that you'll move 3 Na^+ beans out and 2 K^+ beans in. Record the numbers in the chart. Repeat this 4 more times—remember to use an ATP for every cycle of the pump.
7. Where is the Na^+ most concentrated? Where is the K^+ most concentrated? Show this in the cell below.

8. What is the direction of the Na^+ gradient? What is the direction of the K^+ gradient? Show this by drawing arrows in the direction of the gradient (the direction that the ion wants to go) in the cell to the right.



9. Which side is more negative? What is the membrane potential? Put a minus sign (-) where it is more negative.

Activity B. The Leaky K^+ channel.

1. Now make a channel out of another of the sticky-notes. Channels are usually represented by cylinder shapes (so that it looks like a tube that the ion travels through). This channel will be specific for K^+. Put it in the membrane.
2. When the channel is open, the K^+ ions will travel down their concentration gradient. What is the name of this kind of transport?

3. Now, in most cells the K^+ channel is pretty leaky. To show this, move 10 K^+ beans through the channel (make sure you move them in the right direction!). Record the numbers in the chart.
4. What happened to the membrane potential?

5. To demonstrate the balance between the pump and the K^+ channel, you'll need to use more ATP to move the pump through another cycle. Unless you have added pennies from your own pocket to the inside of the cell (which is cheating!), you are out of ATP. How would the cell generate more ATP to keep the pump running?

6. The Na^+ pump works constantly in all cells. What would happen to the ion concentrations and the resting membrane potential if the cell ran out of ATP?

7. You can now flip over the ADP to ATP and use these to make the pump cycle 1 time. Record the numbers in the chart. This membrane potential will be what we call the "resting" membrane potential. Circle it in the chart so that you can remember which one it is.

8. The balance between the Na^+ pump and the leaky K^+ channel is essentially what generates the resting membrane potential. Which one do you think contributes the most to the resting membrane potential (what makes the greatest change)?

9. We say that the cell is "polarized" at the resting membrane potential. Why do you think that term is used?

Activity C. The ligand-gated Na^+ channel.

1. Now make another channel from a sticky-note. This one will be specifically for Na^+. Put it in the membrane. Na^+ channels tend not to leak like the K^+ channel, but they are important in another sense. They only open in response to a specific signal. Sometimes this signal is a chemical ligand, and channels that open in response to these are called ligand-gated channels.

2. For the Na^+ channel to be able to recognize the chemical ligand, the channel must also function as a receptor (something which binds a specific ligand). Draw a receptor attached to the outside end of the channel—this usually looks like the letter "Y" with the bottom part of the letter stuck into the channel and the top part of the letter in the extracellular fluid.
3. The ligand must be a perfect and specific fit for the receptor, so you need to make a triangle that will fit into the "Y." You can do this by tearing off a corner of a piece of paper (or sticky-note), or in some other creative way. Once you have your ligand, label it with an "L." Go ahead and make two ligands. You'll need another one later.
4. The ligand (which just happens to be floating past the cell) binds to the receptor in the Na^+ channel, and causes the channel to open. To show this, put the ligand in the receptor pocket and move 5 Na^+ beans through the channel. The binding of a ligand to a receptor is never permanent. Now that the channel has been opened, allow the ligand to diffuse away. This will cause the channel to close again. Record the numbers in the chart.
5. What happened to the membrane potential?

6. This is referred to as "depolarization." Come up with an explanation for why this term is used.

Activity D. The voltage-gated Na^+ channel.

1. The other type of gated channel is called a voltage-gated channel ("voltage" is simply a fancy word that means the charge difference from one side of the membrane to the other). This type of channel opens in response to a change (from the resting membrane potential) of the charge inside of the cell. This type of channel will only open when another channel has already slightly depolarized the cell (as in the ligand-gated channel above).

2. Make another channel from a sticky-note. This one will also be specifically for Na^+. Put it in the membrane. Each type of voltage-gated channel opens when the membrane potential reaches (or passes) a specific voltage—called a threshold. Let's arbitrarily say that the membrane potential that will trigger this one to open is –15. This means that a voltage sensor (VS) in the channel will trigger the channel to open when the membrane potential passes –15. Write "VS (-15)" on the channel.

3. Will this channel open if the membrane potential is –20? Will it open if the membrane potential is –10? Is the membrane potential in your cell depolarized enough to open the channel right now?

4. Use your second ligand to bind to the ligand-gated Na^+ channel again. Move another 5 Na^+ beans through the channel, and record the numbers in the chart. Is the membrane potential depolarized enough to open the voltage-gated channel now? If it's not, use another ligand to open the channel again.

5. If it is depolarized enough, then this will cause the voltage-gated channel to open. Demonstrate this now by moving 15 Na^+ beans through the channel. Record the numbers in the chart.

6. What happened to the membrane potential?

7. What are some ways that the cell might get it to return to normal (the resting membrane potential)? Come up with at least two ways…one that requires energy and one that does not.

8. Which one do you think will be the fastest?

Activity E. The voltage-gated K^+ channel.

1. Make another channel from a sticky-note. This one will be specifically for K^+. Put it in the membrane. The membrane potential that will trigger this one to open is +10. Write that on the channel VS (+10).

2. Is the membrane potential depolarized enough to open this channel? If so, allow it to open and move 20 K^+ beans through the channel.

3. What happened to the membrane potential?

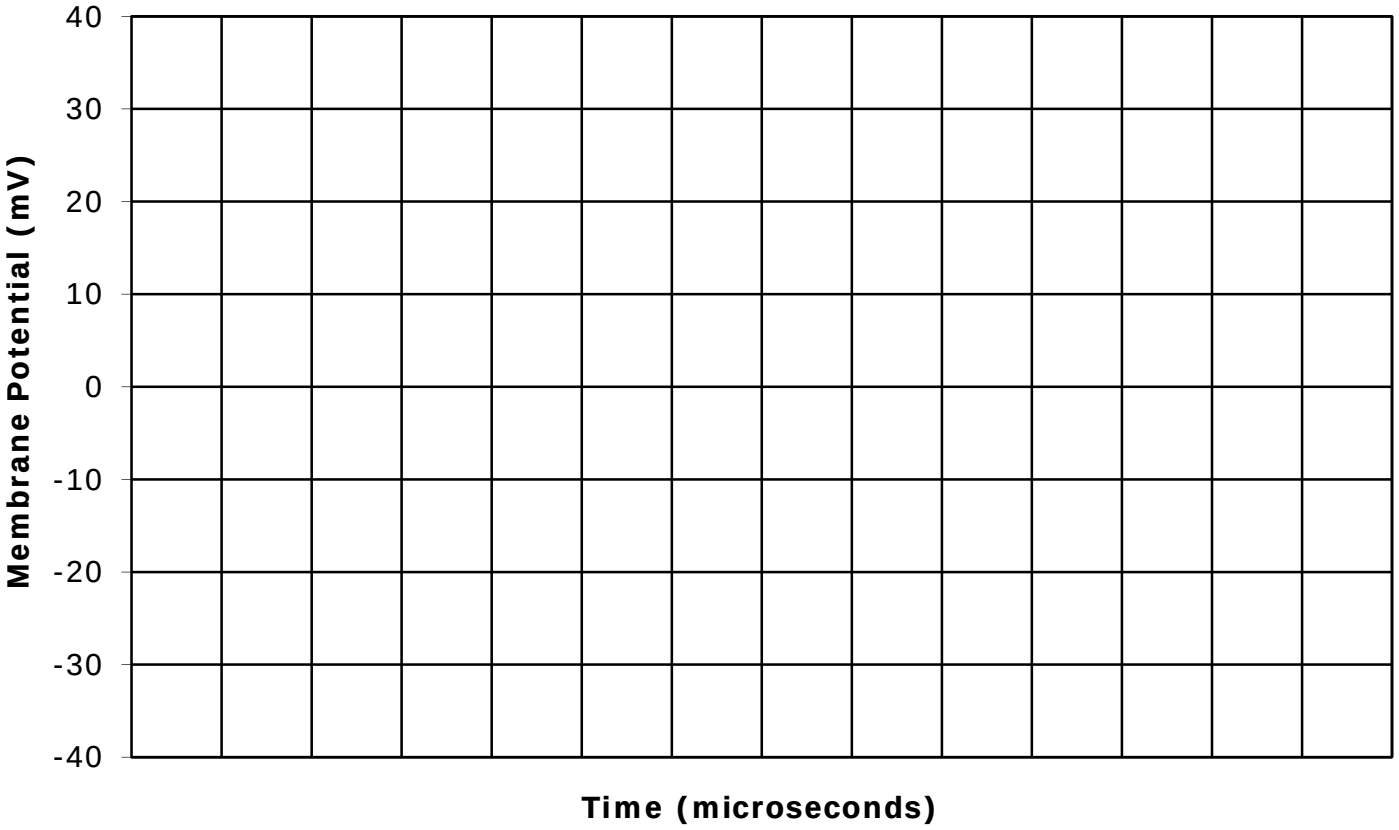
4. What is the status of the concentrations of Na^+ and K^+ inside and outside of the cell?

5. What has to happen to fix this so that the cell returns to its resting membrane potential?

6. Is "resting membrane potential" the best term that you can think of to describe this phenomenon? What might you call it instead?

Activity F. Graphing changes in the membrane potential.

1. In the graph below, plot the membrane potential that was generated in each of the steps (use the numbers that you calculated in the table). Consider each event a microsecond.



2. On the graph, draw a line all the way across to indicate where the resting membrane potential is.

3. Use a marker or a highlighter to color all the parts of the line that are depolarized.

4. Draw an arrow to indicate what direction you think the line would have to go if the cell became hyperpolarized (more polarized than usual).

5. Circle the region of the graph where the membrane is polarized.

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