Computer Lab Worksheet
Characteristics of an Action Potential

Purpose

To explore some of the conditions that promote or inhibit the ability of neurons to generate an action potential.

What is the assignment?

1. Use the results from the program to answer the questions 1-13 (i.e., *Q1 – Q13)* and to fill in empty spaces in Table 1. You will need to use the results in Table 1 to compose a Figure.
2. Hand in a report containing the Figure and your answers to *Q1-13*.

General Information

To load the program, double-click on the "**action potential.rt**" icon. Click on the ARROW button or select "run" from the "operate" menu to begin execution. You may let the program continue to run throughout the exercise, if you so desire. Any of the parameters (e.g. the stimulator or ionic concentrations) can be altered "on the fly" to test their effects on the action potential. To reset all parameters to their default values, go to the "operate" menu and select "reinitialize all to default."

Orientation, and Brief Description of the Model

Load and start the program as described above. While the program is running, but before beginning the laboratory exercises, look at the computer screen and note that there are five general areas displayed on the screen that comprise the model. These five areas include:

1. the extracellular concentration of Na^{+}_{o}, K^{+}_{o}, and Ca^{2+}_{o}
2. the intracellular concentration of Na^{+}_{i}, K^{+}_{i}, and Ca^{2+}_{I}
3. the stimulus parameters (i.e., ways to alter the nature of the stimulation provided to the neural membrane)
3. four different panels showing different features of the response to each stimulation.

The functions of each of each part of the model are described below:

Slider controls for manipulating extra- and intracellular ion concentrations (top left quadrants of computer screen)

The slider controls enable you to manipulate the intracellular and extracellular concentrations of sodium, potassium, and calcium independently. After making a change, you can return the model to its original parameters by pulling down the "operate" menu and selecting "reinitialize all to default."

Controls for manipulating the stimulus parameters (bottom left quadrant of computer screen)

These controls enable you to manipulate several features of the stimulation regime. More specifically, you can vary:

1. the intensity of the stimulation
2. the duration of stimulation
3. the latency between two successive stimulations
4. the quality of stimulation (ramp or pulse)
5. the number of stimulations (1 or 2)

Effect of stimulation on the electrical properties of the membrane (right side of computer screen)

The panels on the right illustrate the effects of each stimulation on:

1. the potential of the neural membrane (E_m)
2. the Na^+ and K^+ current flowing through the membrane at any given time
3. the net current flow through the membrane
4. the timing and magnitude of each stimulation.

Exercises

Threshold and all-or-none property of the action potential

Procedure A: Reset all variables and start the program: stimulator set for a single pulse, DURATION1 = 1 ms; START1 = 4 ms. Now, incrementally increase AMPLITUDE1 (from 0) to find the minimum stimulus amplitude that will trigger an AP.

Q1. What is the minimum stimulus required to produce an action potential (AP)?
Q2. Describe the sequence of current changes that underlie the AP:
Q3. Next, decrease AMP1 until the AP disappears. What term describes the membrane potential at the point where an AP is first produced?
Q4. What happens to the AP as AMP1 is increased well above this point? That is, does it undergo any obvious changes? Explain why or why not.
Q5. Set AMP1= 5.0 ma. Now progressively decrease the extracellular concentration of Na^+. How does this manipulation affect the E_m, the Na^+ and K^+ currents, and the AP? Explain your observations.

Procedure B: Reset AMP1 to the point where the AP first fires. Now set DUR1 = 0.5 ms; note that the AP no longer fires but that Amp1 has to be increased further to trigger the AP. Write the new value down in Table 1. Continue in this manner for the other values of DUR1 until all of the cells in the table are filled. Finally, plot the values on a bivariate graph, with amplitude on the y-axis and duration on the x-axis. This is a well-described relationship that is used clinically to assess recovery of nerve function.

Table 1
Data table for recording the amplitude required to elicit an AP under different durations of stimulation.

Duration of 1 (in msec)	Amplitude of 1 (in mAmps)
0.1	
0.2	
0.5	
1.0	
1.5	
2.0	
2.5	
3.0	

Q6. How would you expect the slope of this curve to differ in a patient with nerve damage? Would it be steeper or shallower? Explain.

Accomodation

Accomodation is a process by which a neural membrane becomes less able to generate an AP following repeated stimulation. The following exercise will illustrate this phenomenon through the use of two type of stimulation: pulse vs. ramp. A pulse stimulation reaches its maximum intensity suddenly, whereas a ramp stimulation reaches its maximum intensity gradually.

Procedure: Reset all variables. Set DUR1 = 15 ms, and determine the minimum value of AMP1 required to fire an AP? Now, keep these settings the same, but switch from a pulse to a ramp stimulus.

Q7. What happens to the AP? Why?
Q8. What is the minimum value of AMP1 required to fire an AP with ramp stimulation?
Q9. Is the shape and timing of the AP under ramp stimulation identical to that under pulse stimulation (switch between pulse and ramp to compare)? What is the molecular mechanism underlying this phenomenon?

Refractory Periods

Procedure A: Reset all variables so that DUR1 = 1 ms; DUR2 = 1 ms; START1 = 4 ms; START2 = 20 ms). Set the stimulator switch for 2 pulses. Set AMP1 and AMP2 to the value in *Q1* that first produced an AP.

> *Q10.* Compare the shape and height of the first and second AP. Do they differ?

Now set START2 = 11 ms. Increase the value of START2 until another AP is fired.

> *Q11.* What was the minimum amplitude required to elicit the second AP? Why was more stimulation required to elicit the second AP when START2 = 11 ms?

Next, set START2 = 10 ms.

> *Q12.* What AMP2 was necessary to elicit the second AP? Why is this value different from that of *Q11*?

Finally, set AMP2 = 400 ma (a maximal stimulus), and incrementally decrease START2 from 10 ms until a clear second AP is not fired.

> *Q13.* What phenomenon are you observing? Why is it impossible to generate an AP under this condition?