Abstract

Mathematical models of neurons or nerve cells are essential for understanding the mechanism through which the neurons generate, transmit and process electrical signals, enabling them to better comprehend intricate behavior of the nervous system. Different mathematical models of the neuron enable the study of the nerve fiber including the behavior of the ion channels, membrane potential, synaptic dynamics, consequences of illness of mutations etc. Moreover, nerve models are also essential for the development of Neuro-prosthetics and Brain-Computer interfaces since they play a vital role to bridge the gap between theory and a real nerve fiber.

The Extracellular Space (ECS) is the region around a nerve fiber which can be considered as a pool of ions and is essential for the generation of action potential. Moreover, studies have also shown that the variation in size, shape and composition of the ECS can have a significant impact on neuronal signaling. Changes to the geometry of the ECS such as its expansion or shrinkage have a significant impact on ion diffusion and neurotransmitter release, local ionic environment, conduction velocity of neuronal signal and extracellular resistance. ECS has a critical role in maintaining neuronal communication and a deeper understanding of its functioning is important for a thorough knowledge of neuronal signal transmission for both normal and diseased conditions like injury, swelling, neurodegenerative disease etc.

It is observed that various mathematical models of neuron such as Hodgkin-Huxley membrane model, Izhikevich neuron model, etc. propose nerve membrane potential expression that consists of the inherent parameters pertaining to the nerve fiber itself. Since ECS is an important parameter that influences neuronal signal transmission, it is essential to consider the fundamental parameters of the ECS while deriving the membrane potential expression. Various mathematical models that involve obtaining the Local Field Potential i.e., the potential of ECS have already been proposed and are well established, but a robust and holistic mathematical model that provides a nerve membrane potential expression incorporating the ECS dependent parameters are still sought. In this regard, this thesis is aimed at bridging this gap and to further explore other phenomena involving the effect of the ECS on neuronal signal transmission.

This work begins with investigating the impact of neuronal activity on neuronal

growth and the effects of varying ECS on neuronal signal through mathematical modeling and simulation. Thereafter, the work involves analyzing the similarities in neuronal signal between two successive Node of Ranvier for different fiber length under the influence of the ECS. This part of the work examines the action potential initiated at a Node of Ranvier and compares it with the signal when it reaches the subsequent Node after travelling via a myelinated segment, highlighting any similarities or differences between the original and the propagated signal.

Thereafter, the work focuses on deriving a nerve membrane potential expression incorporating the fundamental parameters of the ECS through mathematical modeling and simulation, facilitating the study of neuronal signal propagation in healthy and diseased nerve fiber under varying ECS. Additionally, a robust mathematical expression of Rescue Protein mechanism has also been proposed which shows the extent of neuronal recovery completed after mutation induced voltage shift to the gating variables.

The final chapter of this work focuses on mathematical modeling and simulation to investigate how the ECS of varied sizes affects the conduction velocity of neuronal signal. This work is aimed at exploring how different combinations of the fiber anatomy and the size of the ECS influences the nerve conduction velocity which would enable at understanding and considering mitigation of various neurological conditions.

The works involved in this thesis aims towards proposing robust and holistic mathematical models to study nerve signal transmission in which the ECS dependent parameters are incorporated, which is computationally and mathematically less complex and could yield results that are in coherence with biological neurons. The work done in this thesis is intended to pave the way for further understanding of neuronal signal processing and possible early detection and diagnosis of neurological conditions.

Keywords: *Extracellular Space; Neuronal Signal Transmission; Cable Model; Hodgkin-Huxley Model; Rescue Protein; Conduction Velocity*