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An Insight into the Action Potential Generation in the Hodgkin-Huxley model

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Abstract— The brain is one of the most complex organ in the living being and for years its complexity has overwhelmed researchers, physiologists and neuroscientists. Trying to map its behavior right from the start of evolution has brought about only little success. Here we have concentrated on the basic unit of brain "neurons". When the membrane potential reaches a certain threshold value spikes are generated. In this study we have applied concepts of computational modeling to the Hodgkin Huxley model equations which led to some interesting facts.

Index Terms— brain, Hodgkin Huxley, membrane potential, neurons , neuroscientists, spikes, threshold value .

1 Introduction

The Hodgkin Huxley (HH) model was developed by Alan Hodgkin and Andrew Huxley in 1950's for which they won the 1963 Nobel Prize in the field of Physiology or Medicine. Their experiments led to a series of five articles being published in 1952 revealing the properties of ionic conductances dominating the action potential. The final paper laid down the framework for all the modern work in neural excitability [1], [2].

Hodgkin and Huxley choose the squid axon which was large enough to see and stick wires into. They threaded silver wire inside the axon and by doing so they could measure the electrical potential and deliver enough current to maintain a particular voltage despite the efforts of ion channels in the membrane to change it and this was known as voltage clamp .This process gave them the idea about which current is being passed through the membrane and in which direction. They performed the same experiment in potassium or sodium free solutions and by doing so under different voltage conditions they could figure out how sodium and potassium currents changed with the change in membrane potential. They then used these collected data to construct the parallel conductance wherein the electrical properties of segment of a nerve membrane are modeled.

As we can see in fig 1 it consists of four parallel conducting pathways connecting the inside and outside of the membrane. Membrane capacitor and fixed membrane conductance are on the left side. Resistor is connected to a battery and the batteries are denoted by two parallel lines of different length, the long line indicating the positive pole. The passive conductance in this model is called as leak conductance and are not sensitive to voltage hence the leak conductance remains same for all voltage providing constant "leakiness" for current. Potential of the battery with g_{leak} is E_{leak} which is the major determinant of resting potential and its short line is connected to the inside of the membrane making the membrane inside negative [3],[4,[5].

The right side consists of two active branches. The sodium battery and conductance and they are pointed in opposite directions. The potassium battery makes the membrane negative while the sodium battery makes it positive. The arrow in the conductance symbol under each battery means it is a rheostat. Sodium and potassium conductances are turned off at rest so that they don't conduct which means at this time they have no effect on membrane voltage . If anyone is turned on, then associated battery will dominate the membrane potential but if both are turned on at the same time the batteries will discharge massively overheat and blow up [1],[3],[6].

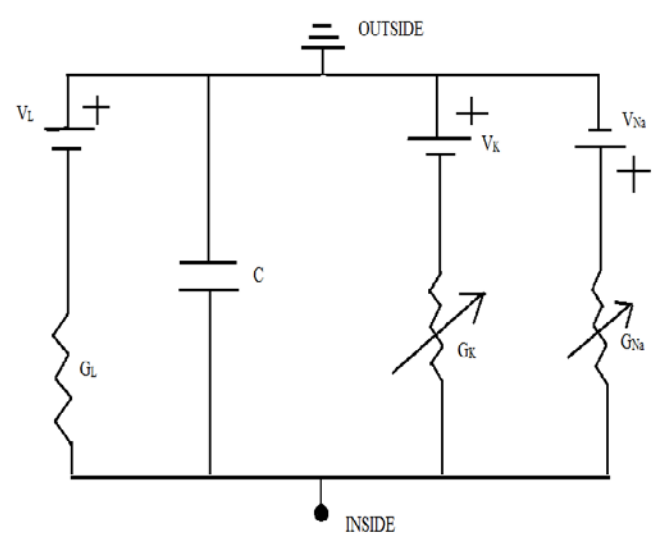

Fig 1: Parallel Conductance Model

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2 The MODEL EQUATIONS

In the parallel conductance model current flowing is carried by the capacitor or by ions. As we can see the resistances relates to charge being carried by sodium and potassium ions and a leakage current. Using Ohm's law (V=IR) the following equations were derived [7],[8].

$$I_{Na} = g_{Na}(V-V_{Na}) \quad (1)$$

$$I_K = g_K(V-V_K) \quad (2)$$

$$I_l = g_l(V-V_l) \quad (3)$$

Where g_{Na} and g_K depend on time and membrane potential. The values of V_{Na}, V_K, V_l, Cm and gL were determined via experimentation and are constants.

To build their mathematical model they used the basic circuit equation

$$I = C_m \frac{dv}{dt} + I_i \quad (4)$$

where

I = the total membrane current density .
I_i = the ionic current density .
V=displacement of the membrane potential from its resting value.
C_m= the membrane capacity per unit area (assumed constant).
t=time.

Further the ionic current was divided into a sodium current a potassium current and a leakage current primarily carried by chloride ions:

$$I_i = I_{Na} + I_K + I_l \quad (5)$$

Here I_{Na} means sodium current, I_K means potassium current and I_l meansleakage current. The model was further expanded by adding (1),(2),(3).

$$I_{Na} = g_{Na}(V-V_{Na}) \quad (6)$$

$$I_K = g_K(V-V_K) \quad (7)$$

$$I_l = g_l(V-V_l) \quad (8)$$

$$V=V-V_R \quad (9)$$

V_R denotes the resting potential.

Again we have

$$g_k=\bar{g}_k n^4 \quad (10)$$

where $\overline{gk}$ is a constant, n is a dimensionless variable that varies from 0 to 1 and is the proportion of ion channels that are open. In order to understand where n comes from we have the equation

$$\frac{dn}{dt} = \alpha_n (1-n)-\beta_n n \quad \alpha_n,\ \beta_n \text{ are rate constants} \quad (11)$$

where alpha (α)is the rate of closing of the channels and beta (β) is the rate of opening. Hence together they give us the total rate of change in the channels during an action potential. Similarly the sodium conductance is described by the equation

$$g_{Na} = m^3 \bar{g}_{Na} h \quad (12)$$

where $\bar{g}_{Na}$ is a constant, m is the proportion of activating sodium ion channels and h is the proportion of inactivation of sodium ion channels. M and h can be further calculated as

$$dm/dt = \alpha_m (1-m)-\beta_m m \quad (13)$$

$$dh/dt = \alpha_h (1-h)-\beta_h h \quad (14)$$

alpha and beta (rate constants) can be calculated as:

$$n_0 = \alpha_{no}/(\alpha_{no} + \beta_{no}) \quad (15)$$

(15)

$$\alpha_n = 0.01\ (V + 10)/((\exp\ (V+10)/10)-1) \quad (16)$$

$$\beta_N = 0.125 \exp\ (V/80) \quad (17)$$

$$\alpha_m = 0.1(V+25)/((\exp(V+25)/10)-1) \quad (18)$$

$$\beta_m = 4\exp(V/18) \quad (19)$$

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

$$\beta_h = 1/(\exp(V+30/10)+1) \quad (21)$$

Therefore the final equation that we have is :

$$I = C_m\, dv/dt + \bar{g}_k n^4 (V-V_K) + m^3 \bar{g}_{Na} h\,(V-V_{Na}) + g_l\,(V-V_l) \quad (22)$$

3 METHODOLOGY

3.1 Simulation of HH model with constant input

In order to mimic the behaviour of membrane potential we resort to simulation technique. Matlab was used for this purpose. As we can see "Fig 2" represents the evolution on membrane potential and spike generation in HH model. We discritize the time interval [0,T] into equal parts of size dt=0.01sec. Euler Maruyama method is applied to simulate the neuronal model. When the membrane potential reaches threshold voltage V_{th} in this case -70 a spike is generated and instantaneously the membrane potential is reset to its resting potential. Thereafter the membrane potential again evolves and reaches the threshold potential to generate another spike [9].Time interval between two consecutive spikes gives the Inter Spike Interval (ISI).

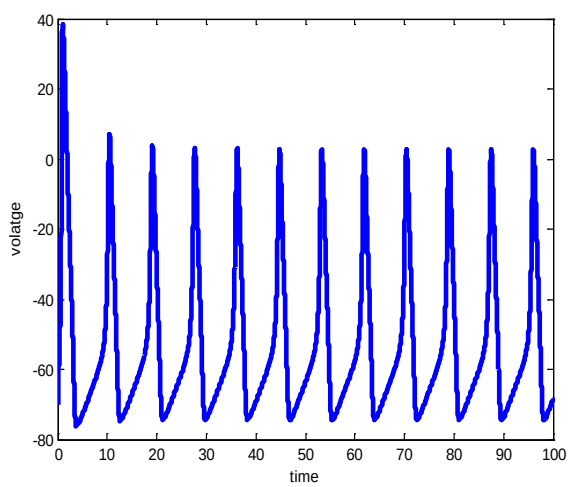

Fig2: Spikes generation with Vth= - 70

TABLE 1 PARAMETERS USED

Variable	Value
Cm	1μF/cm²
dt	0.01ms
Vth	-70 mV
I	50 μA/cm²
VNa	115 mV
VK	-12 mV
Vl	10.6 mV
gbarNa	120 ms/cm²
gbarK	36 ms/cm²
gl	0.3 ms/cm²

3.2 Addition of Noise

Noise and statistical fluctuations are present in all biological systems is now a well established fact. The main challenge across computational biology is understanding its role in cellular dynamics [4].So far we have come to know it can influence information processing [5], spike time reliability [10], stochastic resonance [9], firing irregularity [11],[12], sub threshold dynamics [7],[9], and action potential initiation. During the past few years accurate methods for incorporating noise in the classical Hodgkin Huxley model have been developed [13],[14],[15]. To introduce noise within a differential equation such as that of the HH model, we look for ways of introducing fluctuations into this deterministic system. The three main approaches are as follows [15],[16].

- ***Current noise***

  Replace (22) with

$$I = C_m\, dV/dt + \bar{g}_k n^4 (V-V_K) + m^3 \bar{g}_{Na} h\,(V-V_{Na}) + g_l\,(V-V_l) + \xi_v(t) \quad (29)$$

- ***Subunit noise***

  Replace (11), (13), (14) with

$$dy/dt = \alpha_y(1-y) - \beta_y y + \xi_y(t) \quad (30)$$

where y=n,m,h .

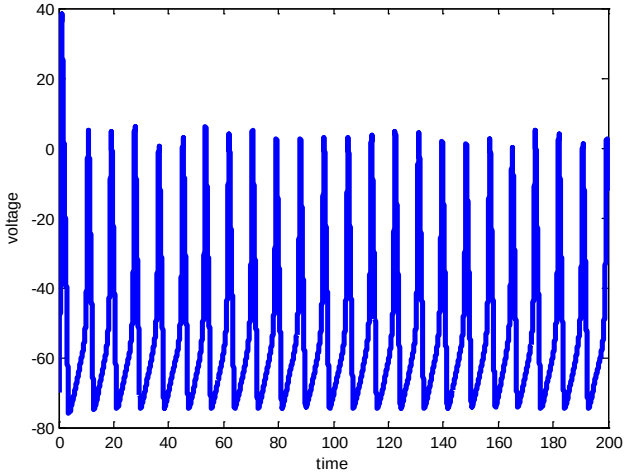

Fig 3: Change in the membrane potential with respect to time

- ***Conductance noise***

Replace (22) with

$$I = C_m \, dV/dt + \bar{g}_K (n^4 + \xi_K(t)) (V - V_K) + \bar{g}_{Na} (m^3 h + \xi_{Na}(t)) . (V - V_{Na}) + g_l (V - V_l) \quad (31)$$

"Fig 3" depicts the results of solving the HH model after the introduction of noise in the model equation.

3.3 Inter Spike Interval

The increase in the membrane potential of the neuron is due to the electrochemical processes inside the neuron [4], [10],[17]. FPT (first passage time) is the time epoch when the membrane potential reaches a certain threshold value for the first time. At this time a spike is generated and then the membrane potential decays to a value known as resting potential. The first passage time is generally random in nature [18]. Inter Spike Interval is the difference between time epochs of two consecutive spikes also known as ISI. Collection of ISI gives the probability distribution.

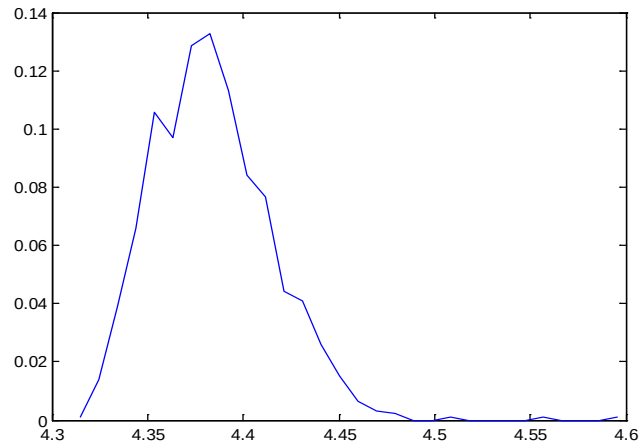

Fig 4: Probabilty Distribution Function of simulated ISI distribution

4 CONCLUSION

Hodgkin and Huxley not only helped scientists understand the concept of generation of action potential, they also laid down the framework for all the modern discoveries made in the field of computational neuroscience. In our quest of understanding of the brain, it will be useful to concentrate on models that suggest new and promising lines of experimentation, at all levels of organization and the best model to choose would be the HH model. We tried to understand how brains compute, using computers to simulate and used our knowledge from various fields such as mathematics, physics and other computational fields.

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