PhD project fully funded

Multiphoton voltage recordings of inhibitory cerebellar circuits participating in pattern separation *in vivo*

Cerebellar neural circuits need to treat and distinguish massively overlapping patterns of inputs, to make sense of sensory-motor information arising during body motion, environmental exploration and perception. This is obtained by so-called pattern separation, a key process implemented in several brain regions. In the cerebellum, the prevailing hypothesis states that the billions of granule cells in the granular layer of the cerebellar cortex perform a combinatorial expansion of the sensory-motor patterns. Separation is then obtained by simple thresholding of the most active granule cells, as operated by the only source of inhibition to granule cells: the network of Golgi Cells (GoC). However, theoretical considerations indicate that a simple homogeneous inhibition would be ill-suited to separate patterns optimally. We posit that the various synaptic circuits which we have recently shown to converge on Golgi cells are able to shape the activity of individual GoCs, within their electrically-coupled population network, to provide meaningful context-dependent inhibitory contrast on the granule cell population.

We have recently performed the world-first optical recordings of membrane voltage from specifically defined cell types in awake behaving mice using custom made two-photon random-access microscopy.[1] Using genetically encoded voltage indicators combined with ultrafast two photon recordings we can now investigate, at the microcircuit level, information transfer in the cerebellum. Specifically, we propose to examine whether, and through which rules and mechanisms, GoC inhibition may participate in pattern separation of granular layer input modalities. We will perform simultaneous presynaptic and postsynaptic optical recordings of activity in granule cells, GoCs and the various inputs controlling the later. By dissecting the input-output relationship of these circuits we should be able to answer whether and how GoCs are instrumental in optimizing the separation of cerebellar input patterns by granule cells.

Our lab, located in the **Institut de Biologie de l'Ecole Normale Supérieure**, provides a rich and vibrant experimental and training environment, in addition to all the required facilities (animal breeding, virus production, imaging, FabLab), to embark on this project. The team is highly multidisciplinary, combining expertise ranging from state-of-the-art molecular biology to physiology, optics and instrumental development. The selected candidate will have full access to unique ultrafast random-access multiphoton microscopy, developed in the lab in the past decade.

References :

1. Villette, V. *et al.* Ultrafast Two-Photon Imaging of a High-Gain Voltage Indicator in Awake Behaving Mice. *Cell* **179**, 1590-1608.e23 (2019).
2. Dugué, G. P. *et al.* Electrical Coupling Mediates Tunable Low-Frequency Oscillations and Resonance in the Cerebellar Golgi Cell Network. *Neuron* **61**, 126–139 (2009).

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