Multilead Measurement System for the Time-Domain Analysis of Bioimpedance Magnitude

Javier Gracia*, Ville-Pekka Seppä, Jari Viik, and Jari Hyttinen

Abstract—Bioimpedance measurement applications range from the characterization of organic matter to the monitoring of biological signals and physiological parameters. Occasionally, multiple bioimpedances measured in different locations are combined in order to solve complex problems or produce enhanced physiological measures. The present multilead bioimpedance measurement methods are mainly focused on electrical impedance tomography. Systems designed to suit other multilead applications are lacking. In this study, a novel multilead bioimpedance measurement system was designed. This was particularly aimed at the time-domain analysis of bioimpedance magnitude. Frequency division multiplexing was used to avoid overlapping between excitation signals; undersampling, to reduce the hardware requirements; and power isolated active current sources, to reduce the electrical interactions between leads. These theoretical concepts were implemented on a prototype device. The prototype was tested on equivalent circuits and a saline tank in order to assess excitation signal interferences and electrical interactions between leads. The results showed that the proposed techniques are functional and the system’s validity was demonstrated on a real application, multilead impedance pneumography. Potential applications and further improvements were discussed. It was concluded that the novel approach potentially enables accurate and relatively low-power multilead bioimpedance measurement systems.

Index Terms—Bioimpedance, frequency division multiplexing (FDM), impedance measurement, interference channels.

I. INTRODUCTION

BIOIMPEDANCE represents a set of electrical properties of living organisms directly related to the composition and distribution of matter. It is traditionally determined by injecting an alternating current excitation signal through the tissue and recording the voltage response (see Fig. 1). Bioimpedance measurement has a wide range of applications, which differ in the excitation waveform and the analysis of the voltage response. The most common analysis techniques are:

1) Frequency domain analysis $\hat{Z}(\omega)$: The frequency response of a single wide-spectrum excitation signal or several individual frequency components provides detailed information about the composition of organic matter. This technique is utilized by different applications to estimate the composition of the human body, tissues, and single cells [1].

2) Time domain analysis $\hat{Z}(t)$: Variations in composition are often related to biological and physiological changes. Tracking the variations in bioimpedance over time enables the extraction of biological signals and dynamic parameters. For example, impedance cardiography tracks impedance changes caused by blood to produce haemodynamic parameters [2]. Typically, time-domain measurements are based on the variations of a single-frequency component excitation signal. Moreover, in many situations, variation in the magnitude $|\hat{Z}|(t)$ is sufficient. This is the case in impedance plethysmography applications such as impedance pneumography (IP). IP estimates changes in lung volume and pulmonary flow rate by monitoring variations in the transthoracic bioimpedance [3].

In certain cases, the information provided by a single bioimpedance measurement may not be enough to resolve complex problems or reliably produce physiological parameters. Often, this lack of information may be solved by combining bioimpedances simultaneously recorded in multiple locations. For example, the combining of multiple signals may allow the removal of movement artifacts [4], as well as the separation of overlapping frequency signals [5]. However, unwanted interactions between single-lead bioimpedance measurement systems working on the same body may degrade the results. It is necessary to use specific methods for multilead bioimpedance measurement.

Most of the actual multilead methods for measuring bioimpedances are aimed at electroimpedance tomography (EIT). EIT is a noninvasive technique that combines bioimpedances recorded between several electrodes to dynamically image body regions [6]. EIT solutions may be unsuitable or excessively complex for other purposes such as the time-domain analysis of bioimpedance magnitude.

This article briefly reviews the existing approaches for multilead bioimpedance measurement and presents the design and testing of a novel system specifically oriented to the time-domain analysis of bioimpedance magnitude in multiple locations.

II. MULTILEAD BIOIMPEDANCE MEASUREMENT BACKGROUND

If multiple single-lead bioimpedance measurement systems are connected to the same organism, their excitation signals may overlap, and the behavior of their electrical circuits may be altered. These effects can cause corrupted results.

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Fig. 1. Ideal tetrapolar bioimpedance measurement circuit. An excitation current $I(t)$ is injected and the resulting voltage response $V(t)$ is recorded. The value of the complex impedance is obtained through $\dot{Z} = \dot{V}/\dot{I}$ (1). $I_+$, $I_-$, $V_+$ and $V_-$ represent the four terminals of the tetrapolar lead.

A. Excitation Signal Overlapping

If two or more excitation signals are simultaneously injected into the same organism, the voltage response corresponds with the sum of the voltage responses that each single excitation signal would produce on its own. Special strategies should be followed to avoid the overlapping of the information conveyed in each individual voltage response signal.

1) Time division multiplexing (TDM): The classic solution utilizes fast switching between multiple bioimpedance leads, resulting in a pseudosimultaneous measurement. Since leads are not connected at the same time, the excitation signals do not overlap. However, an increment of the switching rate may cause transient processes in the tissues and the instrument, which will distort the results [7].

2) Frequency division multiplexing (FDM): Some studies suggest injecting the excitation signals concurrently, and preventing the overlapping using FDM methods [8]. If nonoverlapping frequency signals are injected, their responses can be separated again through frequency separation techniques.

3) Synchronous sampling: A recent study claims that the frequency separation methods utilized in FDM involve high computational resources [9]. The researchers propose basing the bioimpedance analysis exclusively on excitation sine waves. Sampling frequencies and sine waves can be synchronized in order to record when antinodes of a particular sine match with the nodes of the other signals. This method simplifies the signal processing calculations.

B. Electrical Interactions

As Fig. 2 shows, in a real single-lead bioimpedance measurement system, there are two nonideal impedances $Z_o$, $Z_i$ in parallel to the bioimpedance being measured $\dot{Z}$ [6]. The value estimated by the measurement system is equivalent to the parallel circuit of the three elements $\dot{Z}_T$, see Fig. 2. Typically, the two nonideal impedances are significantly higher than the organism’s bioimpedance. Hence, the error they cause may be considered negligible. However, if more leads are connected to the same organism, the number of parallel nonideal impedances increases, and the error may become considerable.

Electrical interactions are not an issue for the TDM method, as it is not a truly simultaneous approach. However, for the FDM and synchronous sampling methods, the only solution is to use circuits with a higher hardware performance.

The design of high output impedance current sources is a common problem in bioimpedance measurement. In the case of simultaneous current feeding, this may become additionally complex. There are two strategies for feeding multiple currents into the body that affect the design of the current sources.

1) Current sources with shared ground: Currents are simultaneously injected in different locations and collected at a common point [see Fig. 3(a)]. This strategy simplifies the system design when measuring contiguous bioimpedances, such as in the case of EIT. Since all current sources share the same ground, current source circuits from single-lead systems can be directly used. Many existing active current source circuits can be employed for this strategy.

2) Independent current sources: Currents are simultaneously fed between two independent points for each lead [see Fig. 3(b)]. This solution facilitates the measurement
of separated bioimpedances. However, it can only be achieved through independent current sources. At the present, there is a lack of current source circuits aimed at independent bioimpedance measurement. To our knowledge, only differential resistive current sources have been utilized for this purpose [9].

III. SYSTEM IMPLEMENTATION

The target of this research was to establish a system for the time-domain analysis of multiple independent bioimpedance magnitudes $|\dot{Z}(t)|$ with maximal measurement accuracy and minimal energy consumption. The system’s design approach and the implementation of a prototype device are presented in this section.

A. Theoretical Approach

1) Electrical Interactions: The improved Howland circuit is one of the most popular active current sources utilized in bioimpedance measurement [10]–[12]. In order to use it as an independent current source, it was fed with an independent power supply. This solution represents the first attempt to apply active circuits for the measurement of independent bioimpedances.

2) Excitation Signal Overlapping: Although synchronous sampling seems to be accurate and computationally efficient for frequency-domain analysis, use of such approach may result a complex solution for tracking only the variations in magnitude. Instead, a simple FDM approach was utilised. This consisted of assigning a different frequency excitation sine signal to each lead, and separating the responses in the frequency domain using fast Fourier transform (FFT).

3) Undersampling: A satisfactory separation of close frequencies can only be achieved through digital methods. Hence, the response signals had to be digitized. The recommended excitation frequencies are over 100 kHz for many applications. Therefore, in accordance with the Nyquist theorem, the response signals had to be sampled at frequencies over 200 kHz. However, the frequency of physiological changes conveyed on the response signal are two to three decades lower. In order to achieve a more efficient use of the hardware resources, an undersampling strategy was applied. Undersampling enables particular kinds of signals to be digitized at below the Nyquist sampling rate without information loss [13]. Consequently, the sampling rate could be reduced to approach the output frequency while maintaining the accuracy.

Fig. 4(a) shows a graphical representation of the effects of undersampling. The whole frequency spectrum can be seen as a fan-fold printer paper. This infinite paper should have the folds in the vertical direction. Hence, in this study, the inward creases correspond to the multiples of the sampling frequency, and the outward creases with the odd multiples of half the sampling frequency. The superimposition of all the sheets after collapsing the paper corresponds to the frequency spectrum after undersampling. Fig. 4(b) shows how a high-frequency band-pass signal can be digitized at a low sampling rate without loss of information. It also highlights the importance of an antialiasing filter. Filtering the target signal before undersampling prevents overlapping with other signals.

B. Hardware

Based on the previous approach, a three-lead prototype device was implemented, as shown in Fig. 5. The independent current sources were composed of a digital signal processor (DSP) to produce the excitation sine signal, and an improved Howland circuit [10]–[12] was used as a voltage-to-current converter. Both were isolated from the main power supply through a dc–dc power isolator. Moreover, a digital isolator was included to enable communication with the DSP. The voltage meter (VM) consisted of an instrumentation amplifier and a second-order antialiasing filter connecting the amplifier to an analog-to-digital converter.

C. Signal Processing

Although the prototype device only implements hardware for three leads, the signal processing was designed for an eight-lead system. As the three hardware leads are frequency configurable,
they were configured to emulate an eight-lead system through multiple rounds of testing.

Given the available resources, the undersampling frequency was set at 10 kHz, providing a 5-kHz output bandwidth. As shown in Fig. 6(b), this 5-kHz wide band was divided into eight frequency channels, one for each of the eight virtual leads. The frequencies of the excitation sine signals after undersampling for each channel are presented in the third column of Table I. It is recommended that excitation frequencies should be above 100 kHz. Therefore, the frequencies of the excitation sine signals were calculated by adding 100 kHz to the corresponding undersampled frequency [second column in Table I; see also Fig. 6(a)].

The antialiasing filters were configured at 100 and 105 kHz for their lower and upper cutoff frequencies, respectively. In order to separate the response signals after undersampling, FFT was computed. The amplitude of a particular excitation signal was calculated from the magnitude of FFT at the signal’s frequency.

| TABLE I
<p>| EXCITATION FREQUENCIES BEFORE AND AFTER THE UNDERSAMPLING FOR EACH FREQUENCY CHANNEL |</p>
<table>
<thead>
<tr>
<th>Frequency Channel</th>
<th>Excitation Frequency</th>
<th>Undersampled Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>f₁</td>
<td>100 750 Hz</td>
<td>750 Hz</td>
</tr>
<tr>
<td>f₂</td>
<td>101 250 Hz</td>
<td>1250 Hz</td>
</tr>
<tr>
<td>f₃</td>
<td>101 750 Hz</td>
<td>1750 Hz</td>
</tr>
<tr>
<td>f₄</td>
<td>102 250 Hz</td>
<td>2250 Hz</td>
</tr>
<tr>
<td>f₅</td>
<td>102 750 Hz</td>
<td>2750 Hz</td>
</tr>
<tr>
<td>f₆</td>
<td>103 250 Hz</td>
<td>3250 Hz</td>
</tr>
<tr>
<td>f₇</td>
<td>103 750 Hz</td>
<td>3750 Hz</td>
</tr>
<tr>
<td>f₈</td>
<td>104 250 Hz</td>
<td>4250 Hz</td>
</tr>
</tbody>
</table>

The second column shows the frequency of the excitation sine signals and the third column presents their value after being undersampled at 10 kHz.

IV. PERFORMANCE TESTING

A. Frequency Channel Interference Tests

Method: The three leads were connected to the same constant resistive value $R_L = 500 \Omega \pm 1\%$ (see Fig. 7), and were configured to work on different groups of frequency channels (see Table I). For all groups, the outputs of the three leads were recorded for a period of 10 s. The mean and variance were calculated for each of the three outputs.

Two groups of triads of frequency channels were selected for two different purposes.
1) The results of $[f_4, f_5, f_6], [f_5, f_5, f_7]$ and $[f_2, f_5, f_8]$ were compared in order to analyze the effects that distance between frequencies may have on the results.
2) The results for $[f_1, f_5, f_3], [f_2, f_3, f_4], [f_3, f_4, f_5], [f_4, f_5, f_6], [f_5, f_6, f_7], [f_6, f_7, f_8]$ were compared in order to verify the correct functioning of the processing block for the eight established channels.

Results and Discussion: The three leads showed constant output values over the 10-s period. The mean values for the three...
TABLE II
LEAD CONNECTION COMBINATIONS USED IN THE ELECTRICAL INTERFERENCE TEST

<table>
<thead>
<tr>
<th>Combination No.</th>
<th>Lead 1</th>
<th>Lead 2</th>
<th>Lead 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>VM</td>
<td>CI</td>
<td>VM</td>
</tr>
<tr>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>2</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>3</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>4</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>5</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>6</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>7</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>8</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>9</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>10</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

X indicates the corresponding voltage meter (VM) or current injector (CI) simultaneously connected to the circuit shown in Fig. 7.

outputs agreed with the load value (500 Ω), with errors lower that the resistance tolerance (±1%). The variance for the three outputs ranged from 0.0083 to 0.0086. Discrepancies in the mean and the variance between triads were lower than 0.01%. These results prove that the undersampling and frequency separation methods work as expected. For the following tests, the triad \([f_1, f_2, f_3]\) was used.

B. Electrical Interference Test

Method: This experiment aimed to quantify the error caused by the addition of leads. The output error for one lead was calculated while the current injectors (CI) and VM from the other leads were connected to the same resistive load \(R_L\) (see Fig. 7) in different combinations (see Table II). Ten different resistors’ between 100 and 1000 Ω were used for \(R_L\). In order to remove the resistors tolerance error from the measure, the measured values \(R_{test:n}(R_L)\) were normalized with respect to the result of lead-1 connected on its own (Combination No.1, \(R_{test:1}(R_L)\)) as

\[
\varepsilon_{test:n}(R_L) = \frac{R_{test:n}(R_L) - R_{test:1}(R_L)}{R_{test:1}(R_L)} \cdot 100.
\]

Each result was presented as the mean value of 50 repetitions.

Results and Discussion: The chart in Fig. 9 illustrates the error for the set of ten resistors for every combination of connections defined in Table I. Although no error exceeded ±0.8%, addition of more leads may increase the error considerably.

The connection of elements involves the addition of an impedance parallel to the load \(R_L\) (see Section II-B). As these impedances are much higher than the load \(R_L\), the error these produce on the measure \(\varepsilon_{test:n}\) should be close to 0 for low loads, and increasingly noticeable for higher load values. The growing rate of the error should differ between experiments and be related to the total impedance value in parallel to the load.

This phenomenon was not noticed in the results. This led us to believe that the current sources had a high output impedance (over 50MΩ). Nevertheless, an unexpected offset error was observed. Discrepancies between the offset errors for the connection of VMs (Combinations No. 5, 6, 7) were less than 0.2%. On the other hand, discrepancies between the offset errors for the connection of CIs (Combinations No. 8, 9, 10) were greater than 1%. It is believed that despite the power isolation, the connection of improved Holland circuits to the same load produces interactions that cause the offset error.

C. Bioimpedance Electrical Model Test

Method: The previous experiments have been based on resistive loads. However, bioimpedances also involves capacitive elements. To assess the accuracy of the device for capacitive loads, the three leads were simultaneously connected to the same bioimpedance electrical model (see Fig. 8) [1]. Eight configurations with different component values were measured (see Table III). The error for each configuration was calculated with respect to the theoretical values as the mean of 50 repetitions.

Results and Discussion: Table III shows the value of the components for the different configurations and the relative error for each lead. The errors did not exceed ±1% and the variation between the three leads was always less than 0.1%. Thus, it is assumed that the errors were mainly caused by the tolerances of the components and the electrical interactions explained in the previous section.
Table III

Component Values and Resulting Relative Error for the Bioimpedance Electrical Model Test

<table>
<thead>
<tr>
<th>Configuration No.</th>
<th>$R_1$</th>
<th>$R_2$</th>
<th>$C$</th>
<th>Relative Error</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lead 1</td>
</tr>
<tr>
<td>1</td>
<td>309 Ω</td>
<td>182 Ω</td>
<td>220 nF</td>
<td>0.67%</td>
</tr>
<tr>
<td>2</td>
<td>475 Ω</td>
<td>442 Ω</td>
<td>100 nF</td>
<td>0.20%</td>
</tr>
<tr>
<td>3</td>
<td>301 Ω</td>
<td>953 Ω</td>
<td>68 nF</td>
<td>0.30%</td>
</tr>
<tr>
<td>4</td>
<td>133 Ω</td>
<td>243 Ω</td>
<td>22 nF</td>
<td>0.11%</td>
</tr>
<tr>
<td>5</td>
<td>475 Ω</td>
<td>442 Ω</td>
<td>10 nF</td>
<td>0.37%</td>
</tr>
<tr>
<td>6</td>
<td>120 Ω</td>
<td>952 Ω</td>
<td>10 nF</td>
<td>0.82%</td>
</tr>
<tr>
<td>7</td>
<td>82 Ω</td>
<td>27 Ω</td>
<td>68 nF</td>
<td>0.96%</td>
</tr>
<tr>
<td>8</td>
<td>180 Ω</td>
<td>243 Ω</td>
<td>10 nF</td>
<td>0.79%</td>
</tr>
</tbody>
</table>

$R_1$, $R_2$ and $C$ correspond to the values of the bioimpedance model circuit in Fig. 8. The error is presented with respect to the theoretical impedance of the model circuit.

Fig. 10. Saline tank test diagram. This shows the dimensions of the tank constructed, the location of the 12 electrodes within the tank and the terminal connected to each electrode.

D. Saline Tank Test

Method: In the previous experiments, the leads always shared the same connections to the same load. However, in a real application, leads will most likely be connected to different locations of the organism. Therefore, there will be some impedance between leads and the load values will differ for each lead. A more realistic test was carried out using a saline water tank.

An elliptic tank 280 cm in length and 160 cm in width was filled with 2 cm of a 1000 ppm NaCl dissolution. Twelve Ag/AgCl electrodes were placed in the inner wall of the tank. Fig. 10 shows the location of the electrodes and the terminals assigned to them.

The theoretical resistive value for each individual lead was calculated with the simulation tool COMSOL Multiphysics. The output of the three leads were recorded for different combinations of lead connections (see Table IV).

Results and Discussion: Table IV shows the results for each lead for the different experiments. Discrepancies between the simulated and measured values were found to be less than 3%. This may be due to environmental factors such as temperature.

Nevertheless, the simulation merely provided a guiding value. More relevant was the error caused by the addition of leads, which less than ±0.4% in all cases. As expected, the addition of leads to the water tank caused an error inferior to the connection of the leads to the same load (±0.8%).

E. Human Testing

Method: In order to demonstrate the correct functioning of the system, it was used in a particular application, specifically the simultaneous measurement of three IP signals. The four terminals of the three leads were connected to a subject through 12 electrodes placed around the thorax at the height of the xiphoid process, as shown in Fig. 11. Variations in transthoracic impedance were recorded while the patient was breathing spontaneously. The lung volume changes were simultaneously recorded with a pneumotachograph (A. Fleisch No. 3, Lausanne, Switzerland with Biopac SS40L pressure transducer, Goleta, CA, USA) by integrating the measured flow rate signal.

Results and Discussion: The charts in Fig. 11 show the output for the three leads and the spirometer over 45 s. A visual inspection showed that the results are in line with previous findings by Seppä et al. [3].

V. DISCUSSION

This study presented the design, implementation, and testing of a novel multilead bioimpedance measurement system. New hardware and new signal processing approaches were introduced. They were proven to be functional and highly accurate for the time-domain analysis of the magnitude of multiple bioimpedances.

A. Hardware

The system showed excellent performance when leads were connected individually to the measurand. The small error (<±0.8%) seen when multiple leads were connected simultaneously is likely to have been caused by the current sources.

The isolation of active current sources has proven to be a promising approach to ensure independence between fed currents. However, the improved Howland circuit may not be the
Fig. 11. Upper pictures show the locations of the 12 electrodes placed around the thorax and the terminal connected to each electrode. The upper chart shows the output signals for the three leads and the lower chart for the spirometer during 45 s of tidal breathing.

best current source circuit for this solution due to electrical interactions.

The lack of solutions for simultaneous independent current feeding calls for further research. We believe that a comparative study of different differential and power isolated current sources should be conducted. The tests presented in this article represent a solid reference for this study.

B. Signal Processing

The combination of FDM and undersampling has been shown to separate frequencies accurately while reducing hardware requirements.

Although energy efficiency was sacrificed in favor of configurability in the implementation of the prototype device, the processing approach potentially enables the reduction of energy consumption. On the one hand, as FDM does not require synchronization between leads, the DSPs can be replaced with analog oscillator circuits. Vuorela et al. [14] have recently demonstrated that this change may provide a decrement of 6 mA per lead. On the other hand, the reduction in hardware requirements enabled by undersampling involves a decrement in energy consumption.

C. Applications

In addition to IP, the developed system can be used for any other application based on time-domain analysis of bioimpedance magnitude. The simultaneous access to multiple bioimpedances is promising for:

1) **Signal separation:** For example, a transthoracic bioimpedance is affected by cardiac and respiratory activities. However, both contributions have overlapping frequency bands that cannot be satisfactorily separated using linear filters. Bioimpedance signals recorded in multiple locations could be combined to separate cardiac and respiratory signals [5].

2) **Motion artifact rejection:** Motion artifacts are a common problem in impedance plethysmographic. The comparison of signals recorded in different locations for the removal of movement effects has been already proven for electrocardiograms [4]. Similar methods could be applied to bioimpedance measurement.

3) **Multiple systems coexistence:** Unlike the TDM or synchronous undersampling, the FDM method does not require any kind of communication between leads. This advantage simplifies the coexistence of independent bioimpedance measurement systems on the same body, providing flexibility to body sensor networks such as the DexterNet [15].

VI. CONCLUSION

A simultaneous access to multiple bioimpedance signals has the potential to improve the accuracy of actual applications, as well as to develop new ones. The design of new approaches out of the main trend focusing on EIT enables the simplification of the hardware and signal processing. It is most promising for increasing precision in measurement and reduce energy consumption.

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Authors’ photographs and biographies not available at the time of publication.