

Non-invasive Assessment of EIS (Electrical Impedance Spectroscopy) based on cell Equivalent Electrical circuit Model

Rabiul Islam, Md. Moznuzzaman, Banaful Paul, Jahidul Alam

Department of Electrical and Electronic Engineering, Chittagong University of Engineering and Technology, Chittagong, Bangladesh.
Email: rabiul.islam07@gmail.com, zaman07eee13@gmail.com, banaful_paul2464@yahoo.com, jahid07eee052@gmail.com

ABSTRACT

Fundamental prerequisite for persistent health-care system is non-invasive detection and monitoring. For tissue level diagnosis there different non-invasive techniques such as ultrasound, X-ray, magnetic resonance and optical imaging. Along with different noninvasive techniques EIS (Electrical Impedance Spectroscopy) is appearing as more suitable technique having some unique advantages. This paper presents a non-invasive technique for bioelectrical impedance estimation by means of Electrical Impedance Spectroscopy (EIS) in MATLAB by using pulsed current-voltage technique. A simple circuit for current pulse injection and voltage pulse detection is accomplished with two electrodes would reduce tissue irritation due to electrode polarization. For sake of simplicity and avoid hazards current source is presented with as low as $100\mu\text{A}$. Both current pulse and voltage pulse stored in MATLAB from which impedance data are assessed. By using serial port interfacing the real time current and voltage pulse signals are plotted in MATLAB. The findings of the work is that serial port interfacing makes bio-impedance spectroscopy easier to save impedance data and also monitor. Along with this variation of cell parameters is shown. Below radio frequency range is the suggested frequency range of bio-impedance measurement because of higher response of permittivity and conductivity of biological tissues in this band than the high frequency band (MHz).

Keywords : Noninvasive detection; Electrical impedance spectroscopy; Bio-impedance; Serial port interfacing.

1 INTRODUCTION

INVASIVE measurement is not certainly going to be popular among the people. Because it excludes the sake of preventive measurement, continuous monitoring and it is sometimes not possible for specific cases (e.g. blood glucose monitoring). Moreover, Invasive methods also cause pain, time consumption, high costs per measurement and also carry potential risk of spreading infectious diseases. This entire factor unavoidably calls for a more reliable noninvasive assessment. There are different popular noninvasive techniques for bio-sensing like optical spectroscopy, ultrasound, X-ray and magnetic resonance imaging which typically measure the effect of absorption, reflection or transmittance of nonionizing radiation that illuminates a portion of the subject. Such techniques offer basic information on mass or proton density distribution only but cannot provide properly.

Bioelectrical impedance provides information on tissue structures and states [2]. The bio-impedance measurements in humans have been receiving considerable attentions during the past two decades because of several advantages, such as low cost, easy application, non-invasiveness and on-line monitoring [3]. Bio-impedance is a non-destructive technique makes use of low level electrical signals such as those which are already present in bio-materials. Accurate measurement of the impedance of bio-materials over broad frequency range yields valuable information about the electrical properties of the materials [4]. This technique is evolved into Bioelectrical Impedance Spectroscopy (BIS) which is also called multiple frequency bioelectrical impedance analysis. It enables us to have an overall figure of impedance. For example, the tissue

impedance at zero frequency corresponding to extra-cellular resistance is useful for the evaluation of mammary and lung cancers and fatty tissues. BIS applies multiple frequency stimulation to measure body impedance and study shows its viability for the applications of body fluid measurement which estimates extracellular fluid, intracellular fluid, and total body water [5][6].

Bioelectricity is fundamental to all of life's processes. Indeed, placing electrodes on the human body or on any living thing, and connecting them to a sensitive voltmeter will show an assortment of both steady and time varying electric potentials depending on where the electrodes are placed. These bio potentials result from complex biochemical processes, and their study is known as electrophysiology. We can derive much information about the function, health, and well-being of living things by the study of these potentials. To do this effectively, we need to understand how bioelectricity is generated, propagated, and optimally measured. Electric fields can arise from a static distribution of charge, whereas electric currents are charges in motion. Since current flow in a volume of fluid is not confined to a linear path as in a wire, currents can flow in many directions. When describing bioelectric currents, we often use a derivation of Ohm's law given in 1.

$$J = \sigma * E \quad (1)$$

Where J =current density, amps/m^2 , σ =medium conductivity, $\text{Siemens}/\text{m}$, E =electric field, volts/m . From this it is well known that the electrical properties of biological tissues differ significantly depending on their structure and characteristics [7]. Experiment shows that extracellular resistance and

intracellular resistance of cancer tissues are significantly higher and plasma membrane capacitance is significantly lower than normal tissues [8]. Experimentally it is shown that significant change in blood conductivity and permittivity due to different level of glucose [9]. Besides, any significant change in tissue characteristics would be detectable with electrical impedance spectroscopy and study shows its viability for visceral fat measurement [10], prostate and lung cancer detection and bone fracture [11]. Biomedical sensing which directly or indirectly related to change in biological tissues, diagnosis based on bioelectrical impedance spectroscopy is emerging with greater prospects for noninvasive bio-sensing than any other noninvasive techniques. This paper present Bio-impedance measurement by simply dividing voltage pulse fetched from cell to current pulse injection into blood equivalent electrical circuit. This paper also include the variation of Bio-impedance parameters R_e , R_i and C_i of electrical equivalent circuit shown in figure 1 with the applied frequency. Here used current source is designed with the option of setting any constant current value as less as 100 μA and Voltage detection is designed with an instrumentation amplifier to provide good noise performance and necessary signal gain. This paper also define about impedance data estimation using serial port interfacing through MATLAB R2009a.

2 METHODS

The electrical equivalent circuit of biological cells is usually represented with similar circuit shown in figure 1 which is comprised of extra-cellular medium resistance, intra-cellular medium resistance and cell membrane capacitance [12]. The cell membrane is composed mostly of a double layer of phospholipid. This structure is called the lipid bilayer and it acts as an electrical insulator (dielectric). The cell membrane maintains an ion concentration gradient between the intracellular and extracellular spaces. This gradient creates an electrical potential difference across the membrane, which is essential to cell survival. Electrical gradients are necessary to support the movement of oxygen, carbon dioxide and nutrients. Therefore, the cell membrane has electrically insulating qualities to maintain an electrical gradient. Thus, impedance of a cell is largely determined by serial connection of the capacitive reactance of the cell membrane, and the resistance of the intracellular liquid. Thus after simplifying we get the electrical equivalent electrical circuit of biological cells which consists of an extra-cellular resistance, R_e in parallel with a series of intracellular resistance, R_i and membrane capacitance, C_i as shown in figure 1. As we know that a discrete pulse contain all frequency components so a short duration current pulse would provide complete frequency response of biological tissues.

The frequency behavior is detected by the distortion in voltage pulse which is solely defined by the electrical behavior of biological tissues and it is important to last the current pulse

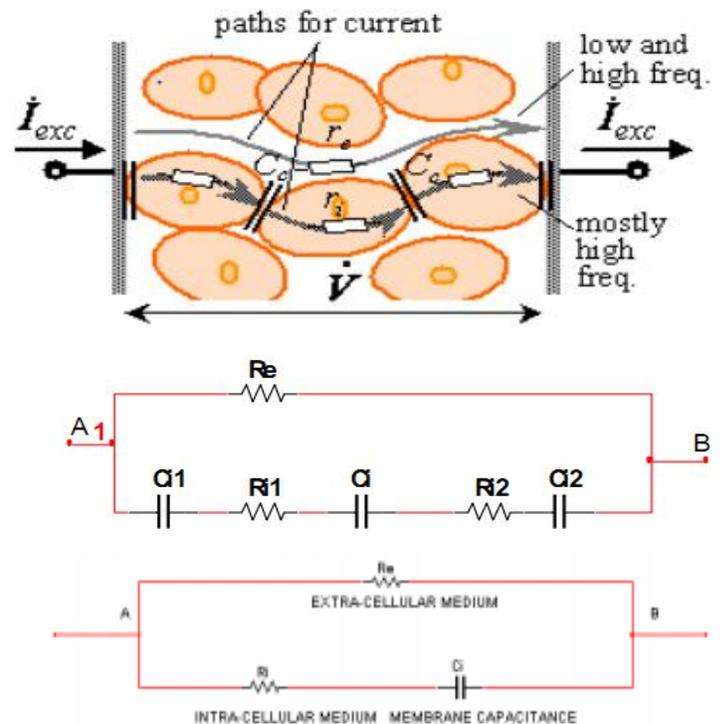


Fig. 1: Electrical equivalent circuit of biological cells

duration until the resulting voltage is stable which practically means that C_i has to be completely charged. The transfer function of bioelectrical equivalent circuit is provided by 2.

$$H(s = j * w) = R_e * (A * s + 1) / (B * s + 1) \tag{2}$$

Where, $A = R_i * C_i$ and $B = A + R_e * C_i$. After injecting a short duration current pulse voltage level is fetched by using time domain convolution of current and transfer function data. So, once the time domain voltage $V(t)$ and current $I(t)$ are acquired. The Laplace transform of voltage gives $V(s)$ and that of current pulse is $I(s)$. The Impedance spectrum is simply found from 3

$$Z(s) = V(s) / I(s) \tag{3}$$

$$|Z(w = 0)| = \max(|Z(w)|) = R_e \tag{4}$$

The frequency transform of voltage and current pulse is plotted in matlab 2009a. The result of this frequency is same as theory explain single sided sinc spectrum is found.

3 SERIAL PORT INTERFACING AND BIO-IMPEDANCE MEASUREMENT SYSTEM

Impedance measurement is accomplished in two sections comprising of current injection and voltage detection and impedance estimation as shown in figure 3.

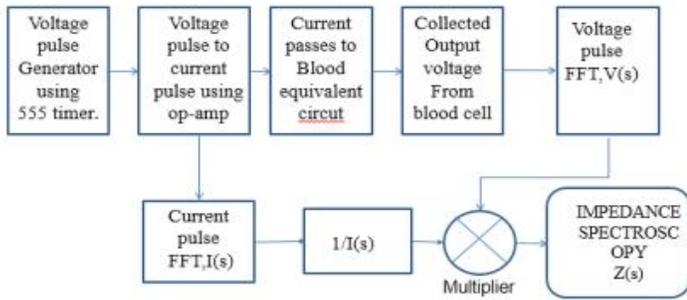


Fig. 2: Simplified Block Diagram of Electrical Impedance Spectroscopy

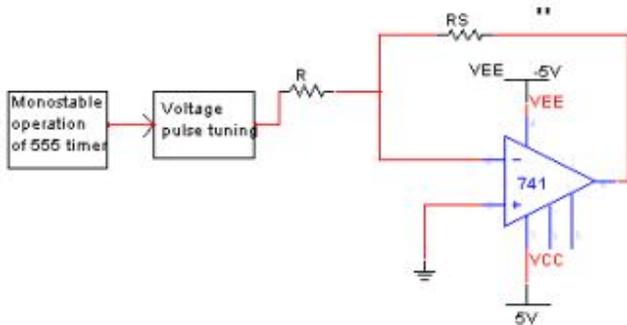


Fig. 3: Current pulse generator circuit [1]

Total system is divided into three section. These are
 1) Current pulse injection
 2) Voltage pulse sensor
 3) Serial port interfacing and impedance plot in matlab

First section involves with constant current injection into blood cell equivalent electrical circuit. Second section involves sensing of voltage pulse using electrode. Third section involves with plot of impedance spectroscopy in Matlab Using serial port interfacing.

3.1 Current Pulse Injection

Current source is the most important part of bioelectrical impedance measurement system. It is also important that the current source must be constant irrespective of load variation. For sake of simplicity and avoid hazards current value should be in 700µA to 1mA [2]. It is also required that current source should have tuning option in amplitude and pulse width.

At first pulse voltage is generated and then converted it into constant current source. In this work voltage pulse is generated by using the monostable operation of 555 timer. The reason is that in monostable operation both amplitude and pulse width is tunable. So we can easily tuning the current pulse width. As the input impedance of the operational amplifier is high we can easily convert voltage pulse to current pulse using operational amplifier. The arrangement of current source generator is shown in figure 3. Here the current to load is solely depended on R , $I = V_{in}/R$, and tunable as low as 100µA. To meet up the stability as a current source against a wide load variation, operational amplifier op-741 is selected with very high differential and common mode input imped-

ance of 1MΩ which makes the circuit applicable for constant current source up to 50KΩ.

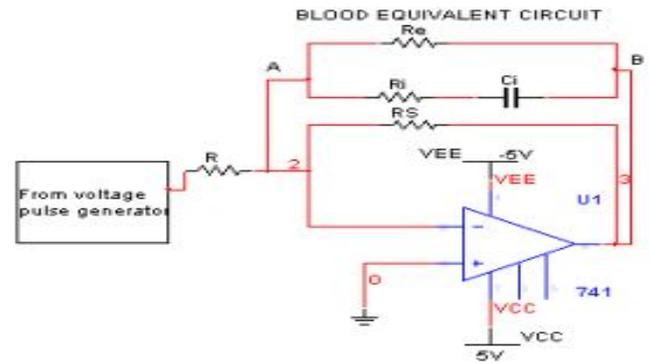


Fig. 4: Two electrode method for voltage detection [1]

3.2 Voltage Pulse Sensor

Tissue impedance must be measured for non-invasive by a couple of electrodes attached to the surface of the sample under study. Impedance measurement system using pulse approach is usually use four electrodes [13], among four electrode two of them are used for current pulse injection and two of them are used for voltage value detection. This method, known as four-electrode method or tetrapolar method, has been used for more than a century and it ideally cancels the influence of the electrode-electrolyte interface impedance. Of course, the four-electrode method is not totally free from errors. Other parasitic impedances (e.g. capacitances between wires or instrumentation input impedances) combined with the electrode-electrolyte impedances cause errors at high and low frequencies and that constrains the useful measurement band of the four-electrode method from some Hz to hundreds of MHz [14]. Under certain circumstances, the measurements performed with two electrodes can be also acceptable because the electrode impedance is negligible compared to the impedance under test. Here two electrode arrangement for both current injection and voltage detection shown in figure 4 which would reduce tissue irritation due to polarization. Here, current is injected by the electrodes A and B where the voltage is detected across electrode B and ground which would be equivalent to voltage across A and B according to the virtual ground phenomenon and makes possible two electrode setup for voltage detection.

Biomedical sensors usually suffer from common mode noise and to implement and manipulate bio-medical electrical signal information, it is very important to deploy the front amplifier with high common mode rejection ratio (CMRR) and high differential gain. This paper presents the instrumentation amplifier setup shown in figure 5 with AD620AN, where the gain G is set at desired value according to 5. Finally, the voltage is acquired with serial port interfacing in MATLAB R2009a for processing and estimation of bioelectrical impedance.

$$G = (49.4K\Omega/RG) + 1 \quad (5)$$

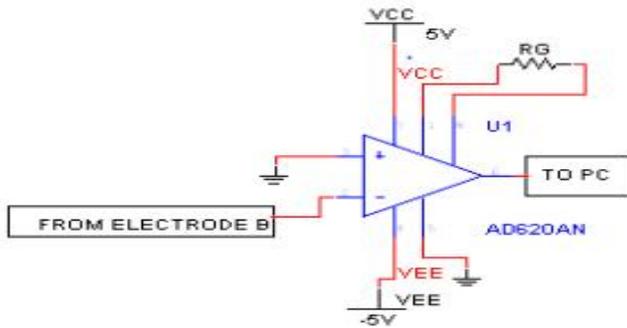


Fig. 5: Common mode noise suppression circuit

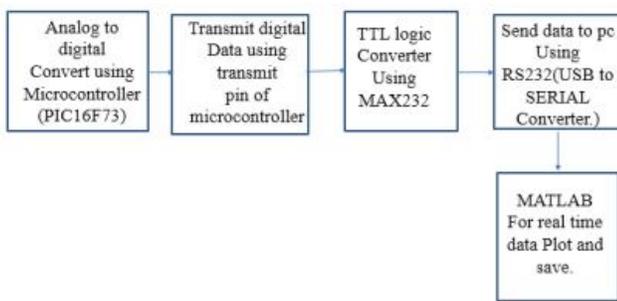


Fig. 6: Block diagram for serial port interfacing

3.3 Serial Port interfacing and Plot in matlab

Once the voltage across bio-logical tissues is fetched, voltage spectrum is found by using FFT in Matlab. By the same procedure current spectrum is also found from known pulse information and together with voltage and current spectrum, impedance spectroscopy is found by 2. For collecting these real time signal into computer some processing activities are required which is simply called interfacing. Interfacing may be serial port interfacing, parallel port interfacing, USB interfacing, sound cord interfacing and so on. In this paper we choose serial port interfacing because of serial port interfacing is one of the easiest methods of introducing external signal into computer. This requires simple arrangement than other ones. Serial communication through computer is widely in different sector of controlling and monitoring. Serial port interfacing increases system reliability. The complete serial port interfacing system is given in figure 6 below. Here at first analog signal is converted to digital signal by using a microcontroller. After A/D conversion the signal is then converted to pc compatible voltage level i.e. TTL logic level by using Max-232 IC. After that the signal is sent to pc by using USB to SERIAL Converter i.e. RS-232. After doing these work a serial plot matlab code is written and run to find voltage, current and impedance spectroscopy.

4 RESULT AND DISCUSSION

After current pulse injection and voltage detection, data are

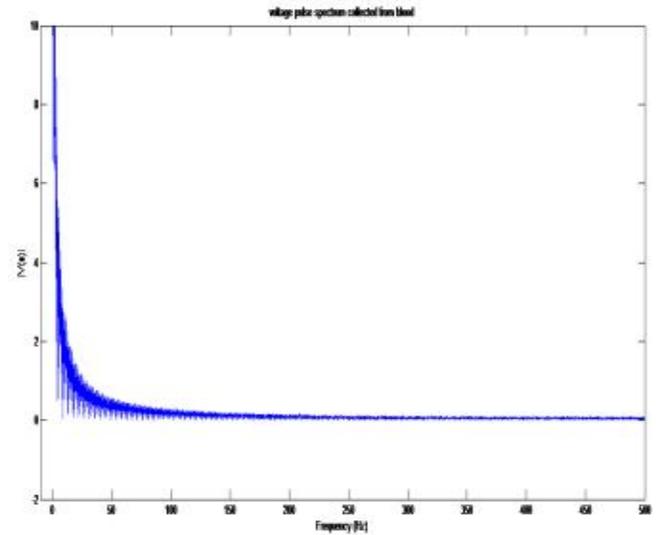


Fig. 7: FFT of voltage pulse collected from blood equivalent

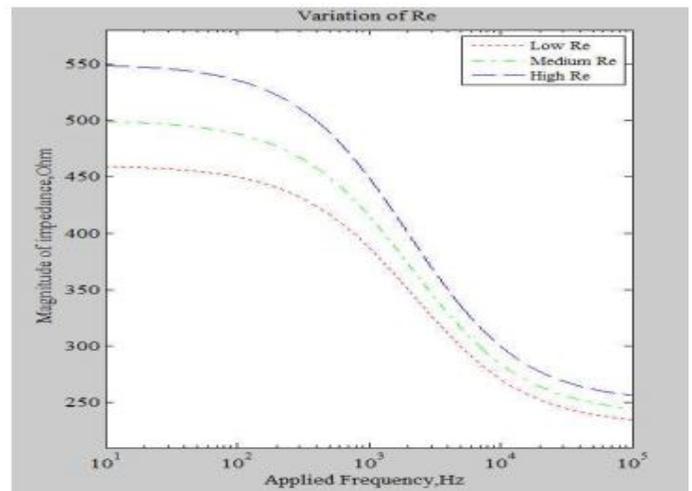


Fig. 8: Variation of impedance spectroscopy with Re

sent to pc by using serial port interfacing and saved as .mat format. After current pulse injection and voltage pulse detection, data are sent to pc by using serial port interfacing and save as .mat format. The voltage pulse fft is shown in figure 7. After this result of different impedance components Re, Ri and Cm from current and voltage pulse, different impedance spectroscopy curves shown in figures 8, 9 and 10 are plotted for the variation of Re, Ri and Cm respectively. Result shows that the variation of electrical impedance for Re is more in lower frequencies (below 1 kHz) although has good variation in higher frequencies too. On the other hand, impedance variation for Cm is strictly within 10 kHz and almost no change thereafter. But it is also found that the bio-impedance change due to Ri (intracellular medium change) is reflected in high frequencies (MHz band). Research shows much more close relation of bioinformation with Re and Cm than Ri and according to the result found, it is suggested to design biomedical sensors below 100kHz rather than MHz band for better sensitivity.

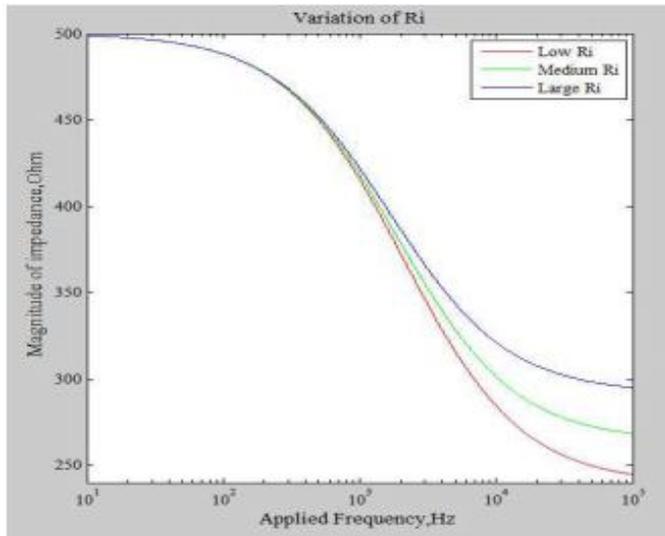


Fig.9: Variation of impedance spectroscopy with Re

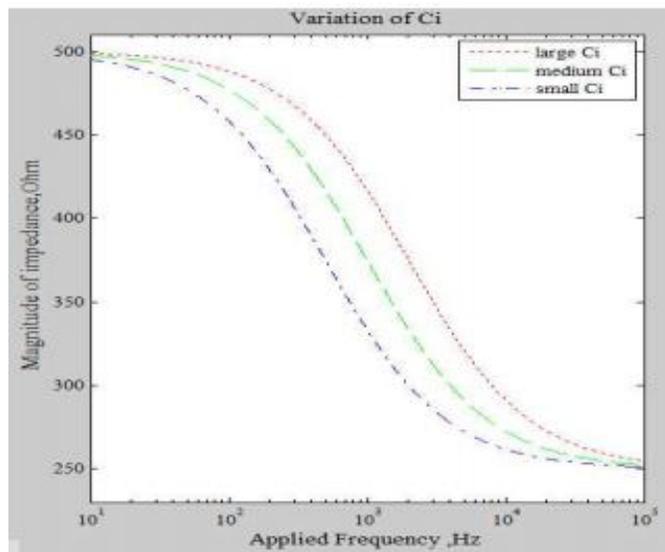


Fig.9: Variation of impedance spectroscopy with Ci

5 CONCLUSION

In present work noninvasive estimation of tissue impedance is performed using pulsatile approach. However stable current source and voltage detection circuit of bioelectrical impedance measurement is presented. Moreover, it is investigated from EIS that the variation of bioelectrical impedance is higher in frequencies less than 100 kHz for inter-cellular medium and plasma membrane capacitance variation. Such findings along with presented impedance measurement system would be applicable for noninvasive impedance estimation on layer structure of based on EIS. By adding some feature it is also possible to continuous monitor of tissue impedance in-MATLAB. Further improvement is needed for use in practical purpose of this method.

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