Graphene-Glial interfaces for the selective modulation of brain signaling

Roberta Fabbri[1], Alessandra Scidà[1], Alessandro Kovtun[1], Andrea Candini[1], Denisa Kirdajova[2], Diletta Spennato[1], Giorgia Conte[1], Emanuela Saracino[1], Katerina Konstantoulaki[1], Chiara Lazzarini[1], Miroslava Anderova[2], Emanuele Treossi[1], Roberto Zamboni[1], Vincenzo Palermo[1], Valentina Benfenati[1]

[1]Institute for Organic Synthesis and Photoreactivity (ISOF), National Research Council of Italy (CNR), Via P. Gobetti 101, 40129 Bologna, Italy

[2]Department of Cellular Neurophysiology, Institute of Experimental Medicine, CAS, Videnska 1083, 142 00 Prague 4, Czech Republic.

roberta.fabbri@isof.cnr.it

Abstract

Among 2D nanomaterials, Graphene has emerged as biomaterial interface due to its outstanding properties, including electrical conductivity, mechanical flexibility and biocompatibility. It is now established that implant devices and electrodes for brain stimulation and recording interact apart from neurons, also with glial cells, called astrocytes. However, evidence is lacking on the possibility to use graphene as electrode interface to modulate the functionality of brain astrocytes. Astrocyte Ca^{2+} signaling is important for the regulation of cognitive and vascular functions, and results compromised in many neurological disorders, such as stroke, epilepsy and spreading depression. In this view, understanding the biophysical mechanisms behind the cell/material interaction has remained a critical challenge. Here, we investigate the unique combination of Graphene-oxide (GO) and reduced GO (rGO) coated electrodes to modulate Ca^{2+} signaling in astrocytes by electrical stimulation. Our results indicate that GO/rGO films are biocompatible coating interfaces, promoting the cell growth with no adverse gliotic reactivity [1]. We found that the electrical stimulation can trigger distinct intracellular Ca^{2+} responses in astrocytes, in vitro and in brain slices, depending on the electrical properties of rGO/GO interfaces. Astrocytes stimulated by conductive rGO electrodes show rapid Ca^{2+} response with oscillating peaks, exclusively mediated by Ca^{2+} release from intracellular stores. Conversely, electrical stimulation delivered by insulating GO electrodes causes slower, sustained Ca^{2+} response, mainly due to external Ca^{2+} influx through membrane channels [2]. We propose a bioelectrical model, hypothesizing that the different conductivity of the substrate influences the electric field at the cell/material or cell/electrolyte interfaces, inducing, respectively, the extracellular Ca^{2+} influx or the intracellular Ca^{2+} release. Graphene-glial interfaces might be extremely promising for neural engineering and neuroscience investigation, offering a new way to dialogue and selectively interact with glial cells in the Nervous System [3].

Supported by US Air Force Office of Scientific Research FA9550-20-1-0386 (AstroLight); Army Research Laboratory W911NF-21-2-0074 (AstroGold); H2020-MSCA-ITN-2020, ASTROTECH (GA956325)

References

[1] M. Durso, A. I. Borrachero-Conejo, C. Bettini, E. Treossi, A. Scidà, E. Saracino, M. Gazzano, M. Christian, V. Morandi, G. Tuci, G. Giambastiani, L. Ottaviano, F. Perrozzi, V. Benfenati, M. Melucci, V. Palermo, J. Mater. Chem. B., 6(2018), 5335.

[2] I. Borrachero-Conejo, E. Saracino, M. Natali, F. Prescimone, S. Karges, S. Bonetti, G. P. Nicchia, F. Formaggio, M. Caprini, R. Zamboni, F. Mercuri, S. Toffanin, M. Muccini, V. Benfenati, Adv. Healthc. Mater., 8(2019), 1801139.

[3] R. Fabbri, E. Saracino, E. Treossi, R. Zamboni, V. Palermo, V. Benfenati, Nanoscale, 13(2021), 4390.