MODELING A TWO COMPARTMENT FAST SPIKING INTERNEURON

Problem Statement: Design a model Parvalbumin-expressing (PV) interneuron with specified passive and firing properties from experimental data.

WHERE DO YOU BEGIN: Compile the .mod files in the Interneuron_Startup files folder using mknrndll. (Drag and drop the folder on MAC, find the directory through the mknrndll executable on Windows). Then run "main.hoc" my double-clicking on it. This is the main interface you'll use to tune the model. You can change parameters like capacitance, leak conductance, etc. all from the GUI, no coding should be necessary.

What properties need to be matched?

1. Passive properties (time constant, resting membrane potential, and input resistance)
2. Firing properties:
   (i) responses to various current injection values by varying only kdr, and
   (ii) the frequency-current response (FIR) curve for the neuron.

Using Real Cell Traces to Match Properties

1. Graphs for observed interneurons have been provided for you to match. MATLAB code and data export is also provided. If you don't have MATLAB, the data is also given in a spreadsheet. Details about the recordings:
   a. Current was injected at 30 pA intervals starting at -60 excluding 0. (-60, -30, 30, 60, 90…)

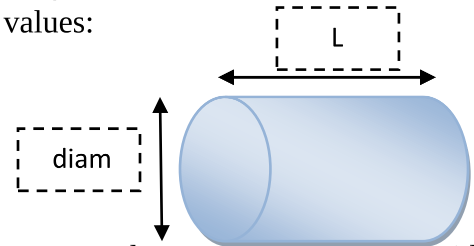
2. Calculate the time constant, resting membrane potential, and input resistance of the experimental cell and document them in an excel sheet. HINT: Look at a current clamp trace where negative current was injected.

3. Try to match the model cell's time constant, resting membrane potential, and input resistance to the experimental values. Document the values you get in your excel sheet. You will likely not be able to match the experimental cell exactly. See the appendix for appropriate ranges of conductances.

4. Now try to match the spiking properties by varying the conductance of the Kdr channel. Show side-by-side plots in your excel sheet of the model and experimental cell. Also plot FIR curves for the experimental and model cell to show how they compare.

Suggestions for model development

- NEURON models the compartment membrane as a cylindrical surface without top and bottom caps. In the template file provided to you, we use L=15 µm, and diam=15 µm for the soma and L=150 µm, and diam=10 µm for the dendrite.
- The default capacitance of the model is 1.0 µm/cm^2
- We use the following reversal potential values:
    - ELeak = - 70 mV
    - Ena = 45 mV
    - Ek = - 80 mV



- Membrane capacitance, channel conductances and output currents are provided per unit area in NEURON, i.e., in the units of S/cm^2, and mA/cm^2, respectively. It takes care of converting values internally.
- The default units for current injection and synaptic currents are nA.
- Useful links:

  NEURON website: http://www.neuron.yale.edu/neuron/node/47

  NEURON official forum: http://www.neuron.yale.edu/phpBB2/viewforum.php?f=15

  NEURON Course Hand-outs
  http://www.neuron.yale.edu/neuron/static/courses/2008/course/handson.html

  Programmer's Reference
  http://www.neuron.yale.edu/neuron/static/docs/help/quick_reference.html

Mod files (.mod) for the following currents are provided to you:

- nainter.mod Fast spike generating Na+ current channel
- kdrinter.mod Delayed rectifier K+ current channel
- leakinter.mod Leak current

APPENDIX

	Conductance range (S/cm2)		
	Min	**Max**	**LA model**
H	1.00E-05	0.0093	1.50E-05
Nat	0.001	0.36	0.027
Nap	1.00E-05	0.005	1.42E-04
Kdr	6.00E-04	0.18	1.50E-03
Kap	8.00E-07	0.096	2.00E-03
Kad	0.04	0.24	
KM	5.00E-06	0.017	6.00E-04
Kca	1.00E-05	0.002	-
sAHP	1.00E-05	0.008	5e-5 to 3e-4
Ca	1.00E-05	0.017	5.50E-04
Leak	1.50E-05	1.00E-04	5.50E-05