# An analysis of the LIF and HH models

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## Introduction

### Leaky Integrate and Fire Model

The leaky integrate and fire model is a computationally inexpensive model that simulates a neuron as a circuit with a capacitor and a resistor. The resistor serves as a sort of "Leak" channel, energy is dissipated out of the neuron through this leak channel. The capacitor part of the circuit simulates the Nernst Potential across the membrane: charge distributed on the two plates of the capacitor behaves in a similar manner to the charge distributed across the membrane. The differential equation for the sub-threshold behaviour of the Leaky Integrate Model is written as:

$$C\frac{dV}{dt} = -g_L(V - V_L) + I$$

Where $g_L$ is the conductance of the leaky resistor ,$V_L$ is the voltage acros the leaky resistor, $I$ is the current injected, $V$ is the total voltage across the neuron membrane and $C$ is its capacitance.

Since the LIF model is supposed to model a neuron, it also needs to take into account its spiking behaviour. However, in the case of this model, the behaviour is inserted in a very ad-hoc fashion. That is, the spiking behaviour is not built into the differential equations, but instead is added as an afterthought, roughly as follows:

$$\text{if } V > V_{th} : V = V_{reset}$$

### Hodgkin-Huxley Model

The Hodgkin-Huxley model is a relatively computationally expensive model which was developed by Hodgkin Huxley following their experiments on the giant axon of a squid. One of the great advantages of the model is that the spiking behaviour is built into the differential equations, there is nothing that needs to be introduced in an ad-hoc manner. The disadvantage that comes with this is that a number of different variables (known as the gating variables) need to be kept track of, each of which is governed by its own differential equations.

The Hodgkin Huxley model is similar to the LIF model in that there is a leak resistance. In all other aspects, however, it is radically different. For one, the HH model treats the currents due to each of the individual ion channels in the neuronal membrane separately. The equation that governs the HH model is:

$$C\frac{dV}{dt} = -\sum_k I_k(t) + I(t)$$

Where the sum over the currents can be opened up as:

$$\sum_k I_k(t) = g_{Na}m^3h(V-E_{Na}) + g_K n^4(V-E_K) + g_L(V-E_L)$$

and this is where the gating variables $m$, $n$ and $h$ come in. These are governed by the differential equations:

$$\dot{m} = \alpha_m(V)(1-m) - \beta_m(V)m$$
$$\dot{n} = \alpha_n(V)(1-n) - \beta_n(V)n$$
$$\dot{h} = \alpha_h(V)(1-h) - \beta_h(V)h$$

Where the $\alpha$ and $\beta$ terms can be thought of as rates of transition from closed to open and from open to closed states respectively. These variables govern the opening and closing of the channels, which in turn governs the firing of the action potential.

### A summary of the analysis

Both of these models were coded up in Python. A github link to the Jupyter notebook that goes through the entire code has been attached [1]. The models were then stimulated with currents of different nature. The LIF model was stimulated with constant, Gaussian White Noise and sinusoidal currents. The voltage responses were recorded. The HH model was stimulated with constant currents of different values. Maximum and minimum spiking frequencies were also recorded for both models. The effect of noise on both of the models was also analyzed.

Finally for the HH model post-inhibitory rebound (the response of the neuron after being released from a prolonged period of under-stimulation) was also analyzed.

## Method

### Environment

All of the code was written in Python 3 within a Jupyter Notebook environment. Any advanced mathematical functions used in the code were imported from the NumPy library. In addition the plotting was done using Matplotlib's pyplot.

#### Models and the parameters used

The LIF model was coded up using the Euler method, whereby the time axis was split into discretized points. Then, starting from an initial voltage of -65 milliVolts, the value of the voltage signal at all of the subsequent points was estimated by multiplying the time step with the value of the slope computed at that point (using the differential equation). The step size chosen for the LIF model was 0.1 milliseconds. This was significantly smaller than the time parameter $\tau$ dictating the time course of the dynamics which had a value of about 10 milliseconds.

The Hodgkin-Huxley model was coded up by evaluating the explicit solutions to the differential equations at each point. This was fairly easy since the form of the differential equations for all four of the dynamic parameters ($m$, $n$, $h$, and $V$) assume the following form after a little manipulation:

$$\dot{x} = \frac{x_{max} - x}{\tau}$$

We used the following functions for the transition rates:

$$\alpha_m = \frac{0.1(v+40)}{1 - e^{-\frac{(v+40)}{10}}} \quad ; \quad \beta_m = 4e^{-0.0556(v+65)}$$

$$\alpha_n = \frac{0.01(v+55)}{1 - e^{-\frac{(v+55)}{10}}} \quad ; \quad \beta_n = 0.125e^{\frac{-(v+65)}{80}}$$

$$\alpha_h = 0.07e^{-0.05(v+65)} \quad ; \quad \beta_h = \frac{1}{1 + e^{-0.1(v+35)}}$$

In addition, the following initial values were used for the four parameters:

$$V(0) = -64.9964 \text{ mV}$$

$$m(0) = 0.0530$$

$$n(0) = 0.3177$$

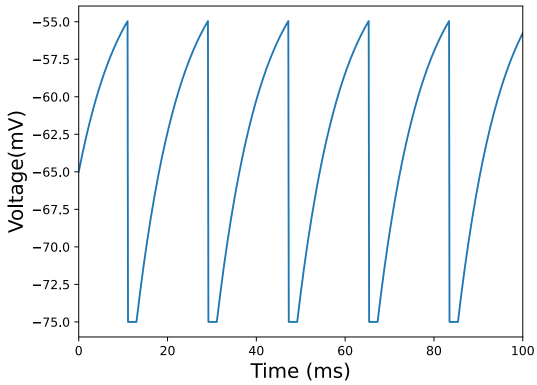
$$h(0) = 0.5960$$

The step size used was again 0.1 milliseconds, this too was significantly smaller than the time constants for each of the parameters.

## Results for the LIF model

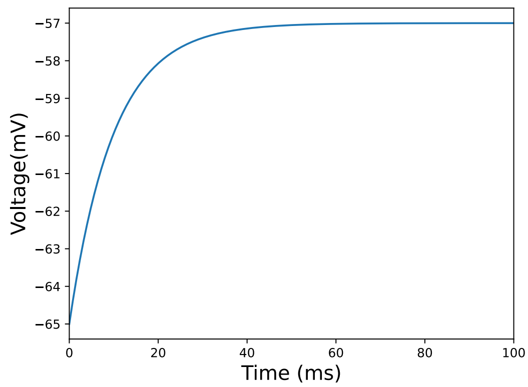
#### Stimulation with constant current

The following are the plots for the responses of the LIF model to constant currents:




What we have plotted above is the response of the LIF model to a constant current of 250 millimAps. It can be clearly seen that the sub-threshold behaviour is that the input gets integrated starting from an initial voltage of -65 (the curved portion shows exactly this integration). This happens until the voltage reaches the threshold value, at which point the if statement kicks in, resetting the voltage to $V_{reset}$. What follows is a period of refractoriness (characterized by the horizontal lines separating the points where the voltage stays at $V_{reset}$. Once the refractory period has elapsed, integration starts again.

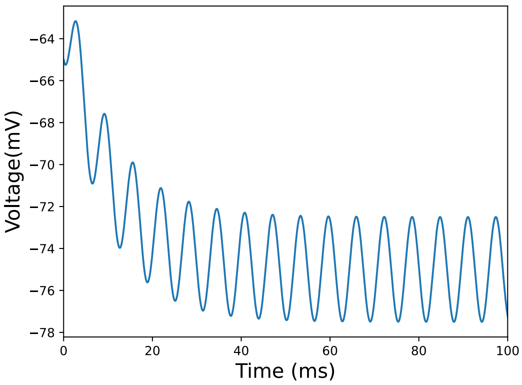
However, this isn't always what will happen. In fact if you plot the model for an input current of less than 200, there isn't enough charge to counter the leaky resistance. This results in no spiking at all. That is what we plot below:



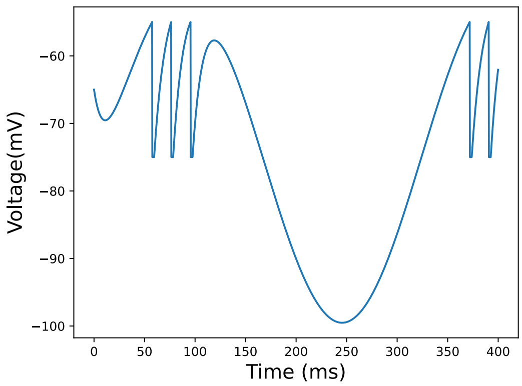

The output voltage plateaus to a certain value below the threshold. This is the farthest it can go. This is essentially because the voltage depends on the charge accumulated on the membrane. If there isn't sufficient charge in the current, the neuron will never spike.

#### Stimulation with sinusoidal current

We now turn towards some more exotic currents. For the original mean current of 250, we apply a sinusoidally varying current of frequency 1mHz:

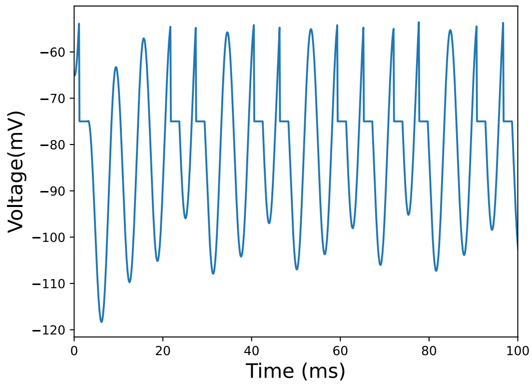



As it stands, this response to the current is quite uninteresting. For one, the output voltage never reaches its threshold value, which means there is no spiking. The reason why this is so is because as it stands, the sinusoidal current has too big of a frequency for the voltage output to be integrated appreciably enough such that it reaches the threshold voltage. What happens instead is that the output becomes a sine wave whose mean decays until it reaches some static value. This is because we started the current at an initial value of -65 mV.




To test the hypothesis that the output is indeed not spiking because of the large frequency I ran the LIF model again, only this time with a prefactor of 0.02 next to the argument of the sine function (this serves to decrease the frequency, giving the output enough time to be integrated so as to reach the threshold frequency). Indeed during the increasing part of the input current there is now spiking.

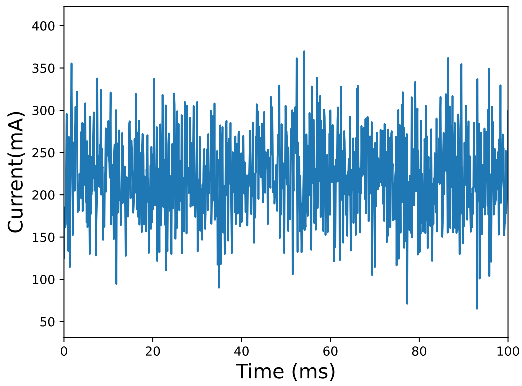
One can also argue that for a given frequency, one might increase the amplitude of the input current to observe spiking. I increased the current to 2500 to see if that happened:



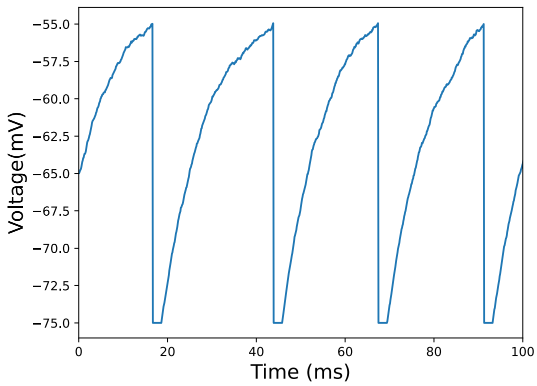

And that is indeed what is seen. If you don't give the signal enough time to integrate upto the threshold voltage, you have to give it more amplitude to get there in a shorter span of time.

### Stimulation with GWN current

A gaussian white noise current with a mean of 220 mA and standard deviation of 0.5 was generated using numpy's randn function. Against time, the current looked as follows:



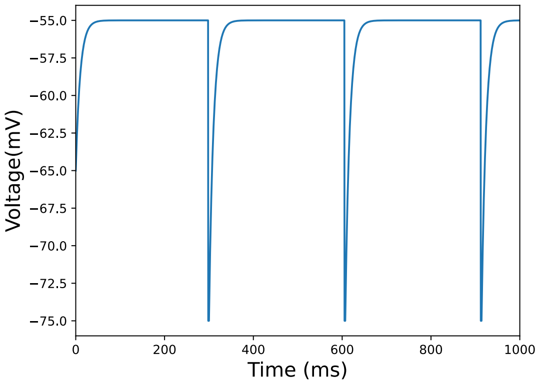

The plot of the voltage response signal against time was as follows:




Clearly the mean was high enough for the provided value of standard deviation for the voltage to be able to generate spikes. Notice that there are small fluctuations in the integration period, these can be attributed to instances where the current suddenly jumps up or down by a large value, causing the integrated voltage signal to either jump up or down relatively drastically.

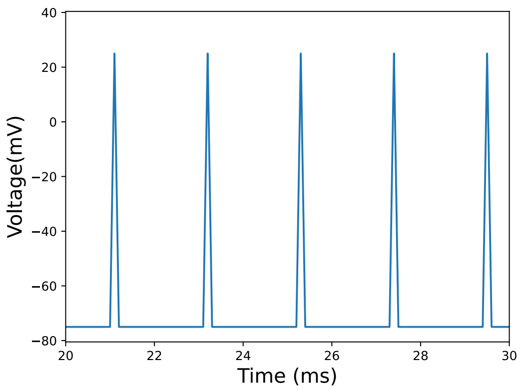
### Maximum and minimum spiking frequencies

After tweaking the value of the input current for some time it was found that the smallest current that generates spikes is actually 200 mA. Any constant current with less amplitude than this does not generate spikes. We perturbed the current to a value only slightly higher than this and then use the numpy ediff1d function to calculate the time duration between successive spikes in our Spikes array. This comes out to be the same for all of the interspike durations.




The above is a plot of the voltage output for the lowest input current possible that generates spikes. We observe that the amount of time required for the signal to integrate upto the threshold value is almost of the order of seconds (the axis in the figure is marked in units of milliseconds).

We then take an arbitrarily high value of the current (100,000 mA in the case of the figure plotted below). Note that this plot does not change in any manner if the current is increased further. This is because the spiking frequency has saturated to the highest possible value:

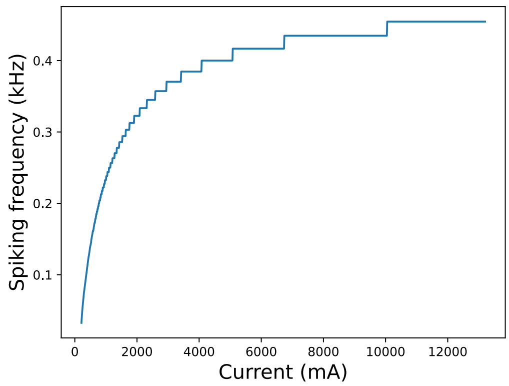



Notice how in the case of this plot, the spiking intervals are of the order of milliseconds. The reason why a saturation in the spiking frequency occurs in the case of our LIF model is simply because we have added a refractory period into the model by hand (2 milliseconds in our case). By making this refractory period arbitaraily small we can make the saturation frequency arbitrarily high. The conclusions were:

- The maximum spiking frequency is: 0.4761 per millisecond
- The minimum spiking frequency is: 0.0032 per millisecond

### F-I curve

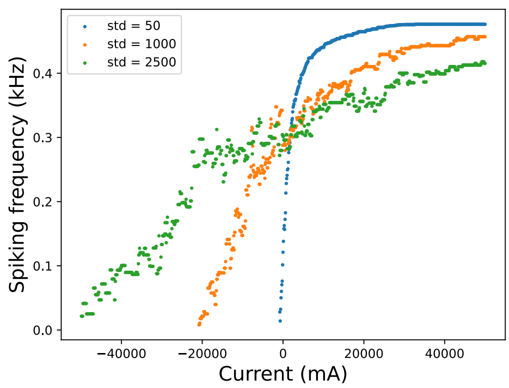
For zero standard deviation, the F-I curve looks as follows:




Notice how the spiking frequency increases as we increase the input current until a plateau is reached. This plateau indicates the point where further increase in current has no effect on the spiking frequency since the refractory period prevents any more spikes from being produced.

### Effect of standard deviation on the F-I curve

In order to study the effect of increased standard deviations in the GWN on the FI curve, I plotted frequency values against current as scatter plots for increasing values of the S.D. The following plots were obtained:



Evidently, increasing the standard deviation has the effect that the spiking frequency gets saturated at higher values of the mean current. We also note that as the standard deviation is increased, the non-linearity in the standard deviation against the current starts to get smoothened out until the function almost resembles a straight line.

### Relation between spiking frequency and the coefficient of variation of the GWN current

The formula for the coefficient of variation ($CV_{ISI}$) is:

$$CV_{ISI} = \frac{\text{std}(isi)}{\text{mean}(isi)}$$

### Effect of Standard Deviation

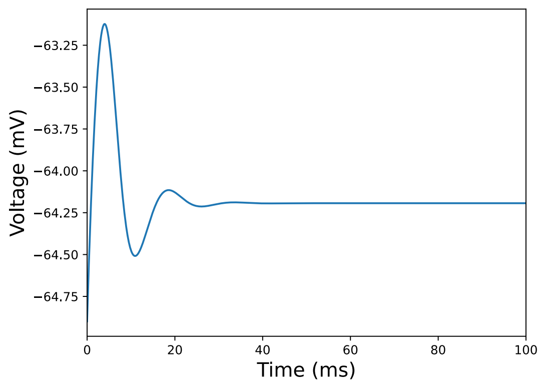
It is evident that increasing the standard deviation of the current increses the coefficient of variation of the interspike intervals. This is precisely because a greater standard deviation for a given mean basically just means that the fluctuations in the current around that mean value are stronger. Since these fluctuations are guassian-random, this means that there are just as many large deviations below the mean as there are above the mean. Consequently, for larger standard deviations, as the LIF is trying to integrate a large positive signal, a large negative incursion immediately afterwards might counter-act it, resulting in less spiking frequency for that particular mean value.

### Effect of Mean

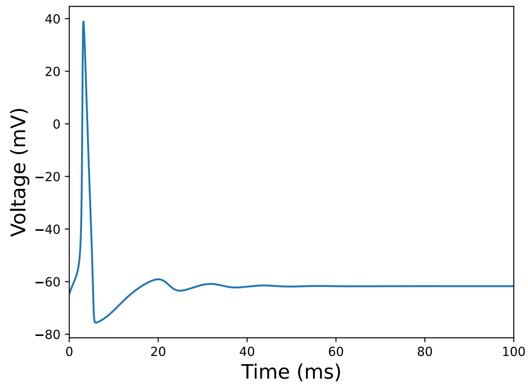
The greater the mean the higher the lower the coefficient of variation in the interspike distances. This is actually quite easy to understand. Since the current fluctuates around the mean, if the mean is higher the output voltage in general fluctuates closer to the threshold voltage. This in turn means that the number/frequency of spikes is larger.

## Results for the HH model

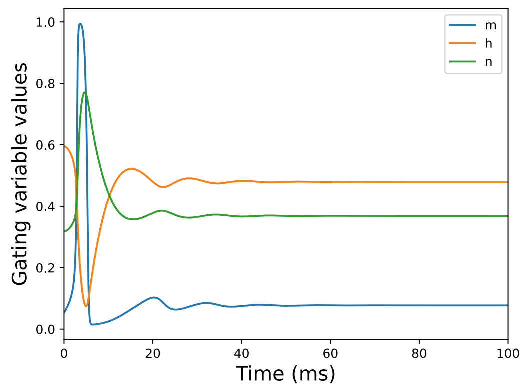
In order to count spikes while simulating the HH model I first decided on a threshold voltage of 0mV such that whenever the output signal exceeded that value, the excursion is counted as a spike.



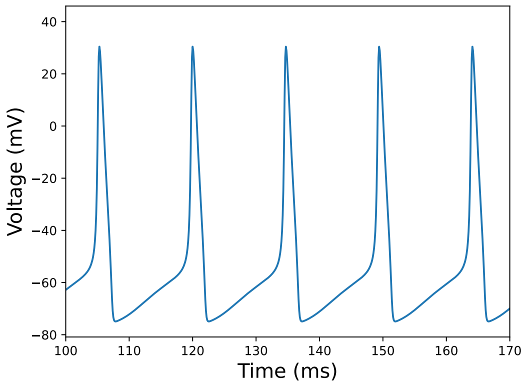

The above is a plot of the response of the Hodgkin Huxley model to a constant current input of about 0.01 units. What is observed is not a spike (the highest value that the voltage reaches is a little over -63.25). The initial kick in the voltage comes from the starting values of the voltage and the gating variables. The current clearly is not enough to generate a spike.



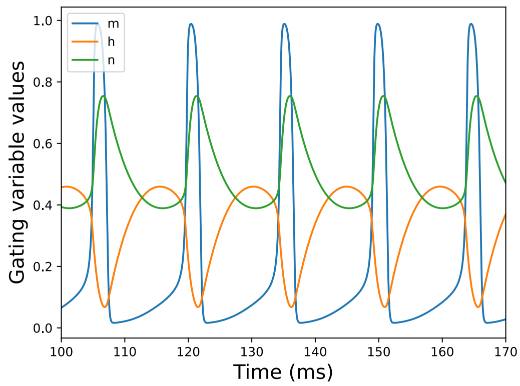

At 0.05 microamperes per millimeters squared, a single spike is observed. This is again because the voltage as well as the gating variables are given some initial value. However, after the spike the constant value of the current is not sufficient to generate subsequent spikes, resulting in a constant voltage.



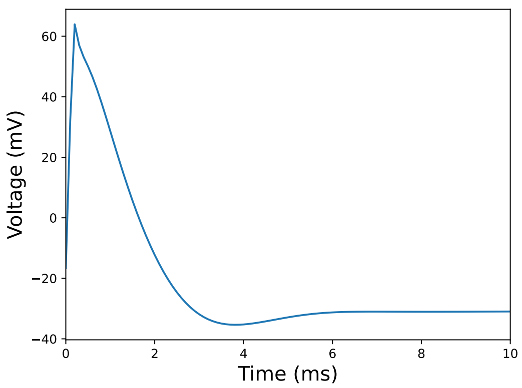

A plot of the gating variables is demonstrative here. Notice how there is a spike in the gating variables m and n initially, denoting the opening of sodium and potassium channels. These variables, however, decay quickly, and there is a gradual increase in h, resulting in the inactivation of the sodium channels. The gating variables eventually attain some steady state values.



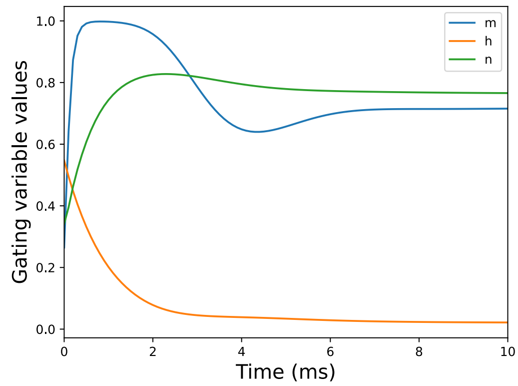

At a constant current of 0.1 microamperes per millimeters squared, a spike train is observed. This can be attributed to the fact that the value of the sustained current is above the threshold value so that everytime the voltage returns to its baseline value there is enough current to generate a spike again.




The gating variables show a type of periodic behaviour - as is expected since multiple spikes are observed and the spikes are qualitatively all the same. However, the general trend is still the same: the gating variable m spikes first, followed immediately by n until. This is followed by a sudden decrease in the values of these gating variables. All the while h increases until it reaches its peak value. The gates open, close and then open again and the process keeps repeating.

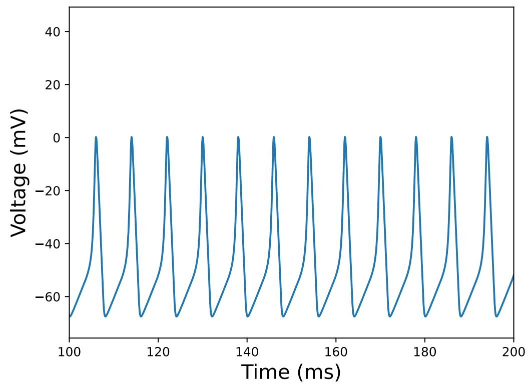



At 5 microamperes per millimeters squared, we only see one spike (which is a lot more spread out than the previous spikes and has a significantly greater amplitude). Plotting the gating variables against time gives us some insight into this behaviour. The peak for the gating variable m is a lot more spread out in time, as a result the spike is a lot more spread out. On the other hand the gating variable h goes to zero after a while, which means the sodium current is cut off completely. Oe can attribute this to the inactivation of the gates beyond a certain current.

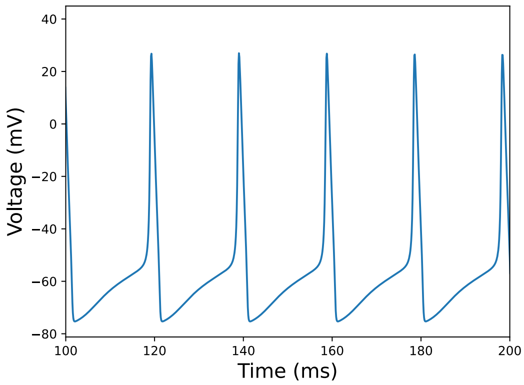



**Maximum and minimum spiking frequencies**

We then tweakead the value of the input current for the Hodgkin Huxley model until we found the maximum and minimum spiking frequencies (in a similar manner to how we did it for the LIF model). Since I decided on an arbitrary threshold value (0mV in our case), I only treated excursions that reached this threshold value as spikes. It was noticed that as the current is increased, while the frequency of spikes increases the amplitude that the spikes reach actually **decreases**.




The above is a plot of the voltage output with the maximum possible spiking frequency. Maximum spiking frequency is observed for a current of about 0.62 microAmps/ millimeters squared. Increasing the current beyond this point results in excursions that do not attain a peak amplitude of 0mV or above and therefore, do not count as spikes.

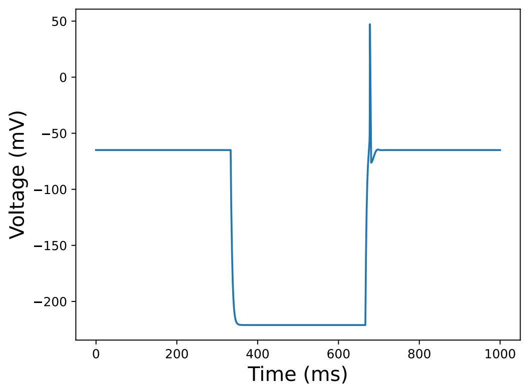



It was found that the smallest value of current that can generate a spike train is about 0.0626 microAmps/ millimeters squared. Decreasing the current below this value does not result in a spike train. The reason why repetitive firing is impossible above the maximum frequency (in the case of the HH model) is simply because beyond a certain value of the current the sodium channels inactivate, preventing spike generation. The conclusions were:

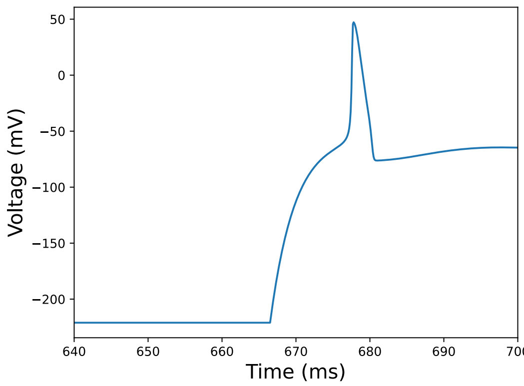
- The maximum spiking frequency is: 0.125 per millisecond
- The minimum spiking frequency is: 0.051 per millisecond

### Post-inhibitory rebound in HH

In order to observe post-inhibitory revound in the Hodgkin-Huxley model, the input current was split into three equal portions in time. In the first portion, the current assumes a value of zero then in the second portion, the current is given a negative value (-0.5 microAmps per mm squared in this case), then in the final stretch, the current jumps back to zero.



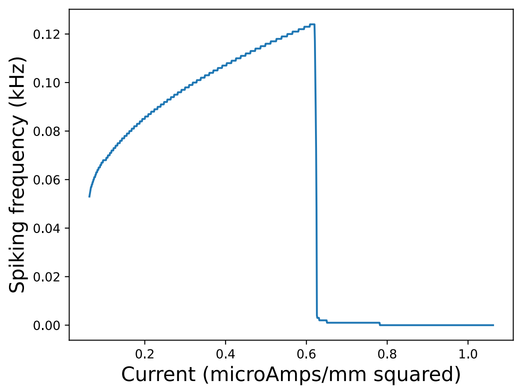

We notice that when the current is set to a negative value, the voltage dips to a lower baseline. Then, immediately after the current is brought back to its original value of zero, a spike is observed before the voltage pleateaus to a larger constant value again. The neuron fired, not as a result of stimulation, but rather as a result of being released from a prolonged state of **understimulation**. This is something that is observed in neurons experimentally and is a feature of the HH model (our LIF model cannot simulate this behaviour).




The above is a zoomed in version of the same plot, showing the spike generated after being released from inhibition.

### F-I curve

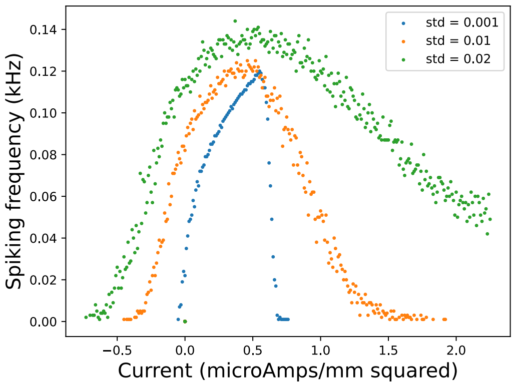
For zero standard deviation, the F-I curve for the HH model looks as follows:




Notice how the spiking frequency increases non-linearly upon increasing current until it reaches its maximum value (that we calculated to be about 0.125 per millisecond). Immediately afterwards, the frequency drops too zero (it takes up small non-zero values before vanishing completely because even when the spike train disappears the initial spike remains for a while). This dip in the spiking frequency can be attributed to the amplitude of the excursions dropping below our threshold voltage of 0mV. As a result, beyond this point, no spikes are counted whatsoever.

### Effect of standard deviation on the F-I curve

In order to analyze the effect of the standard deviation of gaussian white noise current on the hodgkin huxley model, I made scatter plots of the FI curve for three separate values of the standard deviation. The results were as follows:




The following features are worth noting. For small values of standard deviation, the FI curve closely resembles the one we obtained for constant currents (which is to be expected). However, for larger values of the standard deviation, the FI curve starts at a smaller value of the current (this is, indeed, to be expected as well, since for a given mean current a larger standard deviation can cause the input current to attain a high enough value for a spike train to be generated). The peak frequency also increases for larger standard deviations. Finally we notice that for large values of the standard deviation, the frequency drops to zero at higher values of the current.

**Comparison of the qualitative impact of noise on the LIF and HH models:**

**Leaky Integrate and Fire**

The primary effect of increasing the standard deviation on the FI curve of the LIF model is that it linearizes it (for large enough values of the standard deviation, the curve approaches a straight line). However, the qualitative behaviour for large enough current stays the same for the LIF model (no matter the standard deviation): for a chosen duration of the refractory period, the frequency plateaus to a value. This indicates saturation, which is indeed governed by the refractory period in the case of the LIF model.

**Hodgkin-Huxley**

In the case of the Hodgkin-Huxley model, the effect of increasing the standard deviation on the FI curve is that it gets spread out. However, the qualitative features stay pretty much the same: the frequency starts increasing at some value of the current before it approaches a peak value (which is larger for a larger standard deviation) and then starts decreasing until it reaches zero. This is a direct result of the way the gating variables (namely h) behave.

## References

[1] Github page with an ipynb file going through the code. https://github.com/malaikkabir/ComputationalNeuroscience. Accessed: 2023-04-15.