Simulation of Action Potential using the Hodgkin-Huxley cell membrane model

Laboratory Exercise

TBME08 Biomedical Modelling and Simulation

Department of Biomedical Engineering

Place: Zoom (Please see the info available in Lisam)
Software: Matlab with Simulink (Remote access on IMT8 computers)
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Purpose

To give a deeper understanding of how the Hodgkin-Huxley (HH) cell membrane model:

- Can be implemented and simulated numerically in a computer environment.
- Can be used for understanding what bio-electrical properties affect the action potential.
- Can be implemented in different ways, i.e., physical, mathematical and graphical.

Reading material

How to solve and program the Hodgkin-Huxley Equations, J. Kenyon, Department of Physiology & Cell Biology MS 352 University of Nevada School of Medicine. (**Document HH_Kenyon.pdf is found in Lisam**)

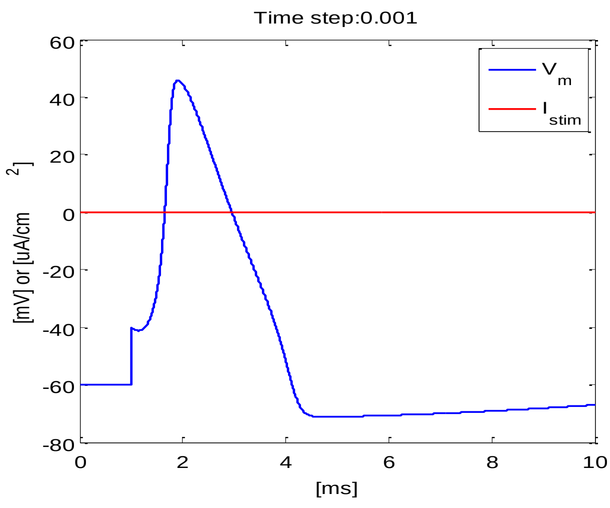
Note: The unit mho (Ohm backwards), is 1/Ohm, m mho is “milli”- mho.

Tasks and report

A Matlab m-file including most of the codes needed is given in Lisam (Hodgkin Huxley Lab.m). To complete the laboratory exercise, additional coding is needed according to the instructions given below. The results, including a brief discussion/reflection on the results, should be summarized in a report. The report must include a brief explanation/introduction of the **mathematical** and **electrical model** of the AP and the simulation performed using numerical methods (the **graphical model** is addressed in task 8). The exercises should be explained by graphs and emphasizing on your understanding of the model. The report should be submitted 10 days after the lab.

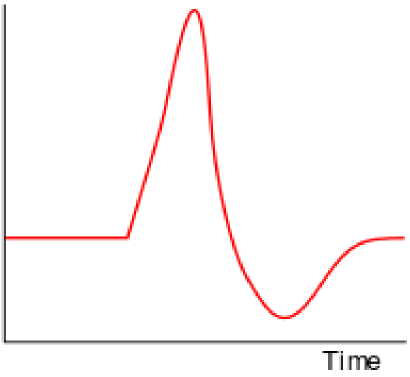
Additional coding

1. Add the calculation of the derivative of the four state parameters
2. Add the iterative update of the state variables using Eulers method.
3. Add the possibility of changing V_m at a single given time point. Test the system by setting $V_m(t = 1 \text{ ms}) = -20$. An AP should be observed.



Preparatory questions:

1. What are the ion exchange mechanisms over a cell membrane that cause an action potential? Describe using the action potential graph below.



2. What are the absolute and relative refractory periods? (show in the action potential graph above)

3. Write the Hodgkin Huxley model and describe each parameter. Which are the state variables? Is the equation linear/non-linear, static/ dynamic?

4. What is the electrical circuit equivalent of the Hodgkin Huxley model? Draw all the electrical components and the ionic and capacitive currents in the circuit.

5. What is the thevenin equivalent of the above circuit and its response time? (You should read the definition of the response time and how it is calculated for an RC circuit in general).

Tasks

Note: Plotting results for each task in one graph, makes the comparison easier.

1. Strength – duration of stimulating current

Start a stimulating current at 1ms with a duration of 0.1 ms. Increase the current amplitude until an action potential (AP) is produced. Find the threshold current (the minimal current needed for an AP to occur). Also observe the timing of the AP for amplitudes just above threshold and higher amplitudes. Continue to find threshold currents for longer stimulus durations up to 1 ms. What is the relationship between the duration and the strength of the threshold current? Plot the strength-duration curve.

2. Rheobase and Chronaxy

Find the Rheobase and the chronaxy points on the strength-duration curve plotted in task 1. Why would it be interesting to find these parameters?

3. Membrane capacitance

Stimulate the membrane using $V_m(t = 1\text{ ms}) = -20$. Change the membrane capacitance. How does this affect the membrane voltage and the depolarization speed? Speculate on how this will impact the propagation speed of the action potential.

(Remember to set the capacitance to the original value when the task is done!)

4. Sodium conductance

Stimulate the membrane using $V_m(t = 1\text{ ms}) = -20$. Lower the sodium (Na) conductance (try at least 1/2, 1/3 and 1/4 of the original value). How does this affect the membrane voltage and the depolarization speed? Speculate on how this will impact the propagation speed of the action potential.

(Remember to set the conductance to the original value when task is done!)

5. Potassium conductance

Stimulate the membrane using $V_m(t = 1\text{ ms}) = -20$. Increase the potassium (K) conductance (try up to 2 times the original value). How does this affect the membrane voltage and the depolarization speed? Speculate on how this will impact the propagation speed of the action potential. (Remember to set the conductance to the original value when task is done!)

6. Refractory period

Increase display time to 20 ms. Set stimulus duration at 0.1 ms and amplitude to produce AP without much delay (i.e. well above the threshold current). Turn on second stimulus delayed 8 ms from start of first stimulus, with same amplitude and duration as first stimulus. Find the threshold amplitude for second stimulus to produce AP. Explain by studying Na- and K-conductances. Find thresholds for delays of 6 and 10 ms.

7. Constant stimulus current

Increase time scale to 50 ms and apply constant current of 15 $\mu A/cm^2$. Try also with 50 $\mu A/cm^2$. Why do they differ?

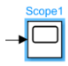
8. Hodgkin Huxley model in Simulink- graphical model

Use the Simulink model (HH simulink) provided in Lisam to generate an action potential. You should first run the file ‘HHparameters.m’ and then the ‘HH.mdl’. Change of parameters should be made in ‘HHparameters.m’. After each change, you need to press **Run** in both files to update the results.

a) Go through the block. What does each part of the model represent? Take a snapshot of the Simulink block diagram, add your explanations to it and compare to the electrical circuit model of the cell membrane.

   In the graphical model in Simulink, locate the part which represents the cell membrane capacitance. Describe the part and relate to the current and voltage in an RC electrical circuit (see lecture slides).

   Hint: You can get information on each block parameter by double clicking on it.

b) Generate one AP using Simulink by clicking on scope 

   In the plotted graph, go to **Tools**, **Axes Scaling**, select **Automatically Scale Axes Limits**.

   Change the model parameters in ‘HHparameters.m’ so that the action potential obtained via Simulink has a shape and amplitude similar to the AP obtained in task 1.

   Hint: To generate single or multiple APs, duration of the stimulation current can be adjusted. Change the resting potential to 0 mV and do not change the sign of the batteries.