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## Enhancing the Study of Quantal Exocytotic Events: Combining Diamond Multi-Electrode Arrays with Amperometric PEak Analysis (APE) an Automated Analysis Code

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Abstract: MicroGraphited-Diamond-Multi Electrode Arrays ( $\mu$ G-D-MEAs) can be successfully used to reveal, in real time, quantal exocytotic events occurring from many individual neurosecretory cells and/or from many neurons within a network. As  $\mu$ G-D-MEAs arrays are patterned with up to 16 sensing microelectrodes, each of them recording large amounts of data revealing the exocytotic activity, the aim of this work was to support an adequate analysis code to speed up the signal detection. The cutting-edge technology of microGraphited-Diamond-Multi Electrode Arrays ( $\mu$ G-D-MEAs) has been implemented with an automated analysis code (APE, Amperometric Peak Analysis) developed using Matlab R2022a software to provide easy and accurate detection of amperometric spike parameters, including the analysis of the pre-spike foot that sometimes precedes the complete fusion pore dilatation. Data have been acquired from cultured PC12 cells, either collecting events during spontaneous exocytosis or after L-DOPA incubation. Validation of the APE code was performed by comparing the acquired spike parameters with those obtained using Quanta Analysis (Igor macro) by Mosharov et al.

Keywords: exocytosis; diamond; multi-electrode array; PC12 cell line; amperometry; dopamine

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## 1. Introduction

For a long time, carbon fibre electrodes (CFE) have been used as an exclusive technique for studying quantal release in neurosecretory cells [1–3]. The applicability of this technique, however, is limited by the low number of cells that can be acquired in each test; for each measurement, a new change in the fiber surface is required when moving from one cell recording to the next. Another important limitation is the need to couple the electrode with a micromanipulator to approach the cell for the measurement. Furthermore, CFEs have a short lifetime [4]. To address these limitations, over the past decade, we have developed prototypes of multi-electrode arrays known as MicroGraphited-Diamond-Multi Electrode Arrays ( $\mu$ G-D-MEAs) [5–7]. These prototypes showcase the capability to simultaneously capture quantal exocytotic events in real-time from both neurosecretory cells and midbrain neurons cultured directly on  $\mu$ G-D-MEAs. Notably, these sensors are among the few devices that enable the simultaneous analysis of amperometric measurements across multiple channels. Remarkably, these devices have shown consistent performance over more than 2 years after daily measurement sessions. The durability and reliability of the device