Software Tool for Analysis of Breathing-Related Errors in Transthoracic Electrical Bioimpedance Spectroscopy Measurements

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Abstract. During the last decades, Electrical Bioimpedance Spectroscopy (EBIS) has been applied in a range of different applications and mainly using the frequency sweep-technique. Traditionally the tissue under study is considered to be time-invariant and dynamic changes of tissue activity are ignored and instead treated as a noise source. This assumption has not been adequately tested and could have a negative impact and limit the accuracy for impedance monitoring systems. In order to successfully use frequency-sweeping EBIS for monitoring time-variant systems, it is paramount to study the effect of frequency-sweep delay on Cole Model-based analysis. In this work, we present a software tool that can be used to simulate the influence of respiration activity in frequency-sweep EBIS measurements of the human thorax and analyse the effects of the different error sources. Preliminary results indicate that the deviation on the EBIS measurement might be significant at any frequency, and especially in the impedance plane. Therefore the impact on Cole-model analysis might be different depending on method applied for Cole parameter estimation.

Keywords: electrical bioimpedance spectroscopy, EBIS artefacts, frequency-sweep EBIS, Transthoracic Measurements, frequency-sweep spectroscopy of time-variant systems

1. Introduction

Electrical Bioimpedance Spectroscopy (EBIS) is widely used for assessing status or composition of tissue. During the last decades, EBIS estimation by using the frequency-sweep technique, i.e. sweeping through a range of different measuring frequencies, has been applied in a range of different areas e.g. Body Composition Analysis (BCA) [1], tissue characterization for skin cancer detection [2], and impedance-based systems for cardiac monitoring [3, 4]. However, the time during which the signal, from for example cardiac activity, can be considered stationary is often shorter than the measurement time for a frequency-sweep. This leads to both under sampling of important information as indicated by Sanchez et al. [5, 6] for real-time monitoring of myocardium tissue, and to measurement artefacts that might ruin the EBIS measurement.
Traditionally the tissue under study is considered to be time-invariant and dynamic changes of tissue activity are ignored and instead treated as a noise source. The error due to frequency sweep measurements under this false assumption of a time-invariant signal is illustrated in figure 1.

Figure 1. Resistance of thorax at four different frequencies (solid, dotted, dashdot and dashed lines); for simplification respiration is considered the only source of variance in thoracic resistance. True (simultaneously sampled) and frequency-sweep measurements are shown by green circle and red square, respectively. A respiration rate of 10 Breaths/Min and a delay of 100ms between measurements were used for this simulation.

This problem, that could have a negative impact, limiting the accuracy impedance monitoring systems and consequently impeding the proliferation of novel and emerging applications of EBIS has to date not been adequately addressed.

In this work, we present a software tool that can be used to simulate the influence of respiratory activity in frequency-sweep transthoracic EBIS measurements and to analyse the effects of the different error sources. The usefulness of the tool is demonstrated by an example of deviations and errors obtained in estimation of Cole parameters.

2. Methods

In this section, the models for creating synthetic EBIS measurements and methods for estimating the Cole parameters and calculating errors are described. EBI data was generated using the Cole equation with biologically plausible values. To model the modulation caused by the respiratory activity, the Cole-model was augmented by adding respiration related time-varying impedance.

2.1. Cole Equation

The Cole Equation (1) is a model for impedance dispersion, which was introduced by Cole in 1940 [7] to fit experimentally obtained Electrical Bioimpedance (EBI) measurements of biological tissue. The model uses four parameters to describe the impedance dispersion, \( R_0, R_\infty, \alpha \) and \( \tau \). Where \( R_0 \) and \( R_\infty \) has a direct interpretation as the impedance response at zero and infinite frequency, the \( \alpha \) describes the models departure from a simple RC circuit model and \( \tau \) is the inverse of the natural characteristic frequency \( \omega_c \) [7].

\[
Z_{\text{COLE}}(\omega) = R_\infty + \frac{R_0 - R_\infty}{1 + (j\omega \tau)^{\alpha}} \quad (1)
\]

The Cole equation is non-linear in the frequency domain and the impedance values generated by \( Z_{\text{COLE}}(\omega) \) in (1) represent a supressed semi-circle when plotted in the impedance plane i.e. resistance vs. reactance [5].

2.2. Modelling and Synthesis of EBIS data

As mentioned earlier, generation of EBI data is simplified by considering time-invariant model for thorax and additive time-variant respiration impedance. Additive white Gaussian noise with mean \( \mu \) and standard deviation \( \sigma \) specified by user is also included to mimic measurement noise.
Thoracic impedance is generated by the tool using the Cole function and user specified values for \( R_0 \), \( R_s \), \( \alpha \) and \( \omega_0 \). Assume \( T \) as duration time of simulation, \( T_d \) as the delay between the measurements at different frequencies in the sweep (step delay) and \( N \) as the number of frequencies in the sweep. The EBIS data for the thorax during simulation time is defined as \( Z_{\text{Thorax}} \). While each row and column shows the value at the corresponding frequency and time, respectively.

\[
t = (1 \ T_d \ 2 \ T_d \ 3 \ T_d \ \ldots \ T)_M \quad , \quad M = \frac{T}{T_d} \quad , \quad f_{\text{Resp}} = \frac{\text{Respiration Rate}}{60}
\]

\[
Z_{\text{Thorax}} = \begin{bmatrix}
Z_{\text{Cole Thorax}}(1) & \ldots & Z_{\text{Cole Thorax}}(1) \\
\vdots & \ddots & \vdots \\
Z_{\text{Cole Thorax}}(N) & \ldots & Z_{\text{Cole Thorax}}(N)
\end{bmatrix}_{N \times M}
\]

According to Brown [8] the impedance change associated with respiration has an inverse relation to frequency (it decreases as the measurement frequency increases). Respiration impedance \( Z_{\text{Resp}} \) is simply modelled as a sinusoid with amplitude generated by a user specified Cole function and phase \( \phi_{\text{Resp}} \) specified by user. \( \phi_{\text{Resp}} \) is used to simulate spectrum measurements which are not synchronized with respiration cycle.

\[
Z_{\text{Resp}} = \begin{bmatrix}
Z_{\text{Resp}}(2\pi f_0)\sin(2\pi f_0 t(1) + \phi_{\text{Resp}}) & \ldots & Z_{\text{Resp}}(2\pi f_0)\sin(2\pi f_0 t(M) + \phi_{\text{Resp}}) \\
\vdots & \ddots & \vdots \\
Z_{\text{Resp}}(2\pi f_{\text{max}})\sin(2\pi f_{\text{max}} t(1) + \phi_{\text{Resp}}) & \ldots & Z_{\text{Resp}}(2\pi f_{\text{max}})\sin(2\pi f_{\text{max}} t(M) + \phi_{\text{Resp}})
\end{bmatrix}_{N \times M}
\]

Simulation of EBIS data has been done by using \( \text{Spectra}_{\text{Measure}} \) and \( \text{Spectra}_{\text{True}} \). True spectra are simply assigned to value of \( Z_{\text{Total}} \) for each frequency at the same time. On the other hand, \( \text{Spectra}_{\text{Measure}} \) elements are assigned to value of \( Z_{\text{Total}} \) for each frequency by considering measurement delay of \( T_d \).

\[
\text{Spectra}_{\text{True}} = \begin{bmatrix}
Z_{\text{Total}}(1,1) & \ldots & Z_{\text{Total}}(1,M) \\
\vdots & \ddots & \vdots \\
Z_{\text{Total}}(N,1) & \ldots & Z_{\text{Total}}(N,M)
\end{bmatrix}_{N \times M}
\]

\[
\text{Spectra}_{\text{Measure}} = \begin{bmatrix}
Z_{\text{Total}}(1,1) & \ldots & Z_{\text{Total}}(1,2N+1) & \ldots & Z_{\text{Total}}(1,M-N) \\
\vdots & \ddots & \vdots \\
Z_{\text{Total}}(N,1) & \ldots & Z_{\text{Total}}(N,3N) & \ldots & Z_{\text{Total}}(N,M)
\end{bmatrix}_{N \times (M/N)}
\]

2.3. Error Analysis

The analysis of measurement error due to the none-simultaneous measurements has been done by studying of Root Mean Square Error (RMSE) and comparing R-fitted Cole parameters for each true and measured spectrum. The RMSE of each measured spectrum compared to true spectrum has been calculated by using Equation 3. Where \( N \) is the number of frequency steps and \( R(\omega) \) and \( jX(\omega) \) are resistance and reactance, respectively.

\[
\text{RMSE} = \frac{\sum(R-R)^2}{N} + \frac{\sum(X-X)^2}{N}
\]

2.4. Software Description

The software is developed by using MATLAB 7.12 (Release 2011a) and its user interface allows us to change simulation parameters and settings, simulate the spectroscopy measurements and plot true and measured spectrum in different planes. The error analysis produces a report containing the RMSE and
R-fitted estimation of Cole parameters compared to the true spectrum. A screenshot of the software is depicted in Figure 2.

Figure 2. Screenshot of the developed software; the user can change simulation parameters and settings, simulate the spectroscopy measurements and plot true and measured spectra in different planes.

3. Results

The results for a simple simulation case are summarized in this section. The thorax and respiration impedance are generated by using Cole parameters $R_0 = 35, R_∞ = 17, f_c = 42000$ and $α = 0.7$ and $R_0 = 3, R_∞ = 1, f_c = 42000$ and $α = 0.7$, respectively.

The simulation has been done in the frequency range of 5-1000 kHz. The spectroscopy frequency-sweep has been done at 16 frequencies with a step delay of $T_d = 100$ ms. The respiration rate is considered at 12 per minute while mean and standard deviation of noise are set to zero.

The spectroscopy measurements and corresponding errors are shown in Figure 3. It can be clearly seen that the error is not negligible for any of the measurements and that the more prominent errors occur at maximum inhalation and exhalation. Figure 4 further illustrates the measured spectrum in different planes (impedance-plane and frequency-plane for resistance, reactance and absolute impedance). The plots in the impedance plane exhibit the variations between the measurements. It is clearly noticeable not only the Cole parameters $R_0$ and $R_∞$ but also for the characteristic frequency $f_c$ and $α$.

| Table 1. Summary of the Error Analysis for Spectroscopy Measurements |
|---------------------------------------------------------------|
| $R_0$ (Error %) | $R_∞$ (Error %) | $f_c$ (Error %) | $α$ (Error %) | RMSE |
|-----------------|-----------------|-----------------|---------------|------|
| True Spectrum 1 | 35.3 (1.4%)     | 17.1 (7.0%)     | 42000.0       | 0.70 |
| Measured Spectrum 1 | 34.8 (1.5%) | 18.3 (7.0%)     | 55420.8 (32.0%) | 0.75 (7.0%) | 1.48 |
| True Spectrum 2  | 37.6 (1.8%)     | 17.9 (7.0%)     | 42000.0       | 0.70 |
| Measured Spectrum 2 | 38.3 (1.8%) | 15.8 (11.6%)    | 35952.1 (14.4%) | 0.68 (3.5%) | 1.76 |
| True Spectrum 3  | 32.5 (0.7%)     | 16.2 (4.0%)     | 42000.0       | 0.70 |
| Measured Spectrum 3 | 32.7 (0.7%) | 16.8 (4.0%)     | 34421.9 (18.0%) | 0.68 (2.6%) | 0.41 |
| True Spectrum 4  | 34.5 (1.6%)     | 16.8 (9.5%)     | 42000.0       | 0.70 |
| Measured Spectrum 4 | 34.0 (1.6%) | 18.5 (9.5%)     | 56156.0 (33.7%) | 0.75 (7.8%) | 1.73 |
| True Spectrum 5  | 37.9 (1.4%)     | 18.0 (10.9%)    | 42000.0       | 0.70 |
| Measured Spectrum 5 | 38.4 (1.4%) | 16.0 (10.9%)    | 38380.0 (8.6%) | 0.68 (2.5%) | 1.52 |
Figure 3. Simulation of spectroscopy measurements; True Spectra, Measured Spectra, Baseline (Thorax) Spectra and Respiration cycle are shown in the upper graph. Measurement error compared to the True spectra and the respiration cycle as functions of time are shown in the bottom graph.

Figure 4. Graphs show measured and time-invariant Thorax spectrum in different planes resistance $R(\omega)$, reactance $\jmath X(\omega)$, impedance $|Z(\omega)|$ and the Cole Plot.

The RMSE obtained for the measured and the true spectrum and the relative error the estimation of the Cole parameters are summarized in Table 1. It is clear that even for the third measurement which has minimum RMSE; the error in estimated parameters is significant. Note that the error in the characteristic frequency is large in most of the measurements.
4. Discussion
The simulation and error analysis of the influence of the time between frequency samples on EBIS measurements indicate that Cole-based analysis done without considering measurement delay can lead to erroneous estimation of the values for the Cole parameters. All parameters suffer from erroneous estimation but the characteristic frequency $f_c$ appears to be the most sensitive parameter.

The deviation of the EBIS measurement is significant in the impedance spectrum for all frequencies and it is more manifested in the impedance plane. Hence it is expected that the performance of Cole parameter estimation methods in different planes might be different. For instance the observed deviations of the impedance data suggest that estimating the Cole parameters from the immittance spectrum instead than in the impedance plane would produce a better result.

The simulation of the respiration-related impedance can be done by using sinusoid synthetized impedance as described in methods or by using empirically respiration impedance measurements. Currently experimental data about transthoracic EBIS measurements during breathing and different activities is collected, thus increasing the capabilities of the software tool to perform more realistic, deeper, and more complex simulations and analysis.

In addition to the search for methods and technics to enhance the analysis of EBIS measurements of the thorax, the software tool can be useful in the design of measurement protocols to be used in studies requiring EBIs transthoracic measurements.

5. Conclusion
The use of the implemented software tool has helped us to confirm our hypothesis that the measurement time delay caused by sweeping between frequencies on the acquisition of EBIS measurements influences on the measured spectrum creating a measurement artefact and consequently taint any subsequent data analysis using Cole parameters characterization. These results encourage to perform more complex studies with more realistic and advanced settings and to include experimental validation. It is expected that as a result of these studies effective tools and methods for removing or avoiding these measurement artefacts and their consequent wrong-analysis will be developed to increase the accuracy of EBIS instrumentation and fostering the proliferation of EBIS-based systems for personalized health monitoring.

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