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Dissecting the mechanisms regulating astrocyte function at the nanoscale with computational approaches

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Astrocytes are cells in the central nervous system involved in numerous functions, from the regulation of neurotransmission to the maintenance of ionic and metabolic homeostasis, as well as memory and learning[1]. However, how astrocytes contribute to these diverse processes is still only partially understood. Here, I will illustrate how computational approaches are providing novel insights into this topic. Our results suggest that the nanoscale morphology of astrocytes leads to the compartmentalization and amplification of signals at synapses[2] and that the spatial properties of calcium stores finely tune local microdomain signals[3]. Our *in silico* experiments suggest that the altered morphology of astrocytes observed in Alzheimer's disease creates diffusional traps at the blood interface. Together, our results reveal mechanisms that regulate astrocyte communication with neurons and mural cells and contribute to the global effort to elucidate the roles of astrocytes in health and disease.

[1] Verkhratsky, A. & Nedergaard, M. Physiology of Astroglia. *Physiol. Rev.* 98, 239–389 (2018).

[2] Denizot, A., Arizono, M., Nägerl, U. V., Berry, H. & De Schutter, E. Control of Ca^{2+} signals by astrocyte nanoscale morphology at tripartite synapses. *Glia* 70, 2378–2391 (2022).

[3] Denizot, A., Castillo, M. F. V., Puchenkov, P., Cali, C. & De Schutter, E. The Ultrastructural Properties of the Endoplasmic Reticulum Govern Microdomain Signaling in Perisynaptic Astrocytic Processes. *Glia* 74, e70091 (2026).

Audrey Denizot is a tenured research scientist in the AIstroSight team at Inria Lyon in France. After her training as a biologist at Ecole Normale Supérieure de Lyon, she obtained her PhD in computational neuroscience at INSA Lyon, France, followed by a postdoc at the Okinawa Institute of Science and Technology, Japan. The main goal of her research is to better understand how astrocytes contribute to brain function in various (patho-)physiological conditions. She does so by developing computational models of astrocytes, in close collaboration with experimentalists. Her work has provided key insights into how the complex nano-anatomy of astrocytes dictates local signaling. Concomitantly, her lab develops open-access tools and codes to foster the application of the FAIR principles within the growing computational glioscience community.

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