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Electrochemical characteristics of ultramicro-dimensioned SIROF electrodes for neural stimulation and recording

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Abstract

Objective.—With ever increasing applications of neural recording and stimulation, the necessity for developing neural interfaces with higher selectivity and lower invasiveness is inevitable. Reducing the electrode size is one approach to achieving such goals. In this study, we investigated the effect of electrode geometric surface area (GSA), from 20 μm^2 to 1960 μm^2 , on the electrochemical impedance and charge-injection properties of sputtered iridium oxide (SIROF) coated electrodes in response to current-pulsing typical of neural stimulation. These data were used to assess the electrochemical properties of ultra-small SIROF electrodes (GSA < 200 μm^2) for stimulation and recording applications.

Approach.—SIROF charge storage capacities (CSC), impedance, and charge-injection characteristics during current-pulsing of planar, circular electrodes were evaluated in an inorganic model of interstitial fluid (model-ISF).

Main results.—SIROF electrodes as small as 20 μm^2 could provide 1.3 nC/phase (200 μs pulse width, 0.6 V versus Ag|AgCl interpulse bias) of charge during current pulsing. The 1 kHz impedance of all electrodes used in this study were below 1 M Ω , which is suitable for neural recording.

Significance.—Ultra-small SIROF electrodes are capable of charge injection in buffered saline at levels above some reported thresholds for neural stimulation with microelectrodes.

Keywords

ultramicroelectrode; neural stimulation; neural recording; sputtered iridium oxide; charge injection; impedance

1. Introduction

An ultramicroelectrode (UME) can be defined as an electrode with at least one dimension smaller than the diffusion layer thickness, which is a measure of the spatial extent over which the concentration of electroactive species in the electrolyte adjacent to the electrode varies from the bulk concentration (Diard *et al* 2005). In the case of planar microelectrodes,

mass transport of electroactive species is perpendicular to the electrode and this forms a linear diffusion profile. In contrast, for a planar UME, transport of electroactive species is radial and a hemispherical diffusion profile is formed (Wightman 1981). The consequence of the hemispherical diffusion profile is that the volume of electrolyte contributing electroactive species to redox process at the electrode is larger per unit electrode area for UMEs compared with microelectrodes.

For typical voltammetric applications, UMEs are $<25\ \mu\text{m}$ in at least one electrode dimension (Wightman 1981, Heinze 1991, Bard and Faulkner 2001). Considering that in voltammetric applications the major transport mechanism is diffusion, UMEs are identified by kinetically-controlled steady-state currents in cyclic voltammetry (CV) measurements (Wightman 1981, Heinze 1991) that result in sigmoidal-shaped CVs, steady state diffusion-controlled currents in chronoamperometry (Heinze 1993), and longer transition time constants compared to microelectrodes in chronopotentiometry (Bard 1961, Lingane 1964, Aoki *et al* 1985). Most UME studies have employed planar surface electrodes, typified by inlaid carbon fiber electrodes (Wightman 1981) or metal wire electrodes made from platinum (Fleischmann *et al* 1984) or from tungsten wires electroplated with gold or platinum (Hermans and Wightman 2006).

Besides their established use for quantifying neurotransmitter release in *in vivo* preparations (Wightman *et al* 1976, Ewing *et al* 1983, Kovach *et al* 1984, Oh *et al* 2018, Park *et al* 2018, Batton *et al* 2019), Ultramicro-dimensioned (UM-dimensioned) electrodes have been employed for recording neural activity *in vitro* (Sekirnjak *et al* 2006, Yu *et al* 2012) and *in vivo* (Schmidt *et al* 1976, Kozai *et al* 2012, Deku *et al* 2018, Gillis *et al* 2018), and for neural stimulation *in vitro* (Grumet *et al* 2000, Stett *et al* 2000, Jensen *et al* 2003, Sekirnjak *et al* 2006) and *in vivo* (Gillis *et al* 2018). One potential advantage of using ultramicro-dimensioned electrodes for neural stimulation and recording is the possibility of designing multielectrode arrays with small shank dimensions that reduce insertion trauma and the chronic foreign body response (FBR) compared to larger microelectrodes. Several groups have reported a reduced FBR to penetrating cortical implants with cross-sectional dimensions of $5\text{--}15\ \mu\text{m}$ (Seymour and Kipke 2007, Stice *et al* 2007, Skousen *et al* 2011) and, consequently, Ultra-small implants may enhance the selectivity of recording and stimulation since viable neurons are expected to be in close proximity to the electrode sites. However, the relevant electrochemical properties of UM-dimensioned electrodes for neural recording and stimulation, such as impedance and charge-injection capacity, remain largely uninvestigated, particularly under the current-pulsing protocols employed in neural stimulation.

As a first-step in evaluating the potential of UM-dimensioned electrodes for stimulation applications, it is desirable to determine their ability to deliver charge without exceeding potential limits considered likely to produce noxious species. In this study, we have characterized sputtered iridium oxide (SIROF) electrodes in an inorganic model of interstitial fluid (model-ISF) using electrochemical impedance spectroscopy (EIS), cyclic voltammetry (CV), and voltage transient measurements during current pulsing. The electrodes are circular with nominal geometric surface areas (GSAs) of $20\text{--}1960\ \mu\text{m}^2$ and minimum linear dimensions ranging from $5\text{ to }50\ \mu\text{m}$, encompassing previously identified

UME and microelectrode dimensions. In addition, some design considerations and fabrication issues related to the use of UM-dimensioned electrodes as neural electrodes are also discussed.

A limitation of the present study is the restriction of the electrochemical measurements to a buffered saline electrolyte. The impact of biomolecule interactions and tissue encapsulation on the charge-injection characteristics of the electrodes remains largely unexplored, particularly for chronic applications.

2. Methods

2.1. Electrode fabrication

Multielectrode arrays were fabricated by depositing a 2 μm amorphous silicon carbide (a-SiC) layer on a silicon wafer by plasma enhanced chemical vapor deposition (PECVD) using established methods (Deku *et al* 2018). Conductive metal traces of Ti(40 nm)/Au(300 nm)/Ti(40 nm) were deposited and patterned on the a-SiC by DC sputtering and lift-off photolithography using the titanium as an adhesion layer between the a-SiC and gold. A second a-SiC layer, also 2 μm thick, was deposited on the patterned Ti/Au/Ti metallization and vias to electrode sites and contact pads on the gold were opened by reactive ion etching (RIE) with SF_6/O_2 using photoresist as an etch mask. The SF_6/O_2 RIE removes both the a-SiC and titanium to expose the gold. The electrode sites were then coated with 300 nm thick SIROF (Maeng *et al* 2019) using a 40 nm thick sputtered titanium adhesion layer between the gold and SIROF. To minimize misalignment, the photoresist etch mask used for the RIE opening of the vias in the a-SiC was also used for the SIROF deposition. A cross-section of the device at an electrode site is shown schematically in figure 1.

Circular SIROF electrodes with GSAs in the range of 20–1960 μm^2 were fabricated. Optical microscopy of a 962 μm^2 electrode, and an SEM image of the typical morphology of SIROF coating is presented in figures 2(a) and (b), respectively. The presence of the hexagonal gold bond pad is readily visualized using the differential interference contrast (DIC) mode on the microscope, even though it is coated with 2 μm of a-SiC. The lip of the via at the electrode site is also coated with SIROF due to slight lateral etching of the photoresist mask during the RIE process for opening vias. As a consequence of this and the sidewall SIROF coating (figure 1), the surface area of the SIROF electrodes are larger than the area defined by the via diameter. Although this is not a significant effect for the larger diameter microelectrodes, it can result in an underestimation of the GSA of the smaller electrodes. A measurement of the effective GSA for these electrodes is difficult because of the likely variation in SIROF thickness on the via sidewalls and the lack of an underlying gold contact on the sidewalls and via rim. Electrical access to the SIROF not directly deposited on the gold contact relies on the lateral sheet resistance of the titanium and SIROF that is difficult to quantify. Due to the relatively high lateral electrical resistance of the Ti/SIROF bilayer compared to gold, any contribution from the Ti/SIROF-coated sidewalls and via rim will occur mostly for slow-sweep-rate cyclic voltammetry and will be less significant for short pulse width current pulsing used for voltage transient measurements. However, because of the uncertainty in electrode GSA when comparing charge-injection capacities, we have primarily used charge/phase rather than the area-normalized charge density.

2.2. Electrochemical measurements

Electrodes were characterized by CV and EIS measurements using a Gamry Potentiostat (Gamry Instruments, Warminster PA). The CV data were acquired at a sweep rate of 50 mV s^{-1} between negative and positive potential limits of -0.6 V – 0.8 V versus Ag|AgCl. Cathodal charge storage capacities of the SIROF electrodes were calculated from the time-integral of the negative current during a complete CV cycle. EIS measurements were made over a frequency range of 1 Hz to 100 kHz about the open-circuit potential of the SIROF using a 10 mV rms sinusoidal excitation voltage. Voltage transient measurements were made in an inorganic model of interstitial fluid (model-ISF). Model-ISF is composed of 110 mM NaCl, 28 mM NaHCO_3 , 7.5 mM KHCO_3 , 2 mM $\text{Na}_2\text{HPO}_4\cdot 7\text{H}_2\text{O}$, 0.5 mM each of $\text{NaH}_2\text{PO}_4\cdot \text{H}_2\text{O}$, MgSO_4 , MgCl_2 , CaCl_2 (Cogan *et al* 2007). The pH was maintained at 7.4–7.6 by purging the electrolyte with a gas mixture of 6% CO_2 , 5% O_2 , and 89% N_2 . The CV and EIS measurements were performed at 37°C and the pH was maintained at 7.4–7.6 by purging the electrolyte with a gas mixture of 6% CO_2 , and 94% N_2 prior and during measurements. Using the mixed gas without oxygen avoids the complication of interpreting UME behavior in the presence of oxygen reduction, although this reaction is thought to be minimal on SIROF electrodes (Cogan *et al* 2010). The ionic conductivity of the model-ISF at 37°C was 14 mS cm^{-1} as measured with an Oakton CON 2700 (Vernon Hills, IL) conductivity meter.

Charge-injection capacities were determined from voltage transient measurements in response to current pulsing. Two approaches to delivering charge-balanced current pulses were employed. For measuring the effect of GSA (from $20 \mu\text{m}^2$ to $1960 \mu\text{m}^2$) and pulse width (from $100 \mu\text{s}$ to $1000 \mu\text{s}$), we employed a 16-channel stimulator (Plexon Inc., Dallas, TX) with cathodal-first, rectangular charge-balanced biphasic pulses with a $100 \mu\text{s}$ interphase delay between cathodal and anodal phases. The current was delivered in a monopolar configuration using a large-area platinum (Pt) counter-electrode. The maximum cathodic potential, E_{mc} , was measured in the interphase interval, during which the electrode is electrically floating, $12 \mu\text{s}$ after the termination of the cathodal current phase. Since the current is zero between phases, ohmic voltage drops in the electrolyte and activation overpotentials do not contribute to the measured E_{mc} . To ensure complete discharge of the electrode between pulses, the stimulation electrode is shorted to the Pt counter-electrode in the interpulse period. The voltage transient was measured in a two-electrode configuration using the Pt counter-electrode as a pseudo-reference electrode. The maximum charge per phase was defined as the charge that polarizes the SIROF electrode -0.6 V with respect to the Pt counter-electrode. Since Pt adopts a potential of about 0.3 V with respect to Ag|AgCl in pH 7.4 saline electrolytes, this is a conservative measure of charge-injection capacity since the electrode should be polarized to only -0.3 V versus Ag|AgCl, approximately 0.3 V positive of the water reduction potential on SIROF. Operating the stimulator in this mode has the effect of positively biasing the SIROF to 0.3 V versus Ag|AgCl in the interpulse period.

We also measured the charge-injection capacity of the electrodes as a function of an interpulse bias from 0.1 V to 0.6 V versus Ag|AgCl. The bias measurements were made with a custom stimulator (Sigenics Inc. Chicago IL) that employs a three electrode configuration in which the SIROF stimulation electrode is biased against a Ag|AgCl reference electrode in

the interpulse period. The polarization of the SIROF was also measured against Ag|AgCl and the maximum charge injection capacity defined as the charge that polarizes the SIROF to an E_{mc} of -0.6 V Ag|AgCl, approximately the potential for the onset of water reduction on SIROF. The stimulator maintains charge-balance by re-establishing the bias potential at end of the current pulse. The electrode is also allowed to electrically float (zero current flow) for approximately $100 \mu\text{s}$ at the end of the current pulse to facilitate measuring E_{mc} (Cogan 2008).

The high impedance and low currents associated with the UM-dimensioned electrodes required the use of a Faraday cage and the shortest practical cable length between the electrodes and measuring equipment. To assess the magnitude of leakage currents arising from the experimental set-up and from capacitive coupling between metal traces on the UM-dimensioned electrode array and between the traces and the electrolyte, some UM-dimensioned electrode sites were not opened. These closed sites were characterized by EIS, CV and voltage transient measurements to provide baseline data on the contribution of capacitive and resistive leakage pathways to the measured SIROF electrode properties.

2.3. Statistical analysis

Data were tested for normality using the Shapiro–Wilk test in Stata 12 (StataCorp, College Station TX) and are reported as mean plus or minus one standard deviation. Typically, four electrodes of each type were measured on a single wafer and the variance reflects intra-wafer variability rather than wafer-to-wafer variability of the fabrication process.

3. Results

3.1. Cyclic voltammetry

Representative CV cycles in model-ISF at 50 mV s^{-1} are compared in figure 3 for circular SIROF electrodes with diameters of $5 \mu\text{m}$ – $50 \mu\text{m}$ ($20 \mu\text{m}^2$ – $1960 \mu\text{m}^2$). The shape of the cyclic voltammograms is similar to that reported previously for SIROF in model-ISF with the redox waves being somewhat less pronounced than those reported in phosphate buffered saline, which typically has a higher buffering capacity than model-ISF (Cogan *et al* 2009, 2007). The cathodal charge calculated from the time-integral of the current in the CVs is shown in figure 4 as a function of GSA. The charge decreases approximately linearly with GSA from $960 \pm 100 \text{ nC}$ to $21 \pm 0.4 \text{ nC}$ ($n = 4$) as the GSA is reduced from $1960 \mu\text{m}^2$ to $20 \mu\text{m}^2$. As shown in figure 5, the cathodal charge storage capacities were approximately independent of GSA from 200 to $1960 \mu\text{m}^2$, varying from 44 mC cm^{-2} to 49 mC cm^{-2} . An increase in cathodal charge storage capacity was observed for electrodes with a $\text{GSA} < 200 \mu\text{m}^2$, increasing to a maximum of $109 \pm 2 \text{ mC cm}^{-2}$ ($n = 4$) for the $20 \mu\text{m}^2$ electrode. In the rest of the manuscript electrodes with $\text{GSA} < 200 \mu\text{m}^2$ and $\text{GSA} \geq 200 \mu\text{m}^2$ are represented with filled and open symbols, respectively.

3.2. Impedance

The impedance magnitude is shown in figure 6 for SIROF electrodes with GSAs from 20 to $1960 \mu\text{m}^2$. As expected, the impedance across the 1 – 10^5 Hz frequency range increases with decreasing GSA with the 1 kHz impedance increasing from $12 \pm 1.4 \text{ k}\Omega$ to $241 \pm 11 \text{ k}\Omega$ ($n =$

4) as the GSA decreases from $1960 \mu\text{m}^2$ to $20 \mu\text{m}^2$. Without the SIROF coating, the impedance of a $20 \mu\text{m}^2$ gold electrode at 1 kHz was $12 \pm 1.8 \text{ M}\Omega$ ($n = 4$).

3.3. Current pulsing

To determine the maximum charge that can be injected during current-controlled stimulation, voltage transients of SIROF-coated electrodes with GSAs of $20 \mu\text{m}^2$ – $1960 \mu\text{m}^2$ were measured. The maximum injectable charge in response to a $200 \mu\text{s}$ cathodal current pulse, defined by a net 0.6 V negative polarization from 0.0 V to -0.6 V versus Pt, was determined from voltage transients, as shown for representative transients in figure 7 and tabulated in table 1. The injectable charge decreases from $28 \pm 5 \text{ nC/ph}$ to $0.7 \pm 0.1 \text{ nC/ph}$ as the GSA decreases from $1960 \mu\text{m}^2$ to $20 \mu\text{m}^2$, whereas the area-normalized charge-injection capacity increases with decreasing electrode GSA from $1.4 \pm 0.2 \text{ mC cm}^{-2}$ ($1960 \mu\text{m}^2$) to $3.3 \pm 0.5 \text{ mC cm}^{-2}$ ($20 \mu\text{m}^2$). The access resistance (R_a), calculated from the current and access voltage (V_a) is also reported in table 1 and increases with decreasing GSA from $6.4 \pm 0.4 \text{ k}\Omega$ ($V_a = 860 \pm 90 \text{ mV}$) for the $1960 \mu\text{m}^2$ electrodes to $63 \pm 2 \text{ k}\Omega$ ($V_a = 140 \pm 15 \text{ mV}$) for the $20 \mu\text{m}^2$ electrodes. The lower V_a results from the greatly reduced maximum current that the smaller GSA electrodes can support without being polarized to the -0.6 V versus Pt potential limit.

In order to compare the effect of pulse width on maximum charge injection capacity of SIROF UM-dimensioned electrodes, SIROF electrodes were subjected to rectangular current pulses with pulse widths from $100 \mu\text{s}$ to $1000 \mu\text{s}$, in steps of $100 \mu\text{s}$. In figure 8, the maximum injectable charge/phase is compared for a $95 \mu\text{m}^2$ SIROF UM-dimensioned electrode and a $1960 \mu\text{m}^2$ SIROF microelectrode. For both electrodes, the average charge/phase increases approximately linearly with pulse width from 2.2 nC/ph to approximately 4 nC/ph for the $95 \mu\text{m}^2$ electrodes and from $37 \pm 0.5 \text{ nC/ph}$ to $67 \pm 1 \text{ nC/ph}$ ($n = 4$) for the $1960 \mu\text{m}^2$ electrodes. The precision of the maximum charge for the $95 \mu\text{m}^2$ UM-dimensioned electrode is limited by the $1 \mu\text{A}$ minimum current resolution of the stimulator and the charge resulting in an E_{mc} closest to -0.6 V versus Pt, either above or below, is reported in figures 8 and 9. When normalized to the electrode surface area (figure 9), the charge-injection capacity is notably higher for the $95 \mu\text{m}^2$ electrode, increasing from 2.3 mC cm^{-2} to $\sim 4 \text{ mC cm}^{-2}$ with increasing pulse width for the $95 \mu\text{m}^2$ electrodes compared with $1.9 \pm 0.02 \text{ mC cm}^{-2}$ to $3.4 \pm 0.05 \text{ mC cm}^{-2}$ ($n = 4$) for the $1960 \mu\text{m}^2$ electrodes. The effect of interpulse bias on the charge-injection capacity of SIROF UM-dimensioned electrodes was assessed using cathodal, controlled-current pulsing. For these measurements, the bias was controlled with respect to a Ag|AgCl reference electrode and the SIROF polarization also measured with respect to Ag|AgCl. A comparison of the maximum charge/phase versus interpulse bias is shown in figure 10 for a range of GSAs from $20 \mu\text{m}^2$ to $1960 \mu\text{m}^2$. As expected, the injectable charge/phase increases with positive bias for all GSAs. For the $20 \mu\text{m}^2$ SIROF maximum injectable charge increases from $0.51 \pm 0.05 \text{ nC}$ to $1.32 \pm 0.03 \text{ nC}$ ($n = 4$) as the bias increases from 0.0 V to 0.6 V versus Ag|AgCl. Likewise, the injectable charge for the $50 \mu\text{m}^2$ SIROF increases from $0.98 \pm 0.01 \text{ nC}$ to $3.1 \pm 0.1 \text{ nC}$ ($n = 4$) as the bias is increased from 0.0 V to 0.6 V Ag|AgCl.

3.4. Inter-trace capacitive coupling

Since electrochemical measurements and charge delivery with UM-dimensioned electrodes are associated with very small currents and high electrode impedances, the potential for errors due to inter-trace shunt capacitance, and capacitance between metal traces and the electrolyte can be significant (Wellman *et al* 2018). The EIS spectrum of a metal trace with an unopened electrode site and a $20\ \mu\text{m}^2$ circular SIROF electrode measured in model-ISF are compared in figure 11. As shown, the impedance of the unopened site, which is representative of trace impedance and capacitive shunting, is at least one order of magnitude higher than the SIROF electrode impedance at frequencies below about 5 kHz. However, as observed in figure 11, at higher frequencies the trace impedance can become comparable to the electrode impedance. Under this circumstance, the shunt capacitance provides a parallel current pathway that can affect electrochemical measurements, particularly voltage transients. As an example, the voltage transient responses of a $20\ \mu\text{m}^2$ SIROF UM-dimensioned electrode is compared in figure 12 for two device configurations, one with narrow traces and $2\ \mu\text{m}$ thick a-SiC encapsulation ((a), figure 12) and a second configuration with wide, large-area metal traces and $0.5\ \mu\text{m}$ thick a-SiC encapsulation ((b), figure 12). Both UM-dimensioned electrodes were subjected to symmetric, biphasic current pulsing with a $200\ \mu\text{s}$ pulse width and the maximum charge-injection current, defined by an $E_{\text{mc}} = -0.6\ \text{V}$ versus Pt, determined to be $4\ \mu\text{A}$ for design (a) and $7\ \mu\text{A}$ for design (b), respectively $0.8\ \text{nC/ph}$ and $1.4\ \text{nC/ph}$. The shunt capacitance in the wide-trace design ((b) in figure 12) dominates the voltage transient with no obvious access voltage at the onset of the current pulse and there is a considerable overestimate of the charge injection capacity. Included in figure 12 is the voltage transient response of a closed electrode site on an array with the low shunt capacitance (design (a)). Based on the slope of the closed-site transient response, the shunt capacitance for this electrode site is approximately $50\ \text{pF}$.

4. Discussion

Previous studies have demonstrated *in vivo* recordings with UM-dimensioned electrodes (Guitchounts *et al* 2013, Patel *et al* 2016, Wei *et al* 2018), but there are only limited reports of *in vivo* neural stimulation with electrodes in this size range (Gillis *et al* 2018). In addition, prior *in vivo* stimulation studies have focused on penetrating electrodes with UM-dimensioned cross-sectional diameters or widths ($<10\ \mu\text{m}$) but with electrode lengths generally greater than $50\ \mu\text{m}$ (Gillis *et al* 2018), resulting in electrode GSAs as large as $2500\ \mu\text{m}^2$ and thus high levels of charge injection (Gillis *et al* 2018). From the charge-injection data in the present study, it is apparent that UM-dimensioned electrodes are capable of supporting high charge-injection densities. However, the charge/phase is low compared to similar SIROF microelectrodes, being less than $4\ \text{nC/phase}$ (at zero interpulse bias) for electrodes with a GSA $< 200\ \mu\text{m}^2$. This raises the concern that the limited charge/phase of UM-dimensioned electrodes will not be sufficient for eliciting functional responses during neural stimulation.

It seems reasonable to use charge thresholds for microelectrode stimulation as a point of reference for assessing the potential of SIROF electrodes with a GSA $< 200\ \mu\text{m}^2$ for neural stimulation. Charge thresholds for microelectrode stimulation have been reported

extensively for both brain and peripheral nerves and, in some cases, are on the order of that deliverable in model-ISF with electrodes having GSAs $< 100 \mu\text{m}^2$. For example, thresholds of 0.8–2 nC/ph were observed for auditory percepts in humans with penetrating electrode arrays in the cochlear nucleus (McCreery 2008). Similarly, reported thresholds for selective stimulation of peripheral nerves with indwelling electrodes range from 0.2 nC to 5.5 nC in some animal and chronic human studies (Dhillon *et al* 2004, Boretius *et al* 2010, Badia *et al* 2011, Davis *et al* 2016).

A compilation of threshold charge levels reported for microelectrodes used in peripheral nerve and brain implants is provided in figure 13. These thresholds are compared with maximum injectable charge levels in model-ISF as a function of GSA for the SIROF electrodes. As can be seen, the maximum charge levels with a 200 μs pulse width for SIROF electrodes with GSAs in the $20 \mu\text{m}^2$ – $95 \mu\text{m}^2$ range are comparable to thresholds reported in a number of *in vivo* studies, particularly if the SIROF is biased to 0.6 V versus Ag|AgCl. However, charge injection capacities measured *in vivo* can be 2–10 times lower than those measured in buffered saline (Leung *et al* 2014, Brunton *et al* 2015, Cogan *et al* 2016) and SIROF electrodes, in particular, exhibit a factor of 2–3 decrease in charge-injection capacity *in vivo*, depending on interpulse bias (Kane *et al* 2013). Whether UM-dimensioned electrodes will have the same threshold charge levels as microelectrodes for eliciting a clinically relevant response also remains to be determined. If the expectation that ultra-small shanks ($\leq 15 \mu\text{m}$ in two dimensions) induce minimal foreign body response (Seymour and Kipke 2007, Stice *et al* 2007, Skousen *et al* 2011) is realized and viable neural cells are in close proximity to the electrode site (Seymour and Kipke 2007), then we might expect lower charge thresholds for neural activation. However, it is also unclear what functional benefit may arise from the excitation of these small volumes of neural tissue. In addition, cells in close proximity to the electrode sites may be susceptible to electroporation, a damage mechanism not usually associated with microelectrode stimulation (Butterwick *et al* 2007, Cogan *et al* 2016).

It is well-established that electrodes with at least one dimension on the order of 25 μm or smaller can exhibit sigmoidal CVs that are characteristic of UME behavior, for the oxidation or reduction of electroactive species whose transport to the electrode is substantially governed by diffusion. These sigmoidal CVs are observed in voltammetry UMEs due to kinetically-controlled redox currents at the electrode which arise when the diffusion rate of electroactive species, to or from the UME, exceeds the reaction rate at the electrode interface (Heinze 1991).

In the case of SIROF charge-injection electrodes, the electroactive species are presumably H^+ or OH^- counterions that maintain charge neutrality during switching of the $\text{Ir}^{3+}/\text{Ir}^{4+}$ redox couple within the SIROF film (Cogan 2008). The availability of the H^+ or OH^- counterions is determined not only by transport in the electrolyte, but by the action of the carbonate and phosphate buffers in the model-ISF, which work to maintain a constant pH of ~ 7.4 at the electrode interface. The availability of buffer is also limited by transport in the electrolyte, particularly the carbonate buffer which relies on dissolved CO_2 , making the analysis of the transport process challenging. The SIROF electrodes in the present study in model-ISF electrolyte did not exhibit the characteristic sigmoidal CV of voltammetry UMEs, over a

sweep rate range of 3 mV s^{-1} – 6400 mV s^{-1} . The CSC values were scan rate dependent, but there was not a marked difference in behavior between UM-dimensioned electrodes and microelectrodes at the current densities encountered in the CVs, which are typically 1–3 orders of magnitude lower than those encountered during measurements of maximum charge-injection capacity. However, there is a notable increase in Q_{inj} of the SIROF electrodes with diameters smaller than $16 \mu\text{m}$ (GSA $200 \mu\text{m}^2$). As shown in figure 5 and table 1, we observe a 70% increase in charge injection capacity for $20 \mu\text{m}^2$ electrodes compared to those with a GSA of $200 \mu\text{m}^2$. Whether this increase is due to an underestimation of electrode GSA or a transition to hemispherical transport of species involved in the redox reactions is difficult to determine.

However, we did observe voltage transient responses of SIROF electrodes with a GSA $< 200 \mu\text{m}^2$, which are suggestive of UME behavior. These voltage transients are shown in figure 14, for electrodes with GSAs ranging 20 – $1960 \mu\text{m}^2$. The electrodes are pulsed at a similar current density, between 20.2 – 23.7 A cm^{-2} , corresponding to a charge-injection density of approximately 4.2 mC cm^{-2} for all electrode GSAs. In current-controlled measurements of this type, the availability of electro-active species supporting the desired electrode reactions can be limited by transport in the electrolyte. In the case of reduction reactions supporting a cathodal-first current pulse, the consequence of the limited availability of the electro-active species is a typically abrupt negative shift in potential to recruit other electrode reactions to support the current flow. For SIROF electrodes, this reaction is likely the reduction of water. The time from the onset of the current pulse to the negative shift in potential is identified as a transition time that for chronopotentiometric measurements, corresponds to the exhaustion, or zero concentration, of electro-active species at the electrode interface (Bard and Faulkner 2001). As observed in figure 14, the larger diameter electrodes ($1960 \mu\text{m}^2$, $960 \mu\text{m}^2$, and $310 \mu\text{m}^2$) exhibit a similar transition time which is indicated by the arrows. For the smaller electrodes, the transition time is longer and for electrodes with GSAs of $20 \mu\text{m}^2$ and $50 \mu\text{m}^2$, no transition time is observed, suggesting that the rate of the $\text{Ir}^{3+}/\text{Ir}^{4+}$ redox reaction and availability of counterions for this reaction is sufficient to support the current density without a transition to water reduction. These observations are consistent with a transition from linear to hemispherical transport of electro-active species to the electrode interface (Bard 1961, Lingane 1964), although we do not consider this definitive evidence of hemispherical transport given the complex nature of H^+/OH^- counter ion availability at the electrode interface by mechanisms not relevant in these earlier studies. In preliminary studies (data not presented), we have investigated UME behavior of SIROF electrodes in a non-aqueous electrolyte with a neutral electro-active species, ferrocene in acetonitrile, and found clear evidence of a linear-to-hemispherical transition in diffusion of ferrocene for $20 \mu\text{m}^2$ and $50 \mu\text{m}^2$ SIROF electrodes. Although these observations confirming that UME behavior is possible with the smaller SIROF electrodes, at least for ferrocene oxidation, further studies would be necessary to confirm hemispherical transport in buffered saline electrolytes or for implanted electrodes.

Whereas the charge injection limits for the smaller SIROF electrodes (GSA $< 200 \mu\text{m}^2$) may exceed some anticipated functional thresholds (figure 13), shunt capacitance, as shown in figure 12, can significantly influence the voltage transient response and current pathways during stimulation pulsing. Consequently, the current and charge delivered through an

electrode will be less than that calculated from the total applied current. Following the discussion by Wellman *et al* (2018), the effect of dielectric encapsulation on shunt capacitance and impedance can be described by the equations

$$C_{\text{shunt}} = k\epsilon_0 A/d; Z_{\text{shunt}} = 1/j\omega C_{\text{shunt}}$$

where Z_{shunt} is the impedance of the shunt capacitance (C_{shunt}), ω the angular frequency, κ the dielectric constant, ϵ_0 the vacuum permittivity, A the trace area, and d the encapsulation thickness. The narrower traces and thicker a-SiC encapsulation of design (a) compared with design (b) in figure 12, demonstrate the effect of trace area and encapsulation thickness and, clearly, narrower traces and thicker insulation reduce shunt capacitance and increase the shunt impedance. The effect of shunt capacitance is more pronounced at higher frequencies as the capacitive impedance decreases, as shown by the comparison in figure 11 of the impedance spectra of a $20 \mu\text{m}^2$ SIROF electrode and a similar electrode trace with a closed electrode site.

Based on the 50 pF shunt capacitance of a closed electrode site (figure 12), we can estimate approximately 0.05 nC of charge will be lost to shunt capacitance for a one volt drop between the metal trace and electrolyte. We assume that the voltage drop along the metal trace is negligible. For the example in figure 12, the maximum voltage excursion from the transient in design a is approximately 0.75 V and, therefore, we expect about 0.038 nC of charge will be lost to shunt capacitance, which is 5% of the nominal charge in the $200 \mu\text{s}$, $4 \mu\text{A}$ (0.8 nC) current pulse. Clearly, the effect of shunt capacitance should be considered when investigating stimulation with UM-dimensioned electrodes. For electrode (a) in figure 12, the metal traces and encapsulation are designed to minimize shunt capacitance, albeit at the expense of some increase in resistance of the metal traces, and the charge lost to shunt capacitance is modest, but still 15%–20% of the lowest intraneural thresholds reported for TIME and LIFE electrodes in peripheral nerve (Boretius *et al* 2010, Badia *et al* 2011). For the wide electrode traces and thin a-SiC encapsulation, design (b) in figure 12, the shunt capacitance dominates the voltage transient response. The absence of a distinct R_a at the beginning or end of the current pulse suggests that the majority of the current flows into the shunt capacitance and not across the SIROF/ electrolyte interface.

5. Conclusion

The electrochemical properties of SIROF-coated electrodes relevant to neural stimulation and recording have been evaluated in an inorganic buffered saline over a range of electrode GSAs from $20 \mu\text{m}^2$ to $1960 \mu\text{m}^2$. We have shown that SIROF electrodes with a GSA as small as $20 \mu\text{m}^2$ can deliver charge in model-ISF at functional threshold levels reported for neural stimulation in brain and peripheral nerve with microelectrodes having a much larger GSA ($\sim 2000 \mu\text{m}^2$). This observation raises the possibility of spatially focal stimulation of neural tissue on a dimensional scale not previously investigated with electrodes that may also induce minimal foreign body response. In addition, the SIROF electrodes with a GSA of $20 \mu\text{m}^2$ exhibit 1 kHz impedance values of approximately 250 k Ω , suitable for neural recording. Our studies also suggest, but do not confirm, that SIROF electrodes with GSAs of

20 μm^2 –200 μm^2 exhibit behavior expected with UMEs where transport of electroactive species to the electrode is via hemispherical rather than linear diffusion. Further investigation via numerical methods is required to confirm the hemispherical transport of reactive species to SIROF electrodes with GSAs of 20 μm^2 –200 μm^2 during voltage transient measurements. The study also demonstrated that careful consideration must be given to the design of multielectrode arrays with UM-dimensioned electrode sites to minimize the effect of shunt capacitance on the delivered charge.

Although SIROF electrodes with GSAs as small as 20–50 μm^2 , exhibit electrochemical properties suitable for neural stimulation and recording in buffered saline, *in vivo* measurements are necessary to establish the potential usefulness of these electrodes in chronic neural applications. It will be necessary in future studies to assess the charge-injection behavior of these electrodes in the presence of a chronic foreign body response. Any significant glial scarring and consequent isolation of the electrodes from the target neural tissue would significantly reduce their effectiveness as stimulation electrodes. In addition, the stability of SIROF, or other electrode coatings, at the high current densities associated with charge delivery with 20–50 μm^2 electrodes should be assessed. Possible stimulation-induced neural damage due to electroporation and tissue or device heating will also need to be evaluated, particularly if viable neural tissue is in close apposition to the electrode sites. Whether UM-dimensioned electrodes offer advantages in terms of increased selectivity of neural stimulation and recording and whether such increased selectivity translates to chronic research or clinical applications remains to be determined.

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Figure 1.

Schematic cross-section of an electrode site on an ultramicroelectrode array showing the amorphous silicon carbide (a-SiC) layers (each 2 μm thick), the Ti/Au/Ti metallization (380 nm total thickness), and the 300 nm thick sputtered iridium oxide (SIROF). The SIROF is also shown on the via sidewalls and on the upper surface of the top a-SiC. A 40 nm thick Ti adhesion layer between the SIROF and Au contact pad is not shown. The width and thickness dimensions are approximately to scale for a 5 μm diameter SIROF electrode.

Figure 2.

(a) Optical image of a sputtered iridium oxide (SIROF) electrode site with a 35 μm via diameter. The hexagonal gold bond pad is readily visualized, although it is coated with 2 μm of amorphous silicon carbide (a-SiC). The SIROF extends from the bottom of the via up the sidewall and forms a narrow ring around the lip of the via, and (b) typical nodular surface morphology of the SIROF electrode coating.

Figure 3.

Comparison of cyclic voltammograms of sputtered iridium oxide (SIROF) electrodes with geometric surface areas (GSAs) ranging from 20 μm^2 to 1960 μm^2 acquired in model-ISF at a 50 mV s⁻¹ sweep rate. For clarity, symbols are plotted every five data points.

Figure 4.

Cathodal charge capacity of sputtered iridium oxide (SIROF) electrodes as a function of geometric surface area (GSA) from 1960 μm^2 to 20 μm^2 . The inset shows more detail of the cathodal charge in the 20–310 μm^2 GSA range. Data are plotted as mean $\pm$ sd ($n = 4$). Where not shown, the standard deviation is smaller than the symbol size.

Figure 5.

Cathodal charge storage capacity (CSC) of sputtered iridium oxide (SIROF) electrodes as a function of geometric surface area (GSA) from 1960 μm^2 to 20 μm^2 . The inset shows more detail of the CSC in the 20–310 μm^2 GSA range. Data are plotted as mean $\pm$ sd ($n = 4$).

Where not shown, the standard deviation is smaller than the symbol size.

Figure 6.

Impedance magnitude in the 1–10⁵ kHz range for sputtered iridium oxide (SIROF) electrodes with a geometric surface area (GSA) ranging from 20 μm^2 to 1960 μm^2 . For clarity, symbols are plotted every fourth data point.

Figure 7.

Representative cathodal-current voltage response of sputtered iridium oxide (SIROF) electrodes pulsed with a symmetric biphasic current pulse with 200 μ s pulse width and 0 V interpulse potential with respect to a platinum counter electrode. Measurements were made in model-ISF at 37 °C. For clarity, symbols are plotted every 25–50 data points.

Figure 8.

Comparison of the maximum charge/phase for a 300 nm sputtered iridium oxide (SIROF) ultramicro-dimensioned (UM-dimensioned) electrode (GSA = $95 \mu\text{m}^2$) and a 300 nm SIROF microelectrode (GSA = $1960 \mu\text{m}^2$) as a function of pulse width. Data are plotted as mean $\pm$ sd ($n = 4$). Where error bars are not shown, the standard deviation is smaller than the symbol size. The dashed line is drawn as an aid to the eye.

Figure 9.

Comparison of the charge injection capacity as a function of pulse width for 300 nm thick sputtered iridium oxide (SIROF) electrodes with 95 μm^2 and 1960 μm^2 geometric surface areas (GSAs) in response to a biphasic current pulsing from a nominal interpulse potential of 0 V versus Pt. Data are plotted as mean $\pm$ sd ($n = 4$). Where error bars are not shown, the standard deviation is smaller than the symbol size. The dashed line is drawn as an aid to the eye.

Figure 10.

Comparison of the charge per phase as a function of interpulse bias for 300 nm thick sputtered iridium oxide (SIROF) electrodes as a function of geometric surface area (GSA) in response to charge-balance current pulsing with a pulse width of 200 μs . Data are plotted as mean $\pm$ sd ($n = 4$). Where error bars are not shown, the standard deviation is smaller than the symbol size. The dashed line is drawn as an aid to the eye.

Figure 11.

Comparison of the impedance of a 20 μm^2 circular sputtered iridium oxide (SIROF) electrode with a closed electrode site of similar geometry both in model-ISF at 37 °C. The impedance of a high-precision 5 GΩ resistor showing the frequency response of the measuring instrument and cables is provided for reference. Symbols are plotted every 5 data points.

Figure 12.

Comparison of voltage transients of $20\ \mu\text{m}^2$ sputtered iridium oxide (SIROF) electrodes with narrow metal traces and $2\ \mu\text{m}$ thick amorphous silicon carbide (a-SiC) encapsulation ((a) in image) and wide metal traces with $0.5\ \mu\text{m}$ a-SiC encapsulation ((b) in image) pulsed with a symmetric biphasic current pulse at $4\ \mu\text{A}$ and $7\ \mu\text{A}$, respectively and $200\ \mu\text{s}$ pulse width ($0.8\ \text{nC/phase}$, $1.4\ \text{nC/phase}$) in model of interstitial fluid (model-ISF) at $37\ ^\circ\text{C}$. A voltage transient showing the shunt capacitance charging at $1\ \mu\text{A}$ of closed electrode site with design (a) is also shown.

Figure 13.

Comparison of *in vivo* stimulation thresholds and the maximum injectable charge/phase of sputtered iridium oxide (SIROF) electrodes pulsed in model of interstitial fluid (model-ISF) as a function of electrode geometric surface area (GSA). The nerve target for the transverse intrafascicular microelectrode (TIME) and thin film longitudinal intrafascicular electrode (tf-LIFE), Utah slanted electrode array (USEA), LIFE, and auditory brainstem implant (ABI) were rat sciatic nerve (Boretius *et al* 2010) (Badia *et al* 2011), human ulnar and median nerves (Davis *et al* 2016), and human ulnar, median, common peroneal nerves (Dhillon *et al* 2004), and human cochlear nucleus (Shepherd and McCreery 2006), respectively. For the $20 \mu\text{m}^2$ – $314 \mu\text{m}^2$ SIROF, the range of injectable charge as a function of interpulse bias from 0.0 V to 0.6 V versus Ag|AgCl in response to charge-balance current pulsing with a pulse width of $200 \mu\text{s}$ is shown.

Figure 14.

Representative cathodal-current voltage response of sputtered iridium oxide (SIROF) electrodes pulsed with a charge-balance pulse with 200 μs pulse width and similar applied current density (20.2 A cm^{-2} – 23.7 A cm^{-2}) with respect to a Ag|AgCl reference electrode. Measurements were made in model-ISF. For clarity, symbols are plotted every 25–50 data points. Dashed arrows show the transition time of different electrode sizes.

Table 1.

Maximum charge injection capacity (CIC) and charge per phase of SIROF electrodes using an E_{mc} of -0.6 V versus Pt obtained from voltage transient measurements.

Diameter (μm)	GSA (μm^2)	Current (μA)	Charge (nC)	CIC (nC cm^{-2})	V_a (mV)	R_a (k Ω)
5	20	3.3 ± 0.5	0.7 ± 0.1	3.3 ± 0.5	204 ± 24	63 ± 2
8	50	8 ± 0.8	1.6 ± 0.2	3.2 ± 0.3	328 ± 16	41 ± 2
11	95	10 ± 0.8	2.0 ± 0.2	2.1 ± 0.2	288 ± 55	28 ± 4
16	201	20 ± 1.3	3.9 ± 0.3	1.9 ± 0.1	380 ± 46	19 ± 2
20	310	30 ± 1	6 ± 0.1	1.9 ± 0.03	440 ± 10	15 ± 0.4
35	962	78 ± 11	16 ± 2	1.6 ± 0.2	770 ± 99	9.9 ± 0.4
50	1960	139 ± 23	28 ± 5	1.4 ± 0.2	860 ± 90	6.4 ± 0.4