Impedance Measurement for 3D Cell Culture Models

M. Favre, M. Giazzon, R. Ischer, G. Andreatta, D. Bayat, M. Liley

Cells grown in a 3D environment have proven to behave in a manner closer to in vivo tissues. Compared to 2D cell cultures, these improved models have several applications such as drug development, toxicity testing or tissue engineering. Measuring the impedance is a non-invasive and real-time technique to monitor cell activities inside 3D constructs. CSEM is currently developing a bioimpedance chamber with integrated electrodes for 3D hydrogel scaffolds.

In vitro 3D cell culture is increasingly used to better mimic in vivo tissues. It has shown an improvement over growing cells on 2D surfaces, but the observation of cellular activities inside the 3D cell culture is much more challenging. Optical microcopy is unsuitable for thick 3D constructs or can only be used as an endpoint analysis with sectioning of the sample.

Electrical impedance spectroscopy (EIS) is a good candidate to get better insight into what is going on inside a 3D construct. This technique consists of applying a defined alternative current and measuring the electrical impedance at different frequencies. The presence of cells, which can be modeled with a resistance (cytoplasm) in parallel with a capacitance (cell membrane), will influence the measured impedance. EIS has potential for simultaneous structural characterisation of 3D scaffolds and evaluation of cellular behaviour (cell proliferation, response to chemicals).

CSEM is developing a biochamber for 3D hydrogel scaffolds with embedded electrodes. COMSOL multiphysics simulations were performed to understand the influence of the electrode shapes, numbers and localisation in the system. Sensitivity distribution of the impedance describes how effectively each region contributes to the measured impedance signal. Depending on the electrode configurations, the measured impedance reflects the whole sample (Figure 1a) or only one region in the sample (Figure 1b). The spatial resolution of the impedance measurement may be enhanced by using an array of electrodes around the conducting volume of interest.

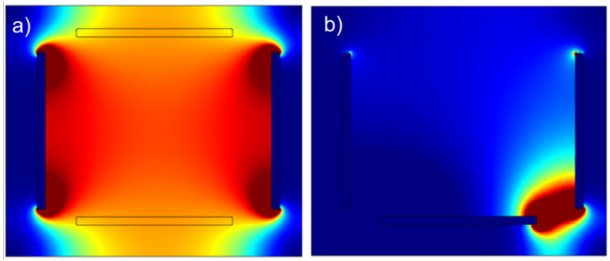

Figure 1: Sensitivity field distribution from COMSOL simulation. Scale from blue (no sensitivity) to red (high sensitivity). a) Sensitivity on the whole sample. b) Sensitivity only in one spot.

The fabricated culture chamber consists of a polycarbonate holder with two microfabricated electrode plates (Figure 2a). A mixture of hydrogel and cells is injected in the chamber between the two electrode plates. Polymerization of the gel is done directly inside the chamber. Platinum electrodes are then connected to an impedance analyzer.

Two different configurations of electrodes were designed. The simplest one consists of a four-point impedance measurement—two electrodes injecting the current and two measuring the voltage. The impedance in this case will give an estimation of the number of cells in the entire scaffold. The second configuration consists of six electrodes on each side of the chamber in order to be able to gather information on the spatial distribution of the cells inside the scaffold.

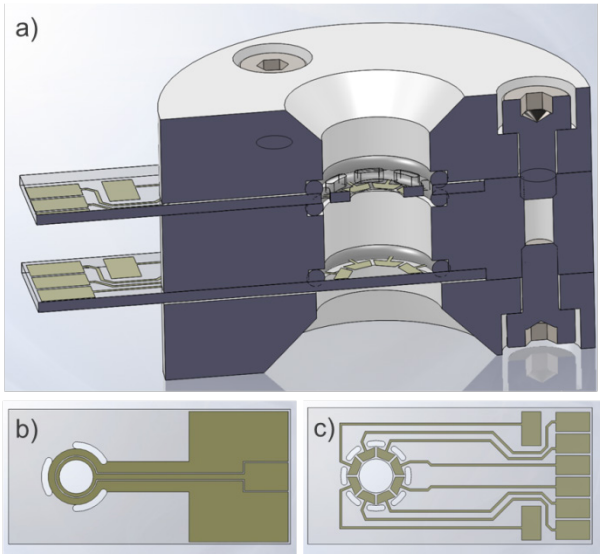

Figure 2: a) Cross-section of biochamber with integrated electrodes; b) Design with 2 electrodes (for one side); c) Design with six electrodes (for one side).

3D cell cultures are used more and more in cell biology as they mimic better the physiological conditions. There is no standard method yet to observe cells inside the scaffold to obtain information on the cell viability, proliferation and migration. As a real-time and non-invasive method, impedance spectroscopy can be a good candidate for the monitoring of large 3D cell culture.

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