**Modeling Analysis of Biomembrane Potential and Action   
Potential Propagation**

Team #: 40

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GitHub Repo: <https://github.com/qiyangsun/6730-final-project>

**Abstract:**

In the past few decades, modeling and simulation of biological membrane potentials have been widely applied in research on computational neuroscience, biomaterials development, and circuit system design [1,2,7]. Several formulas have been proposed from different perspectives, including the Hodgkin-Huxley (H-H) model [3], Morris-Lecar (M-L) model [4], Fitzhugh-Nagumo (FHN) model [5] and others [6]. These models have greatly contributed to our understanding of the underlying mechanisms and principles of the nervous system and other biological systems, and have paved the way for the development of new materials and devices with novel properties and functions. Among them, the H-H model and FHN model are classical models that used to simulate the action potential in neurons, which has been crucial in elucidating the neural code and the basis of information processing in the brain. The M-L model, on the other hand, is another representative model that has been applied to study the dynamics of ion channels and the generation of bursting behavior in neurons. In this project, we intend to implement two typical models: M-L model and FHN model to analyze action potential propagation for those two separate perspectives. Meanwhile, we also notice that most of the muscle contractions are highly related to the membrane potential of the myocyte [8], therefore we would like to further use stochastic crossbridge model along with that two bioelectric models to investigate whether muscle contraction strength is related to electrical signals. Finally, we hope to build a connection between our potential propagation analysis with the crossbridge contraction analysis.

**Project description:**

Therefore, according to the abstract above, the final goal of this project is to use that two models (M-L model and FHN model) to simulate the action potential in neurons.

Here we would also like to give a brief background introduction to our project. As described above, in the real world, information between cells in our body is transduced by electronic signals. This electronic signal, in most cases, is produced by the neuron which is a kind of specialized cell that can convey electric current. Now we have the question: How does a neuron produce and convey the current? The answer is activation potential which means that the membrane of the neuron cell can be depolarized by sodium/calcium ions to produce a positive charge. Therefore, we will find that the key factor of the bio-electric signal is sodium (and potassium/calcium) ions. This gives us a great possibility to simulate the current transduction along the neuron cell - by simulating the calcium/potassium ion dynamics. This is how the M-L model works.

However, if we jump out of the micro-world, we will find another scene. If we consider the neuron stimulation as a whole, regardless of how ions work, we will see that the nerve impulse (neuron current) is also a system that will change over time and convey distance. Therefore, we have another interesting point of view to study the nerve impulse from the systemic perspective. That is how the FHN model works.

We will see the difference between those two models in the following equations.

**Literature review & Conceptual model**

Since we have already included the literature review part in the first two sections (Abstract and Project Description), we will directly introduce the conceptual models we will use in this final project.

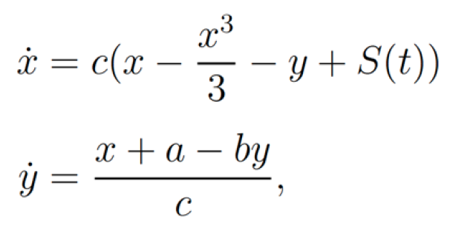
The first model we will use is the M-L model. As introduced above, the M-L model is a neuronal-like model that was originally developed mimic excitability in the barnacle muscle. The model consists of a depolarizing Ca2+-current and a repolarizing K+-current, and the equations involved in this model are:

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The M-L model is a mathematical model that mimics the excitability of barnacle muscle cells. It consists of two main ion channels: a depolarizing Ca2+-current (ECa) and a repolarizing K+-current (EK). The model equations describe the flow of ions across the cell membrane and the resulting changes in membrane potential. The M-L model was originally developed to study the contraction of muscle fibers in barnacles, but it has since been used to model a wide range of biological processes, including the action potential in neurons and cardiac cells.

The second model we will use is the FHN model. FHN models neuronal electrical activity from a systemic perspective, and the equations involved are:



where *a*, *b*, and *c* are parameters and *S(t)* is an applied stimulus.

**Simulation / simulator / simulation model**

The math formulas of those two models are presents in the previous section. We will implement all the models in MATLAB R2019a.

* In the M-L model simulation, we used MATLAB ***pdepe*** solver.
* In the FHN model simulation, we used MATLAB built-in ***ode45*** solver and ***roots*** solver.

Because the model we used is well established, we can easily verify our implement by (1) check the code on the website (2) check the result of the baseline running.

**Experimental results & validation**

**Baseline running**

Firstly, we will show the baseline running result. This is a step to validate our implement by checking if the result is corresponding with our theoretical expectation. The equations of those two models are implemented in MATLAB. By setting the parameter values, we can run the simulator with *pdepe* and *ode45*.

* **Morris-Lecar (M-L) model**

For this model, we have already implemented the model and run it with baseline parameters. We can get the figure about how potential changes with position along the neuron and propagation time. The results are shown as follows:

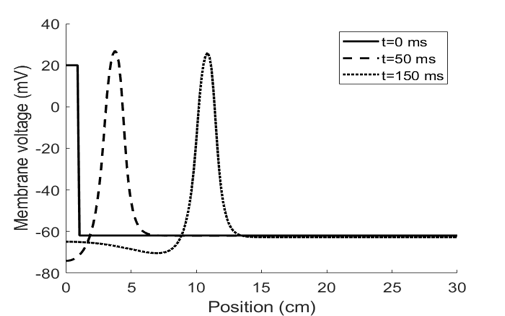


Fig 1. Potential changes with position along the neuron and propagation time

From Fig 1, we can see the scheme of how the action potential was propagated along the neuron at a specific time. For example, at t = 0 ms, we only have the stimulus at the first 1 cm. At t = 50 ms, the first 1 cm where the original stimulus becomes a negative charge due to the repolarization process K+ and other ions fluxing back, and the stimulus triggers an action potential, which then propagates to the position around 4 cm. At t = 150 ms, the action potential propagates to around 11 cm.

Chart, surface chart

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Fig 2. Action potential propagates along neuron as time goes by

From Fig 2, we can see that the action potential propagates along the neuron as time goes by. But the propagation cannot exceed 15 cm beyond which there are no action potentials. There is a subtle change in position potential at >15 cm after 100 ms. The result is corresponding to our expectation.

* **Fitzhugh-Nagumo (FHN) model**

Before, running the model, we first conduct theoretical analysis of this model. We know that this model should be a spiral. Then we run the baseline test. The baseline running result is shown in Fig 3. We choose [-1, -1], [-2, -1], and [1, 0.5] to test the system. Obviously, there is only one fixed point in the model.

Chart, line chart

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Fig 3. Stability test of the FHN model

As can be seen from the figure, the fixed point is a stable spiral and its value is approximately (-1.1, -0.7). This result is corresponding with our expectation. Based on this, we further conduct analysis on the fixed point. We used *roots* function to find the fixed point. The result is shown in Fig 4.

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Fig 4. Roots function result of the fixed point of FHN model

The result shows that this system is **stable spiral**.

Now we have already validate our implement of those two models. Next, we will explore the dependence on initial conditions by simulating from initial voltage pulses of different amplitudes.

**Excitability**

As we know, the most basic question in the neural biology is the excitability of the neuron. In other words, it is how the action potential changes on different stimulus. Biologically, it should follow the “All-or-None law” which means that the action potential will be triggered to the same level only after the initial pulse reach the threshold. Therefore, our model should also mimic this aspect. In this section, we change the initial condition to see how these two models simulate the excitability of the neuron and muscle.

* **Morris-Lecar (M-L) model**

By changing the initial voltage pulse from 20mV to 40mV and 60mV, we have results as follows.

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Fig 5. Action potential on different initial conditions.

In Fig 5, we can find that there is a little left shift when increasing stimulus amplitude, but the overall profile of the action potential is unchanged, and speeds of propagation under different stimulus initial conditions are almost the same*. We can find that the excitability simulated by this model is not affected by the initial condition. This conclusion is also corresponding with the biological intuition that action potential follows the all-or-none law.*

Now we have another question: what the minimum amplitude is required to generate a propagating action potential when the pulse is applied over the first 1 cm on the neuron cell. To answer this, we try to explore the minimal stimulus amplitude to trigger an action potential. By changing the value of Von, we have the following result.

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| --- | --- |
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| Amplitude = -19.1mV | Amplitude = -19.2mV |
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Fig 6. Min value of the initial stimulus to trigger an action potential.

From the result (Fig 6), we can find the min value is around **-19.1 mV**.

* **Fitzhugh-Nagumo (FHN) model**

After studying the excitability pattern of the M-L model, we will do the similar thing to the FHN model. Because this model is not from the ion perspective, we could not know the exact value of the initial voltage. However, we could still analyze the system by changing the initial condition to see whether the “all-or-none law” is still valid in this simulator. In this section, we try to inject a stimulus pulse to investigate excitability.

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| --- | --- |
| Chart, line chart  Description automatically generated | Chart, line chart  Description automatically generated |
| Amp = 1.0 (Blue) & Amp = 0.3 (Red) | Amp = 1 (r), Amp = 0.7 (b), Amp = 0.5 (g) Amp = 0.4 (c) |

Fig 7. Min value of the initial stimulus to trigger an action potential.

From Fig 7, we can also see a significant "threshold" on the action potential initialization. This result, though the model simulates the system from a different perspective than the M-L model, still shows a similar pattern to the M-L model.

*These results (Fig 5-7) together explicitly show the “All-or-None” law in the action potential excitability. Meanwhile, these results are closely corresponding with our biological intuition, which provide a very meaningful understanding of this bio phenomenon from a modeling insight.*

**Wave speed and conductivity**

After studying the excitability of the action potential, we find that the M-L model also have an advantage that it can study the conducting speed. Because this model is based on the ion flow, it has a diffusion coefficient D. By changing this parameter, we can simulate the conductivity.

Our expectation is that the wave speed would increase due to a greater effect of diffusion. To verify this assumption, we run simulation by varying D with increasing values. Results are shown as follows.

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| --- | --- |
| Chart  Description automatically generated | Chart  Description automatically generated |
| D=0.035 | D=0.05 |
| Chart  Description automatically generated | Chart  Description automatically generated |
| D=0.1 | D=0.2 |

Fig 8. Relationship between the diffusion factor and conductivity

In the Fig 8, we can find that when increasing D from 0.035 to 0.2, we will see that the propagation of action potential is going further along the neuron, from less than 15 cm to over the whole length of neuron of 30 cm. The reason is that with greater diffusion coefficient, a greater portion of the previous action potential can propagate to the next position. *This result is corresponding with our expectation that the wave speed would increase as D increases*. *This means that ion flow in the cell membrane is very important to keep the action potential propagation*.

Now we know that the ion flow is critical. However, which ion is the key to positively affect the action potential while which is negatively affect? To further study this question, we vary the *gCa* and *gK* parameters.

**Depolarization and Repolarization**

In this section, we want to study the effect of the calcium ion (which is the same function as sodium ion) and the effect of the potassium ion. Our assumption is that the wave speed would increase when gCa increases, but the wave speed would decrease when we increase gK. Here, we increase that two parameters respectively. Results are shown as follows:

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| Chart  Description automatically generated | Chart  Description automatically generated |
| g\_Ca=4.4 | g\_Ca=5.0 |
| Chart  Description automatically generated with medium confidence | Chart  Description automatically generated |
| g\_Ca=6.0 | g\_Ca=7.5 |

Fig 9. Increase the gCa value will lead to the faster wave speed

From Fig 9, we can see that as the value of gCa getting larger, the wave speed increases. However, the time required to recover to the rest potential also getting longer.

Then we increase the value of gK,

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| gK=8.0 | gK=8.5 |
| A picture containing histogram  Description automatically generated | |
| gK=9.0 | |

Fig 10. Increase the gK value will lead to the slower wave speed

From Fig 10, we can find that as the value of gK getting larger, the wave speed decreases and a lower action potential is triggered. *Combining these two results together, we can see that the Ca2+ ion is a kind of “activating ion” in the action potential propagation while the K+ ion is a kind of “deactivating ion”.*

**Conclusion & Discussion**

In this final project, we systematically studied the action potential propagation from two perspectives: ion-level (M-L model) and system-level (FHN model). We obtained the following conclusions:

* Our results explicitly show the “All-or-None” law in the action potential excitability from the mathematical model level. These results are closely corresponding with our biological intuition, which provide a very meaningful understanding of this bio phenomenon from a modeling insight.
* The diffusion efficiency of the ion is critical to the conductivity of the action potential in the neuron/muscle cell, which means that ion flow in the cell membrane is very important to keep the action potential propagation.
* Ca2+ ion is a kind of “activating ion” in the action potential propagation while the K+ ion is a kind of “deactivating ion”

In the future, we can further connect the action potential propagation with the muscle cell’s crossbridge contraction, as we described in our abstract.

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**Division of labor**

Yuqi Cheng (Y.C.) and Suning Hou (S.H) complete the M-L model implement and corresponding experiments. Shuyan Lin (S.L.) and Qiyang Sun (Q.S.) complete FHN model implement and analysis and contribute to the github repo management. Y.C., S.H., S.L. and Q.S. wrote the manuscript together. All author reviewed the manuscript.