,

Birla Institute of Technology and Science Pilani, Goa

Simulating the Hodgkin-Huxley Model: A Ball-and-Stick Approach to Neural Dynamics

Mihir Thalanki
Kunal Avalakki
Jathin Narayan
Ananth Vishnubhotla
Armaan Chowfin
Vishnu Teja Soorea

Computational Neuroscience - CSF433
Date: **Jan - June 2023**

Introduction

The Hodgkin Huxley paper published in 1952 altered the course of neuroscience as a science, shedding new light on the dynamic characteristics of neurons subject to various conditions. The model mentioned in the paper is a mathematical model that tries to explain how neurons generate and transmit action potentials. It is based on the concept of ion channels and explains how ion channels in the neuron membrane open and close in response to changes in membrane potential, allowing ions to flow through, resulting in the propagation of an action potential.

One way to visualize this model is through the use of a ball and stick model, which represents the electrical properties of different components of the neuron, such as the soma and dendrite. Our study demonstrates the usefulness of this blueprint model in understanding the complex behavior of neurons, and provide a valuable tool for investigating the dynamics of neuronal circuits.

Through this paper, we aim to further understand the properties of neurons through experimental procedures, using the NEURON module in tandem with python code to efficiently simulate neuronal circuits and visualize the resulting graphs.

0.1 Hodgkin Huxley Model

The Hodgkin Huxley uses four differential equations, namely -

- Current per unit Area equation
- Sodium channel activation gate equation
- Sodium channel inactivation gate equation Potassium channel activation gate equation

The Hodgkin-Huxley model is important in understanding the electrical properties of neurons and how they function. It has also been used as a foundation for complex models of neuronal activity, such as the integrate-and-fire model.

In this paper, we present a ball-and-stick model of the neuron that was

created by integrating NEURON library with Python. Using this model, we simulated the experiment conducted by Hodgkin and Huxley and recreated selected figures from the paper - *A Quantitative Description Of Membrane Current And Its Application To Conduction And Excitation In Nerve*

0.2 Ball-and-stick model

The ball-and-stick model is a simplified representation of a neuron that consists of a spherical soma (or cell body) and a cylindrical axon. In this paradigm, the dendrites act as input currents that the soma receives, rather than being explicitly depicted. The model can be used to comprehend the fundamental electrical characteristics of neurons, such as how they produce and spread action potentials.

The Hodgkin and Huxley model is a more detailed model of the neuron compared to the ball-and-stick model, as it includes a comprehensive representation of the ion channels in the neuronal membrane. However, the ball-and-stick model can still be used to simulate the Hodgkin and Huxley model. To demonstrate this, we collected experimental data from the ball-and-stick simulations and compared this with the theoretical data generated by the hodgkin huxley model.

The soma is modelled as a spherical capacitor in the ball-and-stick model, with a capacitance Cm that corresponds to the soma's membrane capacitance. The axon is modelled as a cylindrical resistor with a capacitance Cm representing the axon membrane and a resistance Rm representing the resistance of the axoplasm. Ra, which stands for the resistance of the cytoplasmic link between the soma and the axon, connects the axon to the soma. A current source Ie is used to model the input current to the soma.

Numerous neural phenomena, such as action potential generation and propagation, synaptic integration, and dendritic processing have all been studied using the ball-and-stick model. It can be expanded to more complicated models that integrate dendritic architecture and other characteristics of actual neurons. It is a valuable tool for learning the fundamental concepts of neural computation.

The Hodgkin and Huxley model is a more detailed model of the neuron compared to the ball-and-stick model, as it includes a detailed representation

of the ion channels in the neuronal membrane. However, the ball-and-stick model can still be used to simulate the Hodgkin and Huxley model by incorporating the Hodgkin and Huxley equations for the membrane currents and gating variables into the model equations for the ball-and-stick model.

To accomplish this, we would need to add the Hodgkin and Huxley equations for the membrane currents and gating variables to the model equations for the ball-and-stick model. This would include expanding the model to include more variables to represent the sodium and potassium channel gating variables as well as more equations to calculate the membrane currents based on the values of these gating variables.

One method of incorporating the Hodgkin and Huxley equations into the ball-and-stick model is to describe the propagation of the membrane potential along the axon using the cable equation, and then solve the Hodgkin and Huxley equations to determine the membrane currents and gating variables at each point along the axon. The Hodgkin and Huxley equations would need to be numerically solved in order to use this method at every location along the axon, which can be costly in terms of calculation time.

A different strategy is to utilise a condensed version of the Hodgkin and Huxley equations that only incorporates a portion of the ion channels, including the sodium and potassium channels, and then approximation the rest currents using more basic equations or empirical data. Using this method, a more compact ball-and-stick model that is computationally more effective and captures the key elements of the Hodgkin and Huxley model can be created.

1 Analyzing Gating Variables trends

In the Hodgkin Huxley model, gating variables are the variables that represent the opening and closing of ion channels in the neuronal membrane. They represent the degree of opening of a certain ion channel. The three gating variables that we are dealing with are - n, m and h.The combined action of m and h controls the Na+ channels while the K+ gates are controlled by n. In this paper, we plot all 3 of these gating variables over varying values of voltage to analyze Hodgkin-Huxley's results.

1.1 Potassium Channel

The gating variable n describes the activation kinetics of the voltage-gated potassium channels. Hodgkin Huxley could describe this behavior using an exponential equation:

$\mathrm{n}_\infty = \sqrt[4]{g_K}_\infty \,/\, \bar{\mathrm{g}}_K$
$\alpha_n = 0.01\,(V + 10) \,/\, [\,exp\,((V + 10) \,/\, 10) \;-\; 1]$
$\beta_n = 0.125\,exp\,(V \,/\, 80)$

The curve was obtained from the equation and is seen as an S-shaped sigmoidal shape.

Voltage Clamp recording was obtained from the ball and stick model with parameters from Table 1 of Hodgkin and Huxley, 1952. This was then overlapped on the curve. It can be seen that the experimental values coincide with the theoretical data

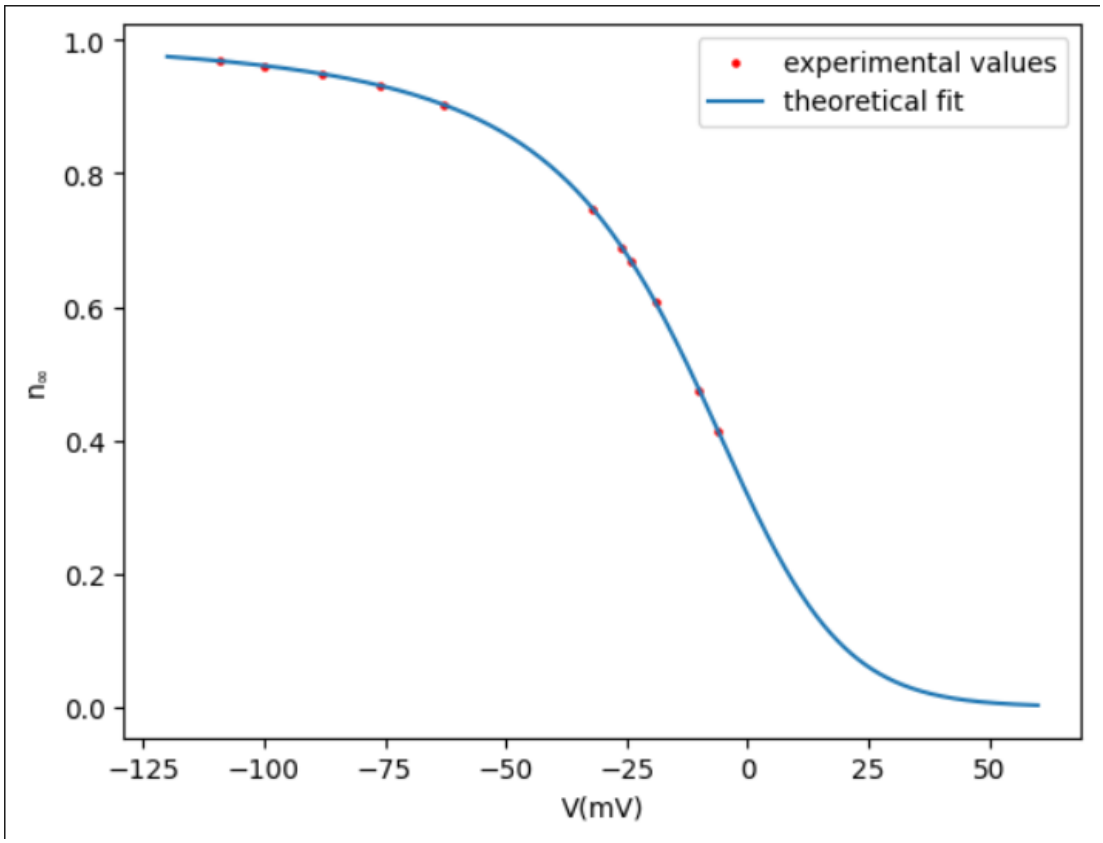

Figure 1.1: Plot of gating variable n at steady Potassium conductance in accordance to membrane potential

1.2 Sodium Channel

Using the same experimental setup as before, we can analyze Hodgkin-Huxley's results for the sodium gating variable.
$m_\infty = \alpha_m \,/\, (\alpha_m + \beta_m)$
$\alpha_m = 0.1\,(V + 25) \,/\, [\, exp\,((V + 25) \,/\, 10) \;-\; 1]$
$\beta_m = 4\, exp\,(V \,/\, 18)$

A similar S-shaped sigmoidal shape is obtained for gating variable m. On overlapping the voltage clamp recorded data, we can see that the Hodgkin-Huxley results coincide with the experimental data.

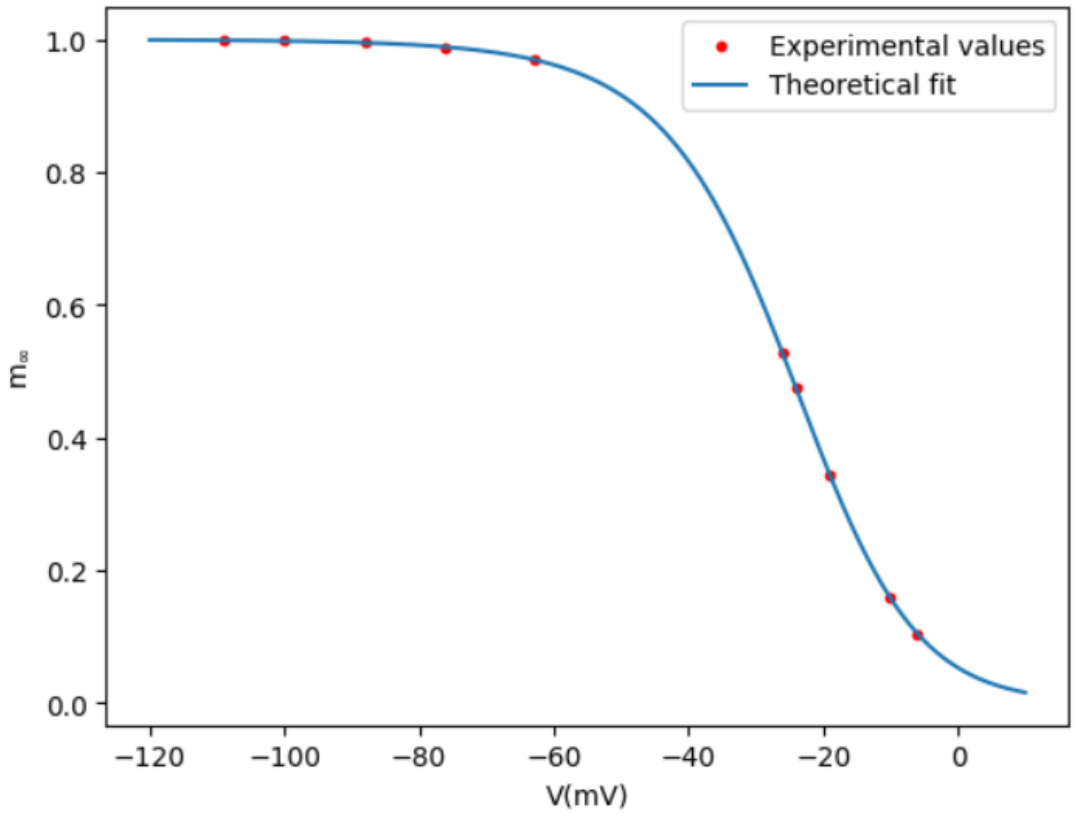

Figure 1.2: Plot of gating variable m at steady Sodium conductance in accordance to membrane potential

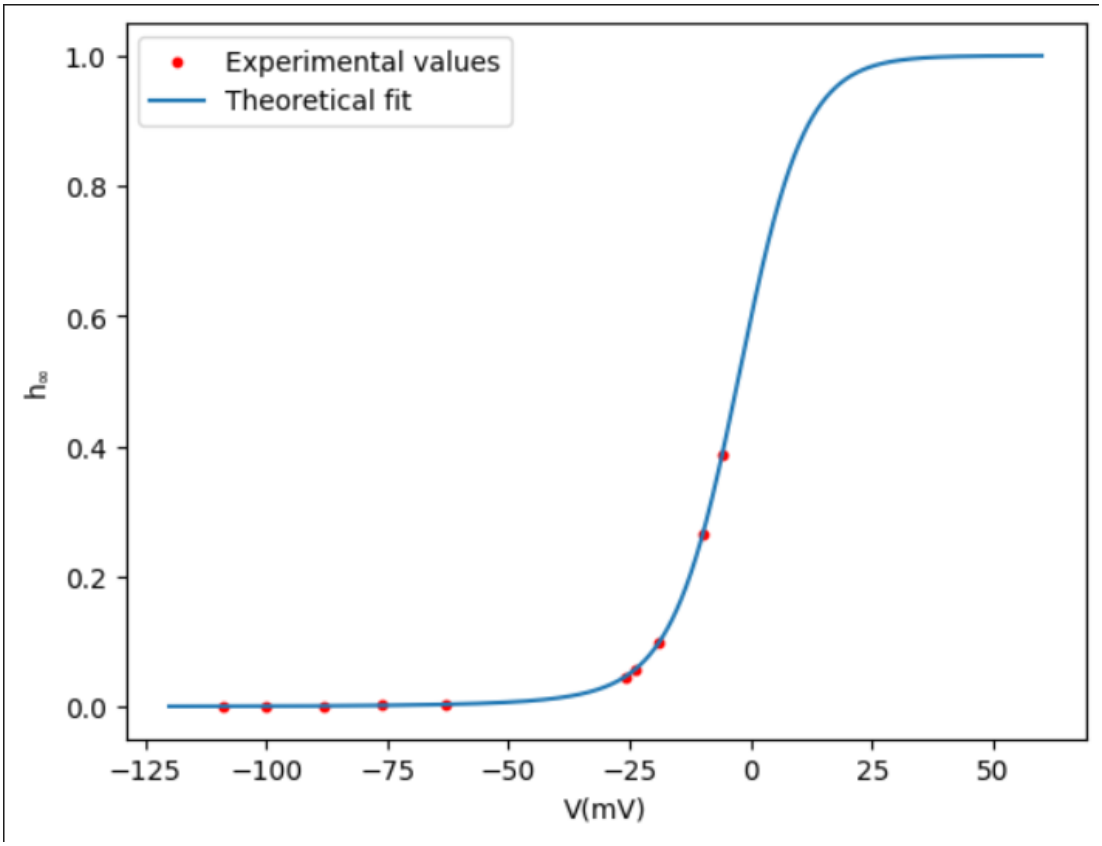

Figure 1.3: Steady state relation between h and V

2 Exploring the relationship between rate constants and membrane potential

2.1 Potassium conductance

The equations used to describe potassium conductance are:

$$g_K = g_K n^4$$

$$dn \,/\, dt = \alpha_n(1 - n) \; - \; \beta_n n$$

where $\bar{g}_K$ is a constant with the dimensions of $conductance/cm^2$, α_n and β_n are rate constants which vary with voltage and have dimension of $time^{-1}$. α_n determines transfer rate from outside to inside and β_n determines transfer rate in the opposite direction.

To understand the relationship between membrane potential and the rate constants α_n and β_n, we plotted the following graph using these equations:

$$\alpha_n = 0.01 \, (V + 10) \,/\, [\, exp \, ((V + 10) \,/\, 10) \; - \; 1]$$

$$\beta_n = 0.125 \, exp \, (V \,/\, 80)$$

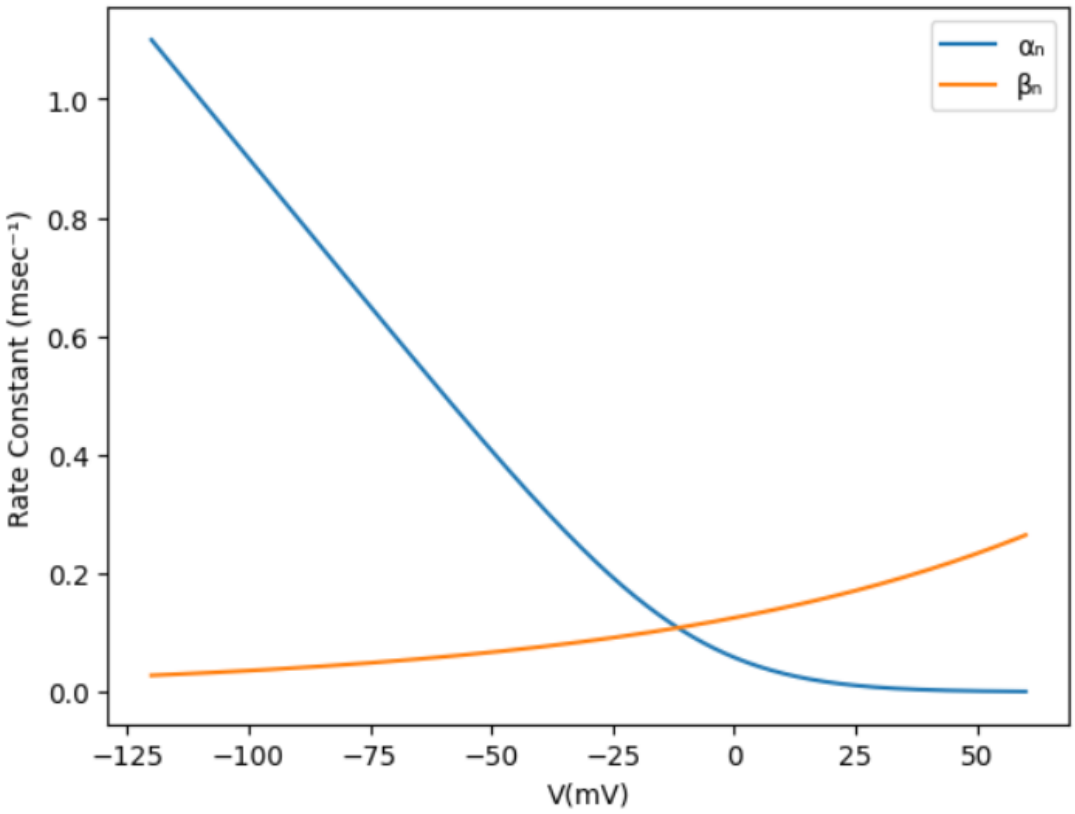

Figure 2.1: Rate constants determining rise or fall of potassium conductance at 6°C vs membrane potential

2.2 Sodium conductance

Out of the possible methods to describe transient changes in sodium conductance, we utlised the one that is determined by two variables each of which obeys a first-order equation. The equation used to describe sodium conductance is:

$$g_{Na} = m^3 h g_{Na}$$

and the 2 first-order equations are:

$$dm \,/\, dt = \alpha_m \,(1 \,-\, m) \,-\, \beta_m m$$

$$dh \,/\, dt = \alpha_h \,(1 \,-\, h) \,-\, \beta_h$$

where g_{Na} is a constant and α's and β's are functions of V but not of t.

The relationship between the rate constants α_m and β_m and membrane potential is determined by the following equations and produces the following graph:

$$\alpha_m = 0.1\,(V + 25)\,/\,[\,exp\,((V + 25)\,/\,10)\;-\;1]$$

$$\beta_m = 4\,exp\,(V\,/\,18)$$

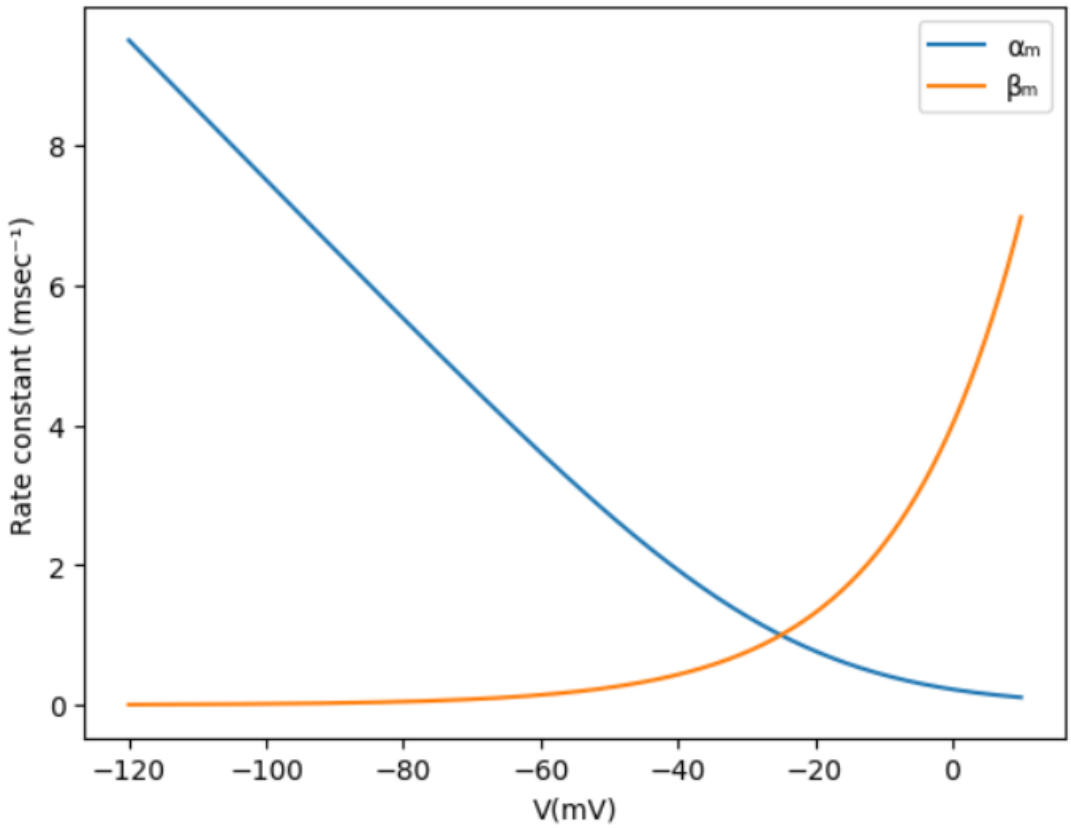

Figure 2.2: Plot of rate constants determining initial changes in sodium conductance at 6°C vs membrane potential

Similarly, the relationship between the rate constants α_h and β_h and membrane potential is determined by:

$$\alpha_h = 0.07\,exp\,(V\,/\,20)$$

$$\beta_h = 1 \,/\, (exp\,((V \,+\, 30) \,/\, 10) \,+\, 1)$$

and produces the following graph:

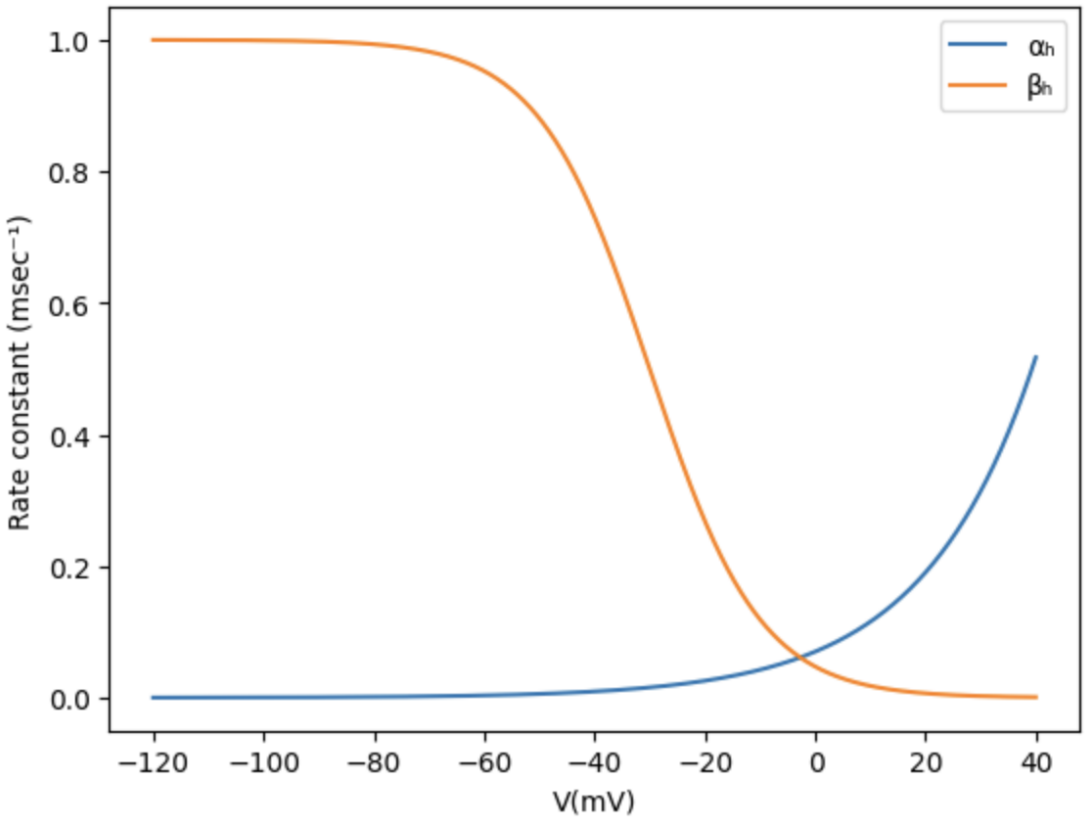

Figure 2.3: Rate constants of inactivation as functions of membrane potential

3 Exploring the relationship between conductance and voltage

3.1 Potassium Conductance G_k

The neuron model presented was subjected to a voltage clamp. The figure below was created using the parameters presented in Table 1 of Hodgkin and Huxley, 1952. We varied the voltages using values from column 1 and the results corresponded with the graph presented in the paper (Fig. 3 of Hodgkin and Huxley, 1952).

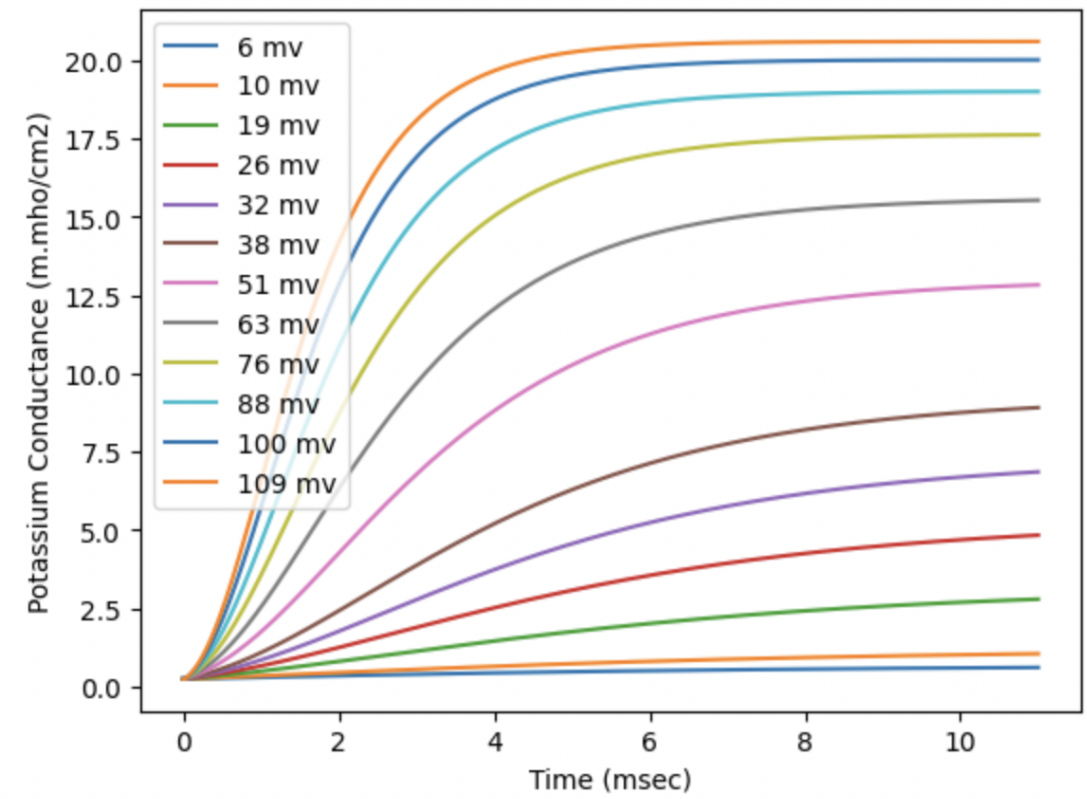

Figure 3.1: Rise of Potassium conductance associated with decreasing depolarizations

3.2 Sodium Conductance G_{Na}

The experiment setup was similar as above. We recorded the Sodium conductance trends for different values of V and got the following results. We also plotted the sodium conductance trends calculated by the hodgkin huxley formulas:

1. $g_{Na} = m^3 h \bar{g}_{Na}$
2. $dm \,/\, dt = \alpha_m \,(1 \,-\, m) - \beta_m m$
3. $g_{Na} = g'_{Na}\,[1 \,-\, exp(-t/\tau_m)]^3\, exp\,(-t/\tau_h)$

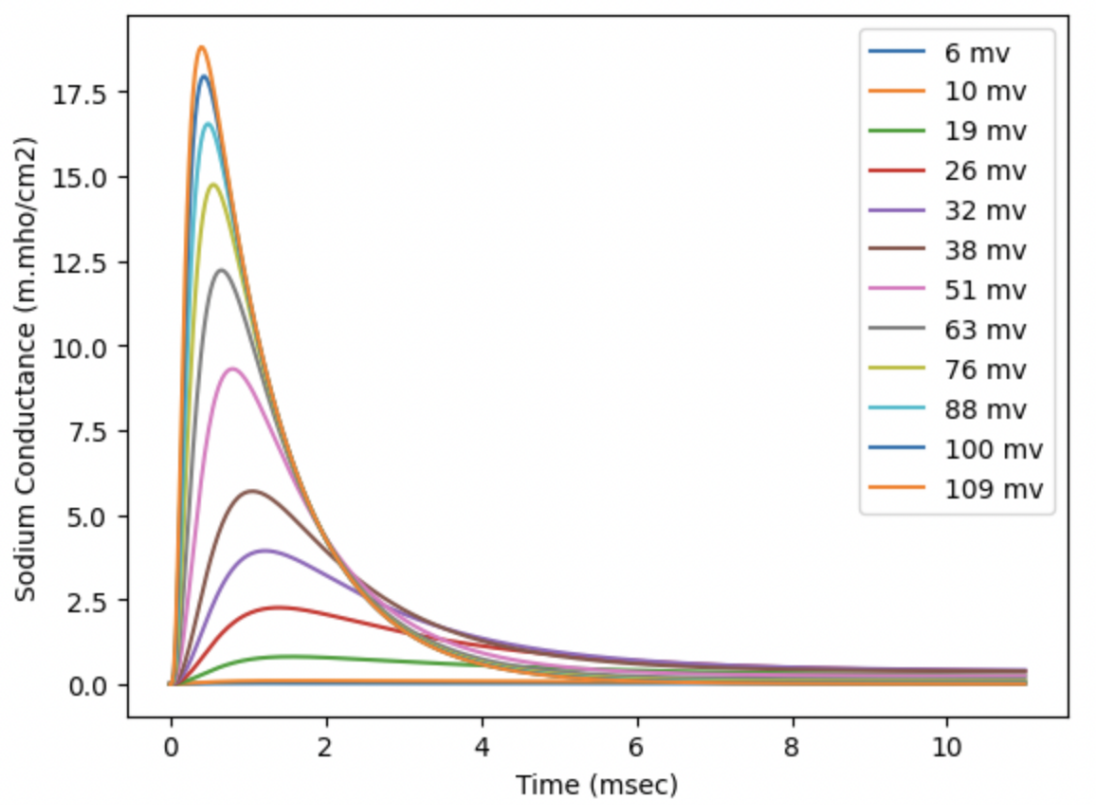

Figure 3.2: Changes of sodium conductance associated with different depolarizations (Experimental values)

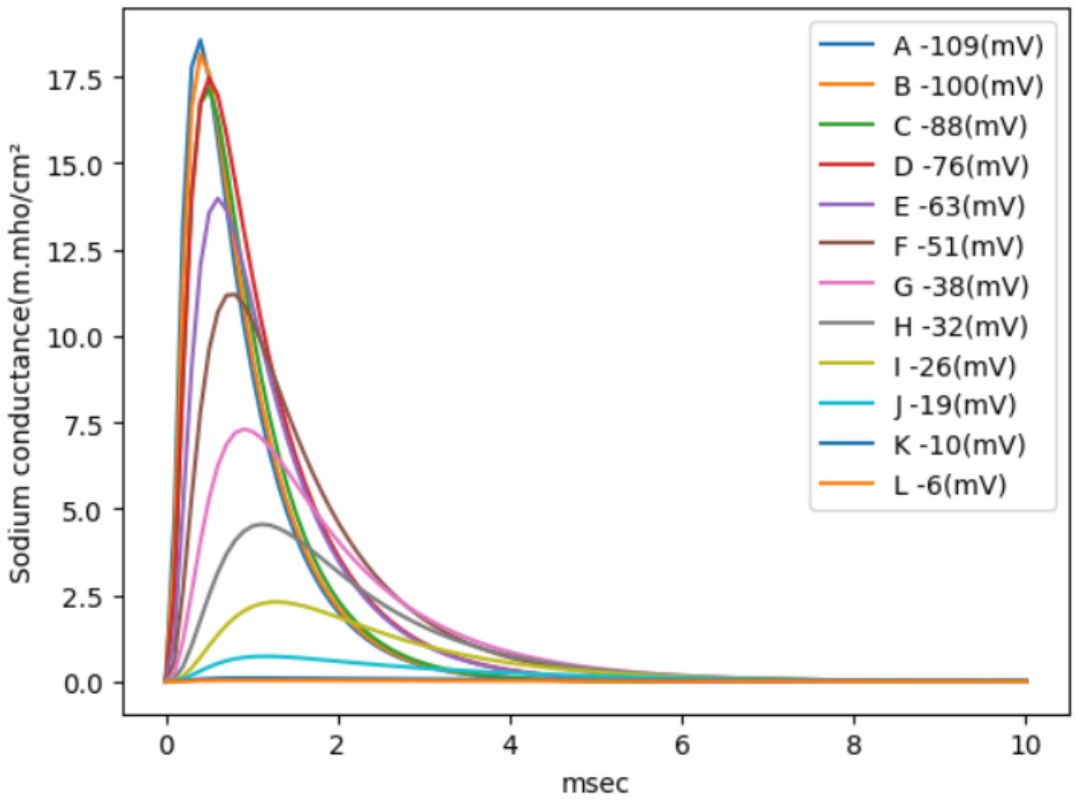

Figure 3.3: Changes of sodium conductance associated with different depolarizations (Theoretical curve to fit experimental values)

Bibliography

Hodgkin, A. L., & Huxley, A. F. (1952). A quantitative description of membrane current and its application to conduction and excitation in nerve. *The Journal of Physiology*, *117*(4), 500–544. https://doi.org/10.1113/jphysiol.1952.sp004764