Investigating Electrochemical Safety Limits of Neural Stimulating Electrodes

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Introduction

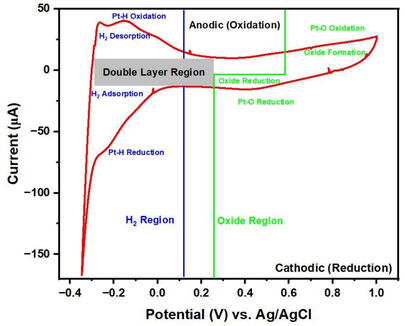
Stimulation of neurons were used to provide sensory input, as successfully demonstrated by cochlear implant devices. The neurons are electrically stimulated by applying charged pulses from a stimulating electrode, thereby creating an ionic gradient in the local environment of the neuron. For efficient stimulation, electrode-neuron interface, biocompatibility and biosafety are the most crucial part in mediating the stimulation from the electrode to extracellular space and then to target neurons.[1] In this work, we have studied the electrochemical properties of nano/microscopic topographic structure of stimulating electrode and their influence on the safe stimulation. The broader scope is to understand the electrochemical safety limits of EVO electrodes. Both physical and electrochemical properties of nano/microscopic topographic structure of EVO electrode and their influence on the safe stimulation were investigated. The charge injection capacity (CIC) & charge storage capacity (CSC) were calculated for geometric and electrochemical surface area as well. Electrochemical characterizations were performed to evaluate the safe charge density (Shannon's Safe Limits) and safe potential/water window for safer stimulation. The evaluation of the biosafety was explored by calculating the concentration of Pt corrosion, with respect to Oticon Medical (OM) stimulation pulse.

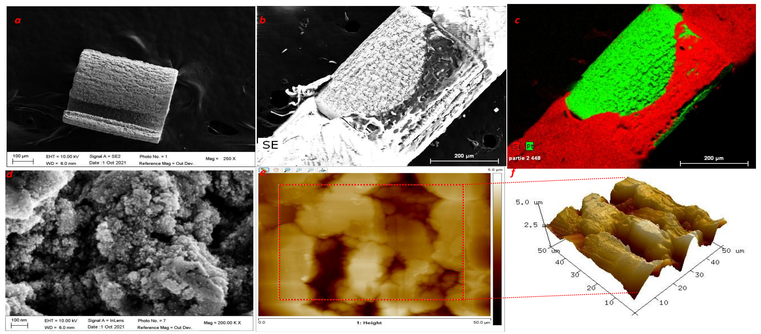
Methods

For this study, Oticon Medical EVO electrodes (0.5 & 0.4 mm) were used. The electrodes were characterised for physical properties using FE-SEM (Sorbonne University) and AFM (Faculty of Medicine, University of Cote D'Azur), whereas Princeton Applied Research Parstat MC potentiostat with a three-electrode system in Artificial Perilymph (AP) electrolyte set-up for electrochemical characterisation and stimulation safety investigations. Electrode corrosion was evaluated by employing ICP-MS/OES.

Results & Discussion

The laser-cut EVO electrodes were imaged using FE-SEM, which provides good detail of 2-D surface morphology showing highly porous structures of micro/nano-nodular topography was observed as well as substantiated with further analysis by Atomic Force Microscopy (AFM). The EDAX data demonstrated that the electrode surface is composed of Pt and Ir without any metal contaminations. Cyclic voltammetry was performed in sulphuric acid and ruthenium complex solutions to determine the electrochemical surface area (ECSA). ECSA was determined from the charge obtained from sulphuric acid hydrogen adsorption region and oxidation/reduction peak current of ruthenium.[2]

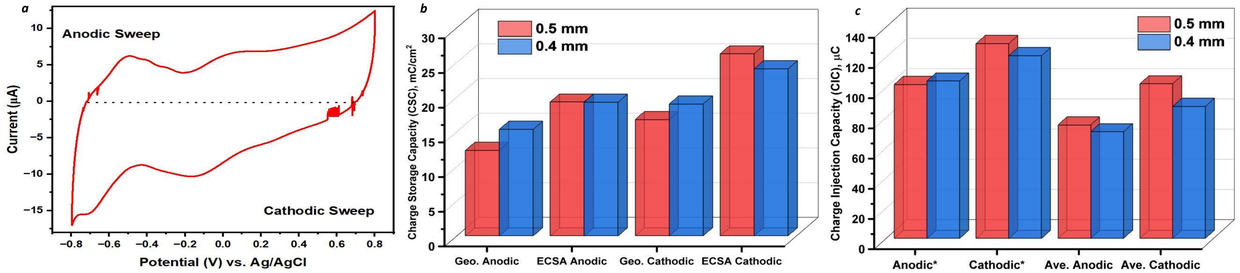




Cyclic voltammetry profile of EVO electrode in sulphuric acid showing hydrogen adsorption and desorption region, the region of interest for electrochemical surface area calculation interfaced with double layer region. Scanning electron microscopic images of EVO electrodes a) Secondary electron image; b) and c) Secondary electron and elemental mapping showing the insulation and EVO electrode without any surface impurities; d) SEM image showing the microscopic and nano-nodular surface structures; e) and f) Atomic force microscopy images showing EVO electrode porosity and surface roughness.

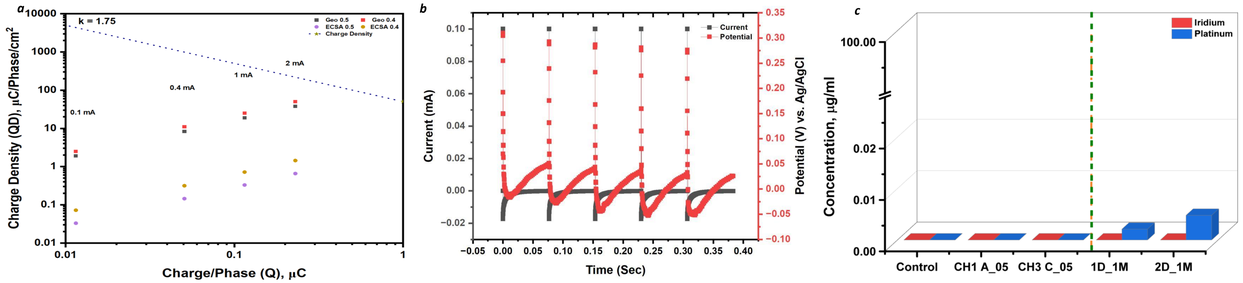
Charge Injection Capacity (CIC), Charge Storage Capacity (CSC)

CIC was calculated for EVO electrodes in Artificial Perilymph (AP) by the total charge delivered/injected in the cathodal/anodal phase with respect to time. CSC was determined by total charge of cathodal/anodal with respect to time divided by electrode area. It is clearly evident from the data obtained, that cathodic charge injection capacity and cathodic charge storage capacity is higher than anodic CIC and CSC. It might be due to the presence of diffused oxygen in AP contributing to the increased cathodic charge by oxygen reduction reaction. Charge Density (QD) was obtained by dividing the charge per phase by the electrode area. Safe limit on the Shannon's plot was determined by the k-value (k = 1.75) and, charge densities below the Shannon's limit were considered as safe. For the ECSA (sulphuric acid) have shown lower charge densities than geometric area and ECSA (ruthenium complexes), due to the influence of double layer capacitance in the active area calculation of sulphuric acid. The Shannon's safe limits for geometric and ECSA for both ruthenium complex and sulphuric acid were below 2 mA of pulse amplitude. Both dimensions of the EVO electrodes were well within the safe limits of Shannon's plot, evidently showing the safety of EVO stimulating electrodes. For geometric area calculation the role of micro/nanoscopic behaviour of the electrode and physical area should be considered for determining the Shannon's safety limit of the electrodes. If not, it would run into erroneous estimation in determining the safety limits resulting in electrode corrosion, generating toxic effects in the body or damaging the tissues and neurons due to unsafe charge densities. It is recommended that care should be taken in estimating the electrochemical surface area, avoiding double layer capacitance, and it is essential that electrochemical behaviour of the stimulating electrodes should be in consideration in determining electrode safe limits.



a) Cyclic voltammetry profile of EVO electrode in Artificial Perilymph (AP) showing anodic sweep and cathodic sweep region, the region of interest for CIC calculations; b) Plot illustrating the difference between the charge storage capacity (CSC) calculated from geometric area and electrochemical surface area for both anodic and cathodic sweeps; c) Data showing the maximum and average (n = 5) anodic and cathodic charge injection capacity (CIC) obtained from cyclic voltammetry of Artificial Perilymph (AP).

Safe Charge Density & Pt Corrosion



a) Shannon's plot showing the safe limits of EVO electrodes obtained from geometric and electrochemical surface area; b) Chronopotentiometric data representing safe water and potential window of EVO electrodes for anodic-first asymmetric charge balanced pulse and; c) ICP results providing the total concentration of Platinum and Iridium dissolution in AP solution after 100 pulses (CH1 A_05 & CH3 C_05) and 1 million pulses (1D_1M & 2D_1M) at 1 mA and 2 mA at 115 µs.

ICP-MS/OES was carried out on single EVO electrode by applying Oticon Medical stimulating pulse for one million pulses in AP solution. All pulses were anodic-first, asymmetric, charge balanced, and cathodic passive discharged. As the charge density increased, the concentration of Pt dissolution increased as well. From an in vitro cellular study, it was reported 50 µg/ml of Pt dissolution concentration has no effect on the cellular viability and >100 µg/ml showed loss of cellular viability and cytotoxicity, due to the changes in the cellular metabolism.[3] Pt concentration assessed in this study has no cytotoxicity and deleterious effects on the cellular metabolism. Pt cytotoxicity might be observed only after 370 billion pulses approximately .

Conclusion

This study offered a better understanding of the electrochemical safety limits of the electrode in terms of deliverable charge (stimulation current), safe window potential and electrode properties. The increased ECSA would lead to better performance of the electrode than geometric area in superior and safer safe charge density limits. And enhanced ECSA would also provide the prospects of reducing the electrode size and sustaining the performance of standard OM electrode size. It is also recommended to consider the electrochemical behaviour of stimulating electrodes in determining the safety limits. The concentration of Pt dissolution measured in this study, is below cellular toxic levels in comparison with literature values, indicating the current level are within the safe limits. This study provides vital information to build on next-generation electrodes with compact dimension and novel materials testing for better, safe and efficient neuronal activation.

References

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3. Wissel, K. Brandes, G., Pütz, N., Angrisani, G. L., Thieleke, J., Lenarz, T., & Durisin, M. Platinum corrosion products from electrode contacts of human cochlear implants induce cell death in cell culture models. PLoS ONE, 13 (2018).

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