Influence of the targeted brain structures on spatial behavior of fiber photometry signals

Cinzia Montinaro[1,2,*], Barbara Spagnolo[1,2], Maria Samuela Andriani[1,3], Marco Bianco[1], Marco Pisanello[4], Antonio Balena[1], Filippo Pisano[1], Francesco De Nuccio[5], Dario Domenico Lofrumento[5], Massimo De Vittorio[1,2,3,†], Ferruccio Pisanello[1,2,†]

[1] Istituto Italiano di Tecnologia (IIT), Center for Biomolecular Nanotechnologies, Via E. Barsanti 14, 73010 Arnesano (Lecce), Italy
[2] RAISE Ecosystem, Genova, Italy
[3] Dipartimento di Ingegneria dell'Innovazione, Università del Salento, Via per Monteroni, 73100 Lecce, Italy
[4] OptogeniX, Via E. Barsanti 14, 73010 Arnesano (Lecce), Italy
[5] Dipartimento di Scienze e Tecnologie Biologiche e Ambientali, Università del Salento, Via per Monteroni, 73100 Lecce, Italy

[†] Co-last authors
* Corresponding author. E-mail: cinzia.montinaro@iit.it

Neuroscience studies aim at a more comprehensive understanding of the brain. The gold standard technique for investigating neural activity is electrophysiology, but it lacks cellular specificity. This can be overcome by taking advantage of genetically encoded light-sensitive proteins to target specific cell subpopulations and by the development of implantable interfaces to optically interrogate neural circuitry. This was followed by research activity to deal with brain opacity due to the scattering of photons in brain tissue, thus limiting the optical access at depth. Neuroscientists therefore focused on the development of implantable devices to deliver and collect light from deep into the tissue, achieving both cell specificity and spatial resolution. Among the available optical neural interfaces, flat-cleaved optical fibers were exploited for optical monitoring of functional fluorescence, a technique called fiber photometry (FP). However, monitoring physiological phenomena through FP requires accurate quantification of differences in photon propagation in different brain regions. In this framework, we estimated how the collection properties of implantable optical devices are affected by different anatomical structures of the mouse brain, estimating the light collection volumes of flat optical fibers into fixed mouse brain slices. We analyzed this in three different brain areas, concluding that their anatomical and cellular peculiarities determine the amount and the depth from which photons can be retrieved. We also present the implementation of a custom optical setup for exploiting optoelectrical neural interfaces based on tapered optical fiber for simultaneous FP and electrophysiology, resulting in a novel multifunctional tool to interrogate brain circuits at depth.