Detection and Characterization of the Fibrosis Induced by Active Cardiac Implant

E. De Roux, M. Terosiet, F. Kölbl, M. Boissière, E. Pauthe, P.H. Aubert, P. Banet, A. Histace, O. Romain
Laboratoire ETIS, ENSEA, UMR8051, Laboratoire ERRMECe, EA1391 and Laboratoire de Physicochimie des Polymères et des Interfaces, EA2528, Université de Cergy-Pontoise, France

Abstract:
The present research work has as principal purpose the study of the fibrosis induced by active cardiac implants. Our goal is to identify an electrical markers (or electromarker) to detect and monitor the mentioned phenomenon. To find the appropriate electromarker the measurement technique known as Electrical Impedance Spectroscopy (EIS) has been used as a method of study and analysis. This method defines the spectrum of the complex electrical impedance as a signature in which the electromarker could be found, under the premise that phenomena at the cellular level occur in different frequency bands and therefore can be differentiated. To find this signature, different systems have been implemented that perform EIS for in-vitro cell culture. One custom designed system, known here as the ISMI system, implements EIS by generating sinusoidal signals of different frequencies within a desired bandwidth. The system is designed with all required capabilities for wireless in-vitro cell impedance measurements. Results performed with human fibroblast cells show a variation in the impedance module and phase that are related to cells growth and extracellular matrix production.

When electrodes, used for electrical stimulation, are implanted inside a living being, the body as an immune response begin to create a fibrous tissue surrounding the electrodes. This fibrotic capsule isolates the electrode from the targeted tissues by physical and electrical means, therefore causing the malfunction of the device. Therefore, it is crucial to detect and measure the evolution of the fibrotic capsule. However, from a scientific point of view, the systematic characterization and monitoring of cells or tissues is still an open issue. We propose the method of Electrochemical Impedance Spectroscopy (EIS) as a practical approach to study the electrical behavior of the fibrotic capsule phenomena. The impedance spectrum signature of cells related to fibrosis (i.e. fibroblast) is found by using a custom portable system (called the ISMI system) that perform wireless EIS of a cell culture.

The system consists of an electronic board and a computer software graphical interface. This hardware-software set is called here the ISMI System. The electronic board is based on the AD5933. With the addition of a digital programmable oscillator the system is able to generate stimulations signals with frequencies between 64Hz to 200KHz, with a 0.1Hz of resolution and a maximum of 255 different equally spaced frequency points per sweep. In addition, the electronic board has the Simblee microcontroller with Bluetooth Low Energy (BLE) communication capabilities that may well be linked to a PC. Finally, the board includes an Analog Front End (AFE) that reduces the output impedance and removes DC offset from the signal and also a 1-to-8 multiplexer to measure up to eight different impedances. A diagram of the functional block of the system is shown in Fig. 1.

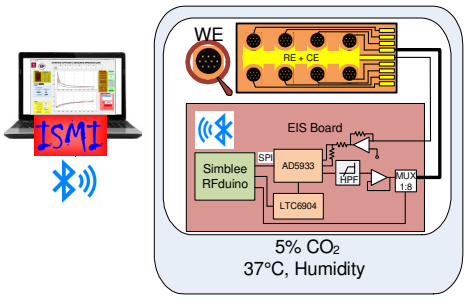

Figure 1. Block diagram of ISMI System

The ISMI System is validated by means of simulations and comparison with a gold standard achieving a minimum of 98% accuracy. Results performed with human fibroblast cells allow a differentiation between cells and the extracellular matrix that they produce since the first are located at higher frequencies than the last one in the spectrum signature.

References:

[1] D.A. Dean, T. Ramanathan, D. Machado, and R. Sundararajan, "Electrical impedance spectroscopy study of biological tissues," Journal of Electrostatics, Volume 66, Issues 3–4, March 2008, pp. 165-177.
[2] B. Kloesgen, C. Ruemenapp, and B. Gleich, “Bioimpedance spectroscopy,” in BetaSys, System Biology Vol. 2, edited by B. Booß-Bavnbek et al. (Springer-Verlag GmbH, Berlin, 2011), pp. 241–264.
[3] M. Terosiet, A. Histace, O. Romain, M. Boissiere, E. Pauthe, "Toward an embedded System for the In-Vitro and In-Situ Cell Proliferation Characterization by Impedance Spectroscopy," Biomedical Circuits and Systems Conference (BioCAS), 2015, doi:10.1109/BioCAS.2015.7348400