

ON-CHIP ELECTRICAL IMPEDANCE TOMOGRAPHY FOR MONITORING THE KINETICS IN THE CELL CULTURE

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ABSTRACT

In this paper, electrical impedance tomography (EIT) is proposed to monitor the kinetics in substrate-based cell culture due to the spatial conductivity distribution within the culturing environment. A circular 16-electrode array was designed for imaging the culturing of *Physarum. Polycephalum*. The theoretical modelling and preliminarily reconstructed image of *Physarum* cell are presented.

KEYWORDS: Electrical Impedance Tomography, Cell Culture, Single Cell Imaging

INTRODUCTION

Electrical impedance spectroscopy (EIS) is a high speed, non-invasive and label-free technique to characterize the dielectric properties of biological tissues and cells. Impedance-based microfluidic cytometers [1] have been fabricated to enable fast and accurate analysis (identification and differentiation) of single cells and other micron-sized particles. By contrast to flow-cytometry, electrical impedance tomography (EIT) can be used to monitor kinetics in substrate-based cell culturing. EIT [2] is a technique for imaging the conductivity/resistivity distribution inside a sample by performing electrical measurements on the periphery of the sample. Electrodes are positioned with equal spacing around the sample. Images are reconstructed by measuring the voltages across sequential electrode-pair combinations, giving a map of the conductivity distribution. EIT has numerous biomedical applications, such as lung function monitoring and the detection of cancer from breast. In our work, a miniaturized EIT system is developed to image a multi-nucleated cell-*Physarum polycephalum* [3].

THEORY AND BACKGROUND

The EIT device contains an array of 16 electrodes arranged around a circular chamber (figure 1). The current is first applied through electrodes 1 and 2. The voltages are measured with successive electrode pairs: 3-4, 4-5, ..., 15-16, giving 13 independent voltage measurements. Then the current is applied through electrodes 2 and 3 giving another 13 sets of voltage data and so on to generate, in total, $16 \times 13 = 208$ voltage measurements.

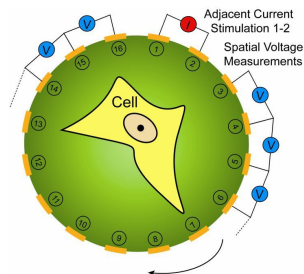


Figure 1. Schematic diagram showing the monitoring of cell culture using EIT.

A finite element model (FEM) of the EIT chip was set up in Comsol Multiphysics (Comsol, Sweden). Two ellipsoidal inclusions are introduced in the background medium (1 S/m), as shown in figure 2a. One has a higher conductivity (10S/m) and the other has a lower conductivity (0.1 S/m) than the medium. Figure 2b shows the reconstructed image of the two inclusions using the EIDORS [4] software package to simulate the results of an EIT experiment. The presence of one high and one low conductivity inclusion can be clearly identified at the correct positions, demonstrating the ability of EIT to image unique electrical properties of inclusions, relative to the background.

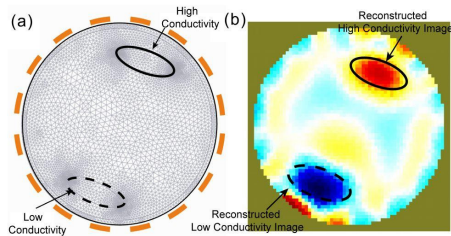


Figure 2. (a) Finite element model(FEM) of EIT chip for imaging two ellipsoidal inclusions. (b)Reconstructed Image

EXPERIMENTAL

A custom-designed electronic platform was developed and built for the real-time multiplexed measurements (Figure 3). Analog chips of 16×8 crosspoint switches (Intersil CD22M3494), connected through a USB controller (FT2232D, FTDI Ltd. UK) to a PC, were used to switch the current stimulation and voltage measurement electrode pairs. The drive current and measurements were obtained using and Alpha-A impedance analyzer (Novocontrol Technologies, Germany).

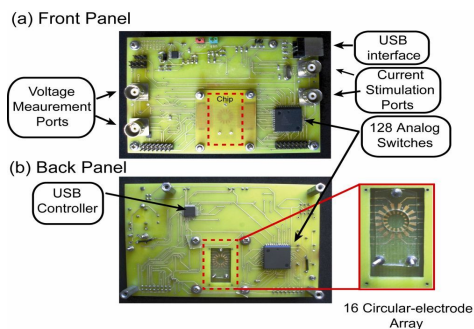


Figure 3. Photograph showing the custom-designed electronic platform for the multiplexing data acquisition.

A polydimethylsiloxane (PDMS) sheet (1 mm thick) with a 4mm diameter well was clamped on the EIT chip and mounted on the platform. The well works as the reservoir of the sample and was sealed by another PDMS sheet on plexiglass at the top to avoid the evaporation. The *physarum* cell was cultured on the 1.5% agar gel and fed with oat flakes and starved at least for 12 hours before the experiments. The electrodes were constructed using PCB printing technology and for biocompatibility, gold was electroplated onto the surfaces of the copper electrodes.

RESULTS AND DISCUSSION

The EIT system was first tested by reconstructing an image of a metal tip in a phosphate buffered saline (PBS) with conductivity of 1.6 S/m. Figure 4a is the photo of a cylindrical metal tip in the EIT chip, showing the position. Figure 4b is the reconstructed image of the tip. The high conductivity region at the corresponding position clearly demonstrates the existence of the metal, showing a successful image

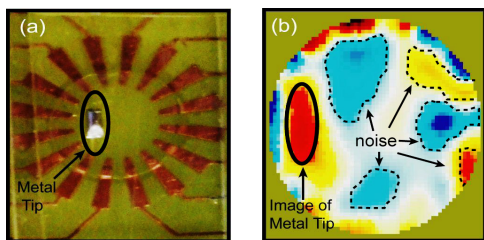


Figure 4. (a) Photograph showing the metal tip in the EIT chip (b) Reconstructed image of the tip.

reconstruction. The noise in the reconstructed image (figure 4b) is more significant than the simulations (figure 2b). This is due to the non-uniformity of the electrodes and the contact impedance between the electrodes and the sample.

The electrical properties of the *physarum* cell were separately characterized by measuring the impedance spectrum of three types of samples in a 3ml tube. From figure 5, it can be seen that the *physarum* cell is more conductive than the agar. As a result, the reconstructed image of *physarum* should exhibit a high conductivity region. Figure 6 shows the *physarum* cell on the agar in the gold-plated EIT chip and the reconstructed image. The higher conductivity region of the cell can clearly be seen.

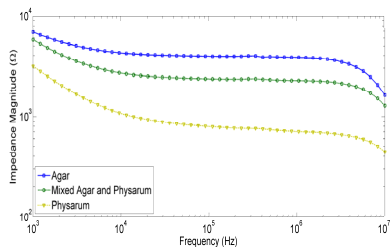


Figure 5. Impedance spectra of 1.5% agar gel, mixture of agar and *Physarum*, and the *physarum*.

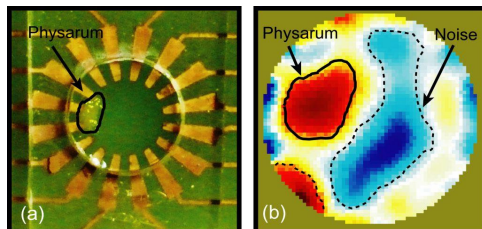


Figure 6. (a) Photograph showing the *physarum* in the EIT chip (b) Reconstructed image of the *physarum*

CONCLUSIONS

A miniaturized electrical impedance tomography system for imaging the cell culture has been developed. In future work, the system will be tested for imaging the kinetics in the cell growth, migration, morphology changes and the time response due to the introduction of a drug.

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