Finite Element Approach Using Electrical Tomography for Bioassay Application

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Abstract. Single-cell imaging is a part bioassay application that is highly used in the studies of microbiology. This bioassay application is used in order to determine the cell activity, behaviour and reaction as well as electrical properties and characteristic. Most of this can be achieved by using mass spectrometry, impedance analyser and flow cytometry. Currently, there is an emerging trend of on-chip integrated device that allows bioassay application to be performed real time. However, in terms of cell monitoring, which allows us to view the cross section image of cell, there is much to be explored. As each cell is composed of different material with specific relative permittivity, Electrical Capacitance Tomography is chosen to determine the electrical properties and spatial distribution of cell. Therefore, the purpose of this research is to simulate Electrical Capacitance Tomography for yeast cell growth in order to determine the most suitable configuration needed for ECT system.

1. Introduction
Tomography refer to the cross-sectional imaging, either 2-dimensional or 3-dimensional, of an object obtained by illuminating the object from multiple viewpoint [1] using the technique of transmission or reflection. Aside from medicinal field, tomography technique is also used in biochemical field as they enabled the researchers to view the reaction of certain substances towards living organism, called bioassay. Bioassay is a successful tool used in estimating and discovering of biologically active substances specifically for the microbiology applications.

One of the method that is use to study the reaction of bioassay is single-cell imaging. Single cell imaging is use to provide cross section image of cell activities, cell pathological as well as its reaction when foreign substances is added. Noted that a single cell imaging assay can also be considered as a technique that allow quantitative analysis of cell signalling pathway. Normally, imaging of single-cell can be acquired through microscopy techniques [3] for example mass spectroscopy and impedance flow
cytometry. Nowadays, there is an emergence of Lab-On-Chip (LoC) technology [4], [5] which combines the function of laboratory operations of single-cell analysis into a miniaturized handheld device.

A research on cell impedance measurement done by [6] using the principle of Electrical Impedance Tomography (EIT) for single cell imaging of P. Polycephalum cell culture. The aim of the simulation is to determine the electrode configuration of the hardware device by introducing two regions with separate conductivity. From the simulation obtain, S. Tsuda created an on-chip EIT device and experiment was done by transferring a section of the cell culture into the sensing region. The result obtain shows that there is difference in cell electrical properties. J Hong on the other hand, develop a microfluidic device using the concept of single cell impedance measurement [7]. The device developed was used to analysed four different kind of cancer cell by supplying several ranges of impedance spectra towards the cells. supplied and based on the impedance measured, the results show that every cell has different tolerances to an electric field.

It can be seen majority of the application of LoC device is used to study the electrical properties of cell. However, there is only few application of cell monitoring provided. Taking the cell properties into consideration, single cell is made up of several components that has different dielectric constants. For example, range of relative permittivity for cell cytoplasm can be from 50-120 while for the cell membrane, the relative permittivity is 2-10 [8]. Thus, Electrical Capacitance Tomography (ECT) is used for cell monitoring in this study by calculating the dielectric constant spatial distribution inside a cell by measuring the capacitance values between electrodes placed on the insulating surface [9].

1.1. Fundamental of Electrical Capacitance Tomography
Electrical Capacitance Tomography (ECT) is a method that belongs to the soft-field tomography. ECT is a part of Electrical Tomography (ET) that uses the principle of electrostatic charge distribution [10] to reconstruct a tomographic image. ECT generally is used to reconstruct a 2-dimensional cross sectional image by measuring the variations of capacitance that exist between electrode pair which represented the spatial distribution [11] of the electrical permittivity of a material.

1.1.1. Electrostatic Behaviour in Electrical Capacitance Tomography. The ECT applied the principle of electrostatics and the system uses electrodes as a measurement tools where the electrode is considered in pair [12, 16]. In order to find the distribution of the electric potential, V, an electrode is excited which causes the electrode to become transmitter (Tx) while the grounded electrode will become receiver (Rx) and an electrical field distribution will exist between those transmitter and receiver. For homogenous condition of capacitance at a given electrode between Tx and Rx, the equation are as follows,

$$C_{ij} = \frac{\int \varepsilon_{ij} \frac{\partial \varphi}{\partial n} ds}{V_j}$$

When a dielectric material is presence is taken into consideration for the heterogeneous condition, the equation is as shown below

$$\Delta C_{ij} = \frac{\varepsilon_0 \int \left( \varepsilon_{ij} \frac{\partial \varphi}{\partial n} - \varepsilon_r \frac{\partial \varphi}{\partial n} \right) ds}{V_j}$$

where $\Delta C_{ij}$ represent change in capacitance due to the presence of dielectric material given $\varepsilon_0$ is the permittivity of free space while $\varepsilon_r$ is related to the permittivity of the sample material [13]. Therefore, based on the equation shown above, we can conclude that the presence of foreign matter will cause changes to electrostatic potential distribution inside the ECT system.

2. Methodology
This research will be using a Finite Element Method (FEM) to perform Finite Element Analysis that is use in solving capacitance calculation between electrode pairs with condition of known sensor structure and given permittivity distribution. Simulation is done by using software COMSOL Multiphysics focusing on single cell imaging of yeast. In this FEM simulation, excited electrode will generate line
projection, that represent electrical field distribution, towards the grounded electrode that act as sensing port.

2.1. Experimental Set-Up
The growth of yeast cell was illustrated by using different radius at different coordinate, in order to study the reaction of sensing electrode and the projection line of electrical field. The coordinate chosen in this experiment are (0,0) and (2,1) while the radius is set to three ranges which were 1.5 mm, 2.5 mm and 3.5 mm. The sensing region is set to radius of 7.5 mm. The size of electrode on the other hand, is set to 2.08 mm width and length is adjusted to 5.0 mm to allow the sensing electrode to fall into the sensing region.

Figure 1. Arrangement of ECT system where (1) copper electrode with measurement 5mm x 2.08mm, (2) yeast cell with radius 1mm, (3) water, and (4) air region

The number of electrode chosen is 8 which produces 28 independent capacitance measurement [4], [14], [15], based on the formula given below

\[ M = \frac{N(N-1)}{2} \]  

(3)

where,

- \( M \) = capacitance measurement
- \( N \) = number of electrode

\[ \text{Figure 1. Arrangement of ECT system where (1) copper electrode with measurement 5mm x 2.08mm, (2) yeast cell with radius 1mm, (3) water, and (4) air region} \]
3. Results and Discussion

The following Fig. 2 shows the simulation result of cell growth.

| Radius of cell (mm) | Coordinate (0, 0) | Coordinate (2, 1) |
|---------------------|-------------------|-------------------|
| 1.5                 | ![Image](image1)   | ![Image](image2)   |
| 2.5                 | ![Image](image3)   | ![Image](image4)   |
| 3.5                 | ![Image](image5)   | ![Image](image6)   |

**Figure 2** Projection of the electrical field lines from the excitation electrode to the receiving electrode

Based on the simulation, the value at the receiver electrode for yeast at both coordinate (0,0) and (2,1) was captured and the graph of measured capacitance when excitation done on electrode 1 (Tx1) is taken. The acquired capacitance value at each receiving electrode (RX 2 to RX 8 as in Fig. 1) is depicted in Fig.3 follows.
The line projection of electrical field diverges between two different dielectric materials within the region of interest. Thus, by observing the projection line for electrical field distribution and the capacitance measurement captured at all grounded electrode, Rx1, Rx2, Rx3, Rx4, Rx5, Rx6 and Rx7, it shows that the value obtains at region adjacent to the excitation electrode, which is Rx2 and Rx8, is the highest. On the other hand, the measured capacitance indicates that the voltage measured for electrical field at sensor electrode Rx3 and Rx4 is the weaker, especially for yeast cell placed at coordinate (2,1). The different placement of yeast cell also plays a part where it will determine the diverging path of streamline. Measured capacitance for yeast cell positioned at coordinate (0,0) is more symmetrically arranged compared to the capacitance measured for coordinate (2,1). This is because, the yeast placed at that position causes the streamline to diverges more towards the other electrode.

4. Conclusion

Based on this research, ECT sensor configuration plays a major part in determining the functionality of ECT device. In this case, the size, angle between electrode and the number of electrode need to be taken into consideration so that the electrode will fall into the sensing region and at the same time, the placement of electrode must not affect the reading taken. The higher the number of electrode will generate more data measurement; however, it can also cause the streamline for adjacent electrode to coincide with one another.

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