PEDOT-CNT-coated low-impedance, ultra-flexible, and brain-conformable micro-ECoG arrays

Elisa Castagnola, Luca Maiolo, Emma Maggiolini, Antonio Minotti, Marco Marrani, Francesco Maita, Alessandro Pecora, Gian Nicola Angotzi, Alberto Ansaldo, Massimiliano Boffini, Luciano Fadiga, Guglielmo Fortunato, Davide Ricci

Abstract—Electrocorticography (ECoG) is becoming a common tool for clinical applications, such as preparing patients for epilepsy surgery or localizing tumor boundaries, as it successfully balances invasiveness and information quality. Clinical ECoG arrays use millimeter-scale electrodes and centimeter-scale pitch and cannot precisely map neural activity. Higher-resolution electrodes are of interest for both current clinical applications, providing access to more precise neural activity localization, and novel applications, such as neural prosthetics, where current information density and spatial resolution is insufficient to suitably decode signals for a chronic brain-machine interface. Developing such electrodes is not trivial because their small contact area increases the electrode impedance, which seriously affects the signal-to-noise ratio, and adhering such an electrode to the brain surface becomes critical. The most straightforward approach requires increasing the array conformability with flexible substrates while improving the electrode performance using materials with superior electrochemical properties. In this paper, we propose an ultra-flexible and conformable polyimide-based micro-ECoG array of sub-millimeter recording sites electrochemically coated with high surface area conductive polymer-carbon nanotube composites to improve their brain-electrical coupling capabilities. We characterized our devices both electrochemically and by recording from rat somatosensory cortex in vivo. The performance of the coated and uncoated electrodes was directly compared by simultaneously recording the same neuronal activity during multiwhisker deflection stimulation. Finally, we assessed the effect of electrode size on the extraction of somatosensory evoked potentials and found that in contrast to the normal high-impedance microelectrodes, the recording capabilities of our low-impedance microelectrodes improved upon reducing their size from 0.2 to 0.1 mm.

Index Terms— micro-electrocorticography, ECoG, PEDOT-CNT coatings, flexible microelectrode array

I. INTRODUCTION

THE ambitious goal of a clinically useful brain-machine interface (BMI) for controlling external devices *via* the human central nervous system requires the stable, long-term recording of large neuron populations from multiple brain areas [1-4]. Single-unit activity (SUA) recorded from the cerebral cortex using intracortical penetrating microelectrodes are the most useful signals for BMI applications and provide the best control in terms of accuracy, speed, and degrees of freedom [1-4]. Unfortunately, despite their great spatial selectivity, the state-of-the-art intracortical microelectrodes – metal microwires [5] and silicon-based neural probes, such as the Utah array [5,6], Michigan array [5,7], or NeuroProbe array [8] – are unable to guarantee safe, accurate, stable, long-term, and bidirectional access to brain signals because of their invasiveness and the induced biological foreign-body response [9]. that encapsulates the neural probes insulating them from the surrounding tissues and inhibiting their ability of discriminating action potentials [1,10]. However, the several types of neural signals – slow cortical potentials (SCPs), sensorimotor rhythms (SMRs), and P300 waves – that can be recorded using noninvasive electroencephalographic (EEG)-based techniques, which avoid the risks of brain surgery, are insufficient for controlling the movement of devices with multiple degrees of freedom, such as arm or leg prostheses [1-4]. Electrocorticography (ECoG) provides a reasonable compromise between invasiveness and signal recording fidelity. The ECoG approach, compared to scalp EEG, improves the spatial resolution, increases the signal-to-noise ratio (SNR), widens the frequency range, and reduces the training requirements [1,2]. At the same time, compared to intracortical implants, it minimizes brain tissue injuries [1,11-13], lowers the clinical risk and increases signal stability over long periods of time [1,2]. Different studies have shown that micro-ECoG arrays, which are characterized by smaller

recording sites and reduced inter-electrode spacing relative to typical clinical ECoG electrodes, could provide motor cortical signals carrying an information density adequate for multiple degrees of freedom BMI [1-4,14-17]. The primary issue with electrode miniaturization is the increased electrical impedance, which results in poor recording quality. A common approach to reduce the impedance of microelectrodes while enhancing their charge transfer capability is to increase the effective surface area [18-33]. Electrochemical deposition allows for the precise placement of a variety of conductive polymers on active electrode sites with excellent thickness control [25,27,28]. Various studies demonstrated that poly(3,4-ethylenedioxythiophene) (PEDOT) and PEDOT-carbon nanotube (CNT) composite coatings drastically decrease the impedance and increase the charge transfer capability of pure metal electrodes, which increases both the selectivity and sensitivity [19-22,24,25,28,29,31-33], and can provide a more adaptable neural tissue interface by reducing the hardness mismatch [24,26,28]. Decreased electrode impedance at sizes of a few micrometers allows for a reduced pitch between electrodes and the exploration of high density microelectrode array designs. Another important area of research is to investigate soft, flexible, and conformable substrates that are capable of accommodating the curvature and movement of the brain to keep each microelectrode in the array intimately contacted with the cortical surface, thus improving the electrical coupling [14,15,34-38]. In this work, we combined a technique for fabricating multi-channel, ultra-flexible and brain-conformable polyimide micro-ECoG arrays less than 10 µm thick with a PEDOT-CNT electrodeposition process to dramatically decrease the metal microelectrode impedance and obtained an ultra-flexible, brain-conformable, low-impedance micro-ECoG device. Finally, we present interesting preliminary results to validate our device *in vivo* by recording somatosensory evoked potentials (SEPs) elicited from rat somatosensory cortex *via* multiwhisker deflections.

II. MATERIALS AND METHODS

A. Ultra-flexible micro-ECoG array fabrication

A 4 µm-thick polyimide (HD2611, HD MicroSystems, Parlin, NJ, USA) layer was first deposited onto an oxidized silicon wafer to overcome sample handling issues during the fabrication process. After curing, to stabilize the polymer on the wafer, a 50 nm-thick silicon nitride layer was deposited *via plasma-enhanced chemical vapor deposition* (PECVD) at a temperature of 250°C to improve the adhesion to the metal layer. Then, a 20 nm-thick titanium layer was sputtered onto the polyimide, a 200 nm-thick gold (Au) film was thermally evaporated onto the titanium, and a sacrificial 20 nm-thick chromium (Cr) layer was used to cover the underlying metal. The microelectrode arrays were then lithographically defined to obtain square 100 µm × 100 µm or 200 µm × 200 µm pads with 200 µm-wide and 4 cm-long metal tracks. Another 4 µm-thick polyimide layer was spin-coated onto the wafer and cured to protect the microelectrodes. Then vias were lithographically defined into a second Cr sacrificial layer and opened using a dry etching technique. The Cr mask and underlying sacrificial Cr layer were removed with a wet-etch solution to uncover the Au pads (Fig. 1a). Finally, the multi electrode arrays were cut out of the holder and were approximately 8 µm thick. To enable the handling and interfacing of the ultra-flexible structures, the structures were bonded to an external flexible PCB containing 17 µm-thick copper tracks using an anisotropic conductive film.
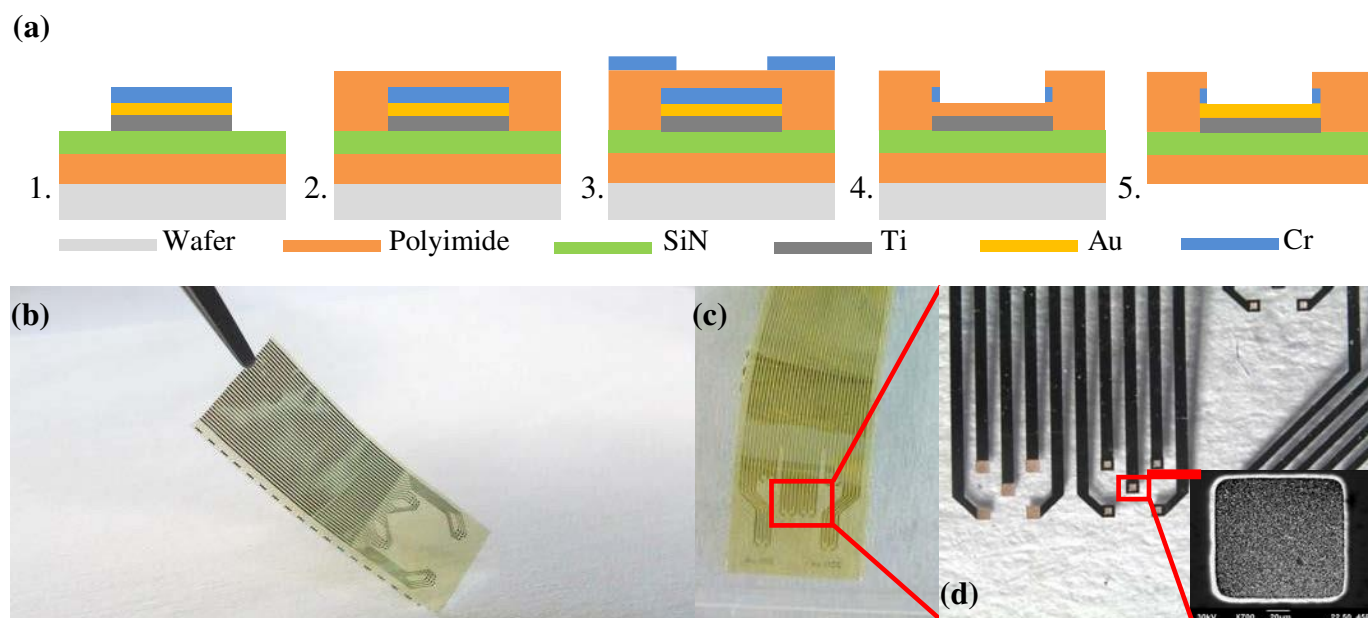
Fig. 1. (a) Main production steps of the ultra-flexible micro-ECoG array: 1. lithographic patterning of metal tracks sputtered and evaporated onto a silicon nitride polyimide layer; 2. deposition of a second polyimide film to passivate and protect this structure; 3. evaporation and patterning of the sacrificial Cr layer; 4. definition of the pathways in the polyimide passivation layer; 5. mechanical detachment of the ultra-flexible array from the rigid wafer. (b) A picture of the ultra-flexible device after detaching from the wafer. (c) One possible micro-ECoG array layout. (d) Details of the two groups of five recording sites 200 µm x 200 µm and 100 µm x 100 µm in size, and a scanning electron micrograph of a 100 µm x 100 µm Au recording site (inset).

B. Electrochemical co-deposition and characterization

Carboxylated multi-wall CNTs (COOH-MWCNT, NC 3151, <4% of -COOH functional groups, Nanocyl S.A., Sambreville, Belgium) were suspended (1 mg ml^{-1}) in ultrapure water (Milli-Q, Millipore, Billerica, MA, USA) *via* horn sonication (6 s, 66% duty cycle pulses, 4 W ml^{-1}, for 30 min) while cooling in an ice bath. Poly(sodium 4-styrenesulfonate) (PSS, Sigma-Aldrich, St. Louis, MO, USA) and 3,4-ethylenedioxythiophene (EDOT, Sigma-Aldrich, St. Louis, MO, USA) were immediately added to this suspension (0.6 wt% and 0.5 M, respectively), and the solution was maintained in a deoxygenated state by bubbling nitrogen through it. The PEDOT-CNT nanocomposite coating was electropolymerized *in situ* onto each electrode at a constant temperature (ice-water bath, 0°C) using 0.8 V *versus* a silver (Ag)/silver chloride (AgCl) reference electrode with 5°C cm^{-2}. The electrochemical behavior of the microelectrodes was studied in a 0.9% aqueous sodium chloride (NaCl) solution *via* both cyclic voltammetry (CV) to quantify their capacitive charging and electrochemical impedance spectroscopy (EIS) to determine the electrical properties of the system over a large frequency range. During the CV tests, the working electrode potential was swept between 0.5 and −0.5 V *versus* Ag/AgCl at a scan rate of 100 mV/s. During the EIS measurements, a sine wave (10 mV RMS amplitude) was superimposed on the open circuit potential while varying the frequency from 10^5 to 1 Hz. All of the electrochemical depositions and characterizations used a potentiostat/galvanostat/ZRA (Reference 600, Gamry Instruments, Philadelphia, PA, USA) connected to a three-electrode electrochemical cell with a platinum counter electrode and Ag/AgCl reference electrode.

C. Neural recording on rat brain and whisker deflection

These experiments were performed on Long-Evans male rats (400-500 gr). Animals were anaesthetized using a mixture of Zoletil (30mg/Kg) and Xylazine (5mg/Kg) delivered intraperitoneally. For recording sessions, the animal was positioned on a stereotactic frame (Kopf, Tujunga, CA, USA), and a small craniotomy was made in the parietal bone, which exposed the vibrissa region of the somatosensory cortex while leaving the *dura mater* intact. A microelectrode array was placed over the cortex between the bone and *dura mater* to record the SEPs elicited *via* multiwhisker deflections. An ultra-flexible micro-ECoG device was tested in nine different cortex positions using consecutive 20 min recording sessions. All surgical procedures were performed in compliance with Italian law regarding the care and use of experimental animals (DL116/92) and were approved by the Italian Institute of Technology Animal Use Committee and the Italian Ministry of Health. The multiwhisker deflections were performed after cutting the whiskers contralateral to the recorded cortex 1 cm from their base and connecting them to a Velcro strip attached to a rod moved by a shaker (Type 4810 minishaker; Bruel & Kjaer, Nærum, Denmark) controlled by a DAQ (National Instruments, Austin, TX, USA). The deflection stimulus consisted of three trains of 10 truncated Gaussians [39] that were 12 ms in duration at 9 Hz followed by a 5 s pause. The stimulus amplitude was changed for each train to obtain multiwhisker deflections of 0.8, 1.1, and 1.3 mm. This sequence was repeated 20 times with a 60 s pause between iterations. We used a compact 16-channel recording system developed in-house that includes a headstage, control unit, and acquisition software to record the evoked neural activity [40, 41]. We can simultaneously record from a maximum of 16 microelectrodes *via* an *ad hoc* adaptor board that allows microelectrode groups to connect to the headstage. Each channel was low-pass filtered using a fourth-order filter with a cut-off frequency set to 8 kHz, whereas a first-order, 3 Hz high-pass filter removed the DC component from the recorded traces before further user-programmable gain amplification. The amplified signals were multiplexed, digitally converted (10-bit, 40,000 samples s^{-1}), downsampled to 1 kHz, and digitally low-pass filtered to obtain the local field potential (LFP, < 250Hz).

D. Signal-to-noise ratio and signal power calculation

We first characterized the overall noise of the recording system. Both Au and PEDOT-CNT-coated microelectrodes and the reference electrode were immersed in a 0.9% NaCl solution, and a 3 min-long recording session was performed. The noise was estimated by computing the spectral power densities (SPDs) of each recorded trace, with a segmentation length of 512 points sampled at a 4000Hz frequency, 0 overlapping ratio of the segments, and a 1-1000Hz window function. Using the same microelectrodes, we recorded from the rat somatosensory cortex both the spontaneous and the evoked neural activity, while varying whisker deflection amplitude. The SPDs of both spontaneous and stimulated activities were computed by averaging signals spectra across the 20 recordings obtained during the different stimulation pattern repetitions. The signal power over the LFP frequency range was computed as the integral of the SPDs of the signals and of the noise. The SNRs were computed as ratio of the different neural signal powers vs the noise power recorded in saline.

III. RESULTS

The previously described lithographic process (Fig. 1a) yielded ultra-flexible polyimide micro-ECoG arrays with a total thickness of approximately 8 μm [42]. Our fabrication technique was compatible with standard microelectronic processing and produced devices with good mechanical strength despite their reduced thickness. Polyimide was chosen due to its biocompatibility [43] and because it easily detaches mechanically from the holder after processing [44]. The array layout was tailored to the type of neurophysiological experiment. Two possible designs are shown in Figs. 1b and c. Fig. 1d presents an optical microscope image of two groups of five recording sites 200 μm × 200 μm (large) and 100 μm × 100 μm (small) in size, and Fig. 1e presents a scanning electron micrograph of a small Au recording site. The

TABLE I
IMPEDANCE AT 100 HZ OF THE COATED MICROELECTRODES

Electrode	Magnitude
100 μm x 100 μm Au-coated	1.6 ± 0.1 MΩ
100 μm x 100 μm PEDOT-CNT-coated	2.1 ± 0.7 kΩ
200 μm x 200 μm Au-coated	509.7 ± 177.5 kΩ

TABLE II
EFFECTS OF REPETITIVE BENDING (10 TIMES) OF COATED ELECTRODES

Radius	$|Z|$ @100 Hz	$|Z|$ @kHz	CTCtot
None	2.43 ± 0.69 kΩ	3.01 ± 0.74 kΩ	31.71 ± 1.09 mC cm^{-2}
1.5 mm	2.48 ± 0.70 kΩ	3.07 ± 0.75 kΩ	31.35 ± 0.58 mC cm^{-2}
0.5 mm	2.66 ± 0.84 kΩ	3.28 ± 0.74 kΩ	34.03 ± 2.52 mC cm^{-2}

PEDOT-CNT nanocomposite was electroplated onto the micro-ECoG recording sites to reduce their impedance and increase their charge transfer capabilities. PEDOT was chosen because of its high conductivity and chemical stability [29,30,32], and PEDOT-CNT composite coatings were particularly preferred because they outperformed PEDOT in terms of impedance reduction, effective surface area increase, conductivity, and mechanical stability, taking advantage of the excellent properties of CNTs [31].

The impedance spectra (Fig. 2a) illustrate how the PEDOT-CNT composite coatings dramatically reduced the impedance of both the small and large recording sites over the entire frequency range (1-10^5 Hz). In particular, the impedance decreased by up to four orders of magnitude in the 1-100 Hz frequency band, where ECoG signals are typically recorded, with a significant downshift of the first frequency response pole. Another consequence of the increased capacitance of the coated electrodes is the downshift of their zero to nearly 0 Hz that, combined with the first pole, induces a pseudo-resistive behavior in the 10-10^5 Hz band for the large recording sites and the 10^2-10^5 Hz band for the small sites, as revealed by the small phase shift. The impedances at 100 Hz (averaged from 10 electrodes) are reported in Table I. The total charge transfer capability (CTC$_{tot}$), calculated as the time integral of an entire CV cycle, increased by approximately 350 fold due to the increased charge exchange between the electrode and solution thanks to the increased effective area of the nanostructured coatings. Typical CVs are shown in Fig. 2b, and the corresponding CTC$_{tot}$ were 40.4 mC cm^{-2} and 64.8 mC cm^{-2} for small and large areas, respectively. The coatings were spongy (Fig. 2c, low-vacuum scanning electron microscopy, LV-SEM). The pictured recording sites coated with PEDOT-CNT composite (Fig. 2d,e, LV-SEM) illustrate that the coating is uniform over the entire surface. In order to check the impact of mechanical stresses induced by bending onto the coated electrodes properties, we systematically performed electrochemical impedance spectroscopy and cyclic voltammetry on five different 100 μm × 100 μm PEDOT-CNT coated recording sites before and after rolling and unrolling repeatedly (10 times) the micro-ECoG device around wires with radii of 1.5 and 0.5 mm. The impedance spectra and voltammograms are very similar, with mean impedance and CTC$_{tot}$ values changes well within the measurement repeatability, as shown in Table II.

To validate the recording capability of our ultra-flexible micro-ECoG arrays, we tested the device *in vivo* on different
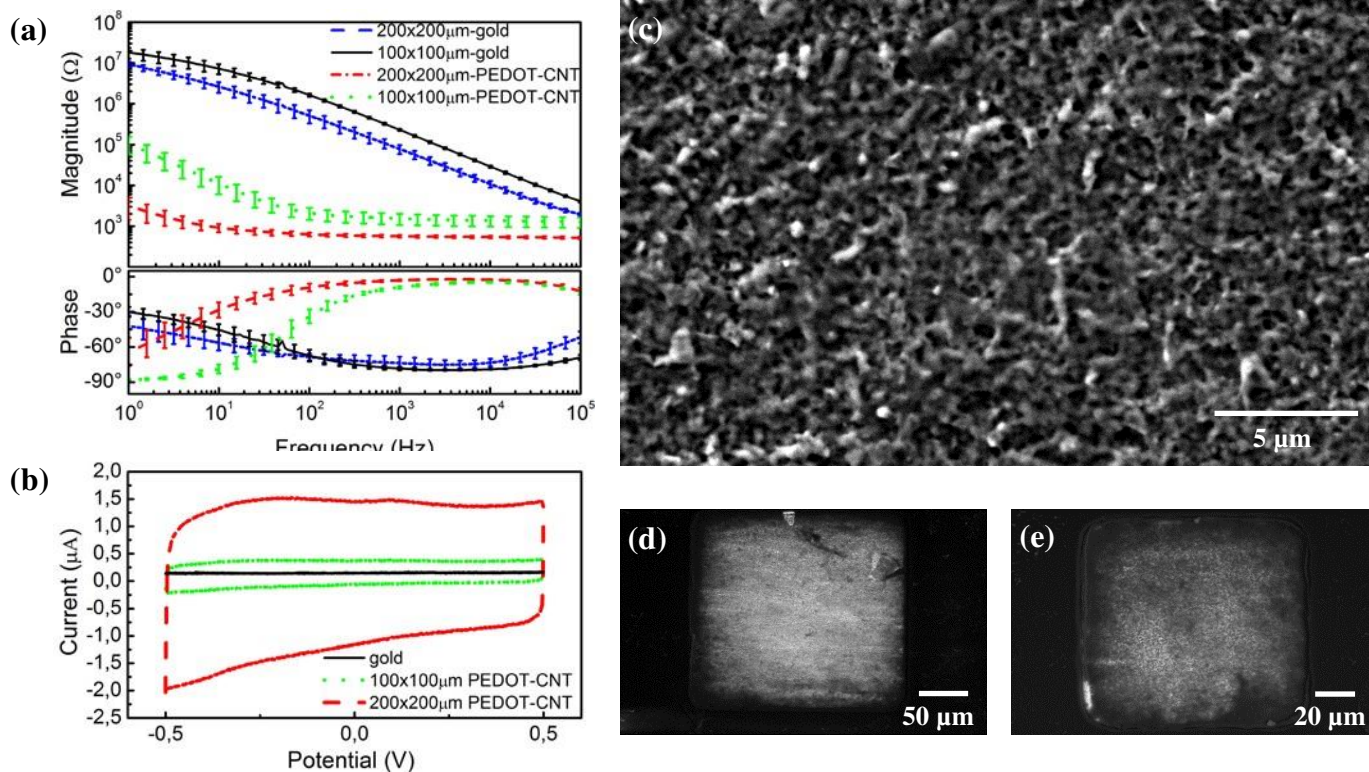
Fig. 2. (a) Impedance spectra of the small and large ECoG array recording sites (mean and standard deviation from 10 recording sites each) before and after PEDOT-CNT electrodeposition; (b) sample cyclic voltammograms of the uncoated (black line, small and large electrodes are not distinguishable at this scale), small PEDOT-CNT-coated (green) and large PEDOT-CNT-coated (red) recording sites; (c) scanning electron micrograph of the PEDOT-CNT coating; (d) a large recording site; (e) a small recording site coated with a PEDOT-CNT composite.
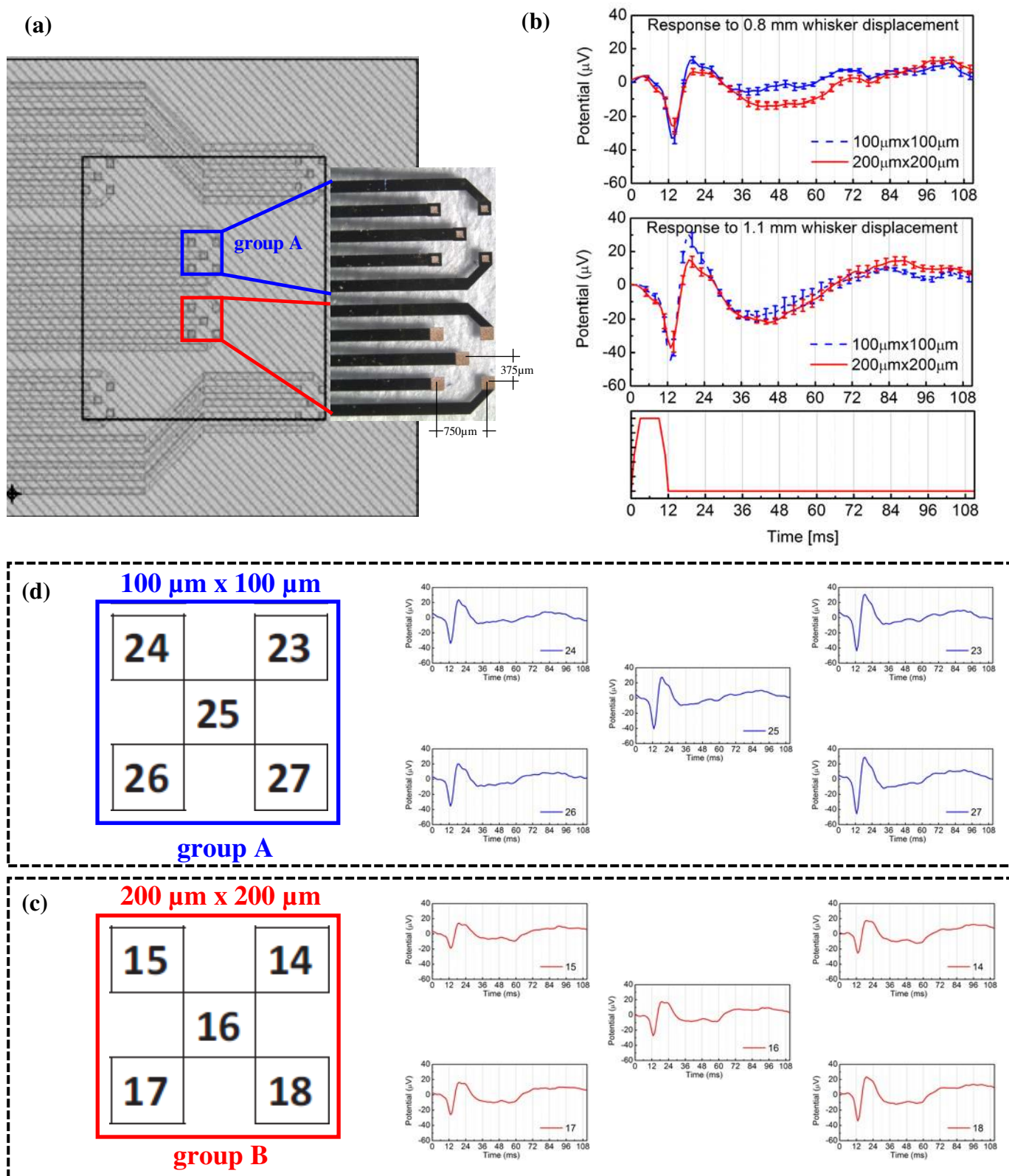
Fig. 3. (a) Layout of the 6 × 5 configuration of the micro-ECoG used to record data from the somatosensory cortex; electrode groups A and B are highlighted. (b) Corresponding optical picture for the two electrode groups (A, small, and B, large). (b) Averaged SEP using a truncated Gaussian of the first 12 ms of the 9 Hz train with a rat multiwhisker deflections of 0.8 and 1.1 mm recorded using the PEDOT-CNT-coated microelectrodes for groups A and B, respectively. Averaged SEP using a truncated Gaussian of the first 12 ms of the 9 Hz train with a multiwhisker deflection of 1.3 mm for each electrodes (c) group A and (d) group B.

positions of the rat somatosensory cortex according to the procedure described above.

To this aim we used a 6 × 5 layout (Fig. 3a). Of the 30 electrodes, we selected two square subgroups of five

(a)

(b)

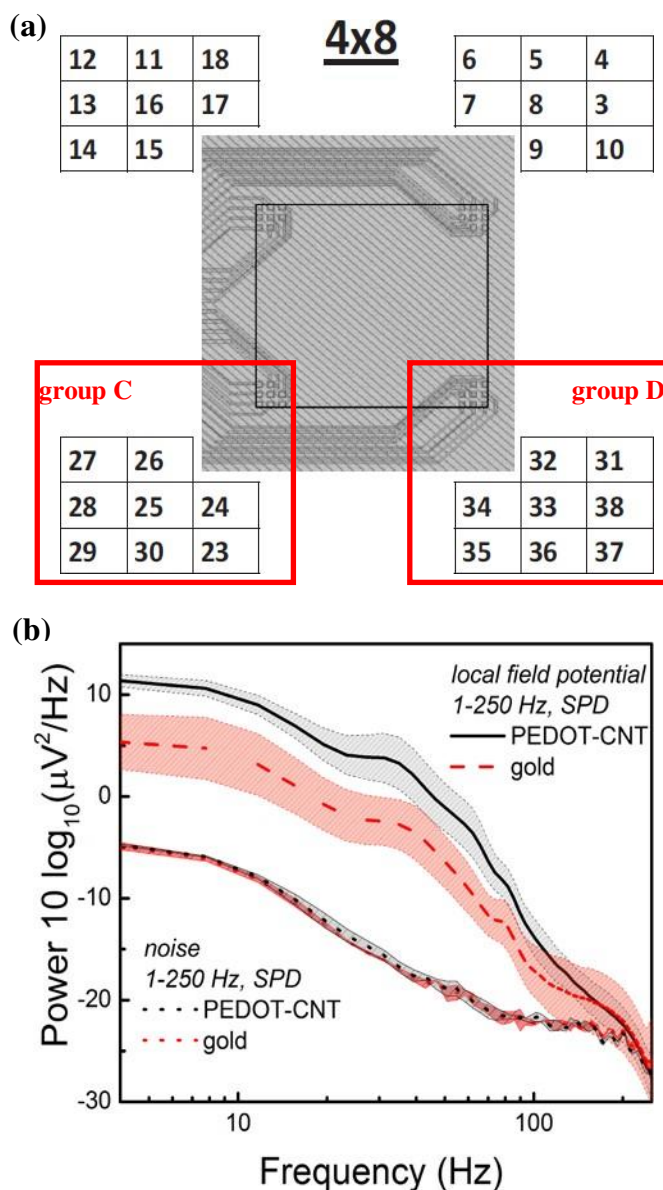Fig. 4. (a) Layout of the 4×8 micro-ECoG array used to record data from rat somatosensory cortex. Groups C and D are highlighted. (b) Averaged noise SPDs (dotted lines) obtained for PEDOT-CNT-coated (black) and Au-coated (red) large microelectrodes immersed in 0.9% NaCl solution, and the spontaneous activity (solid lines) recorded from the rat brain somatosensory cortex using PEDOT-CNT-coated (black) and Au-coated (red) large microelectrodes for groups C and D (mean and standard deviation of coated and uncoated microelectrodes while recording two cortical positions).

TABLE III
SEP PEAK-TO-PEAK AMPLITUDE

Deflection amplitude	Group A	Group B
0.8 mm	32.3 ± 15,2 µV	22.2 ± 10.9 µV
1.1 mm	49.5 ± 27.2 µV	34.2 ± 20.1 µV
1.3 mm	41.4 ± 26.7 µV	28.1 ± 18.1 µV

Group A and group B refer to the electrodes having 100 µm x 100 µm and 200 µm x 200 µm recording area respectively.

traces were obtained by averaging the SEP evoked by 20 stimulation patterns for each microelectrode size (five small and five large, Fig. 3b). All the SEP waveforms have the same shape, and their peak-to-peak amplitudes agree with the changes in whiskers deflection, which clearly indicates the two electrode groups recorded the same neuronal activity. It is important to notice that, due to the geometry of the array the two electrodes groups are 1 mm apart, and the electrodes of the same group have a pitch of 0.75mm, and this distance is comparable to the diameter of individual cortical columns (~0.5 mm). This means that the different electrodes are likely recording from different columns. It is known from literature that there is a significant variability in cell count across different columns [45-47,] but, arguably, it is unlikely that a systematic difference in SEP amplitude between small and large electrodes would be explained by different radial locations as more columns are recorded and averaged by the electrodes belonging to the same group and the experiment is repeated while moving the array in different positions, as explained before. The averaged SEP waveforms recorded by each single electrode for the first 1.3 mm multi-whisker deflection pattern are reported in Figs. 3c and d. The total SEP amplitude for the different whisker displacements (0.8, 1.1 and 1.3 mm) is reported in Table III. The larger SEPs were measured using the smaller microelectrodes for all cases regardless of the stimulus amplitude or electrode positioning. In particular, the average total SEP amplitudes recorded with the 100 µm × 100 µm PEDOT-CNT-coated microelectrodes exceed those recorded with the 200 µm × 200 µm PEDOT-CNT-coated microelectrodes by 31.2%, 30.9% and 31.1% for 0.8, 1.1 and 1.3 mm whisker displacements, respectively. We then computed the SPDs of the SEP recorded by the PEDOT-CNT-coated microelectrodes. The SPD related to the small microelectrodes was greater than that related to the larger ones (4.2%, 5.3%, and 5.5% for 0.8, 1.1, and 1.3 mm whisker displacements, respectively). It seems that, when the impedance is lowered by a coating such as PEDOT-CNT composite the smaller metallic isopotential area underneath the smaller electrode allow a better localized recording that increases the electrode sensitivity to the evoked potential and this sensitivity enhancement clearly derives from the electrode properties because the recorded signal derived from an averaged signal recorded from the same neuronal activity, as previously discussed. Finally, to evaluate how the PEDOT-CNT coating improved the recording quality in terms of the signal power and SNR, we compared two groups of uncoated and PEDOT-CNT-coated 200 µm × 200 µm microelectrodes (Fig. 4a, group C and D 4 × 8 electrode layout) by repeating a

electrodes, one for the small recording sites (group A) and the other for the larger sites (group B). The total area covered by each electrode subgroup was approximately 0.9 mm × 0.9 mm with a 750 µm pitch between the four corner electrodes with a fifth electrode in the center (Fig. 3a inset).

To investigate whether the site size affected the recording quality of the PEDOT-CNT-coated microelectrodes, we tested the recording capability of both groups in three different positions (the geometric area ratio between groups A and B was 1:4). The typical waveform of SEPs elicited using 9 Hz stimulus trains with amplitudes of 0.8 and 1.1 mm, recorded using groups A (blue) and B (red), is shown in Fig. 3b. The

TABLE IV
SNR OF PEDOT-CNT-COATED AND AU-COATED MICROELECTRODES

	PEDOT-CNT-coated	Au-coated
Spontaneous activity	46.1 ± 12.7	13.0 ± 7.9
0.8 whisker displacement	76.9 ± 15.3	26.2 ± 14.2
1.1 whisker displacement	88.9 ± 6.8	26.7 ± 17.9
1.3 whisker displacement	97.7 ± 30.4	27.4 ± 14.6

20 min recording session across five different positions. The eight microelectrodes in each group record a 1 mm × 1 mm area with a total recorded area of 7 mm × 7.3 mm. The distance between two neighboring microelectrodes within the same group was 200 μm, whereas the minimal distance between the two groups was 5.3 mm. We alternately coated the microelectrodes in the two groups with PEDOT-CNT. The electrochemical noise SPD is reported in Fig. 4b, dotted lines. The averaged SPDs of the spontaneous neural activity recorded from the rat somatosensory are reported in the same graph (Fig. 4b, solid lines). These SPD plots show that the PEDOT-CNT coating enhanced the signal power 3.4 times in the LFP (1-250Hz) frequency band. The SNR values are reported in Table IV. In all cases, a three-fold SNR increase occurred when using the PEDOT-CNT-coated microelectrodes.

IV. CONCLUSIONS

In this work, we presented an ultra-flexible and brain-conformable micro-ECoG device with low impedance microelectrodes by combining (1) an 8 μm-thick polyimide-based micro-ECoG array with (2) the electrochemical performance of PEDOT-CNT nanocoatings. We demonstrated that our micro-ECoG electrode arrays are suitable for *in vivo* applications by recording SEP from rat somatosensory cortexes *via* multiwhisker deflections. The PEDOT-CNT coating enhanced the signal power in the 0-250 Hz band by 3.4 fold and increased the SNR by three fold. Furthermore, the recording of the same neuronal activity with the low-impedance PEDOT-CNT-coated microelectrodes indicates that the peak-to-peak SEP amplitude depends on the microelectrode size with the opposite trend to standard high-impedance microelectrodes. In fact, the average SEP amplitudes recorded for the smaller electrodes exceed those recorded for the larger electrodes by over 30% (geometrical area ratio of 1:4, impedance ratio of 3:1). This latter result suggests that a thorough investigation of the neural recording quality dependencies is required once the microelectrode impedances have been reduced to similar values *via* the high surface-+area coatings to account for the recording site size. An in-depth exploration of this aspect may yield useful information on the most appropriate means of optimizing both the size and impedance of microelectrodes to maximize the information extracted from a population of neurons in terms of both spatial resolution and signal properties.

REFERENCES

[1] E. C. Leuthardt, G. Schalk, D. Moran, J. G. Ojemann, "The emerging world of motor neuroprosthetics: a neurosurgical perspective", *Neurosurgery*, vol. 59, no.1, 2006.

[2] E. C. Leuthardt, Z. Freudenberg, D. Bundy, J. Roland,"Microscale recording from human motor cortex: implications for minimally invasive electrocorticographic brain computer interfaces", *Neurosurg Focus*.,vol.27, no. 1, E10, 2009.

[3] S. Thongpang, T. J. Richner, S. K. Brodnick, *et al.*, "A Micro-Electrocorticography Platform and Deployment Strategies for Chronic BCI Applications", *Clin EEG Neurosci*, vol. 42, no. 4, pp. 259–265, 2011.

[4] A. G. Rouse, J. J. Williams, J. J. Wheeler, D. W. Moran, "Cortical adaptation to a chronic micro-electrocorticographic brain computer interface", *J Neurosci*., vol. 33, no. 4, pp. 1326–1330, 2013.

[5] A. B. Schwartz, "Cortical Neural Prosthetics", *Annu. Rev. Neurosci.*, vol. 27, pp. 487-507, 2004.

[6] R. A. Normann, "Technology insight: future neuroprosthetic therapies for disorders of the nervous system", *Nat. Clin. Pract. Neurol.,*vol. 3, no. 8, pp. 444-452, 2007.

[7] R. J. Vetter, J. C. Williams, J. F. Hetke, E. A. Nunamaker, D. R. Kipke, "Chronic Neural Recording Using Silicon-Substrate Microelectrode Arrays Implanted in Cerebral Cortex", *IEEE Trans. Biomed. Eng.*, vol. 51, no. 6, pp. 896-904, 2004

[8] H. Neves, "Advanced in cerebral probing using modular multifunctional probe arrays", *Med. Device Techno.,* vol.18, no. 5, pp. 38-39, 2007.

[9] R. A. Andersen, J. W. Burdick, S. Musallam, B. Pesaran, J. G., Cham, "Cognitive neural prosthetics", *Trends. Cogn. Sci.,* vol.8, pp.486-493, 2004.

[10] C. Marin, E. Fernandez, "Biocompatibility of intracortical microelectrodes: current status and future prospects", *Frontiers in Neuroengineering,* vol.3, pp. 1-6, 2010.

[11] J. A. Brown, J. G. Pilitsis, "Motor cortex stimulation for central and neuropathic facial pain: A prospective study of 10 patients and observations of enhanced sensory and motor function during stimulation", *Neurosurgery*, vol. 56, pp. 290–297, 2005.

[12] E. Margalit, J. D. Weiland, R. E. Clatterbuck, G. Y. Fujii, M. Maia, M. Tameesh, G. Torres,et al., "Visual and electrical evoked response recorded from subdural electrodes implanted above the visual cortex in normal dogs under two methods of anesthesia", *J Neurosci Methods*, vol. 123, pp. 129–137, 2003.

[13] I. Wickelgren, "Neuroscience: Tapping the mind", *Science*, vol. 299, pp. 496–499, 2003.

[14] A. Ritaccio, P. Brunner, M. C. Cervenka, *et al*., "Proceedings of the First International Workshop on Advances in Electrocorticography", *Epilepsy Behav.*, vol.19, pp. 204– 215, **2010.**

[15] A. Ritaccio, D. Boatman-Reich, P. Brunner, *et al*., "Proceedings of the Second International Workshop on Advances in Electrocorticography", *Epilepsy Behav.*, vol. 22, pp. 641– 650, 2011.

[16] E. C. Leuthardt, Z. Freudenberg, D. Bundy, J. Roland, "Microscale Recording from Human Motor Cortex: Implications for Minimally Invasive Electrocorticographic Brain-Computer Interfaces", *Neurosurg. Focus*, vol. 27, E10, 2009.

[17] S. S. Kellis, P. A. House, K. E. Thomson, *et al*., "Human Neocortical Electrical Activity Recorded on Nonpenetrating Microwire Arrays: Applicability for Neuroprostheses" *Neurosurg. Focus*, vol. 27, E9, 2009.

[18] S. A. Desai, J. D. Rolston, L. Guo., & S. M. Potter, "Improving Impedance of Implantable Microwire Multi-Electrode Arrays by Ultrasonic Electroplating of Durable Platinum Black", *Front Neuroengineering,* vol. 3, no. 5, pp. 1-11 , 2010.

[19] S. F. Cogan, "Neural stimulation and recording electrodes", *Rev. Biomed. Eng.,* vol. 10, pp. 275-309, 2008.

[20] J. Yang & D. C. Martin, "Impedance spectroscopy and nanoindentation of conducting poly(3,4-ethylenedioxythiophene) coatings on microfabricated neural prosthetic devices", *J Mater Res,* vol. 21, no. 5, pp. 1124–1132, 2006.

[21] R. A. Green, C. M. Williams, N. H. Lovell, L. A. Poole-Warren,"Novel, neural interface for implant electrodes: improving electroactivity of Polypyrrole through MWCNT incorporation", *Med., J. Mater. Sci: Mater,* vol.19, pp. 1625-1629, 2008.

[22] E. W. Keefer, B. R. Bottermann, M. I. Romero, A. F. Rossi, *et. al.*, "Carbon nanotube coating improves neural recordings", *Nature Nanotechnol,* vol. 3, pp.434-439, 2008.

[23] J. E. Ferguson, C. Boldt, A. D. Redish, "Creating low-impedance tetrodes by electroplating with additives", *Sens. Actuators, A.,* vol. 156, pp. 388-393, 2009.

[24] M. R. Abidian, & D. C. Martin, "Experimental and theoretical characterization of implantable neural microelectrodes modified with conducting polymer nanotubes", *Biomaterials,* vol. 29, pp.1273-1283, 2008.

[25] M. R. Abidian, D. H. Kim, & D. C. Martin, "Conducting-polymer nanotubes for controlled drug release", *Adv. Mater.*, vol. 18, pp. 405, 2006.

[26] W. R. Stauffer & X. T. Cui, "Polypyrrole doped with 2 peptide sequences from laminin", *Biomaterials,* vol. 27, pp. 2405-2413, 2006.

[27] S. M. Richardson-Burns, J. L. Hendricks, B. Foster, *et al.*, "Polymerization of the conducting polymer poly(3,4-ethylenedioxythiophene) (PEDOT) around living neural cells", *Biomaterials,* vol. 28, pp.1539-1552, 2007.

[28] N. A. Kotov, J. O. Winter, I. P. Clements, *et al.*, "Nanomaterials for Neural Interfaces", *Adv. Mater.*, vol. 21, pp. 3970– 4004, 2009.

[29] K. A. Ludwig, J. D. Uram, J. Yang, *et al.*, "Chronic Neural Recordings Using Silicon Microelectrode Arrays Electrochemically Deposited with a Poly(3,4-ethylenedioxythiophene) (PEDOT) Film", *J. Neural Eng.*, **vol.** 3, pp. 59–70, 2006.

[30] D. Khodagholy, T. Doublet, M. Gurfinkel, et al., "Highly conformable conducting polymer electrodes for in vivo recordings", *Adv. Mater.*, vol. 23, pp. H268-H272, 2011.

[31] R. Ferwig, K. Fuchsberger, B. Schroeppel, et al., "PEDOT-CNT composite microelectrodes for recording and electrodtimulation applications: fabrication, morphology, and electrical properties", *Front. Neuroeng.*, vol. 5, no.8, 2012.

[32] M. R. Abidian, D. C. Martin, "Multifunctional Nanobiomaterials for Neural Interfaces", *Adv. Funct. Mater.*, vol. 9, pp. 573-585, 2009

[33] E. Castagnola, A. Ansaldo, E. Maggiolini et al., "Biologically Compatible Neural Interface To Safely Couple Nanocoated Electrodes to the Surface of the Brain", ACS Nano, vol. 7, no.5, pp 3887–3895, 2013.

[34] B. A. Hollenberg, C. D. Richards, R. Richards, et al., "A MEMS fabricated flexible electrode array for recording surface field potentials", *J Neurosci Methods*; vol. 153, pp. 147–53, 2006.

[35] B. Rubehn, C. Bosman, R. Oostenveld, P. Fries, T. Stieglitz, "A MEMS-based flexible multichannel ECoG-electrode array", *J Neural Eng.*, vol.6, 036003, 2009.

[36] S. Thongpang, T. J. Richner, S. K. Brodnick, et al., "A microelectrocorticography platform and deployment strategies for chronic BCI applications", *Clin EEG Neurosci*, vol. 42, pp. 259–265, 2011.

[37] D. H. Kim, J. Viventi et al., "Dissolvable films of silk fibroin for ultrathin conformal bio-integrated electronics", *Nature Materials*, vol. 9, pp. 511-517.

[38] J. Viventi, D.H. Kim, L. Vigeland, E. S. Frechette, J. A. Blanco, et al., "Flexible, foldable, actively multiplexed, high-density electrode array for mapping brain activity in vivo", *Nature Neuroscience*, vol. 14, no.2, 2011.

[39] A. Lak, E. Arabzadeh, J. A. Harris, M. E. Diamond, "Correlated Physiological and Perceptual Effects of Noise in a Tactile Stimulus", in Proc. 2010 Natl. Acad. Sci. U.S.A., 107, p. 7981–7986.

[40] A. Bonfanti, T. Borghi, R. Gusmeroli, et al., "A Low-Power Integrated Circuit for Analog Spike Detection and Sorting in Neural Prosthesis", in Proc. 2008 Systems IEEE Proc. BioCAS , pp. 257– 260.

[41] T. Borghi, A. Bonfanti, R. Gusmeroli, G. Zambra, et al. "A Power-Efficient Analog Integrated Circuit for Amplification and Detection of Neural Signals", in 2008 IEEE Proc. EMBS , pp 4911– 4915.

[42] L. Maiolo, A. Notargiacomo, M. Marrani, A. Minotti, F. Maita, A. Pecora "Ultra-flexible microelectrode array nanostructured by FIB: a possible route to lower the device impedance", *Microelectronic Engineering*, vol.121, pp. 10-14, 2013,

[43] Y. Sun, S. P. Lacour, R. A. Brooks, et al. "Assessment of the biocompatibility of photosensitive polyimide for implantable medical device use", *Journal of Biomedical Materials Research Part A*, vol. 90A, no. 3, pp.648–655, 2009.

[44] A. Pecora, L. Maiolo, M. Cuscunà, et al., "Low-temperature polysilicon thin film transistors on polyimide substrates for electronics on plastic", *Solid State Electron.*, vol. 52, pp. 348–352, 2008.

[45] H. S. Meyer, R. Egger, J. M. Guest, et al., "Cellular organization of cortical barrel columns is whisker-specific", *PNAS*, vol. 110, no. 47, pp.19113–19118, 2013.

[46] R. Egger, R. T. Narayanan, M. Helmstaedter, et al., "3D reconstruction and standardization of the rat vibrissal cortex for precise registration of single neuron morphology", *PLOS Comput. Biol.,* vol. 8, no. 12, e1002837, 2012.

[47] H. S. Meyer, V. C. Wimmer, M. Oberlaender, et al. "Number and Laminar Distribution of Neurons in a Thalamocortical Projection Column of Rat Vibrissal Cortex" *Cerebral Cortex*, vol. 20, no. 10, pp. 2277–2286, 2010.

Elisa Castagnola received her D.Eng. degree in biomedical engineering and the M.D. degree in bioengineering from the University of Genoa, Genova, Italy, in 2005 and 2007, respectively, and the Ph.D. degree in robotics, neurosciences and nanotechnologies from the Italian Institute of Technology, Genova, Italy, in 2011.
While working toward the Ph.D. degree, she defended the thesis, "Carbon Nanotube Based Coatings for Low Impedance Neural Microelectrodes." Since then, she holds a postdoctoral fellowship in the Robotics Brain and Cognitive Sciences Department at Fondazione Istituto Italiano di Tecnologia. Her current research aim is the improvement of long term performance of intracortical and ECoG microelectrodes for neural recording and stimulation applications.

Luca Maiolo received the Master degree in Physics in 2003 and the Ph.D. in 2008, both from "Università degli studi di RomaTre". In 2009 he joined to Robotics, Brain and Cognitive Sciences Department of Italian Institute of Technology in Genova, as post-doctoral fellow, where he developed and tested tactile flexible
sensors for humanoid robot. Currently, he works as researcher at the Institute for Microelectronics and Microsystems of the National Research Council (CNR-IMM). His activity is mainly focused on fabrication and characterization of electronic circuits and smart sensors integrated on ultrathin flexible substrates.

Emma Maggiolini received the B.S. degree in molecular biology and the Ph.D. degree in biomedical, endocrinological and neurophysiological sciences from The University of Ferrara, Ferrara, Italy, in 2004 and 2008, respectively.
Currently, she is a Researcher/Technologist in the
Department of Robotics, Brain and Cognitive Sciences at the Italian Institute of Technology, Genoa, Italy. Her research interests include the development and testing of innovative technology for neural recording for clinical applications.

This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/TNSRE.2014.2342880, IEEE Transactions on Neural Systems and Rehabilitation Engineering

9

Antonio Minotti is currently working at CNR-IMM in Rome as technician. He received the three-year university degree in Material Science in 2002 from " Università degli studi di RomaTre " in Rome. His research activities have been focused mainly on MEMS systems, C-MUT (Capacitive Micromachined Ultrasonic Transducers) and recently on microfabrication processes and thin-film depositions on flexible substrates.

Marco received the Master degree in in 2009 in "Material Science and Technology" from the University of Rome 'Tor Vergata'. From 2013 he's a PhD student in "Electronic Engineering" at the Institute for Microelectronics and Microsystems of the National Research Council in Rome. He's involved in the CORTICONIC EU project and his studies are focused on design, realization and characterization of sensors on flexible substrate for biomedical applications.

Francesco Maita received the Master degree in Electronics Engineering in 2009 and Ph.D. in "Engineering of sensorial and learning systems" in 2013 both from the University of Rome 'Tor Vergata'. From 2012 he's a research fellow at the Institute for Microelectronics and Microsystems of the National Research Council in Rome. His studies are focused on the design and characterization of flexible electronics as read-out interface for sensors.

Alessandro Pecora was born in Rome in 1962. He received the Master's degree in Physics in 1990 from University of Rome "La Sapienza", with a dissertation on solid-surface electron spectroscopy. From May 1990 he is researcher at National Council of Research (currently at the Institute for Microelectronics and Microsystems) where he is responsible of the activity on devices for large area electronics with specific focus about flexible electronics and smart sensors. He participated in several national and European projects and is currently the coordinator of the robotic project "Factory Technologies for Humans Safety" in the framework of National Manufacturing Platform "Factory of the Future". Currently he also holds the position of Scientific Expert at the Italian Ministry of Foreign Affairs.

Gian Nicola Angotzi received the B.S. and Ph.D. degrees in electronic engineering from the University of Cagliari, Cagliari, Italy, in 2003 and 2007, respectively.
He joined the Robotics, Brain and Cognitive Sciences department at the Istituto Italiano di Tecnologia, Genoa, Italy, as a Postdoctoral Fellow in 2008. Currently he is Researcher Technologist in the Neuroscience and Brain Technologies department and his research interests include low-noise and low-power mixed-signal design for high density neural recording systems.

Alberto Ansaldo received the M.S. degree in electronic engineering and the Ph.D. degree in communication science and technology from the University of Genoa, Genova, Italy.
He mainly worked on chemical vapour deposition of carbon nanotubes for electronic applications. Currently, he is a Research Technologist in the Robotics Brain and Cognitive Science Department of the Italian Institute of Technology, Morego, Genoa, Italy, in the Soft Materials Design Laboratory. His research interests encompass nanoscience, robotics and bioengineering, with a focus on the development of technologies based on novel materials such as conductive polymers, and carbon nanomaterials.

Massimiliano Boffini, after a master in Biomedical Engineering, has accomplished a Ph.D in Robotics, Cognition and Interaction Technology at Istituto Italiano di Tecnologia (IIT), studying a method to realize highly stretchable electrodes by depositing metal on medical grade silicone. From genuary 2014 he works in a company as field clinical engineer in the field of neuromodulation for pain therapy.

Luciano Fadiga received the M.D. degree from the University of Bologna, Bologna, Italy, and the Ph.D. degree in neuroscience from the University of Parma, Parma, Italy.

He is a Professor of Physiology at the University of Ferrara, Ferrara, Italy, and Senior Researcher at the Italian Institute of Technology, Genova, Italy. He has a long experience in electrophysiology in monkeys (single neurons recordings) and humans (transcranial magnetic stimulation, study of spinal excitability, and brain imaging). His current research includes the study of the relationships between action and language and the realization of brain-computer interfaces specifically designed for human use.

Guglielmo FORTUNATO is research director and head of CNR-IMM Rome Unit. His main scientific activity is on the physics and technology of thin film transistors based on inorganic (amorphous and polycrystalline silicon) and organic (pentacene) semiconductors. Recently he focused on the development of low temperature process for the fabrication of TFTs on flexible substrates. He has authored more than 200 papers published on international journals and more than 100 contributions to Proceedings of International Conferences, has presented many oral communications and 33 invited talks in International Conferences and is author of 5 invited chapters on books and holds 10 patents.

Davide Ricci received the MSc degree in Physics and the PhD degree in Electronic Engineering and Computer Science from the University of Genoa, Italy, in 1989 and 1993, respectively.

He is currently Team Leader at the Robotics Brain and Cognitive Science Department of the Italian Institute of Technology, Morego, Genoa, Italy, supervising the Soft Materials Design Laboratory. He has authored or co-authored more than 100 papers in peer-reviewed international journals, conference proceedings, and books. His research interests include the integration of novel materials - conductive polymers, nanocrystals and carbon nanomaterials - with conventional technologies, for the development of devices such as neural electrodes for Brain Machine Interfaces, of flexible nano-actuators and sensors for robotics and of smart interfaces for tissue engineering and prosthetics