Dynamics Analysis of Two-Dimensional Systems of the Hodgkin-Huxley Model on Propagatsion of Nerve Cell Impulse

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Abstract. This research aims to assess the environmental quality of Jodipan, Malang through the Comprehensive Assessment System for Built Environment Efficiency (CASBEE) Tools. Jodipan is one of the urban villages in Malang city which stands along in the Brantas riverbanks. It is a high-density settlement with the majority of the population work as a merchant. At 2016, the settlement in Jodipan riverbanks painted colorfully, and it made Jodipan called "Kampung Warna Warni" or Colourful Kampong. Jodipan now became one of the new community-based tourism destinations in Malang and succeeded to attract domestic and international tourist. The existence of this kampong gave a big impact on environmental quality especially river since their communities' activities are very depending on the river. The method based on the triple-bottom-line approach that adopts three classifications of sustainable development which are the environment, society, and economy. The result of environmental quality in Jodipan kampong riverbank was 2.1. This score indicates a low value and below the average of the environmental quality standards.

Keywords: integrated, assessment, quality, riverbank

1 Introduction

Much progress has been made in the study of spike generation since the work of Hodgkin and Huxley. Working without the knowledge of the membrane structure, scientists tried to build models of a neuron by adjusting parameters that were measured and not necessarily from the same neuron. The study of dynamical systems today asks and tries to answer the questions of why two seemingly similar neurons can behave so differently under the same conditions. A dynamical system consists of a set of variables that describe its state and a law that describes the evolution of the state variables with time [1].

The Hodgkin-Huxley model is a dynamical system consisting of the state variables $V, n, m,$ and h with a four-dimensional system of ordinary differential equations governing the evolution of the state variables [2]. We will see that the Hodgkin-Huxley model can be reduced to a two-dimensional model and still produce the same action potentials. Then we will perform analysis on the reduced model to explain some of the dynamics of the squid giant axons. We begin by seeing how other models are analyzed.

Most concepts will be illustrated using the $I_{\mathrm{Na,p}} + I_K -$ model in eq. 3.1 having leak current I_L, persistent Na^+ current $I_{\mathrm{Na,p}}$ with instantaneous activation kinetic and a relatively

ICONQUHAS 2018, October 02-04, Bandung, Indonesia

DOI 10.4108/eai.2-10-2018.2295563

slower persistent K^+ current I_K with either high or low threshold. The two choices of K^+ current result in fundamentally different dynamics of the model. This model is equivalent in many respects to the well-known and widely used $I_{Ca} + I_K$– model proposed by [3] to describe voltage oscillations in the barnacle giant muscle fiber.

Since persistent K^+ current has only one gating variable n, the state of this system is a two-dimensional vector $(V, n) \in \mathbb{R}^2$ on the phase plane $\mathbb{R}^2$. New types of equilibria, orbits, and bifurcations can exist on the phase plane that cannot exist on the phase line $\mathbb{R}$. Many interesting features of single neuron dynamics can be illustrated or explained using two-dimensional systems. Even neuronal bursting, which occurs in multi-dimensional systems, can be understood via bifurcation analysis of two-dimensional systems [4].

Previous research has been conducted by [5]. They studied the four-variable Hodgkin-Huxley cables model by looking at the axon geometry side and the Neuron membrane capacitance.

The problem raised in this research is how to know the dynamics analysis of two-dimensional systems of the Hodgkin-Huxley model to describe the model when there is a change in electric current impulse I_{ext} received by the membrane potential $V(t)$ from outside the Neuron membrane or in other words, when the value of I_{ext} value is fickle. By observe at this change of I_{ext} value is expected to control the magnitude of Neuron membrane potential and the ionic population of Neuron membrane. The numerical simulation conducted in this research is by using ODE45. So the dynamics obtained from changes in the ionic population is controlled by the magnitude of the membrane potential. Thus, the depth of this research is to see how far two-dimensional systems of the Hodgkin-Huxley model analysis of the external current changes. Therefore, it can be concluded how the condition of an ionic population of Neuron membranes to remain balanced.

2 Literature Review

2.1 Two-Dimensional Systems of the Hodgkin-Huxley Model

This research will use systems of nonlinear ordinary differential equations formulated by Izhikevich, (2004). It is consist of two equations, such as membrane potentials and probability of the activation gate to be in the open state for K^+ channels. Let us consider the 2-dimensional leak + persistent sodium + potassium model denoted as: $I_L + I_{Na,p} + I_K$. This model having leak current I_L, persistent Na^+ current $I_{Na,p}$ with instantaneous activation kinetic and a relatively slower persistent K^+ current I_K with either high or low threshold. The state of this systems is a 2-dimensional vector (V, n) on the phase plane $\mathbb{R}^2$ since the Na^+ current has instantaneous activation kinetics, such that its conductance may be considered to be maximal, m_∞, over most all of the time interval. The activation kinetics for n are much slower and so it must be defined by its derivative [6].

2.2 Differential Equations, Vector Fields, and Linear Algebra

Natural, social and artificial systems change hour by hour. Dynamical system is a mathematics for the modeling and the analysis of such systems' behavior. Dynamical systems incorporate the state and its time change in a system. Consider a difference equation or continuous-time dynamical system [7].

$$\frac{d}{dt}x(t) = f\big(x(t)\big), \quad x(t) \in \mathbb{R}^N, \quad 1$$

The solution $x(t)$ which satisfies this differential equation is called an orbit or trajectory of the system (2.1). The state $x(0)$ is referred as the initial state again. The special state point x^* such that $f(x^*) = 0$ is called a fixed point, an equilibrium point or a steady state. The right-hand side (r.h.s.) $f\big(x(t)\big) \in \mathbb{R}^N$ of the differential equation (2.1) is a vector and is called a vector field. The vector field assigns the vector $f(x)$ to each point x of the state space $\mathbb{R}^N$. The simplest example of the continuous dynamical system (2.1) is also the case that the map f is a linear matrix $\boldsymbol{A}$ [8]:

$$\frac{d}{dt}x(t) = Ax(t), \quad x(t) \in \mathbb{R}^N, \quad t \in$$

where A is an invertible $N \times N$ matrix. Note that only the origin $x = (0, \dots, 0)^T$ is the fixed point or an equilibrium point since this system is linear and A is invertible. The general solutions can be obtained by [9].

$$x(t) = \exp(At)x(0)$$

2.3 Linearization and Stabilities

In the case of the continuous-time dynamical system (2.1), the equilibrium point at the origin is stable if the real parts of all eigenvalues of $\boldsymbol{A}$ are less than zero (negative). Next, consider nonlinear dynamical systems. Let x^* be an equilibrium point of the continuous-time dynamical system (2.1), then $f(x^*) = 0$ in (2.1). The Taylor expansion of the function $f(x)$ near the equilibrium point x^* are obtained as follows [10]:

$$f(x) = f(x^*) + \mathcal{D}f(x^*)(x - x^*) + \mathcal{O}\left(||x -$$

where $\left(||x - x^*||^2\right)$ denotes the higher-order terms (second-order terms and higher terms) and $\mathcal{D}f(x^*)$ is the Jacobian matrix:

$$\mathcal{D}f(x^*) = \begin{pmatrix} \frac{\partial f_1(x)}{\partial x_1} & \frac{\partial f_1(x)}{\partial x_2} & \cdots & \frac{\partial f_1(x)}{\partial x_n} \\ \frac{\partial f_2(x)}{\partial x_1} & \frac{\partial f_2(x)}{\partial x_2} & \cdots & \vdots \\ \vdots & \vdots & \vdots & \vdots \\ \frac{\partial f_n(x)}{\partial x_1} & \cdots & \cdots & \frac{\partial f_n(x)}{\partial x_n} \end{pmatrix}_{x = x^*}$$

$$x = (x_1, x_2, \cdots)^T, \quad f(x) = (f_1(x_1, x_2, \cdots), f_2(x_1, x_2, \cdots), \cdots)^T$$

Near the equilibrium point x^*, we can neglect (under some conditions) the higher-order terms $\mathcal{O}\left(||x-x^*||^2\right)$ since $\mathcal{O}\left(||x-x^*|^2\right)$ becomes small when $||x-x^*||^2$ is small. Then, we can obtain a linearized system or linearization of (2.1), respectively as follows:

$$\frac{d}{dt}z(t) = Az(t), \qquad A = \mathcal{D}f(x^*)$$

where we have made use of the change of a variable $z(t) = x(t) - x^*$ [11].

3 Results and Discussion

The model that used in this research is a system of two variables of the Hodgkin-Huxley model that formulated by Izhikevich. The equations is as follows [12]:

$$C\frac{dV(t)}{dt} = I_{\text{ext}} - I_{\text{L}}\big(V(t)\big) - I_{\text{Na,p}}\big(V(t)\big) - I_{\text{K}}\big(V$$

$$\frac{dn(t)}{dt} = \frac{n_\infty\big(V(t)\big) - n(t)}{\tau(V)}$$

where

$$I_{\text{L}}\big(V(t)\big) = g_{\text{L}}(V(t) - E_{\text{L}})$$

$$I_{\text{Na,p}}\big(V(t)\big) = g_{\text{Na}}m_\infty\big(V(t)\big)(V(t) - E_{\text{Na}})$$

$$I_{\text{K}}\big(V(t), n(t)\big) = g_{\text{K}}n(t)(V(t) - E_{\text{K}})$$

$$m_\infty\big(V(t)\big) = \frac{1}{1 + e^{\frac{V_m - V(t)}{\kappa_m}}}$$

$$n_\infty\big(V(t)\big) = \frac{1}{1 + e^{\frac{V_n - V(t)}{\kappa_n}}}$$

The description initial value of variables and parameters that used in the system of two-dimensional systems of the Hodgkin-Huxley model (3.1) can be seen in the appendix. The equilibrium point of the system (3.1) is obtained if $\dot{V} = 0$ and $\dot{n} = 0$. From the system of equations (3.1) is sought the equilibrium point value with the help of Maple to obtain the equilibrium point, is $V^* = -65.95295125$ mV and $n^* = 2.771733422 \times 10^{-4}$. We first need to establish the equilibrium points by studying the nullclines of the state variables. A nullcline is all of the locations in the phase plane where a state variable is at rest. In this system, that would be when $\dot{V} = 0$ and $\dot{n} = 0$. The equation for the V nullcline is:

$$I_{\text{ext}} - I_{\text{L}}\big(V(t)\big) - I_{\text{Na,p}}\big(V(t)\big) - I_{\text{K}}\big(V(t), n(t$$

$$n(t) = \frac{I_{\text{ext}} - g_{\text{L}}(V(t) - E_{\text{L}}) - g_{\text{Na}}m_\infty\big(V(t)\big)(V($$
$$g_{\text{K}}(V(t) - E_{\text{K}})$$

The n nullcline is:

$$n_\infty\big(V(t)\big) = \frac{1}{1 + e^{\frac{V_n - V(t)}{k_n}}}$$

The intersections of these nullclines will be the points where neither of the state variables is changing, so the membrane is at equilibrium [13]. In Figure 3.1, we see the cubic-shaped nullcline for V in purple and the sigmoid-shaped nullcline for n in orange. Their intersection is the equilibrium for this model.

This figure also is demonstrating when $I = 0\ A\ \mathrm{cm}^{-2}$ that some models fail to have "all or nothing spikes". We can see trajectories of the phase plane which have varying initial values for membrane potential but the same initial value for the potassium activation variable, "n". It is apparent that some trajectories follow a subthreshold path to the equilibrium and others take a longer excursion with greater values of membrane potential. So, there are varying amplitudes of action potentials, not "all or nothing" spikes.

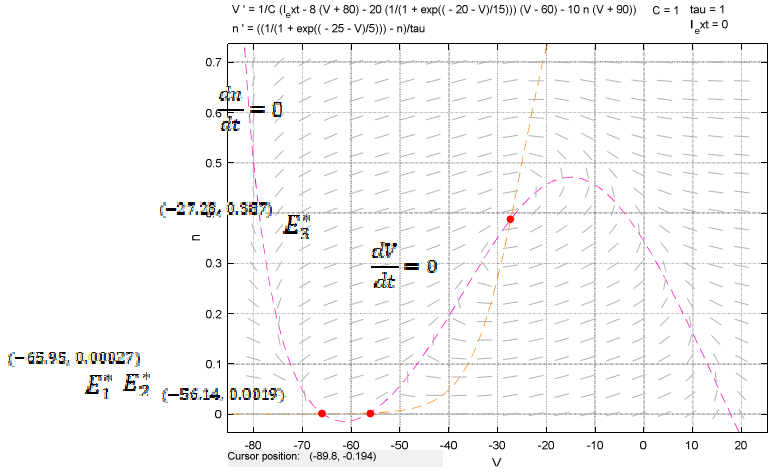

Figure 1. Phase Plane Sub-System $V(t) - n(t)$ *Hodgkin-Huxley* Model

In Figure 3.2, we observe the $I_{\mathrm{Na,p}} + I_{\mathrm{K}}$ low threshold system when $I = 50\ A\ \mathrm{cm}^{-2}$ has trajectories all starting with the same initial membrane potential of $-48\ \mathrm{mV}$, but varying values of initial K^+ activation variable "n". Some trajectories depict full action potentials and some make small excursions and return to equilibrium with subthreshold spikes. We can see that this model has no fixed threshold of membrane potential. All of the action potentials exhibited in Figures 3.1 and 3.2 are transient; they all return to equilibrium values.

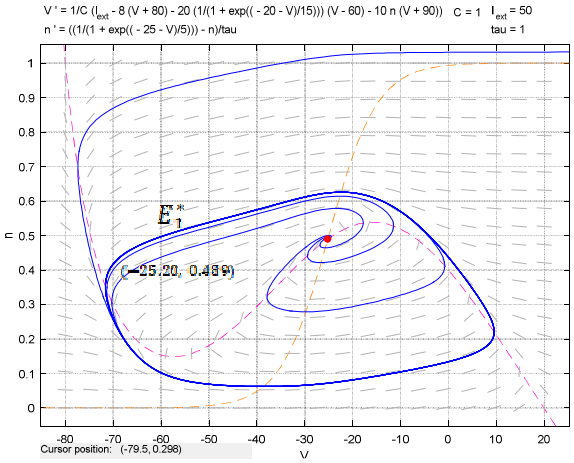

Figure 2. Phase Plane Sub-System $V(t) - n(t)$ when $I = 50\ A\ cm^{-2}$

In Fig. 3.2. It is easy to see how V – and n –nullclines partition the phase plane into four regions having different direction of the vector field: (a) Both V and n increase: Both Na^+ and K^+ currents activate and lead to the upstroke of the action potential. (b) V decreases but n still increases: Na^+ current deactivates but slower K^+ current still activates and lead to the down stroke of the action potential. (c) Both V and n decrease: Both Na^+ and K^+ currents deactivate while V is small leading to a refractory period. (d) V increases but n still decreases: Partial activation of Na^+ current combined with further deactivation of residual K^+ current lead to an excitable period, and possible to another action potential.

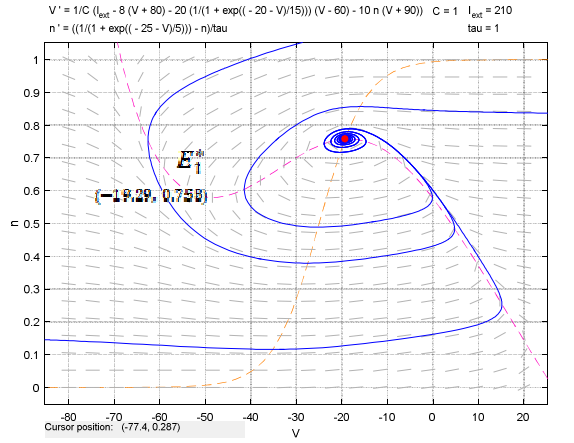

Figure 3. Phase Plane Sub-System $V(t) - n(t)$ when $I = 210\ A\ cm^{-2}$

The intersection of V and n nullclines in Fig. 3.3 is an equilibrium corresponding to the rest state. The number and location of equilibria might be difficult to infer via analysis of equations (3.1, 3.2), but it is a trivial geometrical exercise once the nullclines are determined. Because nullclines are so useful and important in geometrical analysis of dynamical systems, few scientists bother to plot vector fields. Following this tradition, we will not show vector

fields in the rest of the book (except this chapter). Instead, we plot nullclines and representative trajectories.

In Fig. 3.4 we illustrate another dramatic aspect of threshold behavior, which can be explained only by considering joint evolution of V and n. We apply a long pre-pulse current I of various strength to keep the membrane potential of the $I_{Nap} + I_K$ model at various subthreshold values, and then a strong but brief pulse to reset the membrane potential to exactly -48 mV, which is a superthreshold voltage value. As one can see, -48 mV becomes a subthreshold value for positive pre-pulses but remains to be superthreshold for negative and zero pre-pulses.

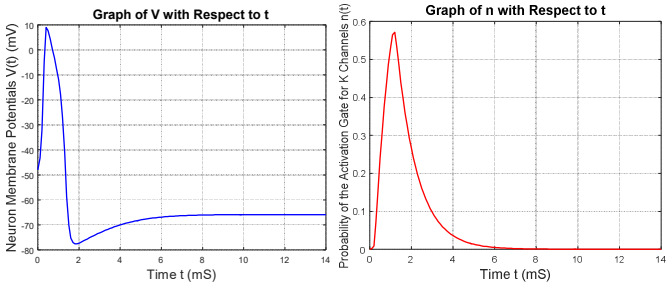

Figure 4. Graph of V, n with respect to t when given $I_{ext} = 0.1\ A\ cm^{-2}$

In Fig. 3.5 we inject $I_{ext} = 4.52\ A\ cm^{-2}$ pulse of current into a brainstem mess V neuron of a rat. When the inhibitory current is removed, the neuron generates rebound action potentials called post-inhibitory spikes. Such spikes are ubiquitous in many neurons, and they are often attributed to the existence of cation inward current with low-threshold K^+ current to generate a post-inhibitory spike in Fig. 3.5. Since the model has neither of the currents, it can produce such a strange phenomenon.

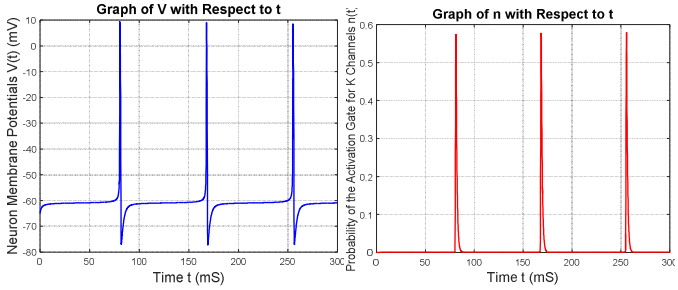

Figure 5. Graph of V, n with respect to t when given $I_{ext} = 4.52\ A\ cm^{-2}$

To explain the mechanism of post-inhibitory spikes, we need to consider joint evolution of the state variables V and n: When the membrane potential is hyperpolarized, the K^+ current, which is partially activated at rest, starts to deactivate, i.e., variable n starts to decrease. When we suddenly remove the inhibitory current, there is a deficit of outward K^+ current (n is too small) and the net membrane current drives V over the threshold. From the dynamical system point of view such post-inhibitory spikes are closely related to the existence of fast damped oscillatory potentials seen in Fig. 3.5.

The approach of the linear system around the equilibrium point V^* and n^* using the Taylor series and cut to first order. After a long process obtained the following linear equations:

$$\frac{dV}{dt} = -1.733914807V - 240.4704$$
$$\frac{dn}{dt} = 5.541930352 \times 10^{-5}\, V - n$$

The Eigen value is obtained by completing $\det(\lambda \mathrm{I} - \mathrm{J}) = 0$. With the help of Matlab program obtained Eigen values $\lambda_1 = -1.715283441931 09$ and $\lambda_2 = -1.018\ 631365068 91$.

At the state of equilibrium point $V^* = -65.95295125$ mV and $n^* = 2.771733422 \times 10^{-4}$ the two-dimensional systems of the Hodgkin-Huxley model is expressed nodes with asymptotically stable because $\lambda_1, \lambda_2 < 0$.

The result of numerical simulation using ODE45 obtained that the two-dimensional systems of the Hodgkin-Huxley model becomes unstable when the external current at the interval of $4.52\ A\ \mathrm{cm}^{-2} < I_{\mathrm{ext}} < 210\ A\ \mathrm{cm}^{-2}$. While at the interval $I_{\mathrm{ext}} \geq 210\ A\ \mathrm{cm}^{-2}$ the graph is stable and goes in the direction of the equilibrium point.

4 Conclusion

Based on the result and discussion analysis of two-dimensional systems of the Hodgkin-Huxley model on the transmission of nerve cell impulse action potential, it can be concluded that: two-dimensional systems of the Hodgkin-Huxley model is expressed nodes with asymptotically stable because $\lambda_1, \lambda_2 < 0$. In the phase-phase analysis, it is understood that the process of transmitting the nerve cell impulse action potential in the $V(t) - n(t)$ sub-system of Hodgkin-Huxley model runs as follows: the resting state → depolarization → decrease of $V(t)$ → increase of $n(t)$ → repolarization.

The result of numerical simulation using ODE45 obtained that two-dimensional systems of the Hodgkin-Huxley model becomes unstable when the external current at the interval of $4.52\ A\ \mathrm{cm}^{-2} < I_{\mathrm{ext}} < 210\ A\ \mathrm{cm}^{-2}$. While at the interval $I_{\mathrm{ext}} \geq 210\ A\ \mathrm{cm}^{-2}$ the graph is stable and goes in the direction of the equilibrium point.

For further research, it is advisable to the reader to examine an analytical solution from two-dimensional systems of the Hodgkin-Huxley model and then compare the results with a numerical solution to see how much approximation error of the numerical method.

Acknowledgements. We would like to thank Prof. Agus Suryanto for fruitful discussions, valuable suggestions, and contribution throughout the first stages of the work. This work was supported in part by the LP2M UIN Malang Indonesia.
This paper in conjuction with the 1st International Conference On Islam, Science, And Technology (ICONIST) 2018, Malang, East Java.

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Appendix

Table 1. Initial Value of Variables

Variable	Variable Description	Initial Value	Unit
$V(t)$	The magnitude of the Neuron membrane potential	-48	mV
$n(t)$	The probability of the activation gate to be in the open state for K channels.	0	$0 \leq n(t)$

Table 2. Initial Value of Parameter

Para-meter	Parameter Description	Initial Value	Unit
I_{exc}	Eksternal membrane current density	0	$\mathrm{pA\ cm^{-2}}$
C_{M}	Membrane capacitance	1	$\mu\mathrm{F\ cm^{-2}}$
g_{K}	Conductance for Potassium	10	mS
E_{K}	Equilibrium potential of Potassium	-90	mS
g_{Na}	Conductance for Sodium	20	mS

E_{Na}	Equilibrium potential for Sodium	60	mV
g_L	Conductance for "leaking" ions	8	mV
E_L	Equilibrium potential for leaking ions	-80	mV
$\tau(V)$	Voltage-sensitive time constant	1	mS
V_m	Parameter satisfies $m_\infty\left(V_{\frac{1}{2}}\right)=0.5$	-20	mV
V_n	Parameter satisfies $n_\infty\left(V_{\frac{1}{2}}\right)=0.5$	-25	mV
k_m	The slope factor of $m_\infty(V(t))$	15	mV
k_n	The slope factor of $n_\infty(V(t))$	5	mV

Table 3. Functions of Systems

Function	Function Description
$I_{Na,p}$	Persistent sodium (applied current inward of $m(t)$ gating activation)
I_k	Potassium (applied current outward of $m(t)$ gating activation)
$m_\infty(V(t))$	The probability of opening for Sodium
$n_\infty(V(t))$	The probability of opening for Potassium