Modeling Membrane Potentials

Objective:

To model physically or with diagrams the role of ion concentrations, ion channels and ion pumps in the maintenance of the membrane potential and the generation of the action potential, at the level of 85% proficiency for each student.

In order to achieve this objective, you will need to be able to:

1. Predict the movement of Na^+ and K^+ across a permeable membrane.
2. Describe the mechanism responsible for the resting membrane potential.
3. Simulate the electrical and chemical changes that occur in the cell during an action potential.

Materials:

Group Supplies

- 1/2 pounds of Black-eyed peas peas = Na^+ (Light beans are positive charged ions)
- 1/2 pounds of Baby lima beans = K^+ (Light beans are positive charged ions)
- 1/2 pounds of Black beans = Cl^- (Dark beans are negative charged ions)
- 2 Post-it-Notes
- 3 Tooth picks
- 6 pie pans per each group of 3 students
- 5 sheets of paper
- 1 sheet poster board (or butcher paper) about 100 x 90 cm
- 1 marking pen
- 1 metric ruler

Methods and Results:

1. Mark the poster board down the center, along its long dimension, with a line that is interrupted in several places for 2 to 3 cm. These interruptions will represent ion channels gates. Place toothpicks along the line where the interruptions have been made to "close" the channels; the toothpicks will be pivoted to "open" the channels. Mark one side of the line "Intracellular" and the other "Extracellular" (see Fig. 1).

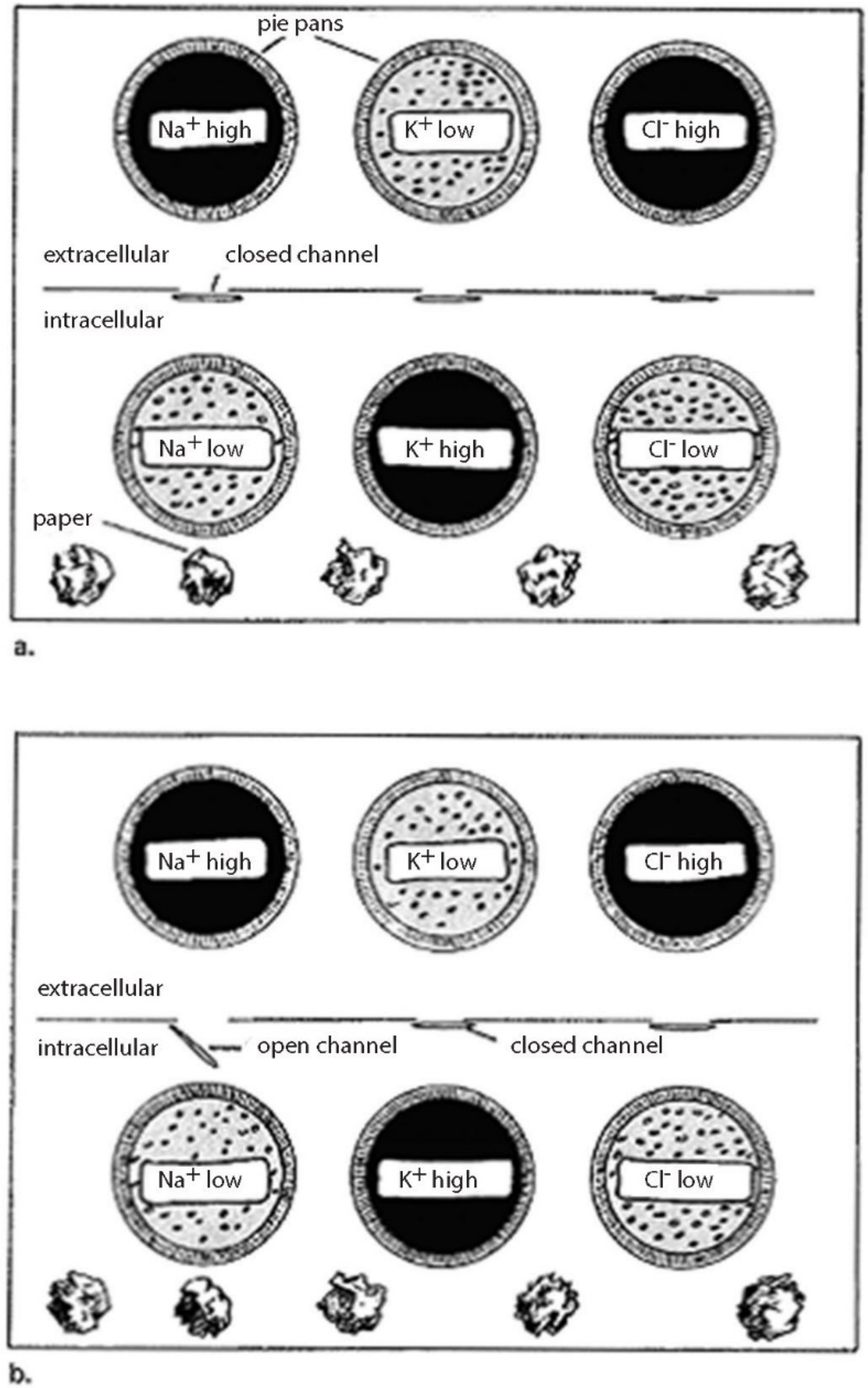

Figure 1. Illustration of student model. (a) Nerve cell "at rest" with all channels closed. (b) Nerve cell with sodium channel having just opened.

2. Fill the pans with peas or beans so that the quantities correspond to the actual concentration of ions. You can estimate the proportions by just looking at them. Table 1 summarizes the approximate concentrations of ions in the extracellular and intracellular fluids for a neuron at rest. You can estimate the proportions by just looking at them.

   * Black-eyed peas (sodium ions (Na^+)): many (140) in one pan, few (15) in another
   * Baby lima beans (potassium ions (K^+)): many (140) in one pan, few (5) in another
   * Black beans (chloride ions (Cl^-)): many (110) in one pan, few (20) in another.

   NOTE: When you are filling the pans to represent the intracellular and extracellular ion concentrations, you are doing the work that is actually done by the Sodium/Potassium (Na+/K+)Pumps and Chloride (Cl-) transporters.

   Table 1. Extracellular and intracellular concentrations of ions.

Ion	Extracellular concentration	Intracellular concentration
Na^+	140 mM/L	15 mM/L
K^+	5 mM/L	140 mM/L
Cl^-	105* mM/L	20* mM/L
Ca^{2+}	3 mM/L	0.0001 mM/L

   *varies during growth and development of nervous system and with specific structures.

3. Wad five pieces of construction paper into tight balls. These wadded-up balls will represent negatively charged proteins that cannot pass through the cell membrane.

4. Arrange the pans and wads of paper on the poster board as shown in Figure 1.

5. Look at the numbers of black-eyed peas representing the <u>sodium</u> ions in the pans inside and outside the cell. If the sodium channel were suddenly opened so that sodium ions (peas) could diffuse (move) across the cell membrane:

   a. Which direction would the <u>sodium</u> ions tend to move based on their <u>concentration</u>; into the cell or out of the cell? Explain.
   b. What effect would the charge of the sodium ions have on their movement? Explain.

6. During an action potential, a sodium channel opens for about one millisecond (one 1000th of a second). You will open the sodium channel for 10 seconds to represent one millisecond. Before opening the sodium channel, decide which direction the sodium ions will move based on your answers to Questions 5a and 5b. When you begin timing, move the appropriate toothpick, to represent opening the sodium channel. Then take the peas out of the pan and drag them through the sodium channel one at a time in the direction you think they will go until 10 seconds has elapsed. (Remember, the sodium ions cannot pass through other channels nor through the membrane where there is no channel.) Close the sodium and leave the sodium ions where they are now as you answer Questions 6a-b below.

   Look at the numbers of sodium ions on each side of the cell membrane now. Compared to the number in each pan at rest, are there:

   a. More sodium ions inside the cell now than there were before opening the sodium channel, or
   b. Fewer sodium ions inside the cell now than there were before opening the sodium channel?

   Based on your answer above, do you think the intracellular fluid of the cell is

   c. More negative than it was before opening the sodium channel, or
   d. More positive than it was before opening the sodium channel? Explain.

   Look at the numbers of lima beans representing the potassium ions in the pans inside and outside the cell. If the potassium channel was suddenly opened so that potassium ions (beans) could move across the cell membrane:

   e. Which direction would the potassium ions tend to move based on their concentration; into the cell or out of the cell? Explain.
   f. What effect would the charge of the potassium ions have on their movement? Explain.

   Relate your findings to the changes in membrane potential that occur an action potential.

7. During an action potential, a potassium channel opens for one to three milliseconds. You will open the potassium channel for 30 seconds to represent three millisecond. Before opening the sodium channel, decide which direction the potassium ions will move based on your answers to Questions 6e and f. When you begin timing, move the appropriate toothpick, to represent opening the potassium channel. Take the beans out of the pan and drag them through the potassium channel one at a time in the direction you think they will go until the 30 seconds has elapsed. (Remember, the potassium ions cannot pass through other channels nor through the membrane where there is no channel.)

   Look at the numbers of potassium ions on each side of the cell membrane now. Compared to the number in each pan at rest, are there:

   a. More potassium ions inside the cell now than there were before opening the potassium channel, or
   b. Less potassium ions inside the cell now than there were before opening the potassium channel?

   Based on your answers above, do you think the intracellular fluid of the cell is:

   c. More negative than it was before you had opened the potassium channel (but after you had opened the sodium channel and moved the peas), or
   d. More positive than it was before you had opened the potassium channel (but after you had opened the sodium channel and moved the peas)? Explain.

8. Sodium channels and potassium channels are often opened in response to electrical signals, such as more positive ions in the intracellular fluid of the cell. Channels of this type are called, respectively, voltage gated sodium channels and voltage gated potassium channels.

   Your instructor will guide you in this activity

   Communication along an axon is due to the sequential opening and closing of **voltage gated sodium channels** and **voltage gated potassium channels**. This process is often referred to as the propagation of an action potential

   We will imagine that each table in the lab is part of an axon of a neuron.

   - At the first table we will start with a **sensory stimulation** that opens **movement gated sodium channels** and makes the intracellular fluid more positively charged.
   - The positive charge also opens **voltage gated sodium channels** at the first table and we repeat steps 6 and 7.
   - The positive charge of the intracellular fluid of the first table quickly **diffuses** to the next table.
   - The positive charge opens **voltage gated sodium channels** and we will repeat step 6 and 7.

9. This process continues from table to table until we get to the last table which we imagine to be the axon terminal and the location of the synaptic bulb.

   When an action potential reaches the axon terminal of the nerve cell, it will then pass information to the next cell. The end of the axon contains **voltage gated <u>calcium</u> channels** which are opened in response to electrical signals, such as the arrival of positive sodium ions in the intracellular fluid of the axon. Due to calcium pumps there are more calcium ions outside of the axons than inside the axons. Thus, when voltage gated calcium channels open, calcium moves into the intracellular fluid of the cell. This stimulates a series of events that cause the **release of a neurotransmitter**.

10. Neurotransmitters can open (gate) a wide variety of channels (**ligand gated channels**) in adjacent neurons, which causes the intracellular fluid to become either more positive (+) (excitation) or more negative (-) (inhibition).

    - A localized increase in intracellular positive (+) charge is called an **excitatory postsynaptic potentials** (EPSP).
        - If <u>sodium</u> channels open, the intracellular fluid of the adjacent neuron becomes positively charged and excites the neuron.
        - If <u>calcium</u> channels open, the intracellular fluid of the adjacent neuron becomes positively charged and excites the neuron.
        - If the localized <u>positive</u> charge (EPSP) is <u>positive</u> enough, it can open voltage gated sodium channels and cause (trigger) an action potential.
    - A localized increase in intracellular negative (-) charge is called an **inhibitory postsynaptic potentials** (IPSP).
        - If <u>chloride</u> channels open, the intracellular fluid of the adjacent neuron becomes negatively charged and inhibits the neuron.
        - If <u>potassium</u> channels open, the intracellular fluid of the adjacent neuron becomes negatively charged and inhibits the neuron.
        - If the localized <u>negative</u> charge (IPSP) is negative enough, it can neutralize the positive charges, prevent the opening of voltage gated sodium channels, and thus prevent an action potential.

Discussion:

1. If sodium channels opened briefly, which direction would the sodium ions tend to move based on their resting concentration; into the cell or out of the cell? Explain.
   a) Would the inside of the cell become more positive or more negative?
   b) What effect would this change in charge have on the movement of the sodium ions? Explain.
2. If potassium channels opened briefly, which direction would the potassium ions tend to move based on their resting concentration; into the cell or out of the cell? Explain
   a) Would the inside of the cell become more positive or more negative?
   b) What effect would this change in charge have on the movement of the potassium ions? Explain.

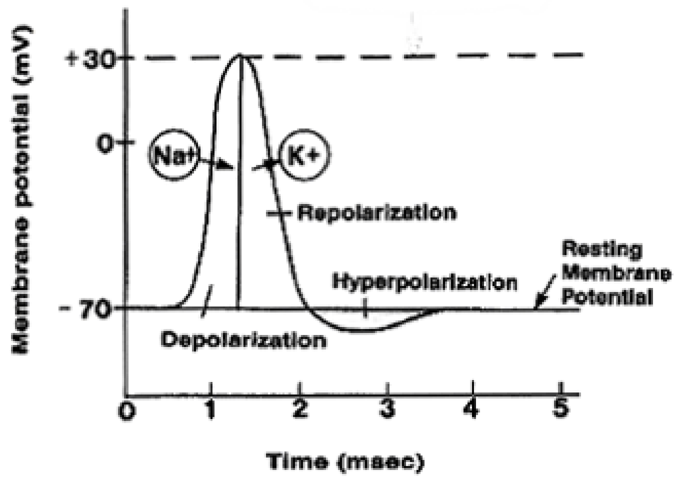

Figure 2. Graph of membrane potential during an action potential.

3. Compare the graph of the membrane potential during an action potential shown in Figure 2 with what you just learned in steps 6 and 7 on the previous pages.
4. After a lot of action potentials have occurred, will there be enough ions moving to change significantly the concentration gradients? Would the sodium and potassium ions continue to move as they did during the action potential?
5. In order to continue to function properly, the cell must now somehow get back to its resting state. Do you have any ideas as to how the cell might do this?
6. When an action potential reaches the end of the axon of the nerve cell, it will then pass on information to the next cell. Do you have any ideas as to how the cell might do this?
7. Can you think of situations in which it would be important for the postsynaptic cell to be stimulated? Inhibited? What kinds of problems might occur if it were not possible to control whether postsynaptic neurons were inhibited or stimulated? For example, what if postsynaptic neurons were always stimulated?