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DYNAMIC OF NEURONAL MEMBRANE USING A NUMERICAL MODEL

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Abstract: The Hodgkin and Huxley model describes the electrophysiology of the membrane of the giant squid's axon. This model was developed from measurements of passive and active electrical behavior of the nerve cell. The four-coupled nonlinear ordinary differential equations, which describe the model, are based on the behavior of sodium and potassium channels. The aim of this work is to study the dynamic behavior of a neuronal physiological system described by the Hodgkin-Huxley (H-H) model through the analysis and interpretation of numerical simulations.

keywords: Modeling, Numerical Simulation and Optimization, System Biology, Time Series Analysis, H-H model, Nerve cell.

1. INTRODUCTION

The physiological process of action potential generation occurs from ions exchange of the extracellular environment to the intracellular neural cell. This process can be analyzed in three distinct phases: depolarization, repolarization and the resting [2] (see Figure 1).

At first, the cell is resting, polarized in a transmembrane potential known as equilibrium potential. In depolarization phase, the membrane has an increased permeability of cations sodium allowing a large number of these ions to diffuse into to cell interior via a simple diffusion, initiating depolarization phase [2-3]. This phenomenon causes the intracellular reverse potential in relation to the rest, being positive. At this point the cell may or may not reach the threshold required for the propagation of the action potential (+30 mV). If it reaches or exceeds this value, an electrical impulse caused by the potential difference will give rise to action potential to be transmitted to the axon.

In repolarization phase occurs the inactivation of sodium channels and activation of potassium channels. Thus sodium will not in the cell and potassium flows into the extracellular medium, reestablishing the resting values of membrane potential. At first, there is a hyperpolarization of the membrane, where it is more negative than the resting values, but gradually the potential of the membrane resumes its resting values.

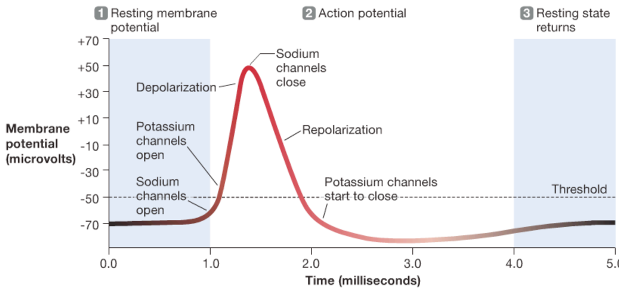

Figure 1 – Action potential
Extracted of <https://www.studyblue.com/#flashcard/flip/5779033>

During the hyperpolarization phase, the cell experiences a period called refractory period. During this period the cell does not respond to the stimuli, regardless of the intensity of the stimulus.

It is important to note there are more than two ions that assist in the process action potential, but they have much less interference values than the main ions. These ions are represented in the H-H model by pouring ion (vaz) [2].

The work aims to evaluate the dynamic behavior of a neuronal physiological system through a numerical model of Hodgkin Huxley equations (H-H model) that simulates transmembrane potential for different stimuli.

2. THE HODGKIN-HUXLEY MODEL

The H-H model, compose by the equations

$$I = Cm\,{}^{dVm}/_{dt} + \bar{G}_{Na}.m^3.h.(Vm - E_{Na}) + \bar{G}_k.n^4.(Vm - E_k) + G.(Vm - E_{vaz}) \quad (1)$$

$$^{dm}/_{dt} = \alpha m(1-m) - \beta m.m \quad (2)$$

$$^{dh}/_{dt} = \alpha h(1-h) - \beta h.h \quad (3)$$

$$^{dn}/_{dt} = \alpha n(1-n) - \beta n.n \quad (4)$$

describes the action potential by non-linear and coupled differential equations. These equations relate the conductance of ions through the respective currents variable activation and inactivation of sodium channels, potassium and leakage (m, n, and h).

Equation (1) relates the capacitance and the membrane potential (Cm and Vm) with the respective potential balance for sodium, potassium and leakage of ions (E_{Na}, E_k and E_{vaz}). The variables m, n and h were experimentally determined and related to the number of particles involved in controlling the conductance. Equations (2), (3) and (4) relate to the α's and β's coefficients, which are functions dependent on Vm determined experimentally to represent the transition rate from state variables of the channels condition activated to inactivated and vice versa [2].

The above set of equations forming the H-H mathematical model for an action potential (AP) neuron.

3. RESULTS

The action potential simulations were performed with the Matlab software and the results to different stimuli are presented and discussed below.

In Figure 1 the stimulus applied is 5 μA/cm^2 between 30 and 32 seconds. We can see the potential shows a behavior governed by the conductance to sodium ions (m), potassium (n) and the inactivation of sodium (h).

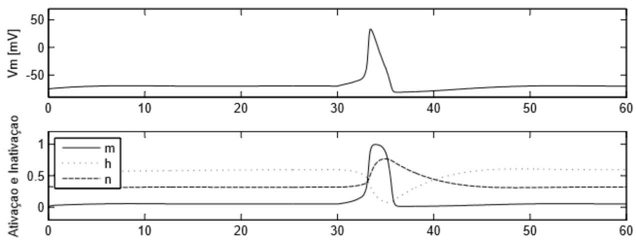

Figure 1 – Above is behavior of action Potential in three distinct moments. Below is behavior of the conductance as a function of sodium channels activation parameters (m), potassium (n) and inactivation of sodium (h).

In Figure 2, a stimulus of 2 uA/cm^2 is applied between instants 30 to 32 seconds. Differently from Figure 1, there is not the curve of AP, but it is possible to observe a slight change in the conductance curves.

Figure 3 shows behavior of a cell that received two stimulations (2 μA/cm^2 between 20s < t < 22s and 3.7 μA/cm^2 between 30 < t < 32s) , but it does not generate any AP. We can observe the "almost" spreading potential and conductance that generated between 30 < t < 40s. It is important to note that there was a change of potassium sodium channels, but not enough to reach the threshold value.

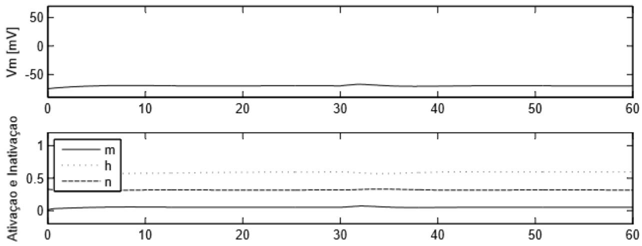

Figure 2 - Above is no threshold potential behavior. Below is the behavior of the conductance as a function of sodium channels activation parameters (m), potassium (n) and inactivation of sodium (h).

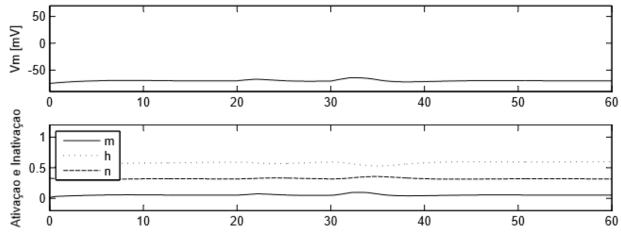

Figura 3 - Above is no threshold potential behavior in two distinct moments. Below is behavior of the conductance as a function of sodium channels activation parameters (m), potassium (n) and inactivation of sodium (h).

Figure 4 shows the situation where two stimuli are applied, with the first between 20 < t < 22s with a lower stimulus value than is necessary for an action potential (3 μA/cm^2) and the second stimulus is applied between 30 < t < 32s sufficient to reach the threshold value (5 μA/cm^2).

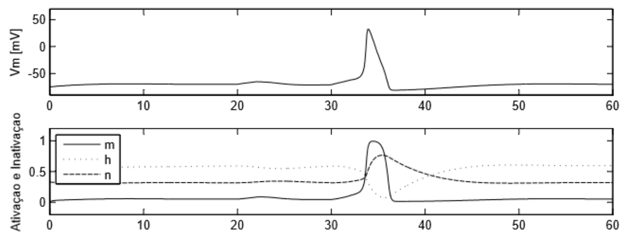

Figura 4. Above is action aotential of behavior in two distinct moments. Below is behavior of the conductance as a function of sodium channels activation parameters (m), potassium (n) and inactivation of sodium (h).

To exemplify the refractory period (Figure 5), two stimuli are applied in sufficient values to reach the threshold value for obtaining an AP. However the time between stimuli was small, i.e, the cell was on the refractory period, and thus it was not possible to obtain an action potential.

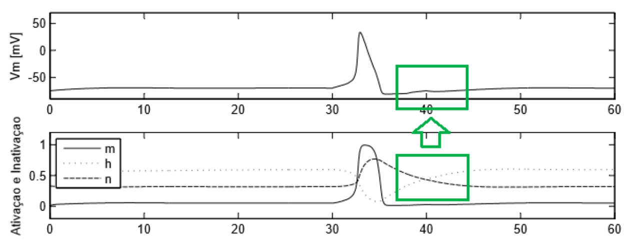

Figura 5. Above is action potential of behavior in two distinct moments. Below is behavior of the conductance as a function of sodium channels activation parameters (m), potassium (n) and inactivation of sodium (h) .

The situation marked by the green rectangle is the second stimulus. It is possible to observe that there is change in conductance, but no trace of potential due to the refractory period.

4. FINAL DISCUSSIONS

This paper presented results of numerical simulation of BP neuronal membrane through the H-H model.

To exemplify and illustrate the model potentials were generated different numerical tests with the aim to illustrate different situations such as when a stimulus is given and it is enough to open the ion channels at the point of the potential difference reach, or even exceed, the value threshold generating an action potential, as seen in Figure 1; and when a stimulus is given and it is not enough to open the ion channels not reaching the threshold value of the potential difference to generate an action potential as exemplified in Figure 2.

When a stimulus is given to an amount sufficient to reach the threshold value triggering an action potential, but when given in sequence, with a very small time interval to the next stimulus, there is no result, since the cell is in its refractory period. It may be noted that there is a change in conductance, but they mean nothing to the cell that is inactive to other stimuli in a given time, as shown in Figure 5.

Based on the results it was concluded that the model responds appropriately to the expected results for the actual neuronal membrane.

The analysis of stimulus values and the action potential itself characterize the research in biophysics area, i.e., reach the biological sphere. Therefore, all this study aims to understand the points which a person can have any shortfall. For example, anyone with some motor problem may have deficiency in sodium and potassium channels, not triggering the PA and the transmission of electrical pulse to reach the receiver, or even present deficiency in the refractory period duration and several other problems involved in this framework. Therefore, these studies increase the horizons diagnoses motor problems.

With the results and conclusions obtained by this stage of the project , we have as next objectives to obtain the intensity x duration curve for the values of stimulatory pulses, determining points of chronaxie and rheobase by Weiss-Lapicque equation, and obtaining the variation the transmembrane potential necessary to generate an action potential, in addition, calculating the absolute and relative refractory period .

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