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Graphene-based devices for selectively triggering calcium signals in brain astrocytes

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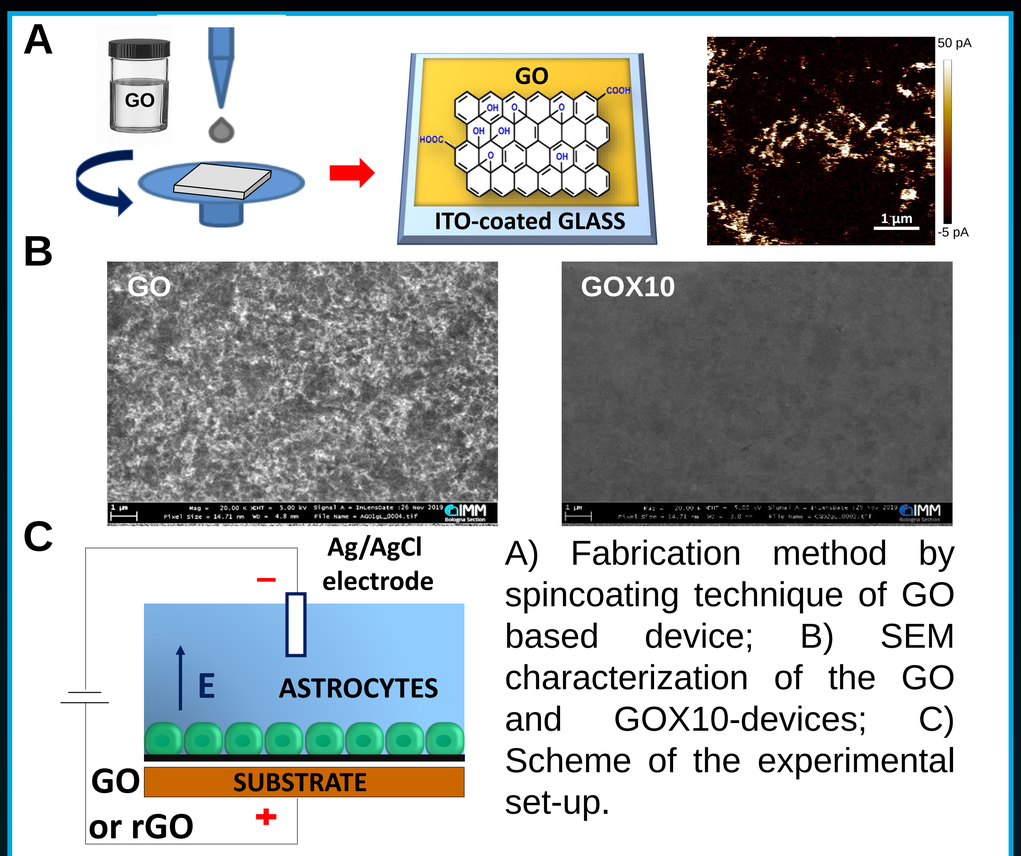
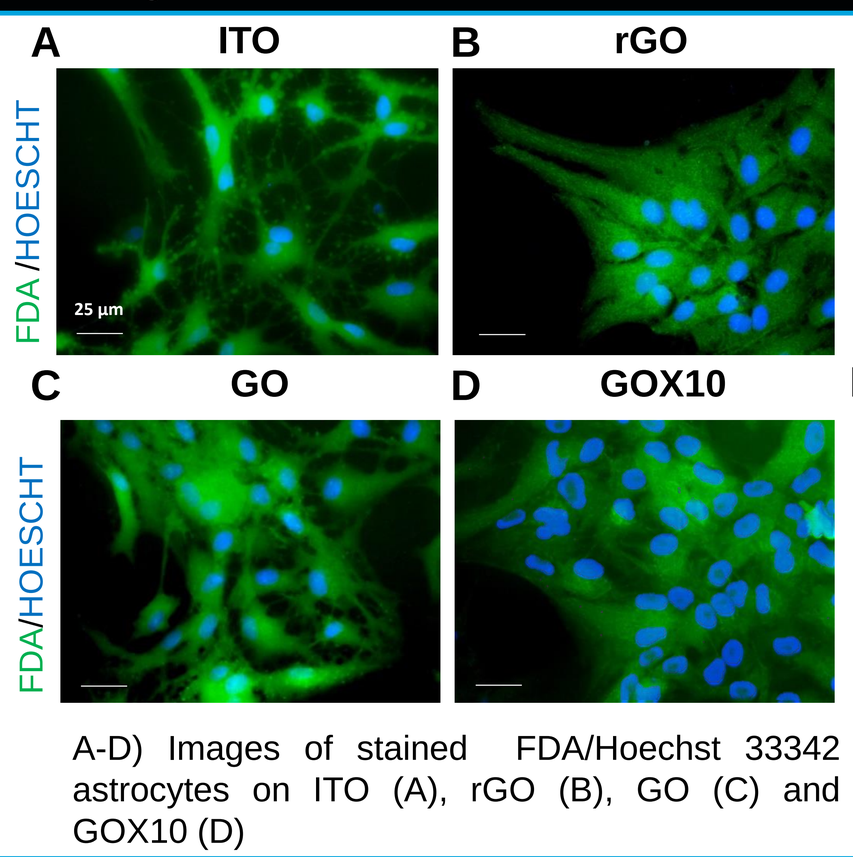
INTRODUCTION Graphene represents a potentially suitable material as neuronal interface. Consolidated evidence highlighted the crucial functions of variation in intracellular calcium concentrations $[Ca^{2+}]_i$ of astrocytes in brain homeostasis and in the control of synaptic transmission. In the present work we sought to investigate the use of **Graphene-based devices to evoke $[Ca^{2+}]_i$ in primary rat cortical astrocytes, by application of extracellular electrical stimulation.**

1) Fabrication and Characterization of the Graphene based-device



A) Fabrication method by spincoating technique of GO based device; B) SEM characterization of the GO and GOX10-devices; C) Scheme of the experimental set-up.

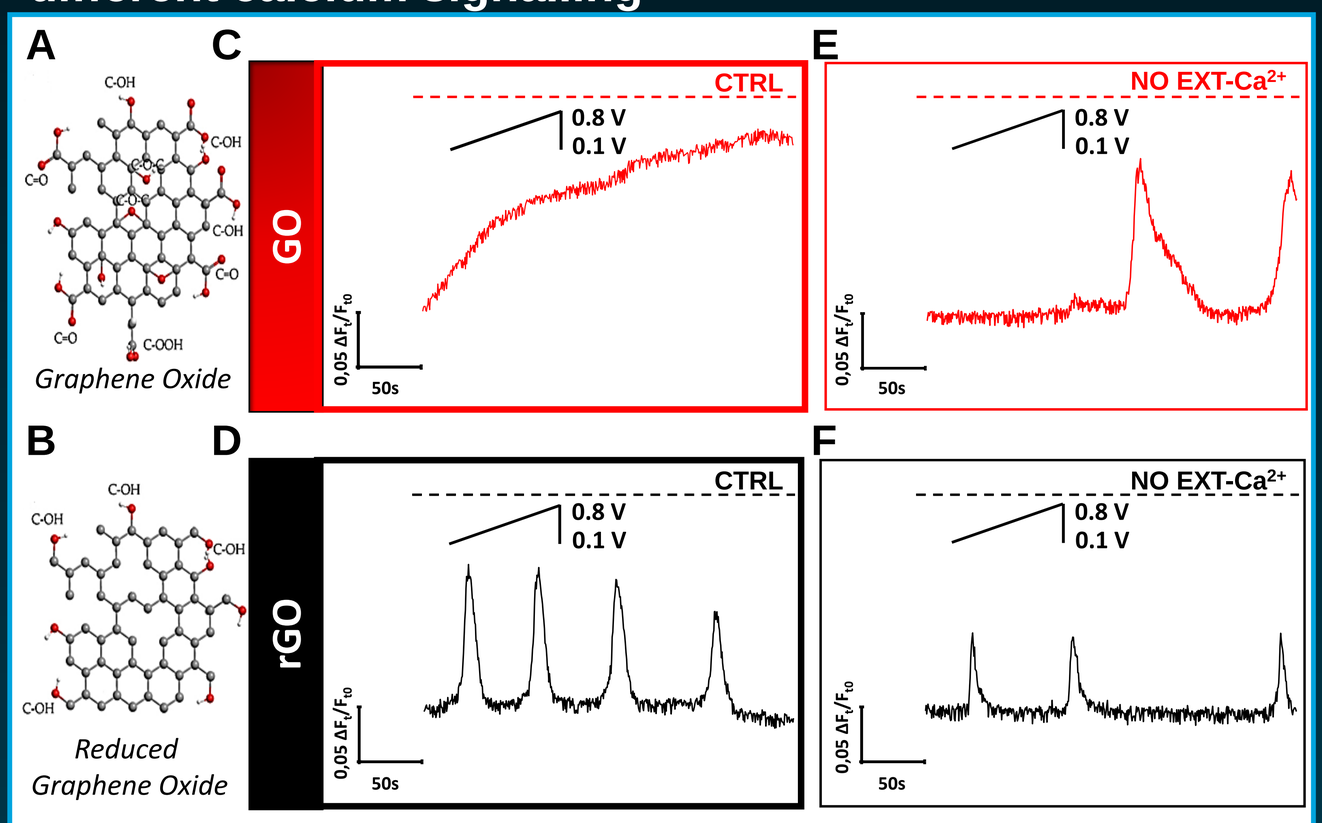
2) Effects of ITO and Graphene based-device on astrocytes viability



A-D) Images of stained FDA/Hoechst 33342 astrocytes on ITO (A), rGO (B), GO (C) and GOX10 (D)

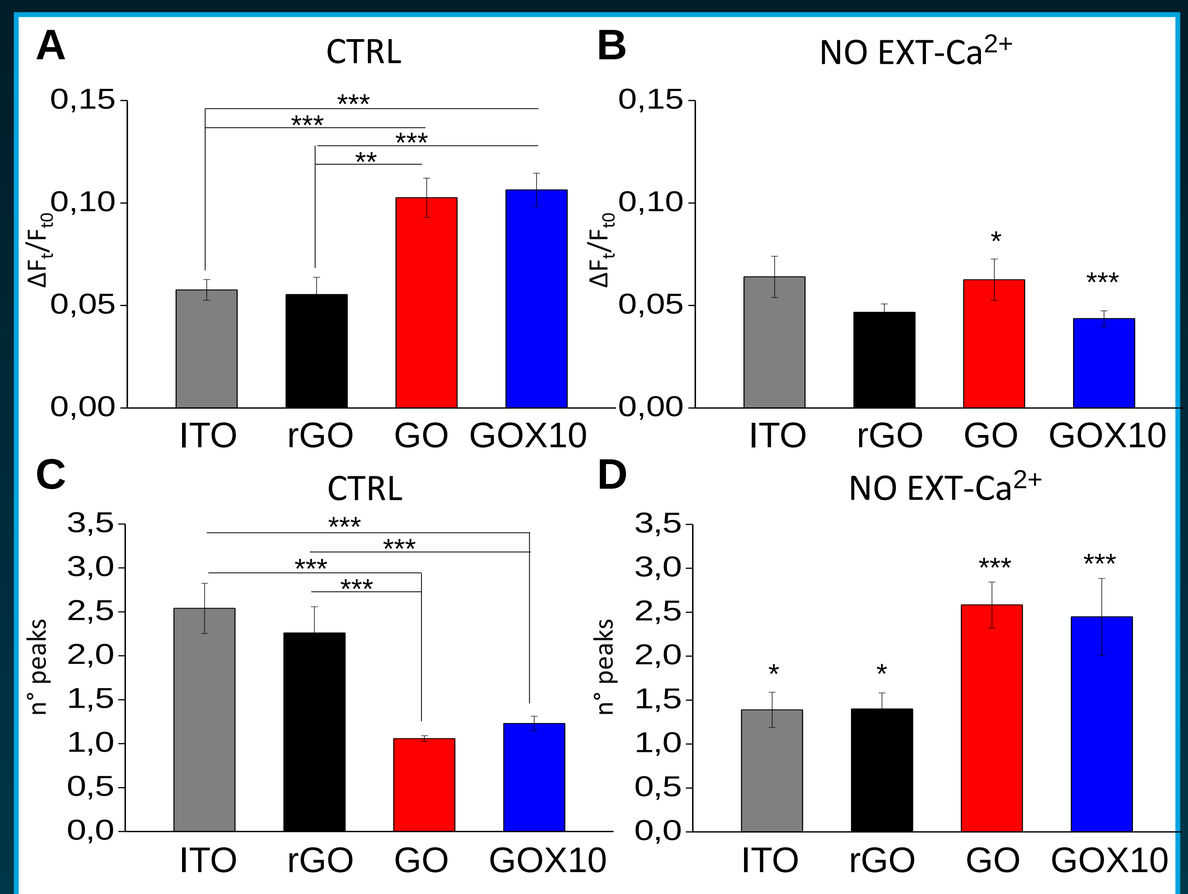
E) Histogram plot showing the number of cells/area (*** $p < 0.001$, ** $p < 0.01$, *$p \leq 0.05$, One-way ANOVA).
The viability on ITO, GO and rGO is comparable

3) Electrical Stimulation by GO, rGO and ITO activates different calcium signalling



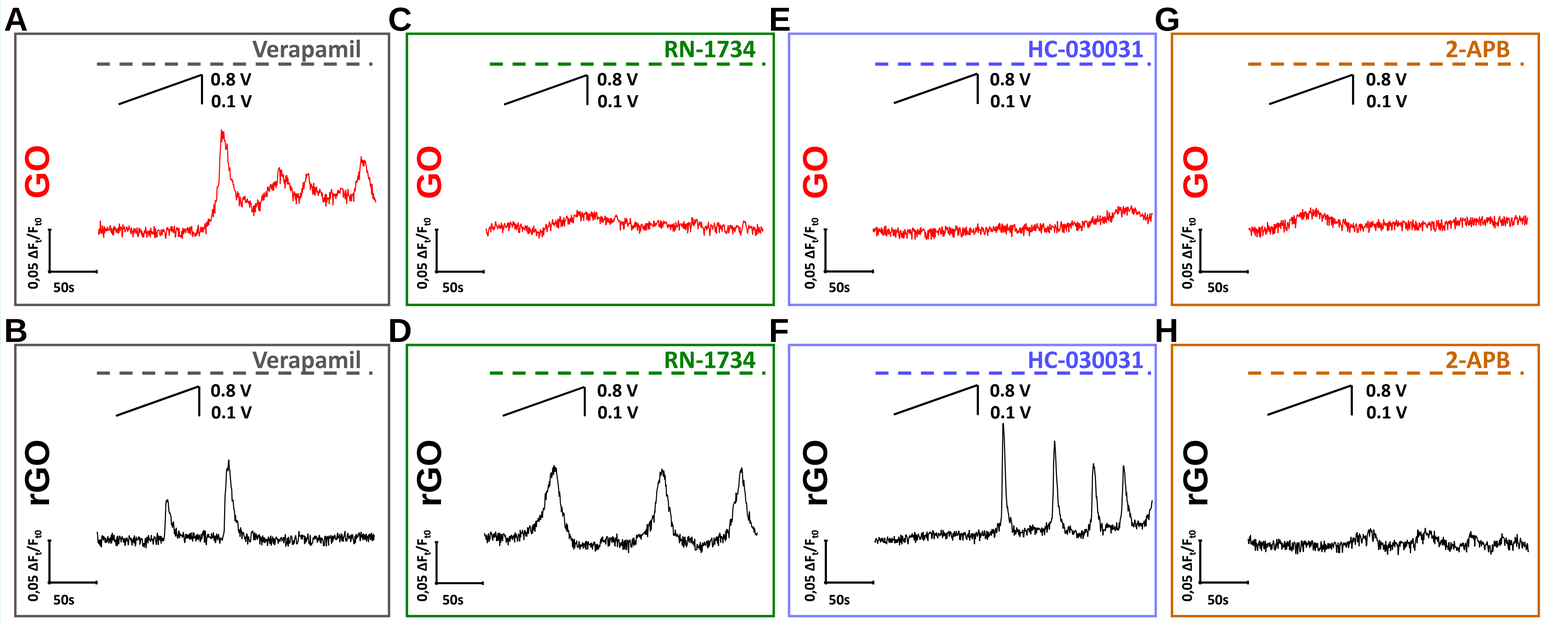
A, B) Chemical structure of GO (A) and rGO (B). C-F) Representative traces of Ca^{2+} imaging experiments performed on GO and rGO-devices in with extracellular solution containing Ca^{2+} (C,D) or in absence of Ca^{2+} (E,F).
Removal of calcium affects only the effect observed in GO device.

4) GO stimulates extracellular Ca^{2+} entry, while rGO and ITO Ca^{2+} release from intracellular stores



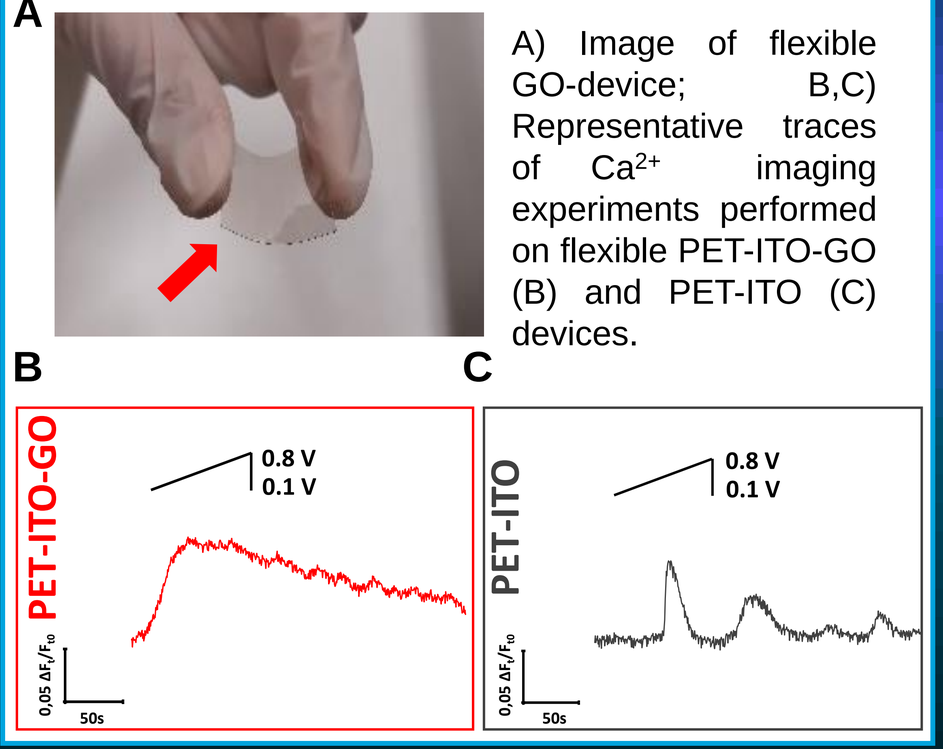
A-D) Bar plots of measurements performed on different GO-devices in with extracellular solution containing Ca^{2+} (A,C) or in absence of Ca^{2+} (B,D).

5) Pharmacology confirms the selective stimulation of $[Ca^{2+}]_i$



A-H) Representative traces of Ca^{2+} imaging experiments performed on GO and rGO devices in presence of VGCC inhibitor Verapamil (25 µM), TRPV4 inhibitor RN-1734 (10 µM), TRPA1 inhibitor HC-030031 (40 µM) and IP_3 inhibitor 2-APB (100 µM).

6) GO-FLEXIBLE devices can be used to stimulate astrocytes



A) Image of flexible GO-device; B,C) Representative traces of Ca^{2+} imaging experiments performed on flexible PET-ITO-GO (B) and PET-ITO (C) devices.

Conclusions: Our results suggest the great potentialities of graphene devices for engineering advanced glial interfaces devoted to the selective modulation of astrocyte calcium dynamics in the study and therapy of brain functions and dysfunctions.

References: A. I. Borrachero-Conejo et al., Adv. Healthcare Mater. 2019, 8, 3, e1801139; M. Durso et al., J. Mater. Chem. B, 2018, 6, 5335; R. Fabbri et al., Nanoscale, 2021, 13, 4390.
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