Dynamic Range Analysis of HH Model for Excitable Neurons

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ABSTRACT

Brain exercises control over other organs of the body. This complex control process, is completed in steps which involves commands issued to the muscles to execute movements, receipt of feedback from sensors reporting the actual state of the musculature & skeletal elements, and inputs from the senses to monitor progress towards the goal. This is made possible by neurons through communicating with each other. Neurons are cells specialised for transmitting and receiving information. Exchange of information between neurons is either in the form of chemical or electrical signals. Electrically information is conveyed in the form of neural electrical signal know as action potential. Hodgkin and Huxley conducted Voltage Clamped experiments to study mechanism for generation and propagation of action potential in giant Axon of Squid and proposed a simple mathematical model known as HH model. Since information is conveyed through time and frequency of action potential, dynamic range becomes an important criterion for analysis. This paper analyse the dynamic range of the HH model through simulation, for its ability to convey information within and between neurons for effective control by brain over other organs.

Keywords

Neuron, Information, Action potential, Voltage clamp, Dynamic range.

1. INTRODUCTION

1.1 The Neuron

Brain acts as the center controlling organ of the nervous system in all vertebrate and most invertebrate animals. A typical human cerebral cortex which is the largest part of the brain, is estimated to contain 15–33 billion nerve cells or neurons, each one is connected by synapses to thousands of other neurons. The human brain is expected to contain on the order of 100 billion neurons. Each neuron "typically" receives ten thousand inputs from other adjoining neurons, but this number may vary widely across neuron types [1]. Neurons communicate with each other by means of electrical signal passing through long protoplasmic fibers known as axons, which carry trains of signal pulses called action potential to distant parts of the brain or body targeting specific recipient neuron or other cells. Neurons are similar to other cells in most of structural aspects, but there is one major difference between neurons and other cells [2]. Neurons are specialized cells meant to transmit and receive information throughout the body. These highly specialized nerve cells are responsible for communicating information in both chemical and electrical forms. There are several different types of neurons responsible for various tasks in the human body. For

example sensory neurons carry information from sensory receptor cells throughout the body to the brain, where as motor neurons transmit information from the brain to other muscles of the body. Responsibility of communicating information between different neurons in the body is of inter neurons.

Neurons have a membrane called axon, which connects it to other neurons and is designed to sends information to other nerve cells [3]. The axon as well as dendrites is also specialized structures of neuron designed to transmit and receive information. The connections between neighboring cells are known as synapses. Neurons release chemicals known as neurotransmitters into these synapses in order to communicate with other connected neurons in the body. Basic neuron structure is shown in Fig 1.
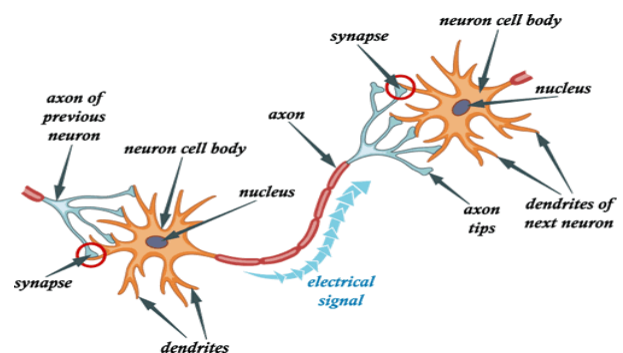

Fig 1: Basic Neuron Structure (helcohe.com/sse/body/neuron)

1.2 Neural Communication and Action Potentials

In order to communicate with each other, neuron needs to transmit information both within the neuron and from one neuron to the other. This process makes use of both electrical signals and chemical messengers [1], [3]. The dendrites receive information from sensory receptors or other neurons in the body. This information is then passed to the cell body and on to the axon. Once the information has arrived at the axon, it travels through the length of the axon in the form of an electrical signal, which is known as action potential [4]. An action potential is an explosion of current caused due to depolarization of its membrane and this current travels along the cell. For an action potential to occur, the depolarization must cross a minimum threshold voltage. Action potentials are generated as an 'all-or-none' response only. This means that action potentials do not vary in size or amplitude and will

not occur if specific threshold voltage is not reached. Action potential can be described as a short-lasting event where the electrical membrane potential of a cell rapidly rises and falls, following a consistent trajectory on each occurrence.

1.3 Historical Perspective

The conception that information is conveyed by sequences of action potentials or spike trains has resulted from more than 100 years of neurophysiologic investigations [5], [6]. It involves both aspects, one is the relation of action potentials to behavior, and another is an explicit, detailed understanding of how action potentials generates and propagates. The latter is the triumph of the Hodgkin-Huxley model. Some of the findings on time line are as follows-

Signals are transmitted from one neuron to another across synapses (Sherrington, 1897).

Action potentials are not graded in intensity; they are "all or nothing" (Adrian, 1926).

Substantial information is contained in the neuronal firing rate (Adrian, 1926; Hubel and Wiesel, 1962; Evarts, 1966).

Action potentials result from the flow of ions across excitable membranes. Membranes can be electrically excitable (Bernstein, 1902; based on Nernst, 1888).

Ion channels gate the flow of ions across membranes (Cole and Curtis, 1939).

Sodium ions (in addition to potassium ions) are involved in action potential generation (Hodgkin and Katz, 1949).

Action potential generation may be described quantitatively using voltage-current-capacitance relationships, and voltage-dependent conductances of distinct ions (Hodgkin and Huxley 1952)

Successes of Hodgkin-Huxley Model can be termed as solution of 150-year-old problem of "animal electricity". The model could do correct predictions of conductances, form of action potential, including it's "undershoot" [4]. Their model, which was developed much before the advent of electron microscopes and computer simulations, was able to give scientists a basic knowledge of how nerve cells work without having a detailed understanding of how the membrane of a nerve cell actually looked like on the micro scale. They even did not know about the existence and structure of ion channels and ion pumps in the membrane.

2. HH MODEL

The Journal of physiology in 1952 published a series of papers that would forever change the relationship between mathematics and physiology [7]. Alan Lloyd Hodgkin and Andrew Huxley authored a series of five papers describing the set of nonlinear ordinary differential equations that model how action potentials can be initiated and propagated through an axon. The Hodgkin-Huxley model for the generation of the nerve action potential is regarded till date as one of the most successful mathematical models of a complex biological process that has ever been formulated.
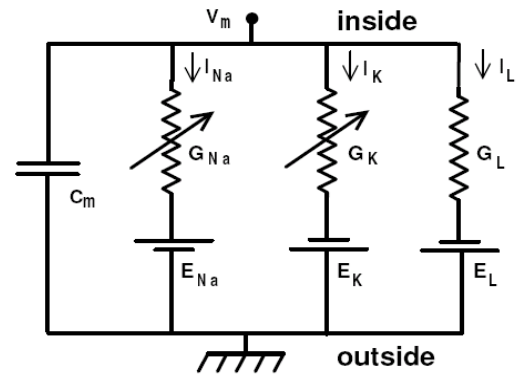

Fig 2: Equivalent electrical circuit of HH Model

The starting point of the HH model is an equivalent electrical circuit of a cellular compartment. There were three types of ionic current in the circuit as shown in Fig 2, sodium current, I_{Na}, a potassium current, I_K, and a current that Hodgkin and Huxley described as the leak current, I_L, which was assumed mostly made up of chloride ions [7]. The sodium and potassium conductances are variable and depend on voltage across the membrane. Since their properties change with the voltage across the membrane, they are treated as active rather than passive elements [8-11]. The voltage-dependence of ionic conductances is incorporated into the HH model by assuming that the probability for an individual gate to be in the permissive or non-permissive ie open or closed state depends on the value of the membrane voltage. The current equation that corresponds to the equivalent electrical circuit is

$$I = I_c + I_i = C_m \, dV/dt + I_i \qquad (1)$$

The total ionic current Ii is the sum of sodium, potassium and leak currents

$$I_i = I_{Na} + I_K + I_L \qquad (2)$$

The magnitude of each type of ionic current is calculated from the product of the ion's driving force which is the difference between the membrane potential and the equilibrium potential of that ion, and the membrane conductance for that ion. For example the sodium driving force is $(V - E_{Na})$ and sodium current is $g_{Na}(V - E_{Na})$

$$I_{Na} = g_{Na}(V - E_{Na}) \qquad (3)$$

$$I_K = g_K(V - E_K) \qquad (4)$$

$$I_L = g_L(V - E_L) \qquad (5)$$

Where the sodium, potassium and leak conductances are g_{Na}, g_K and g_L respectively and E_{Na}, E_K and E_L are the corresponding equilibrium potentials. In the final paper of the series, Hodgkin and Huxley inserted their expressions for the three ionic currents into the membrane equation to give a description of how the membrane potential in a small region of squid giant axon changes over time:

$$C_m \, dV/dt = -G_L(V - E_L) - G_{Na} \, m^3 h \, (V - E_{Na}) - G_K \, n^4 \, (V - E_K) + I \qquad (6)$$

Where, I is the local circuit current, the net contribution of the axial current from neighboring regions of the axon. When this equation is put together with the differential equations for the gating variables *n*, *m* and *h* and the expressions for the rate coefficients, the resulting set of four ordinary differential equations forms the HH model.

Complete Hodgkin–Huxley model is described by following equation for the membrane current by summing up various currents in the membrane, including spatial spread of current from local circuits:

$$Cm\ \partial V/\partial t = -G_L\ (V-E_L) - G_{Na}\ m3h\ (V-E_{Na}) - G_K\ n4\ (V-E_K) + d/4Ra*\ \partial^2 V/\partial x^2$$

Under space clamp conditions there will be no axial current and the last term in the above equation will be zero, thus final current equation will be

$$Cm\ dV/dt = -G_L\ (V-E_L) - G_{Na}\ m3h\ (V-E_{Na}) - G_K\ n4\ (V-E_K). \qquad (7)$$
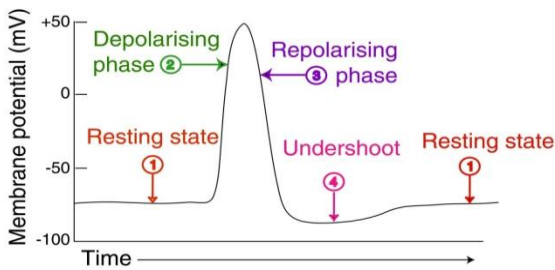

Fig 3: A typical waveform of action potential

3. METHOD AND MATERIAL

A simple neuron of original HH model equations was simulated and tested for generation of action potential [12, 13]. Simulation is done using Matlab 2012 A [14]. Dynamic range was obtained and studied by varying excitation current up to 100 micro amps. Following parameters of HH model were used for simulation [1].

$$\alpha_n = 0.01(v+10)/(\exp((v+10)/10)-1) \qquad (8)$$

$$\alpha_m = 0.1(v+25)/(\exp((v+25)/10)-1) \qquad (9)$$

$$\alpha_h = 0.07\exp(v/20) \qquad (10)$$

$$\beta_n = 0.125\exp(v/80) \qquad (11)$$

$$\beta_m = 4\exp(v/18) \qquad (12)$$

$$\beta_h = 1/(\exp((v+30)/10)+1) \qquad (13)$$

$C_m=1.0\mu\ F\ cm^{-2}$ and I in $\mu\ Amp\ cm^{-2}$

$G_{Na}=120.0\ mScm^{-2}$, $G_K=36.0\ mScm^{-2}$, $G_L=0.3\ mScm^{-2}$

$V_{Na}=-115.0\ mV$, $V_K=12.0\ mV$, $V_L=-10.5989\ mV$

Dynamic range is taken as ratio of maximum frequency to minimum frequency of action potential generated by the model with variation of excitation current. The current is varied from 0 to 100 micro amps and current frequency curve was plotted to study and analyse the dynamic range of excitable neuron represented by HH model.

4. RESULTS

Simulation was done for simple model using equations (7-13) of HH model and tested for ability to generate action potential and to study gating behavior. Fig 4 shows the results of simulation for original HH model. The HH model generates action potential with depolarisation lasting for one m sec and action potential pulse reaches its minimum voltage in three m secs as a result of repolarisation this is followed by prolonged refractory period. It is observed that with increase in excitation current the inter spike interval reduces and the frequency of action potential increases. Initial conditions for m, n and are chosen to be in the middle of their range 0-1 that is 0.5. Their variation with time is plotted in Fig 4 (B). Spike train simulation Fig 4 (c) indicates frequency of approx 70 Hz at excitation current of 10 micro amps.
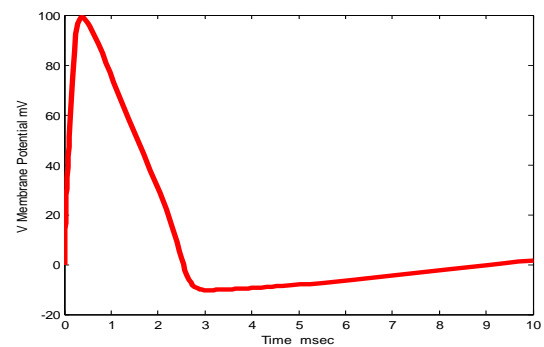
(A)
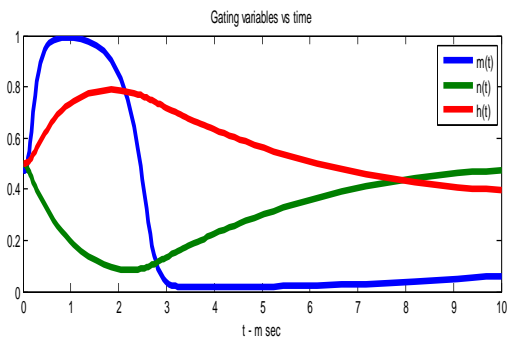
(B)
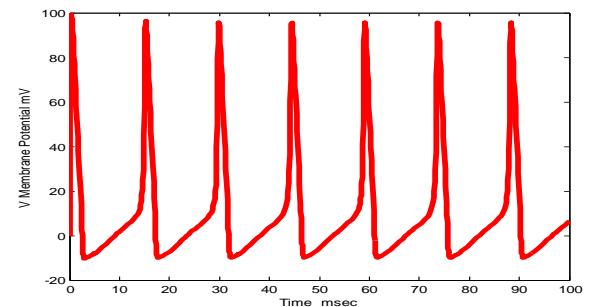
(C)

Fig 4: Simulation of HH model at I=10 µ Amp/Cm² (A) Action potential (B) Gating particle behavior and (C) Spike train
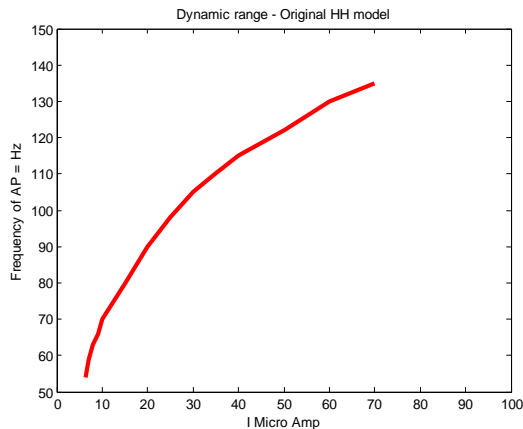
Fig 5: IF curve for HH model

Fig 5 gives current frequency curve for the model. HH model has current threshold of 6.3 micro amps which means below this value of excitation current the model is not able to generate regenerative action potential. At threshold current the frequency of action potential is 54 Hz, which increases as the current is increased. At 70 micro amps the frequency attained is 135 Hz. For excitation greater than 70 micro amps, the model is not able to generate any sustained action potential for excitation currents beyond 70 micro amps. Thus it can be said that original model exhibits frequency range from 54 to 135 Hz that translate in to dynamic range of 2.5.

5.   CONCLUSION

HH neuron generates action potential of frequency from 54 Hz to 135 Hz. Dynamic range exhibited by neuron represented by HH model is 2.5. Since information conveyed depends on time and frequency of action potential thus better dynamic range is desirable [15].

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