Neuromodulation Devices

# Scaling Effects on the Electrochemical Stimulation Performance of Au, Pt, and PEDOT:PSS Electrocorticography Arrays

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The efficacy of electrical brain stimulation in combatting neurodegenerative diseases and initiating function is expected to be significantly enhanced with the development of smaller scale microstimulation electrodes and refined stimulation protocols. These benefits cannot be realized without a thorough understanding of scaling effects on electrochemical charge injection characteristics. This study fabricates and characterizes the electrochemical stimulation capabilities of Au, Pt, poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS/Au), and PEDOT:PSS/Pt electrode arrays in the 20-2000 µm diameter range. This study observes substantial enhancement in charge injection capacity up to 9.5× for PEDOT:PSS microelectrodes compared to metal ones, and 88% lower required power for injecting the same charge density. These significant benefits are strongest for electrode diameters below 200 µm. Detailed quantitative analyses are provided, enabling optimization of charge injection capacity with potential bias and symmetric and asymmetric pulse width engineering for all diameters. These systematic analyses inform the optimal design for acute and potentially chronic implants in regards to safety and clinically effective stimulation protocols, ensure the longevity of the electrodes below critical electrochemical limits of stimulation, and demonstrate that the material choice and pulse design can lead to more energy efficiency stimulation protocols that are of critical importance for fully implanted devices.

such as cochlear implants, deep brain stimulation (DBS), and spinal cord stimulation for the treatment of neurological disease and disorders.<sup>[1-10]</sup> Critical for the success of these devices is to maintain the desired functional response through injection of a safe amount of charge using capacitive and reversible faradaic mechanisms without causing any deleterious effects on either the electrodes or the surrounding tissue.<sup>[11,12]</sup> Previous pioneering work has shown that a variety of factors contribute to safe, efficient, and functional electrical stimulation; factors range from material choices and electrode geometries to stimulation methodology, i.e., controlling stimulation parameters such as pulse width, charge density, interpulse potentials, and bias.<sup>[13,14]</sup> The assessment of micro-/macroneuronal electrodes for functional and safe therapeutic stimulation of physiological tissue and excitable cells hinges on the details of charge injection reactions at the electrode-tissue interface.<sup>[15]</sup> In most clinical applications, electrical stimulation is injected through a biphasic charge-balanced stimulus waveform, which are identified by charge per

### 1. Introduction

Therapeutic electrical stimulation is witnessing an explosion of interest due to the success of recent neuromodulation devices

phase or charge density.<sup>[12,16]</sup> These stimulus pulse parameters are important factors that are usually correlated with thresholds for tissue damage and are traditionally described by the Shannon equation.<sup>[17,18]</sup> Although the precise relation between

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tissue damage and stimulation biproduct and polarization remains unclear, in practice, in vivo charge-injection limits are typically deduced from in vitro charge injection measurements in a buffered physiological saline (PBS) solution to predict potential tissue damage of neuronal electrodes.

The maximum in vitro charge-injection capacity limit is described as the maximum charge delivered through capacitive or reversible faradaic reaction without polarizing the electrode potential beyond the water window limit (reduction and oxidation of water).<sup>[13,19]</sup> Noble metal electrodes, such as Pt and Pt alloys that are presently employed in clinical stimulation and recording (e.g., deep brain stimulation and cochlear implants), possess large electrode areas with limited charge injection limits of 0.3 mC cm<sup>-2</sup>.<sup>[20]</sup> However, for some therapeutic stimulation purposes such as an intracortical microstimulation prosthesis (ICMS), the electrode sizes are chosen to be at microscale dimensions to permit localized stimulation of small neuronal populations. Typically, these prosthesis applications require charge injection densities above 0.5 mC cm<sup>-2</sup>, which might exceed the charge injection limits of noble metal electrodes, resulting in electrode degradation and tissue damage.<sup>[6,21,22]</sup> To provide higher levels of charge injection, different novel coating materials such as IrOx, TiN, and poly(3,4-ethylenedioxythioph ene):polystyrene sulfonate (PEDOT:PSS) have been employed. Iridium oxide and its derivatives, such as activated iridium oxide films (AIROF) that is formed by electrochemical activation of iridium metal, or sputtered iridium oxide films (SIROF) that is deposited by reactive sputtering from iridium metal in an oxidizing plasma, hold great promise as coating materials for next-generation nerve electrodes. These materials are well characterized and optimized for higher charge injection limits  $(3.8 \text{ mC cm}^{-2} \text{ for AIROF and 5 mC cm}^{-2} \text{ for SIROF with the})$ application of positive interpulse bias) enabled by a fast and reversible faradaic reaction involving reduction and oxidation between the Ir<sup>3+</sup> and Ir<sup>4+</sup> states of the oxide.<sup>[23-25]</sup>

In addition to metal oxides, conducting polymers (CPs) have also emerged as prospective coating materials for nextgeneration stimulating and recording electrodes. Particularly, PEDOT:PSS organic coating has been used extensively in neural interface applications.<sup>[26-32]</sup> It is argued that PEDOT:PSS reduces the electrochemical mismatch at the electrode/electrolyte interface due to its mixed electronic/ionic conductivity, and that it helps reduce the mechanical mismatch between electrode and tissue due to its soft nature. Therefore, these organic polymer-coated electrodes are viewed as a serious alternative for metal and metal oxide electrodes.<sup>[33-35]</sup> From a stimulation perspective, PEDOT:PSS coating has also shown a long-term electrochemical stability under in vitro and chronic in vivo conditions with higher charge injection limits compared to metal (PtIr) or metal oxides (IrOx).<sup>[19]</sup> With the growing interest in PEDOT:PSS electrophysiology devices and to facilitate their advancement, a thorough and systematic investigation of their charge injection and storage capacities and how these limits are influenced by the scaling of the electrode size is necessary. PEDOT:PSS is commonly deposited by electrodeposition.<sup>[19,26,27,34,36,37]</sup> This work focuses on PEDOT:PSS that is deposited from solution by spin-casting and patterned peel-off and followed by thermochemical polymerization, developed by Malliaras and co-workers,<sup>[28,29,33]</sup> as described in detail below.

This method provides a smooth PEDOT:PSS surface, and a uniform and identical coating of all electrodes for a given array geometry.<sup>[32]</sup>

Here, we investigated and optimized the charge injection of PEDOT:PSS-coated micro-/macroelectrodes (PEDOT:PSS on Au and PEDOT:PSS on Pt) and quantified their superiority to uncoated Au and Pt electrodes at different electrode diameters for the first time. Given the wide range of electrode geometry choices for different clinical purposes,<sup>[13]</sup> we studied the scaling effects on charge injection capacity (CIC) and charge storage capacity (CSC) for these materials. Additionally, we studied the effect of positive interpulse potential (bias voltage) on the CIC of PEDOT:PSS/Au electrodes and determined a 0.4 V as an optimal interpulse bias. Furthermore, we determined the influence of asymmetric pulse engineering (with different anodal/ cathodal pulse width ratios) on CIC of PEDOT:PSS electrodes. Finally, the frequency dependency and the possible correlation of CIC with charge storage capacity are presented and discussed.

#### 2. Results and Discussion

Neural probes with different electrode materials including Au, PEDOT:PSS/Au, Pt, and PEDOT:PSS/Pt were fabricated on 4-5 um thick parylene C substrate. The details of the fabrication procedure were described previously.<sup>[32,35]</sup> The form factor and electrode layout of PEDOT:PSS/Au electrophysiology device are shown in Figure 1a, which consists of 16 different electrode diameters ranging from 20 to 2000 µm. Each set of the studies presented in this work consisted of four independent devices, where each device comprised all diameters for a given material (Au, Pt, PEDOT:PSS/Au, and PEDOT:PSS/ Pt) fabricated side by side as shown in Figure 1a, to minimize process variations and to permit fair and accurate assessment of the scaling effects across all diameters. Each data point for each diameter is obtained from a single electrode (N = 1). Two layers of 2-2.5 µm thick parylene C film were used to serve as the substrate and passivation layers to form conformal contact to either tissue or electrolyte as shown in Figure 1a. A 10 nm thick Ti adhesion layer followed by a 100 nm thick Au or Pt layers were used as the electrode leads. Anisotropic conductive film bonding was used to connect the device to commercial off the shelf ribbon cables that fit in the external characterization circuitry. Solution-based processing was used to pattern the PEDOT:PSS on top of the metal contacts (Au and Pt); Figure 1d,f,h shows the top-view scanning electron microscope (SEM) images of patterned PEDOT:PSS on Au, Pt, and Au contacts with 150 µm diameter.

To evaluate the morphological characteristics of different films, atomic force microscopy (AFM) was utilized. Surface roughness root-mean-square (rms) values of different electrodes in a  $5 \times 5 \ \mu m^2$  area reveal that Au (11.8 rms) and Pt (12.1 rms) metal contacts possess rougher surfaces compared to the spin-cast PEDOT:PSS film with 4.81 rms value (Figure 1e,g,i). The relatively smooth surface of PEDOT:PSS film is attributed to its monolithic solution-based coating technique that is used for device fabrication. These values however are directly dependent on the surface preparation of the sample and the deposition conditions.





**Figure 1.** Device structural properties and electrochemical characterization methodology for ECoG devices. a) A picture of the fabricated PEDOT:PSS/ Au ECoG electrodes on conformal 4–5  $\mu$ m thick parylene C substrate. Sixteen different electrode diameters ranging from macroscale (2000  $\mu$ m) to microscale (20  $\mu$ m) were included in the device layout (inset). b) An example of injected charge-balanced, cathodal first and biphasic current and corresponding voltage transient with highlighted electrochemical parameters on 500  $\mu$ m PEDOT:PSS/Au electrode. c) An example of cyclic voltammetry (CV) with 200 mV s<sup>-1</sup> scan rate and denoted cathodal and anodal charge storage capacity calculation. d, f, h) Top-view SEM images of PEDOT:PSS/ Au, Pt and Au with 150  $\mu$ m diameter. Atomic force microscopy (AFM) images and roughness root-mean-square values of 5 × 5  $\mu$ m<sup>2</sup> scanned area of e) PEDOT:PSS/Au, g) Pt, and i) Au electrode surfaces.

To assess and compare the stimulation capabilities for the different scaled materials, voltage transient and cyclic voltammetry (CV) were used to measure CIC and CSC, the two major contributing factors to in vivo electrical stimulation performance. Figure 1b shows an example of injected biphasic, cathodal first, symmetric current, and the measured corresponding voltage transient on a PEDOT:PSS/Au electrode with 500 µm diameter. In the current pulse configuration,  $i_c$  and  $i_a$  denote the cathodal and anodal phase currents, respectively. Parameters  $t_{c}$ ,  $t_{a}$ , and  $t_{ip}$ denote the cathodal, anodal pulse widths, and interpulse delay, respectively. In most of our investigations, the applied pulse width was 650 µs and the interpulse delay was 20 µs, unless otherwise specified. In the voltage transient configuration, the interpulse potential,  $E_{ipp}$ , the access voltage,  $V_a$  and electrode polarization,  $\Delta E_p$ , are highlighted. The maximum cathodal excursion potential,  $E_{\rm mc}$ , and the maximum anodal excursion potential,  $E_{ma}$ , parameters which are used to determine CIC, are marked in the voltage transient curve of Figure 1b (all highlighted electrochemical variables and parameters in Figure 1b,c are defined in Table 1). Following the published experimental protocols,<sup>[22]</sup>  $E_{\rm mc}$  and  $E_{\rm ma}$  are the electrode potentials versus Ag/AgCl (reference electrode) evaluated 10 µs after the cathodal and anodal pulses end. This period of interpulse delay (10 of 20 µs) is used to account for the voltage drop across the electrolyte and metal lead series resistance (instantaneous potential drop within 10 µs), resulting in an absolute polarized potential across electrode/electrolyte interface versus Ag/AgCl. CIC was calculated as the injected charge (stimulation current multiplied

by pulse width) at which either  $E_{\rm mc}$  reaches water reduction potential (cathodal limit) and/or  $E_{\rm ma}$  reaches water oxidation potential (anodal limit). The water window limits are considered between –0.6 to 0.8 V for metallic electrodes (Pt and Au) and –0.9 to 0.6 V for organic electrodes (PEDOT:PSS/Au and PEDOT:PSS/Pt).<sup>[13,14]</sup> To evaluate and benchmark the CSCs of different scaled materials, CV has been used within the –0.6 to 0.6 V limit (intersection of two water windows) with 200 mV s<sup>-1</sup> scan rate. An example CV plot for 500 µm PEDOT:PSS/Au diameter is displayed in Figure 1c within the PEDOT:PSS/Au water window (–0.9 to 0.6 V). The cathodal CSC (CSC<sub>c</sub>) and anodal CSC (CSC<sub>a</sub>) are calculated by the time integral of the cathodal and anodal currents over the potential range of water electrolysis window for each material.

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To compare the CIC for the materials investigated here, the electrodes were divided into two groups: macroelectrodes with 200 to 2000  $\mu$ m diameters and microelectrodes with diameters ranging from 20 to 150  $\mu$ m. **Figure 2** shows the CIC analyses of microelectrodes for different materials. The current injection limit ( $\mu$ A) and charge injection capacity (mC cm<sup>-2</sup>) of different microelectrode materials are plotted in Figure 2a,b. The histogram indicates that by increasing the electrode size, the current injection limit is increased. Among all scaled materials, PEDOT:PSS/Pt exhibited the largest and Au the smallest current injection limit and CIC for all diameters ranging from 20 to 150  $\mu$ m. Examples of the corresponding voltage transients at the limiting values for Pt, PEDOT:PSS/Pt, Au and PEDOT:PSS/Au with 50  $\mu$ m diameter are displayed in Figure 2c. It should be

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Table 1. Electrochemical parameters used to extract and calculate the electrochemical quantities with their corresponding sample units and technical/theoretical definitions.

	Parameter	Unit	Description
1	t <sub>c</sub>	[ms]	Cathodal phase current duration
2	t <sub>a</sub>	[ms]	Anodal phase current duration
3	ic	[µA]	Cathodal phase current magnitude
4	i <sub>a</sub>	[µA]	Anodal phase current magnitude
5	t <sub>ip</sub>	[µs]	Interpulse delay between cathodal and anodal phases to facilitate measurement of the access voltage (V <sub>a</sub> ) related to the ohmic drop across the series resistive elements of the electrochemical circuit model
6	D	[µm]	Diameter of the electrode
7	GSA	[mm <sup>2</sup> ]	Geometric surface area = $(\pi \times D^2)/4$
8	V <sub>a</sub>	[V]	Access voltage which is associated with ohmic drop across the resistive elements of the circuit and electrochemical cell. V <sub>a</sub> is calculated as the difference between the bias voltage and the voltage transient (10 μs) after the onset of the current pulse
9	E <sub>mc</sub>	[V]	Maximum cathodally electrochemical potential excursions calculated by subtracting V <sub>a</sub> from the maximum negative voltage transients or the electrode potential immediately, i.e., 10 μs after the end of the cathodic current pulse when V <sub>a</sub> is zero
10	E <sub>ma</sub>	[V]	Maximum anodally electrochemical potential excursions calculated by subtracting V <sub>a</sub> from the maximum positive voltage transients or the electrode potential immediately, i.e., 10 µs, after the end of the anodic current pulse when V <sub>a</sub> is zero
11	OCP	[V]	Equilibrium potential of working electrode (without bias voltage) versus reference electrode (Ag/AgCl) at which the net current flow between the working and the counter electrode is zero (the anodic and cathodic reactions are kept in balance)
12	E <sub>ipp</sub>	[V]	The interpulse potential (bias voltage) of the working electrode relative to a noncurrent carrying reference electrode (Ag/AgCI)
13	$\Delta E_{p}$	[V]	Polarization potential across the electrode/electrolyte interface, $\Delta E_{p} = \Delta V - V_{a}$ , where $\Delta V$ is the voltage transient
14	Current — injection <sub>(Limit)</sub>	[µA]	Maximum delivered (injected) current where $ i_c  =  i_a $ in charge-balanced symmetric bi-phasic current pulse at which either $E_{mc}$ reaches the water reduction potential (cathodal limit) and/or $E_{ma}$ reaches water oxidation potential (anodal limit)
15	$Q_{\text{inj}(c)}$	[mC]	Total delivered (injected) charge in cathodal phase which is the time integral of the current pulse, i.e., $i_c \times t_c$ for a cathodal constant-current pulse
16	$\mathcal{Q}_{\text{inj}(a)}$	[mC]	Total delivered (injected) charge in anodal phase which is the time integral of the current pulse, i.e., <i>i</i> <sub>a</sub> × <i>t</i> <sub>a</sub> for a anodal constant-current pulse
17	$Q_{inj}$	[mC]	$Q_{inj(c)} + Q_{inj(a)}$
18	CIC	[mC cm <sup>-2</sup> ]	The total charge density at which either $E_{mc}$ reaches water reduction potential (cathodal limit) and/or $E_{ma}$ reaches wwater oxidation potential (anodal limit). CIC = $Q_{inj}$ /GSA
19	$Q_{storage(c)}$	[mC]	Cathodic charge storage calculated from the time integral of the cathodic (negative) current in cyclic voltammetry at a specific sweep rate over a potential range within the water window and is related to the total amount of charge that is available for a stimulation pulse to be delivered in a cathodal current pulse without exceeding the water reduction potential
20	$Q_{storage(a)}$	[mC]	Anodic charge storage calculated from the time integral of the anodic (positive) current in cyclic voltammetry at a specific sweep rate over a potential range within the water window and is related to the total amount of charge that is available for a stimulation pulse to be delivered in an anodal current pulse without exceeding the water oxidation potential
21	$Q_{\text{storage(Total)}}$	[mC]	$Q_{\text{storage}(c)} + Q_{\text{storage}(a)}$
22	CSC <sub>(c)</sub>	[mC cm <sup>-2</sup> ]	$Q_{ m storage(c)}/ m GSA$
23	CSC <sub>(a)</sub>	[mC cm <sup>-2</sup> ]	$Q_{storage(a)}/GSA$
24	CSC <sub>(Total)</sub>	[mC cm <sup>-2</sup> ]	$CSC_{(c)} + CSC_{(a)}$

noted that appropriate interpulse bias voltage was applied for each electrode to reach its respective water electrolysis window from both cathodal and anodal limits at the current injection limit (i.e., -0.9 to 0.6 V for PEDOTs and -0.6 to 0.8 V for metal contacts; see Figure 4). To evaluate the scaling effect on current injection limit and CIC, measured values were fitted versus diameter using allometric power functions ( $\gamma = a + b/D^n$ ) where *a* and *b* are constants, *D* is the electrode diameter, and *n* is an exponent that varies between ±1 (perimeter dependence) and ±2 (area dependence). The microelectrode data and fits are shown in Figure 2d,e (also measured values were fitted as a function of geometric surface area (GSA) and presented in Figure S3, Supporting Information). Based on fitting trends, the current injection of all microelectrode materials are almost a function of  $D^2$ . Therefore, by dividing the corresponding injected charge by the electrode area, CICs (mC cm<sup>-2</sup>) become nearly constant and independent of diameter. CIC of PEDOT:PSS/Pt is about 2.71 mC cm<sup>-2</sup> which is 3.2 times larger than its underlying metal contact (Pt) with 0.83 (mC cm<sup>-2</sup>) charge injection capacity. Also, PEDOT:PSS/Au demonstrates 9.5 times larger CIC values (1.9 mC cm<sup>-2</sup>) compared to its underlying metal contact (Au) with 0.2 (mC cm<sup>-2</sup>) charge injection capacity.

Figure 3 shows the CIC analyses of macroelectrodes (200–2000  $\mu m)$  for different scaled materials. Similar to

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**Figure 2.** Microelectrodes current injection limits and charge injection capacities. a) Current injection limit ( $\mu$ A) and b) charge injection capacity (mC cm<sup>-2</sup>) histograms of different materials including Pt (blue), PEDOT:PSS/Pt (green), Au (black) and PEDOT:PSS/Au (red) with diameters ranging from 20 to 150  $\mu$ m. c) Examples of corresponding voltage transients to injected current limits for Pt, PEDOT:PSS/Pt, Au, and PEDOT:PSS/Au with 50  $\mu$ m diameter, limited at their respective water electrolysis window, at both the cathodal and the anodal limits, under application of appropriate interpulse potential bias. Measured and fitted values of d) current injection limits and e) charge injection capacities of different scaled materials as a function of diameter, highlighting the current injection limit and CIC scaling dependencies of each electrode material.

microelectrodes, the current injection limit ( $\mu$ A) histogram (Figure 3a) specifies larger values for larger electrodes. Among all studied materials, in contrast to the microelectrodes, PEDOT:PSS/Au exhibited the largest and Au the smallest current injection limit and CIC (Figure 3b) in the diameter range of 300 to 1000  $\mu$ m. Examples of corresponding voltage transients to injected current limits for Pt, PEDOT:PSS/Pt, Au, and PEDOT:PSS/Au with 500  $\mu$ m diameters are displayed in Figure 3c. To explore diameter dependency of macrodots CICs,

fitted current injection limit and CIC values are plotted on a semilog scale in Figure 3d,e versus diameter, and as a function of GSA in Figure S3 (Supporting Information). Based on fitting trends, the current injection limit of PEDOT:PSS/Au and Au macroelectrodes are scaled by almost  $D^2$  factor (area dependency), whereas PEDOT:PSS/Pt and Pt display *D* and  $D^{1.3}$  size dependency.

Calculated and fitted CICs (mC cm<sup>-2</sup>) values in Figure 3e, showed larger size dependency of PEDOT:PSS/Pt  $(1/D^{1.03})$ 

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**Figure 3.** Macroelectrodes current injection limits and charge injection capacities. a) Current injection limit ( $\mu$ A) and b) charge injection capacity (mC cm<sup>-2</sup>) histograms of different scaled materials, including Pt (blue), PEDOT:PSS/Pt (green), Au (black), and PEDOT:PSS/Au (red), with diameters ranging from 200 to 2000  $\mu$ m. c) Examples of corresponding voltage transients to injected current limits for Pt, PEDOT:PSS/Pt, Au, and PEDOT:PSS/Au with 500  $\mu$ m diameter, limited at their respective water electrolysis window, at both the cathodal and the anodal limits, under application of appropriate interpulse potential bias. Measured and fitting values of d) current injection limits and e) charge injection capacitiess of different scaled materials as a function of diameter, highlighting the current injection limit and CIC scaling dependencies of each electrode material.

and Pt  $(1/D^{0.72})$  compared to nondependency (constant value) of Au and weak dependency  $(1/D^{0.34})$  of PEDOT:PSS/Au macroelectrodes. Figure S1 (Supporting Information) shows this transition on a single diameter axis that covers the whole range of studied diameters. We attribute this result to edge effects that are prominent in PEDOT:PSS/Pt and Pt electrodes. For PEDOT:PSS microelectrodes with diameters smaller than ~150 µm, the whole area of the PEDOT:PSS microelectrode contributes to the electrochemical current or charge exchange between the microelectrode and the solution. As the diameter increases beyond 150  $\mu m$ , the electrochemical charge exchange happens near the edge of the electrode. Therefore, the charge that is injected from the PEDOT:PSS sites near the edge of the electrode builds up a potential that is equivalent to the redox limits without the contribution of the overall GSA near the center of the dot in charge injection. Therefore, if one





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**Figure 4.** Interpulse potential ( $E_{ipp}$ ) effect on scaled PEDOT:PSS/Au and Pt electrodes. Current injection limits of a,c) PEDOT:PSS/Au and b,d) Pt microelectrodes as a function of  $E_{ipp}$  or bias voltage in linear and semilog scale respectively (darker colors indicate larger electrode sizes). Averaged CIC values of e) PEDOT:PSS/Au and f) Pt microdots as a function of  $E_{ipp}$  or bias voltage. Current injection limits of g,i) PEDOT:PSS/Au and h,j) Pt macroelectrodes as a function of  $E_{ipp}$  or bias voltage in linear and semilog scale, respectively (darker colors indicate larger electrode sizes). CIC values of k) PEDOT:PSS/Au and l) Pt macrodots as a function of  $E_{ipp}$  or bias voltage. Filled and open circles indicate the measured cathodal and anodal current injection limits, respectively, and filled triangles correspond to simultaneous anodal and cathodal limits.

normalizes the injected charge by the total GSA for macroscale electrodes, an inactive portion of the electrode area that is not contributing to the electrochemical charge exchange is being included. As such, the calculation results in a reduced CIC for macroscale electrodes. By accounting for this CIC degradation at larger electrode diameters, one is able to calculate the fraction of the electrode surface area that is contributing to the electrochemical activity. This analysis is presented in Figure S2 in the Supporting Information.

It is important to note that there is a thicker PEDOT:PSS layer at the edge of all electrodes, but the difference in the width (broadening) of the edge thickness between the smallest  $(D = 20 \ \mu\text{m})$  and largest  $(D = 2000 \ \mu\text{m})$  is minimal and is measured to be  $\approx 2 \ \mu\text{m}$ .<sup>[38]</sup> Because of the areal dependency of the electrochemical components and the significant enhancement of CIC for the microelectrodes,<sup>[38]</sup> we do not believe that this difference in the edge profile is of significance in the results and analyses provided here. In our previous electrochemical analysis for recording, we found PEDOT:PSS/Au to be advantageous, and that the metal lead resistance for the electron beam evaporated Ti/Au was lower than that of the sputtered Ti/Pt. For a single ECoG device capable of recording and stimulation, fabrication with only one metal deposition step is desired. Therefore, for the next set of optimization for stimulation conditions, we will focus on PEDOT:PSS/Au, and on Pt, which is the better among the two metals studied here in terms of charge injection.

Earlier work by Cogan et al. has shown that charge injection capacity depends on ineterpulse potential values where appropriate bias voltage can further increase the CIC.<sup>[14,22]</sup> To obtain the optimal bias voltage, current injection limits and CICs of scaled Pt and PEDOT:PSS/Au were measured as a function of  $E_{ipp}$  (bias voltage,) as shown in Figure 4 for microdots (blue, 20-150 µm) and macrodots (red, 200-2000 µm). Measured current injection limits of Pt and PEDOT:PSS/Au microdots are plotted as a function of  $E_{ipp}$  in linear (Figure 4a,b) and semilog scale (Figure 4c,d), respectively. Data represented by filled circles indicate a cathodal limited current injection limit/CIC at respective bias voltage, whereas data represented by open circles indicate the anodal limitation. For concurrent cathodal/ anodal limitation state, the data are represented by filled triangles. It is evident that by enlarging electrode diameter (darker color), more current injection is allowed with respect to anodal and cathodal threshold potentials (i.e., a larger current injection limit) for both PEDOT:PSS/Au and Pt microelectrodes (Figure 4c,d). It is important to note that maximum current



injection limits (or CICs) have been measured at 0.4 V (optimal  $E_{ipp}$  bias) in cathodal limited state for PEDOT:PSS/Au and simultaneous cathodal and anodal limits for Pt microdots.

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All calculated CIC values from current injection limits are depicted as general lines for both PEDOT:PSS/Au (Figure 4e) and Pt (Figure 4f) microdots. Maximum CIC of all PEDOT:PSS/ Au microdots with averaged value of  $\approx 1.9 \text{ mC cm}^{-2}$  were calculated at 0.4 V bias voltage with cathodal limited state whereas Pt microdots show 2 to 3 times lower CIC values across different  $E_{ipp}$  biases. Similar to microdots, current injection limits of Pt and PEDOT:PSS/Au macrodots (200-2000 µm) were measured and plotted as a function of  $E_{ipp}$  in linear (Figure 4g,h) and semilog scale (Figure 4i,j), respectively. In a similar behavior as microdots, larger macroelectrodes (darker color), possess larger current injection limit for both PEDOT:PSS/Au and Pt macroelectrodes (Figure 4i,j) that were also measured at 0.4 V (optimal *E*<sub>ipp</sub> bias) for PEDOT:PSS/Au (cathodal limit) and Pt (cathodal/ anodal limit) macrodots. Calculated CIC values of PEDOT:PSS/ Au and Pt macrodots are shown in Figure 4 k,j, respectively, where PEDOT:PSS/Au macrodots showed up to approximately five times larger CIC compared to the same Pt macrodot. The CICs of PEDOT:PSS/Au and Pt electrodes decreased by transitioning from microscale to macroscale across the whole  $E_{ipp}$  biases (Figure 4e,f,k,l).

Asymmetric current pulses can also be employed to surpass the anodal CIC limitation, a technique referred to as pulse engineering. These asymmetric pulses include 1 to 2 (1:2), 1 to 4 (1:4), and 1 to 8 (1:8) cathodal/anodal pulse width ratios, which are applied to PEDOT:PSS/Au macro-/microelectrodes at 0.5 V  $E_{ipp}$  bias whereas current injection limits/CICs were limited with anodal threshold potential (0.8 V for Pt and 0.6 V for PEDOT:PSS electrodes). The optimized current injection limits (and the their fitted lines) for PEDOT:PSS/Au micro- and macroelectrodes are shown in **Figure 5**a,b, respectively, as a function of diameter, and are plotted as a function of GSA in Figure S4 (Supporting Information). Open circles (black) denote the measured current injection limits before pulse engineering with anodal limit at 0.5 V  $E_{ipp}$  (Figure 4). The filled triangles in



**Figure 5.** Pulse width engineering for boosting PEDOT:PSS/Au current injection limits. Measured optimized current injection limits (filled triangles) using asymmetric pulse injection and nonoptimized current injection limits (open circles) using symmetric pulse injection at 0.5 V  $E_{ipp}$  bias for a) PEDOT:PSS microdots and b) macrodots as a function of electrode diameter. Open circles indicate the measured current injection limit at anodal limitation, and filled triangles correspond to anodal/cathodal limits after pulse engineering, which resulted in 13.6% enhancement of PEDOT:PSS/Au microdots and 14.6% enhancement of macrodots current injection limit. Colors denote the asymmetric pulse ratios (cathodal/anodal pulse width ratio; cyan 1:2, red 1:4, blue 1:8). The inset shows the close view of first 4 data points per each plot (20, 30, 40, and 50  $\mu$ m in (a) and 200, 300, 400 and 500  $\mu$ m in (b) diameter sizes). c–e) Examples of different injected asymmetric pulses and the corresponding voltage transients for (c) 40  $\mu$ m (blue 1:8), (d) 150  $\mu$ m (red 1:4), and (e) 400  $\mu$ m (cyan 1:2) diameters.

Figure 5a,b indicate the optimized current injection limits that have been measured with specific asymmetric pulse injection ratio, for each diameter, which resulted in reaching water electrolysis limits from both anodal and cathodal sides at 0.5 V bias voltage. Different types of injected asymmetric current pulses are shown in Figure 5c with their corresponding voltage transient for different PEDOT:PSS/Au electrodes with 40, 150, and 400 µm diameters. To maintain a charge-neutral injected pulse, the anodal phase current should be divided by the respective pulse width ratio as shown in Figure 5c. Overall, pulse width engineering boosted the current injection limit of PEDOT:PSS/ Au by 13.6% for microdots and 14.6% for macrodots.

We also investigated the effect of pulse width on charge injection capacity for safe electrochemical stimulation. CICs of two PEDOT:PSS/Au electrodes with 50  $\mu$ m (microdot) and 500  $\mu$ m (macrodot) diameters were measured under various pulse widths, including 0.35, 0.65, 1, 1.3, and 1.65 ms. Measured and fitted current injection limits and calculated CICs are plotted as a function of pulse width in **Figure 6**a for PEDOT:PSS/Au microdot with 50  $\mu$ m diameter and Figure 6c for 500  $\mu$ m diameter macrodot. The corresponding voltage transients of each injected current limit with varying pulse widths (frequencies) are shown in Figure 6b,d for 50  $\mu$ m microdot and 500  $\mu$ m macrodot, respectively. According to Figure 6a,b, we observed that by choosing a longer pulse width

(lower frequency), the limiting current values for microdots are reduced with  $1/t_c^{0.88}$  ( $f^{0.88}$ ) dependency. The amount of injected charge (or CIC) is increased by applying longer pulse widths (lower frequency). CIC improved by ≈40% by increasing the pulse width from 200 to 2000 µs. Similarly, the macrodot with a 500 µm diameter displayed lower current injection limit (proportional to  $1/t_c^{0.93}$  or  $f^{0.93}$ ) and higher CIC (mC cm<sup>-2</sup>) for longer pulse widths (lower frequency). An ≈21% increase in CIC was calculated by increasing the pulse duration from 200  $\mu$ s duration to 2000  $\mu$ s (Figure 6c). Based on this result, we conclude that clinical stimulation protocols that require long pulse durations (e.g., epiretinal stimulation with 2000 µs pulse width) have a higher CIC allowance. However, clinical stimulation protocols that require shorter pulse widths (e.g., cortical stimulation for vision application with 200 µs pulse width) have a lower CIC allowance. In other words, there is a tradeoff between initiative electrical stimulation (higher frequency) and safe stimulation (higher CIC), and these values scale with different diameters. In general, smaller diameters provide higher CIC allowances.

The last metric relevant to stimulation is the CSC, which is evaluated and compared for different materials using cyclic voltammetry. Given different water electrolysis windows of metallic (Pt and Au, -0.6 to 0.8 V) and organic (PEDOT:PSS, -0.9 to 0.6 V) materials, and for a fair comparison, both



**Figure 6.** Effect of pulse width on current injection limit and CIC of PEDOT:PSS/Au micro and macrodot. a) Measured current injection limit (black) and calculated CIC (blue) as a function of pulse width for a) 50  $\mu$ m diameter size PEDOT:PSS/Au micro dot and c) 500  $\mu$ m diameter size macro dot. Pulse width dependencies are highlighted according to fitting line of current injection limit (dashed black line) and CIC (solid blue line) versus pulse duration. Corresponding voltage transients of injected current pulses with different pulse widths including 0.35, 0.65, 1, 1.3, and 1.65 ms, measured at anodal/cathodal limits (with optimal  $E_{ipp}$  bias voltage), b) for 50  $\mu$ m diameter size PEDOT:PSS/Au microdot and d) 500  $\mu$ m diameter size macrodot.

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**Figure 7.** Assessment of charge storage capacities (CSC) for different scaled materials. Examples of CV characteristics of two microscale electrodes with a) 40 and 100 µm diameters and two macroscale electrodes with b) 0.4 and 1 mm diameters for all electrode materials including Pt (blue), PEDOT:PSS/Pt (green), Au (black) and PEDOT:PSS/Au (red). CVs have been performed in PBS within –0.6 and 0.6 V sweep window with constant scan



cathodal and anodal CSCs were considered through cyclic sweep of tested electrode potential versus Ag/AgCl reference electrode between -0.6 and 0.6 V at constant scan rate of 200 mV s<sup>-1</sup>, as shown in Figure 7. Four examples of measured CVs for different electrode materials including Pt, PEDOT:PSS/ Pt, Au, and PEDOT:PSS/Au are shown in Figure 7a for electrodes with 40 and 100 µm diameters and Figure 7b for electrodes with 0.4 and 1 mm diameters. According to different CV responses, larger electrodes resulted in larger current response through cyclic voltammetry with larger hysteresis loop area, whereas Pt and Au electrodes show the largest and smallest current response, respectively. To evaluate the scaling effect on charge storage ( $\mu$ C) quantitatively, the time integral of both cathodal and anodal currents over a potential range of -0.6 to 0.6 V were calculated. Charge storage values extracted from CV responses of different electrode materials are plotted as a function of diameter in Figure 7c for microscale (20-150 µm diameters) and Figure 7d for macroscale (200-200 µm diameters) electrodes. Pt electrodes exhibited larger charge storage ( $\mu$ C) and dependency to scaling  $(1/D^{1.91}$  for micro and  $1/D^{1.61}$  for macroscale electrodes) compared to other electrode materials whereas PEDOT:PSS/Pt displayed larger charge storage than PEDOT:PSS/Au and Au with smallest charge storage for the whole tested electrode sizes. For further analysis, charge storage capacity (mC cm<sup>-2</sup>) for all electrode materials were calculated: two examples of CV responses of 40 and 100  $\mu m$  diameters are shown in Figure 7e and for different electrodes with 0.4 and 1 mm diameter sizes in Figure 7f. Charge storage capacities for all scaled electrode materials are plotted as a function of diameter for microscale and macroscale electrodes in Figure 7g,h, respectively, as a function of diameter and are plotted as a function of GSA in Figure S5 (Supporting Information). Large electrodes (macro) present lower charge storage capacity (mC cm<sup>-2</sup>) compared to small electrode sizes (micro) as demonstrated by smaller hysteresis loops in Figure 7f than the microscale ones of Figure 7e. Although the CSC is associated with total amount of charge available for a stimulation pulse, there is not a well-established experimental relationship between the CSC, obtained under low-current density, and charge-injection capacity for neural stimulation. The CV response of any electrode material depends on the different electrochemical and also physical properties such as geometrical area and the roughness of the electrodes surface which were depicted in Figure 1. In our earlier recording study,<sup>[38]</sup> we found that PEDOT:PSS-coated electrodes have more facile reversible faradaic (redox) reactions. It is possible that this facile redox capability prevents excess charge storage for PEDOT:PSS while enabling it to possess the highest CIC. Given the different capability of electrode materials for delivering CSC to injected current pulse without exceeding water window, these results indicate higher CIC/CSC ratio of PEDOT:PSS/Au microelectrodes for such charge delivery compared to Au, Pt, and PEDOT:PSS/Pt according to CIC values reported in Figures 2 and 3 and CSCs presented in Figure 7.



Finally, to put these results in perspective of power needed to inject similar charge density for each materials, we measured the voltage transients under biphasic current injection and computed the corresponding absolute power ( $P = I \times V$ ). We applied biphasic square waves with a 0.65 ms pulse width and different amplitudes (noted in Figure 8) into all diameters for all different scaled materials and calculated the corresponding power required for that particular charge injection. Figure 8a,b shows representative measured voltage transients and corresponding absolute power plots for 40 and 400 µm diameter electrodes, respectively. The calculated power consumption per cycle are plotted in Figure 8c for microelectrodes and Figure 8d for macroscale electrodes. For further comparison, the fraction of power consumption for PEDOT:PSS divided by that required for the same charge injection but using the metal electrodes only are plotted as a function of diameter in Figure 8e and as a function of GSA in Figure S6 (Supporting Information). Significant power reduction is observed at the smaller electrode diameters when PEDOT:PSS is used as opposed to metal electrodes. The 20 µm diameter dots of PEDOT:PSS/Au and PEDOT:PSS/Pt require nearly one tenth and one third of the power for injection of the same charge density compared to Au and Pt contacts. The reduction in power requirement can be significantly beneficial for extending the battery life of implanted neuroprosthetic devices. It is important to note that earlier work on electrodeposited PEDOT:PSS observed mechanical failure and delamination that is directly proportional to the film thickness.<sup>[37]</sup> Evaluation of the PEDOT:PSS ECoG arrays prepared using our fabrication method for the purpose of chronic implantation in terms of stability and biocompatibility will be systematically investigated in future work.

To summarize, we investigated the size-dependent electrical stimulation capabilities of Au, Pt, and PEDOT:PSS electrode materials through systematic studies of CIC and CSC. PEDOT:PSS/Au exhibited ≈9.5× larger CIC than Au microelectrodes and PEDOT:PSS/Pt exhibited ≈3.2× larger CIC than Pt microelectrodes for diameters in the range of 20-150 µm. This enhancement is less prominent at macroscale (200-2000 µm diameter) where PEDOT:PSS/Au outperformed other materials by a slight margin that narrows down with diameter. We observed optimal  $E_{\rm ipp}$  bias at 0.4 V for both PEDOT:PSS/Au and Pt micro/macro electrodes where CICs of microelectrodes experienced ≈55% and ≈135% enhancement compared to zero bias voltage, resulting in a maximum 1.88 and 0.8 mC cm<sup>-2</sup> CIC for PEDOT:PSS/Au and Pt microelectrodes, respectively. CICs of PEDOT:PSS/Au micro-/macroelectrodes boosted ≈13-14% further at 0.5 V  $E_{ipp}$  bias by pulse engineering (asymmetric pulse injection). Increased pulse width from 200 µs to 2 ms duration resulted in 40% and 21% larger CIC for PEDOT:PSS/Au microdots and macrodots, respectively. This highlights the importance of accurate regulation of stimulation methodology parameters such as pulse width to make proper balance between safety (higher CIC) and efficacy for neuronal stimulation

rate of 200 mV s<sup>-1</sup>. Charge storages ( $\mu$ C) of different materials plotted as a function of electrode diameter size for c) microscale and d) macroscale electrodes. To show the scaling effect on charge storage values, fitting lines are included with corresponding geometrical dependencies. Examples of CV responses (current densities) of two microscale electrodes with e) 40 and 100  $\mu$ m diameters and two macroscale electrodes with f) 0.4 and 1 mm diameter sizes for all electrode materials. Charge storage capacities (mC cm<sup>-2</sup>) of different materials plotted as a function of electrode diameter for g) microscale electrodes with included fitting lines with corresponding scaling dependencies.







**Figure 8.** Power consumption of current injection through PEDOT:PSS/Au, Au, PEDOT:PSS/Pt, and Pt micro and macrodots. Measured voltage transients and power absolute values of a) 40 μm and b) 400 μm diameter dots with injection of biphasic, cathodal first 7 and 95 μA current pulse, respectively. c) Calculated power consumptions per cycle of Au, PEDOT:PSS/Au, Pt, and PEDOT:PSS/Pt microelectrodes and d) macroelectrodes under the same charge injection with injected current amplitudes highlighted with purple color above each electrode diameter. e) The ratio of power consumption/cycle of PEDOT:PSS/Pt to Pt (green) and PEDOT:PSS/Au to Au electrodes (red). The circles represent experimental measurements and the lines are fits. The largest power reduction of 67% for PEDOT:PSS/Pt compared to Pt and 88% for PEDOT:PSS/Au compared to Au electrodes were observed at 20 μm diameter.

(higher current and frequency). CSC evaluation revealed the largest CSC for Pt micro-/macroelectrodes compared to other electrode materials, whereas PEDOT:PSS/Au micro-/macroelectrodes offered higher capability to convert those available stored charges into an injected electrical pulse (higher CIC/CSC ratio). The required power to deliver the same amount of charge is 88% lower for 20  $\mu$ m diameter PEDOT:PSS/Au electrodes compared to Au microelectrodes and 67% lower for 20  $\mu$ m diameter PEDOT:PSS/Pt compared to Pt electrodes.

Overall, these results provide guidance that addresses considerations with regard to next generation acute mapping and potentially chronic stimulation devices through (1) the evaluation of critical parameters for optimized pulse design that could be safely employed in a chronic scenario and outlining design flexibility that might be useful for finding therapeutic stimulation protocols for each individual patient, (2) ensuring that safe stimulation is also important for electrode longevity, and (3) demonstrating that the material choices and pulse design can lead to more energy efficient stimulation, which is a crucial design consideration for fully implanted devices contingent on material stability *in vivo*.

#### 3. Experimental Section

*Device Fabrication*: The device fabrication is similar to previously established protocols<sup>[32,35]</sup> and is included here for completness. Glass slides (Specialty Glass Products Inc.) were used as substrate carriers for the thin parylene C layers. The glass slides were first solvent cleaned





by rinsing with acetone/isopropanol (IPA)/deionized (DI) water/IPA, then were subjected to ultrasonic agitation in IPA for 5 min, and were then rinsed again with acetone/IPA/DI water/IPA. Diluted Micro-90 (0.1%), an anti-adhesion layer, was spun-cast at 1500 rpm on the glass slide to facilitate the separation of the device after the device fabrication is completed. A first parylene C layer (≈1.9-2.5 μm) was deposited by chemical vapor deposition using a PDS 2010 Parylene coater system. Metal lead patterns were defined and exposed using a Karl Suss MA6 mask aligner using NR9-3000 negative resist. Temescal BJD 1800 electron beam evaporator was used for the deposition of 10 nm Ti adhesion layer and 100 nm Au contact layer, and lift-off process in acetone followed. O2 plasma (Oxford Plasmalab 80 RIE) was then applied for 2 min (150 W RF power) to activate the surface of parylene C for enhancing the adhesion of the subsequent encapsulating parylene C layer. A  $\approx$  1.9–2.5  $\mu m$  parylene C layer was then deposited and followed by coating another Micro 90 anti-adhesion layer. This time, a slightly higher concentrated Micro-90 (1% as opposed to 0.1% for the first layer) was spun-cast at 650 rpm for 10 s on this second parylene C layer for ease of separation of the subsequent layers. A third parylene-C layer was then deposited, followed by the spin-coating and patterning the thick 2010 SU-8 photoresist layer, which was exposed and developed with SU-8 developer. O<sub>2</sub> plasma was used to etch the openings in the third and then second parylene C layers prior to the deposition of PEDOT:PSS. After the O2 plasma etching step, the exposed Au surface was cleaned using moderate sonication while the device was immersed in DI water. 20 mL aqueous dispersion of PEDOT:PSS (PH 1000 from Clevios) was mixed with ethylene glycol (5 mL), dodecylbenzene sulfonic acid (DBSA, 50 µL), and 1 wt% of (3-glycidyloxypropyl)trimethoxysilane (GOPS) and the solution was spun-cast at 650 rpm for 30 s and prebaked at 95 °C for 1 min. The third parylene C layer was then mechanically peeled off in all regions except where PEDOT:PSS made contact with the Au surface on the microarray and macrodot regions. Finally, the devices were cured at 140 °C for 1 h and immersed in DI water to remove any Micro-90 residue from the PEDOT:PSS and parylene C surface. Fabrication of the metal (Pt and Au) microarrays followed similar procedure to that of PEDOT:PSS devices except for the PEDOT:PSS deposition, which was not carried out. For the Pt devices, a 10 nm Ti adhesion layer and 100 nm Pt contact layer were deposited by sputtering.

Device Characterization: The devices were imaged using an FEI SFEG ultra high-resolution (UHR) SEM at 10 kV accelerating voltage. To reduce electron charging in the specimen, a 15 nm thick Ti layer was deposited on the back of the device and that electrically connected the devices to the stage of the system providing a runaway path for impinging electrons. A Veeco Scanning Probe Microscope was used to perform AFM in a noncontact tapping mode. Electrochemical current pulse injection (chronopotentiometry mode) and cyclic voltametry (CV) were performed using a GAMRY interface 1000E in phosphate buffer saline (PBS) solution, using three electrodes configuration, i.e., Ag/ AgCl electrode as a reference, a large platinum electrode as a counter elelectrode, and target micro/macroelectrodes as the working electrode. To calculate the charge injection capacity, cathodal-first, biphasic, charge-balanced current pulse were injected across working electrode and counter elctrode while measuring working electrode's polarization potential with respect to Ag/AgCl reference electrode.  $E_{mc}$  and  $E_{ma}$  were calculated as electrode potential versus Ag/AgCl (reference electrode) 10 µs after cathodal and anodal pulses ended. Charge injection capacity was calculated as the injected charge (by multiplying stimulation current and pulse width) at which either  $E_{mc}$  reaches water reduction potential (cathodal limit) and/or Ema reaches water oxidation potential (anodal limit). Water window limits are considered between -0.6 to 0.8 for metallic electrodes (Pt and Au) and -0.9 to 0.6 for organic electrodes (PEDOT:PSS/Au and PEDOT:PSS/Pt).<sup>[13,14]</sup> To maintain different interpulse potential ( $E_{ipp}$ ) bias for each electrode materials, a net current flowed across the electrode/electrolyte interface with minute current magnitude (typically <10 nA) even for millimeter scale electrodes. CV was performed under low current density, near equilibrium conditions in PBS solution, whereas tested electrode potential was swept cyclically versus Ag/AgCl reference electrode's potential between water window

limits for each electrode material at constant scan rate of 200 mV s<sup>-1</sup> with 10 mV potential steps. The  $CSC_C$  and  $CSC_A$  were calculated by time integral of the cathodal and anodal current (or current density) over a potential range of water electrolysis window for each material.

#### **Supporting Information**

Supporting Information is available from the Wiley Online Library or from the author.

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#### **Conflict of Interest**

The authors declare no conflict of interest.

#### **Keywords**

neuromodulation, PEDOT:PSS, scaling, size, stimulation

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## **Supporting Information**

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Scaling Effects on the Electrochemical Stimulation Performance of Au, Pt, and PEDOT:PSS Electrocorticography Arrays

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## **Supporting Information for:**

## Scaling Effects on the Electrochemical Stimulation Performance of Au, Pt and PEDOT:PSS Electrocorticography Arrays

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Figure S1. Macro and microelectrode current injection limits and charge injection capacities. Measured and fitted values of current injection limits (a) and charge injection

capacities (b) of different scaled materials as a function of diameter, highlighting the current injection limit and CIC scaling dependencies of each electrode material.



Figure S2. Ege effect on CICs of different macroelectrode materials. (a) The injection charge limits of different scaled materials. (b) Charge injection capacities (CICs) of different scaled materials calculated in two methods; (1) using total electrode area  $(A_t)$  shown with solid lines, (2) using active (rings around the edge) electrode area  $(A_{ac})$  shown with dashed line and are constant by extrapolation from the CICs of microscale electrodes. (c) Active area that produces a constant CIC as a function of total electrode diameter; Au seems to have the most active area and Pt and PEDOT:PSS/Pt the lowest. (d) Ratio of active area over total area as a function of diameter. As the diameter increases, the active area in the electrochemical exchange decreases. (e) The width, distance from dot edge, of active region in the electrochemical interaction as a function of total diameter. (f) Ratio of active width over total diameter as a function of electrode diameter.



Figure S3. Micro and macro electrodes current injection limits and charge injection capacities. Measured and fitted values of current injection limit ( $\mu$ A) of different materials including Pt (blue), PEDOT:PSS/Pt (green), Au (black) and PEDOT:PSS/Au (red) as a function of geometric surface area in micro scale (**a**) with diameters ranging from 20  $\mu$ m to 150  $\mu$ m and macro scale (**b**) with diameters ranging from 200  $\mu$ m to 2000  $\mu$ m and for all diameters in log scale (**c**), highlighting the current injection limit areal dependencies of each electrode materials. Measured and fitted values of charge injection capacity (mC/cm<sup>2</sup>) of different materials as a function of geometric surface area in micro scale (**d**) with diameters ranging from 20  $\mu$ m to 150  $\mu$ m and for all diameters in log scale (**f**), highlighting the CIC areal dependencies of each electrode materials.



**Figure S4. Pulse width engineering for boosting PEDOT:PSS/Au current injection limit.** Measured optimized current injection limits (filled triangles) as a function of geometric surface area using asymmetric pulse injection and non-optimized current injection limits (open circles) using symmetric pulse injection at 0.5 V inter-pulse bias for PEDOT:PSS/Au microdots (**a**) and macrodots (**b**) as a function of geometric surface area. Open circles indicate the measured current injection limits at anodal limitation and filled triangles correspond to simultaneous anodal and cathodal limits after pulse engineering. Colors denote the asymmetric pulse ratios (cathodal/anodal pulse width ratio; cyan 1:2, red 1:4, blue 1:8).



Figure S5. Charge storage and charge storage capacities (CSC) of different scaled materials. Charge storages ( $\mu$ C) of different materials, Pt (blue), PEDOT:PSS/Pt (green), Au (black) and PEDOT:PSS/Au (red) plotted as a function of geometric surface area for microscale (a) and macroscale electrodes (b). CVs have been performed in PBS within -0.6 and 0.6 V sweep window with constant scan rate of 200 mV/s. To show the scaling effect on charge storage values, fitting lines are included with corresponding geometrical dependencies. Charge storage capacities (mC/cm<sup>2</sup>) of different materials plotted as a function of geometric surface area for microscale electrodes (d) with included fitting lines with corresponding scaling dependencies.



**Figure S6. The ratio of power consumption/cycle** of PEDOT:PSS/Pt to Pt (green) and PEDOT:PSS/Au to Au electrodes (red) plotted as a function of geometric surface area. The circles represent experimental measurements and the lines are fits. The largest power reduction of 67% for PEDOT:PSS/Pt compared to Pt and 88% for PEDOT:PSS/Au compared to Au electrodes were observed at 20  $\mu$ m diameter.