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# Electrical impedance tomography for sensing with integrated microelectrodes on a CMOS microchip

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**Abstract**

Electrical impedance tomography (EIT) is an imaging method that is capable of reconstructing the three-dimensional (3D) internal conductivity distribution of a body using only electrical measurements made on the surface. This paper explores the theory and the linearisation approach of EIT in brief. A large scale model containing planar electrodes and electrolyte solution is implemented to test the EIT method. In this model, an obstacle made of insulating material is placed on the electrodes to investigate if EIT is able to identify the location of the obstacle. Subsequently, the EIT method is applied to observe biological cells in the micro-scale using measurements made with an array of microelectrodes on a CMOS microchip.


*Keywords:* Electrical impedance tomography; CMOS; Sensors; Microelectrode arrays; Cell culture

## 1. Introduction

Every tissue type exhibits a degree of resistivity that is different from others. It is by this contrasting difference that an impedance imaging method like electrical impedance tomography (EIT) is able to map the degree of resistivity within a tissue layer. The first EIT image that showed an impedance map differentiating between bone and muscle tissue was constructed from a cross-section of a human forearm [1]. EIT has found many applications in areas of biomedical imaging, such as monitoring respiratory cycle [2] and breast scanning for malignant tissue [3]. With EIT, it is also possible to perform subsurface imaging using planar electrodes [4]. The resultant impedance image is a three-dimensional conductivity distribution.

Impedance spectroscopy with microelectrode arrays (MEAs) has been implemented to monitor the cellular behaviour in tissue culture (cell attachment and differentiation) [5], the physiology of a single cell [6] and the reaction to pH changes in a cell culture [7]. The conventional method of analysis only relates the measured impedances to cellular interaction on the electrode surface. Our intention is to implement EIT in a micrometer ($\mu$m) scale using CMOS system with integrated MEAs to monitor cellular behaviour at the electrode surface as well as at distance from the surface of the electrodes. This will allow us to create a three-dimensional conductivity distribution of cells.

## 2. Electrical impedance tomography

EIT uses the electrical measurements made on the surface of a body to estimate the internal conductivity distribution of the body. Typically, the electrical measurements are made through an array of electrodes by injecting currents and measuring the resultant voltages. A set of current patterns where each pattern specifies the value of the current on each electrode is required for constructing an EIT image. A reconstruction algorithm then uses the knowledge of the current patterns and the measured voltages to find the inverse solution for the internal conductivity distribution.

Ideally, the voltages on the surface of the body are measured while a continuous current density is applied to the surface. At low frequencies, the mathematical model describing the electrical properties of the body is a generalised *Laplace's* equation

$$\nabla \cdot (\sigma(x, y, z)\nabla u(x, y, z)) = 0, \quad -\infty < x, y < \infty, z > 0 \tag{1}$$

where $\sigma$ is the conductivity distribution and $u$ is the voltage in the body. Eq. (1) indicates that there are no current sources in the body. The currents are injected into the body via electrodes at

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the surface $z = 0$ to induce a current density distribution whose inward normal is denoted by $j$.

$$\sigma(x, y, 0)\frac{\partial u}{\partial z}(x, y, 0) = j(x, y) \tag{2}$$

Eq. (2) is the Neumann boundary condition for Eq. (1). The reconstruction algorithm is solved in two steps: a forward problem and an inverse problem. In the forward problem, the voltage $u$ is predicted for any given current density on the body, assuming that the body has a constant conductivity $\sigma_0$. As the voltages are theoretically calculated, the forward problem is well-posed.

The inverse problem determines the actual conductivity distribution $\sigma(x, y, z)$ from all possible surface measurements of $(j, u(x, y, 0))$. In other words, it is necessary to solve Eq. (1) given the Neumann boundary condition in Eq. (2). This is a numerical problem that is *ill-posed*, which implies that large fluctuations in the internal conductivities may only correspond to very small changes in the voltage data. Furthermore, this is also a physical problem where data may be limited by the precision of the measuring instruments.

### 2.1. Reconstruction algorithm

The reconstruction algorithm is based on a large scale model for the planar electrode array [8] and it is derived from Eqs. (1) and (2) using *Green's* identity. The algorithm for reconstructing an EIT image is

$$\sum_{l=1}^{L}(U_l^t I_l^m - U_l^m I_l^t) = \sum_{n=1}^{N}\underbrace{(\sigma_n - \sigma_0)}_{\eta_n}\int_{V_n} \nabla\phi^t \cdot \nabla\phi^m \, \mathrm{d}V \tag{3}$$

On the LHS, $L$ is the number of electrodes, $U_l^t$ and $U_l^m$ are the voltages, $I_l^t$ and $I_l^m$ are the injected currents for the theoretical values of dataset $t$ and measured values of dataset $m$, respectively. The subscript $l$ indicates that a surface measurement is made on the $l$ th electrode. On the RHS, $N$ is the number of voxels that are used in representing the internal conductivity distribution. $\sigma_n$ is the actual conductivity of the $n$ th voxel and $\sigma_0$ is an estimated average conductivity. $\eta$ is the perturbation term that represents the difference between the actual conductivity $\sigma_n$ and the best estimate for constant conductivity $\sigma_0$. The volume integral calculates the internal electric field distribution $\nabla\phi^t$ and $\nabla\phi^m$ for the theoretical data set $t$ and the measured data set $m$, respectively.

By defining

$$A(t, m, n) \equiv \int_{V^n} \nabla\phi^t \cdot \phi^m \, \mathrm{d}V \tag{4}$$

and

$$D(t, m) \equiv \sum_{l=1}^{L} U_l^t I_l^m - U_l^m I_l^t \tag{5}$$

the equation becomes a linear system where

$$D(t, m) = \sum_{n=1}^{N} A(t, m, n)\eta_n \tag{6}$$

The solution for the inverse problem is obtained by applying a minimisation routine to Eq. (6).

### 2.2. Solving the linear equation

The reconstruction algorithm is based on the assumption that the fluctuation term $\eta \ll \sigma_0$. Given that this criteria is met, the internal electric field distribution for the body can be approximated by assuming that the body has constant conductivity $\sigma_0$. In using the linear approximation for the internal electric field $\phi^m$, the inverse problem becomes non-linear as matrix $\mathbf{A}$ is ill-conditioned. This problem is solved by regularising matrix $\mathbf{A}$ to become well-conditioned and solving a new problem that is near the original problem. This can be achieved with the *Tikhonov* regularisation routine which solves $(\mathbf{A}^\mathrm{T}\mathbf{A} + \epsilon I)\eta = \mathbf{A}^\mathrm{T}\mathbf{D}$ where $\epsilon$ is a small regularisation parameter. This is equivalent to solving the least-squares minimisation routine with a side constraint.

$$\min_{\eta} ||A\eta - D||_2^2 + \epsilon||\eta||_2^2 \tag{7}$$

This minimisation routine has the effect of damping large oscillations in the least-squares solution to ensure that the solution will converge for $\sigma_n$.

## 3. Implementation

### 3.1. Choosing the current patterns

The effectiveness in detecting an inhomogeneity at a distance from the electrode surface is dependent on the current patterns. The current patterns can be generalised into two cases: one uses only adjacent electrodes and the other uses distant electrodes for current injections. For current injection via adjacent electrodes, the electric field is strongly concentrated near the surface of the electrodes and becomes weaker at a larger distance away from the surface. Hence, this method of current injection is better at detecting inhomogeneity near the surface but weak for inhomogeneity at a distance from the surface. For distant electrodes, the electric field distribution is more uniform across a greater depth and has a higher chance of detecting inhomogeneity at a distance from the surface but suffers accuracy in detecting inhomogeneity near the surface. For the experiments in this paper, the adjacent method was used to test the efficiency of EIT in detecting inhomogeneity near the surface of the electrodes.

### 3.2. Large scale model

The internal conductivity distribution of the body is sufficiently approximated with a large set of $N$ voxels where each voxel is a cuboid space of constant conductivity. The number $N$ is dependent on the number of independent measurements that are achievable from the number of electrodes $L$ on the surface of the body. Therefore, for a system of $L$ electrodes with infinite measurement precision, the maximum number of independent measurements is $L(L-1)/2$ from $(L-1)$ number of linear independent current patterns. If a four terminal measurement method is used, this number becomes $L(L-3)/2$.