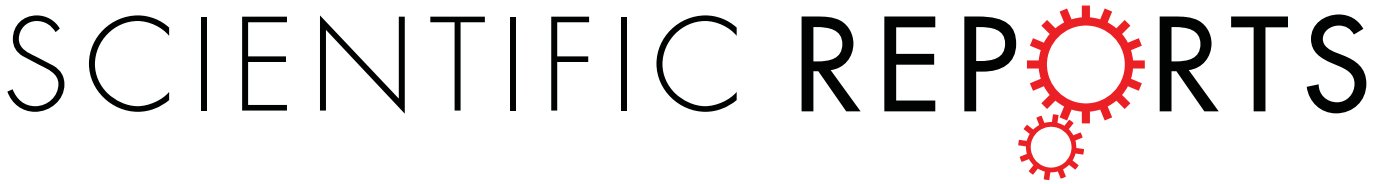

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# All-carbon multi-electrode array for real-time *in vitro* measurements of oxidizable neurotransmitters

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**We report on the ion beam fabrication of all-carbon multi electrode arrays (MEAs) based on 16 graphitic micro-channels embedded in single-crystal diamond (SCD) substrates. The fabricated SCD-MEAs are systematically employed for the *in vitro* simultaneous amperometric detection of the secretory activity from populations of chromaffin cells, demonstrating a new sensing approach with respect to standard techniques. The biochemical stability and biocompatibility of the SCD-based device combined with the parallel recording of multi-electrodes array allow: i) a significant time saving in data collection during drug screening and/or pharmacological tests over a large number of cells, ii) the possibility of comparing altered cell functionality among cell populations, and iii) the repeatition of acquisition runs over many cycles with a fully non-toxic and chemically robust bio-sensitive substrate.**

Synaptic transmission is regulated by vesicle exocytosis. This process occurs when a neuron directs the content of secretory vesicles from the pre-synaptic terminal into the inter-synaptic space, thus delivering neurotransmitter molecules that activate post-synaptic receptors of neighbouring neurons. This release mechanism is common to all neurons and is shared by neuroendocrine cells[1,2], including the chromaffin cells of the adrenal medulla. Such cells release catecholamines (e.g. adrenaline and noradrenaline) following splanchnic nerve stimulation[3]. As such, chromaffin cells are widely used as a model system to study the molecular events underlying exocytosis. The release of oxidazable molecules from individual excitable cells is commonly measured using amperometry, an electrochemical technique that allows resolving the kinetics of single secretory events with a high time resolution[4–7].

Since few decades carbon fibre microelectrodes (CFEs)[4,8] are the most widely employed electrodes to detect the quantal release of catecholamines and still represent the reference technique in this field. Though, parallel recordings of catecholamine release from populations of chromaffin cells still remains a crucial issue that cannot be addressed by means of conventional CFE-based setups. Recently, in order to overcome this limitation, planar multi-electrode devices fabricated from either indium tin oxide (ITO)[9–11], diamond-like carbon (DLC)[12], boron-doped nanocrystalline diamond[13], noble metal (Au, Pt)[14,15] and CMOS silicon-based chips[16] have been successively developed for the simultaneous recording of catecholamine release from chromaffin cell populations.

In the present work, we describe the parallel fabrication of single-crystal-diamond substrates for the realization of micro-electrode array sensors (SCD-MEAs) based on graphitic microchannels, and demonstrate their capabilities in sensing *in vitro* the secretory activity of cultured chromaffin cells. These devices allow to overcome several critical issues of standard devices such as: mechanical and chemical stability over long measurement periods, substrate transparency, biocompatibility, parallel multi-electrode recordings and the possibility of directly culturing the living cells on the substrate.

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