Graphene microelectrode arrays for cell stimulation

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Abstract

The direct electrical interfacing of graphene-based devices with individual neurons is currently being considered for the development of the next generation of neuroprosthetic devices.

Electrical stimulation of neurons can be carried out by voltage-sensitive transmembrane proteins called ion channels embedded in the cell membrane. By modulating the outer potential appropriately it is possible to externally stimulate electrogenic cells. Typically, external stimulation of neural tissue is done using electrodes in direct contact with biological tissue. To date, electrodes have been basically metallic and triggered Faradaic currents, whose reactive redox products could damage the cells. An alternative way to depolarise cells externally is through capacitive currents [1], which require chemically stable electrodes and do not have the problems associated to redox reactions typical of metal electrodes.

Graphene is a very good candidate for external capacitive stimulation of electrogenic cells due to its remarkable chemical and physical properties. Because of its high stability in aqueous environments, no surface layer of dielectric material is required to insulate it from the solution in order to prevent unwanted electrochemical reactions. In addition, its high capacitance up to 2 µF/cm^2 makes graphene an ideal candidate for capacitive stimulation. Furthermore, graphene is known to possess good biocompatibility and facility to be integrated in flexible devices, which is crucial in neuroprosthetic applications [2, 3].

This work will provide a detailed description of the fabrication of chips containing arrays of graphene based solution-gated field-effect transistors (G-SGFET) and microelectrodes (G-MEA) and their use for recording and stimulation of action potentials in cell cultures. Chips (Fig. 1) are fabricated using high quality graphene grown by CVD and standard optical lithography, e-beam and thermal evaporation of metals and oxygen plasma etching. For the characterisation of the devices, Raman spectroscopy, cyclic voltammetry, electrochemical impedance spectroscopy and transistor characterisation at different values of pH and ionic strength are performed. Moreover, electrogenic cells (PC12, HEK and HL-1) are cultured on the graphene chips according to established protocols. Once the devices are fabricated and characterised, mature cells are placed onto them and bioelectronic experiments are performed. Using the patch clamp technique and the arrays (Fig.2) it is possible to record changes of intracellular potential and depolarise cells. The obtained data is finally processed and the triggered action potentials identified (Fig. 3).

References

[1] Schoen, I., Fromherz, P., *Extracellular stimulation of mammalian neurons through repetitive activation of Na+ channels by weak capacitive currents on a silicon chip*, J Neurophysiol 100, 346 (2008).

[2] Hess, L. H., Jansen, M., Maybeck, V., Hauf, M. V., Seifert, M., Stutzmann, M., Sharp, I. D., Offenhäusser, A. and Garrido, J. A., *Graphene Transistor Arrays for Recording Action Potentials from Electrogenic Cells*, Advanced Materials 23, 5045 (2011).

[3] Hess, L.H., Seifert, M. and Garrido, J.A., *Graphene Transistors for Bioelectronics*, Proceedings of the IEEE 100, 1780 (2013).

Figures

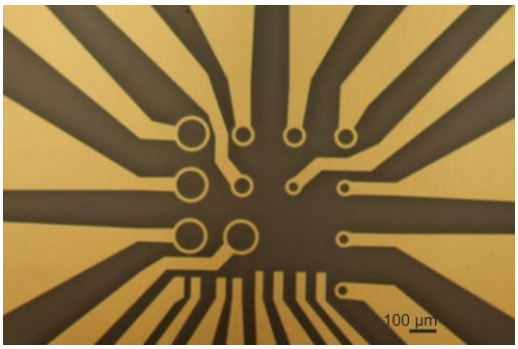

Fig. 1. Optical micrograph of an array with 12 circular electrodes (diameter from 25 µm to 100 µm) and 4 transistors (15x35 μm^2 and 30x70 μm^2).

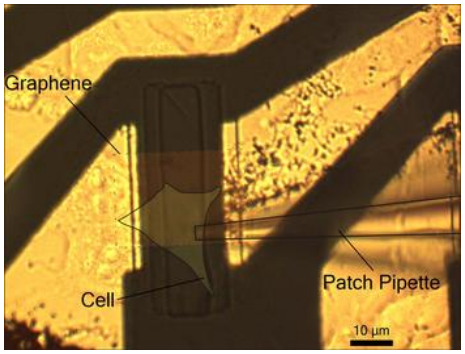

Fig. 2 Electrogenic cell on G-SGFET during patch clamp.

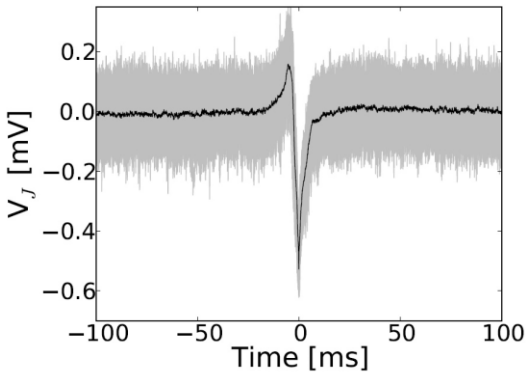

Fig. 3. Average of 83 consecutive action potentials of a electrogenic cell recorded by G-SGFET.