Non-invasive Bio-impedance Measurement Using Voltage-Current Pulse Technique

Sagar K. Dhar and Quazi D. Hossain

Abstract—Noninvasive detection is a fundamental prerequisite for pervasive healthcare system and biosensing. Along with different noninvasive techniques such as ultrasound, X-ray, magnetic resonance and optical imaging, electrical impedance spectroscopy is emerging as more suitable technique for tissue level diagnosis. This paper presents a noninvasive technique for bioelectrical impedance estimation by means of impedance spectroscopy applying voltage-current pulse technique and least square curve fitting method. Simple circuit for current injection and voltage detection is presented with common mode noise suppression circuit requires only two electrodes would reduce problems due to electrode polarization. The current source is presented with constant output current as low as 100 µA, about 1MΩ load variation and 10 MHz mid-range bandwidth. Voltage detection and impedance estimation is done with Data Acquisition (DAQ) tool box of Matlab R2008a and curve fitting technique. Successful simulation results in bioelectrical impedance estimation are found with 1.5% maximum error; suggest impedance measurement below 100 kHz because of higher response of permittivity and conductivity of biological tissues in this band than the high frequency band (MHz band).

Keywords—bioelectrical impedance, impedance spectroscopy, curve fitting, data acquisition tool box, non-invasive biosensing.

I. INTRODUCTION

PERVASIVE healthcare system automatically calls for intermittent, continuous or even contactless (wearable and wireless) and distant biomedical sensing [1]. Such systems not involve pathological patients only but also the healthy people that for the sake of preventive measurement. Therefore, an invasive sensor is not certainly going to be popular among the healthy people. Besides, invasive sensing precludes continuous monitoring and it is sometimes not possible for specific cases (e.g. blood glucose monitoring) which inevitably calls for noninvasive sensors. 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 non-ionizing radiation that illuminates a portion of the subject. Such techniques offer basic information on mass or proton density distribution. On the other hand, one more technique that provides information related to tissue structures and their physiological states and functions is bioelectrical impedance, has been of significant interest because of its several advantages such as noninvasiveness, low cost, ease of application and capability for online monitoring [2], [3] which measures the conductivity and permittivity of bio-logical tissues changed directly or indirectly by the measuring variable.

The original bio-impedance technique was involved with bioelectrical impedance analysis. Within a decade, this technique is evolved into Bioelectrical Impedance Spectroscopy (BIS) which is also called multiple frequency bioelectrical impedance analysis. It enables to have an overall figure of impedance which is of significant interest in biomedical sensing 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 [4], [5] which estimates extracellular fluid, intracellular fluid, and total body water; also applicable for tissue volume change and tissue characterization with impedance plethysmography [6]. It is well known that the electrical properties of biological tissues differ significantly depending on their structure and characteristics [7]. Depending on such variation it is possible to detect benign tissues with Electrical Impedance Tomography (EIT). This has been reported by investigators that electrical properties of tumors get changed significantly and according to Fricke and Morse [8], tumor tissues show higher permeability at 20 kHz compared to that of normal or non-malignant tissues. Study shows that extracellular resistance and intracellular resistance of cancer tissues are significantly higher and plasma membrane capacitance is significantly lower than normal tissues [9]. Similar results also found by other investigations based on microwave bio-sensing. Again, impedance measurement of bodily fluid such as saliva and blood provides much fundamental information on physiological state like glucose level and electrolyte concentration. Study shows significant change in blood conductivity and permittivity due to different level of glucose [10]. Besides, any significant change in tissue characteristics would be detectable with electrical impedance spectroscopy and study shows its viability for visceral fat measurement [11], prostate and lung cancer detection and bone fracture [12].

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 presents bioelectrical impedance measurement by means of voltage current pulse technique. Bio-impedance parameters \( R_e, R_i \) and \( C_m \) of electrical equivalent circuit shown in Fig. 1 are estimated with least square curve fitting method in Matlab 2008a. A current source is designed with the option of setting any constant current value as less as 100 µA, mid-range bandwidth of 10 MHz and load variation up to 1 MΩ. Voltage detection is designed with an instrumentation amplifier to provide good noise performance and necessary signal gain along with parallel port interfacing through Data Acquisition Toolbox of Matlab R2008a.

II. METHODS

The electrical equivalent circuit of biological cells is usually represented with similar circuit shown in Fig. 1 which is comprised of extra-cellular medium resistance, intra-cellular medium resistance and cell membrane capacitance [13]. In every case, subjected electrical current will flow through biological cells or extra-cellular medium. Again, the current through the cells may be classified as the current across the trans-membrane ionic channel (shown as the path with \( R_m \)) or across the plasma membrane. The cell membrane shows dielectric property where the intra-cellular medium and extracellular medium shows resistive behavior represented with \( R_e \) and \( R_i \) which consequently provides the capacitance effect to plasma membrane represented with \( C_m \). Due to the very high trans-membrane channel resistance, it may be ignored and the circuit is simplified with single extra-cellular medium resistance \( R_m \), intra-cellular medium resistance \( R_i \) and cell membrane capacitance \( C_m \).

![Fig 1. Electrical equivalent circuit of biological cells.](image)

Bioelectrical impedance in this paper is measured with electrical impedance spectroscopy by means of voltage-current pulse technique. Since, a discrete pulse contains all frequency components, injection of 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 duration until the resulting voltage is stable which practically means that \( C_m \) has to be completely charged. The transfer function of bioelectrical equivalent circuit is provided by (1) and the change in pulse shape is shown in Fig. 2.

\[
H(s = jw) = \frac{\left(R_e + sR_eR_iC_m\right)}{\left(1 + s\left(R_e + R_i\right)C_m\right)}
\]  

When a current pulse is injected, the voltage across the tissue would be \( V(t) = I(t)*h(t) \) where \( I(t)*h(t) \) represents the convolution sum of time domain current, \( I(t) \) and the impulse response of the bioelectrical equivalent circuit, \( h(t) \). Consequently, the Fourier transform of \( V(t) \) will provide the voltage transform \( V(s) \). So, once the time domain voltage \( V(t) \) and current \( I(t) \) are acquired and are transformed to \( V(s) \) and \( I(s) \), the impedance spectroscopy \( Z(s) \) is recovered by (2) which represents both magnitude and phase of impedance represented by (3) and (4).

\[
Z(s) = \frac{V(s)}{I(s)}
\]

\[
|Z(w)| = \sqrt{\frac{\left(R_e + R_eR_i + R_i\right)^2w^2C_m^2 + w^2C_m^2\left(R_eR_i\right)^2}{1 + \left(R_e + R_i\right)^2w^2C_m^2}}
\]  

\[
\theta(w) = -\tan^{-1}\left(\frac{wC_mR_e^2}{1 + \left(R_e + R_i\right)^2w^2C_m^2}\right)
\]

\[
|Z(w = 0)| = \max\{|Z(w)|\} = R_e
\]

Once impedance data is retrieved from frequency transform of voltage and current pulse, it is enough either to work with magnitude or phase to estimate \( R_e, R_i \) and \( C_m \). In this paper, magnitude data of impedance is fitted with (2) by means of least square method with iterated value of \( R_i \) and \( C_m \) where the value of \( R_e \) is directly calculated with (5).

![Fig 2. Pulse response of bioelectrical circuit.](image)
III. BIOIMPEDANCE MEASUREMENT SYSTEM

Impedance measurement is accomplished in two sections comprising of current injection & voltage detection and impedance estimation as shown in Fig. 3. The first section involves two major hardware parts of impedance measurement system: 1) current source and 2) voltage sensor. The second section involves the software to transform the voltage and current in frequency domain to estimate impedance spectroscopy and impedance parameters $R_e$, $R_i$, and $C_m$ subsequently.

A. Current Pulse Generation

Current source is the most important part of bioelectrical impedance measurement system and should have very good stability in providing current irrespective to the load variation and current value should be in 700 µA to 1mA [2]. Moreover, the current source should have tuning option of both amplitude and pulse width and invariable operation in low and high frequencies simultaneously.

The constant current pulse in this paper is developed by means of conversion of a voltage pulse which is generated with the mono-stable operation of a 555 timer. Since, the voltage pulse width is easily tunable in such operation; it in other words provides the tuning of current pulse width. The voltage pulse is then converted to constant current pulse according to the circuit shown in Fig. 4. The current to load is solely depended on $R_S$, $I = V_{IN}/R_S$, and tunable as low as 100 µA. To meet up the stability as a current source against a wide load variation, operational amplifier AD380JH is selected with very high differential and common mode input impedance of 100 GΩ which makes the circuit applicable for constant current source up to 1 MΩ as shown in Fig. 5. The frequency response of the source in Fig. 6 reveals its mid-range bandwidth as large as 10 MHz.

B. Voltage Detection

Pulse based impedance measurement systems generally use four electrodes [14]: two for current injection and two for voltage detection. This paper presents only two electrode arrangement for both current injection and voltage detection shown in Fig. 7 which would reduce tissue irritation due to polarization. Here, current is injected by the electrodes B and A where the voltage is detected across electrode A 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 Fig. 8 with the common mode rejection performance shown in Fig. 9 where the gain $A_{CM}$ is set at desired value according to (6). Finally, the voltage is acquired with an ADC and parallel port interfacing by the DAQ of Matlab R2008a for processing and estimation of bioelectrical impedance parameters $R_e$, $R_i$, and $C_m$.

$$A_{CM} = 1 + 2R/R_G$$  \hspace{1cm} (6)

C. Impedance Estimation

Once the potential across bio-logical tissues is fetched, voltage spectrum is found 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). At this final point, the magnitude of impedance spectrum data are calculated and fitted to (3) to find impedance parameters $R_i$ and $C_m$ applying least square method as shown in Fig. 10 and $R_e$ is directly found by (5).

IV. RESULT AND DISCUSSION

Electrical impedance is successfully estimated with around 1.5% maximum tolerance. The program of the impedance parameter estimation is run in Matlab R2008a according to the flow chart shown in Fig. 10. To test the accuracy of the curve fitting algorithm, some predetermined value of $R_e$, $R_i$, and $C_m$ are set to create known impedance data and the outcome of the program for $R_e$, $R_i$, and $C_m$ are checked with predefined value. Table I shows some instances of impedance parameter output by the curve fitting program with error percentage. It is found only 1.5% error in curve fitting method.

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>ESTIMATED IMPEDANCE PARAMETERS</th>
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<tbody>
<tr>
<td>$R_e$ (Ω)</td>
<td>Err. % $R_e$</td>
</tr>
<tr>
<td>3.0000e+3</td>
<td>0</td>
</tr>
<tr>
<td>5.0000e+3</td>
<td>0</td>
</tr>
<tr>
<td>6.9999e+3</td>
<td>1.43</td>
</tr>
<tr>
<td>8.9999e+3</td>
<td>0.01</td>
</tr>
<tr>
<td>1.1000e+4</td>
<td>0</td>
</tr>
<tr>
<td>1.3000e+4</td>
<td>0</td>
</tr>
<tr>
<td>1.5000e+5</td>
<td>0.050</td>
</tr>
</tbody>
</table>
After successful estimation of impedance components $R_e$, $R_i$ and $C_m$ from current and voltage pulse, different impedance spectroscopy curves shown in Fig. 11 are plotted for the variation of $R_e$ and $C_m$. Result shows that the variation of electrical impedance for $R_e$ is more in lower frequencies (below 1 kHz) although has good variation in higher frequencies too. On the other hand, impedance variation for $C_m$ is strictly within 10 kHz and almost no change thereafter. But it is also found that the bio-impedance change due to $R_i$ (intracellular medium change) is reflected in high frequencies (MHz band). Research shows much more close relation of bio-information with $R_e$ and $C_m$ than $R_i$ and according to the result found, it is suggested to design bio-medical sensors below 100 kHz rather than MHz band for better sensitivity.

V. CONCLUSION

In the present work, stable current source and voltage detection circuit with common mode noise suppression for bioelectrical impedance measurement is presented. Appropriate signal processing for impedance estimation from impedance spectroscopy is modeled based on least square curve fitting technique. Moreover, it is investigated that the variation of bioelectrical impedance is higher in frequencies less than 100 kHz for extra-cellular medium and plasma membrane capacitance variation. Such findings along with presented impedance measurement system would be applicable for noninvasive bio-sensing based on bioelectrical impedance spectroscopy.

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