International Journal of Biological and Pharmaceutical Sciences Archive

ISSN: 0799-6616 (Online)

Journal homepage: https://ijbpsa.com/

(Research Article)

Simulation of potential action of stimulated external alternating current (AC) in nerve cells using Hindmarsh-Rose model

Siti Aisah Sekar Arum [1,*], Yuyun Yueniwati [2] and Mauludi Ariesto Pamungkas [3]

[1] *Department of Physics, Faculty of Mathematics and Natural Sciences, Brawijaya University, Jl. Veteran, Malang, 65143, Indonesia.*
[2] *Department of Radiology, Faculty of Medicine, Brawijaya University, Jl. Veteran, Malang, 65143, Indonesia.*
[3] *Department of Physics, Faculty of Mathematics and Natural Sciences, Brawijaya University, Jl. Veteran, Malang, 65143, Indonesia.*

International Journal of Biological and Pharmaceutical Sciences Archive, 2021, 01(01), 016–022

Publication history: Received on 03 January 2021; revised on 10 January 2021; accepted on 12 January 2021

Abstract

This paper describes the simulation of potential actions that occur in nerve cells when given frequency variation as a stimulus. The simulation aims to determine the response of nerve cells to various combinations of currents in this case frequency. The simulation results showed that oscillations occur when the given frequency is 0.045 Hz. While the neural cell response occurs when the frequency between 0.055 Hz-0.065 Hz. The method carried out by the author is to modify the model of Hindmarsh-Rose nerve cells and then simulate it using Matlab programming language. Based on the research that has been done it can be concluded that at a frequency of 0.055 Hz a potential signal of action is formed and oscillates. In the human body, nerve cells and muscle cells are cells that have the ability of excitability (stimulated) because it has membrane potential. Short fluctuations of such cells, serve as electrical signals.

Keywords: Potential action; Periodic current; Hindmarsh-Rose model

1. Introduction

Stroke is the second leading cause of death as well as the third leading cause of disability. According to the WHO (World Health Organization), stroke is a condition in which neurons have focal and global deficits that cause death by vascular disorders. Stroke can occur because the blood vessels rupture so that they do not get a blood supply that carries oxygen then causes the death of cells and tissues. Therefore, stroke can cause dementia as well as depression. Stroke is an acute neurological disorder caused by hemorrhagic or ischemic [1].

Several solutions can be done for the healing process of stroke. Includes physiotherapy and alternative therapies using electrical simulations. Electrical stimulation (ES) therapy is one of the therapies in the field of physical doctor and rehabilitation that uses electricity with various types of amplitudes and characteristics of certain electrical flows flowing through the skin. The Verywell Health page writes that electrical therapy is part of physical therapy in the form of electrical stimuli. Electrical therapy is commonly used to deal with nervous diseases, which are characterized by a variety of symptoms. In dealing with nerve diseases, this therapy is thought to work by sending electrical signals and stimulating disturbed nerves to inhibit or reduce the pain of inflammation, also improve muscle function and strength, and blood circulation. But experts argue that electrical therapy still needs proof.

* Corresponding author: Siti Aisah Sekar Arum
Department of Physics, Faculty of Mathematics and Natural Sciences, University of Brawijaya, Jl. Veteran, Malang, 65143, Indonesia.

The human body experiences electrical symptoms. One of them can occur when an impulse-rationing event in nerve cells involves an electrochemical process. Which in the process, there is a potential difference in the cell membrane so that there is an exchange of Sodium(Na) and Potassium (K) ions in certain channels (potential action) to maintain the homeostasis or balance the concentration gradient in the cell due to environmental influences.

Therefore, several types of research related to neural cell models have been widely developed since the 1900s. It began with the thinking of Alan Lloyd Hodgkin and Andrew Huxley in 1952 who stated that nerve cell membranes have channels that can be passed by certain ions. These channels are sodium ion channels, potassium, as well as leakage channels. The mechanism of impulse propagation presented by both is the potential of nerve cell membranes that play a role to receive impulses in the form of currents from the outside as signals. This signal can then activate the mentioned ion channels. Level 1 Sodium ions will pass through the container gate 1 (m). While Sodium 2 ions will also enter the container gate 2 (n). Also, potassium ions will be accommodated by container gate 3 (h). As for ion leakage out towards the membrane. This theory was obtained when he conducted experiments to find out the effect of electricity on octopus muscle fibers. Based on his research, he formulated four differential equations that could describe the potential mechanisms of action [2,3,4,5,6,7].

The model is still very complex even though it has been talking about potential events of action as well as activities that occur in axons. Then in 1961, Richard Fitzhugh simplified the Hodgkin-Huxley model. The theory states that there are only two variables in the impulse propagation process, namely the action period and the recovery period. In his description, he formulates two differential functions capable of explaining the potential process of action more accurately[8,9,10].

Furthermore, there have been many related studies including the modification of Fitzhugh-Nagumo neuron models with external currents as a stimulus was carried out by Mishra in 2006. In this study it can be known that Mishra modified the current in the FitzHugh-Nagumo model with the Rinzel equation Based on the research it can be known that the field image phase was obtained that at the time of Ω= 0.127 neurons experienced chaos. From this, it can be said that frequency is a significant parameter that can affect the characteristics of neurons[11].

But there is another model that can explain the phenomenon of adaptation in neurons, namely the Hindmarsh-Rose model that will be described in the next subsection. Therefore, this simulation is in addition to knowing that the current can affect the response of nerve cells as well as answer the challenges of the above cases.

2. Methods

The Hindmarsh- Rose model is a model developed by J.L. Hindmarsh and R.M. Rose in 1982 by converting linear functions on Fitzhugh's potential variables into cubic functions. This model can explain the phenomenon of adaptation neurons. This model originally had only two nonlineal differential equations as follows [12,13,14].

$$\dot{x} = -a(f(x) - y) - z$$

$$\dot{y} = b(x) - qe^{rx} + s - y$$

$$\text{where, } f(x) = cx^3 + dx^2 + ex + h$$

Then in 1982 Hindmarsh modified the equation based on the analysis of the balance point saddlepoint. In his research, he stated that there are two-phase areas namely limit cycle and balance point. the consequence of such a model is the occurrence of a brief depolarization of changing the silent mode into repeated firing. A third equation is then added so that the burst trigger is isolated, as well as explaining the oscillation phenomenon. which z, y is the coordinates of the model without adaptation. While the values a = 1, b = 3, c = 1, and d = 5. Constant values r and s are r=0.001, s=1. But in experiments using *Lymnaea* the values r and s were r=0.01 and s=4 [4].

$$\dot{x} = y - ax^2 + bx^2 + I - z$$

$$\dot{y} = c - dx^2 - y$$

$$\dot{z} = r(s(x - x_1)) - z$$

In this study, the authors used hardware and software with the following Specifications. The trial process was conducted on an intel PC (R) Atom Dual-Core N3060, up to 2.48 GHz with 2 GB memory. The operating system used is Microsoft Windows 10 Update Assistant and the programming language that has been used is in the application method that is MATLAB R2013a.

The variables used by researchers are as follows. The free variable is the stimulus frequency value in periodic current (AC current), this parameter is indispensable for the modeling process in the development of oscillator motion with the nervous cell system according to the specified case. While the controlled variable is the parameter value of the Hindmarsh-Rose function. Bound variables are x values as a signal of potential action on nerve cells by using the Matlab program application.

The research procedures carried out by the authors are as follows. First, model potential cases of action on nerve cells using the Hindmarsh-Rose equation (a nonlinear differential equation), then assign each of its constant values. Next is to review the variation in stimulus frequency values as external current output. Use the Runge-Kutta numerical solution to solve nonlinear differential equations from the previous point. The step taken by the author is to determine the time range and calculate the constants according to the Runge-Kutta formula. Then, calculate the output value using the Runge-Kutta formula. After that, a program is created using the MATLAB programming language. Finally, from the program that has been created, then run the program in the Command Window.

Here is the Runge-Kutta formula for calculating constants and their output values [15]

$$y_{i+1} = y_i + \emptyset(x_i, y_i, h)h$$

$$k_1 = f(x_i, y_i)$$

$$k_n = f(x_i + p_{n-1}, y_i + \cdots + q_{n-1,n-1}k_{n-1}h)$$

3. Results and discussion

The simulation result of the Hindmarsh-Rose nerve cell model with periodic current variation is shown in the simulation result in the form of a graphic plot is shown in Figures 1-4.

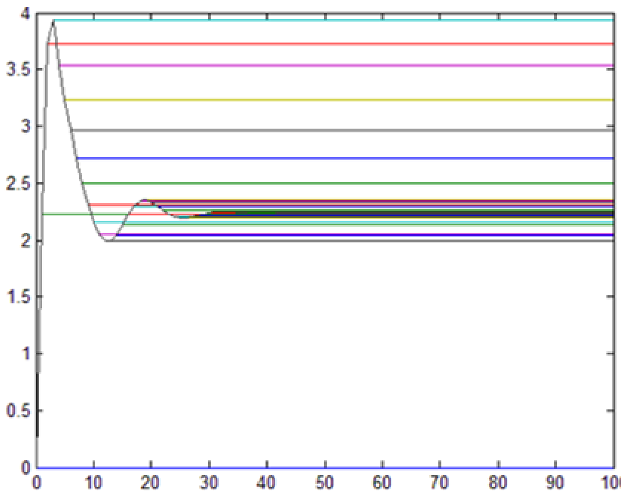

Figure 1 signal the potential action of nerve cells when the current frequency is given as stimulus= 0.035 Hz

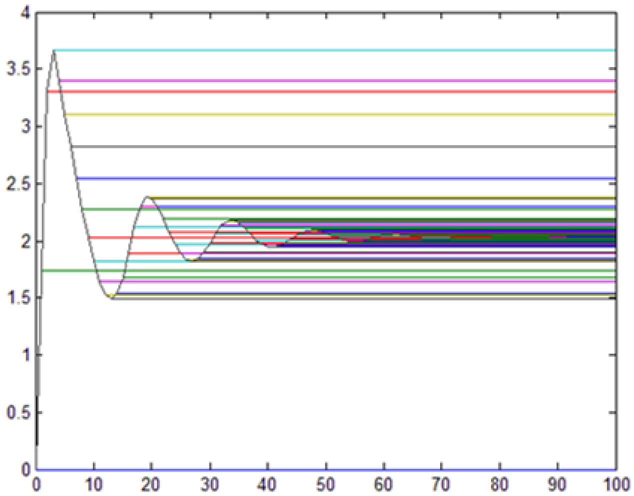

Figure 2 signal potential action of nerve cells when the current frequency is given as stimulus= 0.045 Hz

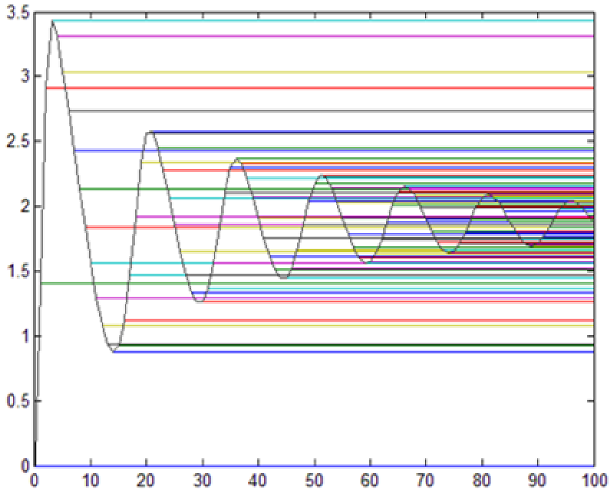

Figure 3 signal potential action of nerve cells when the frequency of current given as stimulus= 0.055 Hz

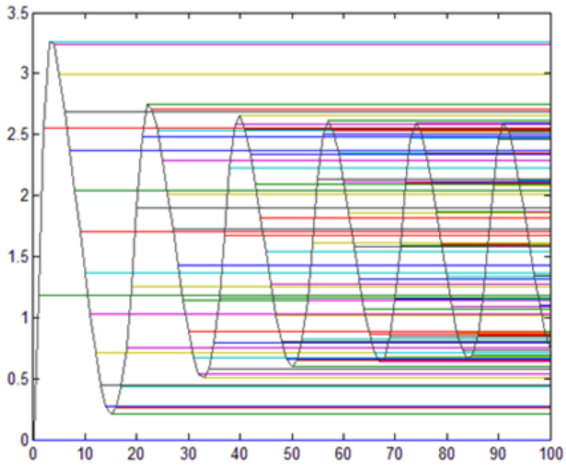

Figure 4 signal of potential nerve cell action when the current frequency is given as stimulus= 0.065 Hz

Potential action on nerve cells can occur when there are stimuli from the outside that reach the threshold. According to Sherwood, Potential action occurs when there is a potential difference in the cell membrane (positive overload) and outside the cell membrane (negative). This difference in charge results in the flow of electric current moving in the direction. Because, if the electric current moves both ways, then a lot of potentials is reflected. That's why there's a refractory period. Which is, this period is set so that the potential action does not return to its original place. Refractory periods can occur after a potential period of action (as Fitzhugh has previously described). The refractory period will ensure that the potential action will not approach the reactivation site [16].

The refractory period also plays a role in determining the upper limit of the potential frequency of action, i.e. this period determines the maximum number of potential new actions that can start and propagate along with fiber within a certain period. The starting place must recover from its refractory period before a potential new action can be formed to follow the potential of the previous action. The length of the refractory period varies for different types of neurons. The longer the refractory period, the longer the pause before a potential new action can form, and the smaller the frequency of nerve cell responses, against the repetitive or prolonged stimulus [16].

Next is a discussion about the response of nerve cells to variations in current frequency. Figure 1 which has been given a frequency of 0.035 Hz resulting in a potential signal of action is not yet visible. So the author increased the frequency by 0.045 Hz (Figure 2) and began to oscillate. This is, the author confirmed that the signal given has not been fully responded to by the cell. In the frequency range between 0.05 Hz (Figure 3) and 0.065 Hz (Figure 4), there has been an oscillation indicating that the external signal (stimuli) has been responded to by nerve cells. This turns out to answer the previous problem that external signals (stimuli) will be converted into electrical signals by nerve cells through potential actions.

The research related to the Hindmarsh-Rose model is the dynamics of the Hindmarsh-Rose model, Aziz Alaoui in 2006. In his research, Alaoui simulated the Hindmarsh-Rose model using Hindmarsh-Rose's coding function and then searched for the clutch strength of each of the neurons and concluded that the more neurons interacted, the smaller the synchronization threshold. In other words, when the number of neurons interacting more and more, it automatically takes only a small clutch constant to produce synchronous signals (corresponding to one neuron to another)[17].

Meanwhile, other research related to the Hindmarsh-Rose model that is influenced by electromagnetic induction states that the effect of electromagnetic induction on the model is that it can respond to fluctuations in membrane potential and signal propagation in neuronal systems can produce drugs and additive currents in the media due to electromagnetic induction [18].

4. Conclusion

This paper shows that nerve cells can respond to any stimulus given according to the threshold or in other words able to convert stimuli from the outside into electrical signals. When the given frequency ≥0.055 Hz, according to the results of the monitoring it can be said that nerve cells respond in the presence of oscillations on the signals that appear. The authors hope this paper will be very beneficial for researchers to develop therapeutic methods that have neurological disorders.

Compliance with ethical standards

Acknowledgments

The authors show their appreciation and gratitude to the Computational Laboratory of Brawijaya University Malang, East Java, Indonesia for the time and place during the research.

Disclosure of conflict of interest

The authors declare no conflict of interest.

References

[1] Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, et al. An updated definition of stroke for the 21st century: A statement for healthcare professionals from the American heart association/American stroke association. Stroke. 2013;44(7):2064–89.

[2] Hodgkin AL, Huxley AF. Currents carried by sodium and potassium ions through the membrane of the giant axon of Loligo. J Physiol. 1952 Apr 28;116(4):449–72.

[3] Hodgkin AL, Huxley AF. The dual effect of membrane potential on sodium conductance in the giant axon of Loligo. J Physiol. 1952;116(4).

[4] Hodgkin AL, Huxley AF. Currents carried by sodium and potassium ions through the membrane of the giant axon of Loligo. J Physiol. 1952 Apr 28;116(4).

[5] Hodgkin AL, Huxley AF, Katz B. Measurement of current-voltage relations in the membrane of the giant axon of Loligo. J Physiol. 1952 Apr 28;116(4):424–48.

[6] Hodgkin AL, Katz B. The effect of sodium ions on the electrical activity of the giant axon of the squid. J Physiol. 1949 Mar;108(1):37–77.

[7] Hodgkin AL, Katz B. The effect of temperature on the electrical activity of the giant axon of the squid. J Physiol. 1949;109(1–2).

[8] Rinzel J, Keller JB. Traveling Wave Solutions of a Nerve Conduction Equation. Biophys J. 1973;13(12):1313–37.

[9] FitzHugh R. Impulses and Physiological States in Theoretical Models of Nerve Membrane. Biophys J. 1961 Jul;1(6).

[10] Nagumo J, Arimoto S, Yoshizawa S. An Active Pulse Transmission Line Simulating Nerve Axon*. Proc IRE. 1962;50(10).

[11] Mishra D, Yadav A, Ray S, Kalra PK. Controlling Synchronization of Modified FitzHugh-Nagumo Neurons under External Electrical Stimulation. NeuroQuantology. 2007;4(1).

[12] Hindmarsh JL, Rose RM. A model of the nerve impulse using two first-order differential equations. Nature. 1982;296(5853):162–4.

[13] Hindmarsh JL, Rose RM. BVP models of nerve membrane (reply). Nature. 1982;299(5881):375.

[14] Hindmarsh JL, Rose RM. A model of neuronal bursting using three coupled first order differential equations. Proc R Soc Lond B Biol Sci. 1984;221(1222):87–102.

[15] Chapra S., Canale RP. Numerical Methods For Engineers with Software and Programming Applications. New

York: The Mc. Graw-Hill Companies, inc.; 2002. 701–702 p.

[16] Sherwood L. Fisiologi Manusia dari Sel ke Sistem. Yusdelita N, editor. Jakarta: Penerbit Buku Kedokteran EGC; 2006. 107–108 p.

[17] Aziz-Alaoui MA. Complex emergent properties and chaos (De)synchronization. Underst Complex Syst. 2006;2006:129–47.

[18] Lv M, Wang C, Ren G, Ma J, Song X. Model of electrical activity in a neuron under magnetic flow effect. Nonlinear Dyn. 2016;85(3).