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Electrical performance of penetrating microelectrodes chronically implanted in cat cortex

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Abstract— **Penetrating multielectrode arrays with electrode coatings of sputtered iridium oxide (SIROF) have been implanted chronically in cat cortex for periods over 300 days. The ability of these electrodes to inject charge at levels above expected thresholds for neural excitation has been examined *in vivo* by measurements of voltage transients in response to current-controlled, cathodal stimulation pulsing. The effect of current pulse width from 150 μs to 500 μs and voltage biasing of the electrodes in the interpulse period at two levels, 0.0 V and 0.6 V vs. Ag|AgCl, were also investigated. The results of *in vivo* characterization of the electrodes by open-circuit potential measurements, cyclic voltammetry and impedance spectroscopy are also reported.**

I. INTRODUCTION

NEURAL stimulation and recording electrodes for intracortical applications involving highly localized and selective neural excitation or recording of single-unit activity, require coatings that provide higher charge-injection capacities and lower impedance than is typically possible with noble metal electrodes [1], [2]. Penetrating multielectrode arrays suitable for intracortical or intraneural stimulation and recording, originally developed at the University of Utah and commonly known as the Utah Array [3], [4], have been coated with sputtered iridium oxide (SIROF) as a low impedance, high charge capacity electrode coating [5]. The SIROF electrodes have been implanted chronically in cat sensorimotor cortex and the stability of neural recordings and the stimulation charge-injection properties for implantation periods from 32 days to over 300 days. In the present work, the stimulation charge-injection properties of the electrodes are reported and analyzed with respect to the long-term capability of the SIROF coatings to provide charge injection above expected functional thresholds without exceeding the potential for water reduction, which is a presumed maximum safe charge-injection limit [1], [2]. *In vivo* cyclic voltammetry and impedance have been compared with measurements prior to implantation in an effort to quantify changes occurring over the course of the implantation period.

II. EXPERIMENTAL

A. Multielectrode Arrays

Multielectrode arrays were fabricated at Blackrock Microsystems using methods that have been described previously [3], [4]. Briefly, each array was fabricated with 16 electrode shafts in a 4 x 4 arrangement and tip-to-tip separation of 400 μm. The electrode tips, which have a nominal geometric area of 2000 μm^2, were coated with sputtered iridium oxide (SIROF) following the procedure described by Cogan *et al.* for coating planar polyimide multielectrode arrays [6], [7]. Each implantable assembly contained two 16-electrode arrays connected to a head-mounted percutaneous connector. The arrays were implanted bilaterally in the sensorimotor cortex of cats.

B. Electrochemical Characterization

Prior to implantation, each SIROF electrode was characterized by cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). The measurements were made in an inorganic electrolyte model of interstitial fluid (model-ISF) having a composition NaCl 110 mM, $NaHCO_3$ 28 mM, $KHCO_3$ 7.5 mM, Na_2HPO_4-$7H_2O$ 2 mM, and 0.5 mM each of NaH_2PO_4-H_2O, $MgSO_4$,

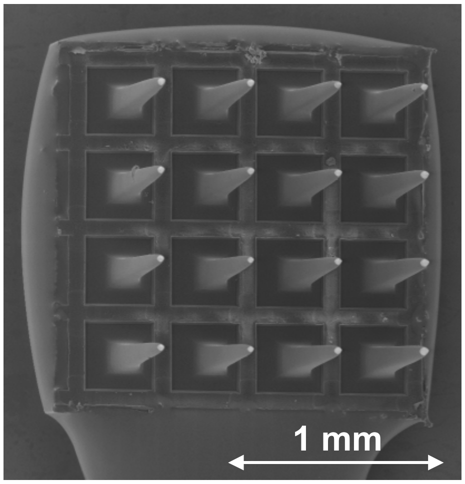

Fig. 1. Scanning electron micrograph of a 16-shaft penetrating microelectrode array with a 400 μm spacing between electrode tips

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$MgCl_2$, and $CaCl_2$ [8]. The pH of model-ISF was maintained at 7.4 by bubbling $5\%CO_2/6\%O_2/89\%N_2$ gas through the electrolyte. All measurements in model-ISF were made at 37^oC. Electrochemical measurements were made in a three-electrode cell using a large-area platinum counterelectrode and a Ag|AgCl reference electrode. All potentials are reported with respect to Ag|AgCl.

CV measurements were made at either 50 mV/s or 50,000 mV/s between potential limits of –0.6 V and 0.8 V. The 50 mV/s CVs were used to calculate the cathodal charge storage capacity (CSC_c), which estimates the amount of available SIROF at the electrode tip and is determined from the time integral of the negative current during a full CV cycle [1]. The EIS measurements were made in model-ISF over a 1 – 10^5 Hz frequency range using a 10 mV rms sinusoidal excitation voltage about a fixed potential of 0.0 V. The impedance data are reported as impedance magnitude versus frequency.

Charge-injection characteristics were determined from potential transients measured during current pulsing. A Sigenics stimulator (Chicago, IL) that delivers monophasic cathodal current pulses from a potentiostatically controlled interpulse bias was used for the pulsing studies. This strategy maintains charge-balance by reestablishing the bias potential in the interpulse period using an anodic recharge current that is sufficient to establish the bias within a few milliseconds of the cathodal pulse [1], [9]. The stimulator is designed to limit the recharge current so that the microelectrode cannot be polarized more positively than the 0.8 V water oxidation limit observed with iridium oxide or platinum electrodes. An interphase period of 1.1 ms between the end of the cathodal pulse and the onset of the anodic recharge current was employed to facilitate analysis of the voltage transients. The maximum negative potential excursion was determined from the transient waveform as the electrode potential immediately after the end of the cathodal current pulse [1]. For all conditions, pulses were delivered at a frequency of 50 Hz.

C. *In Vivo Measurements*

Pairs of microelectrode arrays were implanted bilaterally in the sensorimotor cortex of cats, resulting in 32 electrodes per animal. For electrochemical measurements, a chloridized silver flag and a platinum mesh were placed on the animal's forelimb as reference and counter electrodes, respectively. The forelimb was shaved and electrical contact with the skin maintained with saline-soaked gauze. The electrodes were secured with an elastic bandage. The cat was lightly anesthetized during the measurements.

III. RESULTS

A. *Cyclic Voltammetry*

A representative CV response from one electrode prior to implantation and after 32, 117, and 168 days *in vivo* is shown in Fig. 2. The cathodal charge storage capacity of the electrode increases as a function of time from a pre-implantation level of 24 mC/cm^2 to 41 mC/cm^2 after 168 days. The magnitude of the increase in CSC_c *in vivo* can be large as shown by the comparison in Fig. 3 of the CV response of five electrodes from one array in model-ISF prior to implantation and after 194 days *in vivo*. In this animal, the average CSC_c increases from 36±7 mC/cm^2 (mean±sd n=5) to an *in vivo* value of 135±21 mC/cm^2. While the magnitude of the CSC_c increase varied between electrode arrays, an increase in CSC_c at 50 mV/s was observed for most electrodes over the course of implantation. Mean CSC_c values averaged over all electrodes and animals, for which neural activity was observed, are shown in Fig. 4 as a function of implantation time. The increase in CSC_c appears approximately linear with time as shown by the regression line in Fig. 4. Electrodes that did not exhibit normal neuronal recordings or were obviously non-functioning due to open interconnections were excluded from the analysis. The increase in CSC_c is probably due to current contributions associated with electrolyte leakage under the Parylene insulation at the electrode tip or other leakage paths between the SIROF electrodes and the return electrode on the animal.

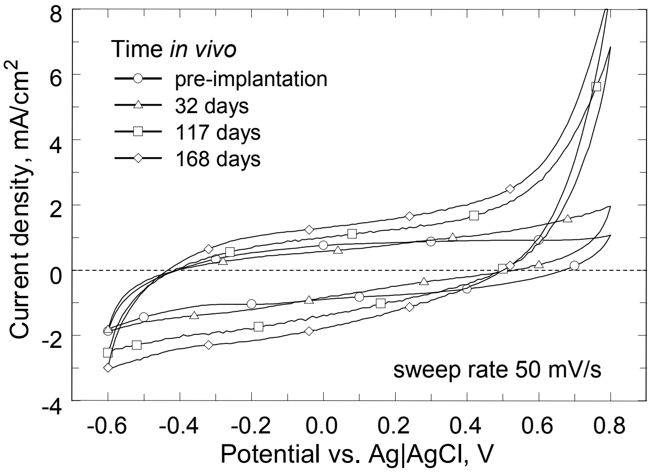

Fig. 2. Representative cyclic voltammograms from a SIROF-coated microelectrode *in vitro* and after 32, 117, and 168 days *in vivo*.

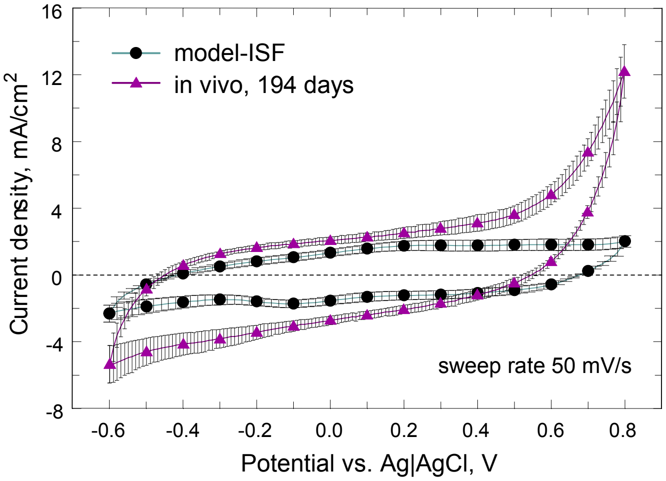

Fig. 3. Averaged CV response for five electrodes on one array in model-ISF prior to implantation and after 194 days *in vivo*. Sweep rate 50 mV/s.

Cyclic voltammetry measurements at a sweep rate of 50,000 mV/s had the opposite behavior to that observed at 50 mV/s, with the *in vivo* CV showing lower currents and a reduced CSC_c compared with *in vitro* measurements in model-ISF. The average CV response from six electrodes on one array measure in model-ISF prior to implantation and 194 days post-implantation is compared in Fig. 5. The average CSC_c decreased from 16±2 mC/cm^2 in model-ISF to 6±1 mC/cm^2 *in vivo* (mean±sd n=6). The high sweep rate cyclic voltammetry reflects processes occurring at the exposed electrode tips and the observed reduction in CSC_c is presumed to be due to higher tissue resistance and reduced counterion transport *in vivo* [1].

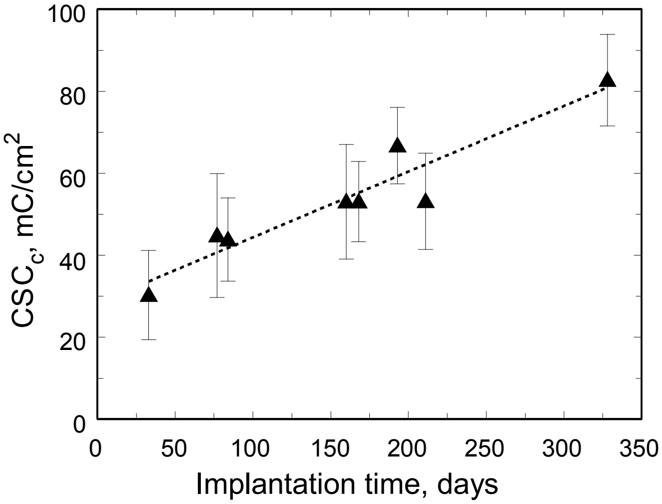

Fig. 4 Cathodal charge storage capacity measured at 50 mV/s averaged over the total number of implanted electrodes studies as a function of time. Error bars are standard deviations.

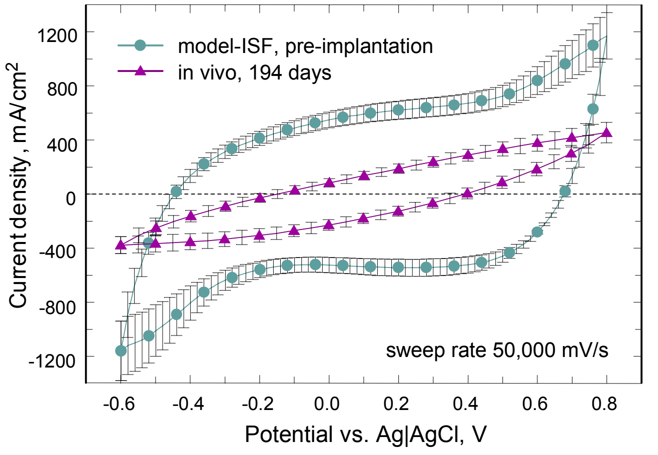

Fig. 5. Comparison of the average CV response of six electrodes pre-implantation in model-ISF and after 194 days *in vivo*. Sweep rate 50,000 mV/s.

B. Impedance Spectroscopy

Impedance measurements over time were consistent with the CV behavior. A general trend towards modestly decreasing impedance over the 1-10^5 Hz was observed with implantation time. A representative example of the impedance behavior is shown in Fig. 6. As anticipated, at higher frequencies, the impedance of the implanted electrodes is generally higher than that of the electrode *in vitro* due to the lower conductivity of tissue and presumably tissue encapsulation around the electrode tip. At 32 days implantation, the low frequency (<10 Hz) *in vitro* and *in vivo* impedance are comparable. However, for longer implantation times the low frequency *in vivo* impedance decreases to values lower than the corresponding pre-implantation impedance. Similar to the comparison between pre-implantation and long-term *in vivo* CV behavior, the decrease in low frequency impedance to values lower than that observed *in vitro* can be broadly interpreted as an increase in the apparent surface area of the electrodes.

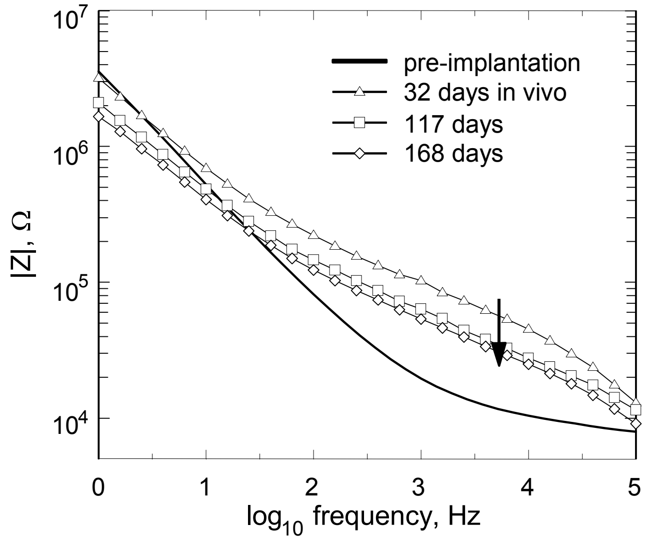

Fig. 6. A representative example of the change in electrode impedance over the course of 168 days implantation. The pre-implantation, *in vitro* impedance is shown for comparison. The arrow indicates the direction of impedance change with implantation time.

The average 1 kHz impedance magnitude recorded from each electrode array at time points from 32 days to 277 days implantation is shown in Fig. 7. The large initial variability in the impedance is probably due to variations in the exposed geometric surface area of the individual electrodes on each array, which has been shown previously to have a significant impact on the electrochemical properties of these electrodes in vitro [5]. The regression line in Fig. 7 suggests that the impedance decreases with implantation time, although the effect is not as strong as observed for the increase in CSC_c with time.

C. Voltage Transients

Voltage transients measured in response to 8 nC/ph (400 µs) current pulses at 50 Hz are shown in Fig. 8 for 12 electrodes on one array *in vivo*. Four electrodes were not characterized due to intermittent electrical contact. The electrodes were pulsed from an interpulse potential (V_{ipp}) of 0.6 V (Ag|AgCl) to maximize charge-injection capacity [10, 11]. The maximum cathodal potential excursion (E_{mc}) for all electrodes pulsed was well positive of the -0.6 V (Ag|AgCl) potential for water reduction on SIROF.

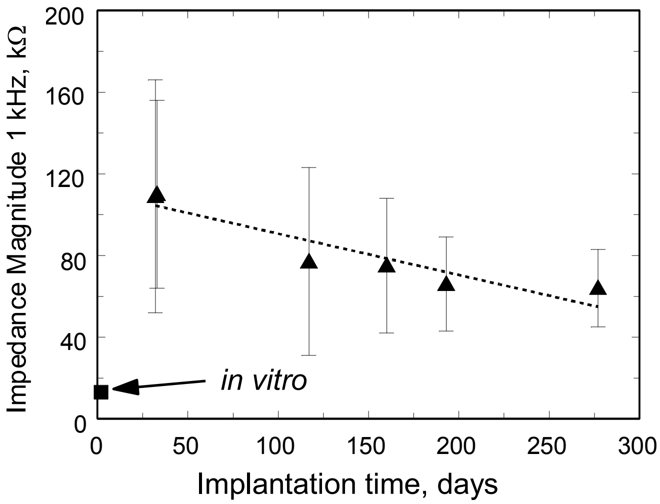

Fig. 7. Mean impedance magnitude at 1 kHz averaged over the total number of implanted electrodes studies as a function of time. Error bars are standard deviations.

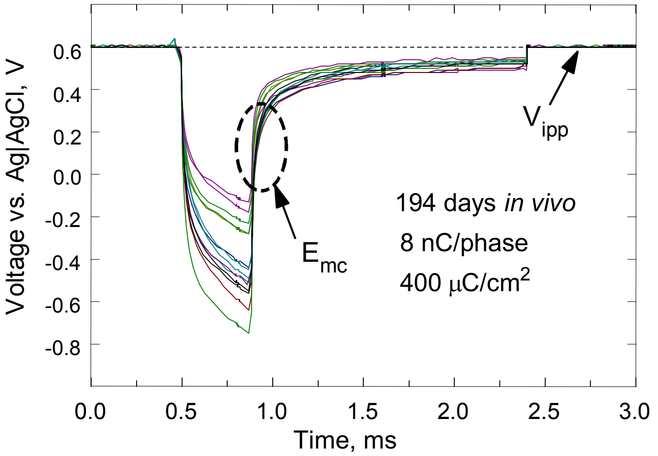

Fig. 8. Voltage transients for 12 electrodes on one array pulsed cathodally at 8 nC/ph (400 μs pulse width, 20 μA current, 50 Hz) corresponding to a nominal charge-injection density of 400 μC/cm^2. The measurements were made 194 days post-implantation.

The SIROF-coated electrodes were capable of supporting charge levels well-above anticipated thresholds for neural excitation with indwelling cortical electrodes, which are typically ~1 nC/phase [12] [13]. However, *in vivo*, the SIROF equilibrated to an open-circuit potential of about 0 V vs. Ag|AgCl and pulsing at 8 nC/ph from an interpulse bias of 0 V (Ag|AgCl) occasionally resulted in electrode polarization beyond the water reduction potential. Based on these observations, and using the avoidance of water reduction potentials as a criterion for maximum cathodal charge injection, 8 nC/phase (400 μC/cm^2) was found to be a reasonable maximum for injecting charge with these electrodes using 20 μA current pulses from a 0 V interpulse potential. Higher charge-injection levels are readily obtained by employing a positive potential bias in the interpulse region, although the long-term consequences of the low net dc current associated with maintaining a non-equilibrium potential have not been fully explored.

While some changes in the electrochemical properties of these electrodes have been observed *in vivo*, robust single-unit neural recordings have been obtained beyond 200 days implantation.

IV. CONCLUSION

Penetrating microelectrodes employing sputtered iridium oxide charge-injection coatings have been evaluated electrochemically for over 300 days in cat cortex. Over this implantation period, at both a 0 V and 0.6 V interpulse bias, the charge-injection capacity of most electrodes was sufficient to support a cathodal charge density of 400 μC/cm^2 without exceeding the water reduction potential. The changes in charge storage capacity and impedance over the same period suggest an increase in the apparent surface area of the electrodes, possibly due to slowly developing leakage current paths. These leakage currents result in some overestimation of the injected charge density.

REFERENCES

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

[2] D. R. Merrill, M. Bikson, and J. G. R. Jefferys, "Electrical stimulation of excitable tissue: design of efficacious and safe protocols," *J. Neurosci. Methods* vol. 14, pp. 171-198, 2005.

[3] P. J. Rousche, and R. A. Normann, "Chronic recording capability of the Utah Intracortical Electrode Array in cat sensory cortex. *J. Neurosci. Methods,* vol. 82, pp. 1-15, 1998.

[4] A. Branner, R. B. Stein, and R. A. Normann, "Selective stimulation of cat sciatic nerve using an array of varying length microelectrodes," *J. Neurophysiology,* vol. 85, pp. 1585-1594, 2001.

[5] S. F. Cogan, J. Ehrlich, T. D. Plante, and R. Van Wagenen, "Penetrating microelectrode arrays with low-impedance sputtered iridium oxide electrode coatings," *Conf Proc IEEE Eng Med Biol Soc.*, 7147-50, 2009,

[6] S. F. Cogan, J. Ehrlich, T. D. Plante, A. Smirnov, D. S. Shire, M. Gingerich, and J. F. Rizzo, "Sputtered iridium oxide films (SIROFs) for neural stimulation electrodes*," J. Biomed. Mater. Res, B Appl. Biomater.*, vol. 89B, pp. 353-361, 2008.

[7] J. O. Winter, S. F. Cogan, and J. F. Rizzo *Neurotrophin-eluting hydrogel coatings for neural stimulating electrodes,* J Biomed Mater Res B Appl Biomater. vol 81B, pp. 551-563, 2007.

[8] S. F. Cogan, P. R. Troyk, J. Ehrlich, C. M. Gasbarro, and T. D. Plante, "The influence of electrolyte composition on the in vitro charge-injection limits of activated iridium oxide (AIROF) Stimulation Electrodes," *J. Neural Eng.,* vol. 4, pp. 79-86, 2007.

[9] P. R. Troyk, D. E. Detlefsen, S. F. Cogan, J. Ehrlich, M. Bak M, D. B. McCreery, L. Bullara, and E. Schmidt, "'Safe' charge-injection waveforms for iridium oxide (AIROF) microelectrodes," *Conf Proc IEEE Eng Med Biol Soc.* vol. 6, pp. 4141-4144, 2004.

[10] S. F. Cogan, P. R. Troyk, J. Ehrlich, and T. D. Plante, "In vitro comparison of the charge-injection limits of activated iridium oxide (AIROF) and platinum-iridium microelectrodes," *IEEE Trans Biomed Eng.*, vol. 52, pp. 1612-1614, 2005.

[11] S. F. Cogan, P. R. Troyk, T. D. Plante, J. Ehrlich, and D. E. Detlefsen, "Potential-biased, asymmetric waveforms for charge-injection with activated iridium oxide (AIROF) neural stimulation electrodes," *IEEE Trans Biomed. Eng.* vol. 53, pp. 327-332, 2006.

[12] D. B. McCreery, W. F. Agnew, and L. A. Bullara, "The effects of prolonged intracortical microstimulation on the excitability of pyramidal tract neurons in the cat." Ann Biomed Eng., vol. 30, pp. 107-119, 2002.

[13] D. B. McCreery, T. G. H. Yuen, and L. A. Bullara, "Chronic microstimulation in the feline ventral cochlear nucleus: physiologic and histologic effects," *Hearing Res.*, vol. 149, pp. 223-238, 2000.