Investigating the effect of nanoscale architecture of astrocytic processes on the propagation of Ca^{2+} signals

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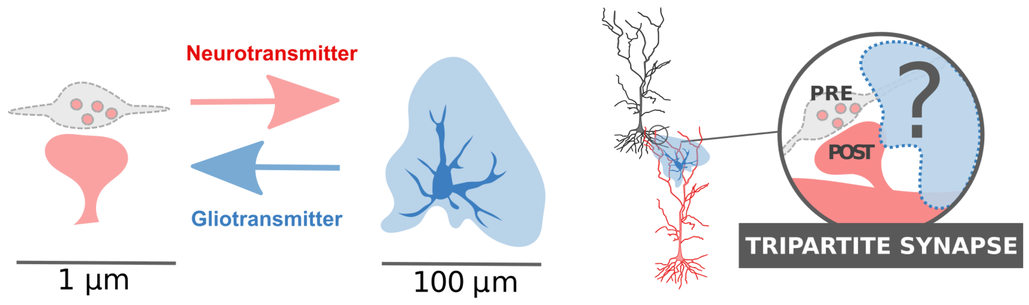
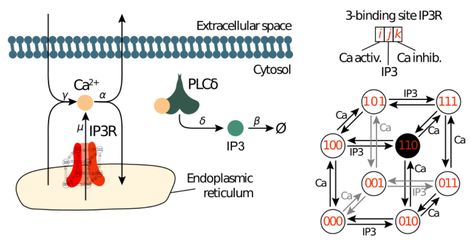
INTRODUCTION

According to the concept of the 'tripartite synapse'[1], information processing in the brain results from dynamic communication between pre- and post- synaptic neurons and astrocytes. Astrocyte excitability results from transients of cytosolic Ca^{2+} concentration. Local Ca^{2+} signals are observed both spontaneously and in response to neuronal activity within fine astrocyte ramifications[2], that are in close contact with synapses[3]. Those fine processes, that belong to the so-called spongiform structure of astrocytes, are too fine to be resolved spatially with conventional light microscopy[4] but can be investigated by super-resolution microscopy and computational modeling. In this study, we investigate the nanoscale architecture of the spongiform domain of astrocytes and its influence on spatiotemporal characteristics of Ca^{2+} signals.



METHODS

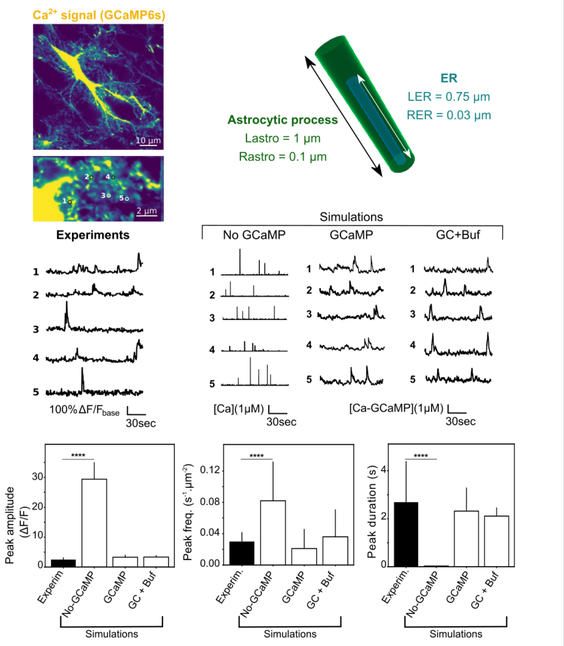


Kitnetic scheme of the model

Because of the low volumes and low number of molecules in processes of the gliapil, we use our stochastic spatially-explicit individual-based model of astrocytic calcium signals in 3D[5], implemented with STEPS[6], which kinetic scheme is presented above.

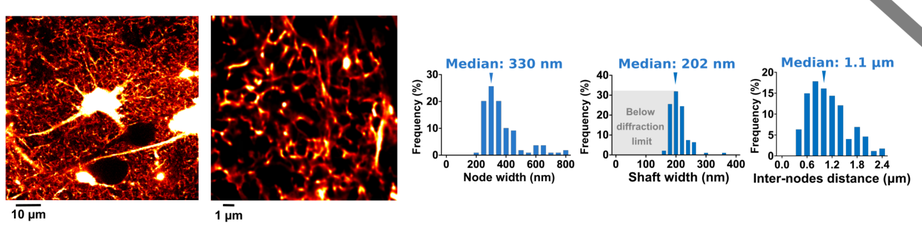
In our recent study[5], we have validated this model by reproducing key parameters of Ca^{2+} signals that we have recorded with high-resolution Ca^{2+} imaging in organotypic hippocampal slices.

Simulations in fine astrocyte process successfully reproduce Ca^{2+} microdomains signals.

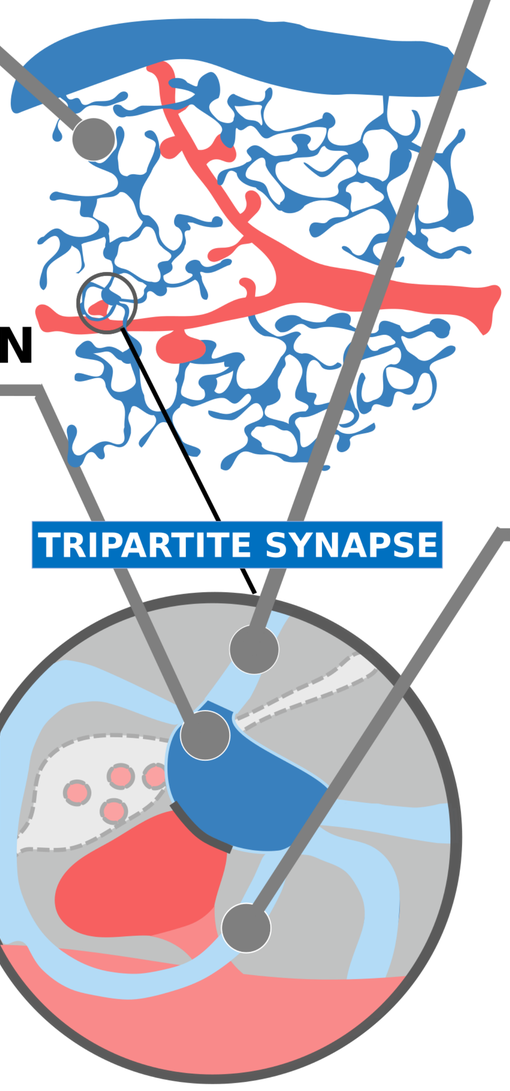


1 RETICULAR STRUCTURE

Morphological structure of the gliapil revealed by STED microscopy

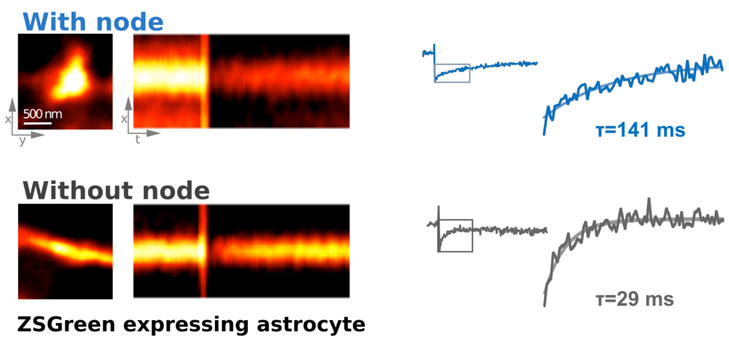


SPONGIFORM GLIAPIL

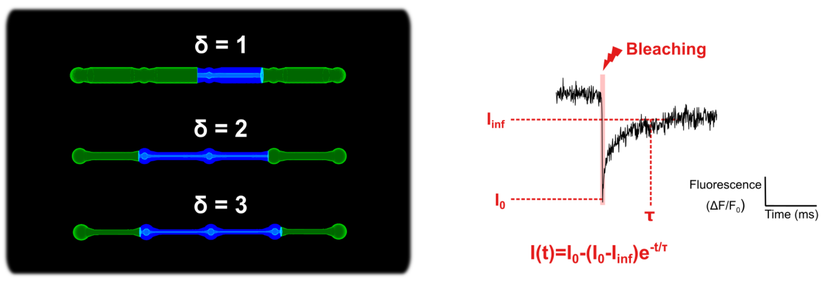


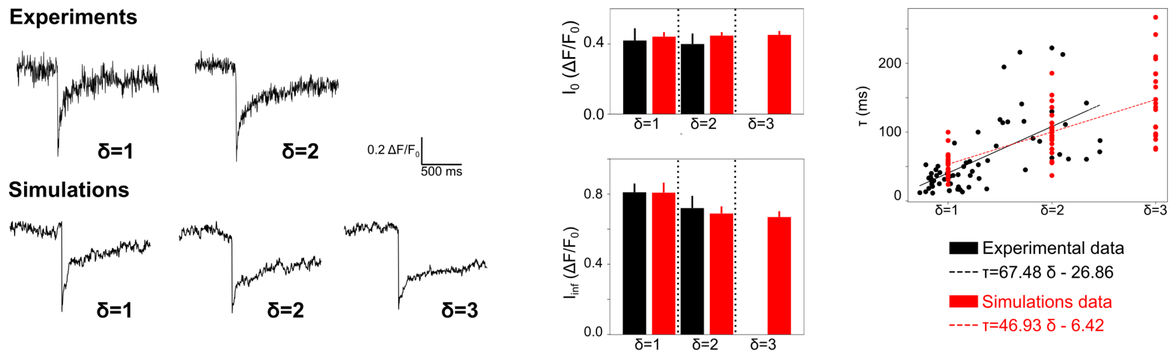
2 NODE COMPARTMENTALIZATION

Nodes are biochemically compartmentalized



Node/shaft geometries designed with different width ratios δ

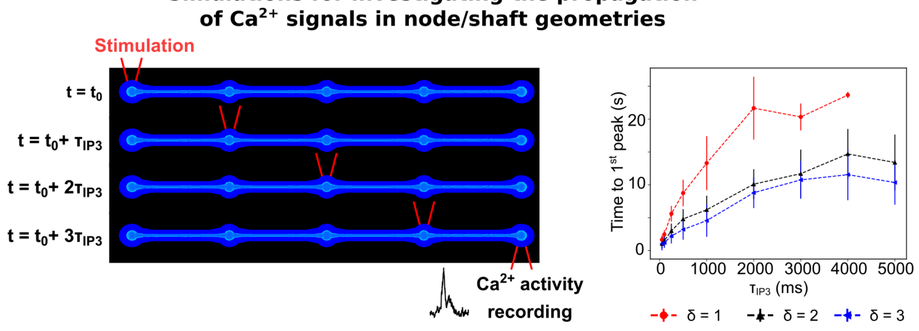




Our model successfully reproduces FRAP experiments and predicts that geometries of varying node/shaft ratios by themselves can result in an increased node isolation.

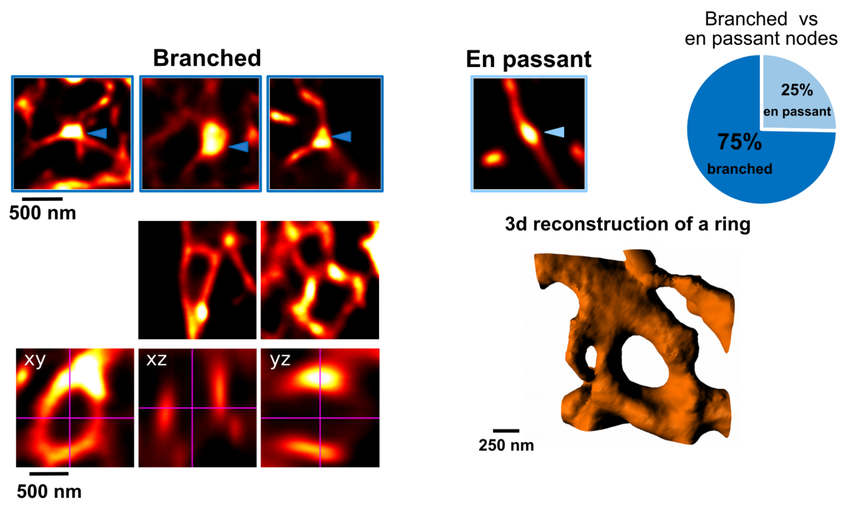
3 SIGNAL PROPAGATION

Simulations for investigating the propagation of Ca^{2+} signals in node/shaft geometries

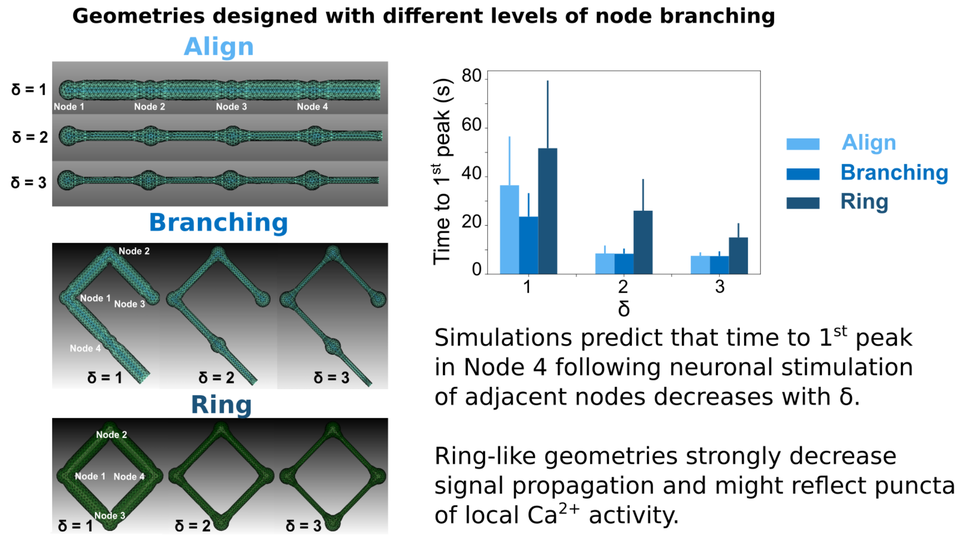


Simulations suggest that signal propagation is improved with high width ratio, especially for long delays between the stimulation of adjacent nodes.

4 NODE BRANCHING



Geometries designed with different levels of node branching



Simulations predict that time to 1st peak in Node 4 following neuronal stimulation of adjacent nodes decreases with δ.

Ring-like geometries strongly decrease signal propagation and might reflect puncta of local Ca^{2+} activity.

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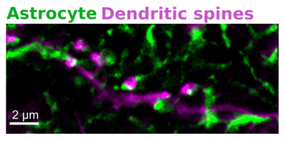
PERSPECTIVES



- **Effect of organellar geometry on signal propagation?**
- **Effect of the geometry of neuron/astrocyte interface on signal initiation and propagation?**
- **Signal integration from different processes?**

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