1.

For a neuron with a surface area of 0.025 mm^2, a specific membrane capacitance of $c_\text{m} = 10\ \text{nF/mm}^2$, a specific membrane resistance of $r_\text{m} = 1\ \text{M}\Omega\cdot\text{mm}^2$, and a resting membrane potential $E = -70$ mV: (a) What is the total membrane capacitance C_m? (b) What is the total membrane resistance R_m? (c) What is the membrane time constant τ_m? (d) How much external electrode current would be required to hold the neuron at a membrane potential of -65 mV? (e) If this amount of current is turned on at time $t = 0$, with the cell initially at -70 mV, and held constant at this value, at what time t will the neuron to reach a membrane potential of -67 mV?

2.

Build a model integrate-and-fire neuron from the equation,

$$\tau_\text{m} \frac{dV}{dt} = E - V + R_\text{m} I_\text{e} \, .$$

Use $E = -70$ mV, $R_\text{m} = 10\ \text{M}\Omega$, and $\tau_\text{m} = 10$ ms. Initially set $V = E$. When the membrane potential reaches $V_\text{th} = -54$ mV, make the neuron fire a spike and reset the potential to $V_\text{reset} = -80$ mV. Show sample voltage traces (with spikes) for a 300-ms-long current pulse (choose a few representative values of I_e that give reasonable, 1-100 Hz, firing rates) centered in a 500-ms-long simulation. Determine the firing rate of the model for various magnitudes of constant I_e and compare the results with the equation,

$$r_\text{isi} = \left(\tau_\text{m} \ln \left(\frac{R_\text{m} I_\text{e} + E - V_\text{reset}}{R_\text{m} I_\text{e} + E - V_\text{th}} \right) \right)^{-1} .$$

3. !!!!!!!!!! Please use these values for the following parameters: c_m = 0.01 microF/mm^2, I_e/A = x*10^-3 microF/mm2, dt=0.01 ms

Build a Hodgkin-Huxley model neuron by numerically integrating the equations for V, m, h, and n given below (see also chapter 5 of the textbook):

$$c_m \frac{dV}{dt} = -i_m + \frac{I_e}{A},$$

where

$$i_m = \overline{g}_L(V - E_L) + \overline{g}_K n^4 (V - E_K) + \overline{g}_{Na} m^3 h (V - E_{Na}).$$

and

$$\tau_n(V)\frac{dn}{dt} = n_\infty(V) - n,$$

$$\tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)}$$

and

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)},$$

(and similar equations for m and h), with

$$\alpha_n = \frac{.01(V + 55)}{1 - \exp(-.1(V + 55))} \qquad \beta_n = 0.125\exp(-0.0125(V + 65)),$$

$$\alpha_m = \frac{.1(V + 40)}{1 - \exp(-.1(V + 40))} \qquad \beta_m = 4\exp(-.0556(V + 65))$$

$$\alpha_h = .07\exp(-.05(V + 65)) \qquad \beta_h = 1/(1 + \exp(-.1(V + 35))),$$

In these equations, time is in ms and voltage is in mV. Take c_m = 10 nF/mm^2, and as initial values take: $V = -65$ mV, $m = 0.0529$, $h = 0.5961$, and $n = 0.3177$. The maximal conductances and reversal potentials used in the model are $\overline{g}_L = 0.003$ mS/mm^2, $\overline{g}_K = 0.36$ mS/mm^2, $\overline{g}_{Na} = 1.2$ mS/mm^2, E_L = -54.387 mV, E_K = -77 mV and E_{Na} = 50 mV. Use an integration time step of 0.1 ms.

a) Use an external current with I_e/A = 200 nA/mm^2 and plot V, m, h, and n as functions of time for a suitable interval.

b) Plot the firing rate of the model as a function of I_e/A over the range from 0 to 500 nA/mm^2. What are the major differences between the firing rate versus current curve for this neuron and the curve you obtained in an earlier assignment for the integrate-and-fire model (focus, in particular, on the region of the curve near where the neuron starts firing)?

c) Apply a pulse of negative current with $I_e/A = -50$ nA/mm^2 for 5 ms followed by $I_e/A = 0$ and show what happens. Why does this occur?