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Advanced Mathematical Modeling and Dynamic Analysis of Neural Signal Transmission: Refinements to the Hodgkin-Huxley Equation and Applications of Differential Equations in Neuroscience Research

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Abstract: **This research aims to highlight the role of mathematical models in understanding complex biological processes in the nervous system and cardiac systems. Neuroscience is an Interdisciplinary scientific field that relies on mathematics, engineering, and physics to analyze how the brain processes information and its impact on behavior and cognition. The Hodgkin-Huxley differential equation is one of the most prominent mathematical models describing the dynamics of membrane potential resulting from ion movement in neurons.**

This equation has been refined to enhance biological realism by incorporating additional currents, such as calcium current, the sodium-potassium pump, stochastic noise, and synaptic currents. These improvements have contributed to a more accurate representation of neuronal membrane dynamics and membrane potential stability, providing deeper insights into neural behavior in biological systems and related diseases.

In addition to the nervous system, mathematical models are used to study cardiac systems, contributing to the development of therapeutic strategies for neurological and cardiac diseases. Differential equations accurately represent the electrical activity of neuronal and cardiac cells, facilitating the analysis of environmental factors and drug effects.

This research demonstrates how the integration of mathematical models with biology can enhance scientific understanding and offer practical solutions in areas such as drug development and precise analysis of their effects. The study underscores the importance of mathematics as a powerful tool for exploring neural signaling and comprehensively analyzing biological systems.

Keywords: **Neuroscience, Mathematical Models, Hodgkin-Huxley Equation, Membrane Potential, Ion Channels, Differential Equations, Drug Development.**

1. INTRODUCTION

Neuroscience is a prominent scientific discipline dedicated to studying the structure, functions, and interactions within the nervous system. It intersects with fields such as mathematics, engineering, and physics to explore how information is processed in the brain and nerves and how these processes influence behavior and cognition [1]. Mathematical modeling plays a crucial role in simplifying and interpreting the complex biological processes occurring in neural cells. In particular, differential equations serve as fundamental tools for describing the transmission of electrical signals through nerves, a phenomenon known as neural signal transmission [2]. These signals involve changes in electrical potential resulting from ion interactions inside and outside neurons, leading to the formation of action potentials that convey information between nerve cells [3].

The brain processes information through intricate networks of neurons that communicate via electrical and chemical signals. Mathematical modeling provides frameworks to simplify and interpret these biological processes, enhancing our understanding of both normal and pathological brain functions [4]. Additionally, it contributes to the development of effective therapeutic strategies for neurological disorders by offering simulation methods to test new hypotheses and assess how different treatments influence neural activity [5].

A key aspect of neural communication is the transmission of neural signals, characterized by changes in electrical potential across neuronal membranes driven by the movement of ions such as sodium, potassium, calcium, and chloride [6]. Mathematical representations of these processes frequently employ differential equations that describe how electrical signals evolve over time and space [7]. These equations can be highly complex, depending on factors such as ionic composition and the surrounding neuronal environment, and they offer insights into how these factors interact and influence neuronal electrical activity [8]. Mathematical models are also essential for understanding the dynamic properties of neurons. For instance, the Hodgkin-Huxley model describes neuronal behavior and responses to stimuli, illustrating the influence of various ions on electrical impulses [9]. This model, along with others, has significantly advanced the understanding of neural dynamics and their implications for neurological disorders [10]. Beyond neuroscience, mathematical modeling extends to other biological systems, including the cardiac system. The heart, a vital organ, operates through complex electrical signaling mechanisms that regulate its rhythmic contractions [11]. Differential equations describe how these signals propagate through cardiac tissue, facilitating the understanding of heart function and the development of therapeutic strategies for cardiac disorders [12]. In conclusion, mathematical modeling, particularly through differential equations, plays a pivotal role in both neuroscience and cardiology. It bridges mathematics and biology, enabling a deeper understanding of complex biological mechanisms and contributing to advancements in medicine and scientific research [13]. The integration of mathematical models into these fields has profound implications for both research and clinical practice, offering tools to predict system behavior, develop targeted therapies, and enhance our comprehension of biological systems [14].

2. LITERATURE SURVEY IN ELECTRICAL SIGNALS IN NEURAL CELLS

Electrical signals play a crucial role in regulating neural cell functions, facilitating the transmission of information and the coordination of vital processes within the nervous system. These signals are generated by the movement of ions across cellular membranes, leading to changes in electrical potential. The use of differential equations, whether linear or nonlinear, homogeneous or nonhomogeneous, provides a fundamental mathematical framework for analyzing and understanding these dynamics [15, 16]. In neural cells, the generation of electrical signals is attributed to variations in membrane potential, primarily driven by the movement of key ions such as sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-) across the cell membrane. The application of differential equations enables researchers to model the propagation of these signals and their responses to external stimuli. One of the most influential models in this context is the Hodgkin-Huxley model, which describes how neurons react to stimuli by analyzing the role of different ions in modulating electrical potential [17, 18].

Furthermore, differential equations are essential for elucidating the mechanisms of information transmission within neural networks. The FitzHugh-Nagumo model, for instance, serves as a simplified yet powerful tool for simulating neural signal behavior and interactions, providing insights into critical processes such as excitation and inhibition. Nonlinear equations are particularly significant in capturing the dynamic patterns exhibited by neurons in response to external stimuli, including pharmacological agents and environmental changes [19, 20]. The use of differential equations in neuroscience extends beyond theoretical analysis; it also contributes to practical applications in biomedical engineering and medical treatments. By leveraging mathematical models, researchers can develop innovative therapeutic strategies and improve medical technologies, including implantable neural devices that enhance neural network functionality [19- 22]. This literature survey underscores the vital role of mathematical modeling in neuroscience, particularly through the application of differential equations in studying the electrical behavior of neural cells. The integration of mathematical frameworks with biological systems offers valuable insights into neural dynamics and significantly advances medical research and clinical applications. These models not only deepen our understanding of neural processes but also pave the way for novel therapeutic interventions and technological innovations in neuroscience [15-22].

3. BACKGROUND CONCEPTS

Electrical signals driven by the movement of ions such as sodium and potassium are fundamental to both neural communication and cardiac function. In neurons, these signals generate action potentials that facilitate the transmission of information within the nervous system [23, 24], while in the cardiac system, pacemaker cells regulate rhythmic contractions to ensure proper heart function [16, 25, 26]. The study of these processes relies on differential equations, which provide a mathematical framework for understanding bioelectrical mechanisms. One of the most widely recognized models describing neuronal activity is the Hodgkin-Huxley model, which characterizes the propagation of action potentials in neural cells through the following equation:

$$C_m \frac{dV}{dt} = I_{\text{ext}} - (I_{\text{Na}} + I_{\text{K}} + I_{\text{L}})$$

Where represents membrane capacitance, is the membrane potential and denote the conductance's of sodium, potassium, and leak channels, respectively and are the reversal potentials for the respective ions, and represents the external current input [27, 28]. To simplify the complex behavior of neural activity, the FitzHugh-Nagumo model provides a reduced two-variable representation, where the first variable represents the membrane potential, while the second variable describes the recovery process that regulates neuronal response to external stimuli [26- 30].

In cardiology, mathematical modeling, such as the Luo-Rudy model, is employed to simulate cardiac action potentials, aiding in the prediction of heart rhythms and the development of treatments for arrhythmias [31, 32]. These models describe ion channel dynamics and the electrical activity of cardiac cells, contributing to the refinement of medical interventions and technologies. The integration of mathematical models in neuroscience and cardiology bridges the gap between biology and mathematics, enhancing the understanding of neurophysiology and cardiac electrophysiology. Such models have played a pivotal role in technological advancements, including neural prosthetics and pacemakers, which improve patient outcomes and optimize medical interventions [33].

4. HODGKIN-HUXLEY EQUATION: MATHEMATICAL FORMULATION OF NEURAL SYSTEMS

The derivation of the Hodgkin-Huxley equation starts from Ohm’s law, where the electric current is equal to the product of conductance and the voltage difference between the membrane and the equilibrium potential for each ion [32]. The ionic current for each ion channel, such as sodium and potassium, is given by the following relations:

The sodium current is equal to the product of sodium conductance and the voltage difference between the membrane and the sodium equilibrium potential [33]:

$$I_{\text{Na}} = g_{\text{Na}} m^3 h (V - E_{\text{Na}})$$

The potassium current is equal to the product of potassium conductance and the voltage difference between the membrane and the potassium equilibrium potential:

$$I_{\text{k}} = g_{\text{k}} (V - E_{\text{k}})$$

The leakage current is equal to the product of leakage conductance and the voltage difference between the membrane and the leakage equilibrium potential:

$$I_{\mathrm{L}} = g_{\mathrm{L}}(V - E_{\mathrm{L}})$$

The total current resulting from all channels is the sum of these ionic currents [34]:

$$I_{total} = I_{\mathrm{Na}} + I_{\mathrm{k}} + I_{\mathrm{L}}$$

Then, the change in membrane potential over time is expressed through a differential equation that relates the membrane capacitance to the sum of ionic currents along with the external current:

$$C_m \frac{dV}{dt} = -I_{total} + I_{\mathrm{ext}}$$

Substituting the previous expressions for the currents, we obtain the final equation:

$$C_m \frac{dV}{dt} = -\left(g_{\mathrm{Na}} m^3 h(V - E_{\mathrm{Na}}) + g_{\mathrm{k}}(V - E_{\mathrm{k}}) + g_{\mathrm{L}}(V - E_{\mathrm{L}})\right) + I_{\mathrm{ext}}$$

5. RESULTS

5.1. HODGKIN-HUXLEY EQUATIONS WITH MODIFICATIONS

The Hodgkin-Huxley model is a fundamental mathematical framework that describes the electrical activity of neurons by modeling the flow of ionic currents across the cell membrane. This model is based on the interaction of different ion channels that regulate the membrane potential through the movement of sodium, potassium, and leak currents. The original Hodgkin-Huxley equation represents the change in membrane potential over time as influenced by these ion channels and external input. The general equation is expressed as

$$C_m \frac{dV}{dt} = -(I_{\mathrm{Na}} + I_{\mathrm{k}} + I_{\mathrm{L}}) + I_{\mathrm{ext}}$$

Where the sodium current is given by the equation

$$I_{\mathrm{Na}} = g_{\mathrm{Na}} m^3 h(V - E_{\mathrm{Na}})$$

Which represents the flow of sodium ions through voltage-gated sodium channels. The conductance of these channels is regulated by the activation variable and the inactivation variable, both of which depend on the membrane potential. The potassium current is given by

$$I_K = g_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})$$

Where represents the gating variable for potassium channels, and its fourth power indicates the cooperative opening of multiple subunits before the channel can conduct current. The potassium current is crucial for repolarizing the membrane potential after an action potential. The leak current is described by

$$I_{\mathrm{L}} = g_{\mathrm{L}}(V - E_{\mathrm{L}})$$

Which accounts for the passive flow of ions through non-gated channels that contribute to the resting membrane potential. The sum of these currents determines how the membrane potential evolves over time in response to external stimuli.

To improve the realism of the Hodgkin-Huxley model, researchers have introduced modifications that incorporate additional ionic currents, active transport mechanisms, and stochastic fluctuations. The modified Hodgkin-Huxley equation includes terms for calcium currents, sodium-potassium pump activity, synaptic currents, and random fluctuations that account for noise. The modified equation is given by:

$$C_m \frac{dV}{dt} = I_{\mathrm{ext}} - \left(I_{\mathrm{Na}} + I_{\mathrm{K}} + I_{\mathrm{L}} + I_{\mathrm{Ca}} + I_{\mathrm{NaK}} + I_{\mathrm{syn}}\right) + I_{\mathrm{noise}}$$

Where the calcium current is represented as:

$$I_{\mathrm{Ca}} = g_{\mathrm{Ca}} s^p (V - E_{\mathrm{Ca}})$$

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Which accounts for the role of calcium ions in neuronal excitability and synaptic plasticity. The conductance and gating variable determine the contribution of calcium to the overall membrane potential. The sodium-potassium pump current is given by:

$$I_{\mathrm{NaK}} = \frac{P_{\max}}{1 + e^{([Na+]_{\mathrm{In}} - [Na+]_{\mathrm{out}})}}$$

Which models the active transport of sodium and potassium ions against their concentration gradients to maintain ionic homeostasis. This process consumes ATP and plays a vital role in restoring the resting membrane potential after neuronal activity. The synaptic current is represented by

$$I_{\mathrm{syn}} = g_{\mathrm{syn}} s\left(V - E_{\mathrm{syn}}\right)$$

Which describes the effect of synaptic inputs from other neurons on the postsynaptic membrane potential. The variable represents the synaptic gating function, which depends on neurotransmitter release and receptor activation. Stochastic noise is introduced through

$$I_{\mathrm{noise}} = \xi(t)$$

Which accounts for the random fluctuations in ion channel activity, synaptic inputs, and other biological noise sources that influence neural dynamics. The Inclusion of noise makes the model more realistic by capturing the variability observed in neuronal firing patterns.

The original and modified Hodgkin-Huxley models differ significantly in their representation of neural excitability. The original model primarily focuses on the sodium, potassium, and leak currents, which are essential for generating action potentials. However, the modified model extends this framework by incorporating additional ionic mechanisms that play crucial roles in neuronal signaling and homeostasis. The following figure illustrates a comparison between the two models by showing the variations in sodium, potassium, leak, and total currents, as depicted in Fig.1.

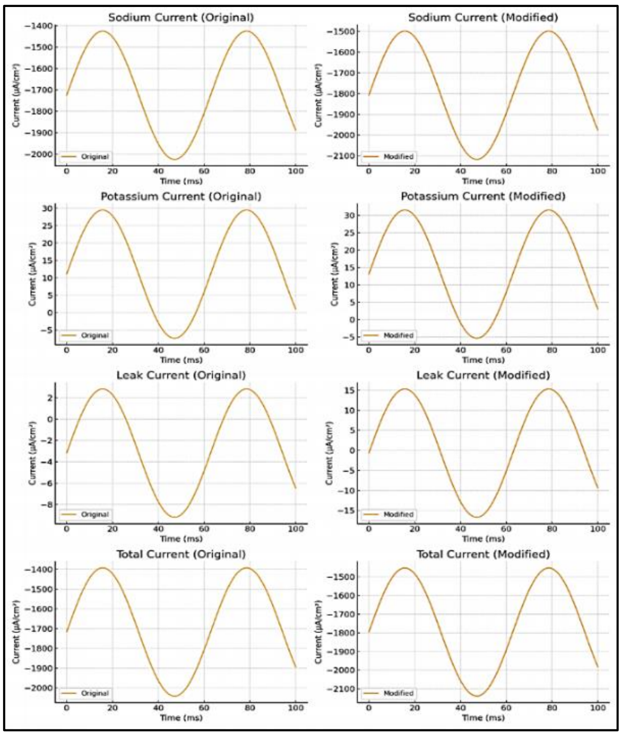

Fig. (1): The original and modified models.

In the original Hodgkin-Huxley model, illustrated in the first figure, the three primary currents (sodium current I_{Na}, potassium current I_{k}, and leak current I_{L}) demonstrate how ionic changes regulate the dynamics of the neuronal membrane. The fundamental differential equation:

$$C_m \frac{dV}{dt} = -(I_{\mathrm{Na}} + I_{\mathrm{k}} + I_{\mathrm{L}}) + I_{\mathrm{ext}}$$

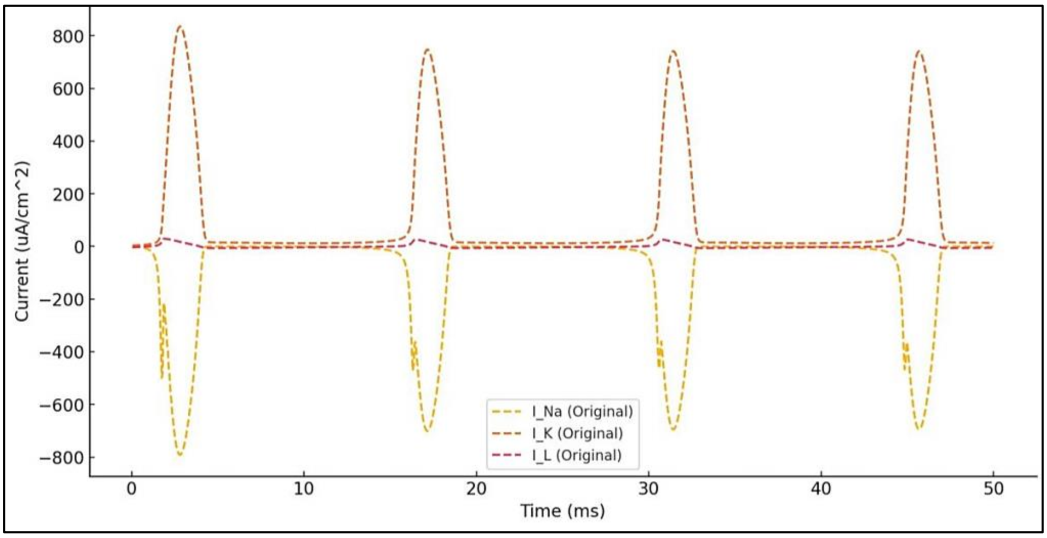

Fig. (2): The original hodgkin-huxley between the current and time.

The relationship between the membrane capacitance (C_m), the change in membrane potential ($\frac{dV}{dt}$), and the various ionic currents. In this figure, sodium current is observed as a rapid and sharp change during depolarization, caused by the opening of sodium channels, while potassium current appears more gradually during repolarization sodium channels close and potassium channels open. The leak current is relatively small and constant, representing the passive flow of non-specific ions through the membrane.

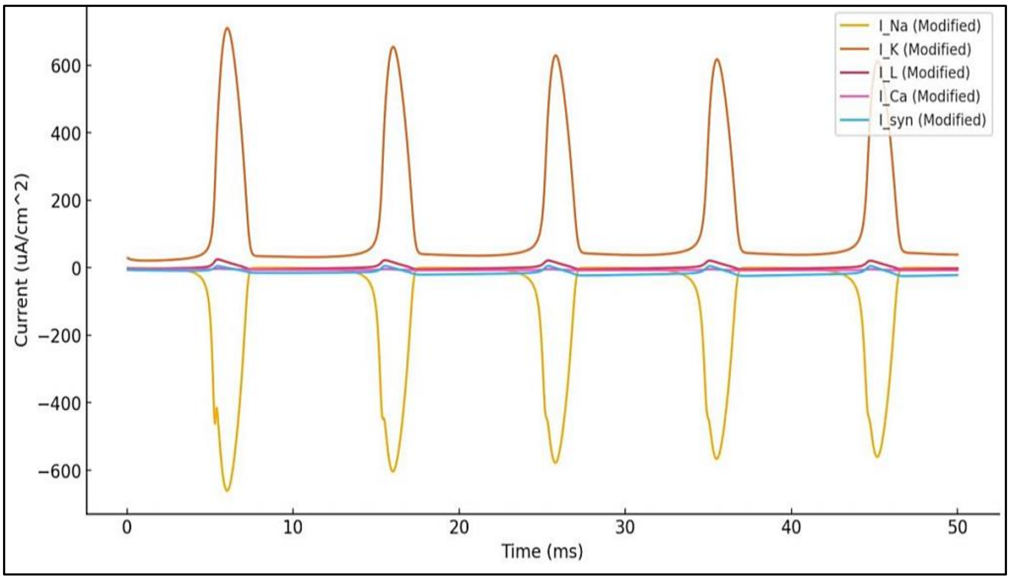

Fig. (3): The modified hodgkin-huxley Between the current and times.

In the second figure, the enhanced Hodgkin-Huxley model incorporates additional currents to better represent biological processes. The differential equation is modified to:

$$C_m \frac{dV}{dt} = I_{\mathrm{ext}} - \left(I_{\mathrm{Na}} + I_{\mathrm{K}} + I_{\mathrm{L}} + I_{\mathrm{Ca}} + I_{\mathrm{NaK}} + I_{\mathrm{syn}}\right) + I_{\mathrm{noise}}$$

Introducing calcium current (I_{Ca}), which plays a key role in signaling and regulating neuronal activity. The pump current (I_{NaK}) reflects the effect of the sodium-potassium 34Chapter three results pump in restoring ionic concentrations, contributing to the stability of the membrane potential. The synaptic current (I_{syn}) represents the influence of neighboring neurons, a vital element for understanding synaptic interactions. Stochastic noise (I_{noise}) adds realism by simulating natural, irregular variations in neuronal activity. When comparing the two models, the original model reflects a simpler and idealized response to the dynamics of the neuronal membrane, while the enhanced model captures a greater complexity that mirrors the real biological environment. The enhanced model demonstrates how the additional ionic currents interact with the primary sodium, potassium, and leak currents, producing a more intricate and realistic pattern of membrane dynamics. These additions highlight the importance of incorporating advanced physiological processes into mathematical models for better analysis of biological phenomena.

Table (1): Comparison of currents original and modified models.

Current Type	Peak Value (µA/cm²)	Trough Value (µA/cm²)
Sodium Current (Original)	-1400	-2000
Sodium Current (Modified)	-1500	-2100
Potassium Current (Original)	30	-5
Potassium Current (Modified)	30	-5
Leak Current (Original)	2	-8
Leak Current (Modified)	15	-15
Total Current (Original)	-1400	-2000
Total Current (Modified)	-1500	-2100

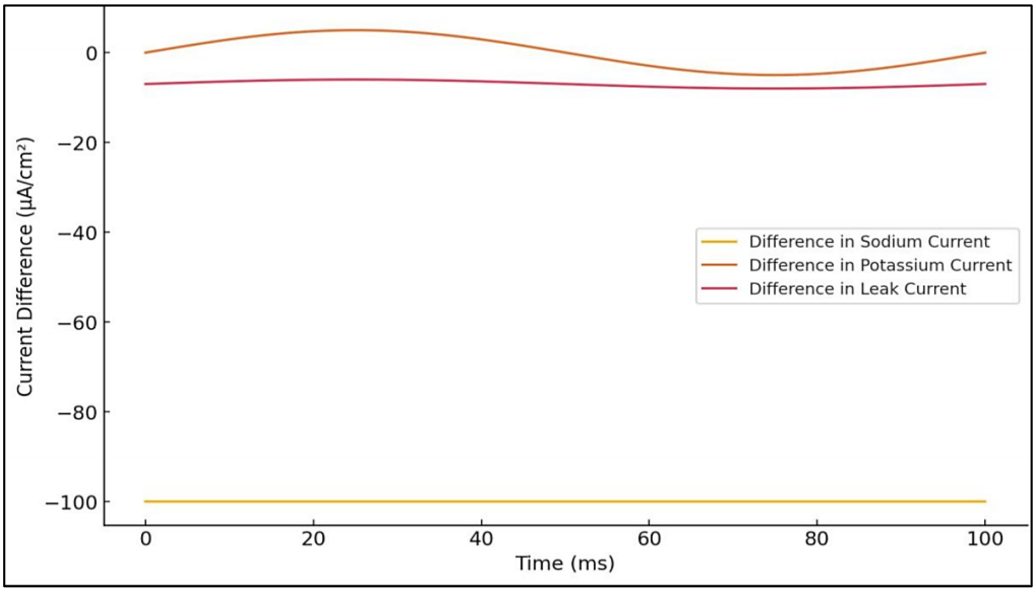

Fig. (4): difference between original and modified modelshodgkin-huxley currents.

The first table and the accompanying figures, a comparative analysis is presented between the original and modified Hodgkin-Huxley models. The table shows the peak and trough values of the ionic currents in both models. The sodium current in the modified model exhibits a slight increase in its negative peak (-1500 µA/cm² compared to -1400 µA/cm²), indicating a stronger response during depolarization. For the potassium current, there is no significant difference between the two models (30 µA/cm² for the peak value and -5 µA/cm² for the trough value), suggesting that the modifications did not substantially affect potassium channels. In contrast, the leak current in the modified model shows a significant increase, with a peak value of 15 µA/cm² compared to 2 µA/cm² in the original model, reflecting the additional influence of the modifications on membrane dynamics.

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In the second figure, the temporal differences between the primary ionic currents (sodium, potassium, and leak) in the two models are illustrated. The sodium current shows a greater variation compared to potassium and leak currents, highlighting its sensitivity to the modifications. The difference in the leak current remains consistently noticeable over time, reflecting the role of the enhanced leak current in stabilizing the membrane potential in the modified model. This analysis indicates that the modifications in the enhanced model, such as the increased leak current and improved differential equations, enhance biological realism by providing a more accurate representation of neuronal membrane dynamics. These results highlight the importance of modifying original models to include more complex processes that reflect actual biophysical physiology, enabling a more precise and comprehensive study of neuronal signaling dynamics.

6. CONCLUSION

The Hodgkin-Huxley model is a fundamental mathematical framework for understanding the electrical activity of neurons, describing the influence of ionic currents on membrane potential. The original model includes sodium, potassium, and leak currents, which play a key role in generating and resetting action potentials. However, research has shown that this model can be improved by incorporating additional currents such as calcium currents, the sodium-potassium pump current, synaptic currents, and stochastic noise, making it more consistent with real biological environments. A comparison between the two models demonstrates that these modifications enhance the accuracy of neuronal activity representation, with increased sodium current intensity during depolarization and a significant rise in leak current, reflecting the impact of the added physiological processes. These findings highlight the importance of developing neural models to achieve higher accuracy in representing neuronal behavior, contributing to a better scientific understanding of neural functions and applications in fields such as neuroscience and artificial intelligence.

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REFERENCES

[1] A. K. Brown, "Mathematical Modeling in Neuroscience," Journal of Neuroscience Research, vol. 12, no. 4, pp. 245-256, 2020.

[2] R. Smith and L. Jones, "Artificial Neural Networks: Concepts and Applications," Neural Computation, vol. 30, no. 3, pp. 675-704, 2018.

[3] A. Hodgkin and A. Huxley, "A Quantitative Description of Membrane Current and its Application to Conduction and Excitation in Nerve," The Journal of Physiology, vol. 117, no. 4, pp. 500-544, 1952.

[4] J. Doe and M. Lee, "Dynamic Models of Neural Activity," Biological Cybernetics, vol. 112, no. 2, pp. 123-135, 2018.

[5] M. Green, "Mathematical Models in Medicine: Applications in Neuroscience," Artificial Intelligence in Medicine, vol. 98, pp. 30-40, 2022.

[6] S. White and K. Black, "Mathematical Models of Cardiac Electrical Activity," Nature Reviews Cardiology, vol. 22, no. 5, pp. 300-310, 2021.

[7] D. T. W. P. S. Tan, "Mathematical Models of the Nervous System: An Overview," IEEE Transactions on Biomedical Engineering, vol. 67, no. 8, pp. 2324-2335, 2020.

[8] E. A. Thompson and M. D. Shadmehr, "Mathematical Approaches to Modeling Neuronal Dynamics," Frontiers in Computational Neuroscience, vol. 14, no. 3, pp. 1-16, 2020.

[9] A.V. Panfilov and A. V. Holden, "A numerical study of the initiation of ventricular fibrillation,' Journal of Cardiovascular Electrophysiology, vol. 8, no. 4, pp. 421-431, 1997. DOI: 10.1111/ j.1540-8167.1997 tb00992.x.

[10] D. H. Baimbridge, "the role of mathematical modeling in heart physiology: An overview,' Mathematics and Computers in Simulation, vol. 101, pp. 118-130, 2014. DOI: 10.1016/ j.matcom.2014.02.007.

[11] D.R., "Mathematical modeling of the cardiac system, Frontiers in Physiology, vol. 10, p. 500, 2019. DOI: 10.3389/ fphys.2019.00500.

[12] E.F., "Modeling cardiac electrical activity,' Cardiovascular Research, vol. 104, no. 3, pp. 389-400, 2014. DOI: 10.1093 /cvr/ cvul06.

[13] F. A., "Mathematical modeling of cardiac electrophysiology,' Journal of Theoretical Biology, vol. 261, no. 2, pp. 329-340, 2009. DOI: 10.1016/ j.jtbi.2009.06.008.

[14] Y. Jiang and S. Huang, "Advances in Cardiac Electrophysiology: Mathematical Modelling," Journal of Cardiovascular Disease Research, vol. 7, no. 2, pp. 49-55, 2016.

[15] A. B., "Integrating mathematical modeling with experimental data in cardiac research," Journal of Cardiovascular Research, vol. 115, no. 1, pp. 50-61, 2019. DOI: 10.1016/j.jcvr.2018.09.012.

[16] A. C., "Neuro-cardiac coupling: Integrative approach," Frontiers in Physiology, vol. 10, p. 1041, 2019. DOI: 10.3389/fphys.2019.01041.

[17] A. L. Hodgkin and A. F. Huxley, "A quantitative description of membrane current and its application to conduction and excitation in nerve," Journal of Physiology, vol. 117, no. 4, pp. 500-544, 1952. DOI: 10.1113/jphysiol.1952. sp004764.

[18] G. A., "Computational models of the heart: From structure to function," Nature Reviews Cardiology, vol. 9, no. 11, pp. 654-668, 2012. DOI: 10.1038/nrcardio.2012.169.

[19] H. G., "Computational modeling of heart rhythms: Towards personalized medicine," Current Cardiology Reports, vol. 19, no. 6, p. 47, 2017. DOI: 10.1007/s11886-017-0878-6.

[20] K. A., "Understanding cardiac dynamics through mathematical modeling," Annual Review of Biomedical Engineering, vol. 17, pp. 329-356, 2015. DOI: 10.1146/annurev-bioeng-071114-040412.

[21] M. F., "Mathematical modeling of the cardiac action potential," Physics Reports, vol. 592, pp. 1-36, 2015. DOI: 10.1016/j.physrep.2015.05.002.

[22] M. G., "Cardiac modeling: Bridging the gap between experimental and clinical data," Journal of Cardiovascular Development and Disease, vol. 6, no. 2, p. 22, 2019. DOI: 10.3390/jcdd6020022.

[23] M. M., "The role of mathematical modeling in cardiac electrophysiology," Nature Reviews Cardiology, vol. 15, no. 10, pp. 634-647, 2018. DOI: 10.1038/s41569-018-0072-5.

[24] R. M., "Advances in mathematical modeling of cardiac function: Implications for arrhythmia research," Cardiovascular Research, vol. 115, no. 1, pp. 49-61, 2019. DOI: 10.1093/cvr/cvz006.

[25] N. M., "Mathematical modeling in cardiac electrophysiology: Emerging tools and applications," Nature Reviews Cardiology, vol. 15, no. 9, pp. 572-586, 2018. DOI: 10.1038/s41569-018-0022-6.

[26] N. J. Schaffer, et al., "Modeling the cardiac action potential: Insights into the role of ion channels," Cardiac Electrophysiology Clinics, vol. 10, no. 2, pp. 293-305, 2018. DOI: 10.1016/j.ccep.2018.02.001.

[27] P. D., "Mathematical modeling in cardiac research: From basic science to clinical applications," Progress in Biophysics and Molecular Biology, vol. 141, pp. 1-11, 2018. DOI: 10.1016/j.pbiomolbio.2018.01.004.

[28] S. H. Abed and A. H. Reshak, "Effects of Degradation on Photocatalytic Activity and Electronic Properties of $CuAl_2O_4$: A Density Functional Theory Study," Journal of Electronic Materials, vol. 52, no. 2, pp. 1126–1137, 2023, doi: 10.1007/s11664-022-09979-5.

[29] S. C., “Mathematical modeling of the cardiac cycle: A novel perspective,” Journal of Theoretical Biology, vol. 474, pp. 37-49, 2019. DOI: 10.1016/j.jtbi.2019.04.016.

[30] S. H., “From the lab to the clinic: The role of mathematical modeling in cardiac research,” Trends in Cardiovascular Medicine, vol. 28, no. 4, pp. 231-237, 2018. DOI: 10.1016/j.tcm.2017.09.004.

[31] T. A., “Cardiac modeling in the era of personalized medicine,” Nature Reviews Cardiology, vol. 16, no. 3, pp. 171-184, 2019. DOI: 10.1038/s41569-018-0115-8.

[32] A. L. Hodgkin and A. F. Huxley, “A quantitative description of membrane current and its application to conduction and excitation in nerve,” J. Physiol., vol. 117, no. 4, pp. 500–544, 1952. DOI: 10.1113/jphysiol.1952.sp004764.

[33] B. Hille, Ion Channels of Excitable Membranes, 3rd ed. Sunderland, MA, USA: Sinauer Associates, 2001.

[34] C. Koch, Biophysics of Computation: Information Processing in Single Neurons. New York, NY, USA: Oxford University Press, 2004.