

Microwell for EIS Based Viability Analysis of Cells

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Summary:

Microphysiological systems enable advanced in vitro studies for drug development and personalized medicine with integrated sensors that allow real-time monitoring of cell behavior in a microfluidic environment. This work presents a compact microwell platform with integrated platinum microelectrodes for electrochemical impedance spectroscopy analysis of cultured cells. The custom designed electronic board enabled real-time EIS measurements on MES-SA human uterine cervical sarcoma cells. In case of UV-irradiation the cells showed decreased impedance, indicating cytoplasmic release and increased ionic concentration.

Keywords: electrochemical impedance spectroscopy (EIS), microphysiological systems, cell viability, integrated electrodes, microfluidics

EIS analysis of cell cultures

Microphysiological systems designed for the examination of in vitro cell cultures represent a significant advancement in drug discovery, screening, and the development of therapeutic applications [1]. Application-oriented devices integrating microfluidic and sensing systems are capable of maintaining cell cultures and tissues under artificial conditions, exposing them to various chemical agents, and monitoring their behavior in real time. This multifunctional operation is essential in personalized medicine and drug development [2].

Electrochemical Impedance Spectroscopy (EIS) is a powerful technique for characterizing physiological properties of cells and cell cultures through their frequency-dependent electrical parameters, while also enabling non-invasive, real-time monitoring. By incorporating integrated microelectrodes, these microfluidic systems become capable of performing impedance-based cell analysis on single cells or cell cultures [3].

Our work demonstrates the applicability of compact microelectrode system for viability testing of cell cultures.

Fabrication and validation of integrated system for EIS analysis

In this work, we present a compact, microwell-based microphysiological platform with an integrated platinum microelectrode array for

real-time EIS measurements (Fig. 1.). Pt electrodes were fabricated on Borofloat™ glass by vacuum sputtering and lift-off lithography. The microwells are made by milling a narrowing cone of 4 to 3 mm into a 6 mm tall polycarbonate cube by CNC machine. The microwell was fixed to the glass chip using a biocompatible Norland UV Curig Adhesive. The electrodes were connected to the PCB by wire bonding. All measurements were performed using the custom-designed PCB.

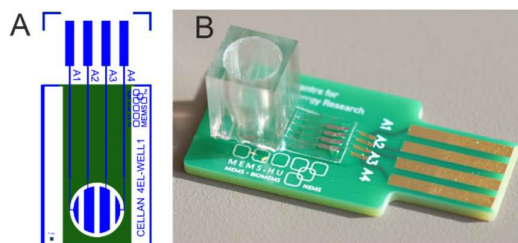


Fig. 1. (A) The layout of the system (green) and the electrodes (blue) and (B) the device itself presenting the PCB and the microwell on top of the chip

The influence of a 30-minute UV irradiation (253.7 nm) on cell viability was tested by following the EIS signal of MES-SA human uterine cervical sarcoma cells cultured in DMEM medium. The microwells were filled with 200 µl of cell solution. Time-resolved EIS measurements were performed before and after

the UV irradiation of an example system and was compared to a control system that received no light exposure. Measurements were made by a PalmSense4 potentiostat. The impedance of the system was measured immediately after the irradiation, after 2 hours and 3 hours and finally overnight incubation of the cells at 37°C temperature and 5% CO₂ environment. To minimize the evaporation, the chips were placed into a Petri dish with wet tissues and then sealed by Parafilm between measurements to keep the humidity constant and to decrease evaporation.

Results

Measurements against a control revealed differences in the EIS measurements of the UV irradiated sample. The control showed no significant difference even after 3 hours while the cells exposed to UV showed a decrease in impedance and a shift in phase (Fig. 2-4.). The change is caused by the death of cells due to UV light exposure that leads to cytoplasmic release and thus increased ionic concentrations. Slight changes are present in the control spectra as well, either signifying cell death independent of the irradiation or the slight evaporation of the medium changing the spectra.

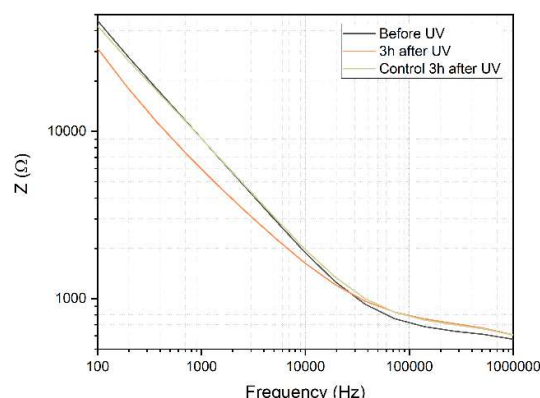


Fig. 2. Difference in impedance of the control and the UV irradiated system before and after 3 hours of light exposure.

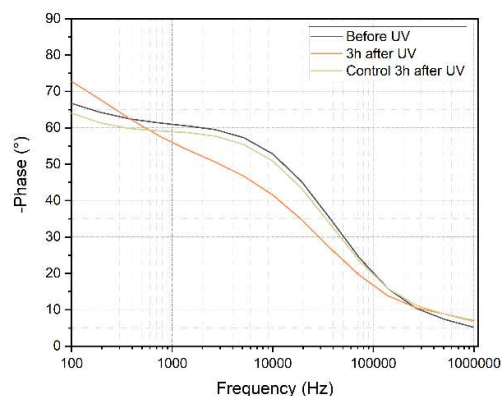


Fig. 3. Difference in phase of the control and the UV

irradiated system before and after 3 hours of light exposure.

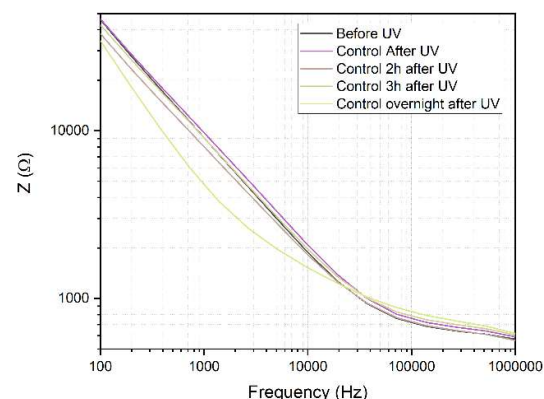


Fig. 4. Difference in impedance of the control system before and after light exposure.

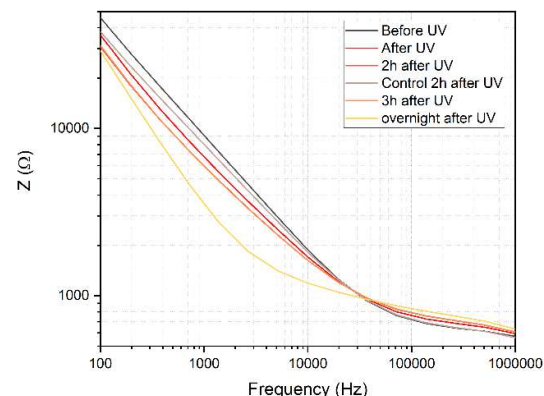


Fig. 5. Difference in impedance of the UV irradiated system before and after light exposure.

Based on the experiments, the system is suitable for longterm monitoring of cells with EIS. In order to follow the changes optically, we are considering modifying the electrodes from Pt to ITO for its transparency. This way the cells could be observed with an inverted microscope that would allow optical characterization with fluorescence methods as well.

References

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