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Planar Diamond-Based Multiarrays to Monitor Neurotransmitter Release and Action Potential Firing: New Perspectives in Cellular Neuroscience

Valentina Carabelli, *,^{†,‡,||} Andrea Marcantoni,^{†,‡,||} Federico Picollo,^{§,⊥,‡,||} Alfio Battiato,^{§,⊥,‡,||} Ettore Bernardi,^{§,⊥,‡,||,∇} Alberto Pasquarelli,[#] Paolo Olivero,^{§,⊥,‡,||} and Emilio Carbone^{†,‡,||}

[†]Department of Drug Science and Technology, [‡]Nanostructured Interfaces and Surfaces Inter-departmental Centre, and [§]Physics Department, University of Torino, 10124 Torino, Italy

^{II}Consorzio Nazionale Interuniversitario per le Scienze fisiche della Materia (CNISM), 10125 Torino Unit, Italy

[⊥]Istituto Nazionale di Fisica Nucleare (INFN), 10125 sez. Torino, Italy

[#]Institute of Electron Devices and Circuits, Ulm University, 89081 Ulm, Germany

ABSTRACT: High biocompatibility, outstanding electrochemical responsiveness, inertness, and transparency make diamond-based multiarrays (DBMs) first-rate biosensors for in vitro detection of electrochemical and electrical signals from excitable cells together, with potential for in vivo applications as neural interfaces and prostheses. Here, we will review the electrochemical and physical properties of various DBMs and how these devices have been employed for recording released neurotransmitter molecules and all-or-none action potentials from living cells. Specifically, we will overview how DBMs can resolve localized exocytotic events from subcellular compartments using high-density microelectrode arrays (MEAs), or monitoring oxidizable neurotransmitter release from populations of cells in culture and tissue slices using low-density MEAs. Interfacing DBMs with



excitable cells is currently leading to the promising opportunity of recording electrical signals as well as creating neuronal interfaces through the same device. Given the recent increasingly growing development of newly available DBMs of various geometries to monitor electrical activity and neurotransmitter release in a variety of excitable and neuronal tissues, the discussion will be limited to planar DBMs.

KEYWORDS: Diamond, multiarrays, chromaffin cells, quantal release, action potential firing, amperometry, cell firing, electrochemical imaging, exocytosis

DIAMOND NEUROBIOSENSORS TO "VIEW" BRAIN FUNCTIONS

Electrical stimulation and recording of brain neurons activity is widely used to understand the molecular and cellular basis of health problems related to chronic pain, paralysis, hearing loss, retinal degeneration, as well as neuropsychiatric and neurological disorders.^{1,2} In in vitro systems, the stimulation and recording of neuronal networks is achieved through extracellular microelectrodes, which require an effective miniaturization to address single neurons and induce minimal tissue damage. Neural microelectrodes work by delivering electrical pulses to neurons and transduce biological events (action potentials and postsynaptic activity) in voltage or current signals to be acquired and stored for continuous online and offline analysis. An ideal microelectrode should provide safe levels of stimulation and record small (μV to mV, pA to nA) and fast electrical signals (milliseconds) without introducing size and time distortion and induction of any chemical reactions on the electrode or in the tissue.

Furthermore, simultaneous recording of action potential waveforms (AP firing) and release of neurotransmitters (pre/

post synaptic activity) is highly desirable in living neurons as they provide a complete framework of the functional or pathological state of the cells. Many neuropsychiatric and neurological diseases derive from defects or alterations of the molecular components regulating vesicle fusion and neurotransmitter release at the *presynaptic terminals* and signals summation and integration at the *postsynaptic site*, where tonic or burst AP firing are generated and propagated.^{3–5} Thus, there is an urgent need for innovative microelectrode arrays (MEAs) to achieve selective stimulation and recording of central neuron excitability as well as precise monitoring of synaptic activity.

This is highly desirable since it promotes new understandings of neuropathologies, formulation of advanced therapies and construction of novel neuroprosthetic devices.

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