BE 521: Homework 2

Modeling Neurons

Spring 2015

44 points

Due: Tuesday, 2/03/2015 11:59 PM

Objective: Computational modeling of neurons.

Homework Policy

1. Piazza should be used for peer discussion for all questions related to course material. Please also use Piazza to contact teaching staff for all questions. TA's will be available to help during office hours and occasionally on Piazza.
2. Submit LaTeX write-up (pdf) and Matlab code to Canvas as pennkey_hwx.pdf, .m before listed deadline.
3. Assignments will be returned electronically on Canvas.
4. Collaboration is encouraged but individual write-ups are required. Please list any collaborators. Honor code will be strictly enforced. Note: submitted code is routinely passed through a plagiarism checker.
5. Late Policy: 5% per day. **No homework is accepted after the 5th late day.** (If originally due Tuesday, 11:59PM, last day to turn in is Sunday, 11:59 PM).

We gratefully acknowledge Dr. Vijay Balasubramanian (UPenn) for many of the questions in this homework.

1 Basic Membrane and Equilibrium Potentials (5 pts)

Before undertaking this section, you may find it useful to read pg. 153-161 of Dayan & Abbott's *Theoretical Neuroscience* (the relevant section of which, Chapter 5, is posted with the homework).

1. Recall that the potential difference V_T when a mole of ions crosses a cell membrane is defined by the universal gas constant $R = 8.31$ J/mol $\cdot$ K, the temperature T (in Kelvin), and Faraday's constant $F = 96,480$ C/mol

$$V_T = \frac{RT}{F}$$

Calculate V_T at human physiologic temperature (37 °C). (1 pt)

2. Use this value V_T to calculate the Nernst equilibrium potentials (in mV) for the K^+, Na^+, and Cl^- ions, given the following cytoplasm and extracellular concentrations in the squid giant axon: K^+ : (400, 20), Na^+ : (50, 440), and Cl^- : (52, 460), where the first number is the cytoplasmic and the second the extracellular concentration (in mM). (2 pts)

3. (a) Use the Goldmann equation,

$$V_m = V_T \log\left(\frac{P_K \cdot [K^+]_{out} + P_{NA} \cdot [Na^+]_{out} + P_{Cl} \cdot [Cl^-]_{in}}{P_K \cdot [K^+]_{in} + P_{NA} \cdot [Na^+]_{in} + P_{Cl} \cdot [Cl^-]_{out}}\right) \quad (1)$$

to calculate the resting membrane potential, V_m, assuming that the ratio of membrane permeabilities $P_K : P_{Na} : P_{Cl}$ is $1.0 : 0.04 : 0.45$. Use the ion concentrations given above in Question 1.2. (2 pts)

(b) Calculate the membrane potential at the peak action potential, assuming a ratio of $1.0 : 20 : 0.45$, again using the ion concentrations given in Question 1.2. (1 pt)

2 Integrate and Fire Model (39 pts)

You may find it useful to read pg. 162-166 of Dayan and Abbott for this section. The general differential equation for the integrate and fire model is

$$\tau_m \frac{dV}{dt} = V_m - V(t) + R_m I_e(t)$$

where $\tau_m = 10\,\text{ms}$ is the membrane time constant, describing how fast the current is leaking through the membrane, V_m in this case is constant and represents the resting membrane potential (which you have already calculated in question 1.3.a), and $V(t)$ is the actual membrane potential as a function of time. $R_m = 10^7\,\Omega$ is the constant total membrane resistance, and $I_e(t)$ is the fluctuating incoming current. Here, we do not explicitly model the action potentials (that's Hodgkin-Huxley) but instead model the neuron's behavior leading up and after the action potential.

Use a $\Delta t = 10\,\mu\text{s}$ (Δt is the discrete analog of the continuous dt). Remember, one strategy for modeling differential equations like this is to start with an initial condition (here, $V(0) = V_m$), then calculate the function change (here, ΔV, the discrete analog to dV) and then add it to the function (here, $V(t)$) to get the next value at $t + \Delta t$. Once/if the membrane potential reaches a certain threshold ($V_{th} = -50\,\text{mV}$), you will say that an action potential has occurred and reset the potential back to its resting value.

1. Model the membrane potential with a constant current injection (i.e., $I_e(t) = I_e = 2\text{nA}$). Plot your membrane potential as a function of time to show at least a handful of "firings." (8 pts)

2. Produce a plot of firing rate (in Hz) versus injection current, over the range of 1-4 nA. (4 pts)

3. `I521_A0002_D001` contains a dynamic current injection. Plot the membrane potential of your neuron in response to this variable injection current. Use Matlab's `subplot` function to place the plot of the membrane potential above the injection current so that they both have the same time axis. (Hint: the sampling frequency of the current injection data is different from the sampling frequency ($\frac{1}{\Delta t}$) that we used above.) (4 pts)

4. Real neurons have a refractory period after an action potential that prevents them from firing again right away. We can include this behavior in the model by adding a spike-rate adaptation conductance term, $g_{sra}(t)$ (modeled as a potassium conductance), to the model

$$\tau_m \frac{dV}{dt} = V_m - V(t) - r_m g_{sra}(t)(V(t) - V_K) + R_m I_e(t)$$

where

$$\tau_{sra} \frac{dg_{sra}(t)}{dt} = -g_{sra}(t),$$

Every time an action potential occurs, we increase g_{sra} by a certain constant amount, $g_{sra} = g_{sra} + \Delta g_{sra}$. Use $r_m \Delta g_{sra} = 0.06$. Use a conductance time constant of $\tau_{sra} = 100\,\text{ms}$, a potassium equilibrium potential of $V_K = -70\,\text{mV}$, and $g_{sra}(0) = 0$. (Hint: what algebraic property might you use to introduce r_m into the g_{sra} differential equation so that you can use the $r_m \Delta g_{sra}$ value to update voltage and conductance separately in your simulation?)

   (a) Implement this addition to the model (using the same other parameters as in question 2.1) and plot the membrane potential over 200 ms. (8 pts)

   (b) Plot the inter-spike interval (the time between the spikes) of all the spikes that occur in 500 ms. (2 pts)

   (c) Explain how the spike-rate adaptation term we introduced above might be contributing to the behavior you observe in 2.4.b. (2 pts)

5. Pursue an extension of this basic integrate and fire model. A few ideas are: implement the Integrate-and-Fire-or-Burst Model of Smith et al. 2000 (included); implement the Hodgkin-Huxley model (see Dayan and Abbot, pg. 173); provide some sort of interesting model of a population of neurons; or perhaps model what an electrode sampling at 200 Hz would record from the signal you produce in question 2.3. Feel free to be creative.

   We reserve the right to give extra credit to particularly interesting extensions and will in general be more generous with points for more difficult extensions (like the first two ideas), though it is possible to get full credit for any well-done extension.

   (a) Briefly describe what your extension is and how you will execute it in code. (6 pts)

   (b) Provide an interesting figure along with an explanation illustrating the extension. (4 pts)