Graphene solution gated field-effect transistors for neurotransmitters monitoring

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The use of the emerging graphene-based field-effect transistors technology has been reported for several applications due to their key advantages such as easy operation and miniaturization, fast response time, label-free and real-time monitoring, multiplexing capability, and possible microfluidic integration.[1] In previous works, we have studied the use of graphene solution gated field-effect transistors (gSGFETs) for developing advanced neural interfaces, taking advantage of its chemical stability to enable dc-coupled recordings[2-3] and for exploring multiplexing readout strategies. In addition, gSGFETs technology allows the monitoring of charge changes on the graphene channel surface in liquid environments, which can be related to the charges introduced upon chemical functionalization, the immobilization of bioreceptors and the detection to an analyte of interest. This feature makes gSGFETs particularly attractive for the development of novel bioanalytical sensors (Figure 1a).

In this aspect, graphene functionalization with linker molecules and the immobilization of bioreceptors is required to perform any detection assay, but the surface modification of graphene has a significant impact on its crystal lattice structure and, consequently, on the electronic properties of these devices. Typically, gSGFETs electrical characterization is performed in steady-state operation mode using transfer curves, in which the Charge Neutrality Point (CNP) value, the minimum of the curve (I_{DS}–V_{GS}), is affected by the introduction of charged species on graphene. Therefore, the variations in the CNP allows to evaluate the chemical functionalization and the sensing response to an analyte of interest (Figure 1b). In parallel, time monitoring experiments can be performed by fixing a certain polarization voltage and measuring the current (I_{DS}). Then transfer curve is employed to calibrate the current-to-voltage conversion during the time measurements.

In this work, we present the evaluation of different types of graphene functionalization strategies, based on different linkers such as pyrene-derivatives, to immobilize neurotransmitters aptamers (Figure 2a). Raman spectroscopy was conducted before and after functionalization for surface characterization, confirming the preservation of the graphene crystalline structure (Figure 2b). The functionalization strategy based on the use of pyrene-maleimide (PMAL) layer is then employed as the linker for serotonin aptamer conjugation. Serotonin neurotransmitter (5-HT) is evaluated due to its importance in neurological diseases such as anxiety, aggression and stress. The serotonin-specific conformational aptamer employed has been previously demonstrated to undergo significant conformational rearrangements upon serotonin recognition in complex environments.[4]

Here, we have employed different gSGFETs array with multiple devices to evaluate the reliability of the functionalization strategies and the subsequent serotonin detection. In order to simulate the neurotransmitter real-time monitoring, the injection of serotonin at different concentrations was performed using a polymethyl methacrylate (PMMA) flow cell chamber with a peristaltic flow pump to control the flow rate (Figure 3a). In addition, we performed the alternation of serotonin injection with 10 mM PBS buffer solution to evidence the reversible nature of the aptamer employed, which is crucial to translate this technology in real scenarios for monitoring neurotransmitters *in vivo* (Figure 3b).

This research validates the use of conformational aptamers with gSGFETs technology as a promising tool for serotonin monitoring and pave the way for the development of neural probes to perform *in situ* sensing of neurotransmitters in brain.

References

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Figures

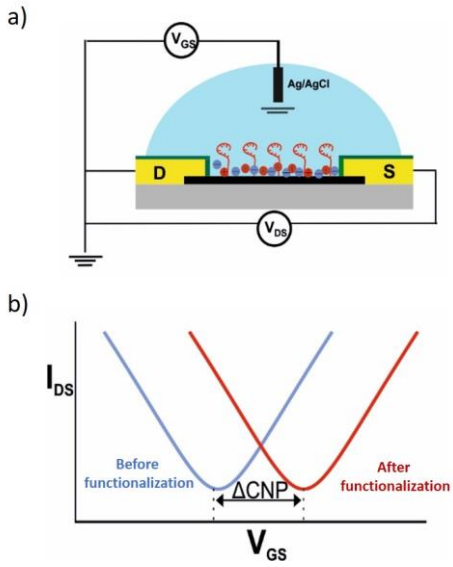

Figure 1. a) Schematic of a graphene solution gated field effect transistor (gSGFET) and b) the typical I-V transfer curves change before and after functionalization.

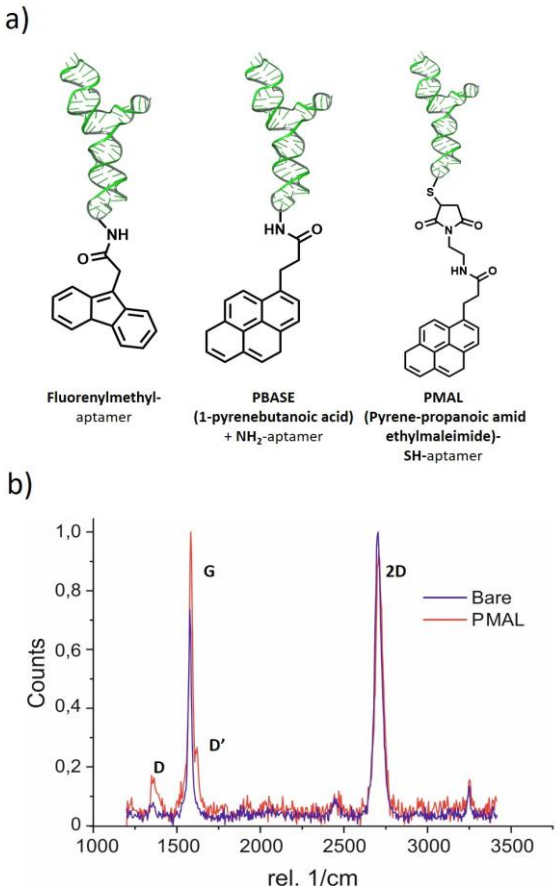

Figure 2. a) Fluorenylmethyl and pyrene-based molecules for serotonin aptamer immobilization. b) Average Raman spectra of graphene from 900 points, before and after 1h incubation with PMAL (5 mM).

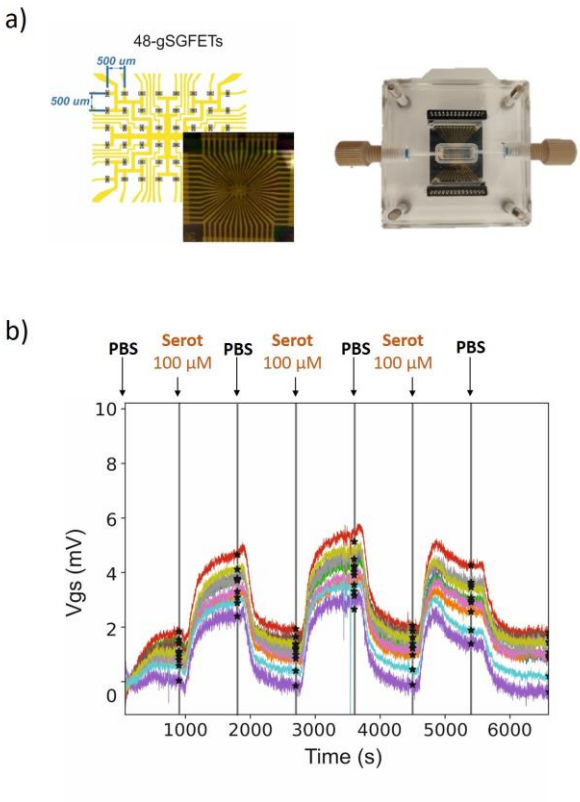

Figure 3. a) Left. Schematic of the layout of a chip with 48-gSGFET array and the optical microscope image of the fabricated chip. Right. Fluidic cell. b) Detection of serotonin, combining cycles of serotonin at 100 µM and PBS 10 mM. Each line represents the response of one transistor from the array.