Bioelectrical Impedance and The Frequency Dependent Current Conduction Through Biological Tissues: A Short Review

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Abstract. Biological tissues are developed with biological cells which exhibit complex electrical impedance called electrical bioimpedance. Under an alternating electrical excitation the bioimpedance varies with the tissue anatomy, composition and the signal frequency. The current penetration and conduction paths vary with frequency of the applied signal. Bioimpedance spectroscopy is used to study the frequency response of the electrical impedance of biological materials noninvasively. In bioimpedance spectroscopy, a low amplitude electrical signal is injected to the tissue sample or body parts to characterization the sample in terms of its bioimpedance. The electrical current conduction phenomena, which is highly influenced by the tissue impedance and the signal frequency, is an important phenomena which should be studied to understand the bioimpedance techniques like bioelectrical impedance analysis (BIA), EIS, or else. In this paper the origin of bioelectrical impedance and current conduction phenomena has been reviewed to present a brief summary of bioelectrical impedance and the frequency dependent current conduction through biological tissues. Simulation studies are conducted with alternation current injection through a two dimensional model of biological tissues containing finite number of biological cells suspended in extracellular fluid. The paper demonstrates the simulation of alternating current conduction through biological tissues conducted by COMSOL Multiphysics. Simulation studies also show the frequency response of the tissue impedance for different tissue compositions.

1. Introduction

Biological tissues are three dimensional (3D) materials which are developed with biological cells. The cells are developed with intracellular fluid (ICF) [1-4] surrounded by the cell envelop. Cells are arranged in a 3D structure and suspended in an extracellular matrix called extracellular fluid (ECF) [1-4]. ICF and ECF provide low resistive properties to an alternating electrical excitation [2, 5] whereas the cell membrane produces some capacitance [2, 5]. Therefore, a biological cell surrounded by ECF collectively produces complex electrical impedance under an alternating electrical excitation [2, 5]. The electrical impedance of biological tissues is termed as bioelectrical impedance or electrical bioimpedance or simply bioimpedance [2, 5-8]. The electrical impedance of the biological tissue depends on the tissue composition, tissue anatomy and frequency of the applied signal [2]. Also, as the capacitive reactance of the cell membrane changes with the signal frequency, the bioimpedance also varies with the frequency of the applied electrical signal. Therefore the current penetration and conduction paths significantly changes with the frequency. Electrical impedance spectroscopy (EIS)
[2, 9-17] studies the frequency response of the electrical impedance of a material and hence it has been applied as an impedance based non-invasive material characterization technique in several fields of engineering, technology and applied sciences [18-27]. As shown in Fig. 1, the EIS applies a constant amplitude electrical signal (current or voltage) to a SUT at different frequency points and the developed signal on the sample surface is measured at all the frequencies using, generally, a linear array of surface electrodes [28-30]. The bioimpedance spectroscopy, which is an EIS technique applied for the biological materials, is used to study and characterize the biological materials for non-invasive analysis of anatomy, physiology and pathology. In bioimpedance spectroscopy, a low amplitude electrical signal is injected to the biological sample (cells, tissues or body parts) and the surface potentials are measured to calculate the bioimpedance for their non-invasive characterization. As the current conduction phenomena is highly influenced by signal frequency, tissue composition and structure, it is important to study the bioimpedance and its frequency response to understand the bioelectrical phenomena as well as to obtain the information required for tissue characterization. Also, the current conduction paths through the tissue can be controlled by suitably changing the frequency which helps us to calculate the impedance of the tissue for different current paths. Therefore, the studies on the current conduction through biological tissue are very important for understanding the tissue behaviour and tissue composition analysis techniques such as bioelectrical impedance analysis (BIA) [7, 31-33]. Visualization of current paths in real materials is very difficult and hence the simulated model analysis with modern softwares helps us to virtually develop the tissue structure and understand the tissue behaviour under electrical excitations and other bioelectrical phenomena. In this direction, the origin of bioelectrical impedance and isolated cell model are discussed and current conduction through biological tissue has been reviewed to present a brief summary of bioelectrical impedance phenomena. The frequency dependent current conduction through biological tissues is also discussed and the simulation of alternating current conduction through biological tissues is studied by COMSOL Multiphysics [34]. The simulation studies are conducted with alternation current injection through a two dimensional model of biological tissues containing finite number of biological cells suspended in extracellular fluid.

![Figure 1. Schematic of the electrical impedance spectroscopy (EIS) of a material.](image)

2. Materials and Methods

2.1. Bioelectrical Impedance
ICF is developed with protoplasm which is composed of nucleus and cytoplasm [4, 35]. Cytoplasm is developed with cell organelles, cytoskeleton, and the cytosol which is made up of cell organelles. ICF is composed of water, salts, and proteins [4, 35] and hence it is found as the good conductor electricity
and produces a resistance \( R_{ICF} \) to the electrical signal applied. The extracellular fluid (ECF) is a collection of extracellular molecules secreted by cells that provides structural and biochemical support to the cells [35]. ECF is developed with the intricate network of macromolecules [35] which are composed of a number of proteins and polysaccharides [35] and produces an extracellular resistance \( R_{ECF} \). The cell membranes are developed with protein-lipid-protein (P-L-P) sandwich structure. Protein is conductor of electricity while the lipid is a poor conductor. Therefore, the P-L-P structured cell membrane produces capacitance called membrane capacitance \( C_M \) under an alternating excitation. If the frequency of the alternating electrical excitation is \( f \), the membrane capacitance \( C_M \) produces a capacitive reactance \( X_M = 1/ωC_M = 1/2πfC_M \) [4] which depends on the membrane structure, membrane composition and the signal frequency. Therefore, a cell surrounded by ECF produces an electrical impedance which is function of \( R_{ICF} \), \( R_{ECF} \), \( C_M \) and \( f \) could be modelled in several ways. A popular model has been shown in the Fig. 2b.

The approximate equivalent electrical model of the cell impedance as shown in Fig. 2b is given by the Eq. 1 which can be resolved to get the real and imaginary terms as described below:

\[
Z_{Cell} = (R_{ICF} - jX_M) || R_{ECF}
\]

\[
Z_{Cell} = \frac{(R_{ICF} - jX_M) \times R_{ECF}}{(R_{ICF} + R_{ECF}) - jX_M}
\]

\[
Z_{Cell} = \frac{R_{ICF}R_{ECF} - jX_MR_{ECF}((R_{ICF} + R_{ECF}) + jX_M)}{(R_{ICF} + R_{ECF})^2 + (X_M)^2}
\]

\[
Z_{Cell} = \frac{R_{ICF}R_{ECF}(R_{ICF} + R_{ECF}) - jX_MR_{ECF}(R_{ICF} + R_{ECF}) + R_{ICF}R_{ECF}(jX_M) + (X_M)^2R_{ECF}}{(R_{ICF} + R_{ECF})^2 + (X_M)^2}
\]

\[
Z_{Cell} = \frac{R_{ICF}R_{ECF}(R_{ICF} + R_{ECF}) + (X_M)^2R_{ECF} - jX_M(R_{ECF}(R_{ICF} + R_{ECF}) - R_{ICF}R_{ECF})}{(R_{ICF} + R_{ECF})^2 + (X_M)^2}
\]
\[ Z_{\text{Cell}} = \frac{R_{\text{ICF}}R_{\text{ECF}}(R_{\text{ICF}} + R_{\text{ECF}}) + (X_{M})^2R_{\text{ECF}}}{(R_{\text{ICF}} + R_{\text{ECF}})^2 + (X_{M})^2} - j \frac{X_{M}(R_{\text{ECF}}(R_{\text{ICF}} + R_{\text{ECF}}) - R_{\text{ICF}}R_{\text{ECF}})}{(R_{\text{ICF}} + R_{\text{ECF}})^2 + (X_{M})^2} \]  

(2)

It is observed from the Eq. 1 through Eq. 2 that, as both the real and imaginary terms of cell impedance (Eq. 2) contain capacitive reactance \( X_M \), they both are found frequency dependent. Also, both the real and imaginary terms are found as the function of \( R_{\text{ICF}} \) and \( R_{\text{ECF}} \) and \( C_M \).

2.2. Electrical Current conduction Through Biological Tissues

Electrical current can flow through the biological tissues depending on the electrical properties of the biological tissues and the property of the electrical signal applied. Bioelectrical impedance is developed with the resistance provided by the ICF \( R_{\text{ICF}} \) and ECF \( R_{\text{ECF}} \) and the capacitance produced by the cell envelop \( C_M \). The capacitive reactance \( X_M \) depends on \( C_M \) as well as the frequency (\( f \)) of the applied signal. At low frequency, the magnitude of the capacitive reactance \( X_M = 1/\omega C_M = 1/2\pi f C_M \) becomes large which does not allow the current to pass through the cell membrane and hence the major part of the electrical current is conducted through the low resistive medium i.e. ECF. But when the signal frequency increases, the \( X_M \) reduces gradually and current start penetrating the cell membrane and passes through the cells. At sufficiently high frequency, the \( X_M \) becomes significantly low in amplitude and hence the current signal easily passes through the cells. Therefore, the impedance measured with low frequency signal provided the information about the extracellular medium only whereas the impedance measured with high frequency signal gives the information of ICF and ECF both. Also, using the low frequency impedance and high frequency impedance we can calculate the compositions of the tissue under test which is the basis of the BIA technique.

![Figure 3](image_url)

**Figure 3.** Electrical current conduction through biological tissues (a) current conduction through biological tissue for low frequency signal, (b) current conduction through biological tissue for high frequency signal.

2.3. EIS

Electrical impedance spectroscopy (EIS) provides the frequency response of the material to study the material properties noninvasively. In EIS, a low amplitude electrical signal is injected to the sample under test (SUT) at different frequencies and the electrical impedance is calculated at each frequency points using Ohms Law. Generally a low amplitude current signal (or voltage signal) is applied to a SUT and the developed surface potential (or current) is measured across (or through) a material segment on the SUT surface using either by two electrode method (Fig. 3a) or four electrode method (Fig. 3b). In two electrode method, current injection and voltage measurement are conducted using the same electrode pairs (Fig. 3a) whereas the four electrode method uses two different electrodes pairs.
for voltage-current data collection (Fig. 3b). As the material impedance depends on the material composition and structure, the electrical impedance could be used as the signature of material information for material characterization. As the electrical impedance is a function of frequency also, the frequency response of the electrical impedance provides more information about the material under test which helps us for better characterization process.

2.4. Bioelectrical Impedance Spectroscopy (BIS)

Bioelectrical impedance spectroscopy (BIS) [36-42] is the impedance spectroscopic technique which is applied for biological tissues. The BIS can be found useful for characterizing the biological mediums such as cells, tissues and biological body parts. Even the BIS can be utilized for single cell spectroscopy also [43-44]. BIS has been found suitable for food analysis [9, 19, 21, 23, 42, 45-50], cell or tissue culture studies [51-55] and the disease detection [56-67] and so on.

2.5. Bioimpedance Studies in COMSOL

To visualize the frequency dependent of bioelectrical impedance and its response to alternating current excitation, the electrical conduction through biological tissues electrical, current conduction studies are conducted with 2 two dimensional (2D) biological tissue model (Fig. 4) using COMSOL Multiphysics software [34].

![Figure 4. Schematic of impedance measurement with two-electrode and four-electrode methods (a) two-electrode method, (b) four-electrode method.](image-url)

![Figure 5. Simulated model of the biological tissue and the bioimpedance simulation in COMSOL Multiphysics (a) 2D model of the biological tissue with electrodes (b) tissue model discretised with the FEM mesh.](image-url)
A 2D model of a square geometry tissue sample containing nine cells has been developed and the tissue model is equipped with two high conductive electrodes positioned on the two horizontal sides of the geometry as shown in Fig. 4a. The tissue sample is discretized with triangular elements mesh (containing 5528 elements) using the finite element method (FEM) [68-72].

The FEM mesh is developed with non-uniform refinement of the elements to obtained optimum results. As shown in the Fig. 4b, the meshing is also made more refined near the electrode region and cell-ECF interfaces with large curvature. The EIS studies are conducted by injecting an alternating sinusoidal current (1 mA amplitude) from 1 Hz to 1 GHz and the current paths through the tissue sample at different frequencies are studied.

3. Results and Discussion

The biological cell model and current conduction has been discussed in this paper. The current conduction paths are visualized with the simulation studies COMSOL Multiphysics software. Fig. 5 shows the current conduction paths obtained from the COMSOL Multiphysics based simulation studies on the multifrequency current injection.

![Figure 6. Current conduction paths through the tissue sample at different frequency of the applied current signal](image)

(a) 1 Hz, (b) 1 kHz, (c) 1 MHz, (d) 1 GHz.

The Fig. 5a, Fig. 5b, Fig. 5c and Fig. 5d show the current conduction paths at 1 Hz, 1 kHz, 1 MHz and 1 GHz respectively. As shown in the figures from Fig. 5a, through Fig. 5d, it is clearly observed that at
the low frequency the current signal tries to avoid conducting through the cells and majorly conducts through the ECF whereas, the penetration of electrical current through the cells increases as the frequency increases. For the current injection with the signal of 1 kHz (Fig. 5b), it is observed that the major part of the current flux lines are trying to avoid the cells whereas the penetration through the cells increases with the increase in signal frequency (Fig. 5b, Fig. 5c and Fig. 5d). At very high frequency the current penetration become maximum and current flux lines become almost linear through the ECF and ICF as shown in Fig. 5d. In the work presented in this paper is the preliminary study on a basic tissue model where the ECF and ICF of a basic animal tissue model have been studied. In the future studies, the current conduction studies with 3D anatomy could be conducted.

4. Conclusions
The origin of the electrical bioimpedance has been discussed from the single cell model and the cell impedance has been deduced to show the frequency dependent behaviour of the impedance and its real and imaginary components. With the mathematical model, it has also been discussed that the bioimpedance and their real and imaginary components depend on the cell composition i.e. ICF, ECF and cell membrane. The COMSOL simulation demonstrates the frequency dependent current conduction through biological tissues. It is observed that the at low frequency, the major part of the current signal avoid to conduct through the cells due to the large capacitive reactance of the cell membrane and prefers to pass through the extracellular fluid region. On the contrary, at high frequency the capacitive reactance reduces and the electrical current penetrates the cell membranes and therefore, it conducts through both the ECF and ICF. The present paper presents a brief review on the bioelectrical impedance and its frequency dependent behaviour to the alternation current. The discussion about the origin of the bioimpedance, equivalent circuit modelling of biological cells and the mathematical representation of the bioimpedance, collectively helps to understand the bioimpedance and bioelectricity basics.

5. References
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