Chapter 1

Introduction

Biological phenomena and processes have long been studied and implemented in terms of biologically inspired algorithms or biomorphic devices to mimic their behavior. A similar congregation can be seen in the field of neural networks, an amalgamation of Neuroscience and connectome theory that tries to simulate the behavior of the primate brain and tries to unravel the mysteries behind learning, cognition, and memory. To some extent, these system has been able to replicate complex brain behavior such as learning, recall, and memory in re-configurable coupled connectivity with other neurons. To perform specific cognitive tasks, artificial neural networks have been built and trained by combining concepts from biological neural networks and connectomics [1, 4, 5]. Nevertheless, these systems oversimplified the working principle of the fundamental entity of the system. The neurons in biological neuronal network are very complex and capable of performing complex computations [6–9]. Very little about the dynamics of neurons has been deciphered and new knowledge regarding the workings of neurons has been put forward with the advent of new technologies and methods.

With the establishment of recent theories in Neuroscience, the study of such dynamic behavior of neurons gained immense popularity in understanding the role of different faculties associated with them. Previously, neurons are perceived as linear Spatio-temporal integrators [10–13]. Sensed signals propagates via the dendrites with attenuation and cumulatively summed & encode in the soma based on some activation function. However, recent findings reveal neurons to be complex entities capable of performing complex computations [14, 15]. Some of the famous literature defines them as active integrator [13, 16–19]. Each faculty associated with neurons (synapses, dendrites, dendritic arbors, cell body and axons) can reshape neuronal behaviors depending on synaptic effects [20–22], connectivity [23–25], morphology [25–27], arbor dynamics, neuronal fiber dynamics [28, 29] and so on. A small change in any of the basic properties can significantly change the response of a neuron toward the same stimuli [26, 30, 31]. Such dynamics and complex behavior brings attention for research works that can facilitate a better understanding of the faculties governing varied responses.

Dendritic morphology and its role in sophisticated neural computation have been established. However, there is a scarcity of neural network models that incorporate linear nonlinear dendritic morphology. A morphologically defined neural network is critical for understanding the computational foundation of arborized dendritic arbour. A morphologically detailed neuron model will improve knowledge of possible arithmetic and logical operations, as well as the function of neuronal assemblies in the formulation of these processes.

The primary focus of the proposed work is to link the bridging gap between neuronal morphologies and structure-function relationships, integrating electrochemical, electrophysiological, and physicochemical attributes of neurons along with connectome specificity. The role of active dendritic integration [14, 32] is considered and investigated to better understanding its role in enhanced functionality, specifically in the retinal ganglion cells (RGC) of the primate visual cortex (PVC). Literature surveys and reviews of the proposed work has put forward some key research issues and challenges as follows:

- Integrating active membrane dynamics to specific locations in the dendritic arbor to mimic similar neuronal dynamics is difficult to model. Compartmentalizing the dendritic arbor with localized active channel dynamics increases the computational complexity with increase in arborization.
- Construction of neuronal morphologies integrating localized active ion channels (AIC) at localized regions with connectome specificity to replicate the intrinsic behavior of RGC is a complex task because of unavailability of definitive connectivity.
- Integrating such RGCs to develop Spiking Neuronal Network (SNN) models to simulate feature extraction (similar to orientation-selective (OS) RGC networks) in the striate cortex of the PVC is computationally expensive as the signal processing aspect needs to convert spatial information into Spatio-temporal signals and vice-versa.

In the proposed work, an attempt has been made to study and mathematically model individual faculties of neurons to replicate their respective behavior by integrating active membrane dynamics with passive neuronal fiber dynamics. The focus has been given to non-myelinated neuron fibers, and dendritic arbors where such active membrane dynamics have been reported at large and can be seen in the PVC and olfactory regions as well.

1.1 Motivation

Significant studies has been reported in the field of Neuroscience in the past decade related to active and passive membrane dynamics, synaptic communications, differential, and gradient localized active ion channel distribution in the dendritic arbor and their potential role in the shaping of neuronal signals. However, a bridging gap exists between the experimental finding concerning electro-chemical, electrophysiological, and physicochemical attributes and connectome specificity with neuronal morphologies and their probable role in shaping the neuronal structure-function relationship. The role of complex morphologies, their importance, and their variation in various parts of the central and peripheral nervous systems have not been thoroughly studied. Rall's equivalent cylinder to accommodate the dynamics due to complex neuronal morphologies or cumulative linear Spatio-temporal integration in the neural network is one of the related works from literature that focus on understanding the mathematical and functional basis of neuronal morphology and their roles in shaping complex biological phenomena such as learning, cognition, and plasticity. Most of the works centered around neuronal morphologies were conducted a few decades back when advanced techniques such as fMRI, calcium imaging had not been introduced and such morphologies are assumed to be passive and linear. Recent literature findings from Ca^{2+} imaging, fMRI imaging responses suggests dendritic arbors as active integrator capable of complex dynamics rather than simple linearly weighted summing units. Active dendritic integration in neurons are proposed due to AIC at specific locations of dendritic arbors that add new dimensions to its computational capabilities. These robust nature of neurons, integrated with its basic faculties, has fascinated researchers to undertake detailed investigations to better understand neuronal dynamics due to morphological components in unison with non-linear active membrane and linear passive membrane dynamics (Hierarchical linear-nonlinear structure (HLNS)).

Neurons are the core computational units capable of complex computations. But non-availability of a detailed neuronal model with electrophysiological, physicochemical attributes, complex neuronal morphologies, and dendritic localized AIC limits understanding of neuronal computation. The model has been extended to be implemented in the PVC to mimic the behavior of RGCs. Different attributes considered for an understanding of the role of complex neurons have been summarized as follows:

- *Active Dendritic Integration and Passive Dendrites:* Dendritic arbors with localized AIC capable of spiking activity initiation and re-encoding of cumulative responses are termed active dendrites, and because of such non-linear integration, such dendritic arbors with localized AIC are known as active integrator. In contrast, dendrites devoid of any AIC are incapable of spiking activity and are passive dendrites, solely responsible for signal propagation with attenuation.
- *Morphology:* Morphology represents a unique structure of neurons corresponding to the complexity of the dendritic arbor and varies significantly from one region to another. The complex morphologies of type-specific neurons are reported to have a significant role in the structure-function relationship and neural computations.
- *Connectomics:* Connectomics represents the connection specificity of one neuron with another, either within the same neuronal network layer or between different layers of neuronal networks. Literature in artificial neural nets shows this neuronal connectomics as the basis of learning and cognitive systems.

In the proposed work, the main focus is on neuronal morphology, active dendritic integration, localized active ion channel distribution, and role of neuronal morphology in the structure-function relationship and neuronal computation.

Recent findings in neuroscience establish neuron as a complex computational unit rather than a simple Spatio-temporal integrator, which is possible because of advances in in-vitro techniques, in-silico models, and sophisticated imaging and measurement techniques. These findings point to neurons as a highly nonlinear system with function formation capability that is directly proportional to dendritic arbor complexity. Aside from function formation and nonlinear computations, localized AICs in dendrites make the neural system dynamic and have instilled an insatiable desire to understand the mathematical aspects of robust parallel computational units. Although several mathematical models have been developed over the years, the majority of them revolve around passive membrane dynamics and active point process models and do not account for the concept of

AICs at specific regions of the dendritic arbor. Therefore, an attempt is made to compartmentalize a morphologically and electro-physiologically detailed neuron and mathematically model different aspects of the compartmentalized neuron and comprehend the effects of such dendritic tree on neural computation. Local membrane dynamics and behavior are modeled and replicated using the cable model.

The visual system also serves as the fundamental architectures responsible for the development of memory, consciousness, concentration, and other sophisticated cognitive abilities. Light stimuli are utilised to retrieve information such as orientation and direction selectivity, object recognition, motion tracking, and many others. The core functions of the V1 layer of the primary visual cortex include direction selectivity, multi-scale feature extraction, and salient mapping in addition to object segmentation and recognition. The contribution of individual neurons in such complicated functionality is far more important than the collective functionality. Especially, it is their morphological structures and fundamental connectomic arrangement that contribute to their robust nature. According to published literature, two-dimensional uniform functional maps exist in the V1 and V2 areas, however other literature discovered incredibly precise micro-architectures in a three-dimensional plane. The literature also implies that cortical maps built with single-cell resolution have a considerable impact on ganglion cell computational capabilities. Along with connectome uniqueness, various dendritic morphologies appear to execute far more sophisticated functional calculations. The neurons' dynamic range of spiking patterns are also seen to reflect their spatial extent and spatio-temporal dynamics. These complicated activity can be linked to single-neuron dynamics, cell biology, and retinal network connectivity. Looking deeper into the layer that connects photoreceptors and direction-selective ganglion cells via ON/OFF bipolar cells, research offers fundamental pattern identification, edge and shape perception, object depth estimation, and so on as possible intrinsic properties. Thus neurons' dynamic behavior brings the need of understanding the mechanisms underlying significance of structural organization, dendritic morphology, and cell biophysics in shaping neuronal response in the PVC.

1.2 Objectives

The objective of the proposed work is to study active channel dynamics and develop a mathematical model of passive dendritic structure. Different faculties of neurons are studied and mathematically modeled. A morphologically detailed

RGC model has been designed integrating active and passive membrane dynamics of neuronal assemblies to understand the role of dedicated neuron morphology and type-specific neuronal computation. The proposed work also aims at the implementation of modeled morphologically detailed neurons in the simulation of primates' primary visual cortex to effectively address the impact of morphology and active dendritic integration in feature extraction type computation. Such a model can be further implemented in biologically inspired SNNs for learning and recognition. In summary, the research work in the thesis proposes to achieve the following objectives:

- Study of active membrane dynamics to replicate localized active ion channel dynamics and mathematical modeling of passive membrane dynamics in passive uniform neuron fiber, tapered and flared neuronal fibers to mimic signal propagation in non-myelinated dendritic fibers. Mathematical modeling and analysis of cell-field interaction and role of non-homogeneous extracellular space in signal transmission in bundled fiber system.
- Designing of morphologically detailed neuron morphology integrating active and passive membrane dynamics to construct a Hierarchical linear-nonlinear structure. Passive fibers replicates the signal propagation whereas non-linearity due to localized active ion channel is modeled using active fiber dynamics. Morphologically detailed neurons are arranged to simulate layers of neuronal network to mimic SNN corresponding to specific regions of visual cortex.
  - Model and simulate orientation selectivity in primates' visual cortex integrating the modeled neuronal faculties.
  - Model and simulate responses of detailed ganglion cell morphology due to similar and antagonistic connectivity with fixed receptive fields (RFs) and network of varying receptive fields.
  - Model and simulate Hubel and Weisel type multi-layer SNN and study neuron population role in learning.

1.3 Scope of Research

The proposed work is centered around role of neuron morphology and their non-linear capabilities. The arborized nature of the dendritic arbor introduces these complex structures being capable of performing multi-level tensor network within a single neuron. When such multi-level tensors are powered by non-linear activation functions at their junctions, can compute much complex input-output relationship that can significantly reduce the size of a learning network. The proposed framework also gives a very good understanding of a static arborized biological neuron morphology and their corresponding role in feature extraction. A similar architecture with dynamic neuronal morphology due to morphological change during learning can give us a better understanding of the computational capabilities of a biological neuron. Similar networks can be incorporated to the current neural network domain that can significantly improve the learning capability and learning accuracy of a neural network learning network model. The dynamic neuron morphology model incorporating computational convergence and non-linearity can be used to incorporate superior feature extraction and complex learning networks across multiple layers similar to graph neural networks.

1.4 Materials and Methods

The importance of a single neuron as a computationally intensive unit is widely acknowledged. Morphological distinctiveness, in combination with unique electrophysiology and localized active ion channel dynamics, is known to shape non-linear attributes of neurons' compute capacity. This work highlights the role of non-linear integration in a morphologically detailed neuron and attempts to imitate it by incorporating the primary attributes. A HLNS neuron with specific morphology is created by combining mathematically modeled neuronal faculties using of Rall's equivalent cylinder. To emulate orientation selectivity in primates' retina, the modeled neuron morphologies were further provisioned to recreate OS RGC dynamics.

Layers of SNN have been designed to simulate scotopic and colour vision in the human retina using the modeled morphologically detailed OS-RGCs. The developed SNN model has also been used to investigate the impact of various RF sizes and their projection onto the parvocellular and magnocellular layers. To investigate its technical feasibility, the SNN model has been extended to reconstruct a simple Hubel and Weisel type of network.

1.4.1 Computational Methods

The well-known cable equation serves as the foundation for modeling neuronal abilities such as passive neuron fiber dynamics, signal propagation in uniform, tapered, and flared fibers, and cell-field interaction in non-myelinated neuron fibers. Equivalent circuits are designed and modeled to replicate dynamics of the neuronal assemblies. Modeling and study of neuronal attributes are divided as following:

- Study of active membrane dynamics and mathematical modeling of passive membrane dynamics
- Mathematical modeling of uniform, tapered and flared 2D Cable model
- Mathematical modeling of cell-field interaction and inter-fiber interference

The morphologically detailed neuron is designed by combining modeled neuronal facets to create HLNS. The non-linear behavior of the neuron is attributed to a linear-nonlinear hierarchy, with the added benefit of investigating different spike encoding patterns. In the proposed framework, rate-based spiking encryption has been used for simplicity. Layers of SNN with layer specific functionalities are formed by arranging morphologically detailed RGCs with connectome specificity. Multiple layers of such SNN are layered to mimic and analyze the edge-estimation, multi-resolution, boundary and contour estimation, and learning behavior of primates' visual cortex extracting features from the inputs using the model. Modeling and study of edge-estimation, multi-resolution, boundary and contour estimation, and learning has been divided as following:

- Designing the morphologically detailed RGC integrating linear and non-linear neuron fiber dynamics
- Construction of single layered OS-RGC SNN in PVC and edge-estimation
- PVC multi-resolution feature extraction in varying RF sizes and visual scene segmentation in RF with unipolar connectivity
- Multi layer SNN in primates' visual cortex and feature interpretation

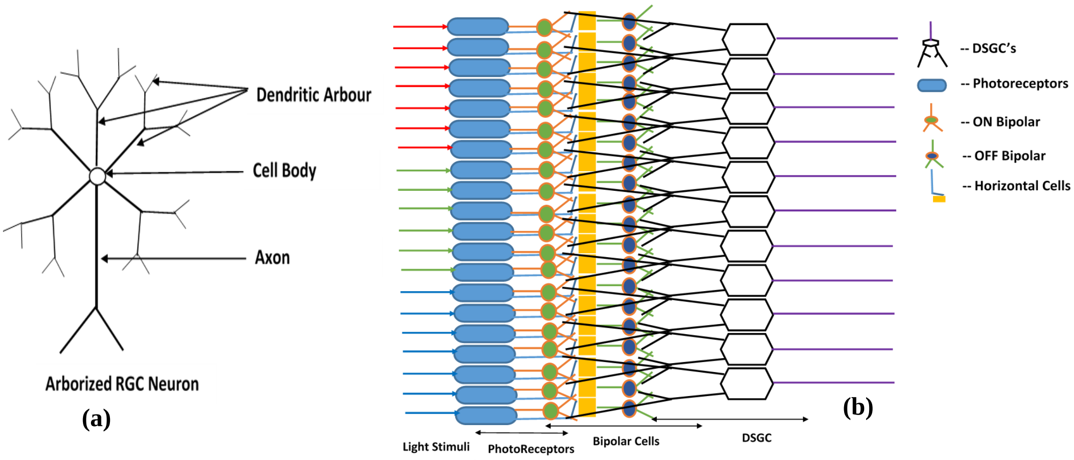

Figure 1-1: The proposed system's conceptual framework.

1.5 Conceptual Framework

Figure1-1 represents a conceptual framework of the proposed work. Shown on the left is a neuron cell with a complex arbor, and different assemblies are mathematically modeled to mimic the local behavior in neurons. Distal dendritic tips, junctions, and cell bodies are modeled as active encoders, whereas dendritic branches are modeled as passive propagators facilitating passive membrane transport. Due to the existence of AIC, the junctions and cell body operate as a summing node that performs a temporal summation of incoming propagating signals and re-encodes the cumulative signals propagating to the junctions and cell body. The overall effect of such composition of active membrane dynamics and passive membrane dynamics results in active dendritic integration. A similar arrangement has been used to construct morphologically detailed RGC neurons to simulate the behavior of the striate cortex of the PVC. In **Figure1-1. (b)** is a single layer SNN consisting of such morphologically detailed RGC cells arranged in a precise, repetitive pattern with single-cell accuracy representing a simple cell network from Poggio, Hubel and Wiesel [33, 34] used to study the structure-function relationship of neuronal morphology.

1.5.1 Single Layered RGC SNN in Primate Visual Cortex for Multi-resolution Feature Extraction and Scene Segmentation

In this proposed work, initially, the same morphology with similar connectome specificity has been integrated with a single layer SNN to investigate the role of dendritic arbor spread and RF. Initial investigation suggests multi-resolution feature extraction in the striate cortex of the PVC. Integrating complex RGC morphology of midget and parasol neurons with active dendritic integration suggests multi-resolution feature extraction where resolution of feature extracted is a function of dendritic spread and RF. A low dendritic spread (corresponding to small RF) focuses on fine feature extraction and a wide spread (corresponding to larger RF) focuses on extracting coarse features. A similar network of SNN has been constructed with the connectivity of neurons specifically with excitatory type of inputs has been investigated. The network under consideration is found to behave as a scene segmentation type system that tries to classify image regions into different clusters. Segmentation of scenes is achieved using three specific cone cells (L, M and S-cone cells) of RGC layers connected to 'Red', 'Green' and 'Blue' color channel affinity cone cells and non-linearly encoded in each layer followed by a linear summation of the cumulative response.

1.5.2 Multi-layer SNN in Primate Visual Cortex

In this proposed work, a multi-layer SNN has been designed to realize the implementation of learning and recognition in the PVC. The multi-layer SNN has been inspired from the works of Hubel and Wiesel [33] and Poggio et. al. [34] where the simple neuron layer 'S1' and 'S2' has been implemented using the proposed morphologically detailed RGC neurons followed by a complex cell layer 'C1' and 'C2' after every simple cell layer responsible for max-pooling operation within a specific pooling range. The simple cell layers behave as band-pass filters responsible for extracting orientational information, contours and combinations of directional features. Complex cells are responsible for max activation information from the RF neighborhood. Preliminary investigations on pattern extraction and content-based information retrieval show some promising results.

1.6 Organization of the Thesis

The thesis is organized as follows:

Chapter 2: Literature Survey

A detailed state-of-the-art literature survey has been conducted on the electrophysiological and physicochemical basis of neuronal membrane dynamics, active and passive fiber properties, AIC in dendrites and their probable role in active dendritic integration. Literature on morphological aspects of type-specific neurons and their probable roles in a structure-function relationship has been conducted in detail.

Chapter 3: Mathematical Modeling and Simulation

This chapter discusses the mathematical model of different neuronal assemblies and processes such as active and passive membrane, signal propagation in a passive membrane, signal dynamics in uniform, tapered and flared fiber, inter-fiber signal interference in non-myelinated bundled nerve fibers and dynamics due to non-homogeneous extracellular space.

Chapter 4: Edge Detection in Primate Visual Cortex

This chapter begins with an overview of signal transduction in the primate retina, followed by a detailed breakdown of the various layers of neuronal cells responsible for some complex operations. A morphologically detailed model of RGC integrating mathematically modeled neuronal assemblies and processes has been constructed to better understand the basis of orientation feature extraction as a function of neuronal morphological structures along with the connectome specificity of a neuron.

Chapter 5: Multi-resolution Feature Extraction and Visual Scene Segmentation of Primate Visual Cortex

In this chapter morphologically detailed model of RGCs with active dendritic integration mimicking midget and parasol cell has been constructed to investigate the structure-function significance of dendritic arbor spread of midget and parasol neurons and RF. The model also explores the change in functionality of neurons with only excitatory inputs and due to a combination of excitatory and inhibitory inputs. Change in RF due to dendritic spread with combinations of excitatory and inhibitory connectivity shows multi-resolution feature extraction functionality whereas neurons with only excitatory type inputs exhibit scene segmentation type functionality.

Chapter 6: Multi-layer SNN in Primate Visual Cortex

In this proposed work, an attempt has been made to reconstruct a detailed multi-layer SNN based on the works of Hubel and Wiesel [33] and Pogoi et. al [34]. Simple cell layers are constructed to replicate the behavior of RGC's tuned to selective orientation feature and complex cell layers are used to replicate max-pooling behavior. Details of morphology and connectome specificity of RGC's in the simple cell and complex cell layer have been discussed in detail.

Chapter 7: Conclusion and Future Directions

This chapter concludes the dissertation and outlines the work done with the scope of possible future research in the field.