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A hybrid PDMS-Parylene subdural multi-electrode array

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A hybrid PDMS-Parylene subdural multi-electrode array

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Abstract In this paper, we report on a cost effective and simple method for fabricating a flexible multi-electrode array for subdural neural recording. The electrode was fabricated using a PDMS-Parylene bilayer to combine the major advantages of both materials. Mechanical and electrical characterizations were performed to confirm functionality of a 16-site electrode array under various flexed/bent conditions. The electrode array was helically wound around a 3 mm diameter cylindrical tube and laid over a 2 cm diameter sphere while maintaining its recording capability. Experimental results showed impedance values between 300 kΩ and 600 kΩ at 1 kHz for 90 μm diameter gold recording sites. Acoustically evoked neural activity was successfully recorded from rat auditory cortex, confirming *in vivo* functionality.

Keywords PDMS · Parylene · Epilepsy · Brain Computer Interface (BCI) · Subdural electrode · ECoG · Flexible electrode

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1 Introduction

Subdural electrodes are used in monitoring cortical activity (electrocorticogram, ECoG) in patients going through pre-evaluation monitoring for epilepsy surgery (Ojemann 1997). These electrodes typically consist of a polydimethylsiloxane (PDMS) sheet with embedded platinum studs connected to the recording apparatus (AD-Tech Medical Instruments Corporation). In addition to epilepsy treatment, subdural electrodes can be used in brain-computer interfaces (BCIs) for recording event-related potentials (Graimann et al. 2004). The subdural ECoG electrodes should be flexible, conformal, biocompatible, accommodating to large areas of the cortex, and low-profile. It is also highly desirable, if possible, to incorporate wireless recording and stimulating systems in close proximity to the electrodes in order to reduce the patient's hospital stay (in the pre-evaluation epilepsy surgery monitoring) and discomfort (in the case of patients implanted with BCI electronics). PDMS is a known biocompatible material with good mechanical properties for flexible electronics applications (E_{PDMS}~0.360–1.24 MPa; Armani et al. 1999; Eddington and Beebe 2005). However, due to its poor adhesion to most metals used in recording and stimulation, it is difficult to embed/deposit electrical interconnects on its surface unless the metallic film is tightly sandwiched between two PDMS layers (Henle et al. 2011). Parylene-C is another biocompatible material that can be used in a flexible array and has material properties that allow for better processability (Rodger and Tai 2005; Toda et al. 2011). However, a very thin Parylene layer (<10 μm) is difficult to handle after its release from the substrate (it folds and wrinkles onto itself) and fabrication of easy-to-handle thicker layers (>50 μm) is not practical (i.e. typically requires long deposition times and results in a stiff, non-conformal film). Another polymeric substrate investigated for subdural applications is polyimide (Rousche et al. 2001; Rubehn et al. 2009; Yeager et al. 2008; Kim et al.

2010). Polyimide is biocompatible and well-suited for integration of electrodes and active electronics. Polyimide is typically spin-coated and cured at high temperatures (several hundred degrees Celsius) in thicknesses ranging from a few tens to hundreds of microns. Thick polyimide substrates allow easy manipulation at the expense of high bending stiffness ($E_{Polyimide}$~2.48 GPa) whereas thinner ones (<5 μm) are difficult to reproducibly spin coat and handle. Although handling of thin polyimide films can be improved with the use of a temporary supporting substrate such as biodegradable silk (Kim et al. 2010); this approach limits the electrode application to a single use and poses difficulty in re-positioning the electrode once the biodegradable backing is dissolved. A thicker permanent backing (e.g., PDMS) would impart repositioning capabilities; however, the high temperatures (>300 °C) (Feger 1989) required for curing polyimide renders this method impractical for *in-situ* deposition and curing on most flexible elastomeric backings. Table 1 summarizes a comparison of several different substrate materials used for fabrication of subdural electrodes. As can be seen, no single material possesses the right combination of mechanical, electrical, and handling/processability characteristics suited for subdural conformal electrode arrays and a composite/hybrid approach provide a more promising solution.

In this paper, we report on a simple method for fabricating hybrid PDMS-Parylene subdural electrode arrays that combines the major advantages of both materials in order to create a platform for passive recording/stimulation and active integration. A thick PDMS backing allows for easy handling while an *in-situ* deposited thin Parylene top layer allows for easy integration of electrodes, interconnects, and active components. Compared to previously reported electrode substrates, the resulting PDMS-Parylene bilayer exhibits a more favorable combination of stiffness and flexibility that improves film manageability while maintaining a straightforward fabrication process. In addition to design and fabrication process, we also present *in vitro* electromechanical characterizations and *in vivo* physiological data recorded from the rodent animal model, demonstrating successful recording capabilities.

2 Methods

2.1 Electrode structure and fabrication

Figure 1a shows a 3D schematic of the electrode array. The electrode array, the back-end contact pads, and the cable connecting the two are made from PDMS-Parylene composite bilayers. Figure 1b shows the cross-section along the dotted line. The PDMS thickness (100–200 μm in thickness) in the electrode area (circular region in Fig. 1a) is greater than that of the flexible interconnect in order to provide easier manageability while placing the electrodes on the cortex. In addition, the extra PDMS mass on the electrodes provides a gentle mechanical force to bring the electrodes into intimate contact with the brain surface while allowing for easy electrode repositioning on the brain. The recording sites and contact pads are connected with a flexible PDMS-Parylene cable (4 cm in length).

Figure 2 shows the fabrication process. First, a mold cavity (100~200 μm in depth) is etched with Deep Reactive Ion Etch (STS ASE DRIE) into a silicon wafer. This defines the PDMS backing in the electrode area, Fig. 2a. The wafer was then silanized (trichloro(3,3,3-trifluoropropyl) silane 97 %, Sigma-Aldrich) in order to facilitate PDMS removal. Next, PDMS (Sylgard 184, Dow Corning) was cast onto the wafer, covered with a polymer film (3M PP2500) for easy removal after curing, pressed with weights (1 kg) on flat steel plate, and cured (60 °C for 4 h) within the cavity, Fig. 2b. Even with a large pressing force, a thin layer of PDMS remained in the areas under the interconnect cable and bonding pads (1–10 μm depending on the force). Although in many applications such a layer is a hindrance, in our case it is beneficial and provides extra flexibility and robustness to the cable and back-end area. After curing, the weight was removed, and the polymer film was peeled off the PDMS. Next, a 5 μm thick Parylene layer was deposited on the PDMS to provide a processable layer for metal interconnect and recording sites, Fig. 2c. The electrical pads and interconnections were then formed by depositing and patterning 0.1 μm gold (evaporation, with a Ti adhesion layer), Fig. 2d; although gold was selected for

Table 1 A *comparison of several substrate materials used for fabrication of subdural electrodes*

Substrate material	Young's modulus	Metal adhesion	Handling
Polyimide	2.48 GPa	Excellent	Easy if >50 μm thick
PDMS	0.36~1.24 MPa	Poor	Easy
Parylene	2.75 GPa	Excellent	Difficult
Hybrid PDMS/Parylene[a]	~2.75 GPa	Excellent	Easy

Sources: (DuPont; Armani et al. 1999; Eddington and Beebe 2005; Specialty Coating Systems)

[a] The hybrid layer assumes Parylene and PDMS layers of similar thicknesses

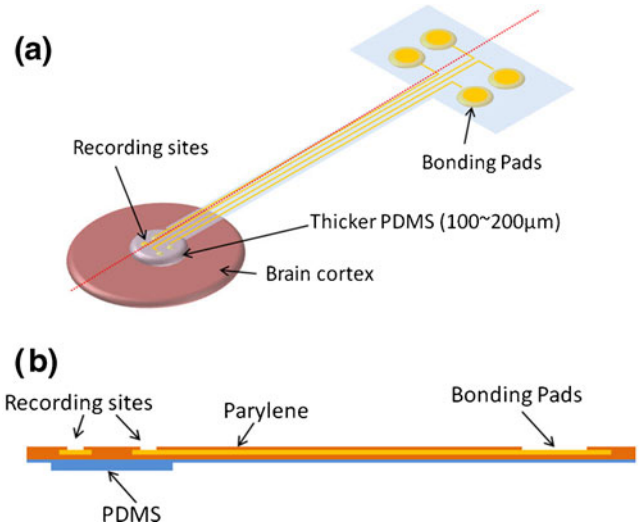

Fig. 1 **a** Schematic view of a PDMS-Parylene subdural electrode array, **b** cross section along the *red dotted line*

the present electrodes, this fabrication procedure can be modified to incorporate other more modern electrode materials such as Pt alloys, Ir oxide, or TiN (Cogan 2008). Following gold deposition, another 0.5 μm of Parylene was deposited (passivation) and patterned (oxygen plasma RIE) to open the recording sites and bonding pads, Fig. 2e and f. The final shape of the electrode was defined with laser micromachining (Universal Laser System, Inc. Professional Series, power 60 W, speed 2 mm/ms, wavelength 10 μm, continuous wave (CW) mode), Fig. 2g. The separated electrodes were then easily lifted off the wafer, Fig. 2h.

2.2 Mechanical and electrical characterizations

The adhesion between PDMS and Parylene layer was evaluated with the standard Scotch tape test (Maissel and Glang 1970). The mechanical flexibility of the electrode array was investigated by rolling (around a cylindrical tube 3 mm in diameter) and bending (placing it on a sphere 2 cm in diameter) the electrode while simultaneously measuring its electrical continuity using phosphate buffered saline (PBS) solution and agarose gel to mimic brain tissue.

The impedance and phase angle values of 16 recording sites (each site 90 μm in diameter) were determined by performing electrochemical impedance spectroscopy (EIS) using an Autolab potentiostat PGSTAT12 (EcoChemie, Utrecht, The Netherlands) with a built-in frequency analyzer (Brinkman, Westbury, NY). A three-electrode setup was used, with a calomel electrode (Fisher Scientific, Waltham, MA) as the reference electrode and a platinum wire as the counter electrode. Measurements were performed in 1X PBS at room temperature. To perform EIS, a 25 mV_{RMS} sine wave was applied to the electrode sites with frequencies ranging logarithmically from 0.1 to 10 kHz. The impedance data collected by EIS were averaged across all sites. The impedances were separated into resistive and reactive components. Nyquist plots (available as Supplementary Material) of the impedance vs. frequency were generated within MATLAB to determine the electrochemical interface between the recording sites and electrolyte.

2.3 *In vivo* experiments

The PDMS-Parylene subdural electrode array was acutely implanted onto the auditory cortex surface of a rat (male, 625 g) for *in vivo* measurements. The experimental procedures complied with the guidelines for the care and use of laboratory animals and were approved by the Purdue Animal Care and Use Committee. During surgery, a craniotomy was performed through the skull over the primary auditory cortex of the right hemisphere. Once the brain was exposed, the area was cleaned and prepared for placing the device onto the dura mater. The PDMS-Parylene microelectrode array was located onto the dura mater first by a micromanipulator and then by Teflon-coated forceps. During the *in vivo* experiment, sound stimuli (white noise 60 dB, RX7, Tucker Davis Technologies, Alachua, FL) were generated and played to the rat. We collected recordings for 300 ms for each acoustic stimulus (100 ms before the stimulus and 200 ms after the stimulus). A total of 200 stimuli were played with a one-second time interval between stimuli. Auditory Evoked Potentials (AEP) was expected to begin approximately 20 ms after the stimulus. Furthermore, due to the tonotopic organization in primary auditory cortex, we expect that different regions would be more sensitive to different sound frequencies. Following the white noise experiments, acoustic tones at specific frequencies (1 kHz, 2 kHz, 4 kHz, 8 kHz, and 16 kHz) were delivered, and neural activities were recorded. Each of the five frequency stimuli was played 200 times in random order for a total of 1,000 trials. The AEPs were sampled at 25 kHz. They were then filtered using a first-order low pass digital Butterworth filter in MATLAB (Natick, MA) with a cutoff frequency of 100 Hz. Subsequently, they were filtered using a second-order IIR notch digital filter with the notch at 60 Hz.

3 Results

3.1 Device

Figure 3a shows a photograph of the laser-patterned electrodes on a 4 in silicon wafer. The electrode contains 16 sensing sites and one circular trace that can be used as a reference electrode. The sensing sites are 90 μm in diameter

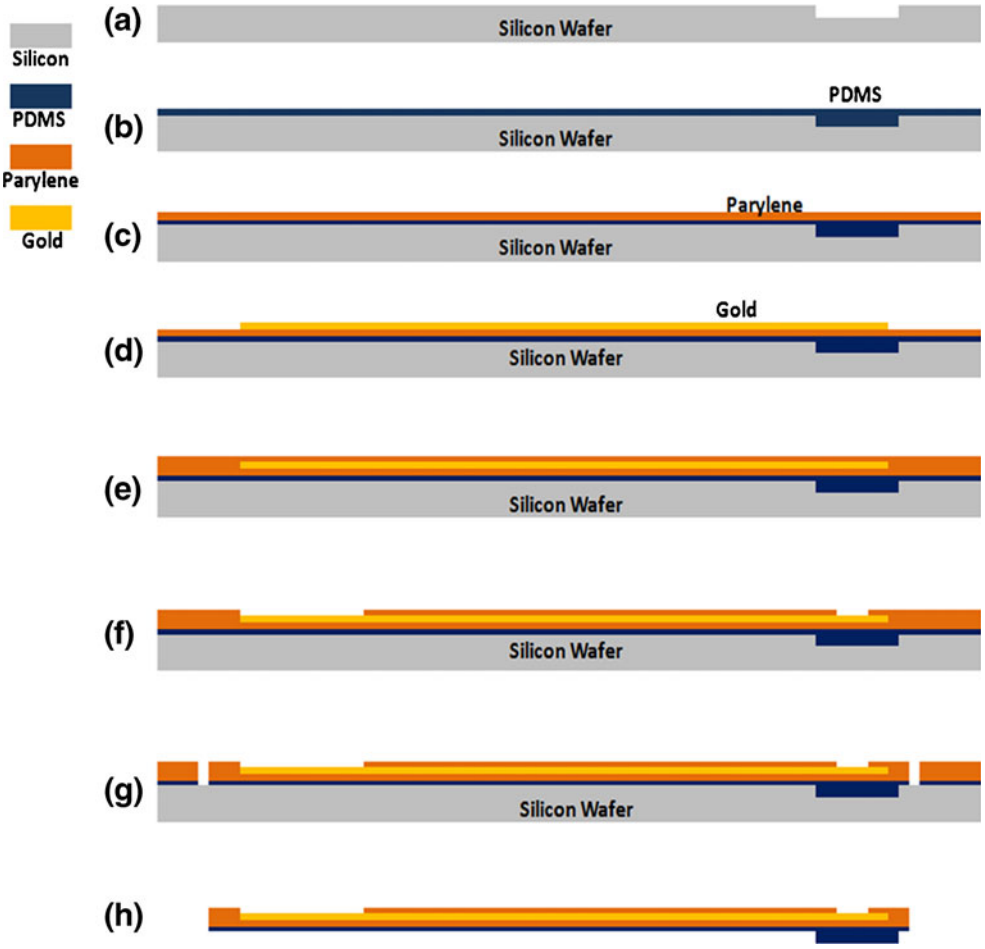

Fig. 2 Fabrication process for a PDMS-Parylene subdural electrode array

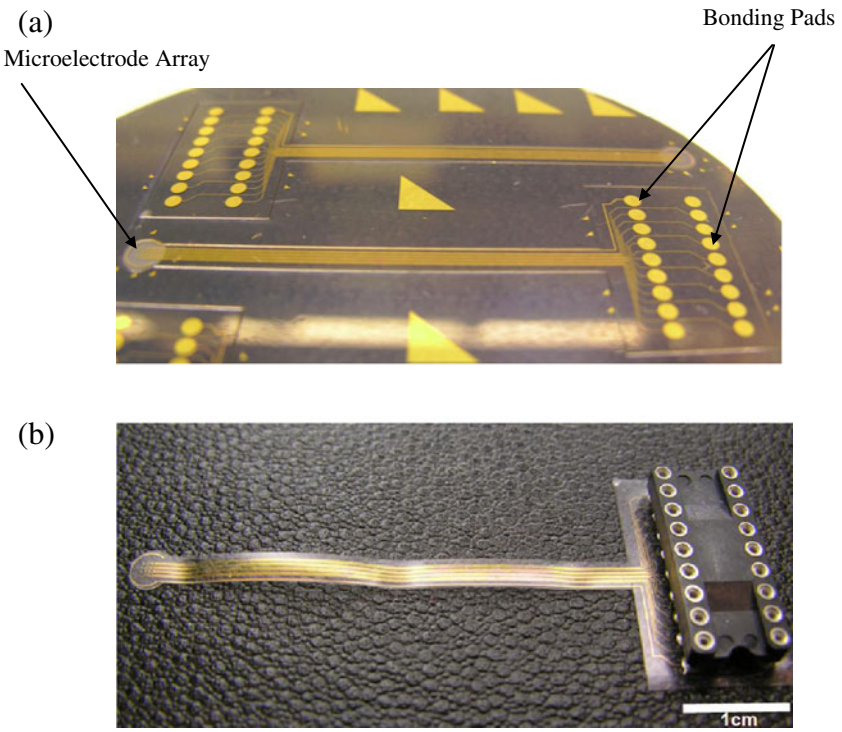

Fig. 3 **a** Laser patterned electrodes on a 4 in silicon wafer, **b** fabricated electrode with a DIP18 package

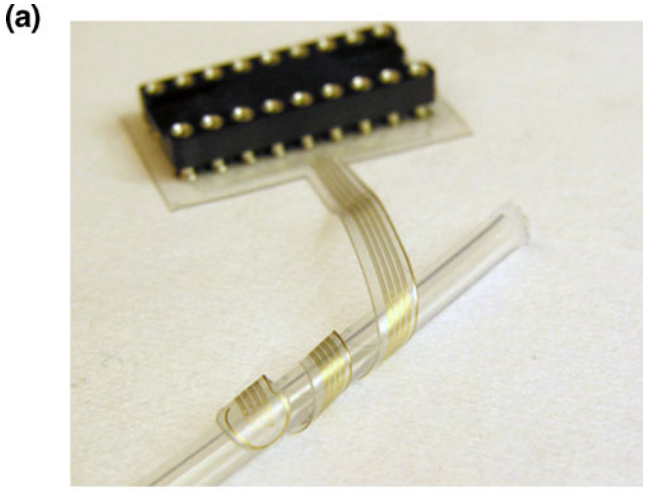

Fig. 4 **a** Fabricated microelectrode array helically wound around a cylindrical tube, **b** recorded signal under helically wound condition, *Top*: input (sine wave 100 Hz, 6.6 Vpp), *Bottom*: measured output (non-distorted sine wave, 100 Hz, 6.4 Vpp)

with 500 μm spacing. The interconnection between the sensing sites and contact sites is a flexible, Parylene-passivated cable (4 cm long). The contact sites are designed to accommodate commercially available DIP18 surface mount packages. The DIP18 connector is mounted onto the electrode with conductive silver epoxy. Figure 3b shows the fabricated device connected to a DIP18 surface mount connector. Although not a focus of this paper, our fabrication method can also be used to make integrated platforms that can incorporate active electronics and wireless interface for a totally self-contained microsystem.

Fig. 5 An electrode array on a 2 cm-diameter hemisphere of agarose gel (0.5 % w/v) shows that all electrode sites are in contact with the gel surface

3.2 Mechanical and electrical characterizations

Scotch tape adhesion tests showed a very strong bond between the PDMS and Parylene. This was expected since the Parylene was deposited *in situ* as opposed to all of the methods reported to date which rely on molding and attaching the PDMS after the Parylene electrode is fabricated. Electrode array impedances were measured over a frequency range from 30 Hz to 10 kHz and values between 300 kΩ to 600 kΩ were obtained at 1 kHz. Electrode functionality under various mechanically deformed configurations was also evaluated. Figure 4a shows the fabricated electrode array helically wound around a cylindrical tube (3 mm in diameter). The device along the tube was immersed into the buffer solution along with a probe which was used to apply a sinusoidal wave (6.6 V_{pp}, 100 Hz). This signal was then measured via the PDMS-Parylene electrode array. We were able to record from all electrodes under such bent condition, Fig. 4b. The experiment was repeated using a 50 mV p-p, 5 Hz sinusoidal wave, and the measured electrode amplitudes are shown in Table 2. For this experiment, noise was measured to have an amplitude of 9.4 mV p-p; hence, 11 of the 16 electrodes (68 %) exhibited satisfactory performance (signal amplitude >9.4 mV p-p). In addition to bent/roll test mentioned above, we also used an agarose covered sphere with a diameter of 2 cm (Fig. 5) to evaluate the electrode's functionality under mechanical conditions similar to rat's brain. After placing the electrode array onto the agarose coated sphere, a sinusoidal signal was injected into the medium and the recorded signals were measured through the recording sites. We were able to successfully record from all the sites, confirming the conformal coverage of the electrode over a curvature of 1 cm^{-1}.

Table 2 Recorded amplitudes of electrodes from an electrode array mounted on agarose gel. The gel was stimulated with a sinusoidal wave (50 mV p-p, 5 Hz). Recorded noise amplitude: 9.4 mV p-p

Electrode #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Amplitude (mV p-p)	17.7	9.4	17.7	23.8	9.4	22.3	21.1	9.4	14.3	18.9	9.4	17.7	23.8	9.4	12.8	14.3

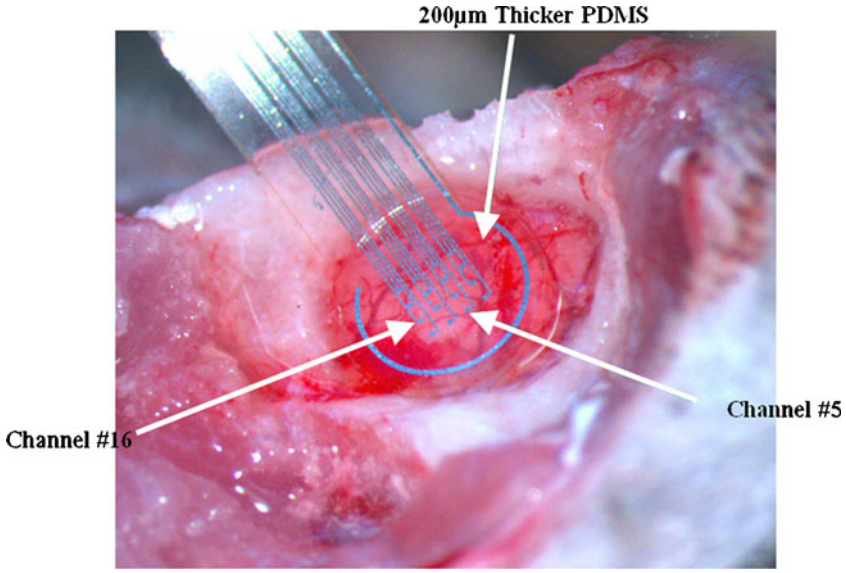

Fig. 6 *In vivo* placement of PDMS-Parylene electrode array over rat auditory cortex

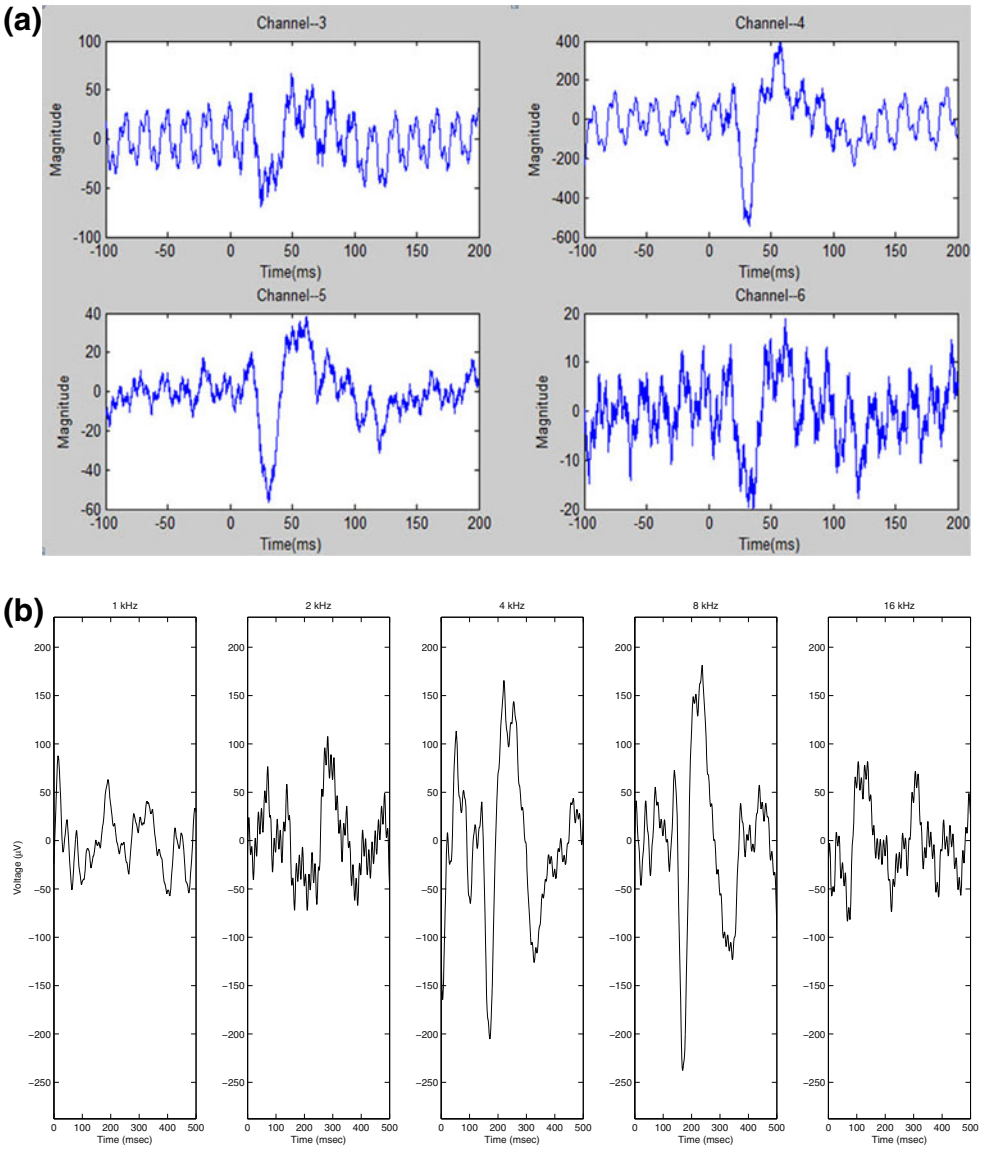

Fig. 7 **a** Averaged recorded waveforms for channels 3, 4, 5, and 6 showing auditory evoked potentials (AEP). Acoustic stimuli (White Noise) was delivered at time $t=0$. **b** Neural responses evoked by presenting acoustic tones of different frequencies. Acoustic stimuli were delivered at time 0. The peak amplitudes of the AEP are frequency-dependent, with the highest AEP evoked by an 8 kHz stimulus

3.3 *In vivo* experiment

During the experiment, the surface electrode array was placed onto the cortex. As shown in Fig. 6, the electrode array exhibits suitable conformal coverage over the cortex. Auditory Evoked Potentials (AEP) was observed as negative-first, biphasic responses occurring approximately 20–40 ms after the acoustic stimulus onset on several channels. The results of 200 trials over 16 channels were recorded and averaged in MATLAB to increase the signal-to-noise ratio (SNR), which was calculated as the ratio of peak-to-peak signal amplitude to root-mean-square of noise (Maynard et al. 2000; Ludwig et al. 2006). The averaged waveforms for channels 3, 4, 5, and 6 are shown in Fig. 7a; these channels exhibited an SNR of about 4.9, 8.6, 6.5, and 3.4, respectively. A noticeable neural response was observed, with a definite AEP beginning 20 ms after the stimulus is played (time=0). Figure 7b presents the recorded waveforms averaged over 16 channels at respective frequencies. The data show a more pronounced AEP recorded at 8 kHz as compared to other frequencies, suggesting that our region of recording was more responsive to the 8 kHz sound stimulus.

These acute experiments were performed as a proof of concept of the device, but they can be expanded for chronic implantations. Chronic use may require optimization of the device dimension (e.g. reducing the thickness of the PDMS at the electrode end to reduce the risk of increased intracranial pressure) or modification of the electrode surface to minimize micromotion concerns (Nair et al. 2008; Wong et al. 2009). Fortunately, the flexibility and biocompatibility of the electrodes, as well as the straightforward fabrication procedure, allow them to be easily altered for chronic implantations

4 Conclusions

In this work, we successfully designed, fabricated, and tested a flexible electrode array for subdural neural recording using a PDMS-Parylene bilayer structure. Together, the two layers form a hybrid structure with straightforward fabrication process that includes low-temperature *in-situ* deposition of Parylene onto the PDMS and superior functionality than either material alone. The thick PDMS layer (~200 μm) allows for easy handling and repositioning of the electrode on the cortex while the thinner Parylene layer (~5 μm) offers a strong, flexible, and processable substrate for electrode and metal interconnects. *In vitro* characterization of the electrode array resulted in 1 kHz impedance values of 300 kΩ~600 kΩ. The electrode array was conformably placed over the auditory cortex of a rat and neural activities (Auditory Evoked Potential, AEP) were recorded.

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