International Journal of Engineering Applied Sciences and Technology, 2022
Vol. 6, Issue 10, ISSN No. 2455-2143, Pages 288-294
Published Online February 2022 in IJEAST (http://www.ijeast.com)

STOCHASTIC BIOLOGICAL MODEL OF NEURON

Prajakta Mhatre
Department of Instrumentation and Control Engineering College of Engineering Pune, Pune
Pune, India - 411005

Dr. Kalyani Bhole
Assistant Professor
Department of Instrumentation and Control Engineering College of Engineering Pune, Pune
Pune, India - 411005

***Abstract*—Brain is the vital organ for action, learning, memory, thought formation and other cognitive activities. The neuron is the fundamental functional unit of the brain. It is a specialized cell created to transmit information and receive information from other nerve cells, muscle cells or gland cells. This paper describes the stochastic behavior of biological model of Neuron and its implementation in MATLAB Simulink to study the behavior of a neuron in a real-time environment. The Hodgkin–Huxley mathematical model describes how initiated and propagated action potentials in neurons takes place are for external stimulus. The stochastic behavior of a Hodgkin-Huxley neuron is studied for various external stimulus and helped to find various action potentials.**

***Index Terms*—Action Potential of Neuron, Hodgkin-Huxley Neuron Model, Neuron Modeling, MATLAB Simulink, Stochas- ticity.**

I. INTRODUCTION

The neuron complex is made up of layers of parallel pro- cessing elements called neurons. Biological Neural Network consists of fast processing speed. Dendrites collects signals and the sends signals of electrical activity through axon to terminal axons. At the end of each terminal axon, synapse takes place with the help of neurotransmitter, gives output as electrical activity. When a neuron receives a input signal which excites it, which is large as compared to the input signal which inhibits it. And then it sends a signal of electrical activity down its axon that is action potential is generated. Neuron model helps to study the effect on nervous system under various stimulus. In this paper we have considered Hodgkin- Huxley (HH) neuron model, added stochasticity and studied how the action potential is generated in neurons and also tried applications based on the concept.

The model for a neuron must be simple to design and efficient of producing firing patterns as produced by actual biological neuron [1]. Neuron models are divided into two categories as per the type of interfacing the model: Electrical input–output relationship voltage of neuron membrane models and Natural stimulus neuron membrane models. The Electrical input–output relationship voltage of neuron membrane models represents the correlation between neuron membrane currents at the input which is external stimulus, and membrane volt- age at the output. This category includes: Hodgkin-Huxley Neuron model, Leaky integrate-and-fire model, Izhikevich (IZ) model [1], Adaptive integrate-and-fire model, Fitzhugh-Nagumo (FHN) model [2], etc. In this paper we are dealing with Electrical input–output relationship voltage of neuron membrane model.

P. Tandeitnik and H. Guterman in [3] performed various experiments on Artificial neuron network and studied various characteristics. Izhikevich in [4] analyzed neurons and com- puted neurons feature and found that Hodgkin-Huxley model exhibited all important biological neuron features.

A stochastic model is the one which has one or additional stochastic element. The system which has stochastic element cannot be answered systematically. In this paper we deal with stochastic behavior and not deterministic behavior because, stochastic model is more informative and better than a deter- ministic model due to varying behavioral characteristics. The probability that spikes are received at the time of synapses based on deterministic study will not be accurate and prac- tical, as further stochastic consideration on spiking neuron is considered [12].

Several inputs, weighting factor are applied to neuron, it sums and gives output when the addition of weighted inputs crosses a certain threshold value. Inputs are of two types either the impulse that excites the neuron or the impulse that inhibits the neuron. Renshaw cell, fond is spinal cord, acts as a safeguard device in case of excessive excitation by creating a negative feedback loop [13].

This paper has been divided into several subsections. Fol- lowed by the introduction given in section I. Biological

Hodgkin-Huxley (HH) Neuron model is explained in Section
II. Hodgkin-Huxley Neuron model is focused in this section as we are going to create stochastic model of it. Section III consists of Stochastic model of Biological neuron. This is followed by some applications in section IV and their effect on action potential of neuron, then follows the conclusion section.

II. BIOLOGICAL HODGKIN-HUXLEY NEURON MODEL

A. Hodgkin-Huxley Model

The Hodgkin–Huxley (HH) model is a mathematical model that shows how action potentials gets are initiates and com-municate in neurons. It consists of set of four nonlinear ordinary differential equations that estimates the electrical characteristics of neurons. Hodgkin and Huxley presented the model to explain the generation of action potential on the squid giant axon. Hodgkin and Huxley mathematical model which represents the neuron membrane is shown in fig. 1

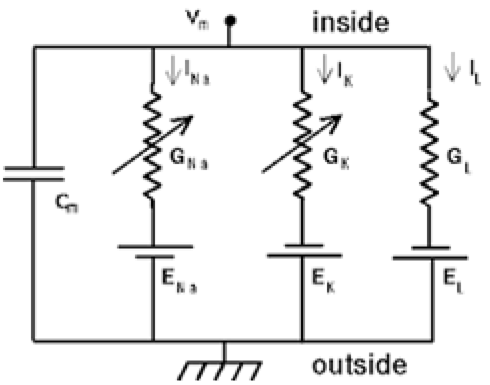

Fig. 1. Circuit diagram of Hodgkin and Huxley Neuron model

Mathematically, the current moving through the bilipid layer is given as:

$$I = C_m \frac{dV_m}{dt}$$

$$C\frac{dV_m}{dt} = I_{ext} - [\bar{g}_K n^4(V_m - E_k)$$

$$+\bar{g}_{Na} m^3 h(v_m - E_{Na}) + \bar{g}_l(V_m - E_l)] \quad ($$

Where I_{ext} is the external simulation current, V_m is the neuron membrane potential, C_m is the membrane capacitance,
the maximum conductance of leak channel; E_{Na}, E_K and E_l represents the potentials for sodium ions, potassium ions and leak ions and m, n, h are the gating variables which regulates the conductivity of Na^+ and K^+ channels. The gating variables follows first order dynamic. If p_o indicates the probability that sodium-potassium pump is open and p_c indicates the probability that sodium-potassium pump is closed [5]. Then according to first order rate process,

$$p_o + p_c = 1 \qquad (3)$$

i.e., $0 < p_{o,c} < 1$ Probability of open of potassium channel is, $p_o = n^4$ and of sodium channel is $p_o = m^3h$.

Rate constant, α, membrane voltage V_m function, is the rate at which sodium-potassium pump closed to open transition takes place. Another rate constant, β, is the rate at which sodium- potassium pump open to closed transition takes place. The probability that sodium-potassium pump is in open state is given by the equation:

b. $E_k = \quad 12mV$

$$\frac{dp}{\cdot} = \alpha_n (1 - n) - \beta_n \quad (n)$$

Initially potential of neuron membrane (V) is taken as zero and then adjusted as per the resting potential of neuron membrane. The MATLAB Simulink model consists of three subsystem of gating variables n, m and h respectively. Fig. 2 represents the subsystem of gating variable n, fig. 3 represents the subsystem of gating variable m, fig. 4 represents the subsystem of gating variable h.

Mathematically the equations are represented as:

i.

$$\frac{dn}{dt} = \alpha(1 - p_o) - \beta(p_o) \qquad (5)$$

$$\alpha_n = \frac{0.1(25 - V_m)}{exp(\frac{10 - V_m}{10}) - 1} \qquad (6)$$

$$\beta_n \quad 80$$

ii.

$$\frac{dm}{dt} = \alpha_m(1 - m) - \beta_m(m) \qquad (8)$$

$$\alpha_m = \frac{0.1(25 - V_m)}{exp(\frac{25 - V_m}{10}) - 1} \qquad (9)$$

$$\beta_m \quad 80$$

iii.

$$dn$$

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80

iii.

$$\frac{dh}{dt} = \alpha_h(1 - h) - \beta_h(h) \quad (11)$$

$$\alpha_h = 0.07 \,\square\, exp(\frac{-V_m}{20}) \quad (12)$$

$$\beta_h = \frac{1}{exp(\frac{30-V_m}{10})+1} \quad (13)$$

Mathematically the equations are:

$$I_k = g_k(V_m - E_k) \quad (14)$$

where,

$g_k = \bar{g}_k n^4$

$\bar{g}_k = 36mS/cm^2$

$$I_{Na} = (V_m - E_{Na}) \quad (15)$$

where,

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

$\bar{g}_{Na} = 120\,mS/cm^2$

$E_{Na} = 120mV$

c.

where:

$g_l = \bar{g}_l n^4$

$\bar{g}_l = 0.3mS/cm^2$

$E_l = 10.6mV$

$$I_l = (V_m - E_l) \quad (16)$$

B. Result

Hodgkin-Huxley neuron membrane model was executed in MATLAB Simulink and the feedback of a neuron to various external stimulus were observed. It was noted that action potential was not generated for the external stimulus below sub-threshold value. And the action potential begins when, the external stimulus overcome the threshold value.

The association between neuron membrane potential, neuron membrane current and the gating variables was studied from the model. The model was simulated using an external stimulus of 10 mA. When an action potential was initiated, the neuron could not stimulate again for a definite time. The time duration when neuron will not respond to any other stimulus is called as refractory period. This period is further divided as: Absolute refractory Period (ARP) and Relative refractory Period (RRP). During the ARP, a new action potential cannot be generated, in this period most of the sodium channels of neuron do not activate, but in RRP, a new action potential can be generated under certain conditions.

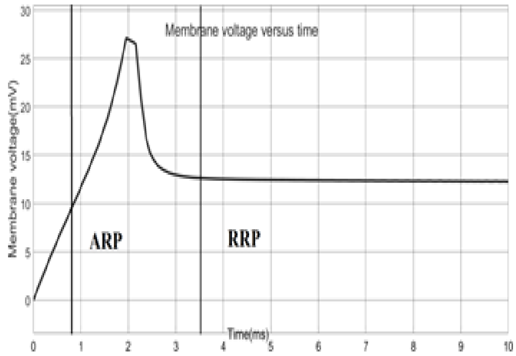

Fig. 2. Membrane voltage v/s time representing ARP and RRP

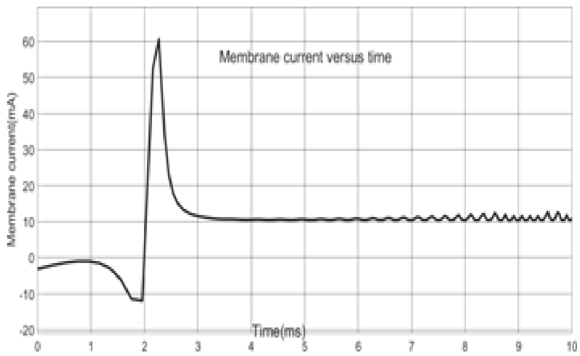

Fig. 3. Membrane current v/s time

ARP is the period when the action potential cycle initiates, additional external stimulus given to neuron at this time interval could not generate a corresponding action potential. RRP is the period when if a powerful stimulus above threshold value is given as the potential of neuron membrane inside the axon membrane becomes relatively more negative than the outside [1]. From fig. 6, left side, as the stimulus is given within 1ms action potential is generated, consists of ARP followed by RRP.

Na+ channels are inactivated in the ARP period, and so the stimulus in depolarization phase cannot initiate an action

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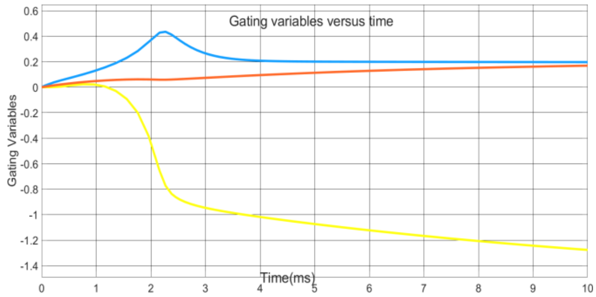

Fig. 4. Diagram representing variation of gating variables

potential. Na+ channels begin to recuperate from inactivation phase after the ARP period, as seen in fig.6. During this time, neuron acknowledge only to an external stimulus, powerful than the threshold value when initially neuron was at rest. As the resting state is recovered, all the ions in Na+ channels turn off as the strength of the external stimulus becomes less than the initial value [5].

As seen in fig. 6 right side, the membrane current initially decreases till -10mA, then increases and reaches at spike value 60mA.

As seen in fig. 7, variation of variable 'm' is restricted for short time interval of the sodium channel, holding up the transient nature whereas variable 'n' expands at a slower rate and comes to its initial value after a brief time interval, holding up the constant behavior of potassium channel.

III. STOCHASTIC MODEL OF BIOLOGICAL NEURON

A. Concept of Stability

According to Bayesian brain hypothesis, brain maintains internal statistical model in the form of a conditional probability density function of the outside world.

According to stochasticity,

$$I_{ext} = I_{ext1} + I_{ext2} + I_{ext3} + I_{ext4} \quad (17)$$

B. Simulink Model

C. Result

External stimulus of 10mA, 20mA, 30mA 40mA are given stochastically. When external stimulus value increases, the firing rate of the neuron increase.

As seen in fig. 9 left side, the ARP period gets reduced in action potential after applying stimulus in stochastic model. After giving stimulus the action potential just starts in less than 1ms. It takes very less time to complete one action potential cycle. The membrane current also increase to a high value in stochastic model as considered to previous also in less time span as seen in fig. 9 right side. According to fig. 10 gating variables get activated in short time span in stochastic model as considered to previous model. Variable 'm' variations as seen in fig. 10 is for very less time interval controlling up the impermanent nature of the sodium channel, on the other variable 'n' value increases very rapidly and come backs to its preliminary value after a brief time interval, holding up

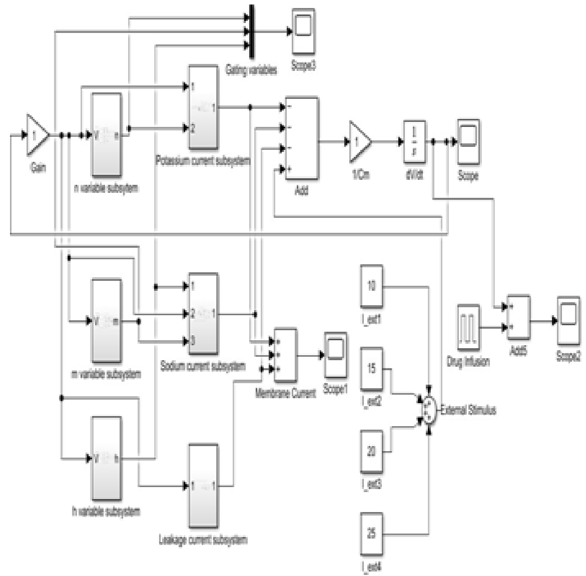

Fig. 5. Simulink model of Stochastic biological neuron model

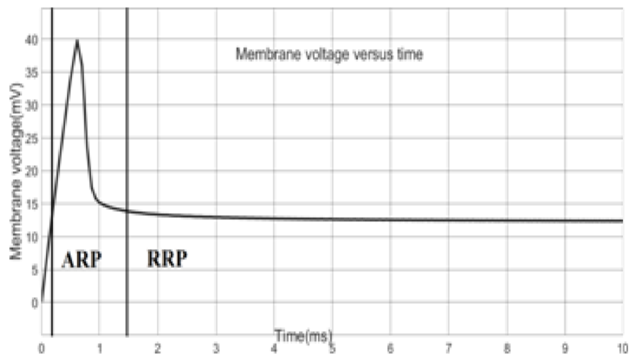

Fig. 6. Membrane voltage v/s time representing ARP and RRP

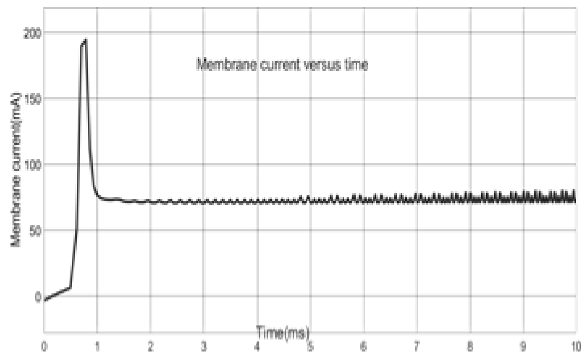

Fig. 7. Membrane current v/s time

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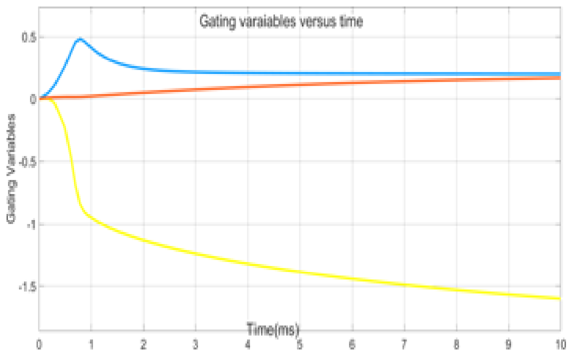

Fig. 8. Diagram representing variation of gating variables

the constant behavior of potassium channel. Thus, the action potential takes less time span in stochastic model as considered to neuron model.

IV. APPLICATIONS

A. Drug Infusion

As neurotransmitters can accelerate or deaccelerate the action potential, drugs can do the same. Messages carried by one neuron to another can also be twisted when hallucinogenic drugs, Opioid drugs are injected in the body. Drugs can cause constant sleep, reduce temperature of the body, reduce the heart rate, blood pressure, and breathing rate. We are trying to study the effect of drugs to a stochastically modelled neuron. Drugs are given as per the quantity and changing the time delay and the effect is studied.

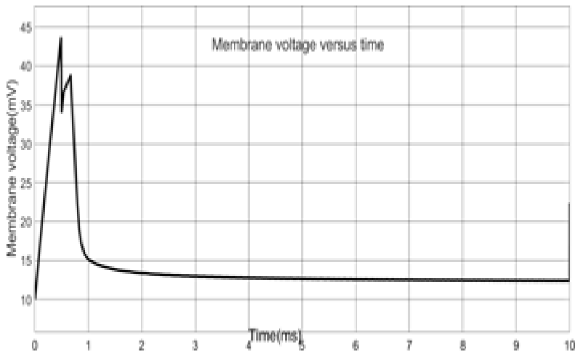

Fig. 9. Voltage membrane versus time graph is obtained for 10mA amplitude drug is infused

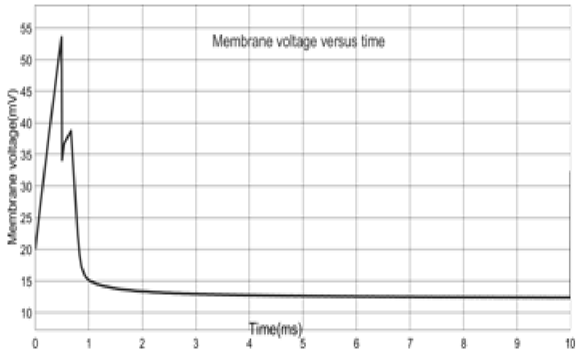

Fig. 10. Voltage membrane versus time graph is obtained for 20mA amplitude drug is infused

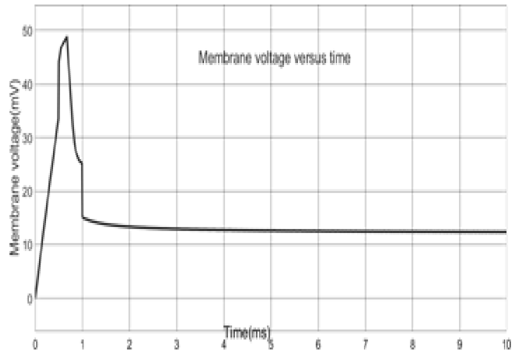

Fig. 11. Voltage membrane versus time graph is obtained for 10mA amplitude drug is infused at a time delay of 0.5msec.

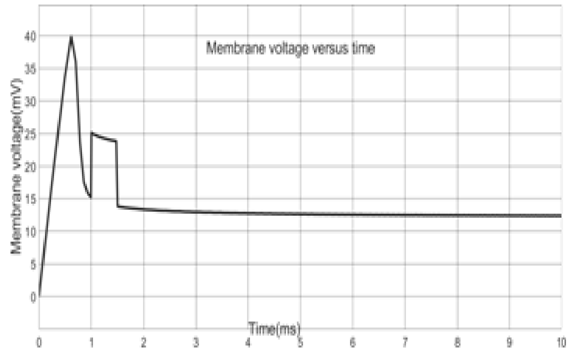

Fig. 12. Voltage membrane versus time graph is obtained for 10mA amplitude drug is infused at a time delay of 1msec

We have already stochastically stimulated the model plus we are infusing drug at 10mA amplitude; the effect is seen in fig. 11 left side. As seen in the figure, depolarization cycle ends and just after the start repolarization cycle another depolar- ization starts i.e., another action potential cycle.

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Drug blocks K+ channels, stopping the flow of potassium ions outside the cell, thus preventing complete repolarization. As seen in fig. 11 right side, 20mA amplitude pulse is given. The refractory period takes for longer time followed by depolarization of another cycle as compared to previous drug infusion of 10mA. In fig. 12 left side we are infusing drug after delay of 0.5msec so second spike is not observed. As per fig. 12 right side as the drug is infused after the action potential is completed, second spike is not obtained.

B. EEG

Electroencephalography, or EEG, a method which captures the electrical signals of the brain.
Frequency ranges / Frequency Bands of EEG signals:

i. Delta wave (1 – 4 Hz): Delta waves are associated with deep sleep stages. As the rhythmicity of delta wave increases, the sleep becomes deeper.
ii. Theta wave (4 – 7 Hz): Theta is correlated with an analytical activity such as creativity, daydreaming, etc. Related with relaxation condition. Helps to find defect whenever there is head injury.
iii. Alpha wave (7 – 12 Hz): Alpha is associated with resting state. In relaxed phase, alpha level value are increases.

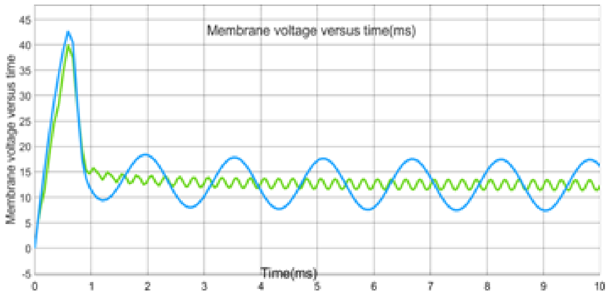

Fig. 13. Model simulated at 4Hz for pulse of 1mA and 5Ma

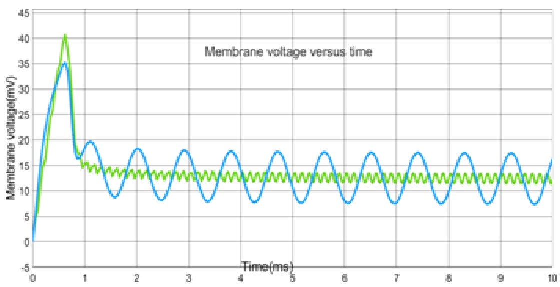

Fig. 14. Model simulated at 7Hz for pulse of 1mA and 5mA

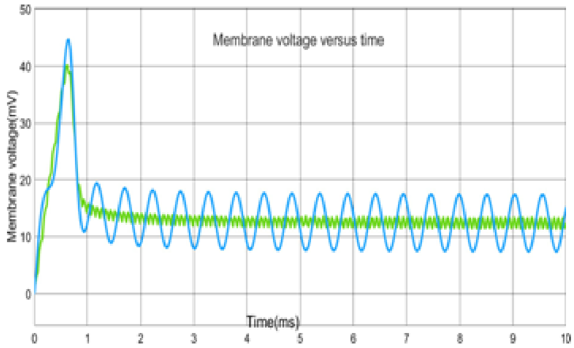

Fig. 15. Model simulated at 12Hz for pulse of 1mA and 5mA

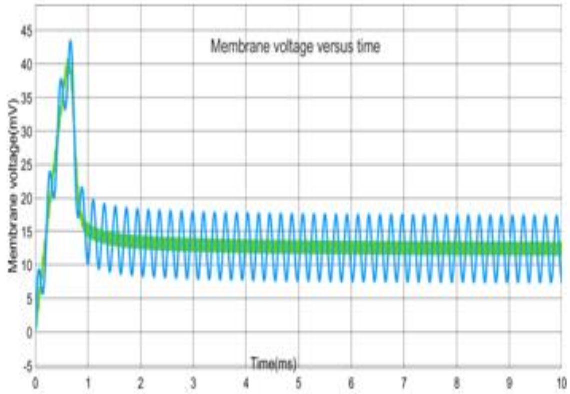

Fig. 16. Model simulated at 30Hz for pulse of 1mA and 5mA

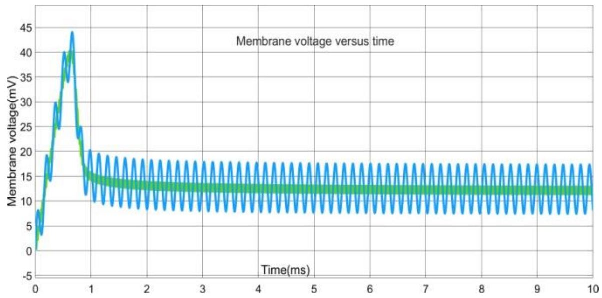

Fig. 17. Model simulated at 40Hz for pulse of 1mA and 2mA

They are well organized and pulsing. They are associated with reducing stress. It is also useful with memory related activities.

iv. Beta wave (12 – 30 Hz): They are commonly observed in awaken state. Beta wave is a fast wave activity, present when we are alert, attentive, focused, mediation, prayer, and engaged in analyzing problem or decision making. They are associated with strongly captured memory.

v. Gamma wave (greater than 30 Hz, typically 40 Hz): Gamma waves are associated with problem solving, concen- tration, etc. It is fastest wave among all waves.

From the figs. 13, 14, 15, 16, 17 we can conclude that as frequency increases the stimulus in the time period increases.

V. CONCLUSION

In this paper, we studied the stochastic behavior of Hodgkin-Huxley model in MATLAB Simulink. In this paper we discussed the outcomes of external stimulus on the stochastic model of neuron. We also discussed the various effects on action potential cycle after the drug infusion as well as the effect on neurons after stimulating to different frequencies. The detailed research and examination of HH stochastic neuron model will help us to strengthen the neurons complex by applying various external stimulus and study its effects on the brain.

VI. FUTURE SCOPE

In this paper as we have seen the drug application on Stochastic behaviour of Neuron, further we can do practical applications of various drugs. We can experiment these drugs individually such as Dopamine, Antidepressants, Antiseizure drugs, etc. .

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