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Charge Storage: Stability Measures in Implantable Electrodes

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Abstract— **Here we report on long-term (300 to 600 hours) stability measures for implantable stimulating electrodes. We have considered several measures of stability as they refer to reliability of charge carrying capacity in implantable electrodes. We have designed and manufactured coatings for large area (1 to 2mm^2) stainless steel substrates. Materials tested were electrodeposited iridium oxide films, multi-walled carbon nanotube mesh, and PEDOT:PSS. Traditional characterization techniques such as cyclic voltammetry and electrochemical impedance spectroscopy cover a small fraction of the characterization framework needed for ensuring the safety and performance of electrodes designed for long-term implants. The stability measures suggested here rely on continuous low frequency cycling and evaluation of cathodic charge storage capacity during cycling. We experimentally show, in this paper, that the stability may be measured and is relevant for long-term applications of such coatings.**

I. INTRODUCTION

ACTIVITY in deep brain structures can be modulated by electric fields applied across neuronal populations. Neuro-disorders are no special case: they are, as the healthy brain, also amenable to such modulation. This idea has been widely used to improve the health of patients over long-term (5 to 10 years) [1]. While the success of stimulation of deep brain structures has driven the implantable device technology to its use in the clinic at a fast pace, the mechanisms of brain and body reaction to such implants have not been elucidated [2], and the requirements for long term implantable electrodes remain to be explicitly written. A better understanding of the chemical stability of electrodes is crucial to the design of better electrode-electrolyte interfaces for *in vivo* use. This problem has been traditionally tackled with methods based on materials research. With new coatings being developed which combine conductive polymers and non-conductive materials, along with the long term implantation in DBS-like applications, the stability of the interface gains relevance: coatings of electrodes need to withstand shear forces of implantation, as well as immediate protein adsorption, and, over time, glial reaction. Here we propose that the *in vitro* stability tests for newly designed electrodes are as relevant as the traditional short term cyclic voltammetry and electrochemical impedance spectroscopy [3],[4], and much more applicable as a characterization tool for long-term (longer than 1 month *in vivo*) applications. We use iridium oxide film, PEDOT:PSS (Poly(3,4-ethylenedioxy-thiophene):poly (styrenesulfonate)), and multi-walled carbon nanotube (MWNT) electrodes to show results on chemical stability for several electrode conditions over periods of 300 to 600 hours of low frequency cycling.

II. ELECTRODE PREPARATION

Coatings were deposited on metallic substrates as described below. Electrodes were subsequently characterized as-prepared or after aging. Aging has been show to modify surface state and thus also impact charge storage capacity. Electrodes are aged between 30days (carbon nanotubes) and 3 years (iridium oxide).

A. Iridium oxide film

Iridium oxide film is electrochemically deposited onto stainless steel substrates [5],[6],[9]. Briefly, working and reference electrodes are immersed in iridium tetrachloride solution (40mM), and 1600 cycles of a voltage controlled triangular waveform is applied between the two electrodes. The scan rate is 100mV/s, with voltages varying from 0 to 0.5V. Then a 1Hz square wave is applied with the same voltage range, but for 2000 cycles. We have tested several substrate sizes, with diameters ranging from 25µm to 250µm 316LVM medical grade stainless steel wire. Insulation on the tested substrates was Teflon (PTFE), polyimide, or parylene. Exposed metallic areas range from 100µm^2 to 2.5mm^2. Unless otherwise stated, the results reported here refer to coatings applied to substrates with exposed areas of 0.7mm^2 and 2.5mm^2.

B. Multi-walled carbon nanotubes

Functionalized (-COOH)MWNT are acquired from a commercial source. As described in detail by our group [8],[9],[10], we use DC (2V) for 5min to electrodeposit a MWNT mesh onto stainless steel substrates with diameter ranging from 25 to 250µm. The surface areas are matched to the iridium oxide deposition. Electrodeposition is realized with a DC-power source and controlled voltage. Current is measured in order to verify deposition. The counter electrode is gold or platinum.

C. PEDOT:PSS

We employ potentiostatic electrochemical polymerization to deposit PEDOT:PSS over stainless steel substrates [11]. Electrodeposition takes place with electrodes immersed in

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an air-equilibrated solution (deionized water) containing ethylenedioxythiophene (EDOT) monomer and polyoxyethylene 10-lauryl ether, along with poly(sodium 4-styrenesulfonate) (PSS). PEDOT is electrochemically formed on the working electrode through voltage controlled deposition.

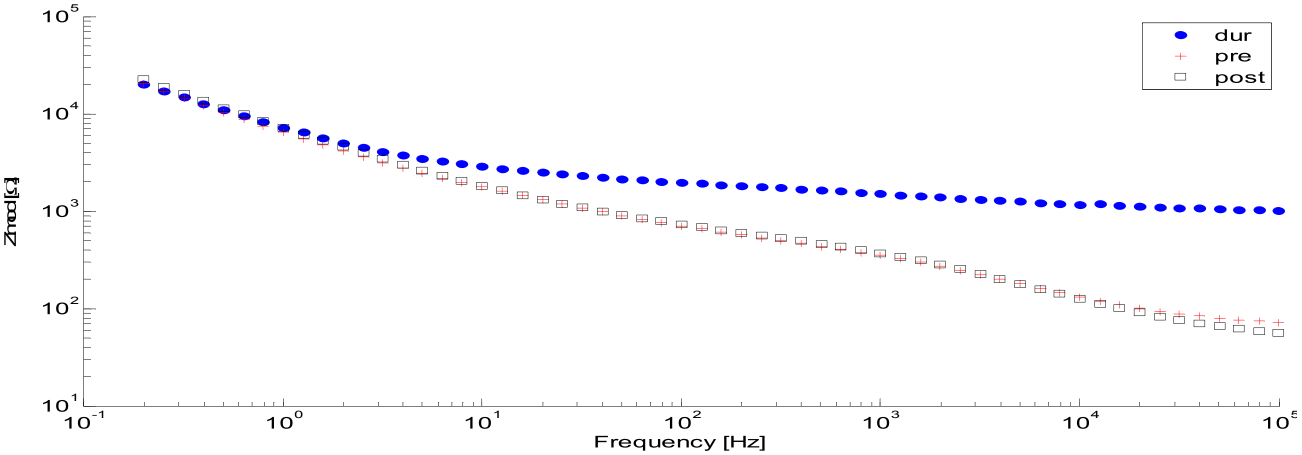

Fig. 1. Electrochemical impedance spectroscopy of an iridium oxide film coated electrode before (red) implantation, during surgery (blue), and after surgery (black squares). Modulus of impedance increases, *in vivo,* for frequencies above 3Hz. EIS ranged from 0.2Hz to 100kHz. At 0.2Hz, in both conditions the electrode presents 20kΩ impedance. However, at 100kHz there is a 10 fold difference between the *in vitro* (lower) and *in vivo* (higher) impedance.

III. IMPLANT PROCEDURES

Acute experiments were undertaken in order to determine electrode performance. All surgeries were approved by the GMU IACUC (protocol 07-0140). Sprague-Dawley rats (250-350g) were anesthetized and stereotaxically implanted in the hippocampus with a coated electrode. For *in vivo* EIS and CVs, the reference and counter electrodes were kept on top of the skull, bathed in physiological saline solution.

IV. CHARACTERIZATION AND STABILITY TESTS

All electrodes are characterized *in vitro* immersed in phosphate buffered saline through cyclic voltammetric techniques at a scan rate of 50mV/s immediately after deposition of the coating. A three electrode setup is used in this case, with silver/silver chloride as reference and platinum as counter electrodes. For iridium oxide and carbon nanotubes the voltage limits go from -0.7 to 0.7V, but for PEDOT:PSS coatings voltage is cycled between 0 and 0.6V.

Electrochemical impedance spectroscopy is also realized (Fig.1), and shows typical profiles of stimulating, large area electrodes. Frequency ranges from 0.2Hz to 100kHz. The modulus of the impedance goes down with higher frequency for all tested electrodes, as expected. However, iridium oxide presents the lowest impedance (for comparable surface area and deposition times) if contrasted with MWNT and PEDOT:PSS electrodes. When implanted, the iridium oxide film electrode shows higher impedance across the spectrum (curve labeled ‘dur’ in the figure), but for the same electrode, if tested *in vitro* after the implant, the impedance profile is not significantly different from the pre-implant picture.

Cyclic voltammetry (CV) spectra are compared over time for each electrode. Figure 2 shows the voltammetry for one MWNT coated electrode followed for five weeks. During the first week, however, the electrode was not cycled. Notice the obvious difference in shape and consequently in the area under the curve for the first week. On the other hand, the following weeks present fairly stable CV.

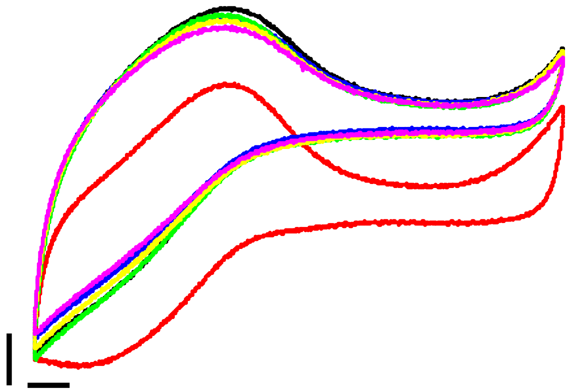

Fig. 2. Cyclic voltammetry spectra of one MWNT electrode; data acquired over 5 weeks. Week 1 (red curve) was taken with no long-term electrode cycling. Weeks 2 through 5 (black, green, yellow, and magenta, respectively) were selected at regular intervals (weekly) from 17 thousand cyclic voltammetric spectra (electrode stability test shown in Fig. 3). Scalebar: 100mV (horizontal) and 2μA (vertical)

In general, unstable electrodes present also unstable CV. This behavior can be captured as a single number, extracted from the CV in real time: the cathodic (or anodic) charge storage capacity. We evaluate the integral of the bottom half of each voltammetric cycle (see for example figures 3 and 4). That number (cCSC), in μC, is then plotted on a graph over time. Figure 3 shows the summary of the cCSC for the MWNT electrode discussed in the previous paragraph. In this case, we recorded 17,833 voltammetric cycles over 600 hours. The mean cCSC was 61.9 μC, and the standard deviation 5.8μC. While the mean and standard deviation alone do not suffice as characterization, the graph over time gives a reasonable picture of the stability of each electrode.

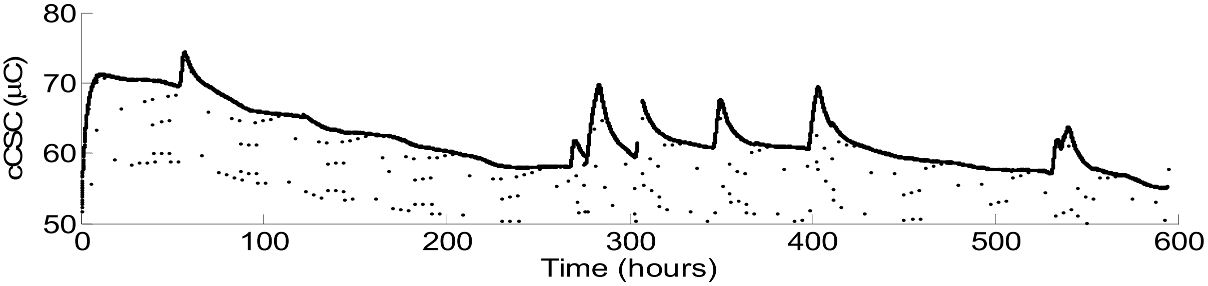

Fig. 3. Stable MWNT electrode tested *in vitro* for chemical stability over 600 hours. Peaks in the graph indicate times of solution exchanging or re-fill of the phosphate buffer saline. Cathodic charge storage capacity (cCSC) in micro Coulombs is plotted over time, in hours. For this particular electrode, 17833 voltammetric cycles were acquired. The mean for the cCSC over the 600 hours is 61.8μC, and the standard deviation 5.8μC.

Due to the long time of each experiment, and consequently evaporation of the phosphate buffered saline, several refills of the electrolyte solution are necessary. These are correlated with the peaks in cCSC observed in Figure 3. In order to make these experiments as close to the *in vivo* situation as possible, the PBS is not agitated. The outliers in figures 3 and 4, always seen below the cCSC level, are due to the evaluation of incomplete CV cycles.

Despite the cCSC measurements, spot checking of cyclic voltammetry spectra taken throughout a long period is necessary. We have implemented random sampling of files in order to compare the morphology of the CV spectra. In the example of figure 4, the electrode coated with iridium oxide film was cycled for 300 hours. We then selected four data points from this graph (labeled A through D) to display their respective CVs. We obviously expect the first (A) to present the largest area of the four, and the last to present the smallest area. Fig. 5 shows the four color-coded cyclic voltammetric curves. From the morphology of these curves one can infer the point-stability of this electrode, as the redox peaks are still present after 300 hours of cycling.

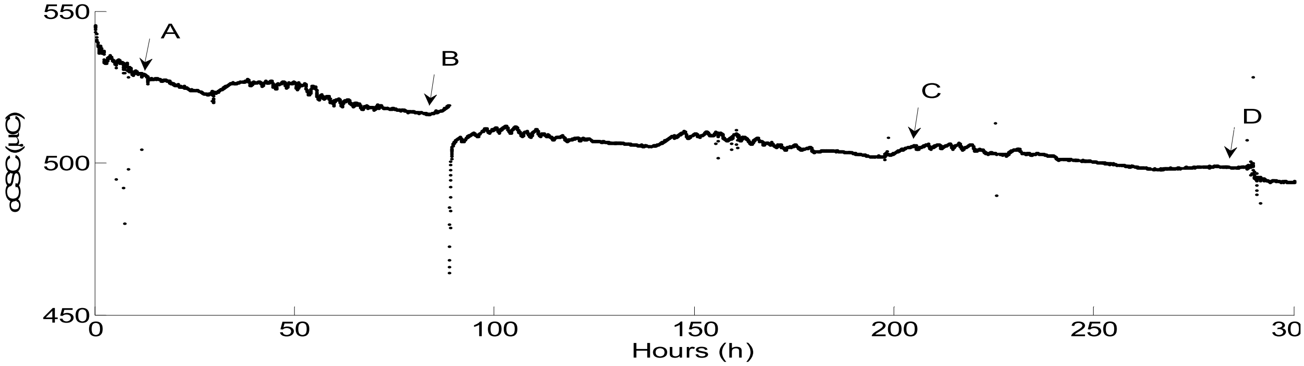

Fig. 4. Chemical stability investigation for iridium oxide film coated electrode. Cathodic charge storage capacity displayed over time for one experiment. 19,024 cycles were acquired over 300 hours. Mean cCSC is 475.0μC, and the standard deviation 82.5μC. Points in the graph labeled with A through D refer to cyclic voltammetry spectra shown in Fig. 5. A, B, C, and D spectra were taken at the following points in time: 12.26h; 83h; 203.77h; 283h.

A measure of stability can be credited to each electrode after such long-term (over 200 hours) experimental runs are completed. It may seem that electrodes (such as shown in Figs 3 and 4) will always hold their charge. That is not the case. As the example in Fig. 6 demonstrates, several coatings tested by us did not remain stable upon cycling. We have examples of MWNT and iridium oxide films prepared which degrade after 200 hours. Differently from testing each electrode once per week, in the cases discussed here we insure continuous cycling. Fig. 6 contrasts an aged (3 years, in air) iridium oxide film electrode with a PEDOT:PSS electrode (as prepared). The PEDOT coating on the electrode (red curve) is not as stable as the aged iridium oxide film. Continuous cycling imposes stress on the coating and forces delamination, as in this case. After 160h the cCSC for the PEDOT electrode is killed by the low frequency stimulation applied, whereas the iridium oxide film has lost 20% of its original cCSC.

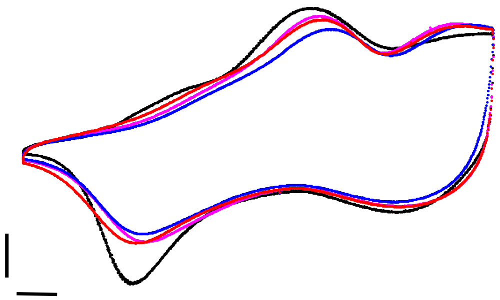

Fig. 5. Iridium oxide coated electrode, cycled for 300 hours. Sample voltammetric curves for 4 non-consecutive days. Voltammetric spectra were taken from labeled datapoints from Fig. 4. Black (A), red (B), magenta (C) and blue (D). Scalebar: 100mV (horizontal) and 10µA (vertical).

V. DISCUSSION AND CONCLUSION

The choice of electrode coating was driven by charge delivery performance of the materials. Iridium oxide presents superior charge than any other substrate, and thus was our first choice. However, its low performance *in vivo* prompted us for the alternative materials discussed here.

Environmental variables were not controlled for in this work. We are aware of the pH dependence of the cyclic voltammetric spectra for iridium oxide, as well as for the MWNT and PEDOT:PSS electrodes. As next steps we plan on incorporating simultaneous measurements of temperature, illumination, volume of solution in the vial being tested, and pH. These variables, and their time course, would help with the definition of a model for each coating tested and with the interpretation of stability results.

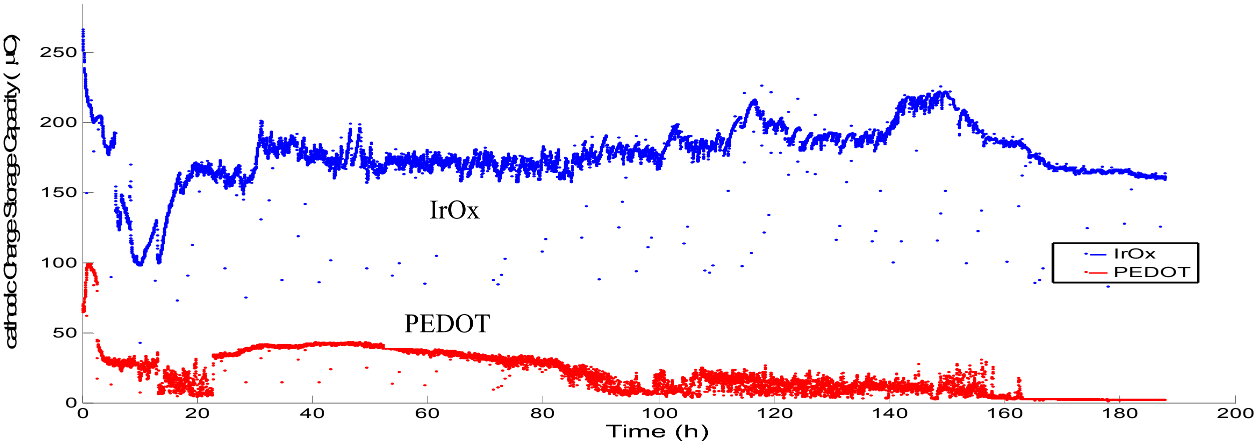

Fig. 6. Comparative stability. Two electrodes are individually characterized with cyclic voltammetry, with scan rate of 50mV/s, 0.7Vpeak, against a Ag/AgCl reference electrode, immersed in PBS. The cathodic charge delivered with iridium oxide coated electrode (in blue, upper curve) is higher than with PEDOT:PSS electrode (red, lower curve). After approximately 6 days the PEDOT:PSS electrode had lost its charge, while the iridium oxide electrode remained within 20% of its initial charge delivery throughout the end of the experiment (8 days).

To our knowledge, there is no single figure of merit which encapsulates all characterizations for implantable electrodes. For stimulation of the nervous system, low impedance and high charge, stable electrodes are needed. These same electrodes can be used for recordings of field potentials or, depending on size (and thus impedance), of single unit activity. The reliability of the recordings and stimulation in *in vivo* situations, either long-term or short-term, will depend on the stability of the interface. We propose that the stability can be quantitatively measured, before implantation, with continuous cycling of the electrode in electrolytic solutions. A stable electrode will survive continuous cycling for over 600 hours (as shown here), while unstable coatings delaminate after 200 to 400 hours. Both stable and unstable electrodes present similar initial impedance spectra and cyclic voltammetric profiles.

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