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Minimizing the Hodgkin-Huxley Model

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Abstract

Memristor (memory resistor) is a passive electrical circuit element whose instantaneous resistance depends not only on the voltage, but the history of the current applied to it. The first memristor was fabricated in 2008 by the HP labs in a semiconductor titanium-dioxide thin film. Apart from its potential for high-density memory storage, the electrical properties of a memristor share similarities with those of ion channels in biological membranes including axons. The electrical response of an axon is traditionally modeled using Hodgkin-Huxley equations. The purpose of this research is to investigate the characteristics that are required to mimic the spiking response of a neuron. We introduce a minimal Hodgkin-Huxley model for steady state stimulus in which the leakage channel, membrane capacitance, and potassium and leakage equilibrium voltages are absent. Our results show that the potassium and sodium ion channels, individually, are essential for action potential; they also show that the generation of action potential requires more than one type of ion channels. Thus, our research sheds light on the feasibility of creating artificial axons (and neural networks) with thin-film memristors.

Keywords: Memristor, Voltage-gated Ion Channels, Hodgkin-Huxley Model

1. Introduction

Neurons are highly specialized for generating electrical signals in response to chemical stimulus and transmitting them to nearby cells. A single neuron consists of soma, an axon, and axonal terminals. Surrounding the soma, cell body, are few tentacle-like branches known as dendrites. Dendrites are essential for receiving signals from other cells. In response to a stimulus, a short term change in electrical potential occurs on the surface of the axon, known as action potential. At the axonal terminal, the electrical signal is converted to chemical signal and is passed to the nearby neuron. [1]

The surface of the axon consists of sodium, potassium, and leakage voltage-gated ion channels that regulate the passage of ions between the inside and the outside of an axon. The imbalance of ionic concentrations between the intracellular fluid and extracellular fluid causes ions to move through their respective voltage-gated ion channels causing a change in potential. When the neuron is depolarized, sodium channels open and sodium ions enter the axon. As a result, the inside of the axon becomes more positive than the outside of the axon which causes potassium channels to open. The movement of potassium ions out of the axon is known as repolarization.[2] Fig. 1 shows a graphical representation of action potential with different phases that resulted from movement of ions.

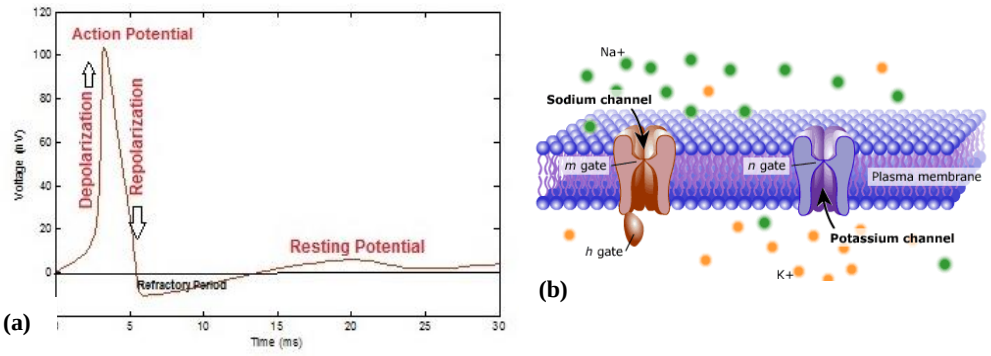

Figure 1. Action potential and axonal membrane

Figure 1. (a) A graph of action potential at applied current of $5\,\mu A/cm^2$. During depolarization phase, sodium enters the axon. During repolarization phase, potassium channel opens and potassium exits the axon. Refractory period is when action potential cannot be initiated. (b) Potassium and sodium voltage-gated ion channels on the membrane of an axon.[3] The green dots represents the sodium ions, most of them are located outside of the axon. Yellow dots are potassium ions, largely distributed within the axon.

In 1952, Alan Hodgkin and Andrew Huxley introduced a scientific model that established that cell membrane behaves similar to an electric circuit (Fig. 2). The capacitor represents the phospholipid bilayer which accumulates charge as action potential, or spikes, occurs. The sodium, potassium, and leakage channels are analogous to variable resistors. The driving force of the ions is donated by the battery symbol.

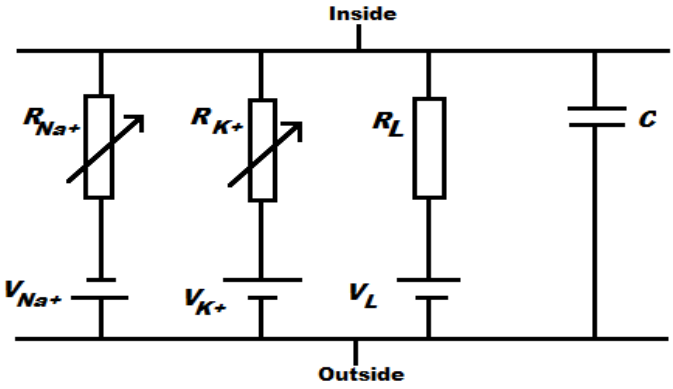

Figure 2. Hodgkin-Huxley electrical circuit model

Figure 2. The electrical circuit model describing the time-dependent action potential. The ionic channels are denoted by resistor, ***R,*** batteries are represented by ***V***, and ***C*** is the capacitor. This model was originally developed for a squid giant axon, remains the standard for computational neuroscience today.[4]

In the Hodgkin-Huxley model, the ionic resistances are arranged in parallel and they assume to obey Ohm's law. Note that in the Hodgkin-Huxley model (Fig. 2) the measurements are made per unit area which has dimensions of cm^2. The membrane potential is given by

$$C\frac{dv}{dt} = I_{app} - I_{ion} \tag{1}$$

where C is membrane capacitance per cm^2, $I_{app}$is the applied current per cm^2, and I_{ion} is the total ionic current which consists of contributions from individual ion species:

$$I_{ion} = g_K(v - v_K) + g_{Na}(v - v_{Na}) + g_L(v - v_L). \quad (2)$$

In equation (2), $g_K, g_{Na},$ and g_L are potassium, sodium, and leakage conductances, inverse of resistances. The sodium and potassium conductances depend on activation and inactivation gates. Flow of the ions through the channels depends on the gates. The great discovery of Hodgkin-Huxley was to realize that potassium conductances depends on four activation gates,

$$g_k(t) = G_k n^4, \quad (3)$$

and sodium conductance depends on three activation gates and one inactivation gate,

$$g_{Na}(t) = G_{Na} m^3 h. \quad (4)$$

In equations (3) and (4), *m* is the activation variable of sodium channel and *h* is the inactivation variable of sodium channel. *n* is the activation of the potassium channel.[2,4,5] The following equations (5)-(13) defines *m*, *n*, and *h* along with corresponding α and β.[5]

$$\frac{dm}{dt} = \alpha_m(V)(1 - m) - \beta_m(V)m, \quad (5)$$

$$\frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V)n, \quad (6)$$

$$\frac{dh}{dt} = \alpha_h(V)(1 - h) - \beta_h(V)h, \quad (7)$$

$$\alpha_m(V) = 0.1\frac{25 - V}{\exp\left(\frac{25 - V}{10}\right) - 1}, \quad (8)$$

$$\beta_m(V) = 4\exp\left(\frac{-V}{18}\right), \quad (9)$$

$$\alpha_n(V) = 0.01\frac{10 - V}{\exp\left(\frac{10 - V}{10}\right) - 1}, \quad (10)$$

$$\beta_n(V) = 0.125\exp\left(\frac{-V}{80}\right), \quad (11)$$

$$\alpha_h(V) = 0.07\exp\left(\frac{-V}{20}\right), \quad (12)$$

$$\beta_h(V) = \frac{1}{\exp\left(\frac{30 - V}{10}\right) + 1}, \quad (13)$$

These parameters, provided in the original Hodgkin-Huxley paper, works well with Hodgkin-Huxley experiment on squid giant axons. However, it is not known where do they come from nor what are the flexibilities of them.

2. Research Problem

In 1976, Leon Chua stated that time-varying conductances, whose variations are functions of first-order differential equations, are actually memristive systems. "In particular, potassium channel of the Hodgkin-Huxley should be identified as a first-order time-invariant, voltage controlled memristive one-port and the sodium channel should be identified as a second-order time invariant voltage controlled memristive one-port."[6] The sodium and potassium channel conductance variations are functions of first order-differential equations and they depend on steady-state values, $m, n,$ and, h. The purpose of this research was to study the characteristics- the input and the output response, state variable dependence, and the current voltage dependence of the channels- that are shared between the biological membrane and memristors. Our research focus on understanding which components of the Hodgkin-Huxley model are necessary to develop a memristor based action potential model.

3. Methods

We solved the Hodgkin-Huxley equations by using a MATLAB code with fourth-order Runge-Kutta method. The Runge-Kutta method, named after two German mathematicians, solves the first-order differential equations by finding the numerical approximation to the solutions.[7] By varying the parameters of ionic conductances, batteries, and equilibrium potentials, we develop an understanding of the Hodgkin-Huxley model and the minimum parameters that are essential for action potential.

We used eliminating method to reduce the Hodgkin-Huxley model (H-H) to a minimal H-H model. First, we eliminated ionic conductances, one-by-one, and examine if action potential still occurs. In certain case when action potential did not occur we concluded that certain conductance is necessary for spiking. Next, the capacitor was gradually reduced while continuously examining the action potential. Lastly, equilibrium potentials were reduced to values that are necessary for action potential.

4. Results

By using the eliminating method we introduce a minimal Hodgkin-Huxley model, shown in Fig. 4, in which leakage channel, leakage equilibrium potential, and potassium equilibrium potential are absent. The value of capacitor is $10^{-2.99}\ \mu F/cm^2$-a value significantly small that capacitor is negligible and therefore is not included in the minimal H-H model. Furthermore, V_{Na} can be reduced to 78 mV from 115 mV. The minimum current required for the minimal H-H model is $5.3\ \mu A/cm^2$. This model preserves the qualitative features of original Hodgkin- Huxley model.

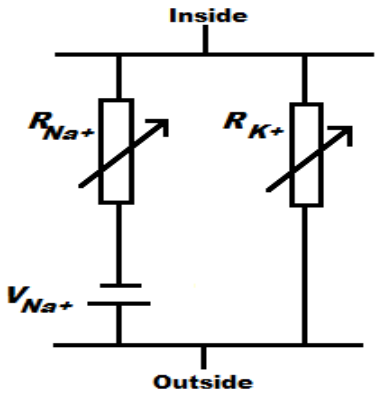

Figure 4. Minimal Hodgkin- Huxley Model

Figure 4. Minimal Hodgkin-Huxley model consists of sodium and potassium resistors and sodium equilibrium potential. These three components of the original Hodgkin-Huxley model are essential for action potential.

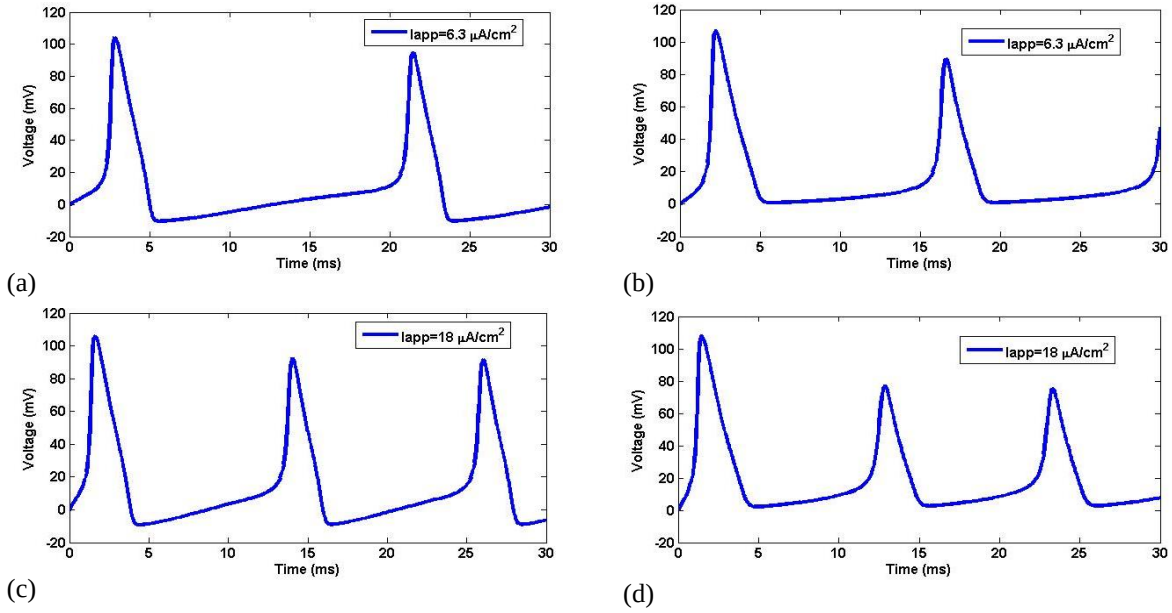

Figure 5. Compares the output response of the original Hodgkin- Huxley model and minimal Hodgkin-Huxley model. (a) and (c) represents the original H-H model and (b) and (d) shows the response of the minimal H-H model.

In Fig. 5, we compare the action potential response for the two models. Fig. 5a and 5c are for the original H-H model and Fig. 5b and 5d are for the minimal H-H model. The input current for the Fig. 5a and 5b is $6.3\,\mu A/cm^2$ and in Fig. 5c and 5d it is $18\,\mu A/cm^2$. These results show that the two models have similar qualitative behavior. Although, in minimal H-H model frequency is slightly increased and the peak voltage for the second and third spikes, have decreased, but the overall behavior of the action potential remains the same.

As the input current is increased by a factor of three, Fig. 5c and 5d, the total number of spikes in the original H-H is three, which is same as the number of spikes in the minimal model. Additionally, the peak voltage of the action potential in H-H model is close to the sodium equilibrium potential, 115 mV, and the minimum value for the potassium equilibrium potential is -12 mV. Similarly, the maximum value of voltage in the minimum H-H model is

approximately 115 mV, which is the value of V_{Na} in the Fig. 5b and 5d, and the minimum voltage is 0 mV, V_K. These results suggest that the minimal H-H model and original H-H model give analogous results.

The minimal model is valuable because it only includes the parameters that are necessary for spiking. This model is useful for understanding what is needed to mimic the behavior of an axon. It does not replace the original H-H model; its job is to help us understand what are the key mechanisms of H-H model that give rise to action potential.

In the H-H model, the presence of a sodium and a potassium channel per area of cm^2 are necessary. When two sodium channels are connected in parallel, instead of a potassium and a sodium channel, spiking does not occur. Similarly, two potassium channel per cm^2 will not give spiking.

Addition to minimizing the Hodgkin-Huxley model, we also studied the effect of increasing the number of channels per square-centimeter on action potential. We did that by multiplying the sodium and potassium currents in equation (2) by a constant. Increasing the number of channels is the same as increasing the conductances by the same factor. For instant, if there are two sodium channels per square-centimeter then twice the conductance, $2g_{Na}$, will give the same results. Our results show that for sodium, increasing the number of channels will decrease the minimum current needed for spiking. For two sodium and one potassium channel in parallel, the input current required for spiking is $-0.99\ \mu A/cm^2$, whereas for one sodium and one potassium channel it is $6.3\ \mu A/cm^2$. In case when only the numbers of potassium channels were changed while keeping the sodium channel to one, spiking does not occur. However, if the numbers of potassium channels are decreased below one (but above $0.08\ \mu A/cm^2$) spiking occurs and minimum current needed for action potential decreases. Lastly, when both the potassium and sodium channels are increased by same factor, spiking occurs.

5. Conclusion

The minimal Hodgkin-Huxley model plays a crucial role in understanding which mechanism are necessary for modeling an axon from semiconductor memristors. Our results show that a single memristor or single-type of memristors will not reproduce the spiking response of a neuron. Therefore, at least two types of memristors are required to mimic the electrical response of a neuron.

6. Acknowledgments

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