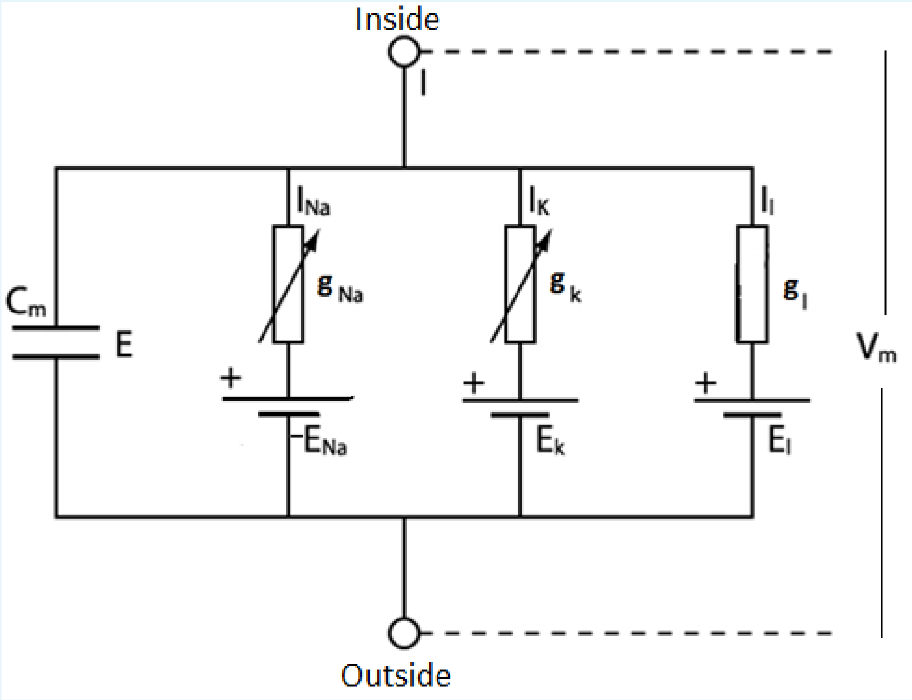
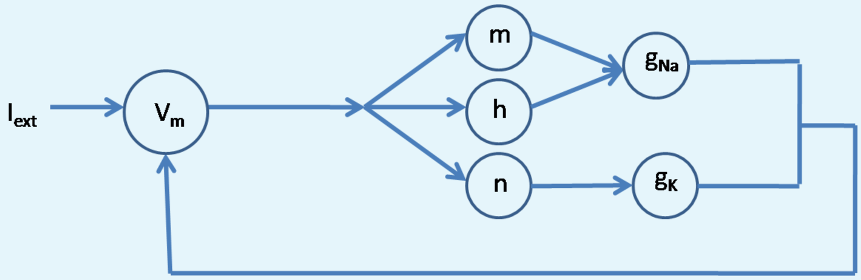
BT6270
COMPUTATIONAL NEUROSCIENCE
ASSIGNMENT 1



Assignment Description

Given is a MATLAB code that simulates the Hodgkin Huxley model.
I have converted the given MATLAB code to Python.



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Question 1

Plot the threshold values for the external applied currents I_1, I_2, and I_3 in which shift of dynamical behavior from one to another is seen, such as no AP, finite number of AP's, Continuous firing and then followed by distortion resulting in no more APs.

Threshold values of External Current:

The below threshold currents were determined via sampling process over a current range, employing a current sampling interval of **0.001**.

The current range considered was **[0, 0.7]** indicating the span of external currents that was applied to the neuron to get the results.

The number of iterations for which I have evaluated the membrane potentials is **10^5**. This essentially increases the precision of model.

- **I_1 = 0.023 uA/mm^2.**
  This value signifies the minimum current required to elicit any significant response from the neuron.
- **I_2 = 0.062 uA/mm^2.**
  This value signifies the current threshold above which continuous firing is observed.
- **I_3 = 0.457 uA/mm^2.**
  This value signifies the current threshold above which the continuous firing may become distorted.

To find the above values, I created two additional functions.

- The first function was to calculate the number of spikes in the ***membrane voltage*** list.
- The second function was to get the currents based on changes in the ***number of spikes*** list.

Assumptions:

The following assumptions were made with respect to Hodgkin Huxley model in the construction of the plots for the "firing rate vs. current" and others.

- **Hodgkin Huxley (HH)** model does not reflect the effect of larger currents on the living cell. The living cell could get electrocuted, however, HH model doesn't explain this behavior.

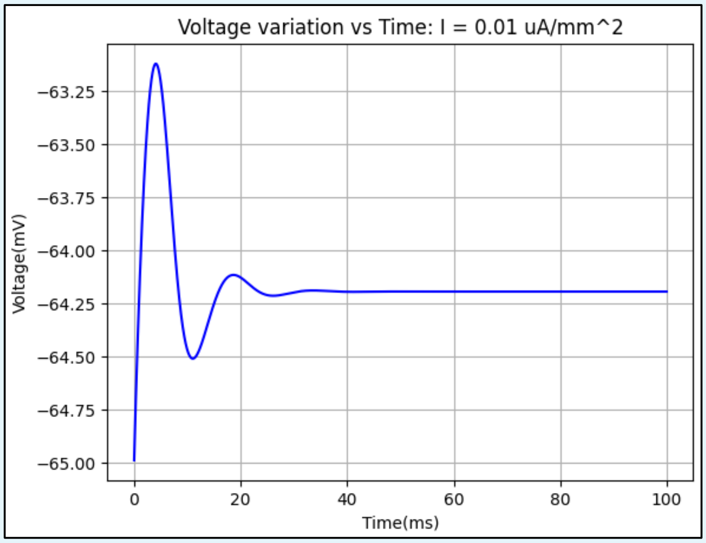
- To count the number of spikes produced at any given current, it is essential to define a voltage threshold. All voltages above that threshold value shall be considered in counting the number of spikes.
  The voltage threshold of a peak is set to **10mV**.

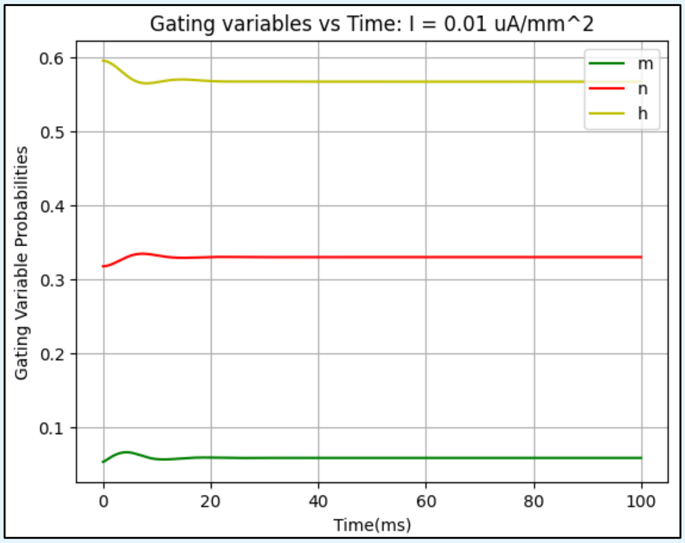
- In order to find the first external input current, $\mathbf{I_1}$, we identify it as the current when the number of spikes becomes **non-zero**.

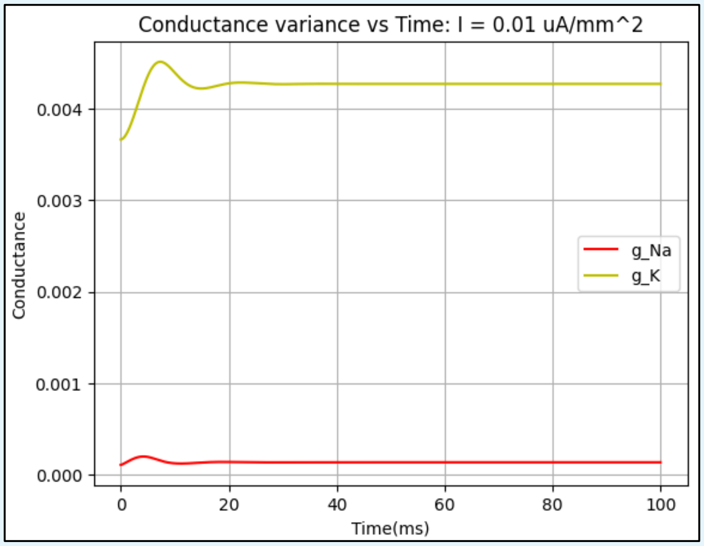
- In order to find the second external input current, $\mathbf{I_2}$, what we need is to identify the current at which we observe a transition from finite number of Action potentials to continuous firing of Action potentials. For this, we identify the current at which the number of spikes **increases by more than 4** in the next current instant.

- In order to find the second external input current, $\mathbf{I_3}$, what we need is to identify the current at which we observe a transition from continuous firing of Action potentials to distorted/no firing of Action potentials. For this, we identify the current at which the number of spikes **decreases by more than 3** in the next current instant.

Value of impulse current = 0.01 uA/mm^2

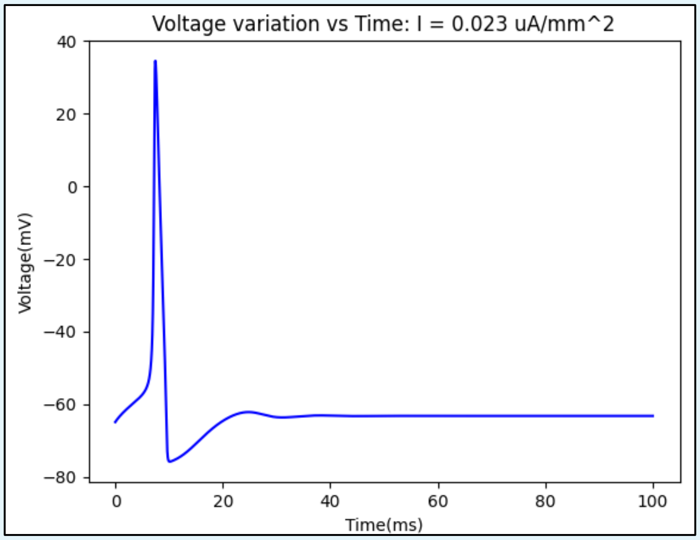


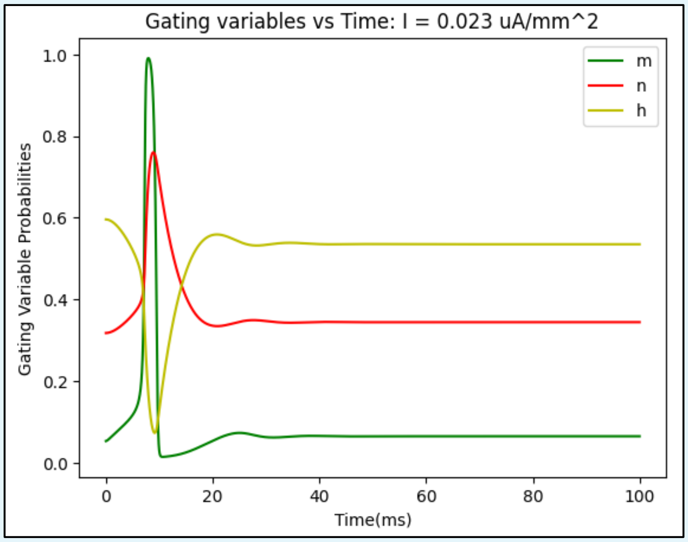


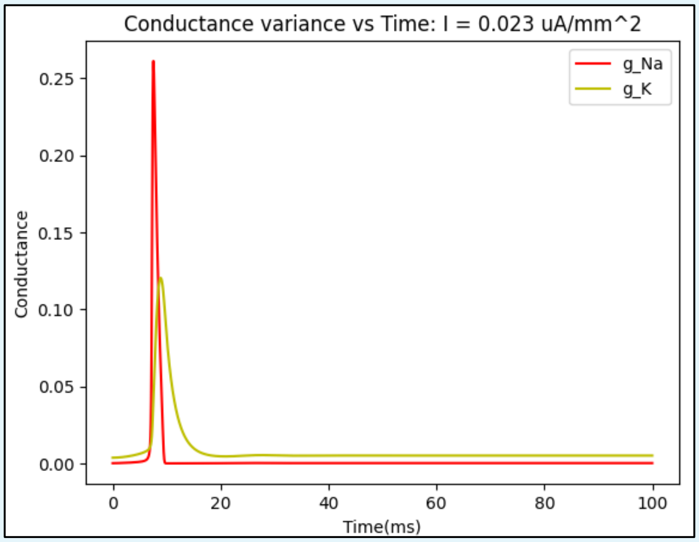


- When an extremely low external current (lesser than I_1) is applied to the neuron, the membrane potential undergoes only a minimal change.
- The tiny current is insufficient to depolarize the membrane to the threshold voltage required to activate the channels.
- Without reaching the threshold, the voltage-gated sodium channels remain in closed state, thus preventing influx of sodium ions.
- As a result, the neuron fails to generate action potentials.
- This condition essentially represents a quiescent, non-excited state of the neuron. Since there is no action potential, the neuron doesn't transmit electrical signals.

Value of impulse current = 0.023 uA/mm^2

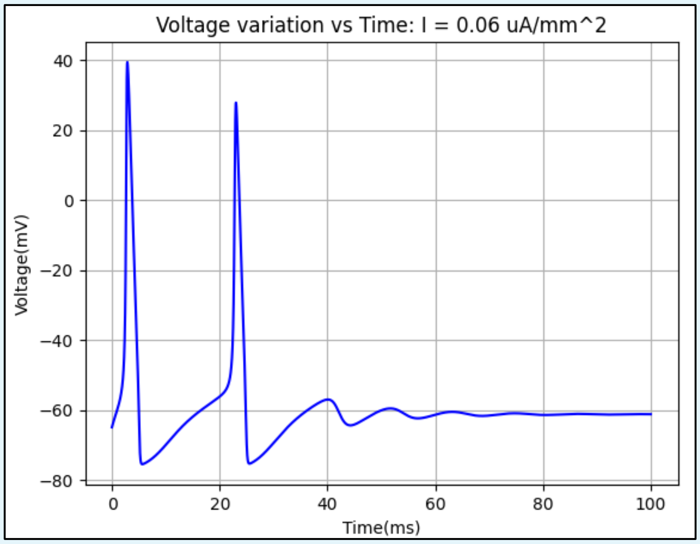


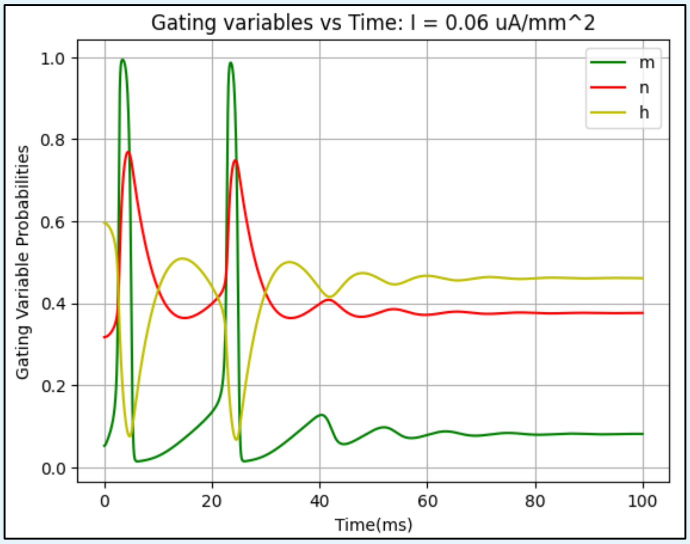


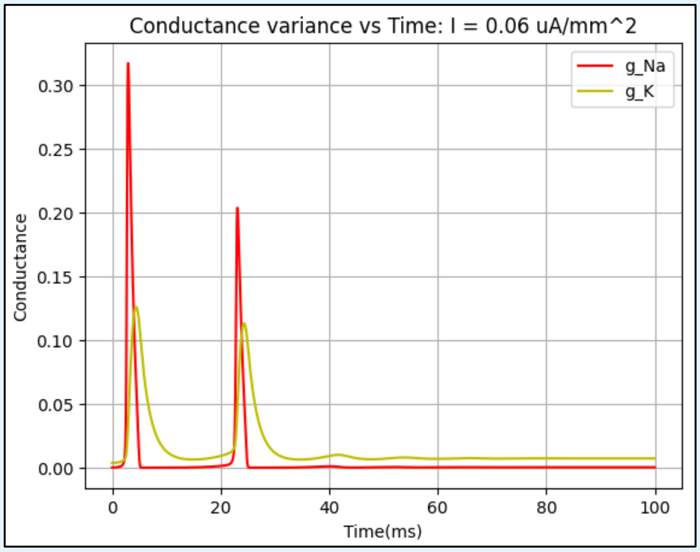


- Above are the graphs at current I_1=0.023 uA/mm^2.
- As I slowly increase the external current value from 0.01 to 0.023 in steps of 0.001, at current 0.023 uA/mm^2 the first action potential is observed.
- At this point, the membrane potential has just crossed the threshold potential.
- At this current only one action potential is observed.
- This current value marks the threshold for transition from no Action potentials to a fixed number of Action potentials.

Value of impulse current = 0.06 uA/mm^2

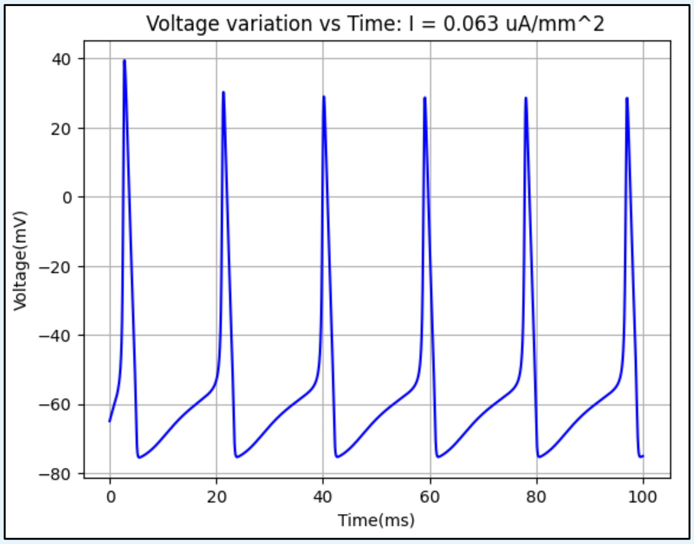


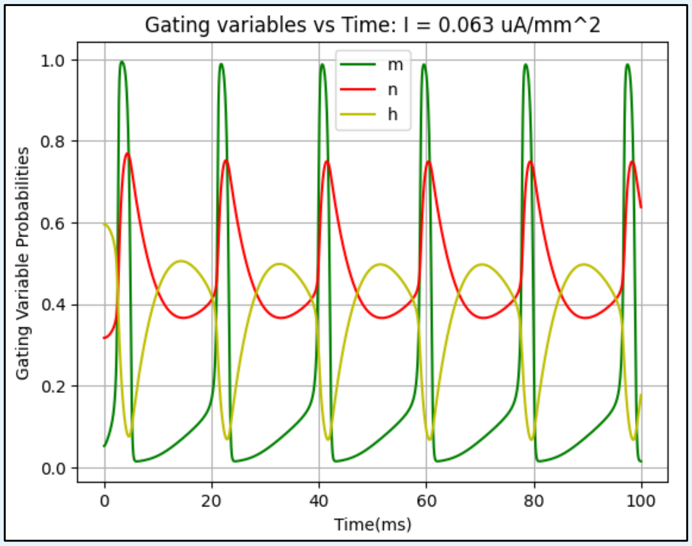


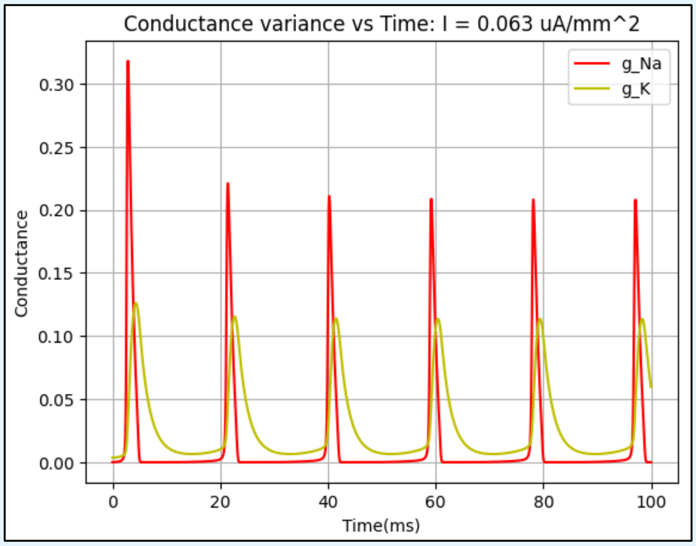


- As the externally applied current increases beyond I_1, however lies below I_2, we observe activation potentials.
- I_1 is therefore considered as first threshold current, as it describes the transition from no activation potential to finite number of action potentials.
- Now, until I_2, we observe a finite number of action potentials being generated. However, at this stage the neuron doesn't fire continuously. Instead, it fires a finite number of action potentials in response to stimulus. This behavior is observed due to the fact that the membrane potential will eventually repolarize, thereby preventing continuous firing.

Value of impulse current = 0.063 uA/mm^2

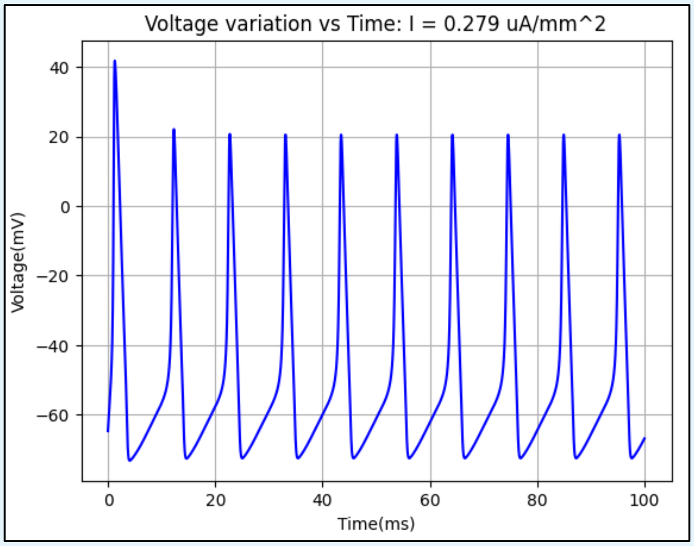


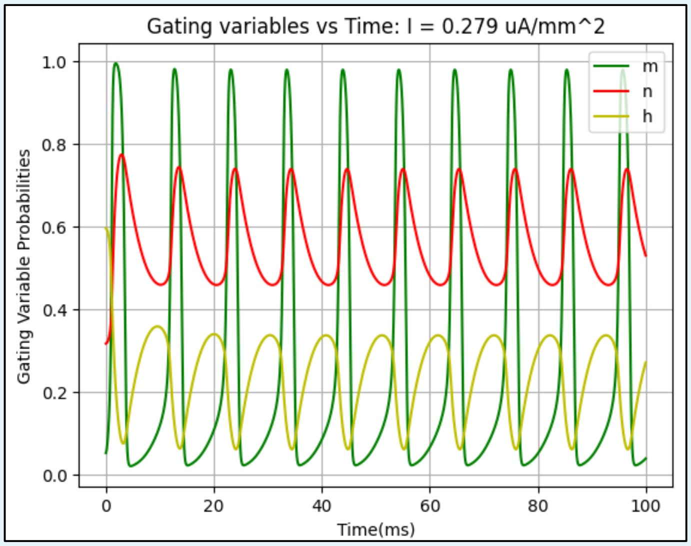


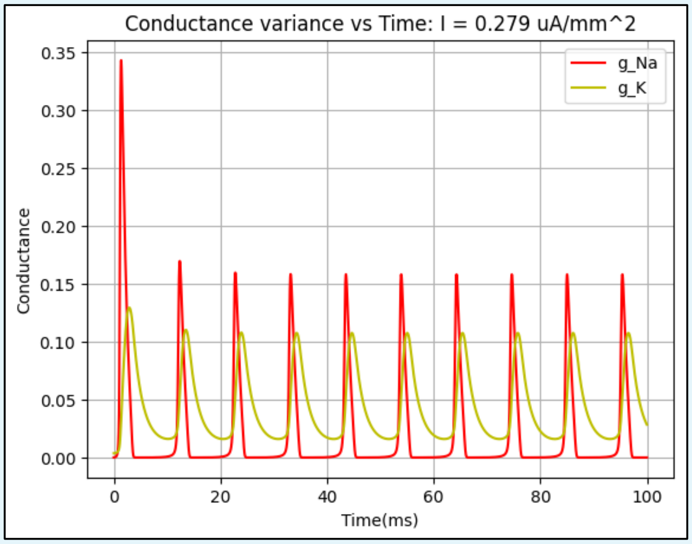


- As the externally applied current increases beyond I_1, the number of action potentials generated gradually start increasing.
- As the current increases, a threshold is reached, beyond which the neurons start to fire action potentials continuously.
- The current threshold at which that occurs for the given HH model is 0.062 uA/mm^2. Given above, at 0.063 uA/mm^2, we observe continuous firing of the action potentials.
- If we analyze the firing rate curve, at this point the firing rate of action potentials experiences as sharp raise.

Value of impulse current = 0.279 uA/mm^2

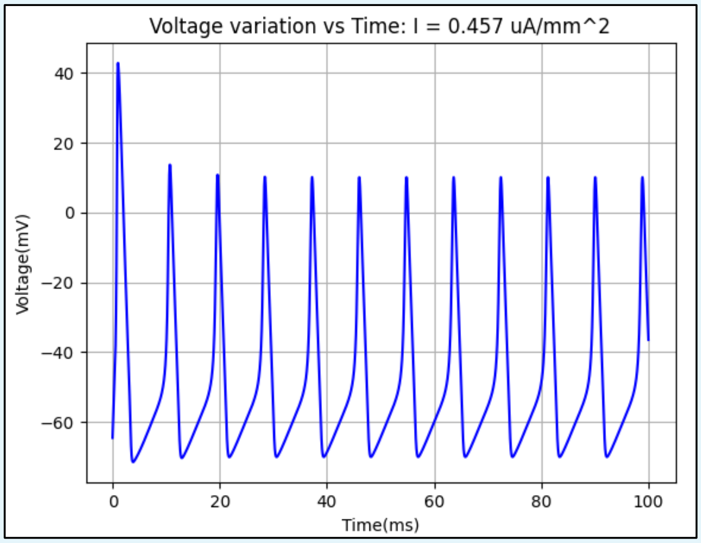


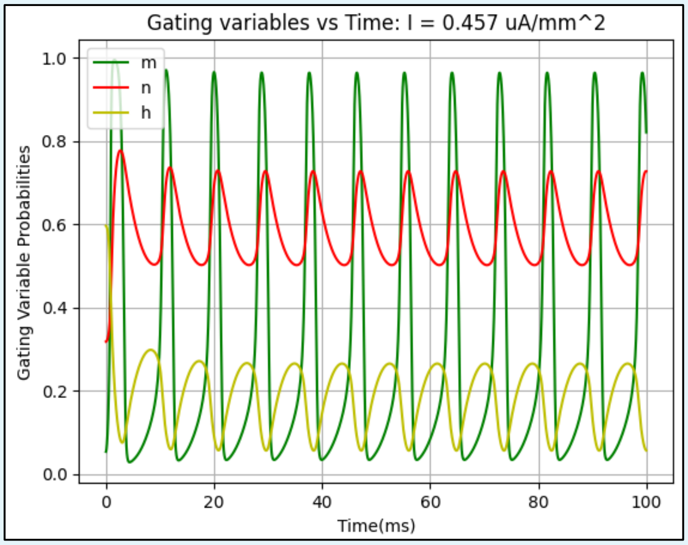


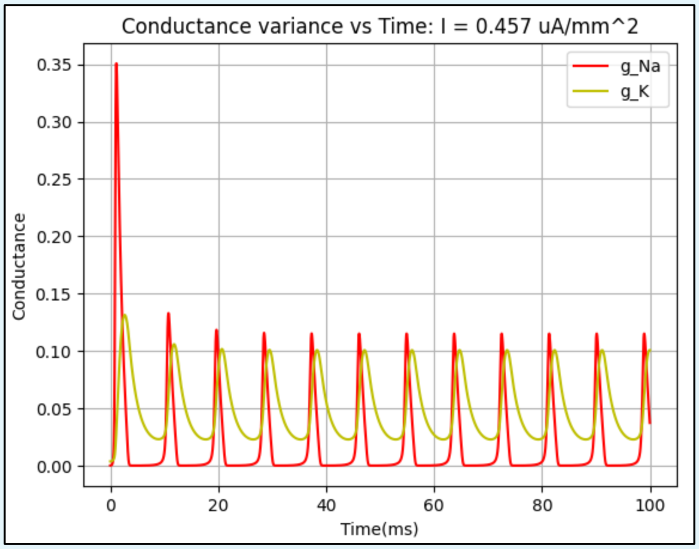


- Further increasing the external current beyond a certain threshold I_2, causes the neuron to fire action potentials continuously.
- The continuous firing occurs owing to the fact that the membrane potential remains depolarized for an extended period, allowing for the rapid reopening of the sodium channels and continuous action potential generation.
- This positive feedback loop of sodium channel activation and membrane depolarization leads to the continuous generation of action potentials until the external conditions change or biophysical limitations come into play.

Value of impulse current = 0.457 uA/mm^2



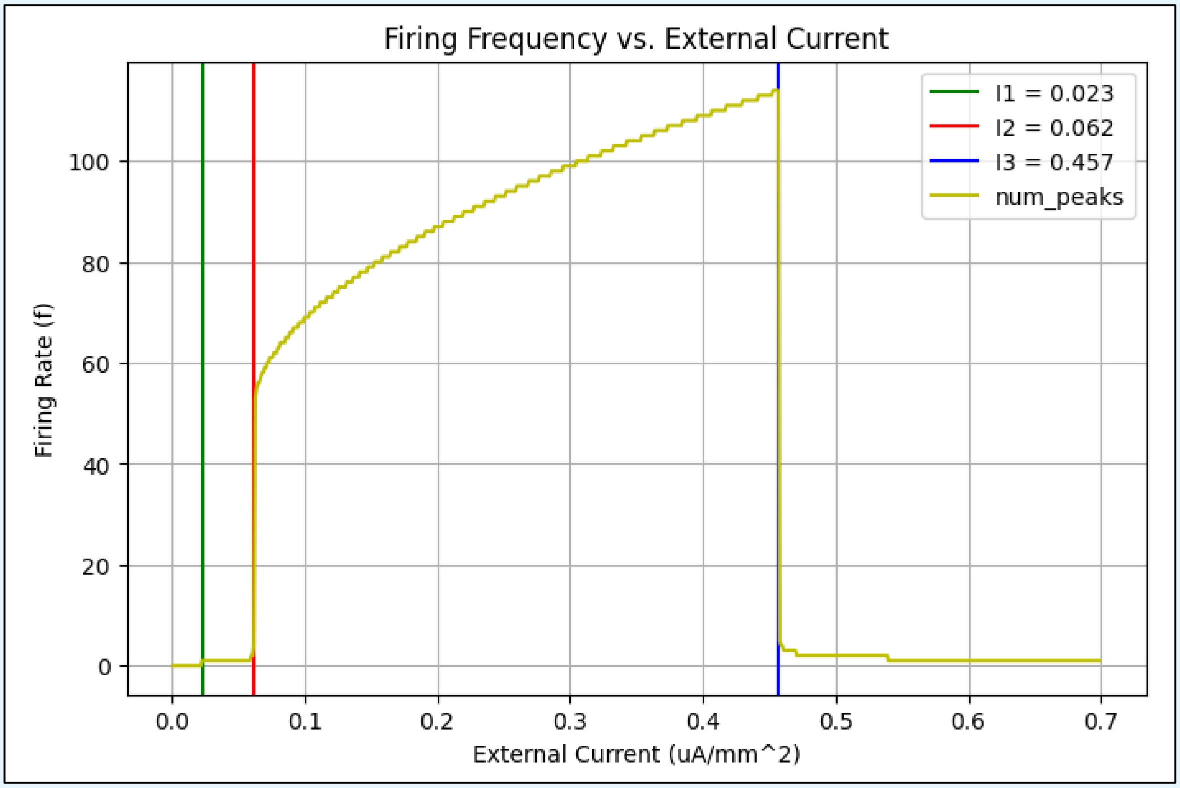




- If the external current is increased to higher levels, there shall arise a threshold current value beyond which the continuous firing pattern may become distorted. That threshold current is I_3.
- It means, that beyond that threshold spikes will occur, however, the maximum voltage reached by these spikes will significantly drop-down and hence they will no longer cross the threshold voltage, thereby resulting in a sharp decay in the firing rate.
- This distortion can be caused by internal factors or biophysical limitations.
- The Hodgkin Huxley model is incapable of explaining the behavior of neurons when exposed to such high external current.

Question 2

Plot a graph which depicts the firing rate (frequency) as you change the applied external current (i.e. I_{ext} vs. Firing rate (f)).




```python
def find_peaks(v_hist):
    threshold_v = 10
    count = 0
    for i in range(1,len(v_hist)-1):
        if(v_hist[i] >= threshold_v):
            if((v_hist[i] > v_hist[i+1]) and (v_hist[i] > v_hist[i-1])):
                count += 1
    return count
```

```python
def find_current(num_peaks):
    I1 = 0
    I2 = 0
    I3 = 0
    for i in range(1,len(num_peaks)-1):
        if(num_peaks[i] > 0 and num_peaks[i-1] ==0):
            I1 = i
        if(num_peaks[i+1] - num_peaks[i] > 4):
            I2 = i
        if(num_peaks[i] - num_peaks[i+1] > 3):
            I3 = i
    return I1, I2, I3
```

Here, I have just enclosed the function used. The entire code has been uploaded as a separate file altogether.

Firing Frequency vs. Ext. Current

The typical dynamics of the Hodgkin Huxley model can be divided into three sections:

1. **Sub-threshold Region ($I < I_1$).**
   At very low external currents, the firing rate is near zero. This region represents the sub-threshold simulation, where the applied current is too weak to elicit action potentials.

2. **Threshold Region ($I_1 < I < I_2$).**
   As the external current is gradually increased within this range, the firing frequency begins to rise. This signifies that the neuron has reached the threshold for action potential initiation.

3. **Saturation Region ($I_2 < I < I_3$).**
   Beyond the threshold represented by I_2, within the given range, the firing keeps increasing slowly with current. Towards the end of this region, it starts to saturate and further increase in external current may not significantly change the firing frequency.

4. **Distortion or Ceasing of Firing ($I > I_3$).**
   In cases of extremely high levels of external current, the firing rate may start to distort or eventually cease. This distortion could occur due to various factors, which include depletion of ions available thereby affecting the action potential and so on.