3D Modelling of a Spatially Resolved Energy Metabolism in Physiological Astrocytic Morphology

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Astrocytes, the most abundant cell in the central nervous system, have a star-shaped morphology and play a central role in brain homeostasis as metabolic mediators between neurons and blood vessels. Recent evidence put astrocytes therefore in the focus of neurodegeneration (ND), since in case of metabolic dysfunctions as e.g. observed in Alzheimer's disease or Parkinson's disease, they cannot provide neurons with sufficient amount of nutrients. Furthermore, progression of ND is often accompanied by changes in astrocytic morphology further indicating the essential role of astrocytes in the brain.

Despite its importance, the complex astrocytic morphology is often neglected in modelling of metabolic reactions [1]. In this study, we propose a computational model that describes cellular metabolism through a reaction-diffusion system including two fundamental pieces of information: the intracellular spatial arrangement of the reaction sites and the real, complex geometries by using the previously developed method CutFEM([2][3]).

Our findings show how intracellular spatial organisation and diffusion limitation as well as the physiological cell shape must be taken into account to go towards biological models that are closer to reality. In particular, the spatial distribution of mitochondria notably impacts the cellular ATP : ADP ratio, which is an indicator of the energetic state of the cell. Finally, we solve our system in a 3D human astrocytic morphology and study the different spatial arrangements of the reaction sites simulating physiological and dysfunctional behaviour. In this regard, we believe, that the proposed model is a useful instrument to gain insights into the role astrocytes play in neurodegeneration.

References

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