Laboratory Rotation Proposal

Calcium Modeling in a Human Purkinje Cell Model

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Abstract

The aim of this project is to build upon and extend the human Purkinje cell model developed in Prof. Erik De Schutter's lab. The goal is to integrate calcium dynamics into the model to investigate the functional implications of human-specific dendritic morphology and calcium signaling. This work aims to advance our understanding of synaptic plasticity, dendritic computation, and cerebellar coding in human Purkinje cells.

Background

Purkinje cells (PCs) are the sole output of the cerebellar cortex and play a central role in sensory and motor encoding. Their extensive dendritic branching enables integration of massive synaptic input, with calcium spikes in dendritic branches being critical for synaptic plasticity and learning [1]. Parallel fibers, originating from granule cells, provide the majority of excitatory input to PCs, and the structural complexity of PC dendrites facilitates precise information processing [2]. Computational models of PCs have largely focused on rodents, leaving significant gaps in understanding human PCs, which exhibit greater dendritic complexity and more prevalent multi-trunk morphologies (Fig. 1) [3]. These morphological differences suggest species-specific adaptations in dendritic computation and information processing. Furthermore, localized calcium dynamics, such as dendritic calcium spikes, play a vital role in synaptic plasticity and cerebellar coding. This project aims to address these gaps by refining the human PC model to incorporate detailed calcium dynamics, providing insights into their role in cerebellar physiology and neuropathologies associated with calcium channel dysfunctions.

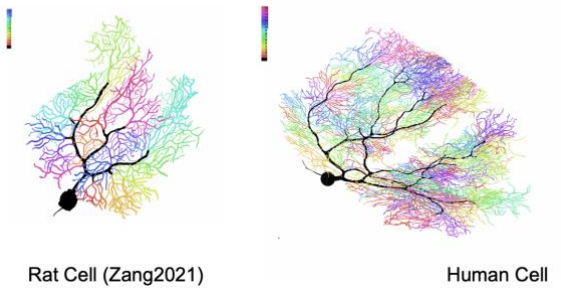

Fig. 1 Difference in morphologies: rat and human Purkinje cell

Objectives

The main objective of this project is to refine and extend the human Purkinje cell model by incorporating calcium dynamics. Specific objectives include:

1. Modify calcium pump expression to eliminate the current unrealistic mini-spikes in the human model.
2. Perform current injection simulations to analyze the firing rate-current (F-I) curve.
3. Investigate the impact of human-specific dendritic trunk morphologies on dendritic computation. Check how different lengths of the trunk impact the firing and the corresponding F-I curve.

Learning Objectives

Through this project, I aim to:

1. Gain a detailed understanding of cerebellar physiology and Purkinje cell function.
2. Learn to use the NEURON simulation environment effectively.
3. Develop skills in working with realistic morphologies and incorporating real data into models.
4. Model calcium dynamics in multiple compartment models.
5. Perform data analysis using Python.

Resources

This project will utilize the NEURON simulation environment to refine the human Purkinje cell model developed in Prof. Erik De Schutter's lab. Existing computational tools and data from prior studies (Cirtala & De Schutter, 2024; Zang & De Schutter, 2021) will provide a foundation for model refinement and simulation experiments. The project will leverage lab expertise and computational infrastructure to implement and test the proposed objectives effectively.

References

1. Cirtala, G., & De Schutter, E. (2024). Branch-specific clustered parallel fiber input controls dendritic computation in Purkinje cells. https://doi.org/10.1016/j.isci.2024.110756
2. Consalez, G. G., Goldowitz, D., Casoni, F., & Hawkes, R. (2021). Origins, Development, and Compartmentation of the Granule Cells of the Cerebellum. Frontiers in Neural Circuits, 14. https://doi.org/10.3389/fncir.2020.611841
3. Zang, Y., & De Schutter, E. (2021). The Cellular Electrophysiological Properties Underlying Multiplexed Coding in Purkinje Cells. https://doi.org/10.1523/JNEUROSCI.1719-20.2020