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Neural Electrode Degradation from Continuous Electrical Stimulation: Comparison of Sputtered and Activated Iridium Oxide

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Abstract

The performance of neural electrodes in physiological fluid, especially in chronic use, is critical for the success of functional electrical stimulation devices. Tips of the Utah Electrode Arrays (UEA) were coated with sputtered iridium oxide film (SIROF) and activated iridium oxide film (AIROF) to study the degradation during charge injection consistent with functional electrical stimulation (FES). The arrays were subjected to continuous biphasic, cathodal first, charge balanced (with equal cathodal and anodal pulse widths) current pulses for 7 hours (> 1 million pulses) at a frequency of 50 Hz. The amplitude and width of the current pulses were varied to determine the damage threshold of the coatings. Degradation was characterized by scanning electron microscopy, inductively coupled plasma mass spectrometry, electrochemical impedance spectroscopy and cyclic voltammetry. The injected charge and charge density per phase were found to play synergistic role in damaging the electrodes. The damage threshold for SIROF coated electrode tips of the UEA was between 60 nC with a charge density of 1.9 mC/cm² per phase and 80 nC with a charge density of 1.0 mC/cm² per phase. While for AIROF coated electrode tips, the threshold was between 40 nC with a charge density of 0.9 mC/cm² per phase, and 50 nC with a charge density of 0.5 mC/cm² per phase. Compared to AIROF, SIROF showed higher damage threshold and therefore is highly recommended to be used as a stimulation material.

Keywords

Functional electrical stimulation; neuronal damage; iridium oxide; pulse DC reactive sputtering; Inductively Coupled Plasma Mass spectrometry (ICP-MS)

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1. Introduction

Functional electrical stimulation (FES) of biological tissue requires transfer of electronic charge from the electrode to ionic charge in the physiological fluid. There are various neural electrodes which can perform FES, for example, the Utah electrode array (UEA) [1]. In order to successfully use these electrode arrays for stimulation in chronic implantation i.e. few years, the electrode material must be both efficacious and safe to use. Efficacy of stimulation primarily means injecting enough charge in the targeted tissue to elicit action potentials. However, in doing so, the electrode itself must not degrade or generate harmful substances or provoke a significant immune response. The active areas of the electrodes must remain stable under the stimulation protocol to achieve a long term functional response. Achieving this remains a challenge as stimulation protocols that permit prolonged excitation of neurons without injuring the tissue or damaging the electrodes are yet to be developed.

The mechanisms for stimulating induced tissue damage are not well understood. The tissue can be damaged primarily due to three reasons: (1) due to surgical trauma while inserting the penetrating electrodes in the tissue, (2) chemical and mechanical bio-incompatibility of the electrode material, and (3) generation of toxic by-products at the electrode-electrolyte interface during electrical stimulation which cannot be tolerated by the physiological medium [2-5] and due to prolonged stimulation induced neuronal activity which changes the ionic concentrations of both intracellular and extracellular, for eg. increase in extracellular potassium, known as 'mass action' theory [6,7].

To reduce the tissue damage from surgical trauma the electrodes can be miniaturized. Selectivity, referred as the ability to stimulate discrete population of nerve fibers without stimulating neighboring population of nerve fibers, may be achieved if one electrode can *communicate* to each fiber. For perfect selectivity the electrode geometry need to be in the range of the nerve fiber. Hence small electrodes or microelectrodes are desirable as far as selectivity and surgical trauma is concerned. However, electrode impedance increases with decreases in electrode size. Since noise accompanies impedance (for thermal noise) lower impedance is preferred when recording action potentials. Higher electrode impedance may be acceptable for stimulation but not desirable. Hence there is a trade-off between selectivity and electrode impedance.

Many researchers have indicated from their studies that neuronal damage is electrochemically induced [8-10]. McCreery et al. attempted to differentiate between electrochemically induced and neuronal activity induced injury by using platinum (faradaic) and tantalum pentaoxide (capacitor) electrodes [11]. However they found equivalent amount of tissue damage under both types of electrodes. All these studies indicates that electrochemically and activity induced injury might not be exclusive.

The guiding design rule to avoid electrode damage while injecting charge is electrochemical reversibility: all processes occurring at an electrode after the application of current pulse are reversed by a second current pulse of opposite polarity. This would eliminate electrode damage and neural damage induced by it. Researchers have showed that the monophasic stimulation waveform is more damaging to the tissue than charge balanced biphasic waveform [9,10, 12-14]. This can be interpreted as the process occurring during the first phase is reversed during the second phase with ultimate goal of no net charge delivered. While in monophasic all injected charge results in generation of electrochemical reaction products. The electrochemical reversibility is measured by charge injection capacity (CIC). The CIC is the total amount of charge per unit area which may be injected in the electrolyte without damaging the electrodes. The 'safe' CIC is when at no point of time the electrode potential exceeds the water window. The water window is defined as the potential region at which oxidation and reduction of water

takes place. If the electrode potential exceeds water window, damage to the electrode can occur in the form of electrode corrosion resulting in dissolution of electrode material in the electrolyte.

For the efficacy of the stimulating electrodes, large CIC is desired. Depending on the electrode material the charge can be injected by double layer capacitance (as in TiN), pseudo-capacitance (as in Pt), or reversible Faradaic reaction (as in IrO_x). However, CIC depends on electrode material, shape and size of electrode, electrolyte used and most importantly on the stimulation waveform.

Fig. 1 summarizes the relationship between injected charge and charge density per phase of the neural electrode with the histological detectable neural injury, for variety of electrodes having different shape, size and geometry, studied in different animals, from various research groups. The tissue damage threshold line is extrapolated from report from McCreery *et al.* They used Pt and activated iridium oxide film (AIROF) electrodes in the cat parietal cortex [6]. Above the extrapolated tissue damage threshold line is a region of unsafe usage of neural electrodes due to neural damage, while below the threshold line is the region of safe usage of neural electrodes. Yuen *et al.* studied neuronal damage in cat parietal cortex using Pt disc electrodes [15]. Agnew *et al.* used AIROF and Pt/Ir (70/30%) electrodes and implanted them on sensorimotor cortex of the cat [16]. Bullara *et al.* used Pt-Ir (30%) electrodes on the ipsilateral pyramidal tract of a cat [17]. To permit selective stimulation of small populations of neurons in close proximity to the electrode, charge injection sites are fabricated with small geometrical areas (cm²), surface area less than 5×10^{-5} cm². The graph also, gives a projection of the neural damage threshold for electrodes with different surface areas. Large area electrodes can inject more charge and still be in a safe operating region; while, small area electrodes, with higher charge density must inject less charge to operate in safe regions. However, there is a trade off. Large area electrodes loses selectivity i.e. ability to activate one population of neurons without activating neighboring populations, hence small electrodes are preferred. There are various ways in which neuronal damage can occur, for example, mechanical constriction of the nerve, neuronal hyperactivity due to stimulation or irreversible reactions taking place at the electrode-electrolyte interface [19]. This paper investigates the stimulation protocol to prevent the irreversible reactions to take place for iridium oxide electrodes.

For chronic stimulation, stability of the electrodes is very important. In this paper, electrode degradation is investigated and the threshold at which degradation occurs is determined. Typically electrodes are coated with a material which has the ability to inject charge into the extracellular fluid. Iridium oxide (IrO_x) was investigated because it has a large reversible charge injection capacity, thus allowing high charge injection without electrolysis or net dc charge transfer. IrO_x permits significantly higher levels of charge injection compared to Pt or Pt-Ir alloys [2,20]. However, the charge injection for iridium oxide depend upon the properties of the IrO_x film, electrode geometry and stimulation waveform. Therefore, it is not possible to specify a charge injection that will be generally applicable to all electrodes. The objective of this study was to determine the charge injection capacity limit (no degradation) of the electrodes coated with sputtered iridium oxide film (SIROF) and activated iridium oxide film (AIROF).

2. Materials and Methods

2.1 Fabrication of microelectrode arrays

Both, SIROF and AIROF were selectively deposited on the tips of penetrating microelectrodes arrays, the Utah Electrode Array (UEA), using Al foil as a mask to cover the shaft and base of the electrodes. A scanning electron micrograph of the UEA is presented in Fig. 2A. The UEA is fabricated from highly doped single crystal silicon and consists of 10×10 array of 1.5 mm long sharp microelectrodes, each of which is surrounded at the base by glass dielectric to

electrically isolate the electrodes. Bond pads on the back of each electrode are wirebonded to an external connector. The UEA is encapsulated by a conformal coating of Parylene-C. The active electrode tips of the UEA are defined by selectively etching the Parylene-C from the tips of the electrodes once again using an Al foil mask. The length of the de-insulated (exposed) electrode tip or *tip exposure* typically ranges from 20 to 100 μm (Fig. 2B). A detailed description of the UEA fabrication is given elsewhere [21]. The tip metallization investigated were deposited in a TM-Vacuum SS-40C-IV multi cathode sputtering system. Prior to any deposition, the load lock chamber was evacuated to 2×10^{-7} Torr using a dry mechanical pump and followed by a cryogenic pump. Ar and O₂ were supplied to the chamber via mass flow controllers (MFC). The effective pumping speed was regulated by feedback controlled throttle valve to achieve a pressure set point. The substrate was not intentionally heated during sputtering.

Titanium—Titanium (Ti) was deposited on the electrode tips of the UEA prior to depositing iridium (for AIROF) or IrO_x (SIROF). Selective Ti deposition on the UEA tip was achieved by using Al foil as a mask during sputtering. Ti acts as an adhesive layer and was deposited using DC sputtering. The Ti layer was sputtered in Ar ambient at a chamber pressure of 20 mTorr with Ar flowing at 150 sccm and sputtering power of 90 W for 5 min. The sputtering parameters were optimized to achieve low stress Ti film. The Ti target was 99.6% pure, 3 inch in diameter and 0.125 inches in thickness (Kurt J. Lesker). The deposition rate of Ti was calculated to be 10 nm/min.

SIROF—SIROF was deposited by pulsed DC sputtering using a RPG 100 power supply (MKS Instruments). The iridium target was 99.8 % pure, 3 inch in diameter and 0.125 inches in thickness (Kurt J. Lesker, Pittsburgh, PA). The SIROF was reactively sputtered in Ar and O₂ plasma with both gases flowing at the rate of 100 sccm for a gas composition of 50%:50% for Ar and O₂, respectively. All the films were deposited at 10 mTorr using 100 W power for 20 min at pulse width 2016 ns. The pulse frequency was constant at 100 kHz. The deposition rate of SIROF was 9.75 nm/min. The above sputtering parameters were selected to yield robust and adhesive SIROF and the ratio of Ir to O concentration was evaluated to be ~0.7 on the planar substrate [22].

AIROF—AIROF fabrication required two steps, the first being iridium metal deposited using DC sputtering on the electrode tips of the UEA. In the second step, the iridium was converted to iridium oxide by potentiodynamic pulsing at room temperature in a process known as *activation* to form AIROF. A process pressure of 20 mTorr was maintained using the throttle valve and an Ar gas flow rate of 150 sccm. The sputtering power was 90 W and deposition lasted 12 minutes. The deposition rate of SIROF was 16.25 nm/min. The iridium electrodes were *activated* to form AIROF by potentiodynamic pulsing between -0.6 V and 0.8 V at 1 Hz for 1350 cycles in phosphate buffered saline (PBS) solution having a composition of 0.13 M NaCl, 0.022M KH₂PO₄·H₂O, and 0.081M Na₂HPO₄·7H₂O (*pH* adjusted to 7.3 ± 0.1 by adding either 5M NaOH or 5M HCl).

2.2 Stimulation protocols

The stimulation waveform utilized a current controlled waveform using a STG 2008 stimulus generator (Multi Channel Systems MCS GmbH, Germany). Biphasic current pulses were delivered as charge-balanced pairs, cathodal first, with equal times and current amplitude for each phase. The pulse frequency was kept constant at 50 Hz for all stimulation protocols. Different stimulation protocols were employed by changing the current amplitude and pulse width. To compare the rate of charge injection, the charge was normalized for 100 μs for all stimulation protocols. Throughout this paper normalized charge is used unless otherwise mentioned. Charge density was calculated per phase. A 20 μs dwell was employed between

phases in each protocol to facilitate measurement of the access voltage (V_a) associated with the resistive (iR) components of the circuit. The voltage waveform was captured by a Tektronix digital oscilloscope.

2.3 Characterization

2.3.1 In vitro electrochemical measurements—To determine the affect of stimulation on the charge storage capacity of the IrO_x film, electrochemical impedance spectroscopy (EIS) data was collected from electrodes in physiological PBS solution before and after stimulation. The data was acquired at room temperature, using a three electrode system in a commercial electrochemical test system (Gamry Instruments PC4 potentiostat, Warminster, PA). A silver-silver chloride electrode (SSE) was used as a reference electrode and a large area Pt wire was used as a counter electrode. All potentials were measured with respect to the SSE. The sinusoidal signal had an amplitude of 10 mV at frequencies from 1 Hz to 100 kHz.

The electrochemical potential transient of the SIROF and AIROF were determined from the voltage waveform by correcting for IR drop. Fig 3 shows the trace of the cathodal first, 100 μA current pulse with a width of 600 μs followed by symmetric anodal charge balance pulse. The graph shows the access voltage (V_{acc}) associated with the resistive (IR) component in the circuit and electrolyte. The maximum cathodic and anodic electrochemical potential (E_{mc} and E_{ma}) excursions of the electrode during pulsing were calculated by subtracting V_{acc} from the maximum negative and positive voltage transient, respectively. Alternatively, E_{mc} is equal to the electrode potential immediately after the end of the cathodic pulse where V_{acc} is zero. Similarly, E_{ma} is equal to the electrode potential immediately after the end of the anodic current pulse [23]. Pulses were delivered at a frequency of 50 Hz, allowing time (~ 18 ms) between pulses. The electrode polarization measurement method is given by Troyk and Cogan [24].

2.3.2 Scanning electron microscopy—The film thicknesses were measured with a Tencor P-10 profilometer on a silicon witness wafer masked to yield a step. The film thicknesses reported are average thicknesses measured over 5 points (top, center, bottom, left and right) on the witness wafer. The surface morphology of SIROF and AIROF (after activation) films and length of *tip exposure* were examined by scanning electron microscopy (SEM) using an FEI Nova NanoSEM microscope. SEM was also utilized to examine the surface morphology of electrode tips which were coated with SIROF and AIROF, before and after the stimulation protocol.

2.3.3 Inductively Coupled Plasma - Mass spectroscopy (ICP-MS)—ICP-MS is a comparative method where the measurement of an unknown sample is based upon chemical standards i.e. the measurement is a comparative process. An Agilent Technologies 7500cx ICP-MS was used and the operating conditions are in Table 1. The samples to measure electrode degradation were stimulated in 10 mL PBS solution. After each stimulation protocol, 2 mL of sample was taken from 10 mL and 0.125 mL concentrated trace metal clean nitric acid was added to it. The total sampled volume was made to 5 mL by adding DI water.

The matrix matched blanks were prepared with 2 mL of PBS solution matrix and 0.125 mL concentrated trace metal clean nitric acid was added to it and finally DI water was added to the sample to make the solution 5 mL. For the matrix matched calibration curve, 999 mg Ir per L standard (Inorganic Ventures, Lakewood, New Jersey, USA) was used to prepare fresh secondary and tertiary solutions with concentrations 0.985 mg/L and 0.972 $\mu\text{g/L}$, respectively. The last solution was used to prepare calibration solutions with Ir concentrations of 0, 2.4, 4.9, 24.3, 48.6 and 97.2 ng/L. 1 mg/L Terbium was used as an internal standard.

3. Results

3.1 ICP-MS, SEM, EIS and CV

SIROF—ICP-MS data were collected as functions of the charge per phase and charge density per phase and are presented in Fig. 4 with data from (a) SIROF and (b) AIROF coated electrodes. The SIROF or AIROF coated electrodes which were not pulsed but soaked for 7 hours had Ir concentration less than 7 ng/L, which was the limit of detection (LoD) of the instrument. For the SIROF coated electrodes which were pulsed, the smallest amount (42 ng/L) of Ir was from the electrode which injected of 80 nC per phase and have a charge density 1.2 mC/cm². Increasing the charge density from 1.2 to 2.5 mC/cm² increased the Ir from 42 to 115 ng/L. However, decreasing the charge density to 1 mC/cm² per phase, Ir was not detected in the PBS solution. On the other hand, Ir was also not detected for the electrode which was pulsed to inject 60 nC per phase with charge density of 1.9 mC/cm².

The ICP-MS results were supported by SEM micrographs shown in Fig. 5. The micrographs of the SIROF electrode pulsed at 80 nC per phase and having charge density of 1.2 mC/cm² is shown in Fig 5 (a) while an electrode pulsed with 80 nC per phase having a charge density of 2.5 mC/cm² is shown in Fig 5 B. As seen in the Fig. 5 B, the pulsed electrodes are ‘SIROF-free’, dissolution of Ir in the solution exposing the underlying substrate. The micrograph shown in Fig 5 C is of electrode pulsed at 60 nC per phase having charge density of 1.9 mC/cm² for 7 hours in PBS solution showed no visible damage to the electrode, as did an electrode which was pulsed with 80 nC per phase having charge density of 1 mC/cm² per phase (not shown)..

Electrical impedance spectroscopy (EIS) data were collected before and after the stimulation protocol. Bode plots of SIROF coated electrodes pulsed with different stimulation protocols are shown in Fig. 6. A significant increase in the electrode impedance was observed for samples pulsed to inject 80 nC per phase of charge having charge density of 1.2 mC/cm² and 2.5 mC/cm². The phase is capacitive for 2.5 mC/cm² compared to 1.2 mC/cm². However, the electrode impedance or phase did not change significantly when 60 nC charge per phase having charge density of 1.9 mC/cm² was pulsed through the electrode. These results are consistent with the absence of degradation observed in the ICP-MS and SEM.

The electrochemical changes that may have occurred due to pulsing of the SIROF coated UEA were also measured by cyclic voltammetry as illustrated in Fig 7 and 8. Fig 7 shows the voltammogram of the electrode which was pulsed at 200 μ A and 300 μ s pulse width per phase. The geometrical surface area of the electrode was 3.1×10^{-5} cm². The electrode was pulsed for 7 h at 50 Hz. The pre and post storage capacity for the electrode with charge density of 1.9 mC/cm² was 1645 and 1654 nC. As seen in the voltammogram there is no significant change in the electrode charge storage capacity. On the other hand, the voltammogram of the electrode which was pulsed at 400 μ A with pulse width of 200 μ s per phase is shown in Fig 8. The electrode surface area was 4.5×10^{-5} cm². The pre and post storage capacity for the electrode with charge density of 1.76 mC/cm² was 490 and 372 nC. At this stimulation protocol the dissolution of Ir is very slow but sure, as confirmed by ICP-MS analysis; 60 ng/L of Ir was found in the PBS solution. The decrease in the charge storage capacity can be attributed to the decrease in thickness of the SIROF.

AIROF—The ICP-MS result for AIROF coated electrodes is illustrated in Fig 4 (b). The lowest amount of Ir in the PBS solution among AIROF coated electrodes was from the electrode pulsed to inject 40 nC charge per phase having charge density of 0.96 mC/cm² per phase. Increasing the charge density from 0.96 to 2.75 mC/cm² increases the concentration of Ir from 28 to 201 ng/L. Ir was not detected in the PBS for electrodes pulsed at 40 nC with charge density to 0.9 mC/cm² per phase, and pulsed at 50 nC per phase with charge density of 0.5 mC/cm².

A SEM micrograph of an electrode pulsed at 40 nC per phase having charge density of ~ 0.96 mC/cm² per phase is shown in Fig 9 A while the micrograph of an electrode pulsed at 40 nC per phase having charge density of 2.75 mC/cm² is shown in Fig 9 B and an electrode pulsed at 50 nC having charge density of 0.5 mC/cm² per phase is shown in Fig 9 C. The electrode which was pulsed 50 nC having charge density of 0.5 mC/cm² per pulse and other electrode pulsed with 10 nC charge per phase having charge density of 2.75 mC/cm² showed no evidence of AIROF damage or delamination (not shown).

The impedance changes from pulsing AIROF coated electrodes are presented by the electrochemical impedance spectra in Fig. 10. The electrode impedance increased significantly when they were pulsed with 40 nC charge per phase having charge density of 0.96 mC/cm² and 0.8 mC/cm². Furthermore, the phase becomes more capacitive after pulsing. However, the electrode impedance did not change significantly when the electrode was pulsed with 50 nC charge per phase having charge density of 0.5 mC/cm². The SEM micrographs, shown in Fig 9, confirm the delamination of AIROF resulting in increase of impedance. The EIS results are consistent with ICP-MS and SEM results.

The representative cyclic voltammogram of the AIROF coated electrode tip of the UEA is shown in Fig 11 and 12. Fig 11 shows the voltammogram of the electrode which was pulsed at 500 μ A with pulse width of 100 μ s per phase for 7 hours at 50 Hz. The electrode surface area was 5.4×10^{-5} cm² making charge density to be 0.9 mC/cm². The pre and post storage capacity, calculated from eq. (1), was 111 and 115 nC. However, the voltammogram of the electrode which was pulsed at 300 μ A with pulse width of 200 μ s per phase for 7 h at 50 Hz is shown in Fig 12. The electrode surface area was 6.2×10^{-5} cm² making charge density to be 0.9 mC/cm². Repetitive cycling produced some changes in the AIROF cyclic voltammogram. At potential more negative than about -0.2 V, there is a loss of charge capacity as indicated by a decrease in cathodal current. The loss of cathodic charge capacity is reflected in overall charge storage capacity which decreased to 150 nC from 174 nC. SEM micrographs of the electrode tip after pulsing, as shown in Fig 5C, confirms degradation of AIROF exposing silicon substrate which can be attributed in decreasing charge storage capacity.

3.2 Potential excursions

Fig. 13 shows the variation of E_{mc} with the charge density of various electrodes coated with SIROF and AIROF. The lowest E_{mc} which damages the electrode was -0.7 V for both SIROF and AIROF. On the other hand, the lowest E_{mc} for not damaging electrode was -0.6 V for SIROF and AIROF. The graph in Fig. 13 shows E_{mc} only, because, for the cathodal first stimulation pulse, E_{ma} does not cross 0.8 V limit without E_{mc} crossing the -0.6 V limit. This is consistent with Cogan *et al.* study on AIROF electrodes [25]. The electrode potential of -0.6 V is not expected to cause dissolution or delamination of SIROF and AIROF under pulse conditions used. However, it is clear that if the electrode gets polarized to voltage which exceeds the water window, SIROF and AIROF degradation occur.

4. Discussion

Fig 14 illustrates the dependence of electrode damage on the charge injection per phase and charge density. The damage was characterized by SEM, ICP-MS, EIS and CV. The *in vitro* damage threshold for SIROF coated on electrode tips of the UEA is between 60 nC per phase having charge density of 1.9 mC/cm² and 80 nC per phase having charge density of 1.0 mC/cm². While for AIROF coated electrode tip, the threshold is between 40 nC per phase having charge density of 0.9 mC/cm², and 50 nC per phase having charge density of 0.5 mC/cm². The SIROF coated UEA electrode damage threshold is higher than the neuronal damage threshold, illustrated in Fig. 1, while AIROF coated UEA damage threshold is less than the neuronal damage threshold. The electrical thresholds density for eliciting neuronal response for cortical

microelectrodes are about 0.1 mC/cm^2 while for deep brain stimulation it is 0.4 mC/cm^2 [26]. Higher charge density may be required for retina prostheses due to smaller microelectrodes required to enhance resolution. Both SIROF and AIROF coated UEA can be used to elicit neuronal response however, AIROF damage threshold is in close proximity to neuronal threshold. SIROF having higher damage threshold would be better electrode material for chronic applications.

It is important to note that charge injection limits for any electrode material depends on the electrode bias level, waveform symmetry, current density employed, pulse frequency, geometry of the electrodes and by properly choosing the stimulation protocol. Cogan et al. showed that asymmetric pulse width and positively biasing the electrode enhances the charge density of both films [26,27]. However, at similar conditions (no electrode bias and symmetric pulse width), the charge density of films studied for present work was at par with published work of other researcher.

The relationship between the electrode damage at high charge density and low charge per phase remains undetermined as it was not possible to fabricate small ($5\text{-}10 \mu\text{m}$) tip exposure by the current fabrication method. Both the factors; charge density and charge per phase, are important to determine whether electrode damage will occur.

Severity of electrode damage increases as charge density and charge are increased beyond the damage threshold. As seen in Fig. 4 as charge or charge density per phase is increased, Ir in PBS solution also increases. Due to the increase of charge and charge density per phase the electrode potential (E_{mc}) decreases. The rate of dissolution/degradation of the film depends on how much lower E_{mc} is compared to the -0.6 V threshold. Lower is E_{mc} faster is the Ir dissolution rate. The exact dissolution rate was difficult to calculate as it is possible that rate of dissolution may vary as time progresses. It is speculated that the rate of dissolution would be slow initially. As the electrode gets 'IrO_x free' the impedance of electrodes increases, therefore, to support the required current the E_{mc} (which is negative) decrease further which in turn, increases the dissolution rate.

The stability of IrO_x is likely to depend on the physical properties of the film such as density, roughness and thickness as well as the details of the pulsing protocol. The better stability of SIROF is attributed to the higher density of SIROF compared to AIROF. Although the density of the SIROF and AIROF studied in the present work was not measured but typically, the density of SIROF and AIROF is 7 and 2 g/cm^3 , respectively [28]. The result shows that the polarization of SIROF is less than AIROF for the same stimulation protocol. Low polarization of SIROF can be attributed to the density of the film, where SIROF has more Ir ions per cm^3 to contribute to the current flow.

Pulsing either type of electrodes (SIROF or AIROF) with current waveforms can enhance activation of the iridium (Ir) metal found in either film to support the charge transfer. Ir metal expands by a factor of ~ 5 as it is converted to IrO_x. This expansion is accommodated in the film. Depending on the amount of Ir present in the film the volume of the film is expanded. Due to this volumetric expansion in the AIROF, the film loses its coherence and is poorly adherent to underlying substrate and may cause dissolution or delamination at low values. On the other hand, SIROF is deposited layer by layer of IrO_x resulting in lower residual film stress compared to that of AIROF.

The charge density is given by total charge per unit geometrical area of the electrode tip. However, the geometrical area differs from real area due to the roughness of the surface and the presence of the deposits or other contaminants which might alter the surface area of the electrode tips. Roughness causes the real surface to be large than the geometrical area, while contaminants reduces the real area. The geometrical areas were measured by linear dimensions

taken from SEM micrographs of the electrode tip. Hence, the actual charge density would be lower than the calculated charge density. Furthermore, the charge density at the surface is assumed to be uniformly distributed, whereas in actual use charge density will be unevenly distributed across the tip due to the unique geometry of the UEA,

It must be noted that the *in vitro* electrode damage threshold established for SIROF and AIROF coated UEA may be different from the *in vivo* electrode damage threshold. Difference in the *in vivo* and *in vitro* electrochemical response and charge injection capability of AIROF electrodes have been found [26,29]. Inferior *in vivo* capability of AIROF electrodes was attributed to the interstitial fluid which had higher buffering capacity than inorganic models of interstitial fluid, such as PBS solution, which was used in this study. It is yet to be investigated if SIROF *in vivo* performance also changes compared to *in vitro*.

For all applications, it is important to limit the voltage excursions within the water window to prevent film damage. The damage threshold limits determined by this study are only for charge injection protocols studied; extrapolations to other stimulation protocols should be made with caution. With the stimulation protocol used in this paper, it is clear that SIROF can support more charge density and higher charge injection compared to AIROF. Though longer periods (months) of pulsing are required to qualify SIROF as a neural electrode material, the ability to inject higher charge and charge density makes SIROF a promising neural electrode material, especially for chronic implantation.

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Fig 1.
The effect of charge and charge density on histologically detectable neural injury.

Fig.2.

(a) Scanning electron micrograph of the Utah Electrode Array (UEA), and (b) a higher magnification image of one electrode depicting tip exposure. The UEA is encapsulated by an insulating Parylene-C layer, with the exception of the tip ($\sim 100 \mu\text{m}$) of the electrode which forms the active site for stimulation and/or recording of neural signals.

Fig 3. Voltage transient of a SIROF coated electrode of the UEA in response to the biphasic, symmetrical current pulses passed at 50 Hz. The current pulse amplitude and width per phase was 50 μ A and 0.6 ms respectively. The figure illustrates the maximum cathodic potential ($E_{mc} = -0.6$ V) and maximum anodic potential ($E_{ma} = 0.6$ V) excursion during a pulse.

(a)

(b)

Fig 4. Effect of charge and charge density per phase on the concentration of Ir found in the PBS solution for (a) SIROF and (b) AIROF coated electrodes.

(a)

(b)

(c)

Fig 5.

SEM micrographs of SIROF coated electrode tips of the UEA. Micrograph of electrode which was (a) pulsed to inject 80 nC having charge density of 1.2 mC/cm² per phase, (b) pulsed to inject 80 nC having charge density of 2.5 mC/cm² per phase, and (c) pulsed to inject 60 nC having charge density of 1.9 mC/cm² per phase for 7 hours.

Fig. 6.

Bode plot of before and after stimulation of SIROF coated electrode tips of the UEA. There is significant increase in impedance when charge or charge density per phase is increased. A silver-silver chloride electrode (SSE) was used as a reference electrode and a large area Pt wire was used as a counter electrode. All potentials were measured with respect to the SSE. The sinusoidal signal had an amplitude of 10 mV at frequencies from 1 Hz to 100 kHz.

Fig. 7. shows the voltammogram of SIROF. The electrode was stimulated with 200 μA pulse amplitude and pulse width was 300 μs per phase having surface area of $3.1 \times 10^{-5} \text{ cm}^2$ for 7 h at 50 Hz. The pre and post stimulation charge was 1645 and 1654 nC.

Fig. 8. shows the voltammogram of SIROF. The electrode was stimulated with 400 μA pulse amplitude and pulse width was 200 μs per phase having an area of $4.5 \times 10^{-5} \text{ cm}^2$ for 7 h at 50 Hz. The pre and post stimulation charge was 490 and 372 nC.

Fig 9. SEM micrographs showing AIROF coated electrode tips of the UEA stimulated with (a) 40 nC per phase having charge density of 0.8 mC/cm² per phase, (b) 40 nC per phase having charge density of 0.96 mC/cm² and (c), 50 nC per phase having charge density of 0.9 mC/cm².

Fig. 10.

Bode plots of pre- and post-stimulation of AIROF coated electrodes. There was significant increase in impedance of the electrode when charge and charge density per phase exceeded threshold. A silver-silver chloride electrode (SSE) was used as a reference electrode and a large area Pt wire was used as a counter electrode. All potentials were measured with respect to the SSE. The sinusoidal signal had an amplitude of 10 mV at frequencies from 1 Hz to 100 kHz.

Fig. 11. shows the voltammogram of AIROF. The electrode was stimulated with 500 μ A pulse amplitude and pulse width was 100 μ s per phase having 5.4×10^{-5} cm^2 tip exposure for 7 h at 50 Hz. The pre and post stimulation charge was 111 and 115 nC.

Fig. 12. shows the voltammogram of AIROF. The electrode was stimulated with 300 μA pulse amplitude and pulse width was 200 μs per phase having $6.2 \times 10^{-5} \text{ cm}^2$ surface area for 7 h at 50 Hz. The pre and post stimulation charge was 174 and 150 nC.

Fig 13.

The variation of potential excursions for SIROF (Δ) and AIROF ($\square$) coated electrodes with charge density. The potential transient was measured with respect to counter Pt electrode. The open symbols are for damaged electrodes and close symbols are for undamaged electrodes. The electrode gets damaged if the potential of the electrode goes below -0.6 V.

Fig. 14.

Synergistic effect of injected charge and charge density per phase of the electrode on the electrode damage. In all the electrodes 1.26 million stimulation pulses were passed at 50 Hz with varying current amplitude and pulse width.

Table 1

ICP-MS operating conditions

Frequency	30 Mhz
RF power	1550 W
Plasma gas flow rate	15 L/min
Auxiliary gas flow rate	1 L/min
Nebulizer gas flow rate	0.95 L/min
Carrier gas flow	0.95 L/min
Make-up gas flow	0.15 L/min
Nebulizer	PTFE 0.4 mL/min
Spray chamber	Scott type
Cones	Platinum
Sensitivity	105 kcps for a 1 microgram Ce/L