

Title: Bridging scales in astroglial calcium dynamics: from nanoproceses to whole-cell modeling in the cerebellum

Authors:

Laura Keto, Tiina Manninen

Keywords:

Neuroscience, bioinformatics and computational biology, cell morphology, software, calcium dynamics

Abstract

Astroglial cells form hundreds of nanoproceses that enwrap neuronal synapses, extend specialized endfeet to the vasculature, and create a rich landscape of calcium signaling. Despite being as essential as neurons to brain function, astroglia remain less studied - particularly in computational modeling. A key challenge is to understand the relationship between astroglial function and morphology. We set out to build a detailed yet computationally feasible full-cell model of a single cerebellar astrocyte, incorporating the major mechanisms underlying astroglial calcium dynamics. Because of the lack of astroglia-specific computational tools, we developed the CellRemorph toolkit (Keto & Manninen, 2023), available on GitHub (<https://github.com/lauraketo/CellRemorph>). Using CellRemorph together with the NEURON simulator (Carnevale & Hines, 2006) and ASTRO framework (Savtchenko et al., 2018), we built a whole-cell Bergmann glial model to investigate how its unique morphology (Grosche et al., 1999; Lippman et al., 2008) gives rise to diverse calcium signaling patterns. At the nanoscale level, we further explored how morphology influences stochastic calcium dynamics within Bergmann glial microdomains using both particle- and voxel-based simulators. This work advances our understanding of astroglial contributions to cerebellar function, bridging scales from microdomains to the whole cell.

Acknowledgements

This work was supported by the Research Council of Finland (decision numbers 326494, 326495, 345280, and 355256). We are very grateful to Prof. Helmut Kettenmann for providing us the video file of Bergmann glia appendage, and to the Doctoral School at Tampere University.