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Label-free biomolecular tissue analysis in the living brain via vibrational fiber photometry at arbitrary depth

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Optical approaches for *in vivo* neural monitoring offer a precious window on brain functions and on the mechanisms of development, ageing or disease progression. Nonetheless, the existing methods still struggle to capture *in situ* the complex biomolecular alterations that accompany physiological and pathological dynamics. As a result, our grasp on the multifaceted components of brain activity is still limited.
To surpass this limitation, we propose a vibrational fiber photometry method based on spontaneous Raman scattering that allows monitoring the biomolecular content of arbitrarily deep brain volumes of the mouse brain *in vivo* without exogenous reporters. To do this, we employed a single, thin tapered optical fiber delivering and collecting optical signals to gather information on the local cytoarchitecture, to sense molecular alterations linked to circuit dysfunction caused by traumatic brain injury, and to detect diagnostic markers of brain metastasis with high accuracy.
In our view, vibrational fiber photometry offers an opportunity to capture a more comprehensive picture of neural activity in the biomolecular context of the local micro-environment. This capability, that can be employed alongside traditional fiber photometry or electrophysiological techniques, is particularly promising for empowering emerging research on brain-immune [1] and brain-cancer [2] bidirectional dynamics.

References

[1] Castellani, G. et al., Science (1979) 380, (2023).
[2] Mancusi, R. & Monje, M., Nature 618, 467–479 (2023).

Primary author: PISANO, Filippo (Department of Physics and Astronomy, University of Padova, Padova, Italy & Padova Neuroscience Center, University of Padova, Padova, Italy)

Co-authors: MASMUDI-MARTÍN, Mariam (Brain Metastasis group, CNIO, Madrid, Spain); SAMUELA ANDRIANI, Maria (Istituto Italiano di Tecnologia, Center for Biomolecular Nanotechnologies, Arnesano, Italy & Dipartimento di Ingegneria dell'Innovazione, Università del Salento, Lecce, Italy); CID, Elena (Instituto Cajal, CSIC, Madrid, Spain); KAZEMZADEH, Mohammadrahim (Istituto Italiano di Tecnologia, Center for Biomolecular Nanotechnologies, Arnesano, Italy); PISANELLO, Marco (Optogenix srl, Lecce, Italy); BALENA, Antonio (Department of Physics and Astronomy, University of Padova, Padova, Italy); COLLARD, Liam (Department of Physics and Astronomy, University of Padova, Padova, Italy); JURADO PARRAS, Teresa (Dipartimento di Ingegneria dell'Innovazione, Università del Salento, Lecce, Italy); BIANCO, Marco (Istituto Italiano di Tecnologia, Center for Biomolecular Nanotechnologies, Arnesano, Italy); BAENA, Patricia (Brain Metastasis group, CNIO, Madrid, Spain); TANTUSSI, Francesco (Istituto Italiano di Tecnologia, Center for Convergent Technologies, Genova, Italy); GRANDE, Marco (Dipartimento di Ingegneria Elettrica e dell'Informazione, Bari, Italy); SILEO, Leonardo (Optogenix srl, Lecce, Italy); GENTILE, Francesco (Nanotechnology Research Center, Department of Experimental and Clinical Medicine, University of "Magna Graecia", Catanzaro, Italy); DE ANGELIS, Francesco (Istituto Italiano di Tecnologia, Center for Convergent Technologies, Genova, Italy); DE VITTORIO, Massimo (Istituto Italiano di Tecnologia, Center for Biomolecular Nanotechnologies, Arnesano, Italy); MENENDEZ DE LA PRIDA, Liset (Instituto Cajal, CSIC, Madrid, Spain); VALIENTE, Manuel (Brain Metastasis group, CNIO, Madrid, Spain); PISANELLO, Ferruccio (Istituto Italiano di Tecnologia, Center for Biomolecular Nanotechnologies, Arnesano, Italy)

Presenter: PISANO, Filippo (Department of Physics and Astronomy, University of Padova, Padova, Italy & Padova Neuroscience Center, University of Padova, Padova, Italy)

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