

Computational Modeling & Simulation I (Interdisciplinary Science)
CS 346

Spring 2020

Homework 3

(Please see the notes below!)

- As noted in email, HW3 is due by 11:59pm (Maine time) on the last day of classes, May 8. Code demos for all CS346 assignments must be completed by the end of the day (Maine time) on Friday, May 15. (You are certainly welcome to submit work and set up code demos before the deadlines, if you'd like.)
- **PLEASE do not wait until the last minute** for code demos! I may be busy at the end of the semester, and if there isn't enough time available for your demo to enable me to fully appreciate your code, it may negatively affect your grade on the HW.
- For HW3 and the Final Project, you may work in teams of two, or you may work individually. If you work in a team of two, you may choose your team; you are permitted to have the same team for both assignments (i.e., both HW3 and the Final Project).
- Please use the string `HW3` as part of (not *all of!*) the folder name (along with names / userids / etc., as required) for submitting this assignment. See documents on the course website for general HW guidelines and submission instructions. (Not following guidelines may result in small deductions on this HW—please see your Prof. with any questions!)

HW3: Runge-Kutta and Hodgkin-Huxley!

This assignment is about implementing Runge-Kutta 4 simulations, building to a simulation of a classic model, the Hodgkin-Huxley model of action potentials in neurons! Here are some introductory notes, some of which are new, and some of which are reminders:

- Please submit code answers to every exercise except for those marked as **write-up only**. The code for one exercise may be very similar to the code for another exercise for the exercises below, but please do not combine responses—submit different, individual code files for each coding exercise.
- Your write-ups for these exercises should explain how the intended model is implemented in your simulations. Some decisions may be subtle and require some explanation, so please explain as needed! For simulations, *unless values are given to you for an exercise* (which is frequently the case on this assignment!), your write-up should include the values of constants / parameters employed for each run of the simulation and a very brief explanation of why you chose to run those particular values for simulations. Descriptions of results should be concise and information-heavy; feel free to include figures (e.g., Matlab plots) in write-ups to illustrate your observations.

If there are any questions about what might be good to include in a write-up, please see documents on the course website, and please feel free to ask me!

- As always, readability is an essential part of the assignment: Make sure both your code and your write-up are easy to read and understand. As part of this, be sure to follow the style guidelines presented in lecture for implementing a Runge-Kutta 4 simulation: Make sure it is easy to tell exactly what function is used to compute the derivative and exactly what arguments are provided to that function for each estimate $\partial_1, \partial_2, \partial_3, \partial_4$.

For example, if you are modeling the dynamics (change in value) of some variable P , then you should have a function `dPdt(...)` somewhere in your code (it could likely be cleanly defined using anonymous function syntax `dPdt = @(...)`), and in your simulation loop, you would have lines that call that function, such as

```
dp1 = dPdt( ... ) * dt;
dp2 = dPdt( ... ) * dt;
dp3 = dPdt( ... ) * dt;
dp4 = dPdt( ... ) * dt;
```

to calculate the estimates $\partial_1, \partial_2, \partial_3, \partial_4$.

Structure like this makes it easy to read and understand an RK4 simulation loop. Code that is not *at least* this easily readable may not merit full credit. Please feel free to ask me any questions about code style and readability for these exercises!

Exercises: Brainpower—The Hodgkin-Huxley Model!

These exercises are based on the Hodgkin-Huxley model of activation potentials in neurons, presented in Chapter 7.9 in your textbook; in particular, they are related (but not identical!) to project 2, on pages 287–288, so please read that project as preparation for these exercises. You will be implementing Runge-Kutta 4 simulations of variations of the Hodgkin-Huxley model (*HH model*, for short), as described below!

Chapter 7.9 presents the model along with a lengthy list of parameters, variables, and equations needed to implement a simulation of the model—please see Table 7.9.1 on page 287 of your textbook! You can use most of the values in that table when you implement your simulations, but with the last eight symbols in that table, use the values / formulas given in Table 1 in this document, instead of the ones in the textbook. (Note: Do not use T or ϕ in your simulation at all!)

1. Implement the HH model as in project 2, Chapter 7.9, but include only the sodium, potassium, and leakage channels, not the Na^+-K^+ -ATPase pump described on page 288. Thus, the model will be consistent with the HH model equation presented on page 285: $\frac{dV}{dt} = (I_{ext} - I_K - I_{Na} - I_L)/C$, with values / formulas for I_K, I_{Na} , and I_L as given in Table 7.9.1 in the textbook. Do not bother (yet!) keeping track of $[Na^+]$ and $[K^+]$ (see the top of page 288), but do implement the voltage-gating on the sodium and potassium channels (as described in the last paragraph of project 2).

Simulate this as described in the textbook (simulating for 3ms, with timestep 0.001ms, and a stimulus current of 15nA, starting at 0.5ms, lasting for 0.5ms), **except that** the threshold for Na channels closing and K channels opening should be 49.3mV rather than the 50mV value given in the textbook. That is, the Na channels should be

Symbol (meaning—units)	Formula / value
a_n (opening rate constant— ms^{-1})	$0.01 \cdot (V + 55)/(1 - e^{-(V+55)/10})$
a_m (opening rate constant— ms^{-1})	$0.1 \cdot (V + 40)/(1 - e^{-(V+40)/10})$
a_h (opening rate constant— ms^{-1})	$0.07 \cdot e^{-(V+65)/20}$
b_n (closing rate constant— ms^{-1})	$0.125 \cdot e^{-(V+65)/80}$
b_m (closing rate constant— ms^{-1})	$4 \cdot e^{-(V+65)/18}$
b_h (closing rate constant— ms^{-1})	$1/(e^{-(V+35)/10} + 1)$
T (temperature— $^{\circ}C$)	Do not include in your simulation
ϕ (factor for temperature correction)	Do not include in your simulation

Table 1: Table of some values and formulas for your Hodgkin-Huxley simulation.

voltage-gated to close, and the K channels voltage-gated to open, at 49.3mV. Show graphs of V , m , n , and h , as in your textbook.

In your write-up, describe the results of the simulation. How well does this simulation match the Hodgkin-Huxley simulation graphs given in your textbook? Be sure to describe your observations of similarities and differences in terms of their neuroscience meanings (e.g., “Without the Na^+ - K^+ -ATPase pump, the voltage V was ... and the value of sodium gating value m was Also, the value of ...”)—the point is not just to point out different shapes on graphs, but to explain how various factors affect the properties and functioning of neurons!

2. Modify the previous simulation to include the Na^+ - K^+ -ATPase pump (*Na-K pump*, for short) as if it’s always on—that is, you will need to modify the equation for $\frac{dV}{dt}$ to include the pump current (call it I_P) in it, but do not bother (yet!) keeping track of $[Na^+]$ and $[K^+]$ concentrations.

As described in the text for project 2 in the textbook, the pump current I_P should have a constant value that counteracts *the initial value* of the leakage current I_L . That way, as long as voltage V is the initial voltage (i.e., the resting voltage, -65mV), the I_P and I_L terms should cancel each other out in the modified $\frac{dV}{dt}$ equation. (Note that as V changes, the value of I_L will change, because I_L is a function of V , but the value of I_P is a constant and will remain unchanged.)

With this modified model, run a simulation with the same parameters and values as in exercise 1. Show graphs of V , m , n , and h , as in your textbook.

In your write-up, describe the simulation. How well does this simulation match the Hodgkin-Huxley simulation given in your textbook? The graphs from exercise 1? Be sure to explain the reasons *why* the differences between this simulation and the simulation in exercise 1 are what they are. (As in exercise 1, be sure to describe your observations in terms of their neuroscience meanings!)

(**NOTE:** Your textbook suggests adding *two* terms to the $\frac{dV}{dt}$ equation, one for current from the Na part of the pump, and one for current from the K part of the pump. For this assignment, that will not be necessary; combining those into a single term I_P is sufficient.)

3. Modify the model from exercise 2 to implement the *Na-K* pump as if it's *not* always on, as specified in the text book: the pump is only on when the concentration of $[Na^+]$ inside the axon and $[K^+]$ outside the axon are both greater than 0. Note that this does not add additional terms to the equation for $\frac{dV}{dt}$, although it requires changes in the way your code handles voltage-gating for the terms already present there.

Simulate this modified model with the same parameters and values as for exercise 2. Show graphs of V , m , n , and h , as in your textbook. In your write-up, describe the simulation. How well does this simulation match the Hodgkin-Huxley simulation given in your textbook? The graphs and values from exercise 2? (As always, please explain the reasons behind your observed similarities and differences, relating them to their neuroscience meanings whenever appropriate.)

4. Now, try simulating the model from exercise 3 with the Na channels voltage-gated to close at 50mV and K channels voltage-gated to open at 50mV, as specified in the textbook. (Please use the rate constants from the table in this handout, though, not the ones from the book.) Implement and run the simulation. What happens? In your write-up, describe the results. (As always, please explain the reasons behind your observations, relating them to their neuroscience meanings whenever appropriate.)
5. Here's a hypothesis: In these HH models, having a voltage-gated leakage channel can result in a higher maximum value for the action potential. To test this, implement the leakage channel so that it is only open when the membrane potential V is such that $V \leq -54.4mV$, and then run a simulation of the system (with the same parameters / values as for exercise 4).

How does this new voltage-gating of the leakage channel affect the simulation when the K and Na channels are voltage-gated at 50mV, as in exercise 4? How well does this simulation match the Hodgkin-Huxley simulation given in your textbook? The results of previous exercises? In your write-up, describe your results. (As always, please explain the reasons behind your observations, relating them to their neuroscience meanings whenever appropriate.)

6. **(For Write-up Only)** What are other ways to get the action potential to a higher maximum value? In your write-up, give some suggestions, and explain the reasons that they would result in a higher maximum action potential. Implement your suggestions, and in your write-up, report the results—what difference does each suggestion make? (You do not need to submit code for this exercise, just a write-up describing how you modified code and describing simulation results. You *may* submit short code fragments in your write-up if you'd like, but not full code files.)

NOTE: In the process of implementing some of the Hodgkin-Huxley simulations with the above specifications, you might find concentrations of some quantities (e.g., sodium or potassium) dropping to zero, or even to negative values. If that happens in your simulations, please make a design decision about how to handle it—e.g., will you sacrifice biological realism and permit such values, or will you do something to prevent them?—and in your write-up, explain what your decision was, why you thought it was the best design choice, and how you implemented it in your code.