Stretchable Bioelectrodes

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*Abstract***— In this paper, we present a stretchable electrode array for studying cell behavior subjected to mechanical strain. The electrode array consists of four gold nail-head pins (250µm tip diameter and 1.75mm spacing) inserted into a** polydimethylsiloxane (PDMS) platform (25.4x25.4mm²). **Fusible indium alloy (liquid at room temperature) filled microchannels are used to connect the electrodes to the outside, thus providing the required stretchability. The electrode platform is biocompatible and can withstand strains of up to 40%. We tested these electrodes by repeatedly (100 times) subjecting them to 35% strain and did not notice any failure. We also successfully cultured mice cardiomyocytes onto the platform and performed electrical pacing.**

I. INTRODUCTION

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STRETCHABLE electrodes as cell culture platforms have studying cellular behavior central to several important pathologies such as traumatic brain injury, cardiomyopathy, and vascular disorders. A central theme common to these diseases is the subjection of tissue to strain. The ability to record and stimulate nerve and muscle cell populations while subjecting them to mechanical strain can provide insights into mechanism of the aforementioned diseases. In addition, stretchable electrodes can be used to study stem cell differentiation since it is widely believed that mechanical cues are important in this process.

Most reported stretchable electrodes are based on the evaporation of a thin gold layer on a PDMS substrate. While many of these electrodes can be stretched to tens of percent, they are not very robust (break after a few rounds of stretch) [1-5]. In this work, we present a stretchable electrode array that alleviates the abovementioned problems by using room temperature liquid-alloy filled microchannels as interconnects and miniature gold nail-head pins as the electrodes.

II. STRETCHABLE PLATFORM

Figure 1 shows a schematic of the cell stretchable electrode array which consists of two PDMS layers. The top layer incorporates sub-surface liquid-alloy-filled microchannels and provides a biocompatible exterior surface for cell culture. The bottom layer is bonded to the top layer, sealing the microchannels. Gold coated nail-head pins acting as electrodes are placed in the channels with their

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sharp head punched through the top PDMS layer and their flange-shaped nail-head bottom flush against the PDMS sealing the junction against the leakage of alloy into the culture medium.

Figure 1. Schematic of the stretchable electrode array.

III. FABRICATION PROCESS

Figure 2 shows the fabrication process. It starts with a SU8 (SU8-2150, MicroChem Inc.) mold on a silicon wafer defining the microchannels $(600 \mu m \text{ height}, 500 \mu m \text{ width})$ and electrode placement areas, Figure 2a. Subsequently, uncured PDMS $(800\mu m)$ thickness) is cast against the mold with polyimide tapes (200µm) as spacers, Figure 2b. After release, the gold coated nail-head pins $(250 \mu m)$ tip diameter and 750µm head diameter, Mill-Max MGF. Corp.) are inserted at electrode locations, Figure 2c. Another thin PDMS layer (300µm in thickness) treated with a high frequency charges generator (BD-10A, Electro-Technic Products, Inc.) is bonded to the top layer, Figure 2d. The bonded layers are kept at room temperature under atmospheric pressure for 24 hours to ensure a strong interfacial bond. Finally, room-temperature-liquid indium alloy (Gallium/Indium = 75.5/24.5, liquidus temperature \geq 15.7ºC) is injected into the channels and thin connecting wires are inserted into the inlet and outlet ports for electrical connections, Figure 2e.

Figure 3 shows a photograph of the fabricated device. The device has total area of $25.4x25.4mm^2$ with four

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electrodes of 1.75mm spacing. The inlet and outlet ports are encapsulated with small PDMS droplets to prevent the leakage and oxidation of fusible indium alloy.

Figure 2. Fabrication Process.

Figure 3. Photograph of a fabricated device.

IV. ELECTRICAL CHARACTERIZATIONS

The stretchable electrode array, without cell culture, was stretched with micro-manipulator to evaluate its electrical properties, i.e., interconnect resistance as a function of applied strain. Figure 4 illustrates the stretch test experimental set-up. The device was clamped to a pair of micro-manipulators with a droplet of phosphate buffer saline

 $(pH = 7.4)$ placed on the device. The impedance was measured between two electrodes at 1kHz with the platform stretched by 5% strain increments and decrements. Figure 5 shows the strain vs. impedance measurements results showing a constant impedance of $\sim 1.1 \text{k}\Omega$ with applied strains of up to 35%. We performed reliability tests by subjecting the platform to 100 cycles of stretch-release, after which, we did not observe any alloy leakage or electrode breakage.

Figure 4. Stretch test setup using a micro-manipulator.

Strain vs. Impedance Measurement

Figure 5. Strain vs. impedance measurement results.

We also performed in vitro tests using agarose gel $(0.2\%$ w/v) to mimic a brain tissue slice [6]. The agarose gel was placed on the stretchable electrode array platform within a PDMS ring container. The entire platform was clamped to a pair of micro-manipulators with a probe inserted into the agarose gel. A sinusoidal signal (100mVpp, 1kHz) was applied to the probe and transmitted voltages were recorded through gold coated nail-head electrodes. Figure 6 shows the recorded waveforms at 0 and 30% strain. The results clearly demonstrate the recording capability of the stretchable electrode array platform within a tissue medium during mechanical deformation.

Figure 6. Recorded signals through an agarose gel (top: signal recorded at 0% strain; bottom: signal recorded at 35% strain)

V. CELL CULTURE EXPERIMENTS

Cell culture experiments with live/dead assay (Invitrogen L3224) were performed to confirm hermeticity of indium alloy inside the PDMS channels. PDMS retaining rings on the devices created a sealed region for cell culture media (Figure 7). Devices were prepared by coating them with 2% gelatin after O_2 plasma surface activation. Human aortic smooth muscle cells were then plated on the devices. Inset in Figure 7 shows the fluorescent microscopic image of the cells after two days with the green being the cell cytoplasm and the red dots the nuclei of dead cells (blue is the bright field image). The presence of live cells is indicated by green cell bodies without red nuclei. These images indicate that cells can survive near and even on the electrodes.

Figure 7. Stretchable cell culture platform populated with human aortic cells enclosed by PDMS retaining ring after 2 days of incubation.

Figure 8 shows cells stretched to 10% strain. As can be seen, cells remained attached to the PDMS surface demonstrating their viability for mechanical studies.

Figure 8. Cells remain attached to the platform and stretch with it upon the application of 10% strain.

 In order to demonstrate the platform functionality with plated cells, we performed electrical pacing of mouse cardiomyocytes. The cell population was prepared and deposited on the device allowing 30 to 90 minutes for cell attachment. Then buffer media containing non-attached cells was aspirated and Tyrode's salt solution was added to the PDMS ring wells shown in Figure 9. Following the preparation of cardiomyocytes, devices wires were connected to a commercial electrical pacer (MyoPacer, IonOptix LLC). A square wave signal (30Vpp, 1Hz) was then applied resulting in contraction of cardiomyocytes on the surface, demonstrating that the device could be utilized for *in-vivo* testing, Figure 9.

Figure 9. Electrically paced mice cardiomyocytes.

VI. SCALABILITY

 The fabrication technique is easily scalable for high density electrode array. We have successfully injected the room-temperature-liquid indium alloy into the PDMS microchannels with $50\mu m$ width. The limiting factor here for scalability is mainly caused by the size of gold coated nail pin (250µm tip diameter and 750µm head diameter). A 16 electrode platform $(250 \mu m)$ electrode spacing) was successfully fabricated and tested, Figure 10.

Figure 10. A 16 electrode stretchable platform.

VII. CONCLUSIONS

We designed a simple and cost effective process for fabricating a stretchable cell culture platform with embedded electrode array using PDMS, room temperature-liquid-alloy, and gold coated nail-head pins. The device was fabricated and fully characterized. It was demonstrated that the platform is biocompatible to human aortic muscle cells and mice cardiomyocyte. The cells adhered well to the substrate during mechanical strain and survived near and on the electrodes after two days of incubation. The platform also maintained its electrical capabilities after being subjected to repeated cycles of mechanical deformation.

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