Modelling of Excitation and Firing in Simple Neural Networks

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Abstract: In the project, the aim is to understand how and under what conditions a neuron can be fired or excited. For that matter, by using NEURON simulation program and Python programming language, a neural network will be designed and be tested with several signals for stimulation purposes. After that, in order to understand further, the concept of firing and excitation of a neuron will be investigated by applying external stimulations in a simulation environment. At the end, how external stimulation techniques could be used to fire or excite a neuron will be answered.

Keywords: Extracellular stimulation, action potential, NEURON, finite-element method (FEM), neuron model, excitable membrane.

I. INTRODUCTION

A neuron is a type of cell that is found in the nervous system. It is specialized for transmitting electrical signals, and it plays a crucial role in many of the body's functions, including sensory perception, muscle control, and behavior. A neuron has a cell body, which contains the nucleus and other organelles, and it has one or more long, thin extensions called dendrites and axons. The dendrites receive signals from other neurons, and the axons transmit signals to other neurons or to muscles or glands [1].

An action potential is an electrical signal that is generated by a neuron when it is stimulated by a certain threshold of input from other neurons. It is a rapid, short-lived change in the electrical voltage across the neuron's membrane, and it travels along the axon of the neuron from the cell body to the axon terminal. When an action potential reaches the axon terminal, it triggers the release of chemicals called neurotransmitters, which then bind to receptors on other neurons, muscles, or glands, and transmit the signal across the synapse to the next cell. In this way, action potentials are the "language" of the nervous system, and they are essential for the transmission of information throughout the body [1].

An axon can be modeled mathematically using a variety of methods and approaches, depending on the specific characteristics and properties of the axon in question. One common method for modeling axons is to use the Hodgkin-Huxley model, which describes the electrical behavior of an axon using a set of coupled nonlinear differential equations. This model accounts for the ionic currents flowing through the axon membrane and the resulting voltage changes, allowing researchers to predict the behavior of the axon under different conditions. Other mathematical models of axons may focus on different aspects of axon function, such as axon guidance or axon regeneration, and may use a variety of different mathematical techniques and approaches [1].

The Hodgkin-Huxley model is a mathematical model that describes the electrical behavior of an axon, which is a long, thin fiber that carries nerve impulses in the body. The model is based on the observation that the voltage changes across the membrane of an axon are caused by the flow of ionic currents through the membrane, and it uses a set of coupled nonlinear differential equations to describe the dynamics of these currents. The equations are based on the kinetics of the ionic channels in the axon membrane, and they describe how the voltage across the axon membrane (V) changes over time due to the flow of ionic currents through the membrane, as well as the dynamics of the ionic activation variables (m and n). The model allows researchers to predict the behavior of an axon under different conditions, and it has been widely used to study the electrical properties of axons and the mechanisms underlying axon function [1].

Finite element method (FEM) is a numerical technique for solving problems in engineering and applied mathematics. It is a mathematical

method that is used to analyze the behavior of complex systems, such as structures, machines, and materials, under a variety of conditions. FEM is based on the concept of dividing a complex system into a number of small, interconnected elements, each of which can be modeled and analyzed separately. By breaking the system down into smaller, simpler components, FEM allows researchers to study the behavior of the system as a whole, as well as the interactions between its individual parts. FEM is widely used in engineering and applied sciences to study and predict the behavior of complex systems, and it is an important tool for design, analysis, and optimization in a variety of fields [2].

Neurostimulation, also known as neuromodulation, is the use of electrical or chemical signals to stimulate specific areas of the nervous system in order to alter nerve activity and treat various medical conditions. It is a form of therapy that is used to treat conditions such as chronic pain, epilepsy, and movement disorders, among others. There are several different types of neurostimulation, including spinal cord stimulation, and deep brain stimulation, among others. These therapies can be used to alter the activity of specific nerves or regions of the brain in order to relieve symptoms and improve a patient's quality of life [1].

II. METHODS

An excitable membrane is a type of biological membrane that is capable of generating and responding to electrical signals. This property is essential for the function of many types of cells, including neurons and muscle cells. Excitable membranes are made up of a special type of protein called an ion channel, which allows ions (such as sodium and potassium) to flow in and out of the cell. When an electrical stimulus, such as a nerve impulse, is applied to the membrane, the ion channels open and allow ions to flow through, creating an electrical current that can be detected and used by the cell to carry out its functions [1].

A. Electrical Model

The electrical activity of an axon can be represented using various types of electrical signals, such as voltage, current, and impedance.

Voltage is a measure of the electrical potential difference between two points in a circuit. In the case of an axon, the voltage across the axon membrane can be measured using microelectrodes or other sensors. This voltage can change over time in response to various stimuli, such as a nerve impulse, and it can be used to represent the electrical activity of the axon [3].

Current is a measure of the flow of electric charge through a conductor, such as a wire or an axon. In the case of an axon, the current can be measured by placing electrodes on either side of the axon and measuring the flow of electric charge through the axon. The current through an axon can change over time in response to various stimuli, and it can be used to represent the electrical activity of the axon [3].

Impedance is a measure of the resistance to the flow of electric current in a circuit. In the case of an axon, the impedance can be measured by applying a small alternating current to the axon and measuring the resulting voltage. The impedance of an axon can change over time in response to various stimuli, and it can be used to represent the electrical activity of the axon [3].

Overall, the electrical activity of an axon can be represented using various types of electrical signals, depending on the specific research question or medical condition being studied, and the specific type of electrical signal used will depend on the particular characteristics and properties of the axon being studied [3].

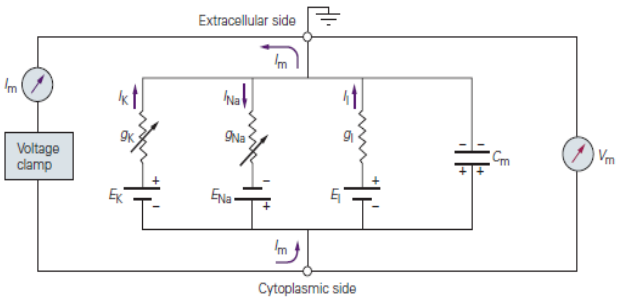

Figure 1: Electrical model for an axon [1]

The Hodgkin-Huxley model is a mathematical model that describes the electrical behavior of an axon using a set of coupled nonlinear differential equations. The model is based on the observation that the voltage changes across the membrane of an axon are caused by the flow of ionic currents through the membrane, and it uses four differential equations to describe the dynamics of these currents []. The equations are as follows:

x	E_x [mV]	G_x [mS/cm^2]
Na	55	40
K	-77	35
CL	-65	0.3

Table 1: Electrical potential and conductivity of voltage gated ion channels [3]

x	α_x (u/mV) [ms^{-1}]	β_x (u/mV) [ms^{-1}]
n	$0.01\ (V + 10) / [-1 + e^{(V+10)/10}]$	$0.125\ e^{V/80}$
m	$0.1\ (V + 25) / [-1 + e^{(V+25)/10}]$	$4\ e^{V/18}$
h	$1 / [1 + e^{(V+30)/10}]$	$1 / [1 + e^{(V+30)/10}]$

Table 2: Coefficient equation for m, n, and h [4]

$$\frac{dn}{dt} = \alpha_n * (1 - n) - \beta_n * n \ (1)$$

$$\frac{dm}{dt} = \alpha_m * (1 - m) - \beta_m * m \ (2)$$

$$\frac{dh}{dt} = \alpha_h * (1 - h) - \beta_h * h \ (3)$$

$$\delta I = C_m \frac{dV}{dt} + G_{Na} * m^3 * h * (V - E_{Na}) + G_K * n^4 * (V - E_K) + G_{Cl} * (V - E_{Cl}) + I_{app} \ (4)$$

These equations describe how the voltage across the axon membrane (V) changes over time due to the flow of ionic currents through the membrane, as well as the dynamics of the ionic activation variables (m, h, and n). The constants G_{Na}, G_K, E_{Na}, and E_K represent the conductance of the sodium and potassium ions, and the reversal potential of the sodium and potassium ions, respectively. The term I_{app} represents an externally applied current, and the functions alpha_n, beta_n, alpha_m, and beta_m represents the kinetics of the ionic activation variables [4].

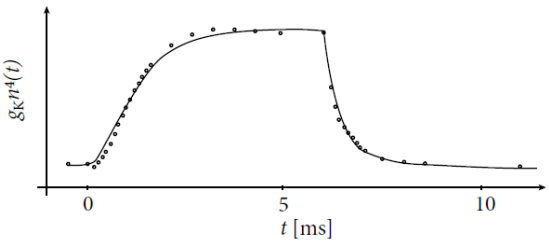

Figure 2: Voltage gated potassium channel graph [3]

The conductivity of ion channels in an axon change according to the membrane potential of the axon. The membrane potential of a neuron is the electrical potential difference across the cell membrane, and it is determined by the concentration and distribution of ions inside and outside the cell. When the membrane potential of an axon is at a certain level, the ion channels in the axon can open or close, allowing ions to flow in or out of the cell and changing the conductivity of the axon [3].

Ion channels are proteins that are embedded in the cell membrane of neurons, and they are specialized for allowing specific ions to flow in or out of the cell. Different types of ion channels are sensitive to different levels of membrane potential, and they can open or close in response

to changes in the membrane potential. For example, when the membrane potential of an axon becomes more positive, certain types of ion channels can open and allow positively charged ions, such as sodium ions, to flow into the cell. This can increase the conductivity of the axon and contribute to the propagation of an action potential [3].

Overall, the conductivity of ion channels in an axon change according to the membrane potential of the axon, and this change in conductivity can affect the ability of the axon to transmit electrical signals. By controlling the opening and closing of ion channels in response to changes in the membrane potential, neurons can regulate the flow of ions into and out of the cell, allowing them to generate and transmit electrical signals [3].

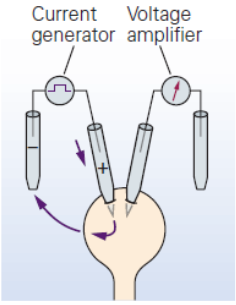

Figure 3: Microglass for current source and microelectrode for action potential recording [1]

B. Physical Model

Microglasses, also known as micropipettes, are very small glass tubes that can be used to deliver tiny amounts of liquid to a specific location in the body, such as a single cell or an axon. They are commonly used in biological research and in some medical procedures, such as intracellular injection [1].

To use microglasses to stimulate an axon, the first step is to locate the axon and gain access to it. This can be done through a variety of methods, depending on the specific research question or medical condition being studied. For example, if the axon is on the surface of the brain, a technique called electrocorticography (ECoG) can be used to place electrodes on the surface of the brain and apply a small electrical current to the axon. If the axon is inside the brain, a technique called micro iontophoresis can be used to inject a chemical compound, such as a neurotransmitter or a drug, directly onto the axon [1].

Once the axon has been identified and access has been gained, the next step is to use the microglass to deliver the stimulus. This can be done by attaching the microglass to a micromanipulator, which is a device that allows the researcher to precisely control the position and movement of the microglass. The researcher can then use the micromanipulator to position the microglass near the axon and deliver a small amount of the stimulus directly to the axon [1].

Overall, using microglasses to stimulate an axon can provide researchers with a high level of spatial and temporal precision, allowing them to study the response of the axon to specific stimuli with a high degree of accuracy [1].

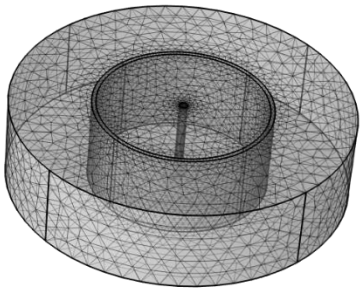

Figure 4: Physical model for axoplasm, membrane and extracellular area of an axon

Finite element method (FEM) could potentially be used to study the behavior of axons and to understand how they work. Axons are long, thin fibers that carry nerve impulses in the body, and they are highly complex structures that can exhibit a wide range of behaviors. FEM could be used to model the electrical and mechanical properties of axons, and to predict how they will behave under different conditions [2].

To use FEM to study axons, a researcher would first need to create a mathematical model of an axon that includes the key electrical and mechanical properties of the axon. This model could include equations that describe the flow of ionic currents through the axon membrane, as well as equations that describe the mechanical properties of the axon, such as its stiffness and flexibility. The researcher would then use FEM to solve the equations and predict the behavior of the axon under different conditions, such as different applied currents or different mechanical loads. By analyzing the results of the FEM simulations, the researcher could gain insights into the behavior of axons and how they function [2].

Overall, FEM is a powerful tool that could be used to study the behavior of axons and to better understand how they work. By creating mathematical models of axons and using FEM to solve the equations, researchers can gain valuable insights into the complex behaviors of these important biological structures [2].

Name	Expression	Value
memb_int_r	1[mm]	0.001 m
memb_r	50000[nm]	5E-5 m
height	1 [mm]	0.001 m
memb_epsilon	5.65	5.65
E_na	55 [mV]	0.055 V
E_k	-72 [mV]	-0.072 V
E_cl	-49.387 [mV]	-0.049387 V
axoplasm_cond	0.5	0.5
axoplasm_epsilon	80	80
extoplasm_cond	1	1
extoplasm_epsilon	80	80
memb_capacitance	1 [uF/cm^2]	0.01 F/m²
hole_r	0.05[mm]	5E-5 m
memb_rest_pot	-65 [mV]	-0.065 V
u	0 [mV]	0 V
memb_pot	u + memb_rest_pot	-0.065 V
g_na_const	120 [mS/cm^2]	1200 S/m²
g_k_const	36 [mS/cm^2]	360 S/m²
g_cl_const	0.3 [mS/cm^2]	3 S/m²
e_na	115 [mV]	0.115 V
e_k	-12 [mV]	-0.012 V
e_cl	10.613[mV]	0.010613 V
g_cl	g_na_const / memb_capacitance	1.2E5 1/s
i_memb	0 [mA]	0 A
memb_cond	1	1

Figure 5: Defined variables for physical model of an axon in COMSOL Multiphysics [5]

III. RESULTS

A. Circuit Model

To model action potentials in Python using the Hodgkin-Huxley model, a set of functions representing the individual ion channels and their conductance, as well as a function describing the overall behavior of the neuron membrane, can be defined. The scipy.integrate.odeint function can then be used to solve the differential equations and compute the voltage of the neuron membrane over time. Simulations can be run to study the behavior of the neuron and the action potentials it produces, and Python can be used to visualize the results of the simulations and to analyze the data to understand the underlying mechanisms of the action potentials.

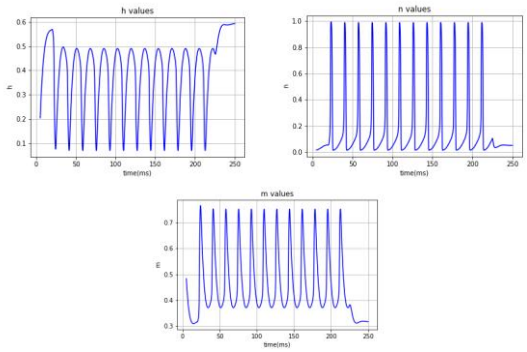

Figure 6: Graphs for m, n, and h values after solving differential equation of the axon model

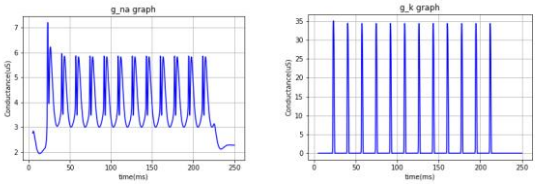

Figure 7: Graphs for G_{Na} and G_K values after solving differential equation of the axon model

The spike rate of a neuron, also known as the firing rate, can be influenced by various factors, including the strength and duration of the external stimuli. The spike rate tends to increase as the strength of the external stimuli increases, but the relationship between the spike rate and the stimulus strength is often nonlinear and may

depend on the specific characteristics of the neuron and the stimuli.

The duration of the stimulus can also affect the spike rate, with a longer stimulus providing more opportunity for action potentials to be generated and a shorter stimulus providing less opportunity. It should be noted that the spike rate is not the only factor that determines the response of a neuron to stimuli, and the pattern of the spikes can also be important for encoding information and transmitting signals in the nervous system.

To study the spike rate in response to different values of external stimuli, simulations with different stimuli can be run and the number of action potentials produced by the neuron can be measured over a given time period. The spike rate can then be plotted as a function of the stimulus strength or duration to see how it varies with different stimuli.

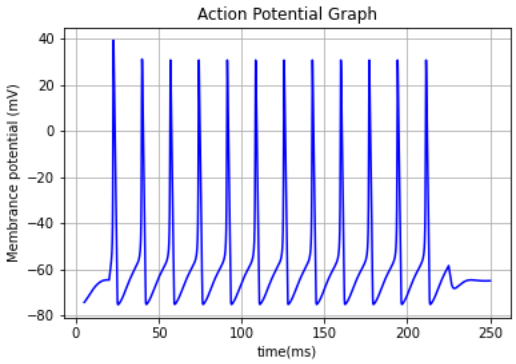

Figure 8: Action potential graph after solving differential equation of the axon model

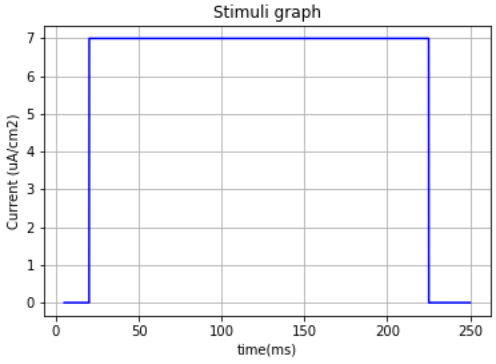

Figure 9: Stimuli for the axon model

B. Physical Model

An axon was modeled in COMSOL using cylinders, with the ion channels in the axon membrane being represented by boundary conditions that specified the current flow through the membrane. External stimuli were implemented by specifying a time-varying electrical current or voltage at the boundary of the axon model, using the "Boundary Current" or "Boundary Voltage" boundary condition. Simulations were then run to study the electrical behavior of the axon and the action potentials it produced, and COMSOL was used to visualize the results and to analyze the data to understand the underlying mechanisms of the action potentials. The accuracy of the simulation results depended on the accuracy of the axon model and the boundary conditions used, which were carefully validated to ensure that they accurately represented the physical system being modeled.

$$D = \epsilon_0 \epsilon_r \boldsymbol{E} \ (5)$$

$$J_c = \sigma \boldsymbol{E} \ (6)$$

$$\nabla \boldsymbol{J} = Q_{j,v} \ (7)$$

$$\boldsymbol{J} = \sigma \boldsymbol{E} + \boldsymbol{J_e} \ (8)$$

$$\boldsymbol{E} = -\nabla V \ (9)$$

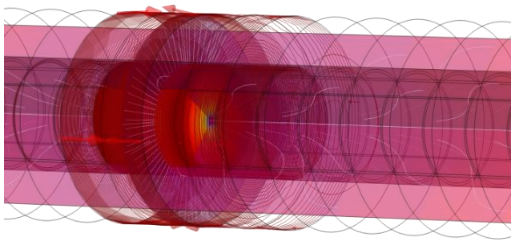

Figure 10: A physical axon model with stimuli

Figure 11: Physical model for axon and **E** field

IV. DISCUSSION

It is not possible to fully model an axon physically, mathematically, or electrically because an axon is a complex structure that exhibits a range of dynamic behaviors that are difficult to accurately represent using any single approach.

One reason why an axon may be difficult to model physically is that it is composed of a number of different types of cells, each of which has its own unique properties and functions. Additionally, an axon is surrounded by other cells and tissues, which can also affect its behavior. As a result, it is difficult to accurately represent the complex interactions between all of these different components using a physical model.

Mathematically, an axon is also difficult to model because it exhibits a range of nonlinear behaviors that are difficult to represent using traditional mathematical models. For example, an axon can exhibit both excitatory and inhibitory behaviors, and its response to a given stimulus can vary depending on the strength and duration of the stimulus. Additionally, the transmission of signals through an axon is influenced by a number of factors, such as the concentration of ions in the surrounding fluid and the properties of the ion channels in the axon membrane, which can also be difficult to accurately represent using mathematical models.

Electrically, an axon is difficult to model because it exhibits a range of dynamic behaviors that are influenced by both electrical and chemical processes. For example, the transmission of signals through an axon is influenced by the flow of ions through ion channels in the axon membrane, which is regulated by both electrical and chemical processes. Additionally, the electrical properties of an axon can vary depending on the state of the axon and the surrounding tissues, making it difficult to accurately represent the electrical behavior of an axon using a single electrical model.

Overall, while it is possible to model certain aspects of an axon using physical, mathematical, or electrical approaches, it is not possible to fully represent the complex behaviors of an axon using any single approach. Instead, a combination of different modeling approaches may be necessary to accurately represent the behavior of an axon as worked to be implemented in the paper.

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SUPPLEMENTARY

The whole codes that are used in the paper and other necessary materials can be found in https://github.com/yakupcatalkaya/Neurostimulation

REFERENCES

[1] Kandel, E. R., Koester, J., Mack, S., & Siegelbaum, S. (2021). Principles of Neural Science. McGraw Hill.

[2] Moulin, C., Gliere, et Al. (2008). A new 3-D finite-element model based on thin-film approximation for microelectrode array recording of extracellular action potential. IEEE Transactions on Biomedical Engineering, 55(2), 683–692. https://doi.org/10.1109/tbme.2007.903522

[3] Gerstner, W., Kistler, W. M., Naud, R., & Paninski, L. (2016). Neuronal dynamics from single neurons to networks and models of cognition. Cambridge University Press.

[4] Hodgkin, A. L., & Huxley, A. F. (1952). A quantitative description of membrane current and its application to conduction and excitation in nerve. The Journal of Physiology, 117(4), 500–544. https://doi.org/10.1113/jphysiol.1952.sp004764

[5] Elia, S., & Lamberti, P. (2013). The reproduction of the physiological behaviour of the axon of nervous cells by means of finite element models. Innovations in Intelligent Machines -3, 69–87. https://doi.org/10.1007/978-3-642-32177-1_5