Submitted for MTH2245 to Dr. Samah El-Tantawy, PhD Associate Professor, Faculty of Engineering.

Modelling of the Neuromuscular Junction

What if we can use math to model the complex geometry of the Neuromuscular Junction, a mathematical masterpiece that is the bridge between nerve and muscle?

NERVOUS SYS-TEAM

Systems & Biomedical Engineering Department

Abstract

This research presents a mathematical model that investigates acetylcholine dynamics in the neuromuscular junction (NMJ) in the context of Myasthenia Gravis (MG), a neuromuscular disorder that leads to weakness of skeletal muscles.

The model utilizes numerical simulations to study the dynamics of acetylcholine release. The simulation results align with the physiological explanation, making this model a valuable tool for studying NMJ dynamics.

Problem Definition

The NMJ is critical component in muscle contraction, facilitating the transmission of signals from motor neurons to skeletal muscle cells through acetylcholine release. However, neurodegenerative conditions like Myasthenia Gravis (MG) can disrupt this process, leading to muscle weakness. Understanding the dynamics of acetylcholine diffusion within the NMJ is crucial for comprehending the mechanisms underlying neuromuscular disorders.

This research addresses the challenge of investigating the complex 3D structure of the NMJ and developing a mathematical model that accurately captures acetylcholine diffusion. Through simulations, our research aims to provide insights into NMJ dynamics, contributing to the advancement of MG research and treatment.

Previous Work

Exploring advanced mathematical models for NMJ synaptic transmission, emphasizing acetylcholine diffusion and receptor-enzyme interactions.

1998 — Smart JL, McCammon JA
Introduces a continuum finite element method for acetylcholine diffusion simulation, highlighting acetylcholinesterase and receptor roles.

2011 — Khaliq A, Jenkins F, DeCoster M, Ali M
A 3D model of NMJ using Finite Element Method, emphasizing asymmetric acetylcholine release.

2013 — Liu D, Wang Y, DeCoster MA
A high-accuracy numerical model using the Spectral Element Method, exploring complex acetylcholine diffusion chemistry in the NMJ.

These models provide a solid foundation for further research using the finite element method to enhance our understanding of NMJ.

Methodology

We implemented the finite element method (FEM) to solve the PDE that describes acetylcholine diffusion. FEM is a numerical technique that divides a given domain into smaller subdomains known as elements. These elements are connected at specific points referred to as nodes, forming a mesh structure. We can then solve the PDEs specified at the nodes of these elements.

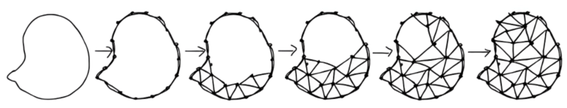

Figure 1. Finite Element Mesh

The NMJ synaptic cleft can be simplified as a slab with the presynaptic membrane located at x=0 and the postsynaptic membrane at x=L.

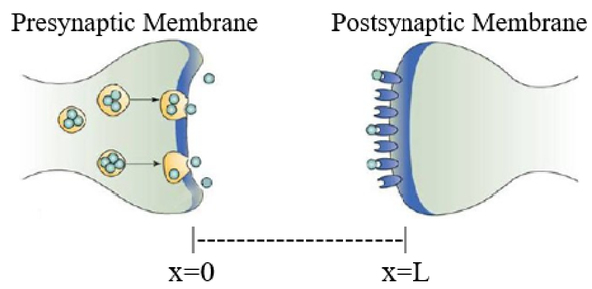

Figure 2. Synaptic Cleft

Chemical Reactions

$$A + E \underset{k_{-E1}}{\overset{k_{E1}}{\rightleftharpoons}} AE$$

$$AE \xrightarrow{k_{E2}} acE$$

$$acE \xrightarrow{k_{E3}} E$$

PDE

$$\frac{\delta A_{(t,x)}}{\delta t} = D\frac{\delta^2 A_{(t,x)}}{\delta x^2} - kA_{(t,x)}$$

Results & Analysis

In our simulation, we decreased the concentration of acetylcholine bound to receptors to illustrate their damaging in the case of Myasthenia Gravis as seen in Figure 3.

For the 3D model, we introduced new terms to represent the faster degradation of acetylcholine in the case of Myasthenia Gravis. The influence of these terms can be seen in Figure 4.

We anticipated a lower concentration of acetylcholine compared to the norm due to a reduced number of active receptors that typically modulate the effect of esterase.

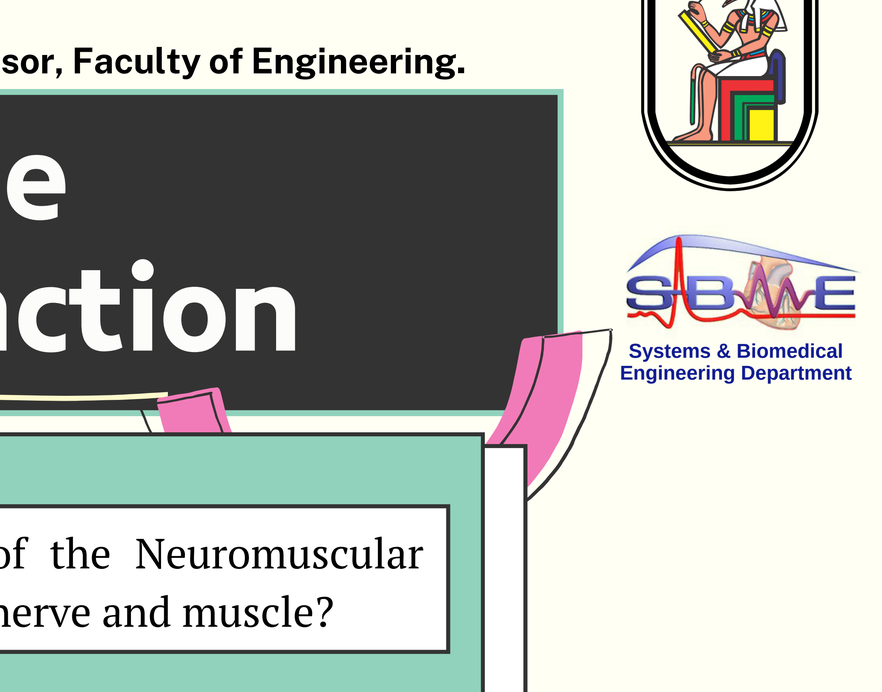

Figure 3. Bound receptor concentration in normal NMJ vs Myasthenia Gravis

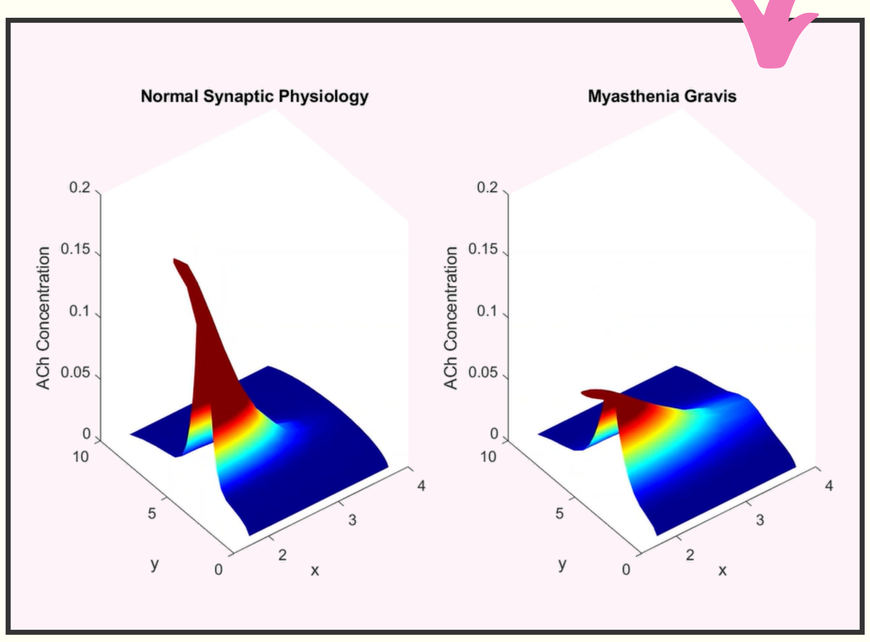

Figure 4. Diffusion of acetylcholine in normal NMJ vs Myasthenia Gravis

Conclusion and Future Work

Our model successfully utilized the finite element method (FEM) to visualize the effect of Myasthenia Gravis on the neuromuscular junction with high accuracy.

Overall, this research demonstrates the potential for advancements in describing and visualizing the difference between functional and defective neuromuscular junctions using PDE models.

Further validation and optimization of the model can be achieved using more complex methods, like the spectral element method (SEM) to achieve even higher accuracy and precision.

GitHub Repo — References

Enjy Ashraf enjy.elsayed03 - **Kirellos Safwat** kerolos.nashed03 - **Mina Raafat** mina.heinen02 - **Mina Wagdy** mina.youssef02 - **Nada Khaled** nada.kotb03 - **Shahd Ahmed Ragab** shahd.qutp04 - **Yasmine Mahmoud** yasmine.fotouh03

@eng-st.cu.edu.eg