ON NON-LINEAR DYNAMIC BEHAVIOR OF THE HODGKIN-HUXLEY MODEL

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Abstract. *The Hodgkin-Huxley model was developed to characterize the action potential of a squid axon. It has served as an archetype for compartmental models of the electrophysiology of biological membranes. Thus the non-linear dynamics of the Hodgkin-Huxley mathematical model have been extensively studied both with a view to their biological implications and as test bed for numerical simulation methods those can be applied to more complex mathematical models. This paper deals with the non-linear dynamics in the Hodgkin-Huxley mathematical model, namely, the existence of quasi-periodic and transient chaotic solutions in the model with its original parameters.*
***Keywords**: Hodgkin-Huxley model, Action Potential, Non-linear Dynamics, Biological Membrane, Complex Mathematical Model*

1. Introduction

The Hodgkin-Huxley mathematical model published in 1952 (Hodgkin, Huxley, 1952), presented the results of a sequence of experiments in which they investigated the flow of electric current through the surface membrane of the giant nerve fiber of a squid. These authors developed a mathematical description of the behavior of the membrane based upon these experiments, which accounts for the conduction and excitation of the fiber. The form of this description has been used as the basis for almost all other ionic current models of exciter tissues.

The mathematical model developed by Hodgkin and Huxley basically states that the total amount of current flow through the exciter membrane is the result of the individual contributions of three different ionic current sources: (1) potassium ionic current, (2) sodium ionic current and (3) a leakage ionic current that accounts for the aggregation of other ionic fluxes such as the chloride and bicarbonate ions. This membrane current depends both on the capacitance of the plasma membrane and the resistance of the ion channels. To put all these together, look at figure 1, where the contributions of all three currents is inherently observed in the parallel connection.

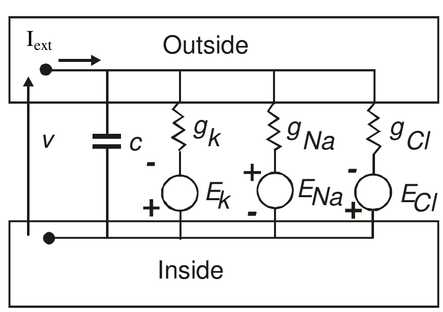


Figure 1. Circuit analog of the Hodgkin-Huxley nerve membrane model.

The basic membrane electric circuit is drawing in Figure 1. This electric circuit is appropriate for simple membrane systems like the squid giant axon or other axonal membranes, where only two voltage-dependent channels are seen. In this model there is a capacitor *C*, to represent the membrane capacitance, a sodium conductance g_{Na}, potassium conductance g_K, and a leakage conductance g_{Cl}. The membrane potential *V* is the potential inside the cell minus the potential outside and there can be a current I_{ext} injected into the cell from an electrode or from other parts of the cell. Consistent with the usual convention, currents are positive in the outward direction.

The mathematical model in Figure 1 represents a patch of membrane, i.e. a small area of membrane which is isopotential, meaning that the membrane potential *V* is constant across the patch. We will consider more general models in which the voltage varies along the extent of the cell. Patch models are appropriate for systems consisting of a large number of channels relatively evenly dispersed across the patch. More specifically, two things are assumed: 1) the number of channels is large enough that individual gating events are averaged out and the *Na* and *K* currents are smooth population currents; and 2) the channels are not arranged in any way which allows special local interactions among small numbers of channels. Such interactions most frequently occur between calcium channels and other channel types through local calcium pools. In this model, the channels interact only through *V*.

The equations describing the patch in the Figure 1., is defined by the four dimensional vector field

$$\overset{*}{v} = I - \left[120m^3h(v+115) + 36n^4(v-12) + 0.3(v+10.599)\right] \tag{1}$$

$$\overset{*}{\mathrm{m}} = (1-m)\frac{\left(\dfrac{v+25}{10}\right)}{\exp\left(\dfrac{v+25}{10}\right)-1} - m\left(4\exp\frac{v}{18}\right) \tag{2}$$

$$\overset{*}{n} = (1-n)0.1\frac{\left(\dfrac{v+10}{10}\right)}{\exp\left(\dfrac{v+10}{10}\right)-1} - n\left(0.125\exp\frac{v}{80}\right) \tag{3}$$

$$\overset{*}{h} = (1-h)0.07\exp\left(\frac{v}{20}\right) - \frac{h}{1+\exp\dfrac{v+30}{10}} \tag{4}$$

with variables (v, m, n, h) that represent membrane potential, activation of a sodium current, activation of a potassium current, and inactivation of the sodium current and a parameter I that represents injected current into the space-clamped axon. Recall that the Hodgkin-Huxley convention for membrane potential reverses the sign from modern conventions, and so the voltage spikes of action potentials are negative in the Hodgkin-Huxley model. While improved models for the membrane potential of the squid axon (Clay, 1998) have been formulated, the Hodgkin-Huxley model remains the paradigm for conductance-based models of neural systems. From a mathematical viewpoint, varied properties of the dynamics of the Hodgkin-Huxley vector field have been studied by a number of authors. We mention, with deserve others, the works of (Fukai *et al*, 2000; Doi,, Kumagai, 2000; Guckenheimer, Labouriau, 1993; Hassard, 1978; Hassard, Shiau, 1996; Labouriau, 1989; Rinzel, Miller, 1980).

Functionally, the dynamic behavior represented by this set can also be modeled in terms of the closed-loop system in Figure 2. A depolarizing stimulus that exceeds the threshold produces an increase in sodium conductance, with allows sodium ions to enter the intracellular space. This leads to further depolarization and greater increase in sodium conductance. This positive feedback effect is responsible for the rising phase of the action potential. However, fortunately, there is a built-in inactivation mechanism (represented by h) that now begins to reverse the depolarization process. This reversal is aided by the negative feedback effect of the increase in potassium conductance, which follows a time-course slower than of the sodium conductance. The outflow of potassium ions leads to further repolarization of the membrane potential. Thus, the action potential is now in its declining phase. Due the potassium conductance remains above its resting level even after sodium conductance has returned to equilibrium, the nerve cell continues to be slightly hyperpolarized for a few milliseconds following the end of the action potential. Figure 3, reproduced from the original Hodgkin-Huxley paper, by us, shows, the time-courses for V, g_{Na}, and g_k as predicted by the model to occur during an action potential. The curve labeled g represents the time-course of the membrane conductance. Multiplying this function with V allows us to predict the time-course for the net membrane current during the action potential.

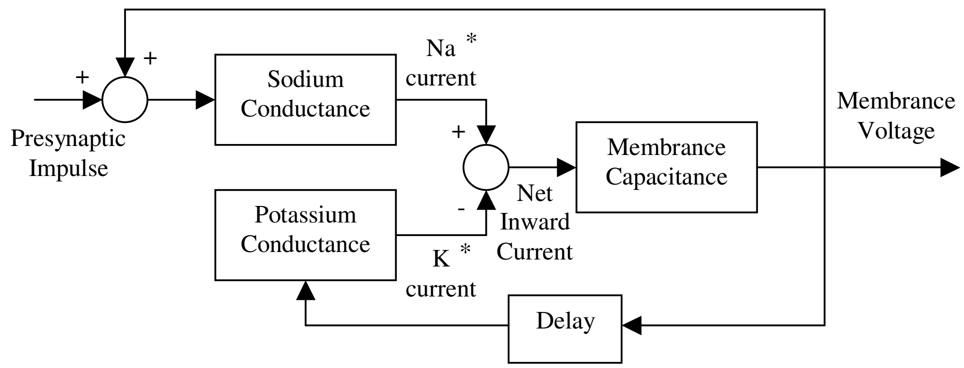


Figure 2. The Hodgkin-Huxley model as a closed-loop system with negative and positive feedback.

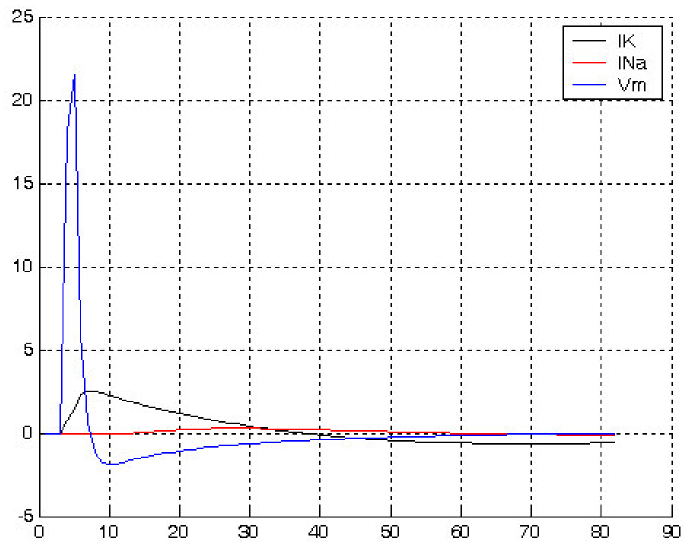


Figure 3. Time course of ionic conductance's and membrane potential during an action potential, as predicted by numerical solution of the Hodgkin-Huxley equations.

2. Nonlinear Dynamic behavior of the System

A stringent definition of chaos in a discrete dynamical system is that there is an invariant subset on which subset the transformation is hyperbolic and topologically equivalent to a sub shift of finite type (Guckenheimer, Holmes, 1983; McDonald *et al*, 1985). Continuous time dynamical systems are reduced to discrete time maps through the introduction of cross-sections and Poincaré return maps (Guckenheimer, Holmes, 1983).

An important concept for (chaotic) dynamics system is the notion of Lyapunov exponents, introduced by Oselec (1968). Lyapunov exponents are numbers, which describe the average behavior of the derivate of a map along a trajectory.

The trajectory of a point x is called a chaotic trajectory if (1) the trajectory of a is bounded and is not asymptotic to either a fixed point or a periodic orbit, and (2) F has at least one positive Lyapunov exponent at x.

In this subsection we study the dynamics of the Hodgkin-Huxley model for different types of input. Without input, i.e., I=0, constant input, and since input are considered in turn. These input scenarios have been chosen so as to provide an intuitive understanding of the dynamics of the Hodgkin-Huxley model.

We see form Figure 4a current input is 0. As indicated in Figure 4b, show the potential action general for the model with I=0. In the Figure 4c the phase plane (v, h) generated and Figure 4d, show the dynamics of lyapunov exponents for I=0.

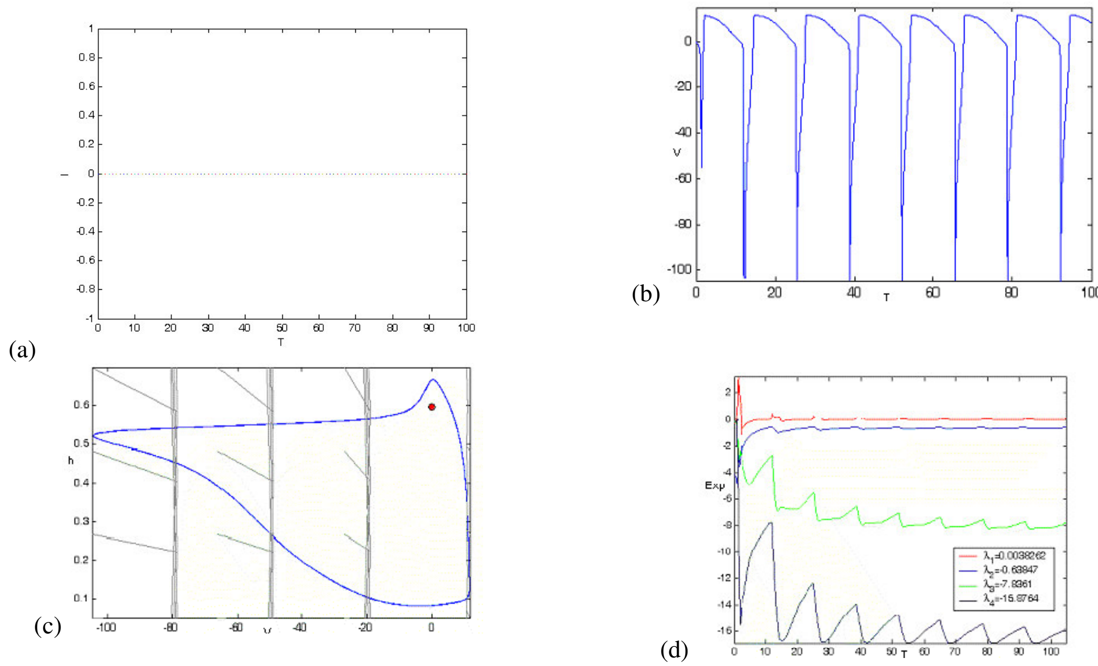


Figure 4. (a) Current Inject. (b) Action Potential. (c) Projection of the phase space (v, h). (d) Dynamics of Lyapunov exponents

We see form Figure 5a current input is 3.2. As indicated in Figure 5b, show the potential action general for the model with I=3.2. In the Figure 5c the phase plane (v, h) generated and Figure 5d, show the dynamics of lyapunov exponents for I=3.2.

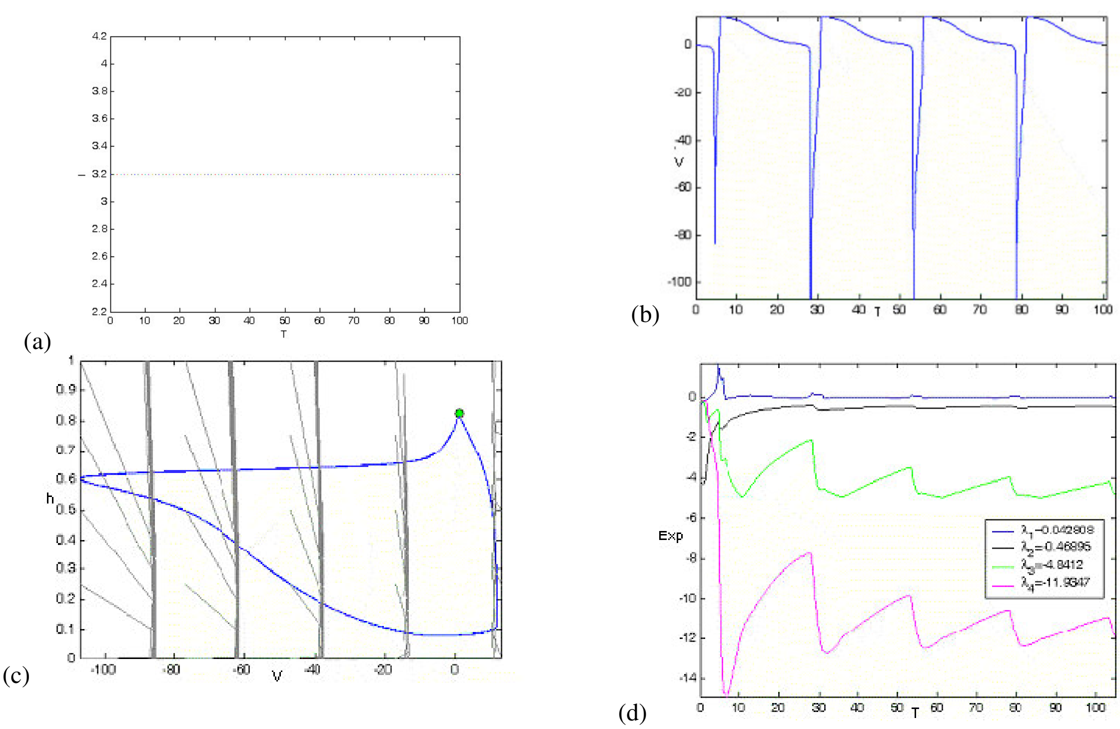


Figure 5. (a) Current Inject. (b) Action Potential. (c) Projection of the phase space (v, h). (d) Dynamics of Lyapunov exponents

We see form Figure 6a current input is sine form. As indicated in Figure 6b, show the potential action general for the model. In the Figure 6c the phase plane (v, h) generated and Figure 6d, show the dynamics of lyapunov exponents.

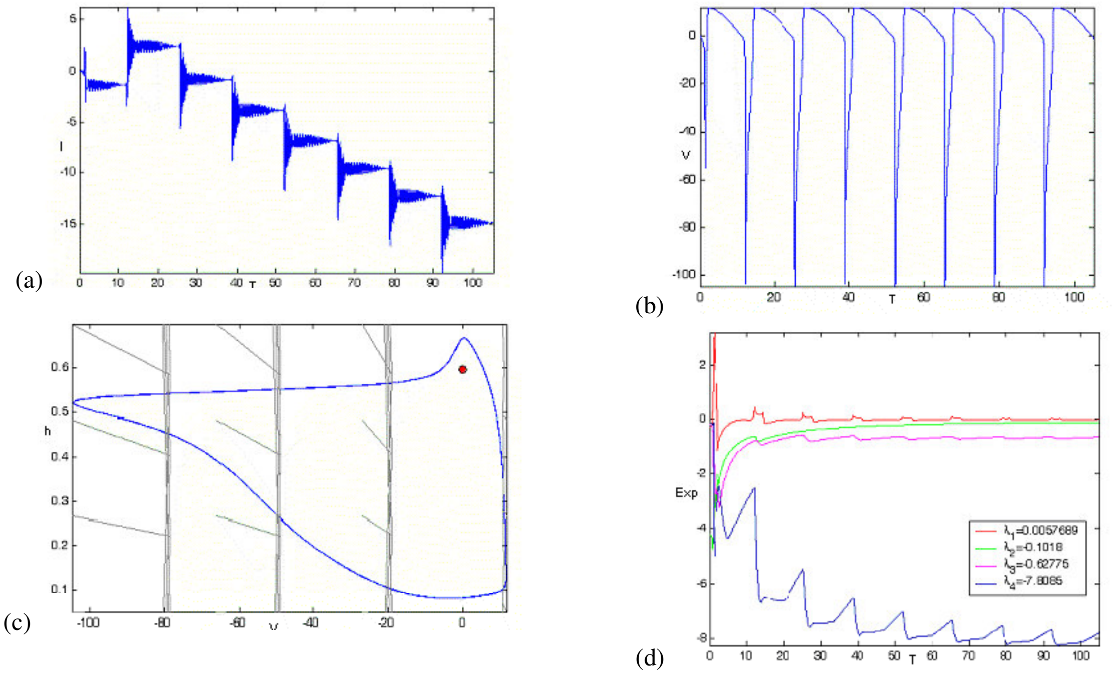


Figure 6. (a) Current Inject. (b) Action Potential. (c) Projection of the phase space (v, h). (d) Dynamics of Lyapunov exponents

We turn now to the significance of this nonlinear dynamic behavior of the Hodgkin-Huxley model. The invariant above is a highly unstable structure associated with the "threshold" for action potentials. Action potential of neurons is large all-or-nothing voltage spikes. In axons that are not space-clamped, like those represented by the Hodgkin-Huxley model action potentials propagate along axons as traveling waves and stimulate synaptic currents in adjacent postsynaptic neurons. Threshold is the magnitude of an input that must be exceeded for an action potential to fire. This definition is based upon the assumption that there is a critical current *I* above which the axon will fire an action potential when given a brief stimulus of magnitude *I* and below which it will not.

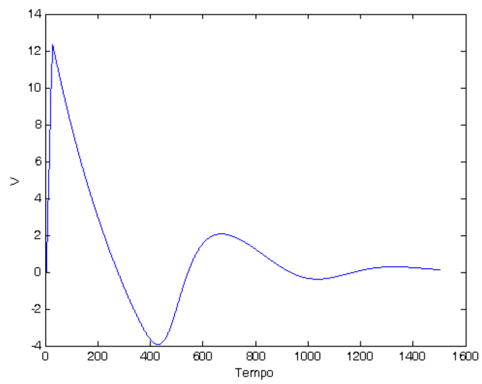
If our conjectural description of the phase space of the Hodgkin-Huxley model is correct, then there is a degree of unpredictability about show how the system will respond to stimulation. Brief current inputs to the axon that evolve to the stable steady state and those that evolve to the firing state are finely interleaved with each other as the amplitude of the current input is varied. The dynamics underlying action potentials yield an inhered lack of predictability in determining how large an input is required to cross the threshold for firing action potentials.

We believe that the phenomenon seen here on fine scales may well be present on larger scales in other neural systems or for different parameter values of the Hodgkin-Huxley model. The significance of our results is that they establish the subtlety of the concept of threshold: the excitability of a neural membrane to fire an action potential may be more complex than a smooth hyper surface that divides sub threshold and suprathreshold membrane potentials.

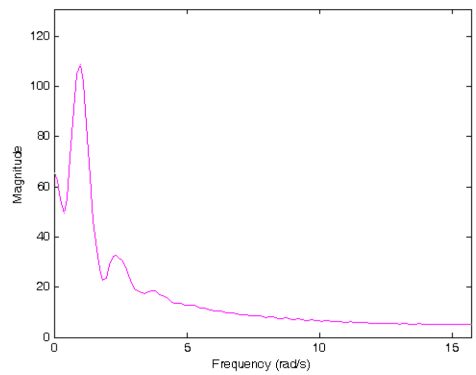
According to results obtained through Figures 4d, 5d and 6d by using three different inputs (0, 3.2 and sine form), we will obtain quasi-periodic motions according to the value of the Lyapunov exponents (around zero), in this case the obtained solution in a larger interval.

Guckenheimer and Labouriau obtained the existence of horseshoes and transient chaotic behavior in the unforced Hodgkin-Huxley equation. The system experiences a transient period of exponential instability before entraining to the input. This transient chaos is caused by a horseshoes (Guckenheimer, Labouriau, 1993).

In particular, chaotic behavior has long been observed in numerical studies of neuronal models: in the Hodgkin-Huxley system driven by periodic pulse trains, in them we apply 1, 2, 3 and 4 pulses in the systems and we show in illustrations 7a, 8a, 9a, and 10a its dynamic behavior.



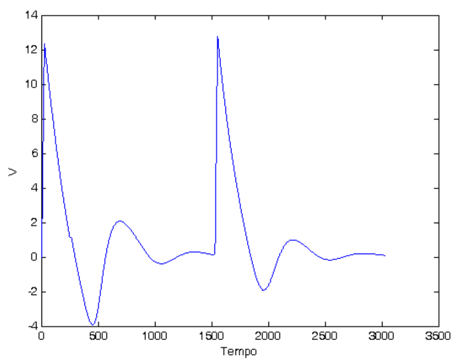
a)



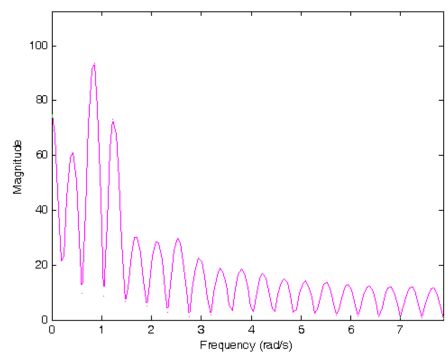
b)

Figure 7. (a) Action Potential for One Exciter . (b) Frequency Spectrum for One Exciter

In the Figure 7a show the potential action general for one nervous impulse and the Figure 7b show the frequency spectrum for this impulse.



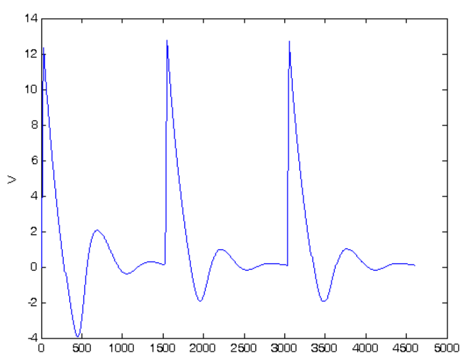
a)



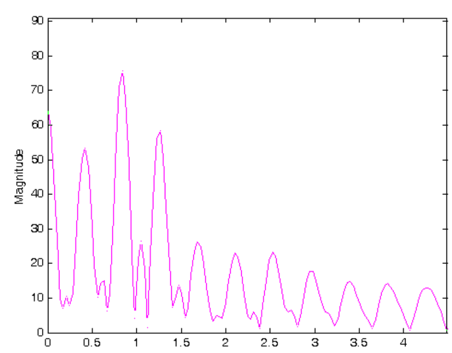
b)

Figure 8. (a) Action Potential for Two Exciters . (b) Frequency Spectrum for Two Exciters.

In the Figure 8a show the potential action general for two nervous impulses and the Figure 8b show the frequency spectrum for this impulse



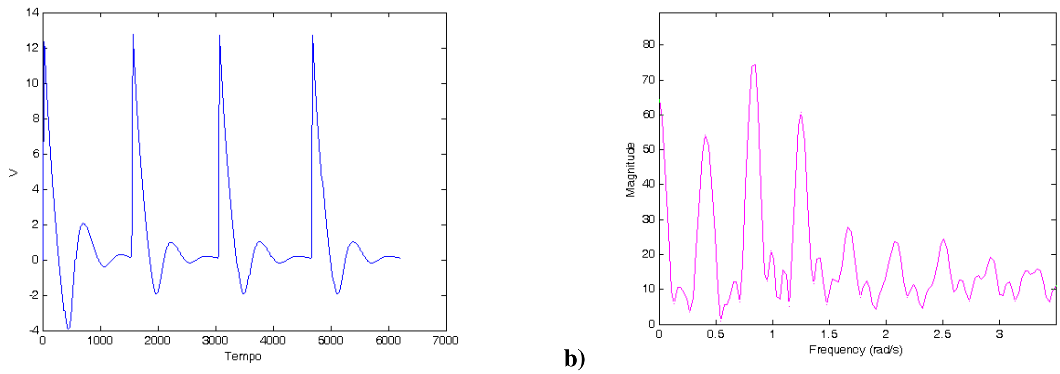
a)



b)

Figure 9. (a) Action Potential for Three Exciters . (b) Frequency Spectrum for Three Exciters

In the Figure 9a show the potential action general for three nervous impulse and the Figure 9b show the frequency specttrum for this impulse.



a) **b)**

Figure 10. (a) Action Potential for Four or More Exciters . (b) Frequency Spectrum for Four or More Exciters

In the Figure 10a show the potential action general for four nervous impulses and the Figure 10b show the frequency spectrum for this impulse. We can observe for illustrations 8b, 9b and 10b, that the frequency specter demonstrates the presence of transient chaos in the system during the presence of more of the one than a followed nervous impulse. We still observe, that above of four nervous pulses the specter of the system it remains continues, we remember that finished the impulse nervous the system comes back the stability, normally.

3. Conclusions

A non-linear dynamics characteristic of the Hodgkin-Huxley mathematical model was analyzed by using numerical simulations. They were based on their biological implications. This paper also discusses the existence of quasi-periodic solutions in the used model with its original parameters. We also comment the transient chaotic behavior of the nonlinear dynamics, by using Frequency Spectrum analysis.

4. Acknowledgements

The authors acknowledge FAPESP and CNPq.

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