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The Use of Electrical Impedance Spectroscopy for Medical Application: A Mini Review

El Asri S*

Faculty of Sciences Semlalia, Cadi Ayyad University, Morocco

***Corresponding author:** Saloua El Asri, Laboratory of Materials, Energy and Environment, Faculty of Sciences, Semlalia. B.P. 2390, Marrakech, Morocco, Email: saloua.el.asrii@gmail.com

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Abstract

Electrical impedance spectroscopy (EIS) has emerged as a powerful technique in biophysics, enabling the analysis of biological tissues, cell behavior, and the development of biosensors. By measuring the impedance response of biological systems across a range of frequencies, EIS provides valuable insights into the electrical properties and structural characteristics of tissues and cells. This paper provides an overview of fundamental principles of EIS and the application of impedance spectroscopy in biophysic, highlighting its potential in understanding tissue properties, monitoring cell behavior, and designing biosensors for various biomedical applications.

Keywords: Electrical Impedance Spectroscopy (EIS); Biological Tissue; Cell Behavior; Biosensors

Abbreviations: EIS: Electrical Impedance Spectroscopy; AC: Alternating Current; Z_R: Real Part.

Introduction

Electrical Impedance Spectroscopy (EIS) is a powerful technique used to investigate the electrical properties of electrical systems. EIS is known as a technique widely used in various scientific and engineering fields, including the medical field. It involves measuring the electrical impedance of a system over a range of frequencies and is particularly useful for characterizing the electrical properties of biological tissues [1,2], cells [3,4], and other medical materials as biosensors [5,6]. Concerning biological tissue analysis, EIS offers a non-invasive and label-free approach to assess tissue composition, hydration, and physiological changes [7]. By measuring the impedance spectrum, EIS can provide information about tissue architecture, cellular organization, and even detect abnormal conditions such as cancer. This technology holds promise for applications in fields like oncology, dermatology, and tissue engineering, enabling clinicians and researchers to obtain valuable information about tissue properties without the need for invasive procedures.

Cell analysis represents another area where impedance spectroscopy has found significant utility. By monitoring the electrical properties of cells, EIS can provide insights into cell viability, proliferation, migration, and differentiation [8]. The technique allows for real-time and continuous monitoring of cellular behavior, offering a valuable tool for studying cellular responses to various stimuli, drug testing, and tissue engineering applications EIS-based biosensors have several advantages over other detection methods, such as high sensitivity, specificity, and real-time monitoring capabilities [9,10]. Impedance spectroscopy is a valuable tool for the development and characterization of biosensors, providing researchers with detailed information about the electrochemical properties of the biosensing platform and the biological recognition element. Hence, a better understanding of measuring principals of impedance spectroscopy will definitely enhance the development of new biosensors. This mini review aims to delving into the fundamental principles of EIS and some ways in which impedance spectroscopy is used in biophysics.

Basic Principles of EIS

EIS uses an alternating current (AC) excitation signal to analyze the system's response at different frequencies. The AC excitation allows the measurement of impedance over a wide frequency range, providing insights into the system's electrical behavior at different time scales [11] Figure 1.

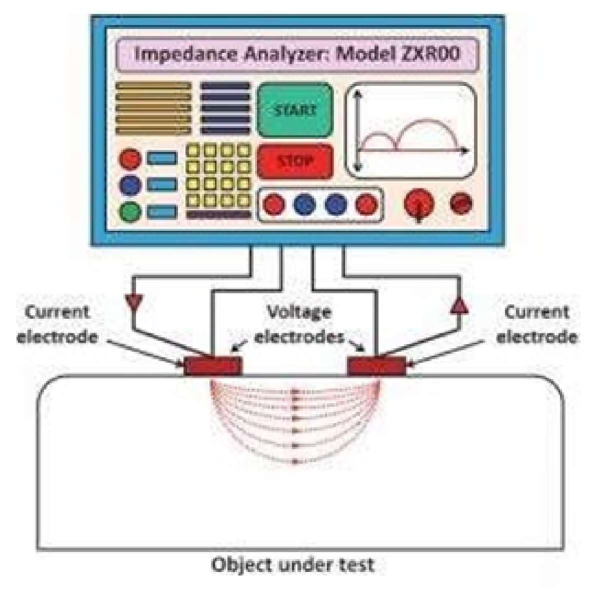

Figure 1: EIS measurements with an impedance analyzer using two-electrode method [12].

The impedance of an analyzed system is a complex quantity that comprises two components: resistance (Z_R) (real part) and reactance (Z_i) (imaginary part). Resistance represents the opposition to the flow of current in a system, while reactance captures the effects of capacitance and inductance. The complex impedance is denoted as $Z = Z_R + jZ_i$, where j represents the imaginary unit [13]. EIS typically involves sweeping the frequency of the excitation signal over a specified range. The frequency sweep can be performed in a logarithmic or linear manner, depending on the application. By measuring impedance at different frequencies, the system's response across a wide frequency spectrum can be characterized and modelized.

Data Presentation

EIS data is often presented using Nyquist plots and Bode plots. A Nyquist plot displays the imaginary part of the impedance (Z_i) on the y-axis against the real part (Z_R) on the x-axis. It provides information about the system's capacitive and inductive behavior. A Bode plot shows the magnitude of the impedance (|Z|) and the phase angle (θ) as a function of frequency. Bode plots help visualize the system's frequency-dependent behavior.

Modeling

Impedance spectroscopy can be used to model a system using an equivalent circuit. This latter represents the electrical elements (resistors, capacitors, inductors, etc.) that matching the behavior of the system under investigation [14]. By fitting the measured impedance data to an equivalent circuit model, it is possible to extract information about the system's electrical properties and underlying processes Figure 2.

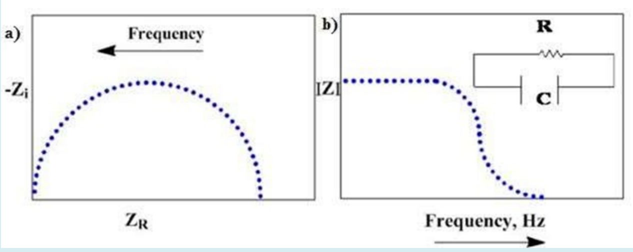

Figure 2: (a) Nyquist plot and (b) Bode plot for the simple equivalent circuit where resistor and capacitor in parallel [15].

Medical Application of EIS

Biosensors

AC impedance spectroscopy is utilized in biosensors for detecting and analyzing biological substances. Biosensors based on impedance measurement can detect changes in impedance caused by the interaction of target analytes with specific receptors or biological materials. This enables the detection and quantification of various analytes, including proteins, DNA, antibodies, and pathogens [16-18]. Impedance-based biosensors find applications in medical diagnostics. In fact, EIS shows potential advantages including: AC impedance spectroscopy allows label-free detection of biomolecules and cells. By measuring changes in impedance caused by the interaction of target analytes with specific receptors immobilized on the sensor surface, it enables direct detection without the need for additional labels or markers [10,19]. This approach simplifies the sensing process and reduces the risk of interference or false results. Furthermore, ac impedance spectroscopy provides real-time monitoring capabilities, allowing continuous and dynamic measurements of biological events. It enables the detection of binding events, conformational changes, and other biological processes in real-time, providing valuable kinetic information [20]. This feature is particularly useful in applications such as drug screening, enzymatic activity monitoring, and studying cellular behavior.

In fact, EIS-based biosensors have the potential for point-of-care testing. Portable and handheld impedance-based devices allow for on-site and near real-time analysis of biomarkers, facilitating rapid disease diagnosis, monitoring, and management at the point of care [21]. This makes EIS-based biosensors valuable in resource-limited settings, remote areas, and emergency situations.

Tissue Characterization

AC impedance spectroscopy can be employed to analyze the electrical properties of biological tissues. By measuring the impedance of tissues at different frequencies, it is possible to obtain information about their electrical conductivity, capacitance, and dielectric properties. This technique is used in areas such as cancer detection, tissue engineering, and wound healing research. Resistive component (impedance magnitude at low frequencies) reflects the tissue's ionic conductivity and cell membrane characteristics. Changes in this component may indicate alterations in cell density, extracellular fluid volume, or the presence of cellular abnormalities [22,23]. At different frequencies, tissues display varying levels of resistance and reactance. This behavior can be attributed to the complex electrical properties of tissues, including the conductivity and permittivity.. These frequency-dependent patterns can be analyzed to extract information about tissue composition, fluid distribution, or cellular characteristics.

Capacitive component (impedance phase at high frequencies) represents the tissue's ability to store charge and is influenced by factors such as cell membrane capacitance and cell size. Variations in this component can indicate changes in tissue structure or cell membrane integrity.

Cell Analysis

AC impedance spectroscopy is widely used in cellular studies. By measuring the impedance of cells in suspension, researchers can extract valuable information about cell size, morphology, viability, and membrane properties [3]. This technique is utilized in various applications, including cell counting, cell differentiation, drug discovery, and monitoring cellular responses to stimuli. Valuable information can be recongnazied by Cell analysis using electrical impedance spectroscopy including:

Cell Size and Morphology

The amplitude and shape of the impedance spectrum can provide information about the size, shape, and volume of the cells [24]. Cells with larger sizes or irregular morphologies will exhibit different impedance responses compared to smaller or more spherical cells.

Membrane Integrity and Cell Viability

Changes in the impedance spectra can indicate alterations in cell membrane integrity. Disruptions in the cell membrane, such as cell swelling or cell lysis, can lead to variations in the impedance measurements, providing insights into cell viability and membrane integrity [25].

Cytoplasmic Properties

The electrical properties of the cytoplasm, such as conductivity and permittivity, can influence the impedance spectrum. Changes in these properties can reflect variations in cellular composition, cytoplasmic viscosity, or the presence of organelles [26].

Cell Adhesion and Aggregation

Impedance spectroscopy can be used to study the adhesion and aggregation of cells. By monitoring changes in impedance over time, it is possible to observe cellular behaviors such as cell adhesion, migration, or aggregation [27].

Conclusion

In conclusion, impedance spectroscopy has proven to be a versatile and powerful tool in biophysics. Its applications in biological tissue analysis, cell behavior monitoring, and biosensors development have shown great potential in advancing our understanding of biological systems and enabling innovative biomedical applications. As research continues to advance, impedance spectroscopy is expected to play an increasingly integral role in biophysical studies and contribute to advancements in medical diagnostics, therapeutics, and bioengineering.

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