In-vitro Modeling of Electrode-tissue Parameters

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1 OBJECTIVES

The long-term causes underlying the failure of neural recording electrodes is an active question in the community of neural implant users and developers. It is known that a variety of phenomena contribute to signal degradation, but to engineer better devices, the impact of each factor must be quantified and prioritized. Excluding modes of general implant failure such as connectors and meningeal responses (Barrese, et al., 2013), the causes of gradual loss of signal fidelity on individual electrodes include: 1) insulation breakdown (Prasad, et al., 2014), 2) biofouling (Malaga, et al., 2015), 3) glial ensheathment (Polikov, et al., 2005), and 4) neuronal death (Biran, et al., 2005). It is difficult to identify the dominating problem based on existing literature, which offer different conclusions (Prasad, et al., 2014; Malaga, et al., 2015).

One challenge to teasing these factors apart is that they occur simultaneously in-vivo. Another is that impedance, the primary method of monitoring electrode status, is affected by multiple factors. Not surprisingly the correlation between impedance and signal quality has been reported to be weak in longterm studies of intracortical arrays, and changes in strength and direction during different time periods post implantation (Barrese, et al., 2013).

The purpose of this project is to build a simple and cost effective in-vitro setup to model each phenomenon individually, and quantify its impact on both impedance spectra and electrophysiological recording quality.

2 METHODS

2.1 Hardware Components

A custom adapter board was built to interface with commercially available multi-electrode array (MEA) plates (single well plate, Axion Biosystems). Electrical contact is made via Z-axis elastomer, and secured in place with a 3D printed housing. The adapter board was laid out such that electrode positions in the MEA mapped to a corresponding field of headers.

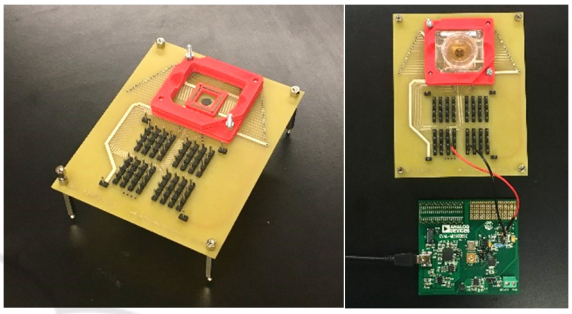

Figure 1: A. Adapter board for interfacing with MEA plate. B. MEA plate seated in adapter board, two electrode sites connected to impedance converter board.

A single-chip impedance converter / network analyser (AD5933, Analog Devices) is used to perform electrochemical impedance spectroscopy. The device was modified for optimal measurement of 1Khz -10Khz range by adding a 4Mhz oscillator.

A generic data acquisition module with built-in instrumentation amplifier (DAQPad-6259, National Instruments) and custom LabVIEW programs were setup for electrophysiological recordings.

2.2 Biological Components

Culture of rat embryonic (E18) cortical neurons and postnatal (P1) astrocytes and microglia will be used to model neural and glial-scar tissue in the MEA plate. Inflammation inducing factors (such as TGFβ1) will be added to convert glial cells to a state of reactive gliosis. The HEK293 cell-line is used to generate reference data on effects of cell density.

2.3 Test Conditions

The four conditions will be modelled as follows:

- Biofouling: incubate MEA plate with 100% fetal bovine serum (FBS).

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- Glial ensheathment: seed glial cells at various densities on top of a neural culture.
- Neuronal death: increase distance between MEA surface and neural culture with hydrogel coating or a dense glial layer.
- Insulation breakdown: natural degradation of the MEA plate (insulation layer begins to detach with repeated usage/sterilization).

3 RESULTS

Preliminary testing of the in-vitro setup showed sufficient sensitivity and consistency in impedance measurements to proceed to electrophysiological experiments.

Differences in spectra were observed after modifications to the MEA surface: before and after PDL coating (Figure 2A), after one day of FBS incubation (Figure 2B), and at HEK293 cell densities of ~50% and ~80% confluence (Figure 2C).

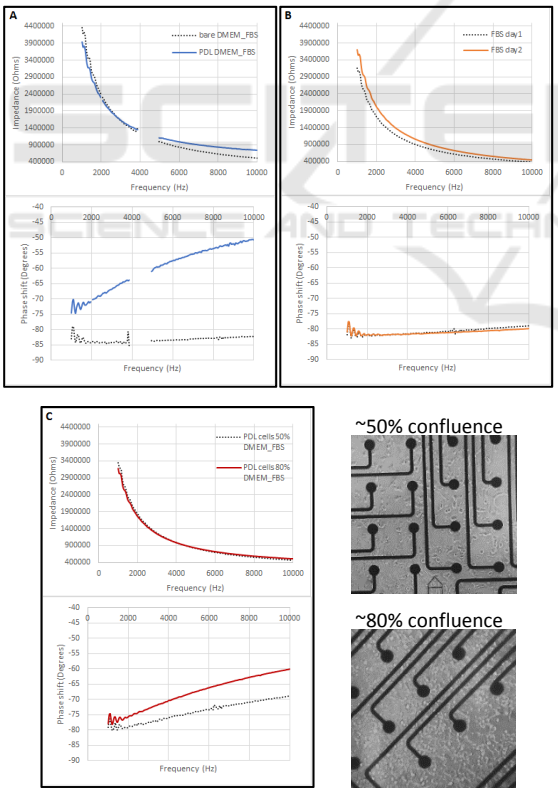

Figure 2: A. Before and after PDL coating, measured in DMEM solution with 10% FBS (typical for HEK293 cell culturing). B. After one day of incubation in serum (100% FBS). C. HEK293 cell culture at different densities.

4 DISCUSSION

This system for in-vitro impedance testing and electrophysiology combines relevant aspects of a neural electrode to tissue interface in a simple setup. Commercial disposable MEA dishes are affordable, well fabricated to work with in-vitro methods, and transparent for convenient imaging. The custom adapter board enables flexible access to MEA sites for connecting to any instrumentation. The single-chip impedance converter and general purpose data acquisition box provide low-cost and programmable options for interrogating the MEA plate.

Preliminary impedance data show promise that different electrode-tissue conditions yield different spectra. This may offer a means to reconcile observations in the literature regarding impedance and signal quality trends. A potential further application of this system is screening of electrode coating materials for enhancing biocompatibility.

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