

Purpose:

To demonstrate the unique physiological properties of the action potential in a CNS neuron.

General Information:

Program name = "CNS AP.rt"
Location = Any of the Power Macintosh computers in the MSL

Directions:

- 1) Double click on the "CNS AP.rt" icon to load the program.
- 2) 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.
- 3) 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.
- 4) To reset all parameters to their default values, go to the "operate" menu and select "reinitialize all to default".

Problems:

1) **Threshold.** This exercise will illustrate the all-or-none property of the action potential.

a) Reset all variables and start the program (stimulator set for a single pulse, DURATION1 = 1 ms, START1 = 4 ms). Incrementally increase AMPLITUDE1 (from 0) to find the minimum stimulus amplitude that will trigger an AP = _____. Identify the various phases of the AP: _____

Describe the sequence of current changes that underlie the AP: _____.
Decrease AMP1 until the AP disappears; what term describes the membrane potential at the the point where an AP is first produced? _____. What happens to the AP as AMP1 is increased well above this point? _____.

Set AMP1= 10.0 ma. Now progressively decrease $[Na]_{out}$ and describe the effects on E_m , i_{Na} and i_K : _____.

b) Reset all variables.

Set AMP1 again to the values at which 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 the Table to the right. Then complete the Table for other values of DUR1 (numbers <0.5 need to be typed in).

<u>Duration1</u>	<u>Amplitude1</u>
0.1 ms	
0.2	
0.5	
1.0	6.4 ma
1.5	
2.0	
2.5	
3.0	

Finally, sketch a rough plot of the Amplitude (y) vs Duration (x). (This is a well-described relationship that is used clinically to assess recovery of nerve function).

2) **Accomodation.**

a) Reset all variables. Set DUR1 = 12 ms, what is the minimum value of AMP1 required to fire an AP? _____.

b) Keep these settings the same but switch from a pulse to a ramp stimulus. What happens to the AP? Why? _____.
Now what is the minimum value of AMP1 required to fire an AP? _____.
Is the AP identical to that in question 2a (switch between pulse and ramp to compare)? _____.

What is the mechanism behind this phenomenon? _____.

3) Refractory Periods.

a) Reset all variables (DUR1 = DUR2= 1ms, START1 = 3 ms, START2 =13 ms).Set the stimulator switch for 2 pulses. Set AMP1 and AMP2 to the value in question **1a** that first produced an AP. Compare the second AP to the first: _____. Why?_____. Now set START2 = 10 ms (i.e. so the second pulse is delivered during the after-hyperpolarization phase of the first AP). Increase the value of START2 until another AP is fired. START2 = _____. What is the term for the difference between START2 and START1? _____.

b) Set START2 = 8.0 ms. At what value of AMP2 will an AP first fire? _____. Is the AP identical to the first one? ____ Why or why not? _____.

c) Set START2 = 7.0 ms. At what AMP2 does an AP fire? _____. Why is this value different from that in **4b**? _____.

d) Set AMP2 = 400 ma (a maximal stimulus). Now incrementally decrease START2 from 7 ms until a distinct second AP is not fired. START2 = _____. What is the term for the difference between START2 and START1? _____.

4) Spontaneous Depolarization.

Reset all variables. Keep AMP1=0 and increase $[K]_{out}$ until an AP is fired. $[K]_{out} = \underline{\hspace{1cm}}$? How is the AP different than in **1a**? _____. What is E_{rest} at this point? _____.

5) Anodal break.

Reset all variables. Progressively decrease AMP1 below zero. Describe the changes in E_m when AMP1 pulses are positive or negative: _____.
Can an AP ever be fired using a hyperpolarizing stimulus pulse? ____ Why or why not? _____

_____.

6) Selective Channel Blockade

a) Reset all variables. One difference between an AP in a peripheral neuron verses an AP in a CNS neuron is the contribution of Ca to the AP in central neurons. To observe this, set AMP1 = 20 ma and decrease the [nifedipine]. Describe how the AP shape changes: _____. Why? _____
(nifedipine is an L-type Ca channel blocker). The difference in the two APs, although somewhat exaggerated, illustrates an important difference between central and peripheral neurons.

b) To reinforce this concept, describe what happens when voltage-gated Na channels are progressively blocked by increasing the [TTX] (leave the nifedipine concentration lo): _____.
What ion is carrying the majority of inward current under these conditions? _____. Why is the upstroke phase different than in exercise #1? _____.

c) To further exaggerate the effect, describe what happens when K channels are partially blocked (increase [TEA] but don't change any other settings): _____.

_____.

The shape of the AP is now approaching that observed in what (non-neuronal) cell type ? _____.

d) To observe the effects of K channel blockade in a peripheral neuron, reset all variables, set AMP1 = 20 ma, then increase the [TEA]. Compare the effect of TEA now with that in **6c**: _____. (The effect is more subtle and difficult to illustrate if (as in this model) K channels are not completely blocked by TEA; a more complete block would necessitate compensatory adjustments of AMP1).