Bioinspired Silicon Neuron

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Abstract—*The Hodgkin-Huxley model of neuron showed how a neuron is excited, an action potential generated in a neuron and how a conduction current is generated. The model discussed in this paper is a reduction of the Hodgkin-Huxley model, where it shows the individual effect of an excitatory and inhibitory neurotransmitter as well as their combined effect.*

1. INTRODUCTION

Neurotransmitters are released when an external stimuli is applied. On application of external stimuli, two types of neurotransmitters may be released–excitatory and inhibitory. This leads to the generation of an action potential, which propagates through the neuron and the information is relayed. This is how neurotransmitters and neurons work in relaying any kind of information.

1.1 Neurons

Neurons are cells that processes and transmits signal either through chemical or electrical signals. The signals travel through the dendrites and then through the cell body called soma and ultimately through the axon. The axon can be myelinated or non-myelinated. The signals that travel are in the form of pulses called action potentials and have amplitude in the range of millivolts (mV).

1.2 Synapse

The synapse is the gap between two adjacent neurons. Also known as the synaptic cleft, here is where the neurotransmitters of the pre-synaptic neuron are released, to be received by receptors in the post-synaptic neuron. It is around 20 nm wide. The neurotransmitters usually take 1-2 ms to travel through the synapse.

1.3 Neurotransmitters

Neurotransmitters are the chemicals that are released into the synaptic cleft by the pre-synaptic neuron. These help in generating an action potential in the post-synaptic neuron after it binds with the receptors. The receptors allow specific ions viz-a-viz sodium (Na), potassium (K), chlorine (Cl), etc to enter or exit the cell membrane of the neuron, thus generating an action potential.

Neurotransmitters can be of two types–excitatory and inhibitory. Excitatory neurotransmitters help in the conduction of signal due to the action of external stimuli. It increases the probability of an action potential occurring in a post-synaptic neuron [1]. The inhibitory neurotransmitters inhibit the action of external stimuli. Examples of excitatory neurotransmitters are–Acetylcholine, Glutamate, Catecholamines etc. Examples of inhibitory neurotransmitters are–GABA, Dopamine, Glycine etc.

1.4 Generation of Action Potential

In a neuron, the inner side of the cell membrane is filled with potassium (K^+) ions whereas the outer side has sodium (Na^+) and potassium (K^+) ions, along with some other ions like chlorine (Cl^-). This makes the inner side of the cell membrane slightly negative as compared to the outside environment. The effect of other ions outside the cell can be neglected as its amount is negligible. At resting state, the sodium channels present in the membrane are closed whereas some potassium channels are open. Due to this, there is continuous influx of potassium ions into the cell. Thus a potential difference is generated between the inner and outer sides of the cell membrane. This is known as the resting potential and its value is almost -70 mV.

In case of excitatory neurotransmitters, when an external stimulus is applied, the sodium ion channels open.. Due to this there is influx of sodium ions into the cell membrane. This causes a change in the potential difference between the inner and outer environment of the cell membrane. The voltage changes from -70 mV to 30 mV, and after sometime it gradually stabilizes to -70 mV.

In the case of inhibitory neurotransmitters, on application of an external stimulus, the chloride ion channels open leading to an influx of chloride ions. This changes the potential difference between the two sides of the cell membrane. The voltage almost reaches -90 mV before stabilizing again at -70mV.

1.5 The H-H Model

Many experiments were performed on neurons to study its various functions and effects. The most popular being the Hodgkin-Huxley Model (H-H Model). Many research works

have been done based on it. The H-H model describes the membrane current that is quantitative and how it is applied to the conduction and excitation in nerve. Many electronic circuits have been developed, over the years, and are also being developed, to reproduce the behaviour of neurons [2]-[6].

In the H-H model, C_M denotes the membrane capacitance. The permeability of Potassium, Sodium, and other ions is given by g_K, g_{Na} and g_o respectively, which were found to be time dependent. E_K and E_{Na} represent the chemical potentials of Potassium and Sodium, as shown in Fig.1.

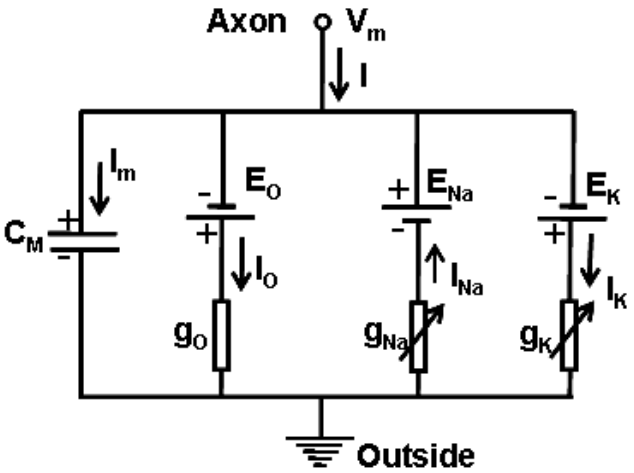


Fig. 1: H-H model

In this model the total current is given by:

$$I=I_m+I_o-I_{Na}+I_K \quad (1)$$

If the post-synaptic membrane potential is represented by V_m, then the capacitive membrane current and ionic current can be given as:

$$I=C(dV_m/dt)+g_o(V_m-E_o)-g_{Na}(V_m-E_{Na})+g_K(V_m-E_K) \quad (2)$$

Equations (1) and (2) are known as the H-H equations.

This work was performed to develop a model, based on the H-H model, using ENFET, which shows the individual effect of an excitatory neurotransmitter, an inhibitory neurotransmitter and the combined effect of both. For this work, two types of neurotransmitters were taken into consideration. For excitatory neurotransmitter, Acetylcholine was chosen, whereas for inhibitory neurotransmitter, GABA was chosen. The simulation of the work has been done in MATLAB environment.

2. MODELLING AND SIMULATION

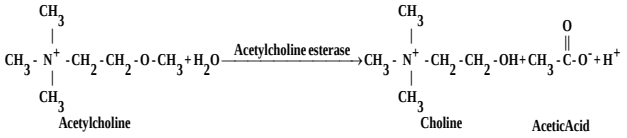
When the excitatory neurotransmitter, acetylcholine, is released from the pre-synaptic neuron, it diffuses through the synapse to bind with specific receptors - nicotinic acetylcholine receptors (AChR). This opens the sodium ion channels to allow the sodium ions to enter the cell. The threshold voltage required for an action potential to generate depends on the number of open channels. Thus an action potential will be generated when a sufficient number of channels are open.

The acetylcholine–receptor binding activity is governed by the following reaction:

$$2ACh + AChR(closed) \underset{K_2}{\overset{K_1}{\Leftrightarrow}} 2ACh - AChR(open) \quad (3)$$

Here K_1 is the forward and K_2 is the backward rate constants.

The reaction in the ENFET is in accordance with the following reaction based on the hydrolysis of acetylcholine in the presence of Acetylcholine Esterase (AChE):



(4)

In case of the inhibitory neurotransmitter, GABA, after its release from the pre-synaptic neuron, it also diffuses through the synaptic cleft and binds to specific receptors, called GABA receptors, present in the post-synaptic neuron.

When it reaches the post-synaptic neuron and it binds to specific receptors present there, the chloride ion channels open to allow the chloride ions into the cell. This results in a negative current which hyperpolarises the cell membrane and if sufficiently large number of chloride channels opens then an action potential will be initiated by the membrane potential in the negative direction [7].

The GABA molecules bind to a receptor to open the ion channels. The GABA–receptor binding activity is governed by the following reaction:

$$2GABA + GABA(R) \underset{K_2}{\overset{K_1}{\Leftrightarrow}} 2GABA - GABA(R)(open) \quad (5)$$

Here too K_1 is the forward and K_2 is the backward rate constants.

When Glutamate decarboxylase (GAD) is immobilised on the surface of gate oxide (Al_2O_3), the GABA sensitive ENFET can be prepared. The reaction follows the biocatalyzed hydrolysis of GABA.

$$2H_2O \rightarrow 2NH_4^+ + 2CH_3COO^- + C_4H_7O_2^- + H^+ \quad (6)$$

The proton generated in equations (4) and (5) brings about a change in the value of pH of the enzyme in the ENFET, which then changes the voltage. $V_{Th(IS)}$ is the threshold voltage of the ENFET, a function of pH of solution [8], is dependent on the concentration of acetylcholine or GABA. The conductance of

ENFET, for very small value of V_{ds}, which is the drain-to-source voltage of ENFET, can be expressed as:

$$G_{ds}=\beta(V_{gs}-V_{Th(IS)}) \quad (7)$$

Where β represents the geometric sensitivity parameter which can be expressed as

$$\beta=\mu C_{ox} W/L \quad (8)$$

here the oxide capacitance per unit area is given by C_{ox}, L and W are the length and width of the channel respectively. The channel electron mobility is represented by μ. Applied voltage to the reference electrode is V_{gs} and $V_{Th(IS)}$ is the threshold voltage of the ENFET. V_{gs} and β are constants and the only input variable in an ENFET is $V_{Th(IS)}$. Thus G_{ds} depends on the threshold voltage, $V_{Th(IS)}$, which is analogous to the ion channels conduction of post-synaptic membrane dependent on the binding activity. The acetylcholine or GABA sensitive ENFET can represent the neurotransmitter gated ion channels because of the changing conductance with respect to voltage.

Both acetylcholine-receptor binding activity and GABA-receptor binding activity are dependent on time and the number of transmitter gated ion channels that open will vary with time. $V_{Th(IS)}$ in equation (7) can be modelled as [7]-[9]

$$V_{Th(IS)}(t)=V_{THO}[1-\exp(k_1 t)+\exp(-k_2 t)U(t-t_m)] \quad (9)$$

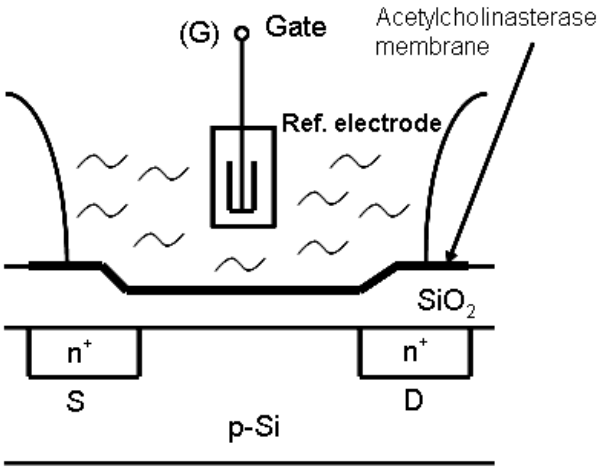


Fig. 2(a).

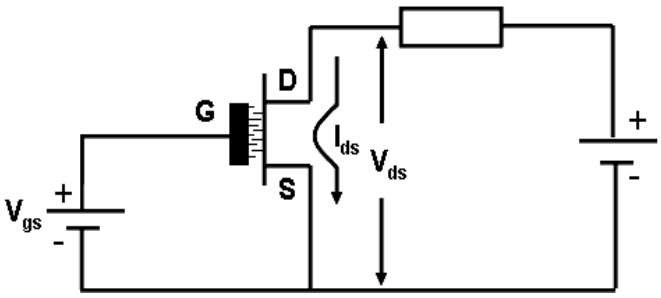


Fig. 2(b).

Fig. 2: ENFET (a)Schematic diagram (b)Electronic diagram

Here k_1 and k_2, the rate constants are analogous to the rate constants of equations (3) and (5). $U(t-t_m)$ is known as the Heaviside function. When all the sodium ions channels are open, $V_{THO,}$ the threshold voltage, is proportional to the maximum attainable conductance.

Fig. 3 and 4 shows the post-synaptic membrane circuit model in case of excitatory and inhibitory action. In Fig. 3, the excitatory action is only because of the sodium ion channels, hence to represent spatial summation of the sodium current controlled by g_{Na1}, g_{Na2} and g_{Na3}, the post-synaptic membrane is divided into three patches, where

$$I_{Na}=I_1+I_2+I_3 \quad (10)$$

So that, $I=I_m-I_{Na}+I_K$ =

$$C_m\frac{dV_m}{dt}-g_{Na}(V_m-E_{Na})+g_K(V_m-E_K) \quad (11)$$

Where g_{Na} is the total sodium conductance.

Similarly in Fig. 4, only chloride ion channels are responsible for the inhibitory action, hence to represent the spatial summation of the chloride current by g_{Cl1}, g_{Cl2} and g_{Cl3} which is the total chloride conductance, the post-synaptic membrane is divided into three patches.

$$I=I_m+I_{Cl}+I_K \quad (12)$$

$$=C_m\frac{dV_m}{dt}+g_{Cl}(V_m-E_{Cl})+g_K(V_m-E_K) \quad (13)$$

Where g_{Cl} is the total chloride conductance.

For both, g_K is the non-gated potassium conductance. V_{g1}, V_{g2} and V_{g3} are the voltages applied to the reference electrodes of the ENFETs.

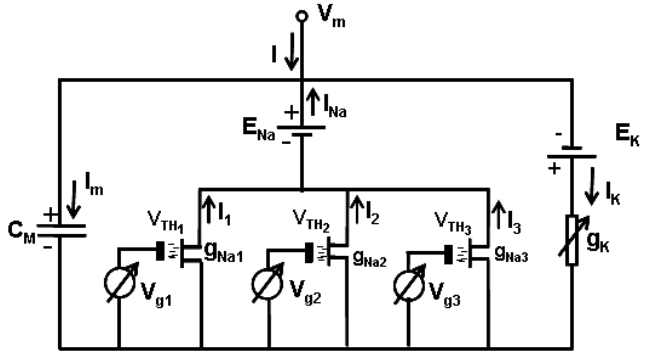


Fig. 3: Post-synaptic membrane circuit model for acetylcholine

The simulation was done in MATLAB environment, with the following the following values taken from the reference [9]: C_m=-90μF/cm^2, g_K=1ms/cm^2, E_{Na}=60mV, E_{Cl}=-100mV and

E_K=-90mV. I=0, L=15µm, W=2µm, t_{ox}=100nm, µ=600cm^2/V-sec. The exponential function parameters in equation (9) applied are: V_{THO}=-2Volts. t_m=600µsec, K_1 = K_2 = 1msec. The ENFETS gate-to-source voltage i.e. V_{g1}, V_{g2} and V_{g3} are kept constant at 1 volt each. The three, ENFET input parameters, namely V_{TH1}, V_{TH2} and V_{TH3} dependent on acetylcholine or GABA concentrations are applied at 1.5 msec intervals in a staggered sequence. It was done for the simulation of time variation in acetylcholine transmitter-receptor binding or GABA transmitter-receptor binding with respect to different patches of post-synaptic membrane.

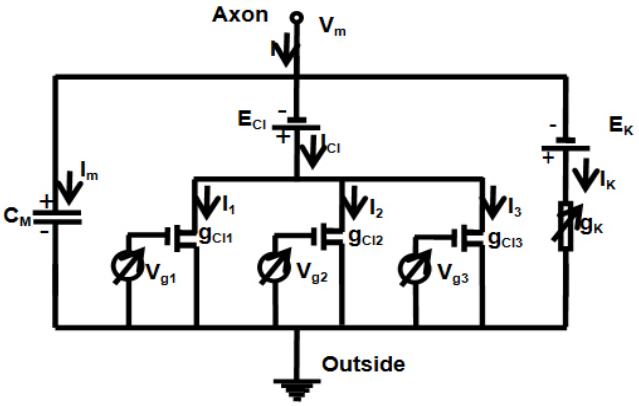


Fig. 4: Post-synaptic membrane circuit model for GABA

3. RESULTS

When the MATLAB simulation was done, the following outputs were observed. Fig. 5 is the waveform of an excitatory neurotransmitter. Here it can be seen that after the membrane potential exceeds the threshold value, an action potential is generated, which rises from around -70mV, peaks at about 35 mV and again settles down at -70 mV.

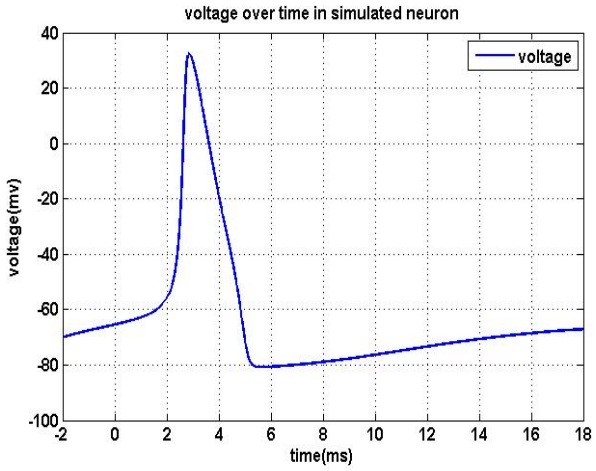


Fig. 5: Action potential of an excitatory neurotransmitter

Fig. 6 shows the action of an inhibitory neurotransmitter. Here the response is negative, as expected, from an inhibitory neurotransmitter. The initial potential is at about -70mV. An excitation pulls the potential down to around -90mV. After sometime the potential again comes back to its resting potential.

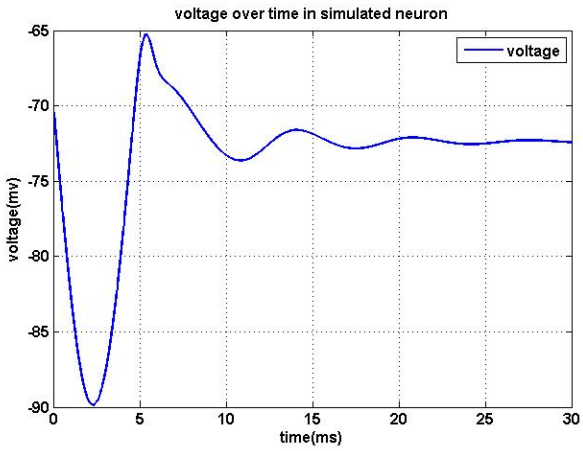


Fig. 6: Action potential of an inhibitory neurotransmitter

Fig. 7 is the result of the combined effect of an excitatory neurotransmitter and an inhibitory neurotransmitter. The combined effect shows that the excitatory effect is more than that of inhibitory. It is similar in shape as that of the action potential of an excitatory neurotransmitter.

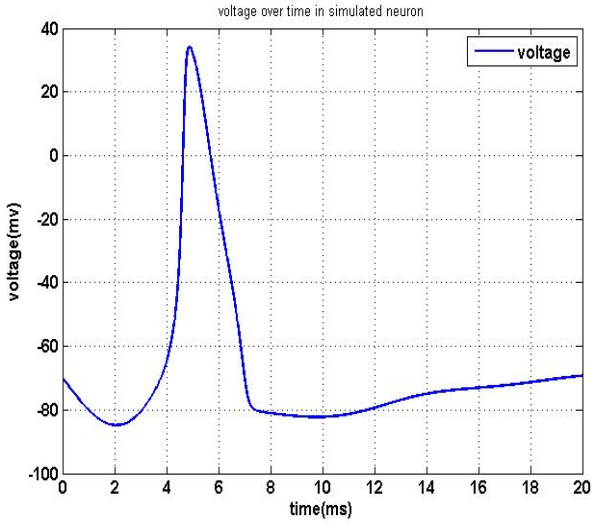


Fig. 7: Action potential of the combined effect of excitatory and inhibitory neurotransmitter

4. CONCLUSION

The aim of the work was to show how an excitatory and an inhibitory neurotransmitter generate an action potential in a circuit based environment using ENFETs which shows an analogy to the actual process. The combined effects of both

were also studied. The ENFET based circuit model is a biologically motivated model which can be used in research work and as a teaching unit in neurology and related areas of interest and also in bioelectronics.

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