Research Interns: Assignment II

Passive neuronal properties

Important note for this and the upcoming assignments: For each question, give me relevant voltage/current traces and graphs that you derived from these traces. Make sure you have comments at the end of your answer to each subquestion, linking your observations to theory and what insights you got from performing this simulation. Submit these traces, plots and comments as a separate PDF file, and send me your codes as well.

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1. Take a single passive compartmental model of 80 μm diameter and 70 μm length. Set R_m to be 35 kΩ.cm^2, and C_m to be 1.5 μF/cm^2. Inject a current pulse of appropriate duration of any amplitude and direction (positive or negative), to the center of this compartment. Record the voltage response from the center of the compartment. Alter dt (from the range of 1 μs to 10 s using appropriate steps in between), and plot the charging curve for each of its different values. How does this alter the charging curve or the steady-state response? How does this alter the time taken for completing the simulation? Relate your outcomes to theory and explain.

2. Take a passive single compartmental model of 80 μm diameter and 70 μm length. Set R_m to be 35 kΩ.cm^2, and C_m to be 1.5 μF/cm^2. Inject a current pulse of appropriate duration of any amplitude and direction (positive or negative), to the center of this compartment. Record the voltage response from the center of the compartment. Compute input resistance of the compartment as the ratio of the amount of steady-state voltage deflection to the amplitude of current injected. Do the following:

    a. Vary C_m and R_m over a range of values, and plot input resistance as functions of these two parameters.

    b. Plot input resistance as functions of diameter and length of the compartment.

    c. Theoretically estimate the input resistance (you should be able to calculate it from these parameters) and its dependencies on these four parameters, and ask if the empirical outcomes match with the theoretical prediction.

    d. Comment on what these dependencies of input resistance on morphological as well as passive properties would mean physiologically for various compartments in a given neuron.

3. Take a single long dendrite of 1500 μm length and 3 μm diameter. Set R_m to be 35 kΩ.cm², R_a to be 250 Ω.cm and C_m to be 1.5 μF/cm². Compartmentalize the dendrite using space constant at 100 Hz. Inject a current pulse of appropriate duration at one end of this dendrite (chose any value for the injected current!). Measure voltage response at various locations along the dendrite, and plot steady-state voltage response as a function of distance from the point of current injection. Answer the following questions based on simulations:

a. How does distance-dependent steady-state attenuation change as functions of R_m, R_a and C_m? Plot steady-state voltage response *vs.* distance for various values of R_m, R_a and C_m in different graphs for each of these three parameters, and explain the outcomes theoretically.

b. How does distance-dependent steady-state attenuation change if length of the dendrite or its diameter is changed? Plot steady-state voltage response *vs.* distance for various values of length and diameter in different graphs for each of these two parameters, and explain the outcomes theoretically.

   Remember to recompartmentalize the dendrite appropriately after changing the parameter values in both the above cases. Also when measuring steady-state voltages, recall the definition of steady state in assigning an appropriate value for the duration of current injection.

c. For the default values of all these parameters, reduce or increase the number of compartments (nseg for NEURON) from the default value that you would have obtained with the d_λ rule. Say, if N_c is the number of compartments you arrived at using the d_λ rule, vary the number of compartments from 2 to $2*N_c$. How does this increase or decrease in the number of compartments alter the steady-state voltage response *vs.* distance curve? Explain using theory.

4. Take a soma of 80 μm × 70 μm. Connect a dendrite of 1250 μm length and 2.5 μm diameter to this somatic compartment. Choose the values of uniform passive parameters: R_m to be 35 kΩ.cm², R_a to be 250 Ω.cm and C_m to be 1.5 μF/cm². Compartmentalize appropriately using the d_λ rule. Place a single-electrode voltage-clamp mechanism at the soma. Let the initial and final voltages for the voltage pulse be −70 mV, and let the holding voltage be +50 mV. Answer the following questions.

a. Record the voltage at the soma, and comment on the trace that you obtain, comparing it with the trace that you wanted!

b. Plot the voltage at various points along the dendrite (every 300 μm distance from the soma; i.e. 300, 450, …, 1500) and comment on the traces that you obtain. Is the voltage-clamp covering the entire neuron? Are there any deficits in clamping that you notice?

c. Record the maximum voltage reached at various locations along the dendrite, and plot a distance-dependent graph of the maximum voltage you record at various locations. If the entire neuron were clamped to the same voltage as the somatic clamp voltage, then this should be a straight line with a value of +50 mV for all possible locations. Is that the case? Is the whole neuron clamped to same voltage? If not, what explains the discrepancy?

d. Vary R_m, R_a, C_m, diam and L and plot the distance-dependence curve for various values of each of these parameters. <u>Comment on the outcomes, relating them to theory.</u>

For 2–4, use the minmax mechanism that we introduced in the lectures and automate the parametric dependence using appropriate loops. Remember, you will have to run “nrnivmodl” in the directory (with the minmax.mod file present) for Unix/Linux/MacOS machine or run “mknrndll” on the directory (again, with the minmax.mod file present) in a Windows machine. The details are available online in the NEURON website (see
http://www.neuron.yale.edu/neuron/static/docs/nmodl/mswin.html
http://www.neuron.yale.edu/neuron/static/docs/nmodl/macos.html).