Computational and experimental approaches to uncover the integration of visual information and internal states in the mouse visual system

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Rationale & Hypothesis: Sensory circuits receive complex features from their respective sensory organs and must integrate these unimodal signals with other sensory modalities and the animal's behaviorally relevant internal states. We will combine computational and experimental techniques to study how such integration occurs in the mouse visual system, where retinal ganglion cells (RGCs) output to the superior colliculus (SC) for the formation of visual reflexes, and to the lateral geniculate nucleus (LGN) for conscious vision. Recent advances in neurophysiological tools allow for large-scale recordings of neural populations, including local circuits and long-range axons from other brain areas. Because each neuron pools inputs from local and distant sources, conventional pairwise analysis methods are not sufficient to fully understand the contribution of each input to the circuit's neuronal activity. A new theoretical framework beyond simple correlations is required to uncover the functional connectivity patterns among individual neurons, and ultimately form robust, testable predictions on the causal relationships between them.

In this proposal, we focus on two complex computations performed by the visual system using in vivo calcium imaging data of the awake, head-fixed mouse. First, we will characterize functional responses of RGCs projecting to the SC, and how such information is modulated by inputs from the primary visual cortex (V1) under different behavioral states. Second, we will use similar approaches to determine how binocular responses are produced at the LGN, which involves an interplay between neurons responding to each eye as well as feedback from V1. In both systems, it is unclear how modulatory feedback signals shape visual responses under different behavioral conditions. We will then develop and use advanced analytical approaches to reveal the functional connectivity patterns of these circuits, including the role of long-range RGC feedforward and V1 feedback inputs, in particular predicting synaptic weights and other causal relationships. Finally, we will integrate these connectivity patterns into a neural network model of this visual pathway.

Aims: We will build a comprehensive model of how local circuits of the SC and LGN in mice integrate feedforward sensory inputs from RGCs and feedback modulatory signals from V1. Our preliminary data suggest spatio-temporal correlations among the activity of SC soma and V1 feedback input axons, as well as how RGCs converge to produce binocular responses in the LGN. Our analysis and modelling of the functional correlations between RGCs, V1 inputs, and their thalamic and collicular targets will determine the presence and role of causal interactions among them, such as the role of V1 feedback in shaping behaviorally-tuned visual responses and the circuit computations underlying binocularity.

Significance & Impact: We will discover new computations and functions of an important visual pathway that integrates sensory signals with internal states. We will develop and use novel and versatile data analytics and modeling techniques that will applicable to experiments involving different brain regions and that have the potential to become key tools to establishing structure-function relationship in the brain.

Integration of Expertise of Partners: This interdisciplinary project offers to ambitious candidates a unique opportunity to learn both the cutting-edge neurophysiological expertise of the Asari and Rompani labs at EMBL Rome, and the advanced computational expertise of the Panzeri lab at IIT. The Asari and Rompani labs have established in vivo two-photon calcium imaging in the head-fixed, awake mouse. This allows them to monitor the visual responses of local neurons together with either RGC axons carrying feedforward visual inputs or V1 axons carrying feedback signals, with the Asari lab focusing on the SC and Rompani lab on the LGN. The Panzeri lab at IIT specializes in developing analysis and modelling tools in neuroscience. The combination of the experimental and theoretical tools of the IIT/EMBL labs will allow uncovering to an unprecedented level how visual circuits integrate complex inputs.