Non-Linear Dynamics & Neurobiology

Course Project for PH 567 - Non Linear Dynamics

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This report is aimed at exploring the dynamics of electrical conductance signals in the human body. Among the various mathematical models developed to describe the same, we focus on the equations used by ***Alan Hodgkin & Andrew Huxley*** *in their 1952 paper -* ***'A Quantitative Description of Membrane Current and its application to Conduction and Excitation in Nerve'*** *for which they received the Nobel Prize in Physiology and Medicine in 1963. We try to analyse the behaviour of membrane potential, when subject to various external stimuli, by numerically integrating the Hodgkin-Huxley Model. The book* ***Theoretical Neuroscience*** *by* ***Peter Dayan & L.F. Abbott*** *has been our major source for understanding the biology behind the system.*

1 Introduction

Neuron systems are one of the prominent examples of how non linear dynamics affect our day-to day life. The conductance of a nervous signal throughout our body is governed by chaotic systems which hasn't been fully mapped yet but the scientific community has come up with numerous mathematical models to understand some of its basic underlying principles.
One of the earliest (1950) and most accurate spiking neuron models is the **Hodgkin-Huxley Model**. It is a set of nonlinear differential equations that approximates the electrical characteristics of excitable cells such as neurons and describes how the nervous signals are initiated and propagated. Based on their experiments, Hodgkin and Huxley found that the ion current in the axon consists of three different types: Sodium current Na^+, Potassium Current K^+ and a leak current consisting mainly of Cl^- ions. The Potassium and Sodium currents have specific voltage-dependent ion channels which regulate their flow through the cell membrane. The leak current takes care of the other channel types.
In this report we have dealt specifically with the behaviour of Na^+ and K^+ channels and the membrane potential when a pulse is introduced for a short while or as a series of regular spikes. It is also an interesting fact that the results were derived by Hodgkin and Huxley based on their experiments on a giant axon of a squid but it explains the human system surprisingly well.

Motivation for the project

One of the most intriguing aspects of taking up this project was the opportunity to explore the interdisciplinary nature of Physics (specifically in the domain of Biology) which we have heard about but never experienced first hand. Although most of our computation deals with the physics behind the neuron system, it is not possible to compute it without actually understanding the biological reasons behind it. The topic in itself served as a perfect blend for exploring the dynamics in the human body and the evolution of non-linear systems - Biology and Physics at their best.

2 Description

The Hodgkin-Huxley Model is based on the relation between total membrane current density $I(t)$, ionic current density i_m and membrane capacity current $C\frac{dV}{dt}$

$$I(t) = C_m \frac{dV}{dt} + i_m \tag{1}$$

The ionic current i_m is determined to have the following dependencies on the gating variables.

$$i_m = \bar{g}_L(V - E_L) + \bar{g}_K n^4 (V - E_K) + \bar{g}_{Na} m^3 h (V - E_{Na}) \tag{2}$$

Based on the the above equations the model can be represented as a capacitor-resistor circuit with 4 parallel paths - 3 with resistors describing the ion currents and the one with the capacitor representing the conductance due to charge accumulation on the membrane. The closing and opening of the ion gate channels can be equated to the conductance in the respective pathways.
Hodgkin and Huxley experimentally determined that the base potentials (the E's) and maximal conductances (the g's) of these channels can be taken as a constant (values used in the model are mentioned below). In the diagram attached (copied from the original paper [1]), the resistance (conductance^{-1}) of the leakage current is a constant (voltage-independent) while the resistance of the K^+ and Na^+ channels are variables (dependent on the membrane potential). Based on the experimental data, these values were fitted to the differential equations which form the differential equations in the Hodgkin-Huxley Model. The Outside current in the circuit represents the external pulse or I(t) provided to the membrane.

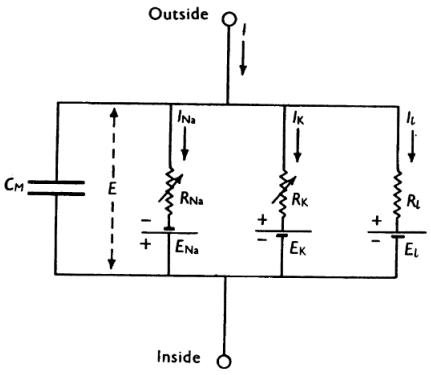


Figure 1: Electrical Circuit representing membrane

2.0.1 Gating Variables

The gating variables m and n represent the probability of gate being open in the Na^+ and K^+ channels respectively. h represents the probability of the gate not being blocked in the Na^+ channel. The value of these probabilities depends on the membrane potential and are determined by the following subfunctions α and β of membrane potential:

$$\alpha_n(V) = 0.01\frac{V-10}{1-e^{\frac{-(V-10)}{10}}} \qquad \beta_n(V) = 0.125e^{-0.0125V}$$

$$\alpha_m(V) = 0.1\frac{V-25}{1-e^{\frac{-(V-25)}{10}}} \qquad \beta_m(V) = 4e^{-0.0556V}$$

$$\alpha_h(V) = 0.07e^{-0.05V} \qquad \beta_h(V) = \frac{1}{1+e^{\frac{-(V-30)}{10}}}$$

The α and β of each of the gating variable is related to it by the following diffrential equation:

$$\frac{dx}{dt} = \alpha_x(1-x) - \beta_x x \qquad \text{where } x = n, m, h$$

This equation can be modified to determine the fixed point value n_∞, m_∞ and h_∞ of n, m and h with time constants τ_n, τ_m and τ_h respectively.

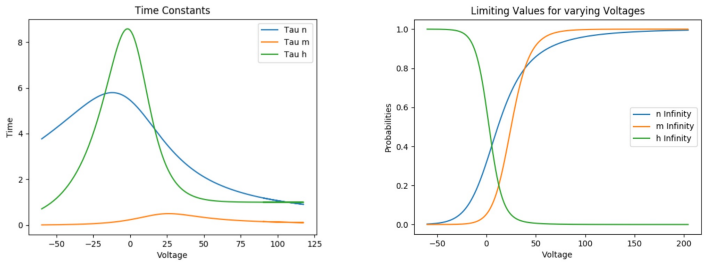
$$\tau_x = \frac{1}{\alpha_x + \beta_x} \qquad x_\infty = \frac{\alpha_x}{\alpha_x + \beta_x} \qquad \text{where } x = n, m, h$$

3 Summary of Results

Using the above equations and functions, we made a python program with the following constants: The maximal conductances and reversal potentials are g_L = 0.003mS/mm^2, g_K= 0.36mS/mm^2, g_{Na} = 1.2mS/mm^2, E_L = -54.387 mV, E_K = -77 mV and E_{Na} = 50 mV. C_m was taken $1\mu F$. The values of n, m and h for one spike and multi spike input were taken for membrane potential = -60 mV.

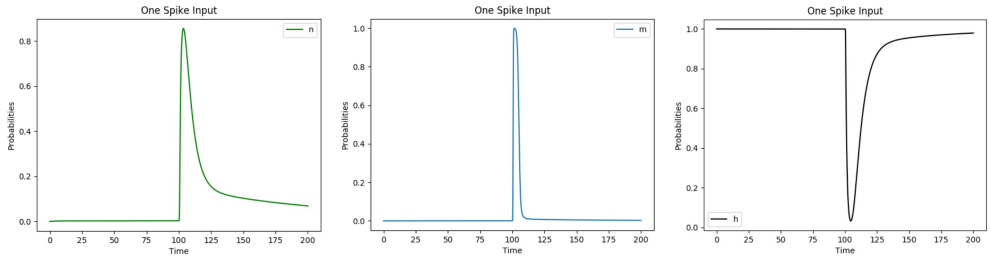
Link to access the python code.

3.1 Time constant and Fixed Point Values of n,m and h



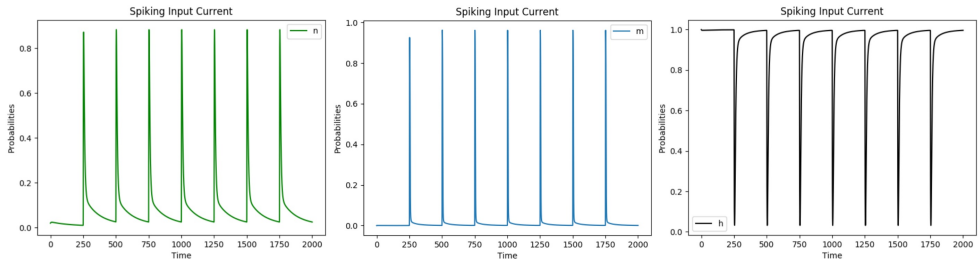
Here, we show the maximum attainable values of the gating variables, for a range of membrane potentials. It's evident that at $-60mV$, the fixed points for n and m is 0 and for h it are 1. The nature of the plots in the time constant graphs give us an idea of the rate at which n, m and h approach their steady state values. Current will flow in a channel only if all its gating variables are non zero which corresponds to very few voltages for the Na^+ channel. Hence Na^+ channel is responsible for Transient Conductances (short signals) while K^+ is responsible for persistent conductances (long signals).

3.2 n,m,h Vs time (single spike input)



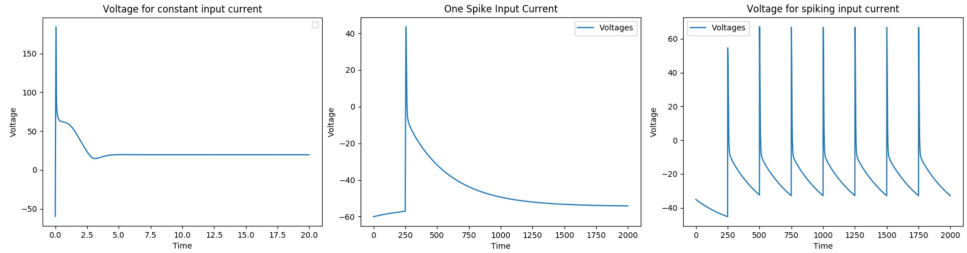
Upon supplying a single current spike, the plots reveal that the values of n and m shoot up to 1 as there is an input pulse and hence flow of ions and increase in the membrane potential V. As soon as the pulse is removed they decay back to 0 which signifies closing of the gate. h dips close to 0 due to the input pulse. This signifies the tendency to block the gate to stop the flow of ions and decrease the membrane potential to its original value. As V decreases h also tends to its steady state value of 1.

3.3 n,m,h Vs time (multiple current spikes)



Supplying a series of short bursts of current to the membrane causes the gate variables to fluctuate periodically. At the end of each burst, they revert back to their steady state values. We observe that m and h are able to attain it faster than n because they are responsible for transient signals while n is responsible for persistent signals.

3.4 Voltage Vs time (constant current, single and multiple current spikes)



The first graph shows that when a constant stimulus is supplied, the membrane potential shoots up, then irregularly settles down to a fixed value, which in turn depends on the value of the stimulus. Here input current is $20\mu A$ and the steady state voltage is $20mV$. The second graph illustrates the effect of a single current spike. Potential shoots up and then smoothly decays to a fixed value ($-54V$ in this case) which is the equilibrium voltage. Third plot shows that the expected regular pattern of rise and fall is followed for a periodic stimulus. The rise is steep as the input pulse forces the membrane potential to supercharge. Initially the decay is also very steep as all the channels tend to discharge, but after a while the effect becomes less pronounced.

4 Conclusion

Shortcomings of the Model

- The HH model clubs together all the channels, apart from Sodium and Potassium channels, into a single leakage channel. This simplification compromises the accuracy of the results.
- In reality, the membrane capacitance also varies with membrane potential, while we made an assumption to simplify integration.
- The Hodgkin-Huxley Model was derived based on the experiments performed on an axon. A system of axons which deals with complex geometric arrangement of axons and dendrites (such as a human system) would require much higher insight.
- From a computational point of view, this model is not suitable for a large scale simulation of a group of neurons. Simplified models like the FitzHugh-Nagamo Model (which deals only with the mathematical dynamics of a neuron system) are preferred which employ less of biology and more of physics.

Our Observations

- For a constant current supply, fixed point of membrane potential varies with the supplied membrane current, however, for short bursts of input, membrane potential always tends to a constant fixed point.
- While determining the impact of a current spike on membrane potential, the quantity that matters is the product of interval of burst and the current supplied (i.e. the total charge supplied in a single burst).

5 References

1. Hodgkin A.L. and Huxley A.F. : **A Quantitative description of Membrane Current and its application to Conduction and Excitation in a Nerve**, Physiological Laboratory, University of Cambridge (1952)

2. FitzHugh, R.A.: **Mathematical models of excitation and propagation in nerve**. Schwan, H.P. (ed.) Biological Engineering. McGraw-Hill, New York (1969)

3. Ivancevic T., Laxmi Jain, John Pattison and Alex Hariz : **Non linear dynamics and chaos methods in neurodynamics and complex data analysis** (2008)

4. Online tutorials from https://neuronaldynamics.epfl.ch/online/Ch2.S2.html

5. **Theoretical Neuroscience**: Computational and Mathematical Modeling of Neural Systems by Peter Dayan and Abbott L.F.