# Action Potential Generation Simulation using the Hodgkin-Huxley Model

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***Abstract*—This document is a project report, for which an action potential is simulated by using the Hodgkin-Huxley Model in MATLAB. This model is based on the rate constants for ionic channel conductivities determined by Hodgkin and Huxley. In this simulation, for the ordinary differential equations describing the phenomenon, Forward Euler Method is used. User specifies the number of stimulations and delay between them. Moreover, for applied input current, its amplitude and duration are chosen by the user. All the outputs are taken out in a graphical form for a smooth visualization of the data in a certain time interval to observe the effect of the stimulations.**

***Index Terms*—Biomedical engineering, Hodgkin-Huxley Model, action potential, simulation, MATLAB, METU, EE416**

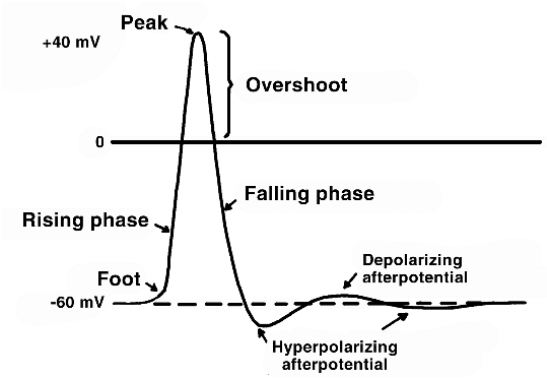


Fig. 1: Action Potential

## I. Introduction

THERE are several types of ion channels in a biological membrane, and naturally ion activity occurs due to trans-membrane voltage. There is a process called action potential across the membrane from a generated electrical pulse. This process starts with membrane depolarization, which is an increase in potential, and it is followed by a recovery to rest conditions. In other words, if a situmulus current is applied, membrane voltage shows a response, thus action potential appears, shown in Figure 1. This behaviour has been experimantally observed thanks to the giant axon of the squid and voltage clamp experiments. Later, Hodgkin and Huxley have authored five papers describing this phenomenon and presenting a model how action potentials can be initiated and propagated through an axon. [2]–[6] In this paper, a brief introduction to squids and voltage clamp experiments in Section II-A, a detailed analysis of the Hodgkin-Huxley model including the mathematical expressions and its explainations in Section II-B are presented. In addition to the explanation of the theory, algorithm for the simulation of the model and the over-all results including several properties of excitable membranes (accommodation, refractory period, temporal summation, etc.) of the simulated model in MATLAB are given in Section II-B2 and Section III, respectively. The main aim of this project is to implement a code to model the excitable membrane of an axon using the Hodgkin-Huxley model and to understand and to visulize the prodecure happening in the membrane better by generating some graphical outputs, which is indeed done in Section III.

## II. Theory

### A. Squids, Voltage and Space Clamp

The voltage clamp is an experimental method introduced by Hodgkin and Huxley to seperate the current components of the membrane, mainly capacitive, sodium and potassium currents. Measurements and experiments are done on the squid axon. The reason why the squid was chosen is that it has the largest nerve axons, up to 1 mm in diameter, whereas human nerve axons are 0.001-0.020 mm in diameter. The main objective of the experiment is to seperate the current into individual ion components since action potential is affected from all kinds of currents together. There is a capacitive current during the action potential, as the structure of the membrane acts like a capacitor. Firstly, to eliminate this current component, membrane voltage is chosen at a certain level, i.e. a voltage step input, which simplifies the analysis. Moreover, Hodgkin and Huxley did not include the chloride contribution directly, it was regarded as a small leakage current. The hardest task was seperating sodium and potassium contributions. Hodgkin and Huxley made a key assumption that the sodium and potassium ion fluxes are independent of each other (asserting the independence principle). [1] It is done by altering the sodium concentration outside the axon and applying voltage clamp at sodium Nernst voltage, which eliminates the flow of sodium ions. By this way, behavior of potassium ions is observed alone. By measuring the membrane current under normal conditions, and subtracting the potassium current from the total current, the sodium current component is obtained.

In addition to voltage clamp, space clamp is used, which is stimulating the axon simultaneously throughout the entire length of the preparation. This is done in order to avoid the currents being a function of space variables.

### *B. The Hodgkin-Huxley Model*

Hodgkin and Huxley's model is based on the experiment explained in Section II-A. The model is created not from the exact equations but from the insight of the theory and mathematical fitting of the data obtained from the experiments. For voltage clamp experiment, only variable is time and capacitive current is zero due to the unchanged voltage. Although the sodium and potassium conductances are evaluated at a fixed voltage with voltage clamp experiment, their values differ in different voltages. Thus, the membrane conductance for sodium and potassium are functions of transmembrane voltage and time. However, the leakage conductance is constant, whose magnitude is small most of the time compared to conductances of sodium and potassium.

Equivalent circuit schematics for the Hodgkin-Huxley model is shown in Figure 2 and the expression for the total transmembrane current density is given in Equation 1.

$$I_{\mathrm{m}} = C_{\mathrm{m}}\frac{dV_{\mathrm{m}}}{dt} + (V_m - E_{\mathrm{Na}})\, g_{\mathrm{Na}} + (V_m - E_{\mathrm{K}})\, g_{\mathrm{K}} + (V_m - E_{\mathrm{L}})\, g_{\mathrm{L}} \tag{1}$$

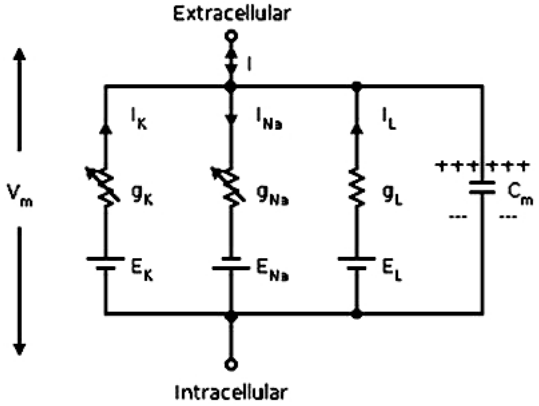


Fig. 2: Equivalent Circuit Schematics for the Hodgkin-Huxley Model

#### *1) Hodgkin-Huxley Conductance Equations:*

i) Mathematical Model for Potassium
Conductance for potassium can be given Equation 2 and derived from either Equation 1 or Figure 2.

$$g_{\mathrm{K}}(t) = \frac{I_{\mathrm{K}}(t)}{(V_m - E_{\mathrm{K}})} \tag{2}$$

Hodgkin and Huxley assigned the fourth power to $n$ in Equation 3 since it was the best fit to potassium ion data, it was interpreted as the probability of finding any four of the particles in the open state. [1]

$$g_{\mathrm{K}} = \bar{g}_{\mathrm{K}} n^4 \tag{3}$$

For finding $n$ from Equation 4, the rate constants for $n$, $\alpha_n$ and $\beta_n$, which are called constants as they are constants at each voltage clamp experiment while they are actually functions of $v_m$, should be determined. From the collected data set for $\alpha_n$ and $\beta_n$, Hodgkin and Huxley chose the analytical functions in Equations 5 and 6.

$$\frac{dn\,(t, v_m)}{dt} = \alpha_n\,(v_m)\,(1 - n) - \beta_n\,(v_m)\,n \tag{4}$$

where

$$\alpha_n = \frac{0.01\,(10 - v_m)}{\left[\exp\left(\frac{10 - v_m}{10}\right) - 1\right]} \tag{5}$$

$$\beta_n = 0.125 \exp\left(\frac{-v_m}{80}\right) \tag{6}$$

ii) Mathematical Model for Sodium
Conductance for sodium can be given Equation 7 and derived from either Equation 1 or Figure 2.

$$g_{\mathrm{Na}}(t) = \frac{I_{\mathrm{Na}}(t)}{(V_m - E_{\mathrm{Na}})} \tag{7}$$

Hodgkin and Huxley assigned product of two variables $m$ and $h$ to sodium conductance in Equation 8, where $m$ was the activation parameter and $h$ was the inactivation parameter. $m^3h$ can interpreted as the probability that a sodium channel is open. [1]

$$g_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}} m^3 h \tag{8}$$

Similarly, for finding $m$ and $h$ from Equations 9 and 10, the rate constants $\alpha_m$, $\beta_m$, $\alpha_h$, and $\beta_h$ should be determined. Hodgkin and Huxley chose the analytical functions in Equations 11, 12, 13, and 14.

$$\frac{dm}{dt} = \alpha_m(1 - m) - \beta_m m \tag{9}$$

$$\frac{dh}{dt} = \alpha_h(1 - h) - \beta_h h \tag{10}$$

where

$$\alpha_{\mathrm{m}} = \frac{0.1\,(25 - v_{\mathrm{m}})}{\exp\left[0.1\,(25 - v_{\mathrm{m}}))\right] - 1} \tag{11}$$

$$\beta_{\mathrm{m}} = 4 \exp\left(-\frac{v_{\mathrm{m}}}{18}\right) \tag{12}$$

$$\alpha_h = 0.07 \exp\left(-\frac{v_{\mathrm{m}}}{20}\right) \tag{13}$$

$$\beta_{\mathrm{h}} = \left\{\exp\left[\frac{(30 - v_{\mathrm{m}})}{10}\right] + 1\right\}^{-1} \tag{14}$$

iii) Leakage Current
By knowing that there are other currents apart from the sodium and potassium currents, the Hodgkin-Huxley model introduces the leakage current, which is given in Equation 15.

$$I_L = g_L\,(V_m - E_L) \tag{15}$$

*2) Simulation of Membrane Action Potentials:* Since all the equations describing each ionic current is developed for any voltage clamp experiment, a model of the behaviour of the membrane can be constructed. This is true because by fitting the data for all the voltage clamp experiments done, we can simulate at any voltage clamp experiment. Thus, the equations respond for naturally changing voltage values. Since differential equations cannot be solved exactly, numerical methods should be followed. Forward Euler Method is one of the methods which can be used, and the suggested algorithm, given in Step ii, is based on this method. [8]

i) Sum of Currents

$$I_m = I_{\mathrm{K}} + I_{\mathrm{Na}} + I_L + I_C \tag{16}$$

ii) Algorithm for Advancing throuh Time

- Determine $I_m$

$$\begin{aligned} I_m &= 0 && t < t_0 \\ I_m &= I_s && t_0 \leq t < t_0 + T \\ I_m &= 0 && t_0 + T \leq t \leq t_1 \\ I_m &= I_s && t_1 \leq t < t_1 + T \\ I_m &= 0 && t_1 + T \leq t \leq \infty \end{aligned} \tag{17}$$

- Estimate $\Delta V_m$

$$\begin{aligned} \Delta V_m^i &= \frac{\Delta t}{C_m}\left[I_m^i - I_{\mathrm{ion}}^i\right] \\ &= \frac{\Delta t}{C_m}\left[I_m^i - I_{\mathrm{K}}^i - I_{\mathrm{Na}}^i - I_L^i\right] \end{aligned} \tag{18}$$

$$\begin{aligned} I_{\mathrm{K}}^i &= g_{\mathrm{K}}^i\left(V_m^i - E_{\mathrm{K}}\right) \\ I_{\mathrm{Na}}^i &= g_{\mathrm{Na}}^i\left(V_m^i - E_{\mathrm{Na}}\right) \\ I_L^i &= g_L\left(V_m^i - E_L\right) \end{aligned} \tag{19}$$

$$\begin{aligned} g_{\mathrm{K}}^i &= \bar{g}_{\mathrm{K}}^i n_i^4 \\ g_{\mathrm{Na}}^i &= \bar{g}_{\mathrm{Na}}^i m_i^3 h_i \end{aligned} \tag{20}$$

- Estimate $\Delta n$, $\Delta m$, and $\Delta h$

$$\Delta n^i = \Delta t\left[\alpha_n^i\left(1 - n_i\right) - \beta_n^i n_i\right] \tag{21}$$

$$\Delta m^i = \Delta t\left[\alpha_m^i\left(1 - m_i\right) - \beta_m^i m_i\right] \tag{22}$$

$$\Delta h^i = \Delta t\left[\alpha_h^i\left(1 - h_i\right) - \beta_h^i h_i\right] \tag{23}$$

- Advance to the next time

$$\begin{aligned} V_m^{i+1} &= V_m^i + \Delta V_m^i \\ n^{i+1} &= n^i + \Delta n^i \\ m^{i+1} &= m^i + \Delta m^i \\ h^{i+1} &= h^i + \Delta h^i \end{aligned} \tag{24}$$

## III. Results

There are some basic concepts associated with the activation process of the membrane. Activation is very relevant with the duration and strength of the stimulus. Threshold, which will be explained later, can be reached by not only a strong stimulus but also weaker but longer stimuli. Sometimes, it is shown with a curve in strength-duration domain. All of the properties of the excitable membranes must be satisfied by the Hodgkin-Huxley Model, thus the simulation written in MATLAB must give correct visual outputs for each property of the excitable membrane. Before trying whether these properties are satisfied by the model or not, a general view for the output can be given in Figures 3 and 4.

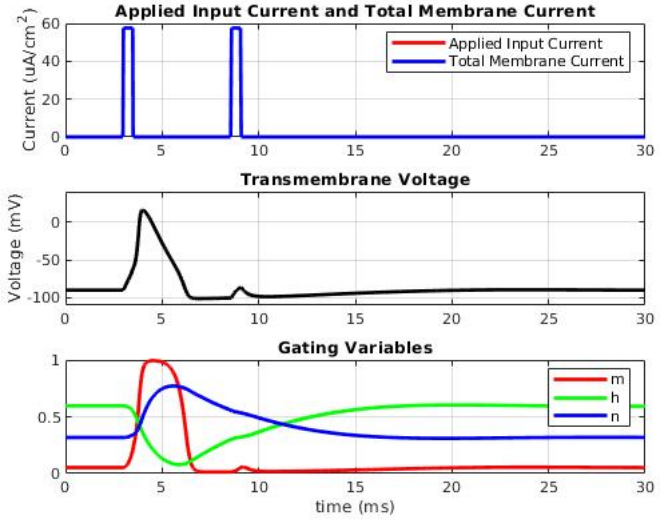


Fig. 3: Membrane Action Potential Using the Hodgkin-Huxley Equations

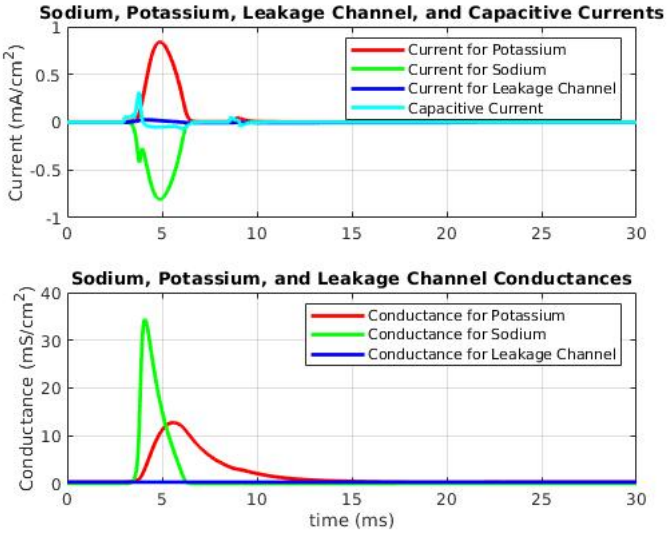


Fig. 4: Sodium, Potassium, and Leakage Conductances, and Corresponding Currents

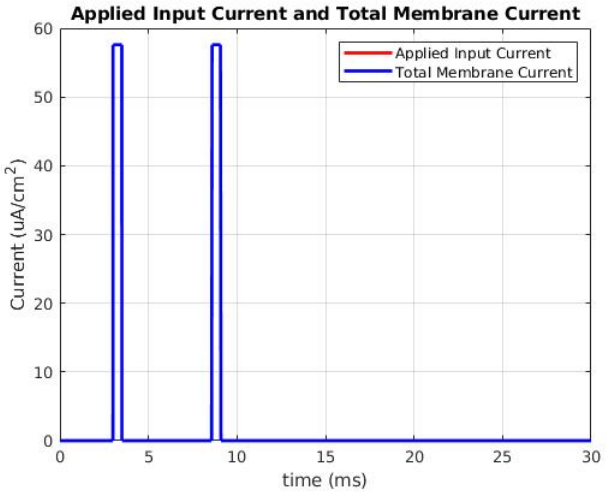


Fig. 5: Applied Input Current and Total Membrane Current

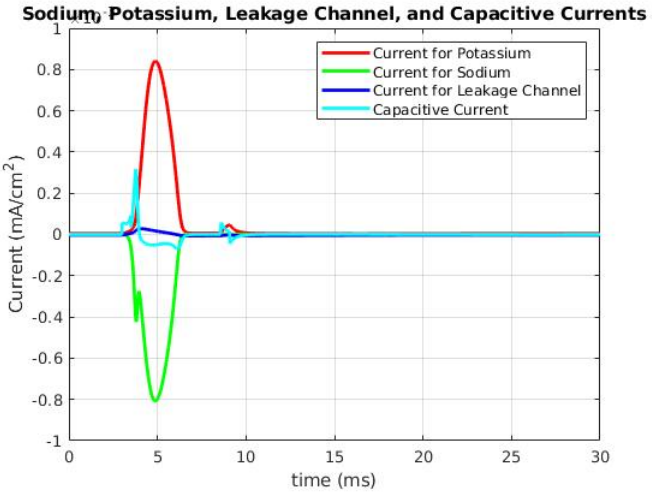


Fig. 8: Sodium, Potassium, Leakage Channel, and Capacitive Currents

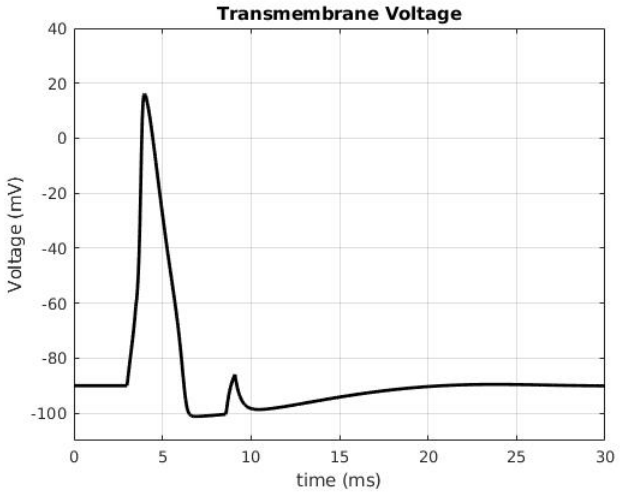


Fig. 6: Transmembrane Voltage

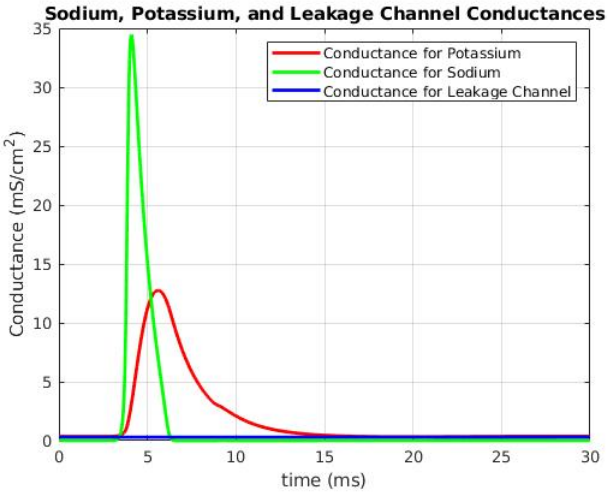


Fig. 9: Sodium, Potassium, and Leakage Channel Conductances

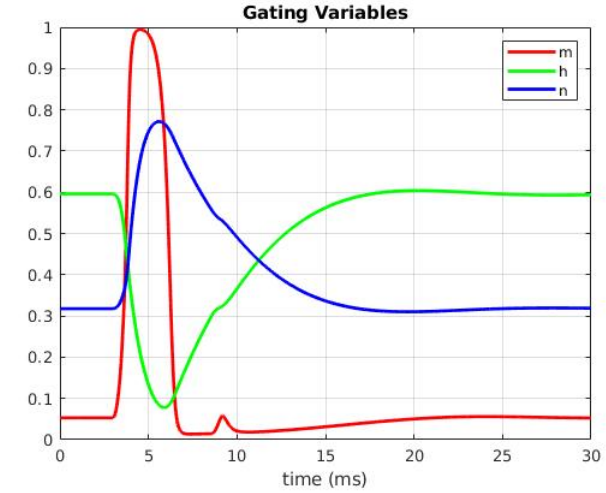


Fig. 7: Gating Variables

For a better visualization, all five plots are given seperately, in Figures 5, 6, 7, 8, and 9.

### A. Qualitative Description of AP Generation

*Sodium*

A current originates, thus the potential inside the membrane increases before the sodium conductance. In this stage, total membrane current is mainly capacitive, since conductances of the sodium and potassium are low. When the membrane depolarizes, i.e. voltage increases $m$ increases. Hence, sodium conductance increases, which allows sodium ions to go into the cell. The cell potential increases.
$\rightarrow$ $m$ increases, $g_{\mathrm{Na}}$ increases.
Effect of $h$ ends this process, with $h$ decrasing.
$\rightarrow$ $h$ decreases, $g_{\mathrm{Na}}$ decreases.

*Potassium*

Because of the initial depolarization, $n$ rises with some time constant, meaning it takes a time to reach the maximum. Thus, $g_{\mathrm{K}}$ starts to be prominent when $g_{\mathrm{Na}}$ is decaying. Increase in $g_{\mathrm{K}}$ causes potassium to go out of the cell, which leads the potential to decrease. Voltage at the peak occurs when the flow of both ions are equal to each other. At this moment, the capacitive current will be zero instantly. The transmembrane voltage will decrease as $g_{\mathrm{Na}}$ decreases and $g_{\mathrm{K}}$ increases. As the voltage decreases, $n$ will decrease, which causes $g_{\mathrm{K}}$ to go down. When the conductances reach their resting value, the membrane voltage reaches its resting voltage.

### B. Action Potential Characteristics

The properties of the excitable membranes can be listed as follows:

1) *Threshold*
2) *Accommodation*
3) *Latency*
4) *Refractory Period*
5) *Temporal Summation*
6) *Pulse Frequency Modulation*
7) *Anode-Break Excitation*

Each will be defined and tested with the model constructed.

*1) Threshold:* the critical voltage to which a membrane potential must be depolarized to initiate an action potential.

As seen in Figure 10, the stimulus given is not enough to initiate an action potential. To initiate an action potential either the strength or the duration of the stimulus should be increased.

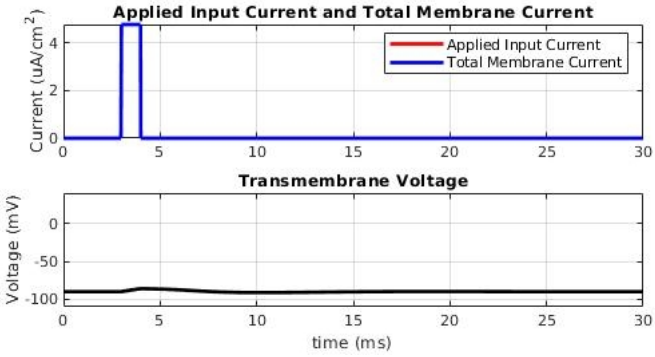


Fig. 10: Threshold

*2) Accommodation:* the adaptation to a continuing or repetitive stimulus, which is characterized by a rise in the excitation threshold.

As seen in Figure 11, the stimulus given is a continuing stimulus. Accomodation can be observed from the second action potential.

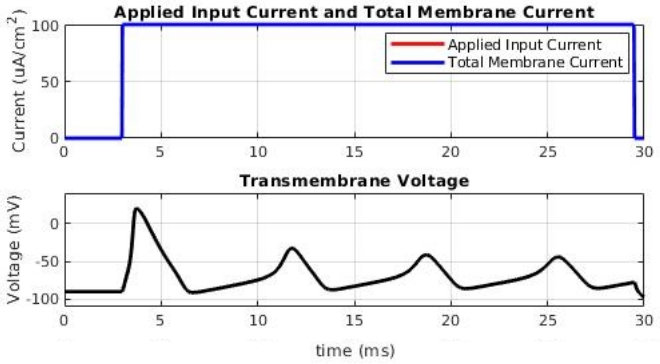


Fig. 11: Accomodation

*3) Latency:* the time between applied input pulse and the beginning of the activation.

As seen in Figure 12, there is a time difference between the applied input signals and the beginnig of the action potential, it is called latency.

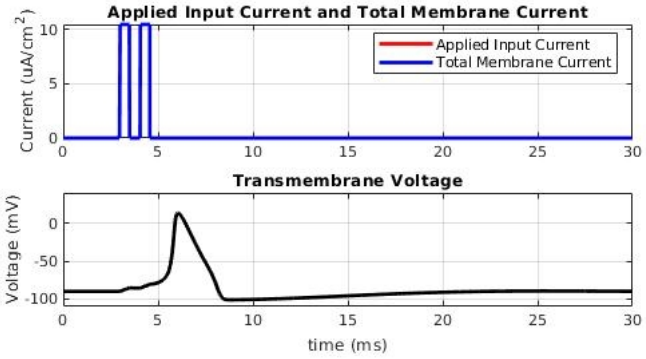


Fig. 12: Latency

*4) Refractory Period:* the time when membrane is insensitive to new stimuli. There are 2 different refractory periods.
*The absolute refractory period:* Once activation has been initiated, the membrane is insensitive to new stimuli, no matter how large the magnitude.
*The relative refractory period:* Near the end of the activation impulse, the cell may be activated, but only with a stimulus stronger than normal. [1]

As seen in Figure 13, even if the inputs are the same, which means it is enough to initiate an action potential, second stimulus does not initiate due to the refractory period.

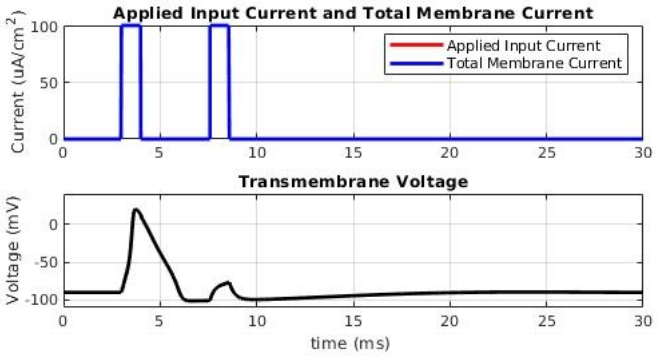


Fig. 13: Refractory Period

*5) Temporal Summation:* the situation where the second stimulus can start an AP whereas the first stimulus could not initiate an AP, and there is not much delay between them, which occurs since the effect of the first stimulus has not vanished. As seen in Figure 14, the first stimulus could not initiate an AP, however in Figure 15, the second stimulus starts an AP.

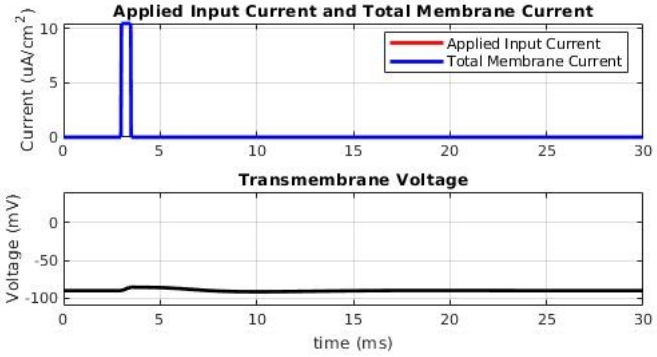


Fig. 14: Temporal Summation

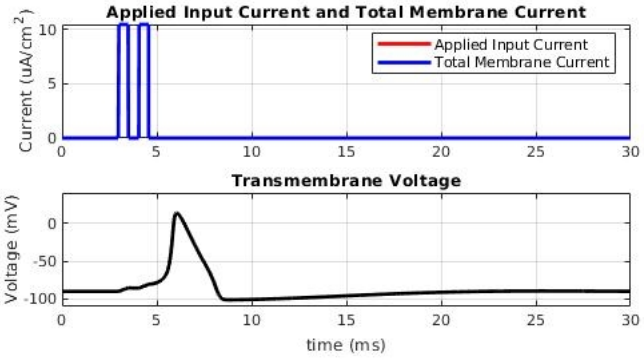


Fig. 15: Temporal Summation

*6) Pulse Frequency Modulation:* the situation where a step current is applied, whose magnitude is larger than rheobase current, a continuous series of action potentials are generated, which can be seen in Figure 16.

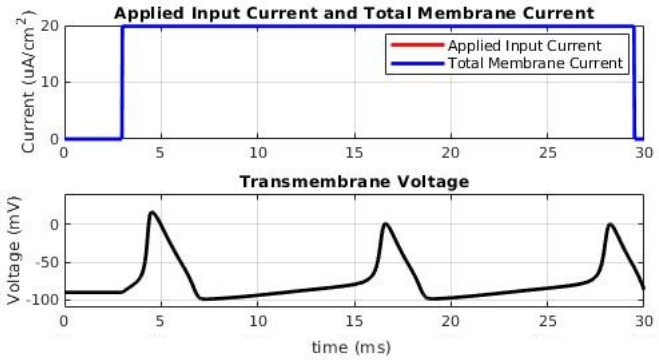


Fig. 16: Pulse Frequency Modulation

*7) Anode-Break Excitation:* the situation where a negative current pulse of long duration (or large magnitude) is applied, and one or more APs may appear, seen in Figure 17.

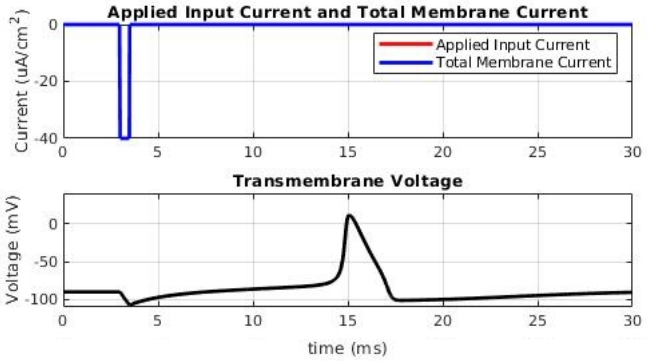


Fig. 17: Anode-Break Excitation

## IV. Graphical User Interface

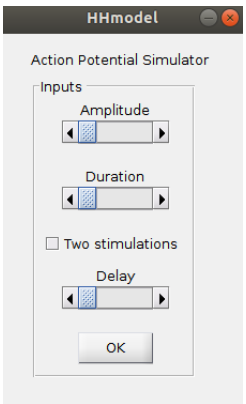


Fig. 18: GUI

## V. Discussion and Conclusion

This project does not only give an insight about what happens when the neurons are communicating with each other but also gives a deep understanding about the model mathematically. It is very fascinating to see such a complex behaviour like this can be expressed and modelled with so few equations. To think all is possible thanks to squids and clever people who can set up a hard experiment as such, which in this case Hodgkin and Huxley, is influential. What is done is that an idea is constructed by using voltage and space clamp techniques and then controllable experiments are conducted with giant axon of the squid. Theory is builded and on top of that mathematical functions are found to approximate the data set experimented on. All of this phenomenon is qualitatively described by using these mathematical functions.

In conclusion, for this project, explanations of the Hodgkin-Huxley Model are made by providing examples, figures and equations. The importance of the experiment is emphasized. A software implementation is prepared in MATLAB, and simulation of the behaviour of the membrane is done. Simulation results were given in graphical form for easy interpretation of the model, and explained detailly. Moreover, the code was tested in many situation where action potential characteristics are observable, such as accommodation, latency, refractory period, etc. In addition to implementation, although its usage is relatively easy, a basic GUI is created. MATLAB code and GUI can be found in Appendix A.

## Appendix A
### Associated MATLAB code

Click here.

## References

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