Technical Note

Soft Neural Interfacing based on Implantable Graphene Fiber Microelectrode Arrays

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ABSTRACT

Microelectrode Arrays (MEAs) neural interfaces are considered implantable devices that interact with the nervous system to monitor and/or modulate brain activity. Graphene-based materials are utilized to address some of the current challenges in neural interface design due to their desirable features, such as high conductance, large surface-to-volume ratio, suitable electrochemical properties, biocompatibility, flexibility, and ease of production.

In the current study, we fabricated and characterized a type of flexible, ultrasmall, and implantable neurostimulator based on graphene fibers. In this procedure, wet-spinning was employed to create graphene fibers with diameters of 10 to 50 µm. A 10-channel polyimide Printed Circuit Board (PCB) was then custom-designed and manufactured. The fibers were attached to each channel by conductive glue and also insulated by soaking them in a polyurethane solution. The tips were subsequently exposed using a blowtorch. Microstructural information on the fibers was obtained using Scanning Electron Microscopy (SEM), and the measurements of Electrochemical Impedance Spectroscopy (EIS) were conducted for each electrode.

Flexible MEAs were created using graphene fibers with diameters ranging from 10 to 50 microns with a spacing of 150 microns. This method leads to producing electrode arrays with any size of fibers and a variety of channel numbers. The flexible neural prostheses can replace conventional electrodes in both neuroscience and biomedical research.

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Keywords

Microelectrodes; Neural Prostheses; Implantable Neurostimulators; Neurosciences; Biomedical Research

Introduction

Microelectrode Arrays (MEAs) have the potential to help better understand the neurophysiological processes that underlie many aspects of human function and have also shown promise in restoring lost neurological functions due to disease, stroke, or injury [1]. Metal wire electrodes with a diameter of 10-200 µm and an uninsulated tip are one of the most common and long-established arrays [2]. Such arrays provide certain challenges in clinical trials due to their insufficient long-term stability, which prevents stimulation and recording of neuronal cells and increases the risk of device failure [3]. The carbon-made microelectrodes, such as carbon nanotubes and carbon fibers, can overcome the limitations of metal-based arrays because of their small size, flexibility, minimal tissue reaction, and suitable mechanical and electrochemical characteristics [4-6].

Many studies [4, 7-8] have shown that graphene electrodes can be utilized for neural stimulation and recording. For example, reduced graphene oxide-based fiber-structured electrodes seem effective in recording from the cortex and triggering retinal ganglion cells [4]. Graphene-based multielectrode arrays have the potential of extracellularly detecting action with a high signal-to-noise ratio in vitro investigation of both a cardiac-like cell line and cortical neural networks [7]. Furthermore, deep brain stimulation and functional magnetic resonance imaging using graphene fibers have resulted in a comprehensive activation pattern in Parkinsonian rats [8].

In this study, a novel graphene fiber-based Microelectrode Array (MEA) was developed and analyzed, which was penetrating and flexible with ultrasmall dimensions. The small fiber diameters, comparable to the size of a single neuron, lead to MEA suitable for high-precision stimulation and recording, resulting in the targeting of individual neurons rather than large populations of neurons.

Technical Presentation

Fabrication

The fabrication of graphene fiber in the MEAs can be summarized as follows: the graphene fibers were produced using a wet-spinning process. Graphene powder (a few layers, technical grade) was purchased from united nanotech innovations. The Polyacrylonitrile (PAN) powder with a molecular weight of 250000 g/mol was purchased from Lianxu, China. Then, the graphene and PAN powders were dissolved in polar solvents, such as Dimetylformamide (DMF). In more detail, PAN powder and graphene powder were weighted using a scale. First, 5 wt% PAN was prepared by dissolving it in DMF. Then, graphene powder in graphene: PAN 70:30 ratio was added to the solution. The solution was heated and dissolved at 60 °C for 1 hour using a heating and stirring plate and a stirring magnet to prepare a uniform spinning solution. A syringe pump is employed to provide a consistent throughput (30 ml h^{-1}) of the solution. A spinneret is then used to guide the solution into a coagulation medium that is made up of water and DMF in a 1:1 ratio. The medium also known as an anti-solvent, in which the spun or accrued fibers coagulate. A spool collects the produced fibers. Figure 1 depicts the wet-spinning process for producing graphene fiber. They can be washed and dried at room temperature, in the furnace, or the like.

In the second step, a PCB, made from a flexible, double-sided, insulating substrate and 10-channel featured with an electrode pitch of 150 µm, was designed using layout software to specify the number, width, and pitch of channels. Next, the PCB was soldered to a connector to enable connection to the appropriate source.

In the third step, graphene fibers were cut to a few millimeters in length using a razor blade and then placed in silver epoxy-filled traces, and were briefly soaked in a polyurethane solution for insulation. The very tips were exposed by fire-sharpening. To further sharpen the fibers, the array was immersed in a bowl of deionized water, with the tips of the fibers visible above the surface. A blowtorch was then passed back and forth over the top of the fibers to sharpen graphene fibers.

Surface Characterization

The morphology of the graphene fibers was obtained with Scanning Electron Microscopy (SEM).

Impedance Characterization

A potentiostat was used to measure impedance spectroscopy, and obtained by immersing the electrodes in an electrochemical cell with three electrodes, in which the counter and reference electrodes are made of platinum and Ag/AgCl, respectively. Without nitrogen gas bubbling, all tests were conducted in 1 M

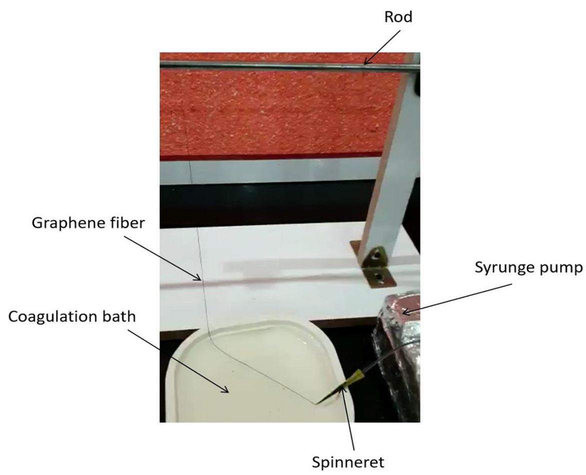

Figure 1: An image of an apparatus for continuously manufacturing fibers using a wet-spinning process.

phosphate buffered saline (PBS) at ambient temperature.

Results

The microstructure of graphene fiber was investigated by SEM. Figure 2 shows that fibers with an average diameter of around 30 μm were formed with a rough surface, as irregular particles can be seen on the surface of fibers. The images show that in the PAN, graphene sheets can bind together to form homogeneous structures of fibers with no pores or voids.

Figure 3 displays the MEA made using graphene fibers, with 10-channel features and a 150-micrometer pitch distance. The diameter of the graphene fibers ranges from 10 to 50 microns.

Impedance is frequently used for evaluating electrodes, and Figure 4 displays the impedance spectrum of the graphene fiber MEA, which is approximately 30 kilohms at 1 kHz.

Discussion

The degree of glial scarring that occurs around brain implants is influenced by both the elastic modulus and the size of the implant, with implants smaller than 50 μm displaying higher proximal neuron survival and less severe foreign body reaction than 200 μm implants. Larger electrode leads, such as those now utilized in commercially available implantable electrode systems, will have much greater stiffness values due to the increased size and higher elastic modulus of the materials [4]. Flexible implants also cause less micromotion-induced damage due to their shock absorption and vibration dampening characteristics [3]. Moreover, Low impedance in the range of tens of kilohms can enhance the stimulation and recording properties of MEAs, leading to a suitable candidate for closed-loop neuromodulation [5, 6].

Several studies have been carried out in order to develop flexible single fiber electrodes for closed-loop systems [4-6]. For instance, liquid crystal graphene oxide (LCGO) single fiber with a cylinder diameter of 50 μm are utilized for neural stimulation and recording [4]. It was revealed that 10 μm carbon fiber with nitrogen-doped ultra nanocrystaline diamond collect single unit activities from the visual cortex and stimulate neural

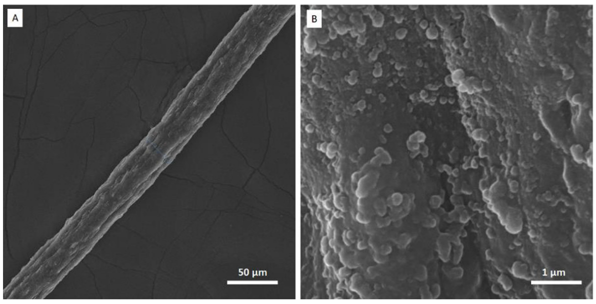

Figure 2: Scanning Electron Microscopy (SEM) picture of the graphene fibers, based on the wet-spinning process.

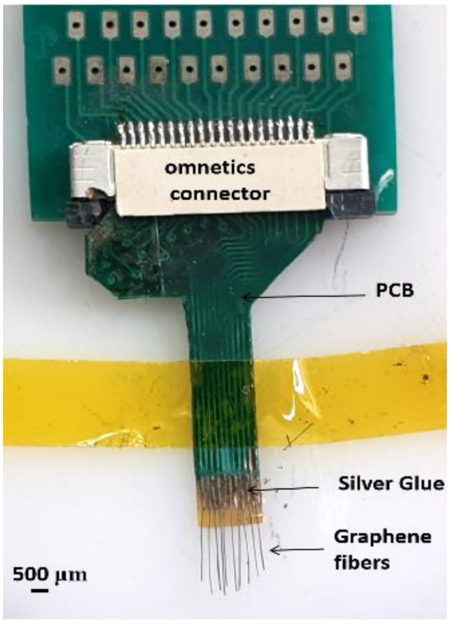

Figure 3: The final preparation of the graphene fiber electrode array. (PCB: Printable Circuit Board)

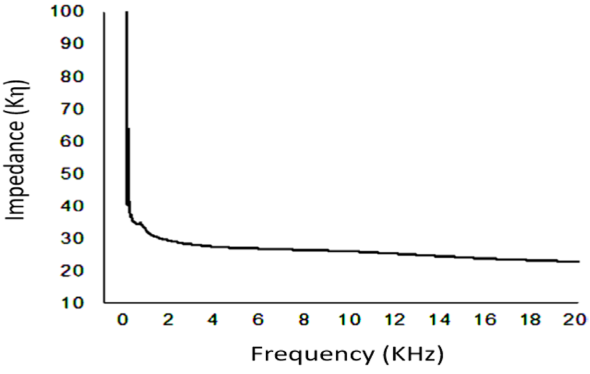

Figure 4: Modulus of the impedance of graphene fiber electrode.

activity in explanted retina [5]. 10 μm coated carbon fiber with boron-doped carbon nanowall was used to activate the nervous system. Furthermore, they obtained a high single to noise ratio from in vivo recording and high resolution retina ganglion cell stimulation [6].

However, there have been no reports of the manufacture of flexible fiber-structured microelectrode arrays (MEAs) for use in a closed-loop system capable of providing information from a vast area of the brain. Flexible graphene fiber-shaped MEAs can be employed for this purpose in the long term to simultaneously gatter data from a large group of single neurons without eliciting an inflammatory tissue response in the host body.

Conclusion

In this study, we fabricated and characterized a flexible, ultrasmall, and implantable MEA constructed of graphene fiber for high-accuracy neural interfaces. Wet-spinning is used in the fabrication method, which is easy, quick, and affordable. The MEA 10-channel is a high-density graphene electrode array with a 150-micron pitch. Furthermore, the low impedance in the tens of Kohms region makes this electrode a viable candidate for neural recording and stimulation. When compared to typical metal electrodes, graphene fibers have a cross-section as small as 10 microns and are flexible, which may boost long-term durability. Large-scale graphene fiber neural recording and stimulation arrays are a promising technology for reducing the inflammatory response and increasing the information density.

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Authors' Contribution

The concept was proposed, expressed, and data was gathered by MA. Hejazi. SA. Seyedi assisted with data collection. AR. Mehdizadeh was the supervisor and consultant during the design of experiments and data collection. All the authors read, modified, and approved the final version of the manuscript.

Conflict of Interest

AR. Mehdizadeh, Editor-in-Chief, and Chairperson were not involved in the peer review and decision-making processes for this manuscript. The non-author, Editorial Board, and reviewers oversaw the peer review process for this paper.

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