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A diamond-based biosensor for the recording of neuronal activity

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ABSTRACT

We have developed a device for recording the extracellular electrical activity of cultured neuronal networks based on a hydrogen terminated (H-terminated) conductive diamond. GT1-7 cells, a neuronal cell line showing spontaneous action potentials firing, could maintain their functional properties for days in culture when plated on the H-terminated diamond surface. The recorded extracellular electrical activity appeared in the form of well-resolved bursts of fast and slow biphasic signals with a mean duration of about 8 ms for the fast and 60 ms for the slow events. The time courses of these signals were in good agreement with those recorded by means of conventional microelectrode array (MEAs) and with the negative derivative of the action potentials intracellularly recorded with the patch clamp technique from single cells. Thus, although hydrophobic in nature, the conductive H-terminated diamond surface is able to reveal the spontaneous electrical activity of neurons mainly by capacitative coupling to the cell membrane. Having previously shown that the optical properties of H-terminated diamond allow to record cellular activity by means of fluorescent probes (Ariano, P., Baldelli, P., Carbone, E., Giardino, A., Lo Giudice, A., Lovisolo, D., Manfredotti, C., Novara, M., Sternschulte, H., Vittone, E., 2005. Diam. Relat. Mater. 14, 669–674), we now provide evidence for the feasibility of using diamond-based cellular biosensors for multiparametrical recordings of electrical activity from living cells.

1. Introduction

The recording of electrical activity from neuronal networks, both *in vitro* and *in vivo*, has experienced substantial advances in the last few years, owing to the design and fabrication of improved microelectrode arrays and to the development of suitable software tools (Le Van Quyen and Bragin, 2007; Hofmann and Bading, 2006). By these means, long time recordings of electrical activity (see e.g. Potter, 2001) and of its modulation by agonists and pharmacological agents from single elements of a neuronal population have seen widespread applications (see e.g. Stett et al., 2003). Most systems presently available suffer, however, from some limitations, particularly regarding surface reactivity and optical transparency, critical for obtaining long term recordings of multiple parameters (e.g. optical and electrical).

Among the materials investigated as potential substrates for the fabrication of biosensor devices, diamond is a relatively new entry; however its peculiar properties, such as chemical inertness, biocompatibility, optical transparency, high conductivity when the surface is properly functionalized, have attracted increasing interest from biochemists, biophysicists and material scientists (see e.g. Martinez-Huitle, 2007; Carlisle, 2004). Relevant results are represented by the development of diamond-enzyme interfaces exploiting electron transfer mechanisms (Härtl et al., 2004; Zhao et al., 2006) and of microchambers for DNA synthesis (Adamschik et al., 2001). These examples highlight the feasibility of building diamond-based molecular biosensors: the main biological achievement would be however to develop cellular sensors to record electrical and optical activity from cultured cells and by means of implanted devices. Some preliminary steps have been accomplished: one group has described the ordered growth of neurons and of their processes over single, oxidised diamond crystals on which grids of adhesion molecules were drawn (Specht et al., 2004); others (Chong et al., 2007) have described how adhesion and survival of fibroblasts and non-differentiated PC12 neuronal cells (both electrically unexcitable) can be modulated by surface topography and functionalization. In a previous paper (Ariano et al., 2005), employing more physiologically relevant models (primary cultures

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