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The use of a novel carbon nanotube coated microelectrode array for chronic intracortical recording and microstimulation*

Rebecca A. Parker, Sandeep Negi, Tyler Davis, Edward W Keefer, Harvey Wiggins, Paul A House, Bradley Greger

Abstract— **Micro-electrode arrays (MEAs) have been used in a variety of intracortical neural prostheses. While intracortical MEAs have demonstrated their utility in neural prostheses, in many cases MEA performance declines after several months to years of *in vivo* implantation. The application of carbon nanotubes (CNTs) may increase the functional longevity of intracortical MEAs through enhanced biocompatibility and charge injection properties. An MEA metalized with platinum (Pt) on all electrodes had a CNT coating applied to the electrodes on half of the array. This Pt/Pt-CNT MEA was implanted into feline motor cortex for >1 year. Recordings of action potentials and 1 kHz impedance measurements were made on all electrodes to evaluate device functionality. Additionally, electromyogram (EMG) responses were evoked using micro-stimulation via the MEA to measure device performance. These metrics were compared between Pt and Pt-CNT electrodes. There was no significant difference in the data acquisition or micro-stimulation performance of Pt and the Pt-CNT electrodes. However, impedances were lower on the Pt-CNT electrodes. These results demonstrate the functionality of CNT coatings during chronic in vivo implantation. The lower impedances suggest that for microstimulation applications CNT coatings may impart enhanced interface properties.**

I. Introduction

Micro-electrode arrays (MEAs) are promising devices that enable bidirectional communication with the central nervous system. MEAs provide a high-selectivity method for recording information from and imparting information to neural tissue. While MEAs have already proven their utility for clinical neural prosthetic applications [1], it has been noted that over time, the ability of MEAs to obtain high-yield, stable action potential recordings decreases [2], [3], [4]. Many underlying causes have been hypothesized to account for these dynamics in performance, including device damage, cortical plasticity, and the tissue response to the implant. Tissue response is a particularly complicated problem that is known to occur with any type of injury to the cortex. It comprises a complex, interconnected network of mechanisms, including macrophage activation, disruption of the blood brain barrier, and glial scarring, all of which can cause both neuronal death and changes in neuronal signaling [5], [6]. Many surface modification intervention strategies have been tested in order to attenuate the tissue response, and thus improve long-term MEA performance in cortical applications [7], [8]. One such promising modification is the use of carbon nanotubes (CNTs) [9]. CNTs have a variety of beneficial electrical properties, such as high capacitive charge injection limits and high conductivity which make them ideal for use in electronic interfaces with the brain. Furthermore, CNTs offer a variety of methods for the attachment of biomolecules, including covalent modification, non-covalent attachment, and biomolecule wrapping [10]. CNT coatings have been shown to improve neuronal recordings [11]. In this study, we further characterized the long-term performance of a CNT coating applied to a chronic intracortical MEA used for both microstimulation and recording, in order to determine if the beneficial electrical properties imparted enhanced stimulation ability, and to ensure that CNTs do not adversely affect long-term MEA performance.

II. Methods

A. Micro-electrode array

The MEA used in this study was a commercially obtained 96-electrode platinum (Pt) Utah Electrode Array (Blackrock Microsystems, Inc.). 48 of the 96 electrodes were coated with commercially obtained multiwalled CNTs (CheapTubes, Inc.) by Plexon, Inc. as described in [11]. Prior to implantation, the array was imaged under scanning electron microscope (Figure 1), and electrochemical impedance spectroscopy and cyclic voltammetry (Figure 2) were performed to confirm the presence of the CNT coating.

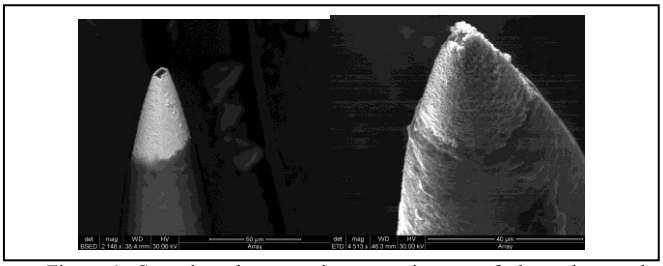

Figure 1. Scanning electron microscope images of electrodes on the CNT/CNT-Pt array prior to implantation. While CNTs could not be visually verified, their presence was confirmed using cyclic voltammetry and electrochemical impedance spectroscopy. The general integrity of the MEA and the metallization on electrode tips was found to be adequate for implantation.

B. Feline implant

Implantation was conducted in January of 2011 by a clinical neurosurgeon. Implantation procedures followed those described in [4]. Briefly, the cortex was exposed over

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R. A. Parker is with the Interdepartmental Program in Neuroscience, University of Utah, Salt Lake City, UT 84112 USA (phone: 801-865-8029; e-mail: parker.becca@gmail.com).

S. Negi is with the Electrical and Computer Engineering Department, University of Utah, Salt Lake City, UT 84112

T. S. Davis and B. Greger are with the Bioengineering Department, University of Utah, Salt Lake City, UT 84112

E.W. Keefer and H. Wiggins are with Plexon, Inc., Dallas, TX 75206

P.A. House is with the Department of Neurosurgery, University of Utah, Salt Lake City UT 84132

the right motor cortical region, and the array was pneumatically inserted to minimize tissue disruption. The array was then covered with a silicon polymer, the percutaneous connector was attached to the skull using bone screws, and the scalp was sutured shut. The animal was given 48 hours to recover prior to attempting data acquisition.

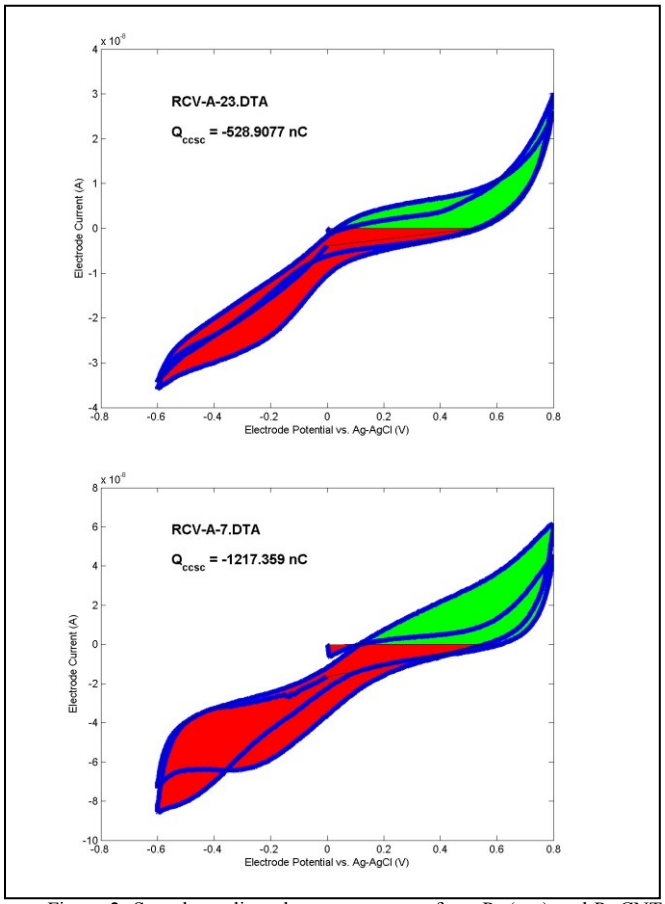

Figure 2. Sample cyclic voltammetry traces from Pt (top) and Pt-CNT electrodes (bottom) taken prior to implantation. Both cyclic voltammetry and electrochemical impedance spectroscopy confirmed the presence of CNTs on half of the array.

C. Neural data acquisition

Neural recordings were obtained daily for the first 90 days following implantation, and at least weekly for the subsequent 3 months. Recordings were made using a patient cable, amplifier, and Cerebus system from Blackrock Microsystems, Inc. Sample data is shown in Figure 3. During data acquisition, the awake animal was placed in a standard pet carrier and the patient cable was attached to the percutaneous connector. The animal was allowed to behave as normal during two 5-minute recordings, band-pass filtered at 0.3Hz – 7.5 kHz and acquired at 30 kHz. Following neural data acquisition, 1 kHz impedance measurements were made using a proprietary mechanism built into the Blackrock patient cable.

D. Micro-stimulation and electromyogram

During micro-stimulation sessions, the feline was anesthetized with Telazol in order to prevent spontaneous movement. Micro-stimulation was performed under current control using an IZ2 system fed through the feline's percutaneous connector (Tucker-Davis Technologies, Inc.) The voltage excursion of this system is ±15V, allowing for micro-stimulation currents of up to 300 µA across a 50 kOhm load. Stimulation amplitude was varied from 50-300 µA in intervals of 50 µA. Trains of 25 biphasic pulses, at pulse durations of 0.2-1 msec, were applied one electrode at a time to all electrodes of the array on two occasions in order to determine the amplitude of current required to evoke a motor response. Motor responses were sampled at 25 kHz using an Intan amplifier board (Intan Technologies, Inc.) and bipolar fine-wire electrodes placed in the hind limb, trunk, and neck muscles of the feline. Data acquired using the Intan board, recording of stimulation parameters through the Cerebus system, and information from the stimulator was synchronized using in-house Matlab (The Mathworks, Inc.) code.

E. Data analysis

Action potentials were extracted from the 0.3Hz – 7.5 kHz data using a modified t-dist EM principal component analysis algorithm [12]. Following spike sorting, a 90 µA threshold was applied to sorted action potential data in order to remove noise clusters using in-house Matlab code. All local field potential, impedance, and statistical analysis was also performed using in-house Matlab code.

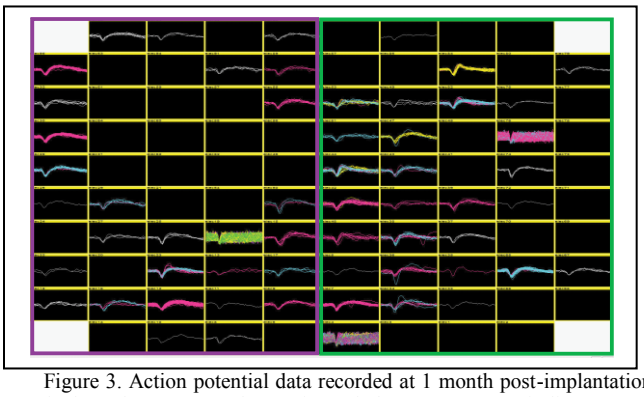

Figure 3. Action potential data recorded at 1 month post-implantation. Purple box denotes Pt-only portion of the array; green indicates CNT coated electrodes. Note similar numbers of well-formed action potentials on both sides of the array, as well as noise recordings on both portions.

III. Results

Results of recordings, stimulation, and impedance measurements were compared between the Pt-only and CNT portions of the array as an internal control. Further comparisons were made between the long-term performance of the novel array and sputtered iridium oxide film arrays previously implanted in the same intracortical feline preparation by our group [4].

A. Pt and CNT electrodes exhibit similar recording performance

Number of well-isolated action potentials was used as a measure of performance over time. As seen in Figure 4, the number and amplitude of recorded well-isolated action potentials changed over time, but there was not a significant difference in the number of action potentials recorded

between Pt and CNT portions of the array. The yield over time of action potentials recorded was similar to the fade-in, high yield, fade-out pattern observed in SIROF array animals [4].

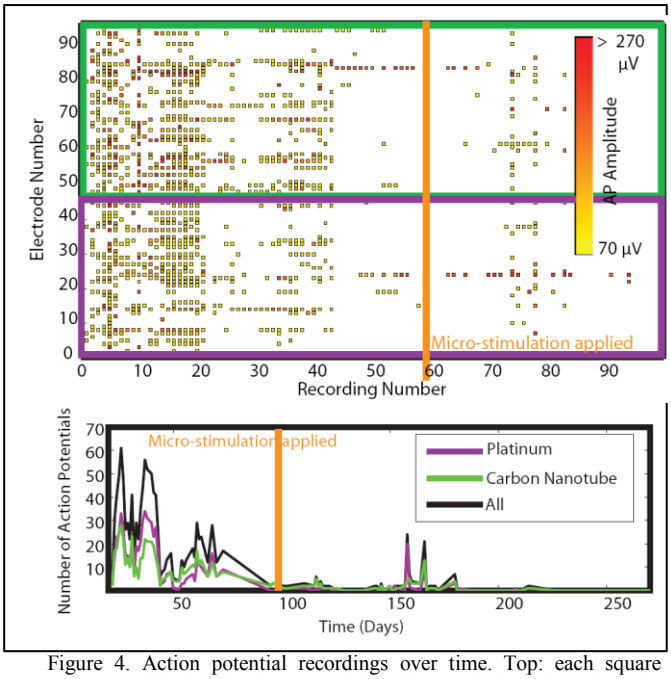

Figure 4. Action potential recordings over time. Top: each square represents a well-isolated action potential, with amplitude indicated by the color of the square. Purple box denotes Pt electrodes, while green box denotes CNT. The orange line represents the first application of micro-stimulation. The ability to record action potentials was maintained following micro-stimulation. Bottom: yield of action potentials, Pt yield, and CNT yield.

B. *CNT coated electrodes retain the ability to stimulate to physiological effect*

Stimulation sessions were performed on all electrodes of the array, one at a time, on two separate occasions, with EMG recordings as a measure of efficacy. Shown in Figure 5 is a sample mean binned rectified EMG response across 5 100 Hz trains of 25 biphasic pulses, 0.4 msec/phase and 100 µA current on a stimulated CNT channel. Few such response were evoked on either side of the array, but were evoked via micro-stimulation of both Pt and CNT channels.

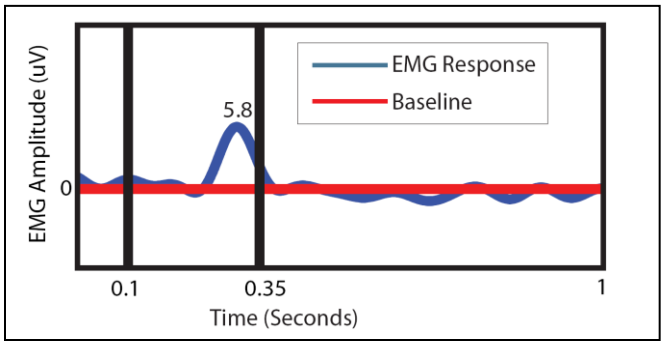

Figure 5. Example of mean binned rectified electromyographic response to stimulation applied. Stimulation was applied in 25 biphasic pulses at 100 Hz between 0.1 and 0.35 seconds on a CNT electrode following >3 months of implantation. Muscle twitches such as this one recorded via electromyogram were used to indicate efficacy.

C. *CNT electrodes retain significantly lower impedances than bare Pt electrodes*

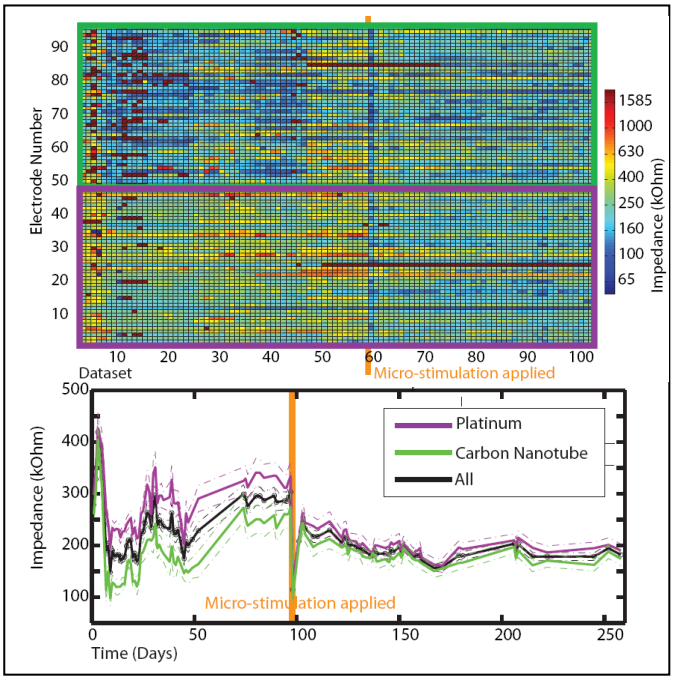

Figure 6. 1 kHz impedance measurements over time. Top, each box represents the impedance on one electrode during one data acquisition session. The value of the impedance is denoted by the color of the box. CNT electrodes are outlined in green, Pt electrodes in purple. The impedances for the CNT portion of the array were lower than that of the Pt. Impedance decreased abruptly following the initial micro-stimulation session, shown by the orange bar. Bottom, mean impedances across days.

1 kHz impedance measurements were used to evaluate the state of the electrode-tissue interface over time (Figure 6). It was found that CNT electrodes exhibited lower impedances over time (Wilcoxon's signed rank test, $p < 0.05$). Furthermore, the pattern of mean impedance followed a similar pattern to that previously observed in animals implanted with SIROF arrays for both Pt and CNT electrodes, namely, an initial increase to a plateau value followed by fade out over time. Impedances did decrease acutely with the application of micro-stimulation on both Pt and CNT electrodes, but recovered towards baseline after 24 hours.

IV. Discussion

A. *Chronic recording performance*

Action potential yield followed a fade-in (low yield during the first days), high-yield (plateau over several weeks), fade-out (gradual decline in yield) pattern similar to that described in [3] and [4], which is generally accepted as the time course of recording performance for most MEAs. This pattern may be a result of the tissue response to the implant. The initial trauma of implantation is known to disrupt the local vasculature, which may cause the initial low yield of action potentials. Over the first few days of implantation this response clears and gives way to the chronic response, during which time the yield of action

potentials increases. Over time, however, the glial scar may push neurons outside the recording radius of electrodes, lead to neuronal death, or cause neurons to cease signaling, which may result in the observed fade-out of action potential yield. As no significant differences were observed between CNT and Pt portions of the array, it seems that CNTs do not exacerbate this tissue response. Furthermore, nine months of action potential recordings demonstrate that tissue is still viable in the 100-200 microns surrounding the electrode tips during this time.

B. Impedance measurements

Impedance measurements on both Pt and CNT electrodes also followed patterns previously observed in the literature, namely, impedances gradually increased over the first few weeks of implantation, consistent with the formation of a glial scar [13]. Impedances decreased after reaching this high point for the duration of the implant, which may reflect changes in the ionic environment surrounding the electrodes.

Mean impedance of the CNT electrodes was significantly lower than the Pt electrodes. This is consistent with pre-implantation impedance spectroscopy (mean 1 kHz impedance for Pt = 231.98±107.8, CNT = 49.71±5.07) and is expected both due to the electrical properties of CNTs as well as the increased geometric surface area resultant from the application of a coating. This lower impedance was maintained for the duration of the implant, suggesting that the CNT coating was retained throughout processes of implantation and tissue response. Furthermore, it suggests that CNTs may retain an increased conductivity when compared to Pt even following multiple months of implantation.

Impedances dropped acutely with the application of stimulation on both Pt and CNT, but recovered towards pre-stimulation values. This is consistent with findings in the literature [4]. Such acute drops in impedance suggest that acute electrochemical changes occur in the electrode, device damage occurs, or that some disruption of the tissue response surrounding the electrode results from stimulation. While it is unclear to what extent each of these processes plays a role in the observed phenomenon, the recovery of impedances towards baseline suggests that the effect is not only reversible, but that no permanent damage to the electrodes or CNT coating occurred.

C. Conclusions and future directions

Performance of CNT electrodes over several months of intracortical implantation and micro-stimulation was similar to both internal Pt controls and previously observed SIROF MEAs in many respects, including yield of action potential recordings, impedance dynamics, and ability to stimulate to effect. While CNTs did not show enhanced action potential recording ability, as their electrical properties might suggest, it is hoped that their ability to scaffold biomolecules will prove useful in attenuating tissue response and thus enhancing performance. Work is underway to determine if the lower impedances of CNT electrodes correspond with an enhancement of stimulation ability, i.e. an ability to stimulate to effect on more electrodes with lower currents than Pt counterparts.

Histology on the implant is underway, in order to determine the effect of CNTs on tissue. Local field potentials were also recorded during neural data acquisition, and an analysis of the LFP recording performance of CNT electrodes compared to Pt is also being performed. It is expected that CNTs will show an enhanced recording ability in some frequency bands of neural data, which could potentially be used for neural decodes.

This pilot study has demonstrated that CNTs perform similarly to Pt in chronically implanted devices. It is hoped that these results will encourage further chronic *in vivo* studies of CNTs to systematically determine their potential for recording and microstimulation in neural prosthetic devices.

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