Optimization of an impedance spectroscopy system for measuring cultured epithelial tissue integrity

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Abstract

The project “Optimization of an impedance spectroscopy system for measuring cultured epithelial tissue integrity” is support by the school of Biomedical Engineering and Electrical engineering of Dalhousie University. In the project, we will use the impedance spectroscopy technology to design an electronic system to measure the real-time impedance of an epithelial tissue and get a relationship between the impedance and integrity. It needs to show the user once the impedance of the tissue changes, the integrity also changes.

Introduction

The project started from Jan 7th, 2020 and will be end in Dec,2020. Our team has three team members, and they are ShiyuXia, Xiaoyang Li, Xiaotong Lu. This project will be submitted and used by the client, Dr Leung, which is a professor in school of biomedical engineering. Dr. Leung will provide the epithelial tissue that we need to test in dentistry building in Dalhousie University. Our designing and testing will be taken place in Dr. Adamson's lab in Sexton campus of Dalhousie University. Dr. Adamson is our internal supervisor and Dr. Leung is our client and external supervisor.

Some cancer patients undergoing chemotherapy have suffered very painful sores in the mouth. These sores can cause extremely painful, pose an infection risk in patients who already have a compromised immune system. Different Physiological tissues may have their specific electrical impedance characteristics. We will use impedance spectroscopy technology to measure the impedance of the epithelial tissue. The change of the epithelial tissue’s impedance can show some important information about the tissue and the entire organism. Through figuring out the epithelial tissue’s electrical characteristic, its pathological condition can be predicted. This is why we need to design a real-time impedance measurement system. Our client needs the system to figure out the characteristics of the tissues and treat more patients and contribute to the world's medical science. Our system provides the real-time impedance and spectroscopy of the acini. With these results, the system shows the integrity of the tested epithelial tissue. The importance of making the measurements and plotting automatization is our clients get the reliable results quickly, easily and efficiently which will benefit their research furthermore. Also, these are some extremely important implicants of the project.

Epithelial is the cover and protector of the organs and skins. It is important to have a real-time measurement of the integrity of the epithelial. We cannot use DC source because the DC is damaging to the cell.

The overall performance goal is an operating prototype that can measure the impedance of an epithelial cell and covert the data into the MATLAB to generate a relationship between the impedance and the integrity of the tissue. The impedance of the tissue should have an uncertainty within 5%. The system connects with the tissue and the input current in different frequencies. And it detects the voltage across the cells, and then the software will automatically draw the spectroscopy and show the real-time impedance of the epithelial tissue.

Right now, we've got a detailed plan and some outcomes for the "holder PCB module", "AC current source module", "voltage measurement module", "processor module" and "software module".

We cannot just connect two electrodes on two sides of the tissues. So, we use a PCB board to be the holder which has multiple holes to hold the tissues and has some electrodes to connect to "AC current source module", "voltage measurement module" to get the current and voltage. AC module produce a suitable current and voltage module provide a voltage and go through an amplifier and a microcontroller to convert the analog signal to digital signal using ADC function. The program reads the digital signal, process the data, plot the curve and show whether the tissue is integrity or not to client.

Methods and Materials

1. Impedance spectroscopy is a technology that can measure the resistance and capacitance of a material via application of a sinusoidal AC signal. An impedance spectrum is obtained by varying a range of frequency. Impedance spectroscopy can be used to detect immunological binding events such as antibody binding occurring on the electrode surface. The technique has recently been applied to cell toxicology studies, monitoring changes in the cell motion and morphology.
2. Transepithelial/trans endothelial electrical resistance (TEER) is the measurement of electrical resistance across a cellular monolayer and is a very sensitive and reliable method to confirm the integrity and permeability of the monolayer. By doing some research and reviewing some literatures, we decided to use this method to design the circuit. It is a quick, label-free, and non-invasive method. TEER measurement has an advantage that it can be performed in real -time if the measurement electrodes are integrated into a microfluidic organ-on-chip device.
3. Materials: PCB board, AD 9201 board, AD 9959 current source, epithelial tissue, programming software and lab equipment.

Design

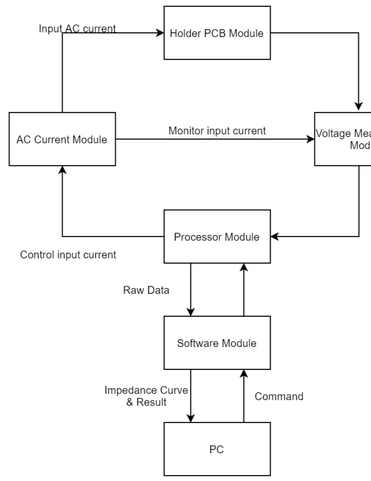

Figure 1. System Architecture

1. The user uses a PC to send a command to Processor Module via Software Module.
2. Processor Module adjusts the frequency of the input current and AC Current Module inputs an AC current through the tissue via Holder PCB module.
3. Voltage Measurement Module monitors the input current and detects the voltage on the tissue. Then, send the data to Processor Module.
4. Processor Module converts the analog signal to digital signal by ADC function and send the data to Software Module.
5. After the analysis, Software Module provides an impedance curve to the user and determines the integrity of the tissues.

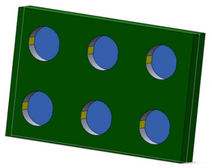

Figure 2. Holder PCB Module

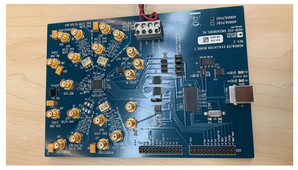

Figure 3. AC current source

Figure 4. Controller Module

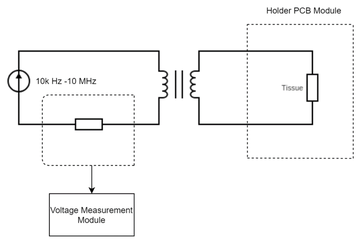

Figure. 5 AC Current Module circuit

- Provides a suitable current that won’t damage the tissue.
- The transformer decreases the input current to protect the tissue.

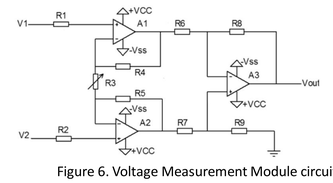

Figure 6. Voltage Measurement Module circuit

- Amplifies the output Voltage to 0 – 5V.
- Decreases the error of ADC’s sampling process.
- Monitors the output voltage and the input current at same time.

Discussion and Challenge

Biological Challenges:
The tissue sample required around a week to grow and we need to make sure cells are not damaged when transferred.

Hardware Challenges:
1. The noise of building the amplifier on the breadboard is a lot. It should be built on a prototype board.
2. Amplimer circuit can operate under the range of the AC current source which is between 10 kHZ to 10 MHZ

Software Challenges:
1. Our team does not have much experiences in programming the GUI on either Excel Visual Basic or MATLAB
2. The ADC sampling rate should reach 20 MHZ since the maximum current source frequency is 10 MHZ. Another ADC needed to add on the system

Future Work

1. Project Design: The designing of the amplifier, system circuit design and PCB semantic drawing.
2. Project Test: The testing process includes three rounds.

- The first round is mainly focus on the electric side which includes the functioning of the amplifier, the voltage measurement monitor circuit and the PCB board functioning
- The second round will testify the software modulation: Current source control panel, ADC function and the impedance plot of the measured tissue.
- The third round will testify the integrity of the entire system includes how fast the system gives the result, how accurate it can be and weather the GUI can control the system well

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