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Validation of graphene-based devices for neurophysiological recordings

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The fabrication of probes through microtechnologies has fostered critical advances in the understanding of brain neuronal networks in recent years, mainly by allowing multiple simultaneous recordings through silicon probes. Microelectrodes in neuroscience are needed for the efficient and selective stimulation or recording of different groups of neurons, as a basic tool to increase the knowledge about brain baseline functionality or even for diagnostics or treatment of neurodegenerative diseases. In this sense, we previously reported biosensors with optimal probe design for neural recording [1] and the integration of C-based material such as CNT[1b, 2] and graphene[1a, 1c, 3]. Recently we started to study and develop devices for neural recordings based entirely on graphene (Figure 1b). Taking advantage of the intrinsic properties [4] of graphene, such as the flexibility, transparency, biocompatibility, good electrode-electrolyte interface, and compatibility with standard microtechnologies, we hypothesized that graphene neural devices with enhanced performance with respect to the silicon-based ones could be developed. In this abstract, we present graphene based neural probes that can endow the neuroscience with an improved tool in contrast with the regular metallic sensors widely used by the neurophysiologists, which present many drawbacks. These disadvantages such as the electrode material degradation, the high laceration due to the rigidity in the mechanical device insertion, the foreign body response and the difficulties for obtaining and maintaining good recordings, arise mainly as a consequence of a lingering technological bottleneck that is the realization of a soft, minimal invasive, micron-sized electrodes capable of recording neuronal activity without causing neither electrode nor tissue damage.

Graphene has been envisaged to be a material with realistic chance to become the next disruptive material thanks to the combination in the same material of the intrinsic properties of graphene above mentioned. Motivated by this combination of properties, we fabricated a novel flexible neuronal microelectrode device based entirely on graphene technology with the capability of obtaining brain recordings and open of the double use as recording/stimulating electrodes plus compatibility with magnetic resonance imaging techniques.

Specifically, the main objective with these devices is to detect signals with a functional signal-to-noise ratio. This noise can be divided into neural noise + thermal noise. This last one is associated to the electrode impedance, and the strategy in commonly used metallic electrodes to decrease this parameter and obtain good recordings is to increase the effective area by increasing the surface roughness. In the case of a graphene based device, the electrode is addressed to be purely capacitive, with no CPE behavior, eliminating by this way the thermal noise and so increasing the signal-to-noise ratio.

The devices consist of conducting graphene material embedded in a flexible and biocompatible support such as COP of 40um thick, through transference from the grown CVD graphene, and then the graphene is protected by SU-8 polymer as a passivation layer. In this process standard microelectronic technology such as optical photolithography has been used to obtain a perfect defined area of the electrode from 500um to 10um diameter (Figure 1c). Once obtained the sensor it is encapsulated into a PCB to perform the final device. (Figure 1a). We currently explore the possibility of using the photolithography to perform devices with multiple electrodes. These devices have been characterized by impedance measurements and cyclic voltammetry to assess the viability for the recording experiments.

The device has been tested in *in vivo* experiments to perform recordings of the neural activity and the results seem to be very promising in order to confirm that high quality brain recordings can be obtained with a satisfactory signal to noise ratio (Figure 1d).

In contrast to the technology for flexible devices developed until know, here we present a *promising and simple* technology which uses a combination of *micro and nano schemes* for obtaining a nearly purely capacitive microelectrode entirely based on graphene with a defined area for neural applications.

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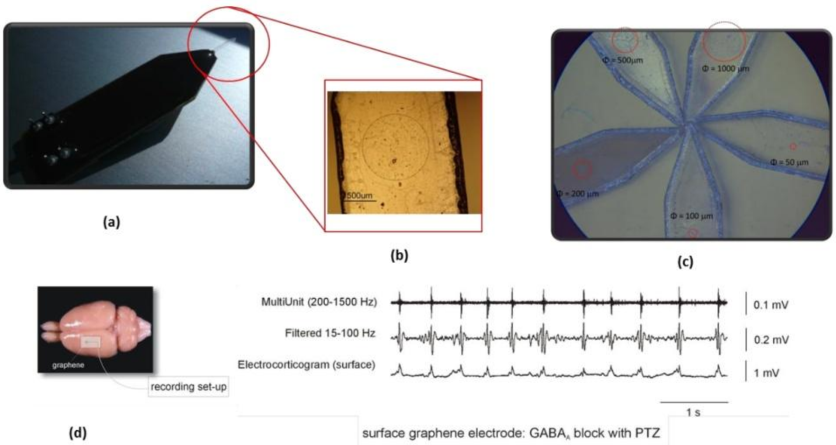

Figure 1. a) Neural probe entirely based on graphene, b) Graphene electrodes defined after photolithography, c) Encapsulated graphene neural probe d) Neural recordings made with the graphene probe prototype from the surface of the cerebral cortex of an anesthetized mouse. Recordings were obtained in the presence of GABA$_A$ receptor blockade.