IMPLANTABLE, MICROFIBER NEUROELECTRODES FABRICATED OUT OF POLYCRYSTALLINE DIAMOND AND BORON-DOPED DIAMOND

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ABSTRACT

This abstract presents micromachined, implantable, all diamond microfibers to facilitate reliable, precision recording of extracellular biopotentials and neurotransmitter concentrations in neural networks (**Fig. 1**). Each of such microfibers consists of a conductive boron-doped polycrystalline diamond (BDD) core encapsulated in a thin insulating polycrystalline diamond (PCD) cladding. The BDD core enables single-unit recording and neurotransmitter sensing from target neurons with high spatiotemporal resolution and fidelity, while the PCD encapsulation serves as a biocompatible and hermetic package as well as a dielectric barrier to prevent signal cross-talking. The fully developed fibers had been successfully tested *ex vivo* in different chemicals under different concentrations.

Keywords: Boron Doped Diamond (BDD), Polycrystalline Diamond (PCD), Neurotransmitter, Neural Recording.

INTRODUCTION

The central nervous system (CNS) consists of large networks of neurons that communicate with each other both electrically and chemically for information processing, analysis, and generation of outputs to achieve complex brain functions and behaviors. Rapid, transient, long-distance communication in neural circuits primarily occurs via electrical impulses (action potentials) along the axon, while neuron-to-neuron communication occurs chemically at the synapses [1]. Dysregulated level of neurotransmitters (NTs) in the brain is believed to be the main cause of several neurological disorders, such as Parkinson's and Alzheimer's diseases, schizophrenia, and epilepsy [2-4]. In particular, dopamine (DA) is one of the most important NTs that modulates motor activity, motivation, reinforcement learning, among many other functions. Abnormal DA activity in the basal ganglia has been demonstrated as an important indicator for monitoring Parkinson's disease and schizophrenia [5-8]. Hence, a complete understanding of these brain diseases will require real-time monitoring of dynamic changes in both extracellular electrical and DA signaling.

Such comprehensive research demands advanced brain mapping tools with minimal invasiveness and high spatiotemporal resolution. Of many different mapping approaches, implantable microelectrodes capable of recording extracellular biopotentials and neurochemical signals from small, targeted groups of neurons have shown great promises for neuroscience research and emerging clinical applications. While extremely popular in their use, metal microwires and silicon-based microelectrodes suffer from signal instability and degradation after chronic implantation for several months to a few years, resulting primarily from inflammatory responses and fibrous encapsulation evoked by electrode insertion and subsequent relative motion [9, 10]. Increasing evidence suggests that the dimension and stiffness of implanted electrodes contribute greatly to tissue damage and fibrosis in chronic implantation [11]. To overcome the problem of traditional hard material-based electrodes, soft electrode technology has been

explored aggressively to reduce their mechanical mismatch with the surrounding tissues [12]. However, fabrication of soft electrodes with small dimensions and good durability is still challenging due to the physical limitations and tradeoffs between size and mechanical strength. Recently reported carbon fiber (CF) ultramicroelectrodes have a small cross-sectional footprint (8-9 μm diameter) and low stiffness that promise to reduce chronic tissue damage and neuron death upon implantation [13, 14]. Despite their many advantages, currently, fabrication of these carbon fiber electrodes requires laborious and time-consuming alignment and assembly of individual fibers onto pre-patterned printed circuit board (PCB) substrates, which is impractical for building high-channel-count carbon fiber electrode arrays. In addition, thin polymer encapsulation does not provide an impermeable barrier for carbon fiber electrodes [15], and its long-term efficacy for chronic implants remain undefined.

In this paper, we present a micromachined, implantable, all diamond fiber ultramicroelectrodes to facilitate reliable, precision recording of extracellular biopotentials and chemical signals from brain networks for potential applications in both neuroscience and clinical research. Our device takes advantages of the unique properties of polycrystalline diamond (PCD) thin films, such as high biocompatibility, long-term stability, and biochemical inertness [16]. Compared to commonly used electrode materials (e.g. platinum and glassy carbon), diamond also exhibits excellent chemical non-reactivity, low double-layer capacitance, and a wide aqueous potential window, which make it an ideal material for neurotransmitter sensing [17, 18]. Our diamond microfibers are completely made of thin films of doped and undoped microcrystalline diamond and differ from conventional diamond electrodes, in which only the tips of sharpened and insulated metal wires were covered by a thin layer of boron-doped polycrystalline diamond (BDD) [18].

DEVICE DESIGN

As shown in Fig. 1, the unassembled fiber contains three main parts: a fiber shank, a contact pad, and an anchor. The fiber shank consists of a conductive BDD core encapsulated in a thin insulating PCD cladding. The BDD core is exposed at the tip with a small cross-sectional area to enable single-unit recording and neurotransmitter sensing from target neurons with high spatiotemporal resolution and fidelity. The PCD encapsulation serves as a hermetic package and a dielectric barrier to prevent signal cross-talking during neural recording. The anchor is designed to fix the fibers onto the silicon wafers during fabrication, and eventually will be removed by cleavage, in order to expose the fiber end as the recording site. The contact pad, as illustrated in Fig. 1, has the exposed BDD layer to form interconnect to a custom-designed, printed circuit board (PCB) using conductive epoxy. The PCB is connected to testing instruments via a surface-mount connector and ribbon wire. The devices designed for rat's model have different widths of 10-20 μm , lengths of 1-3 mm, and an overall thickness of 6.9 μm . The contact pads are designed in two different ways, one with holes that go through the pads in order to

Fig. 1: Conceptual diagram of the all diamond fiber microelectrode

fix the pads with the silver epoxy, and one without the holes. Besides single-shank microfibers, two-dimensional (2D) fiber arrays are also designed, combining multiple shanks with the same or various lengths and widths on a single platform.

FABRICATION METHOD

Fig. 2 shows details of the fabrication process. As illustrated, in the step a), a 1.9- μm -thick polycrystalline diamond layer (PCD) was deposited on top of a 3-inch silicon wafer as the bottom insulator, and a 3.7- μm -thick boron-doped-diamond (BDD) layer was deposited on top of the PCD insulating layer. Both diamond layers were synthesized using a custom-designed 2.45 GHz microwave plasma assisted chemical vapor deposition reactor (MWPACVD) with a gas mixture of hydrogen-diborane and methane (1%) in a hydrogen atmosphere, under a 700 °C temperature. The B-to-C ratio was 20,000 ppm and the B-to-H ratio was 200 ppm. The deposited BDD layer was initially terminated by hydrogen, and after being exposed to air for a long time, the surface was converted gradually to a partially oxygen-terminated surface.

In step b), a 1.3- μm -thick copper layer was deposited using thermal evaporation (Edward Auto306 thermal evaporator, Edward, Inc.), and patterned via ultraviolet (UV) photolithography (ABM, Inc.) and chemical etching of copper to be used as a hard mask for the following diamond etching step. In the diamond etching step, BDD and PCD layers were patterned by being etched in an electron cyclotron resonance reactive ion etcher (RIE, Lambda Technologies, Inc.) using $\text{SF}_6/\text{Ar}/\text{O}_2$ with a microwave power of 400 W and a radio-frequency (RF) bias of 100 W (150 V). After the diamond layers were patterned, the copper mask was removed by the copper etchant.

In steps c) and d), another layer of PCD with a thickness of 1.3 μm was grown on top of the patterned diamond layers and exposed regions of the silicon wafer, using the above equipment and approach. Afterward, another copper layer was deposited and selectively patterned on top of the new PCD layer to be used as the hard mask for etching the top PCD layer. In order to be sure that the needle part of BDD layer underneath would be fully covered, the copper mask is slightly larger (from 2-10 μm) than the BDD layer. This mask also exposes the contact pad at the backbone of the fiber, so after the top PCD layer was removed from the contact areas, the BDD layer underneath would be exposed for good connectivity. The top PCD layer would be patterned using the RIE method with the new copper mask. After that, the device was released from the wafer using chemical etching of silicon in a hydrofluoric acid/nitric/acetic acid (HNA) solution (step d)). Then the anchor on the tip end of the fiber was cleaved using a pair of tweezers in order to expose the recording site at the tip of the fiber (step e)). Finally, the released

Fig. 2: Process flow for making the all diamond microfibers. a) Deposit BDD /PCD thin films on top of the Si substrate; b) Pattern BDD/PCD with a copper mask; c) Deposit the top PCD layer and pattern the Cu mask; d) Etch the top PCD layer and remove the Cu mask; e) Release the device and open the tip of the microfiber.

device was bonded onto the PCB stick using the conductive silver epoxy.

DEVICE CHARACTERIZATION AND RESULTS

A. Fabricated Diamond Microfiber

Fig. 3 (a) shows prototypes of the fabricated diamond microfibers. The cross-sectional view in Fig. 3 (b) gives clear indication that the BDD microfiber core was completely insulated by the dense PCD cladding. The tip had a trapezoidal cross section due to isotropic nature of plasma etching of diamond films. Our fabrication method allows batch production of diamond electrodes with different geometries on the same wafer and is compatible with conventional microfabrication techniques. Each 3-inch silicon wafer contains 440 devices, including 248 single microfibers and 32 2D arrays each of which includes 6 fibers.

B. Mechanical Flexibility

Analytical approaches were used to study the mechanical properties of the diamond microfibers since the previous studies show that mechanical property mismatch between the hard implant and soft tissue may increase risks of negative neural response, glial scar formation, inflammation, and mechanically induced trauma [11, 19, 20]. Although diamond has a relatively high Young's modulus (1050 GPa), the bending stiffness of the microfiber is a more relevant indicator of device-tissue interactions than Young's modulus [21]. Given the rectangular cross-section of the fiber, its bending stiffness can be calculated by: $F/d = (4Ewt^3)/L^3$, where F is the force, d is the deflection, E is Young's modulus, w is the width of the cross-section area, t is the thickness of the cross-section area, and L is the length of the device. As such, our diamond fibers are relatively compliant with the F/d value ranging from 511 mN/m to 27.59 N/m depending on different dimensions of the fibers.

Fig. 3: (a) SEM images of a microfabricated, all diamond microfiber array. Inset shows a released single fiber. (b) SEM image shows the cross-section of a diamond microfiber with dimensions of $\sim 17.4 \mu\text{m}$ in width and $\sim 3.7 \mu\text{m}$ in thickness.

However, the flexibility of the fiber imposes a challenge for device insertion into the brain tissue. It is well known that fibers with large lengths and small cross section diameters may mechanically buckle under minor loads, which can be studied using the critical buckling force: $F_{\text{buckling}} = (\pi^2 Ewt^3)/(5.88L^2)$. As a result, the critical buckling load for different fiber designs varies from 643.3 μN to 11.6 mN, which is mostly larger than the insertion force required to penetrate brain tissue ($\sim 1 \text{ mN}$) [22].

C. Electrochemical Properties

Experiments were performed to evaluate the general electrochemical characteristics of the all diamond microfibers using electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV). All measurements were done with a three-electrode cell comprised of the diamond microelectrode as a working electrode (WE), a platinum wire as a counter electrode (CE), and a standard Ag/AgCl electrode as a reference electrode (RE). The electrochemical impedance of the electrode at 1 kHz was 1.3 M Ω , in an acceptable range of the extracellular recording. Cyclic voltammograms (CVs) of the devices were measured in different chemicals, including phosphate-buffered saline (PBS), ferri/ferrocyanide ($\text{Fe}(\text{CN})_6^{3-/4-}$), ruthenium hexamine ($\text{Ru}(\text{NH}_3)_6^{2+/3+}$), and DA. Fig. 4 (a) shows the CVs of the diamond microfibers in pH=7.4 PBS under various scan rates. The double-layer capacitance (C_{dl} in $\text{F}\cdot\text{cm}^{-2}$) of 18 $\mu\text{F}/\text{cm}^2$ was calculated based on $C_{dl} = i_{av}/\nu A$, where i_{av} (in $\text{C}\cdot\text{s}^{-1}$) is the average current of the forward and reverse sweeps of the CV, and ν (in $\text{V}\cdot\text{s}^{-1}$) is the scan rate of the CV, and A (in cm^2) is the electrode area [23]. CVs of two one-electron transfer redox couples, $\text{Fe}(\text{CN})_6^{3-/4-}$ and $\text{Ru}(\text{NH}_3)_6^{2+/3+}$, are shown in Fig. 4 (b). In both cases, the diamond microfibers exhibit the trademark sigmoidal response characteristic of microelectrodes, occurring when the radius of the electrode is smaller than that of the diffusion profile of the analyte. The magnitude of the steady-state current responses for the anodic and cathodic scans are nearly identical, indicating a reversible electron

transfer process. The BDD electrode exhibits featureless background current and a much wider potential window in PBS ($\sim 3.8 \text{ V}$) than standard gold, platinum, and glassy carbon electrodes Fig. 4 (c), permitting detection of analytes across a wide range of voltages without the interference of faradaic background current.

Square-wave voltammetry (SWV) was used to demonstrate the feasibility of *ex vivo* DA sensing using the fabricated microfibers. In this case, DA was serially diluted in 0.1 M, pH=7.4 PBS. Fig. 5 shows the response at lower DA concentrations of 0-25 μM ; sharp

Fig. 4: Cyclic voltammograms (CVs) of the diamond microfiber measured (a) in the pH=7.4 PBS buffer under various scan rates and (b) in two redox couples. (c) Comparison of the potential window of various electrode materials.

Fig. 5: SWVs of the diamond microfiber measured under different dopamine concentrations of 0-25 μM . The inset shows the linear fitting of dopamine concentration vs. peak area.

and well-resolved oxidation peaks in response to different dopamine concentrations were observed. A direct correlation between the dopamine concentration and the current amplitude was observed with excellent linearity ($R^2 = 0.999$) over the tested concentration range.

CONCLUSIONS

This paper reports the design, fabrication, and characterization of all diamond microfibers for potential applications in neurophysiological recording and neurotransmitter sensing. A wafer-level approach was developed to monolithically fabricate the microfibers with high yield and productivity. The fabricated microfiber has a small cross-section area that matches the size of neurons, suitable for single unit recording. Results of electrochemical measurements demonstrate that the diamond fiber is able to detect low concentrations of DA with excellent linearity. Ongoing work includes *in-vitro* and *in-vivo* characterization of the devices using cell cultures and rat's models.

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