Instituts thématiques Inserm
Institut national de la santé et de la recherche médicale

Institute of Psychiatry and Neuroscience of Paris

Université Paris Cité

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(Host: Gilles Huberfeld)

Beyond 2P microscopy: optogenetic probing of large and deep neuronal circuits in freely moving mice

In the past 15 years, the synergy of two-photon (2P) microscopy and optogenetics has transformed neuroscience, enabling high-resolution imaging and precise photostimulation of neuronal activity. Today, understanding how specific patterns of neuronal activity influence perception and behaviour, requires to push the limits of 2P microscopy. This involves studying freely moving animals engaged in natural tasks and accessing thousands of neurons across superficial and deep brain regions, as well as distant yet interconnected areas.

In this presentation I will outline our recent endeavors towards these goals. I will first show how 2P holographic photostimulation is capable to precisely target individual neurons within a large volume1; I will then describe how we can use minimally invasive GRIN lenses to access deeper brain regions2; finally, I will detail our most advanced technique: a novel fiber-based miniaturized microscope to image and photostimulate neuronal activity in freely moving mice3,4. In the last part of the talk, I will present future directions for further developments and applications.

1.Accanto, N. et al. Multiplexed temporally focused light shaping for high-resolution multi-cell targeting. Optica 5, 1478 (2018).

2.Accanto, N. et al. Multiplexed temporally focused light shaping through a gradient index lens for precise in-depth optogenetic photostimulation. Sci. Rep. 9, 7603 (2019).

3.Accanto, N. et al. A flexible two-photon fiberscope for fast activity imaging and precise optogenetic photostimulation of neurons in freely moving mice. Neuron 111, 176-189.e6 (2023).

4.Lorca-Cámara, Antonio, Blot, Francois & Accanto, N. Recent advances in light patterned optogenetic photostimulation in freely moving mice. Neurophotonics 11, S11508 (2024)