INV20

Glial engineering & interfaces: organic/hybrid materials and devices to probe and sense the "other brain"

Valentina Benfenati[1]
Consiglio Nazionale delle Ricerche, Istituto per la Sintesi Organica e Fotoreattività, via Gobetti 101, Bologna, Italy.
Author e-mail address: valentina.benfenati@isof.cnr.it

1. Main text

Studies over the past four decades have enlightened that the correct human brain function is dependent on the activity of glial cells called astrocytes.[1] Although uncapable of action potential, astrocytes are far to be passive cella, merely supporting the function of neurons. Astrocytes can sense and respond to chemo-physical changes in the extracellular environment, by alteration in their bioelectrical properties as well by variations in intracellular calcium concentration ($[Ca^{2+}]_i$). Accordingly, the role of ions and water channels mediating dynamics, waves and signaling of astrocytes is recognized as critical for brain homeostasis and neurovascular coupling, while it is assuming relevance for brain communication and information processes, typically univocally assigned to neurons.[1,2]

A major obstacle in studying astrocytes is that most of the technologies used to probe and sense them are derived from those developed to study neurons.[2]

In this respect, the concept of glial interfaces and glial engineering[2,3] is herein reported and proposed to meet the demand of technologies targeting glial cells and in particular astrocytes, to develop ad hoc tailored tools to probe and sense their peculiar structural and functional properties.

Advances and results are presented, achieved using organic/hybrid material interfaces and devices that interact with astrocytes. In particular, results will be overviewed obtained by: 1) using engineered organic/hybrid biomaterials and nanostructured interfaces to provide in vivo-like in vitro models for controlled & reliable studies of astrocytes in vitro;[4,5] 2) using organic semiconductor & polymers, carbon-based materials in electronic and photonic devices methods for spatially precise stimulation of specific astrocytes ionic currents and selective calcium signalling;[2-7] 3)validating a nanostructured device that enable noninvasive extracellular recording of the slow-frequency oscillations generated by differentiated astrocytes.[4]

It will be shown the ability of these approaches to reach unprecedented insights into the mechanism underpinning the role of astroglial cells in brain function and dysfunction.

Finally, the potential of glial engineering to enable significant advancement of knowledge surrounding cognitive function, and to generate alternative therapeutic approaches to achieve neuromodulation is discussed.

2. References

[1] Verkhratsky A, Nedergaard M. Physiology of Astroglia. Physiol Rev. 2018; 98(1):239-389.

[2] Borrachero-Conejo AI, Saracino E, Natali M, Prescimone F, Karges S, Bonetti S, Nicchia GP, Formaggio F, Caprini M, Zamboni R, Mercuri F, Toffanin S, Muccini M, Benfenati V. Electrical Stimulation by an Organic Transistor Architecture Induces Calcium Signaling in Nonexcitable Brain Cells. Adv Healthc Mater. 2019 Feb;8(3):e1801139.

[3] Maiolo L, Guarino V, Saracino E, Convertino A, Melucci M, Muccini M, Ambrosio L, Zamboni R, Benfenati V. Glial Interfaces: Advanced Materials and Devices to Uncover the Role of Astroglial Cells in Brain Function and Dysfunction. Adv Healthc Mater. 2021 Jan;10(1):e2001268.

[4] Saracino E, Maiolo L, Polese D, Semprini M, Borrachero-Conejo AI, Gasparetto J, Murtagh S, Sola M, Tomasi L, Valle F, Pazzini L, Formaggio F, Chiappalone M, Hussain S, Caprini M, Muccini M, Ambrosio L, Fortunato G, Zamboni R, Convertino A, Benfenati V. A Glial-Silicon Nanowire Electrode Junction Enabling Differentiation and Noninvasive Recording of Slow Oscillations from Primary Astrocytes. Adv Biosyst. 2020 Apr;4(4):e1900264.

[5] Fabbri R , Saracino E , Treossi E , Zamboni R , Palermo V , Benfenati V . Graphene glial-interfaces: challenges and perspectives. Nanoscale. 2021 Feb 28;13(8):4390-4407. d

[6] Borrachero-Conejo AI, Adams WR, Saracino E, Mola MG, Wang M, Posati T, Formaggio F, De Bellis M, Frigeri A, Caprini M, Hutchinson MR, Muccini M, Zamboni R, Nicchia GP, Mahadevan-Jansen A, Benfenati V. Stimulation of water and calcium dynamics in astrocytes with pulsed infrared light. FASEB J. 2020 May;34(5):6539-6553.

[7] Durso M , Borrachero-Conejo AI , Bettini C , Treossi E , Scidà A , Saracino E , Gazzano M , Christian M , Morandi V , Tuci G , Giambastiani G , Ottaviano L , Perrozzi F , Benfenati V , Melucci M , Palermo V . Biomimetic graphene for enhanced interaction with the external membrane of astrocytes. J Mater Chem B. 2018 Sep 7;6(33):5335-5342.

3. Acknowledgements

Valentina Benfenati. is grateful to the co-authors and collaborators that contributed to the presented results. Among the others acknowledged are E. Saracino, D. Spennato, R. Fabbri, R. Zamboni, M. Melucci, E. Treossi and V. Palermo at CNR-ISOF; L. Maiolo & A. Convertino at CNR-IMM,

INV20

M. Muccini, A. Borrachero-Conejo, CNR-ISMN, L. Ambrosio and V. Guarino from CNR-IPCB, G. P. Nicchia, University of Bari, M. Caprini and F. Formaggio from FABIT-UNIBO, M. Chiappalone and M.R. Antognazza, Fondazione Istituto Italiano di Tecnologia; W. Losert and K. O'Neil from University of Maryland, S. Hussain from Air Force Research Laboratory, A. Mahedevan-Jansen,W. Adams from Vanderbilt University, M. Hutchinson, from University of Adelaide, Dr Karma Perry and Dr. Shashi Karna from Army Research Laboratory.
Sponsored by MSCA-ITN-2020-ASTROTECH (GA956325), by the following grant from Air Force Office of Scientific Research (AFOSR): ASTROLIGHT (FA9550-20-1-0386), 3D NEUROGLIA, FA9550-18-1-0255 (V.B., V.G., L.A.), ASTRONIR, FA9550-17-1-0052 and "Decoding Astrocytes Rhythm" and by Army Research Office grant ASTRO-GOLD (W911NF2120074).