ASSIGNMENT - 1

ANALYSIS OF HODGKIN-HUXLEY MODEL

BT6270 Computational Neuroscience
Fall / Odd Semester 2025
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Introduction

The Hodgkin-Huxley model is a foundational mathematical framework developed to describe the temporal variation of action potentials and the behavior of voltage-gated ion channels in neural cells.

The model is based on the following assumptions:

- **Spatial Homogeneity**: The membrane is considered uniform in its properties at every point, eliminating local variations in ion channel density or membrane characteristics. Additionally, in the extracellular space and cytosol, respectively, the concentration of ions is assumed to be uniform throughout space.

- **Infinitely Large Membrane Sheet**: The system under study is assumed to be an infinitely large membrane sheet. This geometric assumption chosen to facilitate computational analysis by eliminating tricky boundary effects.

- **Uniform Current Density**: To satisfy the above assumptions, any current applied to the membrane is presumed to spread evenly across the sheet, rather than being localized to a specific region.

Assumptions

In the following section, we shall classify the thresholds of voltage-gated ion channels in the membrane, define an action potential, and clarify all assumptions made for this assignment.

Voltage-Gated Ion Channels

Two voltage-gated ion channels are considered in this model, and their activity is vital in the non-linear dynamics exhibited by neurons in response to an applied external voltage.

- **The voltage-gated sodium-ion channels:** These channels open rapidly in response to membrane depolarization at around -55 mV, allowing an influx of Na^+ ions. The concentration of Na^+ ions within the cell is lower than the concentration outside, thus the opening of the channels leads to a sharp spike in membrane potential (depolarization phase of the action potential). They reach peak conductance at a membrane potential of 20–30 mV.

  Following this, these channels inactivate quickly and close entirely when the membrane potential reaches around -55 mV [1].

- **The voltage-gated potassium-ion channels:** The concentration of K^+ ions within the cell is higher than the outside; therefore, these channels are involved in the cell membrane's repolarization. K^+ channels conduct ions at an extremely fast rate. Three major families of voltage-gated potassium-ion channels exist: K_f, K_v, and K_A [2].

  K_f is a fast, transient potassium channel subtype critical in repolarizing membrane voltage once the voltage-gated sodium channels open. Their threshold voltage for activation is around -22 mV. These ion channels open gradually, with peak conductance of these channels occurring at a membrane potential of approximately 10 to 20 mV [3].

  These channels inactivate slowly at approximately -70 mV, leading to hyperpolarization of the membrane. Following this phase, the membrane potential returns to its resting state due to the activity of constitutive ion channels. The concentration gradients of Na^+ and K^+ are maintained by the Na^+-K^+-ATPase pumps.

The various voltage thresholds of these ion channel gates are summarized in Table 1 below.

Channel	Activation Threshold	Maximum Conductance (Voltage)	Deactivation Threshold	Notes
Voltage-gated Sodium-ion Channels	~ -55 mV	25 to 30 mV	~ -55 mV	Rapid activation & inactivation
Voltage-gated Potassium-ion Channels	~ -22 mV	10 to 20 mV	~ -70 mV	Delayed & gradual opening, gradual closing

Table 1: Threshold voltages of voltage-gated ion channels

Action Potential

In literature, an action potential is typically characterized by two parameters: the spike width and the peak membrane voltage attained during the event. Since temporally distorted action potentials are not encountered for this assignment, we will focus solely on the peak voltage criterion.

Specifically, we will require that an action potential reach a minimum peak voltage of 10 mV. This criterion ensures that only biologically relevant spikes are recorded as action potentials, reflecting the requirement that a majority of voltage-gated K^+ channels are open—a condition generally met at voltages between 10 and 20 mV, as previously discussed. Therefore, a threshold of 10 mV is adopted to maintain biological consistency in action potential identification.

(a) Characterizing System Response to Input Currents

1.No Action Potential Regime

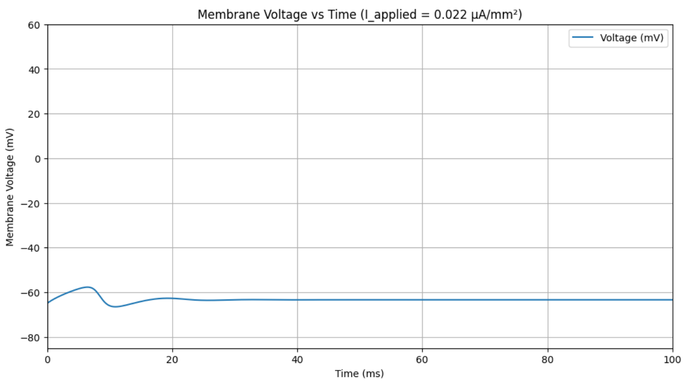

Figure 1.1

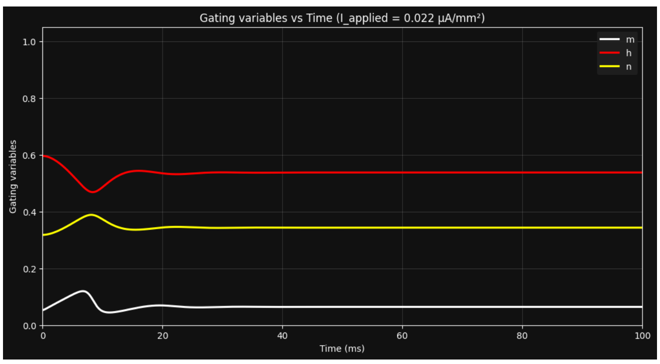

Figure 2.1

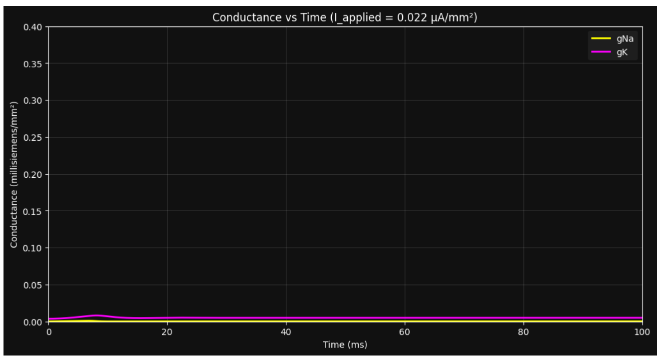

Figure 3.1

For applied currents below 0.0222 μA/mm^2, the system remains in the no action potential regime. The peak membrane voltage stays below -55 mV, so the sodium channels responsible for rapid depolarization do not open, as their activation threshold is not reached. This leads to the brief depolarization of the cell membrane following which it quickly returns to it's resting potential.

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2. Finite Action Potential Regime

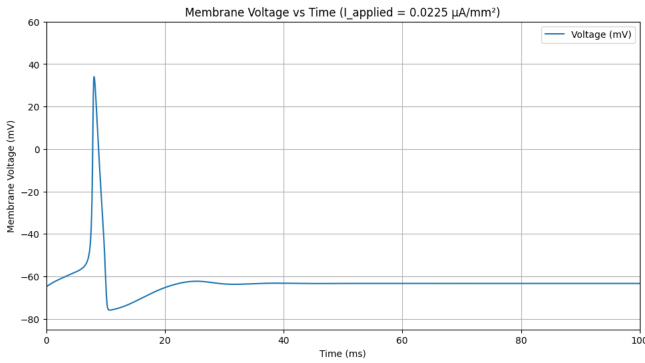


Figure 2.1 (a)

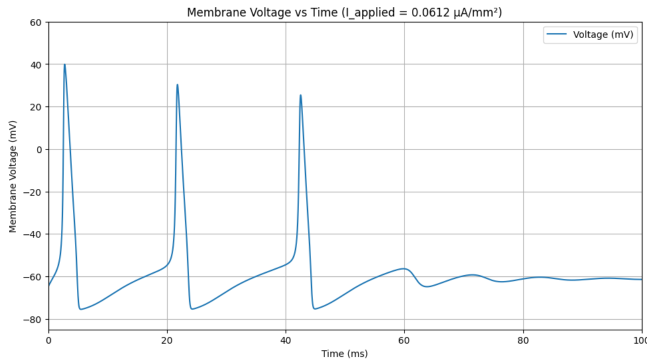


Figure 2.2 (a)

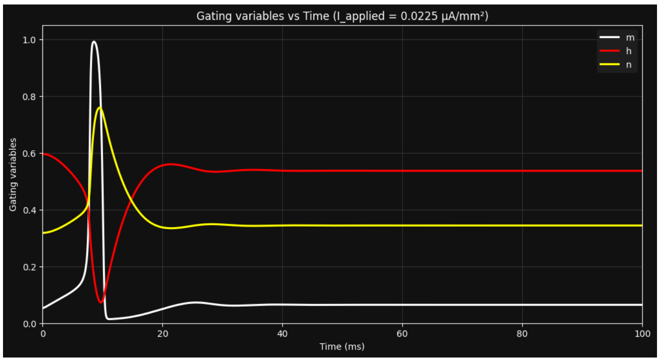
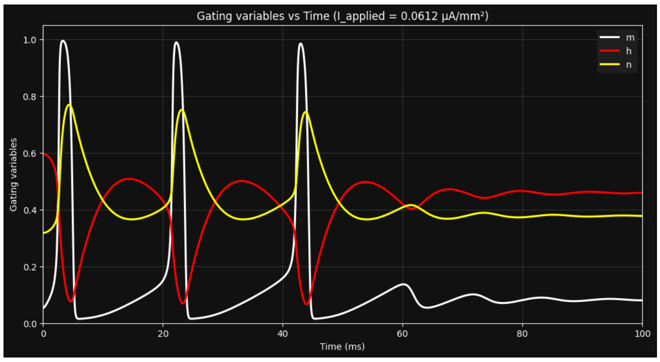


Figure 2.1 (b)



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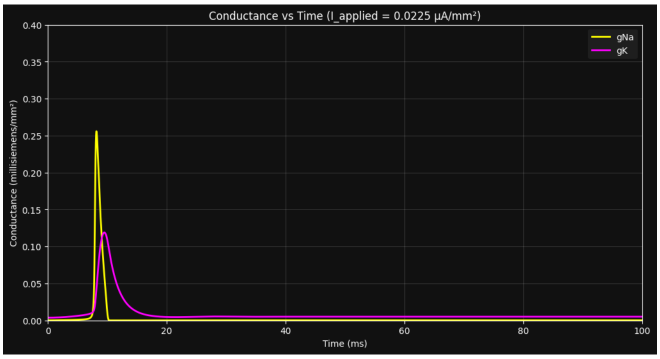

Figure 2.1 (c)

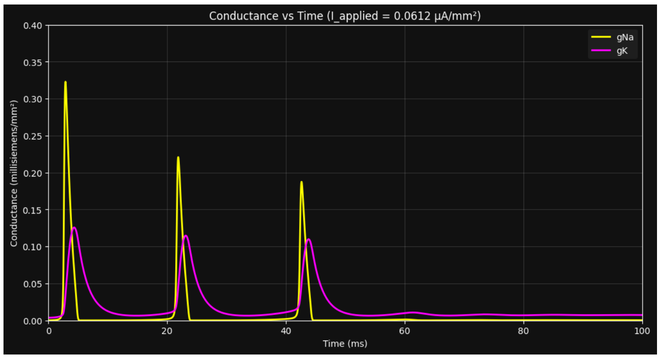

Figure 2.2 (c)

For applied currents between 0.0223 μA/mm^2 and 0.0612 μA/mm^2, the system enters the finite action potential regime. In this range, the membrane voltage transiently exceeds -55 mV, allowing the sodium channels to open and initiate one or more action potentials.

After firing a finite number of spikes, the membrane potential returns to rest.

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3. Continuous Action Potential Regime

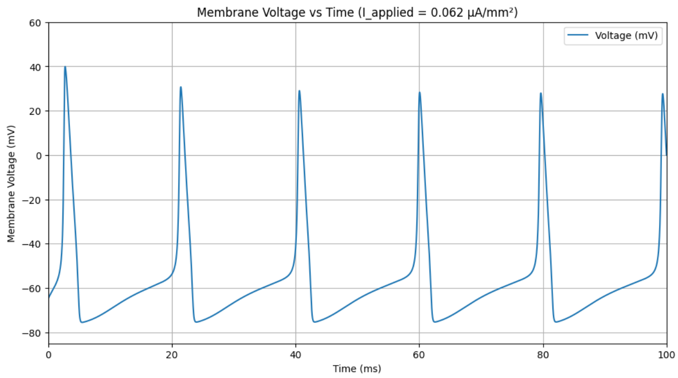


Figure 3.1 (a)

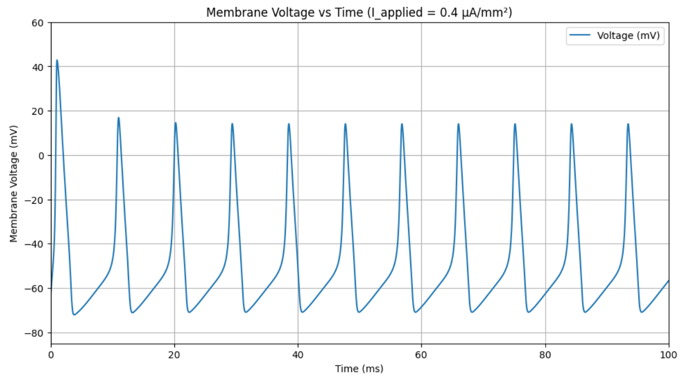


Figure 3.2 (a)

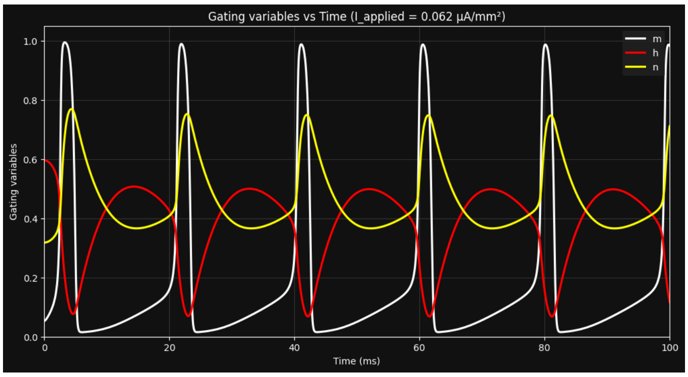
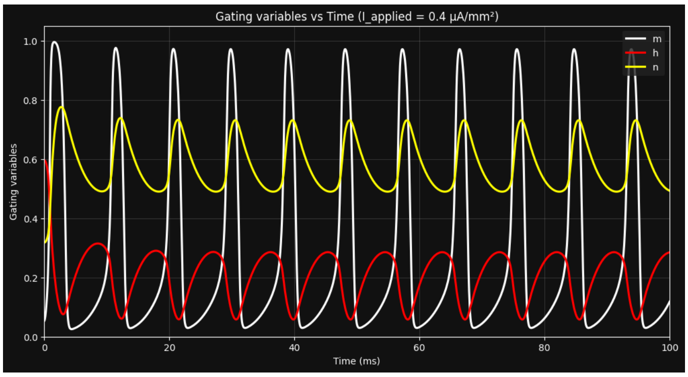


Figure 3.1 (b)



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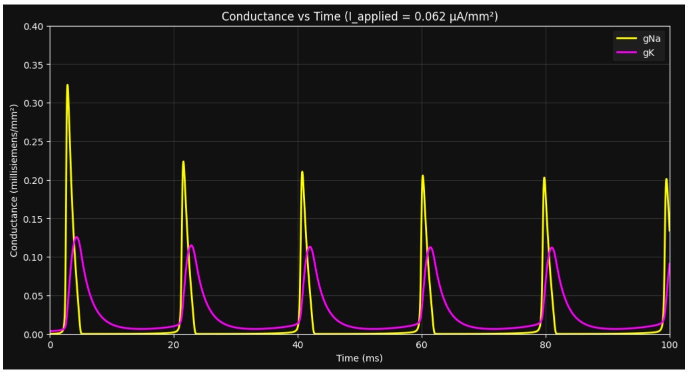

Figure 3.1 (c)

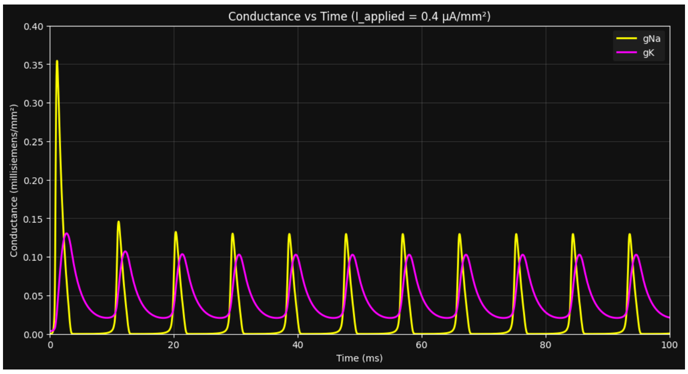

Figure 3.2 (c)

For applied currents between 0.0622 μA/mm^2 and 0.465 μA/mm^2, the system enters the finite action potential regime. In this range, the system displays sustained, regular action potentials.

As the Applied current is increased in this regime 2 phenomena are observed.

1. The frequency of action potential firing increases with applied current, exhibiting a rise similar to that of a square root function, i.e., $f \propto \sqrt{I_{\text{applied}}}$.
2. The peak voltage of each action potential decreases as the applied current is increased (As observed between Figure 3.1 (a) and Figure 3.2 (a)).

4. Deformed Spikes (No Action Potential) Regime

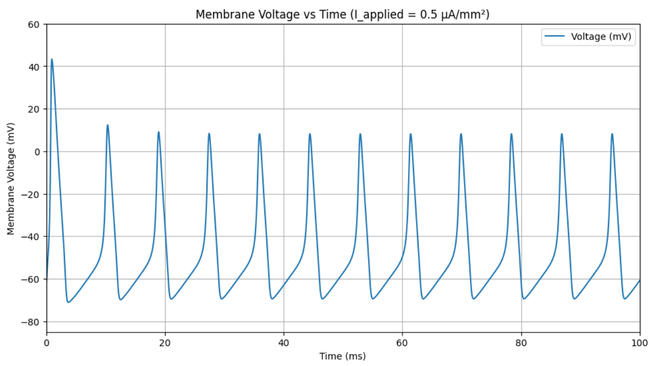

Figure 4.1 (a)

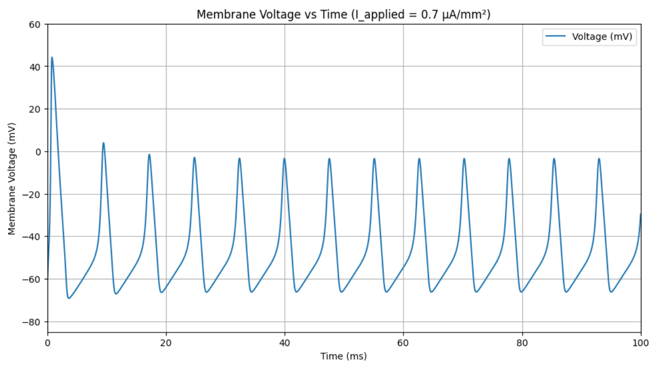

Figure 4.2 (a)

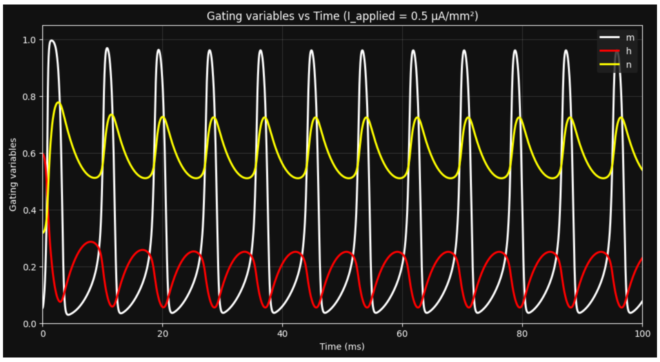

Figure 4.1 (b)

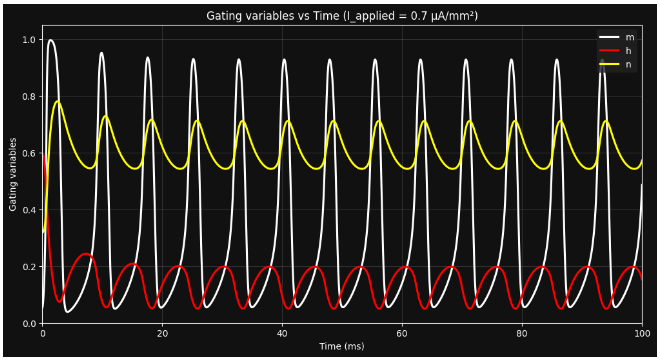

Figure 4.2 (b)

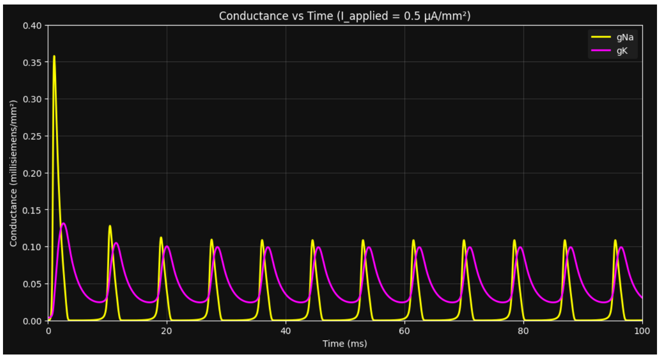

Figure 4.1 (c)

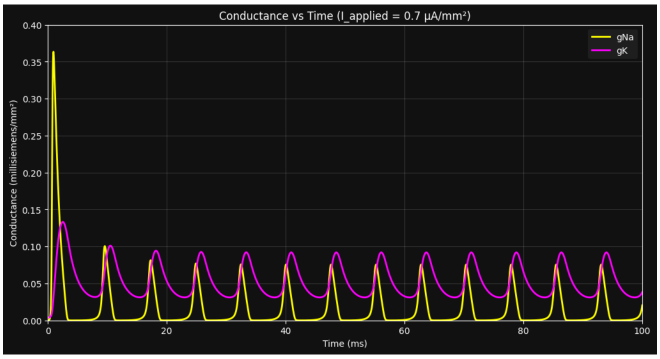

Figure 4.2 (c)

In this regime, an initial action potential is observed, followed by a series of distorted voltage spikes whose maximum amplitude falls below the action potential threshold of 10 mV for all applied currents greater than 0.465 μA/mm^2. As the applied current increases, these voltage spikes become increasingly distorted.

Regime	**Current Range (μA/mm^2)**
No Action Potential	$I_{applied} \leq 0.0222$
Finite Number of APs	$0.0223 \leq I_{applied} \leq 0.0617$
Continuous Firing (Periodic)	$0.0618 \leq I_{applied} \leq 0.465$
Spike Distortion	$I_{applied} > 0.465$

Table 2: Current ranges and corresponding neuronal behavior

(b) Applied Current vs. Action Potential Firing Rate

The model was used to simulate voltage dynamics over a duration of 1000 ms (1 second) for different applied current inputs. For each applied current value, the total number of voltage spikes with peak amplitudes exceeding 10 mV was counted and plotted, as shown below.

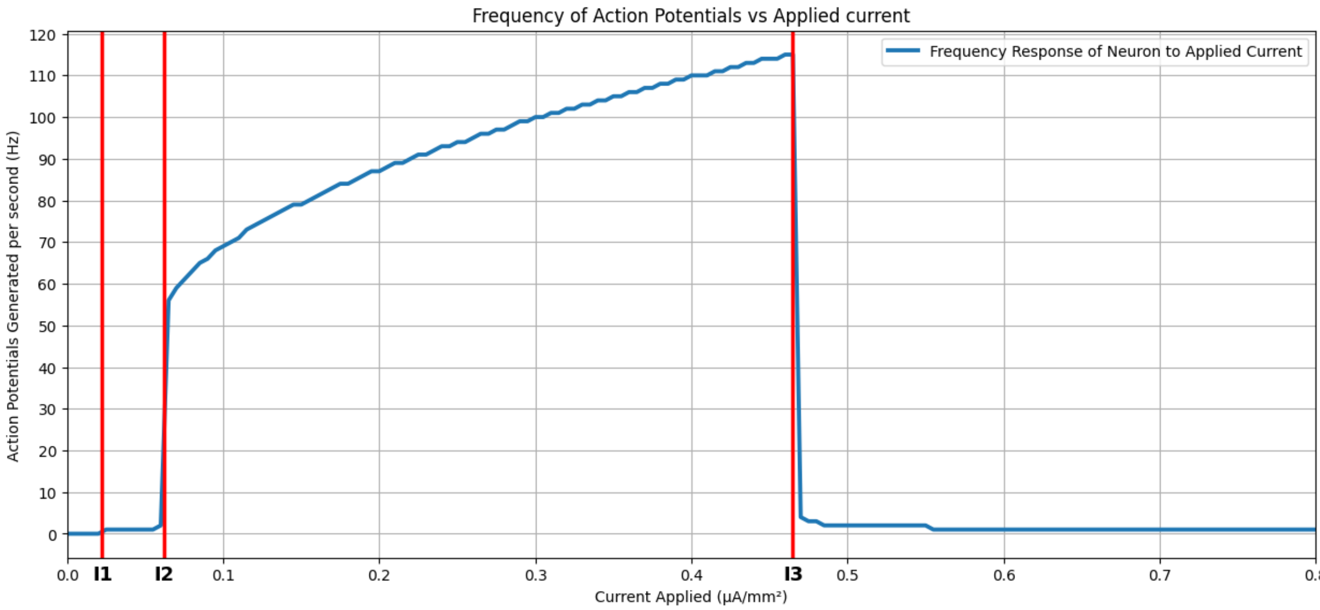

Figure 5 : Action Potential firing rate vs Applied external current

In the above plot:

- $I_1 = 0.0225\ \mu\text{A/mm}^2$. $I_{applied}$ less than I_1 belongs to the no AP regime.
- $I_2 = 0.062\ \mu\text{A/mm}^2$. Between I_1 and I_2 is the finite AP regime.
- $I_3 = 0.465\ \mu\text{A/mm}^2$. Between I_2 and I_3 lies the continuous AP regime.
- Beyond I_3 lies the distorted voltage spiking regime (No APs are observed here).

As stated earlier, in the continuous AP regime where $I_2 \leq I_{\text{applied}} \leq I_3$, the firing frequency increases. It resembles:

$$f \propto \sqrt{I_{\text{applied}}}$$

References

1. Voltage-Gated Sodium and Potassium Ion Channels.
2. Kim DM, Nimigean CM. Voltage-Gated Potassium Channels: A Structural Examination of Selectivity and Gating. *Cold Spring Harb Perspect Biol.* 2016 May. PMCID: PMC4852806.
3. Kang J, Huguenard JR, Prince DA. Voltage-gated potassium channels activated during action potentials. *J Neurophysiol.* 2000 Jan. PMID: 10634854.
4. BT6270 - Computational Neuroscience, course notes and slides.