Computer Lab Worksheet - SYNAPSE

Purpose:
To demonstrate the basic physiological properties of a neuron-neuron synapse.

General Information:
Program name = "**synapse**"
Location = PowerMac and Wintel computers in the LRU or MSL rm. 180; or downloaded from Davis' website link.

Directions:
1) Double click on the "**synapse.rt**" (Mac) or "**synapse.exe**" (Wintel) icon to load the program.
2) Click on the arrow button or select "**run**" from the "operate" menu to begin execution.
3 To reset all parameters, go to the "**operate**" menu and select "**reinitialize all to default**".

Exercises:

1. Temporal summation. This exercise demonstrates how stimulation of a single presynaptic cell generates EPSPs that summate over time.

RESET all variables and set A=fire. Click the ARROW to RUN. Note the shape of the EPSP (a rapid rise in E_m with exponential decay back to the resting potential). What accounts for this shape? _____.

Set Pulses=4 and RUN. Note that a train of 4 AP's traveling down cell A produces 4 individual EPSPs on cell C and that no summation occurs. Now sequentially increase the firing rate of A from 1 to 9 and RUN the model after each increase. Temporal summation should be observed; what is the maximum amplitude of the summed EPSP? _____. At the highest firing rate (=9), how many pulses are required to reach the threshold (-60 mV) for firing an AP on cell C? ____ (progressively increase the # pulses and RUN each time to find out.) What should happen to the E_m tracing if the threshold is reached?_____.

2. Effects of Changing the Time or Length Constant of Cell C. The values of tau (time constant) and lambda (space constant) influence the degree to which EPSPs summate on the surface of the postsynaptic cell.

a. Keep all variables the same as they were at the end of exercise **1** (i.e. a rapid train of pulses firing on cell A that gives a large but NOT-QUITE-threshold EPSP on cell C. Now change tau from 0.4 to 0.5. What is the effect? _____.

b. To observe the effect of changing tau on a single EPSP, RESET all variables, set A=fire, Pulse=1. RUN. Change tau and repeat. Describe how changing tau alters the EPSP magnitude: _____ and EPSP shape: _____.

c. RESET; A=fire, Pulse=1. Compare the EPSP amplitude with lambda set to 1.0 vs 0.1: _____ _____. Set Pulses=3 and A_{rate}=9, RUN. Compare the maximum EPSP amplitude with lambda set to 1.0 vs 0.1: _____. [note: changing the length constant of cell C would not affect EPSP amplitude or temporal summation directly under the terminal bouton of A, but remember that the E_m tracings are being measured at the axon hillock; therefore, decreasing lamda reduces the amplitude of the EPSP as it travels from the bouton to the axon hillock. Thus, the concept that increasing tau enhances temporal summation while increasing lamda enhances spatial summation is valid].

3. Spatial summation. This exercise demonstrates how stimulation of multiple presynaptic inputs can generate EPSPs that sum over distance.

RESET. Compare the amplitude of the EPSP on cell C when A fires 1 pulse vs when A and B both fire one pulse in synchrony. A alone (set A=fire): ____ A+B (set A and B=fire): _____. To more clearly observe that summation occurs, try increasing the delay of cell B to ≈ 1.4 ms: amplitude=_____. At what value of B_{delay} does no

summation occur? ____. What is the maximum EPSP amplitude that can be achieved in this model with spatial summation alone (i.e. without increasing the # of pulses)? ____. Why? _____.

4. Combinations of Spatial and Temporal Summation.

RESET, set A=fire, Pulses=5, A_{rate}=8, RUN. What is the maximum EPSP amplitude? _____. What type of summation is involved? _____. Now add excitatory input from cell B (B=fire, B_{rate}=5). What is the maximum EPSP amplitude now? _____. Progressively increase B_{rate} to determine at what minimal rate an AP fires on cell C: ____. Keep these settings and then increase B_{delay} to 1.2 ms (this should change the degree of summation slightly but enough to prevent an AP from firing).What happens? _____.

For another example of the interaction between temporal and spatial summation, RESET, set A=fire, B=silent, A_{rate}=9, Pulses=5, tau=0.6 then RUN. Note that threshold is not quite reached, but if cell B fires even once (set B=fire to see this), an AP fires on cell C.
[This shows how cell B could act as an ON-OFF gate to control "information" transfer from cell A to cell C, i.e. if B is off, then repeated bursts of firing by cell A do not elicit APs from cell C, but if B fires a pulse during that time (B_{delay}= 1.0 to 2.0 ms), an AP fires on C. Try to verify this].

5. Effects of Changing Transmitters or Post-synaptic Conductances. [it may be useful to run the program in continuous loop mode for exercises **5 and 6**, by pressing the loop button rather than the arrow button to run the model].

a. RESET, set A=fire. Measure the amplitude of the EPSP: _____. This might simulate the effects of ACh as the transmitter released from cell A, because ACh typically increases the membrane conductance of the postsynaptic cell to <u>both</u> K^+ and Na^+ ions. To illustrate how this can cause a depolarization (despite K efflux), compare the size of this EPSP with one resulting from a selective increase in gNa (i.e. change A_{cond}="Na"): ___ _____.

b. Now set A_{cond}="Cl" and note the magnitude of the EPSP: _____. Explain the difference: _____. Compare this with the IPSP amplitude when A_{cond} = "K+Cl": _____ or when A_{cond}="K" _____. If changes in gCl have "no effect" on E_m why is the IPSP amplitude smaller when A_{cond}="K+Cl" than when A_{cond}="K" alone? _____.

6. Presynaptic inhibition. Demonstration of this phenomenon requires an anatomical change in the configuration of the cells. RESET all variables, then set Wiring=A->B and RUN <u>once</u>.

a. Set A=fire, B=silent. Now what effect does cell A firing have on the E_m of cell C? _____ Why? _____ _____.
Now set A=silent, B=fire. You should see a "normal" EPSP on cell C. What happens when cell A fires also (set A=fire)? _____.
What mechanism underlies this phenomenon?
_____
_____.
Keep the settings the same. What happens if the B_{delay} is progressively increased to 3.0?
_____. Why? _____.

[Extra: How/why are the answers to the last two questions affected by increasing the time constant of C?]