MICRO BIOIMPEDANCE TOMOGRAPHY FOR CONTINUOUS MONITORING OF CELLULAR PROCESSES
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ABSTRACT
Electrical impedance tomography (EIT) is an imaging technique which, on a large scale, has been used to visualize and monitor physiological functions. The focus here is make this technique viable for monitoring cellular processes. To this end, an EIT-based sensor system is currently being developed and characterized. Initial testing with the setup allows for detection and location information of a 700 microns glass bead. Current efforts are focusing on increasing the spatial resolution of EIT by employing a greater number of electrodes (16 or 32) and decreasing the size of the probe area.

KEYWORDS: Impedance, Tomography, Imaging, Conductivity, Label-free

INTRODUCTION
Electrical impedance tomography (EIT) is a technique used to acquire three dimensional images of the conductivity distribution of a body. The technique can be considered as an extension of the four electrode electrical impedance spectroscopy (EIS) [1] to a system with greater number of electrodes. Current is injected into the object via two source electrodes and surface potentials are simultaneously or sequentially measured using multiple electrode pairs. Each pair of voltage measuring electrodes measures a different potential based on location around the imaged object, consequently providing spatial information. This information can then be processed to get a 2D or 3D image of the object based on the material conductivity. The use of impedance tomography has been proposed for a number of applications, particularly within the medical field. Although this technique does not provide as high of a spatial resolution as MRI and CT, it is relatively inexpensive, non-invasive and does not require any labeling. In 2011, the first product (Pulmo Vista 500®, Dräger Medical) to monitor lung ventilation was released in Europe.

Recently, some research groups have demonstrated the use of EIT for imaging of cells and tissue culture [2, 3]. The long term goal of this work is to improve the spatial resolution of EIT to allow monitoring of live cell cultures which will help understand complex cell processes and quorum sensing. Here, the setup and initial testing of a system designed for this purpose is introduced.

EXPERIMENTAL
The setup includes a glass slide on to which a variable number of Platinum electrodes are microfabricated around a small circular probe area (Fig.1).

Figure 1: Six Pt. electrodes are microfabricated on a glass slide around a central probe area (see inset). The alignment marks are used to place the fluidic cavity on the slide such that only the tips of the electrodes are exposed. The distance between the tips for the shown electrode is 500μm.
The glass slide is aligned with a micromachined fluidic well (Fig. 2). A Howland current pump is used to apply a stable AC current stimulus. The stability of this circuit is dependent upon the balancing of $R_{11}$, $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ in the following ratio:

$$\frac{R_{14}}{R_{15}} = \frac{R_{11}}{R_{12} + R_{13}}$$

A microprocessor is programmed to control a bidirectional switch such that the current stimulus is applied to one pair of electrodes while the voltage is measured from other pairs. The stimulus pair is then switched and the process of reading voltage from all the other pairs is repeated.

**RESULTS AND DISCUSSION**

The initial testing of the EIT system has been demonstrated by finding the change in voltage due to presence of glass bead(s) in the probe area. The voltage is first measured with only PBS in the probe area. Thereafter, the glass bead is placed in the PBS at various locations and the voltage response is measured again. The difference between the two data is evaluated using a simple ‘sums-of-the-difference’ calculation for each pair of electrode. The results show that even a simple six electrode system can not only detect the presence of the bead but can also indicate its approximate location. For instance, when the bead is present between two electrodes, the voltage difference data accordingly shows a peak for that pair (Fig. 3). The system is most sensitive when the bead is present between the electrodes and not as much when bead is on the electrodes. When the bead is in the center of the probe area then there is an equal increase in voltage of all pairs. Presence of two particles correspondingly causes the voltage of respective pairs to increase (data now shown).

The data is verified by COMSOL simulations (Fig. 4). The reconstruction is accomplished using a freeware finite element based EIT program, called EIDORS, written for MATLAB software (Mathworks,
The program allows comparisons between simulated data of particle versus background as well as comparison of experimental data. The program can be customized for number, size and shape of electrodes. Initial modeling of the six electrode system has been created to perform reconstruction with impedance data from glass bead experiments.

CONCLUSION
An EIT-based sensor system is currently being developed and characterized. Initial testing with the setup allows for detection and location information of a 700 microns glass bead. With the setup in place, the current efforts are focusing on increasing the spatial resolution of EIT by employing a greater number of electrodes (16 or 32) and decreasing the size of the probe area.

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REFERENCES:

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Figure 3: The location of the bead can be ascertained by the measured voltage data for each electrode pair. (Left) A glass bead between electrodes causes the largest voltage change. (Middle) The electrodes are less sensitive to presence of the bead on the electrode. (Right) With the bead in the center, the change in voltage is roughly the same for all electrode pairs.

Figure 4: COMSOL simulations with and without a cell shows the greatest change in voltage for electrode 0 where the cell is located.