Advanced electrochemical sensor methods turn neural implant electrodes into long-term stable sensors

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Introduction

Electrochemical sensors allow the continuous monitoring of the chemical microenvironment around implanted microsensors with high spatial and temporal resolution. Noble metal electrodes, e.g. Pt or Pt/Ir, are widely used in neural implants, ranging from deep brain stimulation electrodes to the cochlear implant. Our approach is to develop advanced electrochemical methods in order to use unmodified noble metal electrodes of neural implants as in situ chemical sensors.

Methods

We developed a unique electrochemical sensor protocol based on chronoamperometry and active potentiometry. Surface processes of the platinum were investigated by chronocoulometry, so that we could successfully separate surface from analyte redox processes. A major challenge was the measurement of both oxidizable (reactive species) and reducible (dissolved oxygen) with the same electrode. The cyclic nature of the multi-step protocol ensures long-term stability and at the same time also provides fundamental information on the state of the electrode.

Results

We successfully demonstrated the sensor performance of our method in vitro. Oxygen as the key metabolite, hydrogen peroxide as reactive species, and ascorbic acid as biogenic interferent were measured with high precision and stability, even in the presence of proteins. Platinum microelectrodes were implanted into the brain of rats. Our method was able to turn these electrodes into fully functional, stable oxygen sensors. At the same time, it was possible to both restore and quantify the loss of electrocatalytic properties over four weeks of implantation.

Conclusion

We developed a universal sensor protocol to turn platinum electrodes into chemical sensors at neural interfaces in vivo. Catalytic properties of the electrodes were lost over weeks of implantation and successfully restored by our method. Various types of neural implants may therefore benefit from such a preconditioning method to prevent degradation over the implant's lifetime. The relevance of our work extends towards in situ corrosion measurements and implant-life-long sensing.

Spectrally selective activation of the auditory nerve using an optical cochlear implant based on thin-film micro LEDs

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Introduction

Hearing is partially restored in the deaf by electrical cochlear implants (eCIs) enabling speech comprehension in more than half a million users worldwide. However, hearing with state-of-the-art eCIs suffers from a limited spectral selectivity caused by current spread around each stimulation site resulting in poor speech recognition under background noise. This limitation might by circumvented by optogenetic stimulation of the auditory nerve as light can be spatially better confined.

Methods

Multi-channel optical cochlear implants (oCI) comprising 16 micromachined thin-film light-emitting diodes (µLEDs, 460 nm, 60□60 µm^2) arranged along a flexible epoxide substrate. The GaN-based µLEDs were transferred from the sapphire epitaxy substrate using a wafer level bonding and laser-lift off process followed by encapsulation in silicone rubber. Acute optical stimulation experiments were performed in adult Mongolian gerbils with the auditory nerve being manipulated by virus-mediated gene transfer. The neural reponse was monitored using linear 32-channel multi-electrode arrays implanted in the central nucleus of the inferior colliculus (ICC).

Results

The oCIs providing a maximum power output of individual µLEDs of 0.76 mW at LED currents up to 10 mA were successfully inserted into the cochlea via the round window or a cochleostomy using a retroauricular approach. The average threshold of neural activation in the ICC upon oCI stimulation in the cochlea was found to be 0.52 mW. Using the cumulative discrimination index based on recorded spike rates in the ICC, we demonstrated that average spatial spread of excitation upon optical stimulation is reduced by a factor of 2.2 compared to an electrical stimulation.

Conclusion

This study applied multi-channel µLED-based optical cochlear implants to activate the optogenetically modified auditory nerve. We successfully combined biomedical and optoelectronic approaches towards optogenetic hearing restoration, and demonstrated in vivo functionality and high spectral selectivity of optogenetic stimulation by µLED-based oCIs.

Modelling Electrochemical-Structural Failure Mechanisms in Active Medical Implanted Devices (AMID)

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Introduction: Demand for accelerated uptake of simulations due to MDR

The MDR causes reduced innovation at many places as ressources are shifted into regulatory field. One approach coping with this is the development of tools that reduce the amount of necessary tests and testing time computer simulations. Their objectives are device reliability assessment made available as software package as early as in the design phase and an increased reliability and prognosis precision from short term observation under true conapplication conditions by widened parameter sets.

Methods: Complex modelling and true data verification

Starting from typical device failure of class IIb and III devices, they undergo identification of contributing parameters with transfer into software modules of industry standard programmes. The widely applied Arrhenius approach is extended towards pressure and concentration of body fluid constituents. Novel electrode materials that are exceeding the performance of currently used metals are described by ab-initio calculated Pourbaix diagrammes.

Results: First parametrization

For PDMS we investigate the pressure dependence of saline water. Pressure increase slows down the intake of water, but going down to pressures below ambient pressure enhances the uptake, which may be due to a widening of the polymer matrix for eased diffusion. The initial uptake of water, however, is enhanced by increased pressure. Thus, future pressure-accelerated testing seems to be feasible by pressure variation. Based on this, interface diffusion is explored at the delamination points where a four-phase boundary needs to be introduced. Whilst the intact polymer-metal interface is governed by classical adhesion via surface energies, the growth rate of the corresponding 4-phase boundary shuld speed up with reduced dimensionality, but might also be limited by inhibited transport processes of a body fluid through narrowed gaps. For the corrosion of the metals themselves, classical water-metal models need to be extended towards body fluid ions.

Conclusion: Roll out and challenges

In order to avoid home-made, academic test specimen, the access to data available from industry's testing labs are paramont. However, the MedTech industrial field shows a defensive attitude towards all variants of "Data Sharing" (see ongoing discussion on OEM/PLM and Art. 61 (4-5) MDR). Hence, an industry communication program must be installed as a substantial parallel action that paves the way for the necessary paradigm change. The technical solutions themselves need regulatory backing, uptake into standardization and finally, harmonization. In addition, modelling will ask for experimental data that never envisioned to be necessary by the companies. As long term experiments cannot be repeated in the course of 4 years, methodologies of survival with "weak data" are another challenge for the realization of exact modelling of failure mechanisms in AMID.

The role of structural biocompatibility for tissue integration of intracortical neural probes

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Introduction

Intracortical neural probes are known to induce a scarring reaction in the brain which is both electrically insulating and deplete of functional neurons. This reaction occur over the first weeks to months following implantation and is the reason why long term stable connection to intracortical neurons has been so challenging to accomplish. Strategies for improving tissue integration can be divided into those addressing surface and structural biocompatibility respectively. Much point to that the dominant part of the tissue reaction to neural probes relates to their insufficient structural biocompatibility, rather than is modulated by the surface. In this study we investigated the collective impact of combining a flexible substrate material (polyimide) and a small cross-section, two aspects of importance for structural biocompatibility of a neural probe.

Methods

Through polyimide thin-film microfabrication two types of flexible neural probes were realized, with smaller (10 x 30 μm^2) and larger (10 x 100 μm^2) cross-section. In order to investigate how size and flexibility of an intracortical probe influence tissue integration over shorter (1-8 weeks) and longer (12-16 weeks) time, the two types were implanted in rodent cortex. The impact of size on tissue integration was evaluated histologically, and compared to signal quality of recoreded spikes.

Results

Over the shorter time interval histology showed comparable tissue integration regardless of device type. Over the longer implantation times, larger devices showed a disproportionate increase in scarring while smaller devices, in contrast, were close to seamlessly integrated with the surrounding tissue. Interestingly, the difference in histology was not reflexcted in recorded signals, which were comparable for both types of devices.

Conclusion

When desigining intracortical neural probes it is of critical importance that both mechanical and geometrical factors are optimised to get the best possible tissue integration. Seamless tissue integration is accomplished first when both aspects are optimised.

Plasma-Coatings for controlled adhesion processes on inner ear prostheses

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Introduction

More than 460 million people worldwide suffer from hearing loss. This fact has a socioeconomic impact on each individual and on the society as a whole. Cochlear implants (CI) are the treatment of choice to treat severe cases. Although CI are remarkably successful in restoring hearing, they present several insufficiently addressed limitations. Of these limitations, foreign body reactions to the implant material and therewith associated fibrotic formations around the device may impact the performance of the CI. The aim of the study was to test the influence of different plasma surface coatings on the adhesion of fibroblasts, the main cellular components leading of fibrotic tissue formation.

Methods

Glass surfaces have been prepared with different coatings (plasma nanofilm I, III and V). These nanofilms were applied by magnetron enhanced plasma polymerization from methane and oxygen precursors. The surfaces were engineered to adsorb proteins in different amounts and conformations. This was achieved by tailoring the surface hydrophilicity as well as the swelling degree of the coatings. Fibroblast-cell lines (NIH 3T3) were seeded at a defined density on the surface and allowed to adhere and proliferate for 48 hours (h). The confluence of cell growth was determined thereafter.

Results

From the three different coatings, one (I) was repellent for fibroblasts. Not a single cell was attached to the surface after 48 h, despite some limited attachment and growth initially (after 24 h). For the coatings III and V, good attachment and proliferation was achieved.

Conclusion

Our preliminary results show that plasma nanofilm seem to be a suitable approach to control cell adhesion and proliferation of fibroblasts. This approach will be applied to primary cells derived from the inner ear (including auditory neurons and whole organ explants) to investigate the effect of such coatings of the cells of the cochlea. Furthermore, the feasibility of using such coatings on CI electrode arrays will be investigated in future studies.