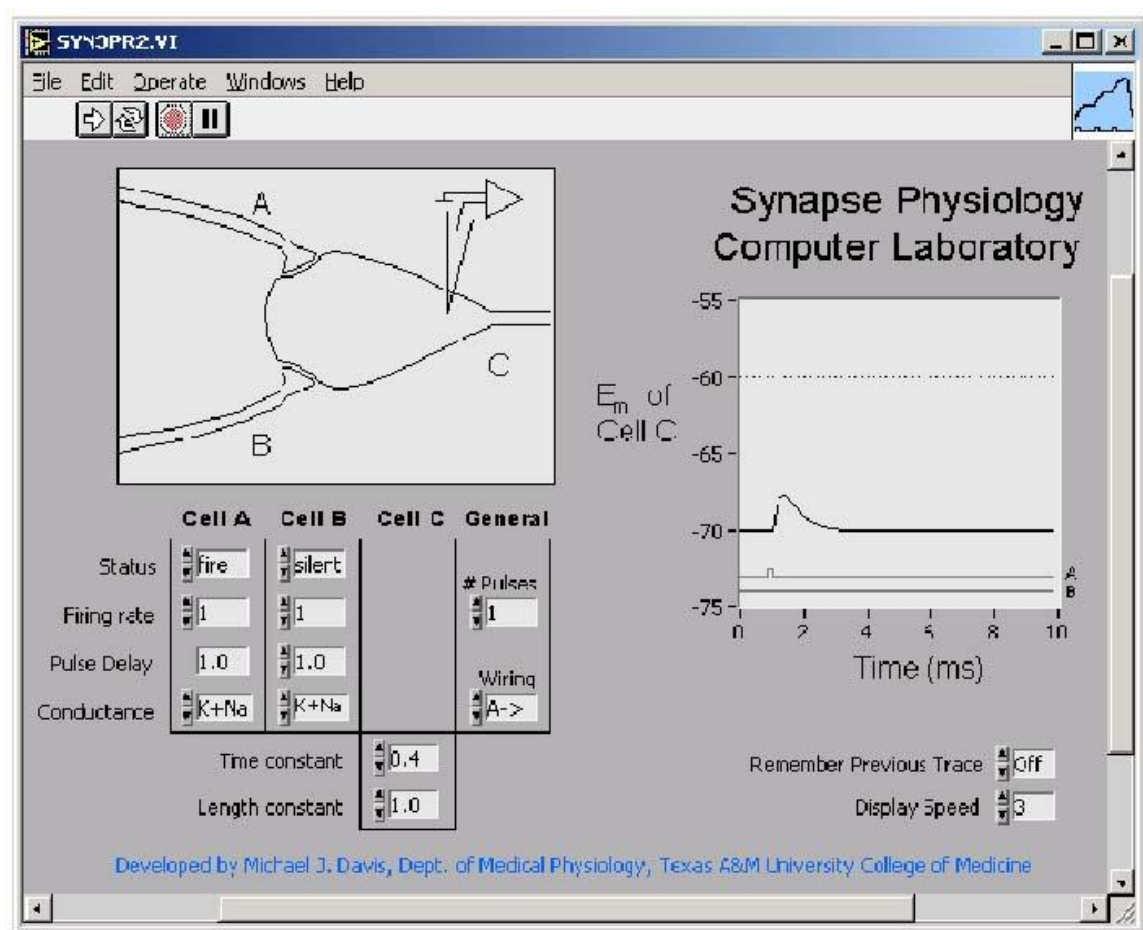


Modeling Synaptic Integration



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Objective:

To model with simulation or with diagrams the major features of synapses and the processing of nervous signals including temporal and spatial summation, excitatory and inhibitory neurotransmission and presynaptic inhibition, at the level of 85% proficiency for each student.

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

1. Define Excitatory Postsynaptic Potential (EPSP)
2. Define Inhibitory Postsynaptic Potential (IPSP)
3. Compare and contrast Temporal Summation and Spatial Summation.
4. Explain the generation of post-synaptic potentials seen with a combination of temporal and spatial summation.
5. Explain the generation of post-synaptic potentials seen with the opening of various ion channels that reflect excitatory and inhibitory neurotransmission.

Materials and Methods:

The simulation program is **SYN3P-R2.EXE** for Windows based computers.
To load the program, in the desktop double-click on



Alternatively, if needed, you may download the program from my website:
https://www.dgward.com/pdf/physo101/pdf_other_physo101.htm

After it loads, the program draws the displays. Run the program either by clicking on the "**Run**" button (→) in the upper left-hand corner of the program window, or by selecting "**Run**" from the "**Operate**" menu at the top of the program page. The program can be stopped at any time by clicking on the "**Stop**" button (stop-sign symbol) in the upper left-hand corner of the program window. If necessary, the model parameters can be reset to their initial conditions at any time by selecting "**Reinitialize All to Default**" from the "**Operate**" menu at the top of the screen.

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 exercise, look at the computer screen and note that there are three general areas displayed on the screen. These areas include:

A. Display of Neuronal firing (top left side of screen):

On the left side of the screen is a display of the anatomical connections between two pre-synaptic neurons (cells A and B) and one post-synaptic neuron (cell C). A recording electrode is placed near the axon hillock of cell C to measure membrane potential (E_m).

With the default settings, neurons A and B each synapse on the cell body of neuron C. Neuron A will be stimulated with one pulse at the lowest stimulation (firing) rate. At any time the user may pull down the "Operate" menu at the top of the program page and select "Reinitialize All to Default" to reset the program to the default conditions.

B. Controls (lower left side of screen):

Below the neuron display are various controls to alter the stimulus parameters, the anatomical arrangement between the neurons, and the properties of ion channels in the post-synaptic neuron. Each pre-synaptic stimulus will produce an action potential in the respective pre-synaptic neuron, which will travel down to that cell's synaptic bulb and release transmitter

The controls are organized such that there are four for each pre-synaptic cell, two for the post-synaptic cell (C), and two general controls. The "Status" control for each pre-synaptic cell refers to whether that cell is being stimulated to generate an action potential. "Firing Rate" determines the impulses per second if multiple stimuli are delivered to the pre-synaptic cell (1 = lowest rate, 10 = highest rate). "Pulse Delay", "Time Constant" and "Length Constant" are not used in this lab. "# Pulses" determines the number of stimuli delivered to the pre-synaptic cell(s) and can be used to generate a "train" of action potentials.

C. Graph of Membrane Potential (E_m) vs Time for Neuron C (right side of screen):

The graph on the right shows the change in membrane potential (E_m) of neuron C as a function of time. The timing of the pre-synaptic stimulus pulses is marked on the graph by gray pulses just below the trace of the membrane potential (E_m).

D. Optional controls.

Turning the "Remember Previous Trace" switch 'On' preserves the previous graph, allowing the traces associated with two sets of parameters to be easily compared. Increasing the 'Display Speed' allows the drawing to be slowed down for use on faster computers.

Terminology:

E_m – Membrane potential – the voltage of the intracellular fluid relative to the extracellular fluid.

EPSP – Excitatory Postsynaptic Potential – a localized increase of positive charge in intracellular fluid that is too small to trigger an action potential

IPSP – Inhibitory Postsynaptic Potential – a localized increase of negative charge in intracellular fluid

Amplitude – the size of a response (EPSP, IPSP, membrane potential)

Conductance – the flow of ions through a channel – specific ions are conducted through specific channels

Temporal summation – accumulation of ion charge over time (repetitions)

Spatial summation – accumulation of ion charge over space (from different locations)

Temporal summation

This exercise demonstrates how stimulation of a synaptic site generates EPSPs that can accumulate over time.

- A) Reinitialize all variables, set cell A **“conductance”** = **“Na”**, and then Click the **“Run”** button.
Note the shape of the EPSP (a rapid rise in membrane potential (E_m) with exponential decay back to the resting potential). What accounts for this shape?
- B) Set **“# Pulses”** = **“3”**, and then Click the **“Run”** button.
Note that a train of three action potentials (APs) traveling down cell A produces three individual EPSPs on cell C without any summation.
- C) Now *sequentially* increase the **“firing rate”** of Cell A from **“1 to 9”** and Click the **“Run”** button *after each* increase. (**“1” “Run”**, **“2” “Run”**, **“3” “Run”**..., **“9” “Run”**)
Temporal summation should be observed; what are the maximum amplitudes of the summed EPSP? When was an action potential generated in cell C?

Spatial summation

This exercise demonstrates how stimulation of synaptic sites at separate locations generate EPSPs that can accumulate together.

- A) Reinitialize all variables, set cell A **“conductance”** = **“Na”**, and then Click the **“Run”** button.
What is the amplitude of the EPSP in cell C?
- B) Set **“status”** = **“fire”** for both Cell A and Cell B. Set **“conductance”** = **“Na”** for both Cell A and Cell B. Click the **“Run”** button.
What is the amplitude of the EPSP?
Compare the amplitude of the EPSP in cell C under these two conditions.

Temporal and Spatial summation

This exercise demonstrates how stimulation of multiple synaptic sites can generate EPSPs that can accumulate over time and location.

- A) Continue from where you stopped above.
Set **“# Pulses”** = **“3”**, and then Click the **“Run”** button.
What is the amplitude of the EPSPs in cell C?
- B) Now *sequentially* increase the **“firing rate”** of Cell A and Cell B from **“1 to 5”** and Click the **“Run”** button *after each* increase. . (**“1”**, **“Run”**; **“2”**, **“Run”**; **“3”**, **“Run”**;....)
Temporal and spatial summation should be observed. What are the maximum amplitudes of the summed EPSP? When was an action potential generated in cell C?

Compare the amplitude of the EPSP on cell C under these condition with those used to show just temporal summation.

Effects of changing post-synaptic electrolyte conductance (opening different ion channels)

This exercise demonstrates how the opening of different types of ion channels affects EPSPs and IPSPs.

- A) Reinitialize all variables, set cell A **“conductance”** = **“Na”**, and then Click the **"Run"** button.
What is the amplitude (size) of the EPSP in Cell C?

- B) Set **“status”** = **“fire”** for both Cell A and Cell B. Set **“conductance”** = **“Na”** for Cell A. Set **“conductance”** = **“K”** for Cell B. Click the **"Run"** button.
What is the amplitude of the EPSP in Cell C?

- C) Set **“status”** = **“fire”** for both Cell A and Cell B. Set **“conductance”** = **“Na”** for Cell A. Set **“conductance”** = **“Cl”** for Cell B. Click the **"Run"** button.
What is the amplitude of the EPSP in Cell C?

Explain the differences between A), B), and C).

Discussion:

1. Explain the differences among Membrane Potential, Excitatory Postsynaptic Potential (EPSP), Inhibitory Postsynaptic Potential (IPSP), and Action Potential.
2. The conductance of which ion (s) cause an EPSP; an IPSP?
3. Explain the difference between Temporal summation and Spatial summation.
4. What is the significance of summation of postsynaptic potentials in neural processing?
5. Why does conductance of potassium ions (K^+) have a greater inhibitory effect than conductance of chloride ions (Cl^-)?