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Parylene-based flexible neural probes with PEDOT coated surface for brain stimulation and recording

V. Castagnola [a,b,*], E. Descamps [a,b], A. Lecestre [a,b], L. Dahan [c], J. Remaud [c], L.G. Nowak [d], C. Bergaud [a,b]

[a] CNRS, LAAS, 7 avenue du colonel Roche, F-31400 Toulouse, France
[b] University of Toulouse, LAAS, F-31400 Toulouse, France
[c] Centre de Recherche sur la Cognition Animale (CRCA), University of Toulouse, France
[d] Centre de Recherche Cerveau et Cognition (CerCo), CNRS, Toulouse, France

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ABSTRACT

Implantable neural prosthetics devices offer a promising opportunity for the restoration of lost functions in patients affected by brain or spinal cord injury, by providing the brain with a non-muscular channel able to link machines to the nervous system. Nevertheless current neural microelectrodes suffer from high initial impedance and low charge-transfer capacity because of their small-feature geometry (Abidian et al., 2010; Cui and Zhou, 2007). In this work we have developed PEDOT-modified neural probes based on flexible substrate capable to answer to the three critical requirements for neuroprosthetic device: efficiency, lifetime and biocompatibility. We propose a simple procedure for the fabrication of neural electrodes fully made of Parylene-C, followed by an electropolymerization of the active area with the conductive polymer PEDOT that is shown to greatly enhance the electrical performances of the device. In addition, the biocompatibility and the very high SNR exhibited during signal recording make our device suitable for long-term implantation.

1. Introduction

Many different disorders can disrupt the communication of the brain with the external environment. Neuroprosthetics may offer the possibility to restore sensory or motor functions by providing the brain with an external communication and control channel, as in the Brain Computer Interface (BCI). Moreover neural probes are employed for the treatment of numerous diseases such as Parkinson's disease, dystonia and chronic pain (Hochberg et al., 2006; Schwartz et al., 2006). The implantation of neural interfaces for long periods of time has rapidly becoming an invaluable clinical and diagnostic tool (Kipke et al., 2008). Although neural electrodes have been successfully used and demonstrated clinical relevance (deep brain stimulation, cochlear implants) some issues remain to be addressed. In particular, the efficiency, the biocompatibility and the stability of the implanted electrodes are far from being optimized; in many cases, penetrating recording electrodes fail within weeks or months (Griffith and Humphrey, 2006) because the recording capability usually deteriorates over time. This lack of long-term reliability must be improved to make these technologies viable for widespread use (Polikov et al., 2005). The degradation of signal quality in chronically implanted microelectrodes is attributed to both biotic factors, such as the hypothesis that the glial scar, constituted primarily by astrocytes and microglia, encapsulates the electrodes (Kotov et al., 2009), functionally insulating the recording surfaces, and to abiotic factors, such as insulation delamination, corrosion and strain due to micromotions (Streit et al., 2012; Biran et al., 2007). Another reason for electrode failure can be breakage of electrode leads caused by mechanical stress. Moreover, a common hypothesis is that micromotions or rather microforces between the implanted probe and the tissue cause small injuries that constantly maintain an inflammatory process (Polikov et al., 2005). Histological studies (Biran et al., 2007; Kim et al., 2004) report that the strain induced immune response, caused by the rigid tethering of the electrode to the skull, leads to an increase in microglial activity in the implanted tissue as compared to untethered electrodes (Gilletti and Muthuswamy, 2006). Quantitative studies have shown that electrode with low Young's modulus material or redefined geometry for high compliance can provide front-end strain relief and polymers such as polyimide and Parylene-C, with their good biocompatibility, have been the choice of researchers for electrode substrate materials(Sankar et al., 2013; Seymour et al., 2011; Ziegler

* Corresponding author at: CNRS, LAAS, 7 avenue du colonel Roche, F-31400 Toulouse, France.
E-mail addresses: vcastagn@laas.fr (V. Castagnola), edescamp@laas.fr (E. Descamps), alecestr@laas.fr (A. Lecestre), lionel.dahan@univ-tlse3.fr (L. Dahan), jessica.remaud@univ-tlse3.fr (J. Remaud), lionel.nowak@cerco.ups-tlse.fr (L.G. Nowak), bergaud@laas.fr (C. Bergaud).

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et al., 2006; Kim, 2013; Rodger et al., 2008; Metallo et al., 2011). Furthermore it is well known that the miniaturization of the electrode size is a critical requirement for single neuron recording and for electrical stimulation restricted to small populations of neuronal elements. In fact, a single square millimeter of brain tissue contains approximately one million neurons. To match this number and density, future BMIs must feature smaller and denser electrode arrays in order to precisely monitor and control neural circuit activity. Unfortunately a significant reduction in electrode size greatly increases electrode impedance, limiting the recording sensitivity and the maximum stimulating current deliverable through the electrode–tissue interface. Chronic implantable microelectrodes should exhibit low impedance for recording or safe charge injection for stimulation to ensure a good quality of bidirectional communication with the neural tissue. In order to address these issues, a reduction in electrode size should not be done at the expense of electrode function and the interface, where the physical contact between the brain and the neuroprosthesis occurs, is then the key element of the device.

Conductive polymers, serving as stable electron- and ion-conducting biomaterials, are widely used as interfaces with nerve cells for recording their activities (Abidian et al., 2010; Asplund et al., 2010; Harris et al., 2013). Among conductive polymers, poly(3,4-ethylenedioxythiophene) (PEDOT) has been the subject of much interest because of its well-known properties such as high-conductivity, biocompatibility, excellent stability and transparency in its doped state (Aregueta-Robles et al., 2014). Yamato et al. (1995) reported that PEDOT:PSS was more chemically stable than PPy:PSS (Polypyrrole).

In this work we propose a simple fabrication procedure for neural probes fully made of Parylene-C in which, for the first time on a highly flexible multielectrode device, the active electrode area is electrochemically modified with PEDOT, in order to enhance the electrical properties and the stability at the electrode–tissue interface. By combining the capability of Parylene-C to conform to living tissue with the modification of the electrode interface, we propose an answer to the major critical requirements for long-term implantation of a neural probe.

2. Experimental

2.1. Materials

The Parylene C (PXC) dimer was provided by Comelec SA. Both the 3,4-ethylene dioxythiophene (EDOT) and the Poly (sodium 4-styrenesulfonate) (NaPSS, average Mw=70,000) were provided by Sigma Aldrich and used as received. Deionized water was used to prepare all solutions. Dulbecco's Modified Eagle Media (D-MEM), Horse Serum (Heat Inactivated), Fetal Bovine Serum, Antibiotic–Antimycotic (containing penicillin–streptomycin), and Trypsin were purchased from Thermo Scientific (HyClone). SH-SY5Y cell line was kindly provided by the Institut de Pharmacologie et de Biologie Structurale (IPBS) of Toulouse. The LIVE/DEAD Viability/Cytotoxicity Kit for mammalian cells was purchased from Invitrogen.

2.2. Fabrication of Parylene-based neural probes

The implantable microelectrodes fabrication process is schematized in Fig. 1.

A standard 4 p-type silicon wafer of (100) orientation with a thickness of 525 μm was used as a substrate for the whole process. Parylene-C (Fig. 1a) was deposited through thermally activated CVD machine C30S, provided by Comelec SA at the pyrolysis temperature of 700 °C. The thickness of the deposition, measured each time by standard Profilometer (KLA Tencor), is directly related to the mass of precursor dimer loaded in the sublimation chamber. A 23 μm-thick PXC (Parylene-C) film was obtained starting from 80 g of precursor. It will constitute the substrate of the final device.

Gold (Au) circular electrodes were patterned on the PXC surface thanks to a metallization followed by a lift-off process. First, a negative photoresist (AZ-nLOF 2035, MicroChemicals) was patterned on the wafer (Fig. 1b), using a Mask Aligner MA150 (Karl Suss), then a 200 nm-thick Au layer was evaporated on the wafer (a 50 nm-thick Ti layer, also obtained by evaporation, was used to improve adhesion between PXC surface and Au). The electron beam physical vapour deposition was performed using the equipment EVA 600 (Alliance Concept) at room temperature (20 ± 1 °C) at a working pressure of 2×10^{-7} mbar, leading to a deposition rate of 1 nm/s both for Au and Ti. A lift-off process was performed after the Ti/Au evaporation by dipping the wafer in an acetone bath overnight (Fig. 1c). After the Au electrode patterning, a thin layer of PXC (about 800 nm obtained from 1.6 g of precursor) is deposited on top of the wafer as a passivation layer (Fig. 1d). The electrode surfaces and the contacts were opened by dry etching of the PXC using a photoresist mask (AZ-ECI 3027, MicroChemicals) with a thickness of about 2 μm (Fig. 1e). The plasma etching has been performed using a Plasma equipment RIE-ICP (Trikon Omega 201). The etching parameters have been optimized as follows: $T=10$ °C, $O_2=20$ sccm; $P_r=20$ mT; $P_{ICP}=500$ W; $P_{bias}=10$ W. The etching rate of PCX with these parameters was found to be

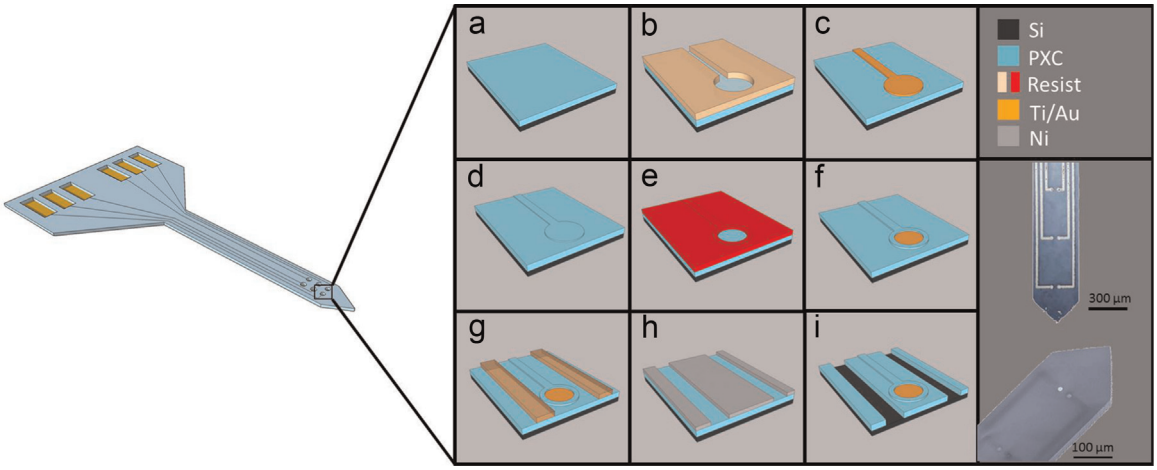

Fig. 1. Schematic illustration of the main steps to fabricate the Parylene-based microelectrodes.