HW #1: Math and Hodgkin & Huxley
Neuro 120
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Due: October 4, 2018

Problem 1. Numerical Integration

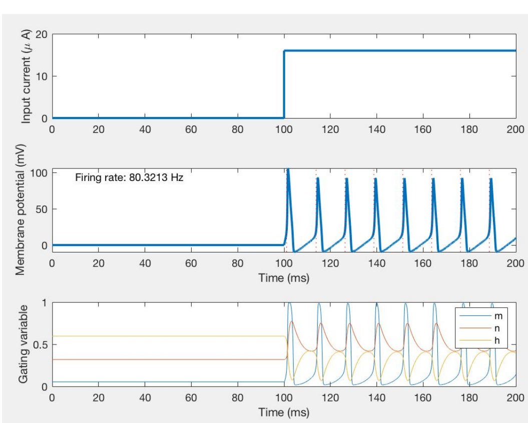
a) Implement euler integration.

Below is a screenshot of the implementation of euler integration within euler_solver.m.

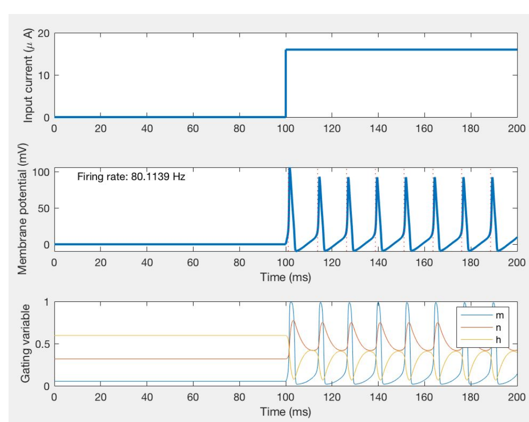
```
function [t, y] = euler_solver(odefun, tspan, y0, dt)
% Solve differential equation y' = f(t,y), from time tspan = [t0 t_final],
% with initial condition y0. Here odefun must be a function with signature
% odefun(t,y), which for a scalar t and a vector y returns a column vector
% corresponding to f(t,y). The solver uses the integration timestep dt.
% Each row in the solution array y corresponds to a time returned in the
% column vector t.

n=ceil((tspan(2)-tspan(1))/dt);              %%Calculate total number of trials
y=zeros(n+1,length(y0));                     %%Initialize output variables
t=zeros(n+1,1);
y(1,:)=y0;                                   %%Initial condition set to first row
yderiv=zeros(length(y0),1);                  %%Initialize variable used in loop

for i=2:n+1
    t(i)=(i-1)*dt;                           %%Update time vector
    yderiv=feval(odefun,t(i),y(i-1,:));      %%Evaluate derivative at time point
    y(i,:)=y(i-1,:)+dt*yderiv';              %%Euler's method equation
end
```

To check our work, we compared the output of our euler_solver to the built-in ODE. Below are the two outputs, indicating no significant difference in the HH model simulation.

Output of our euler_solver:

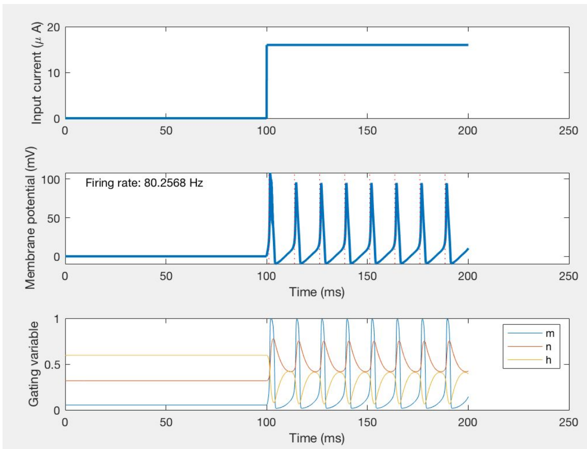


Output of the built-in ODE:

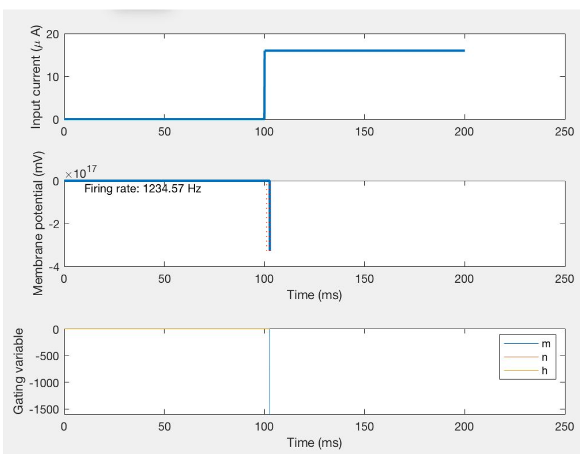


b) **Test the effect of the Euler integration step size (which is set in simulate_hh.m). The default used by simulate_hh.m is Δt = 0.01.**

What happens when Δt = 0.07?



What happens when Δt = 0.09?

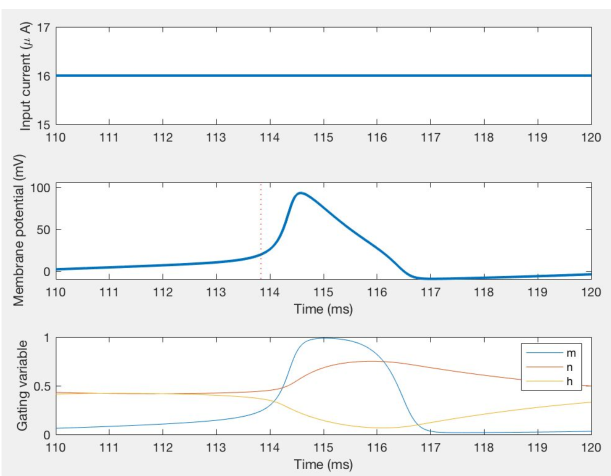


The Euler integration method breaks when the time steps are too large. As is evident by the gating variables, the rapid decrease in m resulting from repolarization of the neuron initiates a positive feedback loop which reinforces this decrease in activation below 0, at which point the governing equations break down, since the gating variables are only defined in the range [0,1]. Thus, the rapid dynamics of neuronal firing necessitate a smaller time step.

Problem 2. Basic Spike Generation

With our simulator in hand, (or by setting use_euler=false), investigate the spiking behavior of the HH model. Zoom in to one action potential. Explain the generation of this action potential by examining the gating variables.

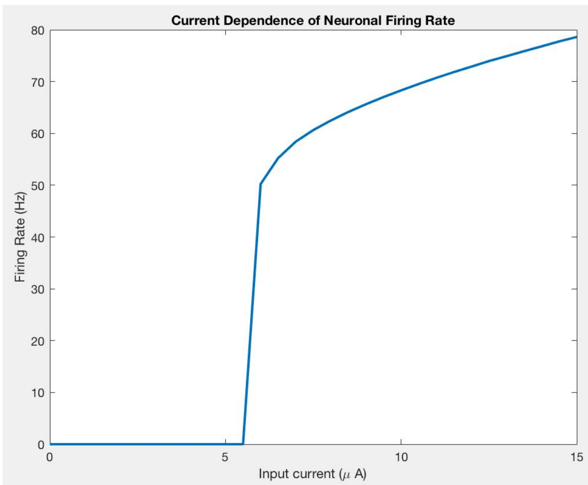
The action potential generation can be described as a function of the gating variables, which describe the behavior of voltage-dependent Na+ and K+ channels. The variable **m** describes the opening of sodium channels, while **h** describes the inactivation of the Na+ channels and has the opposite voltage-dependence of **m**. The variable **n** describes the activation of the K+ channels. In order to initiate the action potential shown below at ~114ms, Na+ channels must open to depolarize the neuron. In terms of the gating variables, we see that the **m** value increases drastically at 114ms, while **h** begins to decrease. This increase in **m** leads to a higher sodium channel conductance, while the slower dynamics of **h** cannot prevent net channel opening of Na^+ channels. The Na+ channels are opened, and Na+ flows into the neuron, leading to a quick depolarization (the positive feedback loop pushes the voltage over the threshold, causing a reinforcing depolarization). After the depolarization causes a significantly positive membrane potential, the conductance of the K+ channels increases in response, as shown by an increase in **n**. At the same time, the Na+ channels are now more inhibited, as **h** decreases due to the depolarization, increasing the Na+ channels' probability of inactivation. As a result, a net outward current flows from the cell due to sodium channel inactivation and potassium channel activation, thus repolarizing the cell. Continued activation of potassium current leads to a brief hyperpolarization before returning to resting potential.



Problem 3. Firing Rate for Constant Inputs

a) **Generate a plot of the firing rate as a function of the applied input current. See the "configure input current" section of simulate_hh.m to adjust the input current. Try currents in the range [0 15]. You can do this by hand or by writing code to do it. The file simulate_hh.m contains a section which estimates the firing rate.**

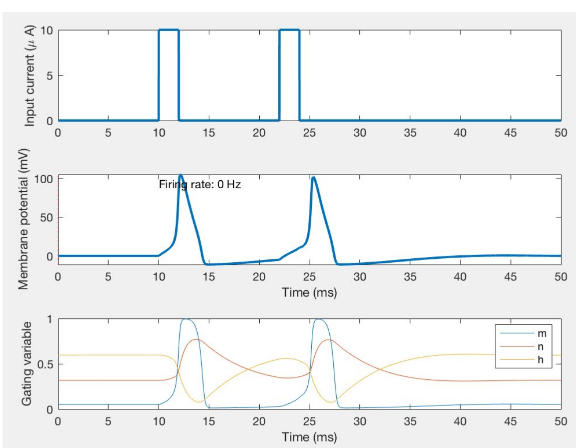
The plot of the firing rate as a function of the applied input current in the range [0 15]:



b) **What is the minimum sustained firing rate for the HH model?**
The minimum sustained firing rate for the HH model is 50Hz.

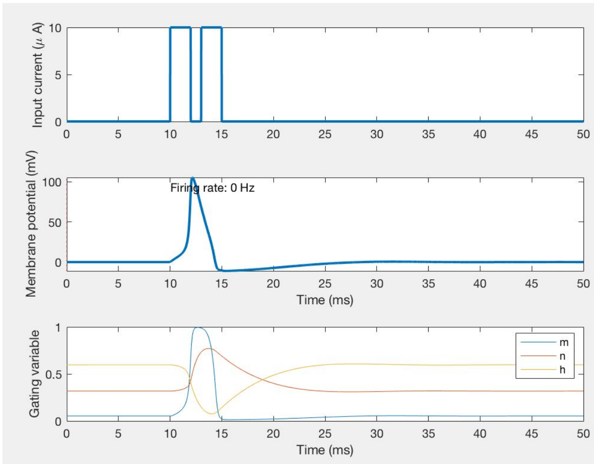
Problem 4. Refractory Period

a) **How many spikes are fired in response to two pulses separated by 12ms?**



In response to two pulses separated by 12ms, 2 spikes are fired.

b) How many spikes are fired in response to two pulses separated by 3ms?



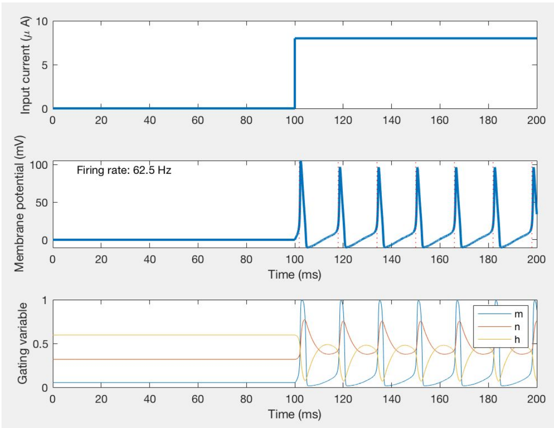
In response to two pulses separated by 3ms, 1 spike is fired.

c) By investigating the gating variables, explain the source of this phenomenon?

When two pulses are separated by 12ms, 2 spikes are fired because the neuron is able to overcome the refractory period after the first spike, which allows for a second action potential. When the first input is presented at 10ms, m increases, n increases after a short delay, and h decreases. The cell repolarizes as sodium channels are inactivated, which leads to an increase in h. However this increase in h is slow, which, in conjunction with an elevated potassium conductance, gives rise to the refractory period. Therefore, the cell must wait until enough sodium channels are no longer inactivated, and enough potassium channels have closed, to allow for another action potential. Therefore, when two pulses are separated by just 3ms, the slow dynamics of h and n prevent the initiation of a second action potential.

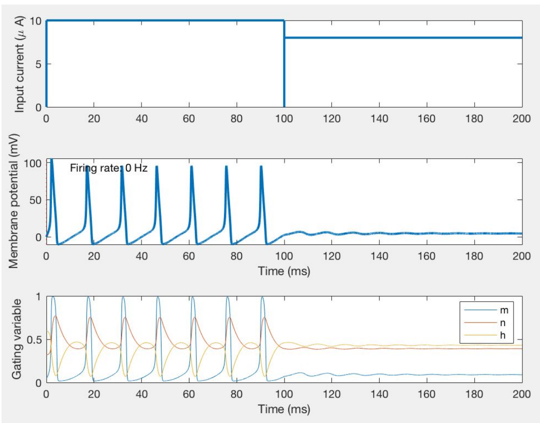
Problem 5. History Dependence

a) **Uncomment the input current which begins at 0μA and rises to 8μA. What is the firing rate (after the rise to 8μA)?**



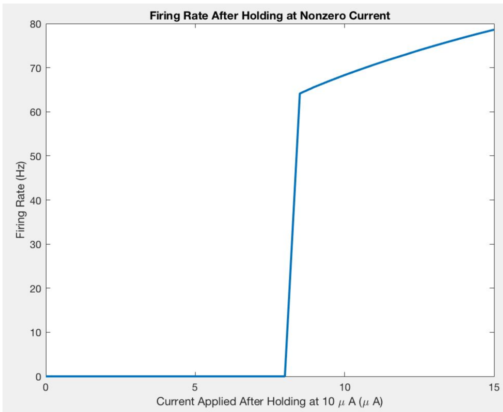
The firing rate is 62.5 Hz after the rise to 8μA.

b) **Uncomment the input current which begins at 10μA and drops to 8μA. What is the firing rate (after the drop to 8μA)?**



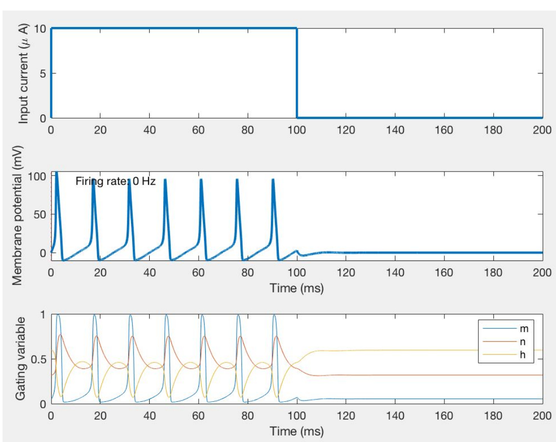
The firing rate is 0 Hz after the drop to 8μA.

c) **Generate a firing rate curve as in part 3a, but starting at 10 μA, and compare to that in 3a.**



Compared to the firing rate curve in 3a, we see that a higher current threshold is required in order to have a minimum sustained firing rate when applying current after holding a 10μA current in the neuron rather than applying current with no existing current input. We hypothesize that when holding the current above 8.5μA, an increase of h over n combined with a larger increase in m create the potential for an oscillatory feedback loop which allows continued depolarizations and neuronal firing. This phenomenon does not similarly occur at 8μA.

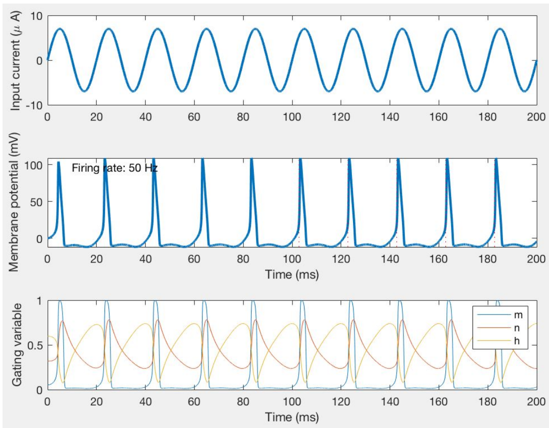
d) **Uncomment the input current which begins at 10μA and then turns off (0μA). Explain the resulting behavior by investigating the gating variables.**



The neuron stops firing when the input current turns off. Without an external input to depolarize the cell, the values of **m, h,** and **n** return to their resting values as the neuron returns to resting potential. After the final action potential initiated by the 10μA input is completed, the Na+ channels are not opened because there is no external input for depolarization, and no new action potential is initiated.

Problem 6: Oscillations

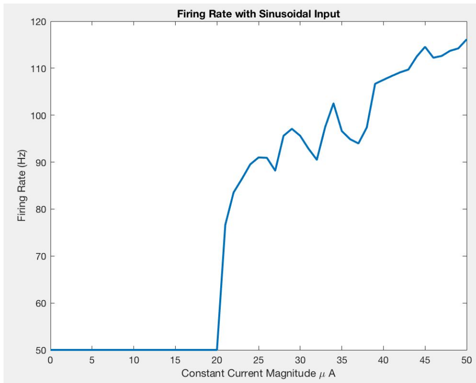
a) **Manipulate ω. What is the firing rate of the neuron?**



The firing rate of the neuron matched the value of **ω** with a lower bound of 19Hz and an upper bound of 74Hz, given an $I_0 = 0$. Above the upper bound, the neuron cannot match the oscillation rate and we see multiple oscillations per spike. Below the lower bound, we see multiple spikes per oscillation.

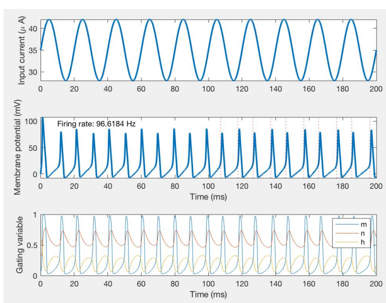
b) Generate a firing rate curve by varying I_0

Firing Rate Curve

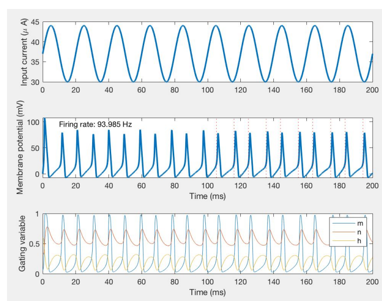


We provide the firing rates from 3 specific current values in order to demonstrate the existence of local minimi in the firing rate even as current is steadily increased.

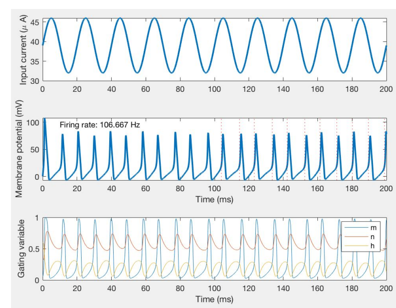
35 μA I_0



37 μA I_0

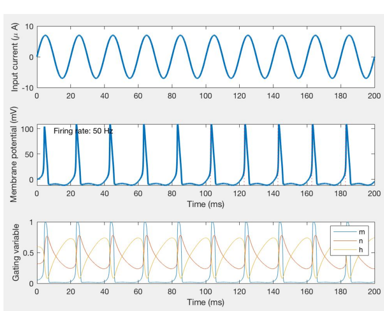


39 μA I_0

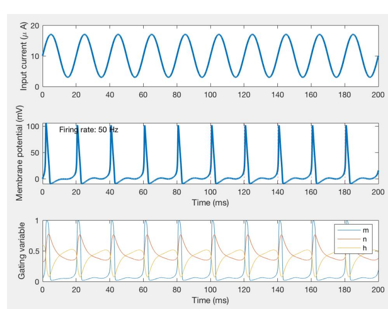


c) Manipulate I_0 in the range where one spike is fired per oscillation cycle. What effect does I_0 have in this case?

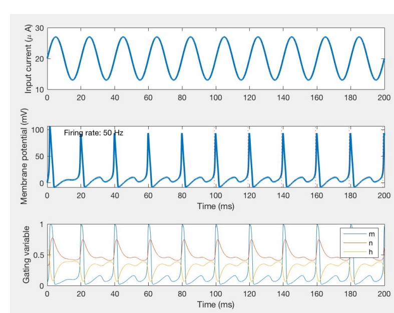
1 μA I_0



10 μA I_0



20 μA I_0



Increasing the magnitude of I_0 serves to decrease the maximum amplitude of the action potential, and increases the magnitude of the subthreshold oscillation between each spike.