Rubén Buendía López

Model Based Enhancement of Bioimpedance Spectroscopy Analysis: Towards Textile Enabled Applications

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Dedicado a mi Familia y a Sarah
ABSTRACT

Several signal processing approaches have been developed to overcome the effect of stray capacitances in Electrical Bioimpedance Spectroscopy (EBIS) measurements. EBIS measurements obtained with textile-enabled instrumentation are more vulnerable to stray capacitances. Currently, the most widespread approach for correcting the effect of stray capacitances in EBIS is the time delay ($T_d$) compensation method, which also has several drawbacks. In this study, the $T_d$ method is revisited and its limitations and its lack of a scientific basis are demonstrated. To determine better ways to overcome the effect of stray capacitances, a simplified measurement model is proposed that is based on previous models of artefacts in EBIS measurements described in the literature. The model consists of a current divider with a parasitic capacitance ($C_{par}$) in parallel with the load. $C_{par}$ creates a pathway for the measurement current to leak away from the load, provoking a capacitive leakage effect. In this thesis, three approaches with different limitations are proposed to overcome the capacitive leakage effect. The first approach estimates $C_{par}$ and subtracts it from the measurements, thus finding the load. $C_{par}$ can be estimated because the susceptance of biological tissue is null at infinite frequency. Therefore, at high frequencies, the susceptance of the tissue can be neglected, and the slope of the susceptance of the measurement is $C_{par}$. The accuracy of $C_{par}$ depends on the maximum frequency measured and the value of $C_{par}$. Therefore, it may not be possible to accurately estimate small values of $C_{par}$ in the typical frequency ranges used in EBIS. The second and third approaches use the Cole fitting process to estimate the Cole parameters, which form the basis for most EBIS applications. Because the conductance of the measurement is free from the effect of $C_{par}$, performing Cole fitting on the conductance avoids the effect of $C_{par}$ in the fitting process. With a poor skin-electrode contact, this approach may not be sufficiently accurate. The third approach would be to perform the Cole fitting on the modulus with a reduced upper frequency limit because the modulus and the low-medium frequencies are very robust against the effect of artefacts. In this approach, a slight capacitive leakage effect is unavoidable. Since it is common to find tainted measurements, especially among those obtained with textile-enabled instrumentation, it is important to find viable methods to avoid their effect. The three methods studied showed that they could reduce the effect of tainted measurements.
ACKNOWLEDGEMENTS

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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>Ag/AgCl</td>
<td>Silver / Silver Chloride</td>
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<tr>
<td>BCA</td>
<td>Body Composition Assessment</td>
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<tr>
<td>EBI</td>
<td>Electrical Bioimpedance</td>
</tr>
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<td>EBIS</td>
<td>Electrical Bioimpedance Spectroscopy</td>
</tr>
<tr>
<td>ECW</td>
<td>Extracellular Water</td>
</tr>
<tr>
<td>EIT</td>
<td>Electrical Impedance Tomography</td>
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<tr>
<td>FFM</td>
<td>Fat Free Mass</td>
</tr>
<tr>
<td>FM</td>
<td>Fat Mass</td>
</tr>
<tr>
<td>ICG</td>
<td>Impedance Cardiography</td>
</tr>
<tr>
<td>ICW</td>
<td>Intracellular Water</td>
</tr>
<tr>
<td>MAPE</td>
<td>Mean Absolute Percentage Error</td>
</tr>
<tr>
<td>REBIS</td>
<td>Resonant frequency Electrical Bioimpedance Spectroscopy</td>
</tr>
<tr>
<td>RS</td>
<td>Right Side</td>
</tr>
<tr>
<td>SF-BIA</td>
<td>Single Frequency Bioimpedance Analysis</td>
</tr>
<tr>
<td>SF-EBI</td>
<td>Single Frequency Electrical Bioimpedance</td>
</tr>
<tr>
<td>TBC</td>
<td>Total Body Composition</td>
</tr>
<tr>
<td>TBW</td>
<td>Total Body Water</td>
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LIST OF SYMBOLS

\( \sigma \)  Conductivity
\( \varepsilon \)  Permittivity
\( \rho \)  Resistivity
\( \rho_e \)  External Resistivity
\( \rho_i \)  Internal Resistivity
\( \rho_{ae} \)  External apparent Resistivity
\( C \)  Capacitor
\( C_m \)  Membrane Capacitor
\( R_m \)  Membrane Resistance
\( R_e \)  Extracellular Resistance
\( R_i \)  Intracellular Resistance
\( Z_{meas} \)  Measurement Impedance
\( V_{meas} \)  Measurement Voltage
\( I_{meas} \)  Measurement Current
\( Y_{meas} \)  Measurement Admittance
\( G_{meas} \)  Measurement Conductance
\( S_{meas} \)  Measurement Susceptance
\( Z_m \)  Measurement Impedance
\( Z_{Cole} \)  Cole Impedance
\( Y_{Cole} \)  Cole Admittance
\( G_{Cole} \)  Cole Conductance
\( S_{Cole} \)  Cole Susceptance
\( Z_{corr} \)  Corrected Impedance
\( Z_{comp} \)  Compensaed Impedance
\( V_m \)  Measurement Voltage
\( I_m \)  Measurement Current
\( Z_{Tissue} \)  Tissue Impedance
\( Z_{TUS} \)  Tissue Under Study Impedance
\( Z_{ep} \)  Electrode polarisation Impedance
\( V_{ep} \)  Electrode polarisation Voltage
\( I_{ep} \)  Electrode polarisation Current
\( Z_{in} \)  Input Impedance
\( Z_{out} \)  Output Impedance
<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>$I_0$</td>
<td>Reference Current</td>
</tr>
<tr>
<td>$R_0$</td>
<td>Resistance at DC</td>
</tr>
<tr>
<td>$R_\infty$</td>
<td>Resistance at Infinite Frequency</td>
</tr>
<tr>
<td>$\omega$</td>
<td>Natural Frequency</td>
</tr>
<tr>
<td>$f_c$</td>
<td>Characteristic Frequency</td>
</tr>
<tr>
<td>$\omega_c$</td>
<td>Characteristic Natural Frequency</td>
</tr>
<tr>
<td>$V_{Body}$</td>
<td>Body Volume</td>
</tr>
<tr>
<td>$D_B$</td>
<td>Body Density</td>
</tr>
<tr>
<td>$H$</td>
<td>High</td>
</tr>
<tr>
<td>$W$</td>
<td>Weight</td>
</tr>
<tr>
<td>$k_b$</td>
<td>Body Constant</td>
</tr>
<tr>
<td>$T_d$</td>
<td>Time Delay</td>
</tr>
<tr>
<td>$C_{par}$</td>
<td>Parasitic Capacitance</td>
</tr>
<tr>
<td>$X_{C_{par}}$</td>
<td>Parasitic Capacitance Reactance</td>
</tr>
<tr>
<td>$S_{C_{par}}$</td>
<td>Parasitic Capacitance Susceptance</td>
</tr>
<tr>
<td>$I_{leak}$</td>
<td>Leakage Current</td>
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Chapter 1

Introduction

Increases in life expectancy and society’s growing demands on health and wellness services augment the cost of health services. Hospitals require enormous investments in infrastructure as well as high cost due to clinical staff salaries. One of the most effective ways to reduce the cost of healthcare is Home Healthcare.

Current information and communication technologies are capable of supporting the implementation of efficient, user-friendly, home monitoring devices. Physiological measurements are a key part of home monitoring systems, but measurements taken by the patients are not always reliable.

When dealing with noninvasive electrode-enabled measurements, well-defined measurement protocols together with a supervisory system may improve the reliability of the performed measurements; however, the electrode placement as well as the lead connections and the skin electrode contact would require a technological solution. Smart Textiles could be a very good approach.

During the last few years, the European Union has financed research activities focused on home healthcare monitoring systems. Smart Textiles is included as a part of these systems. These research activities have been funded through different projects, e.g., MyHeart FP6-IST-2002-507816, STELLA FP6-IST-028086 and HeartCycle FP7-216695. As a result of this research, new conductive fibres, textile electrodes and garments with integrated electrodes have been developed.

The success of textile transducers in health monitoring systems requires appropriate medical instrumentation and textile technology as well as medical signal processing applied to physiological measurements. For several decades, Electrical Bioimpedance (EBI) technology has played an important role in electrophysiology and biophysics. Currently, EBI provides means of noninvasive, quick and relatively affordable assessment of tissue composition. EBI applications for skin cancer detection (Aberg et al., 2005) or dry weight determination (Kuhlmann et al., 2005) have increased during the last decade.

Home monitoring applications based on Body Composition Assessment (BCA) determined using EBI, such as early diagnosis of lung oedema (Beckmann et al., 2007) or hydration status (Medrano et al., 2007) are recent promising applications which may utilize portable devices and textile electrodes, also known as Textrodes.

The most common tool for BCA is EBI spectroscopy (EBIS). This approach consists of fitting the EBIS raw data to the Cole function proposed by Cole (1940) to estimate the Cole parameters from which the BCA parameters are computed.

To obtain a reliable estimate of the Cole parameters and then conduct an analysis, reliable measurements are needed. However, the measurements obtained with Textrodes and portable
devices, especially when taken by the patients outside the laboratory or clinical environment, are more susceptible to noise and artefacts.

The electrode polarisation impedance ($Z_{ep}$) of Textrodes varies more than that in conventional electrodes. Textrodes are also more susceptible to motion artefacts. Therefore, they may be influenced by stray capacitances (Scharfetter et al., 1998) as well as $Z_{ep}$ mismatch between electrodes (Bogónez-Franco et al., 2009). The presence of artefacts in EBIS measurements often leads to faulty estimation of the Cole parameters and errors in any subsequent analysis. Therefore, their effect must be minimised. Even if several analyses of measurement errors have been reported and recommendations for measuring practices have been provided (Bogónez-Franco et al., 2009; Bolton et al., 1998; Sverre Grimnes et al., 2006; Scharfetter et al., 1998), there is a lack of signal processing approaches to solve the problem.

1.1 Aim

The main aim of this thesis is to propose and validate robust and reliable estimation methods for obtaining Cole parameters from nonideal EBIS measurements.

In this work, different sources of measurement errors that are derived from a nonideal measurement system and influence the immittance spectra are identified, analysed and modelled. Then, different approaches are proposed to overcome the effect of these measurement errors on the estimation of the Cole parameters.

1.2 Structure of the Thesis

Chapter one is a general introduction of the home health care monitoring need and how Smart Textiles can facilitate home monitoring. In addition, an introduction to EBI and its applications in the home monitoring field, the challenges of EBIS measurements obtained with Smart Textiles and a contribution to solve the challenges are provided. Chapter two provides the theoretical basis of the thesis. Chapter three is a description of the problem. Chapter four offers an analysis of the source of errors in EBIS measurements and a critique of the current method to compensate for such errors. In addition, an introduction to alternative ways to minimise the influence of the measurement artefacts is provided. Chapter five proposes three approaches to overcome the effect of the errors described in chapter four. Chapter six presents experimental validation of the approaches proposed in chapter five. Finally, in chapter seven, the results are discussed, the conclusions are drawn, and future work is outlined.
Chapter 2

Theoretical Frame

2.1 Dielectric Properties of Biological Tissue

Biological tissue mainly consists of extracellular fluid and cells. The cells contain organelles and intracellular fluid inside a lipid bi-layer membrane known as the cell membrane. The extracellular fluid is the medium surrounding the cells, the extracellular space (Guyton et al., 2001). The electrical properties of the tissue are determined by the electrical characteristics of its constituents.

Because both intra- and extracellular fluids contain ions, they are considered to be electrolytes. These ions can move freely and are able to transport electrical charge. Therefore, from an electrical point of view, biological tissue may be considered an ionic conductor at low frequencies.

The cell membrane electrically isolates the cell because its conductive properties are very low. Thus, a conductor-dielectric-conductor structure is created by the intracellular space, the lipid bi-layer membrane and the extracellular space. The most common ions contained in the extracellular fluid are Na\(^+\) and Cl\(^-\); the potassium ion K\(^+\) has the highest concentration in the intracellular fluid. The existence of charges free to move at both sides of the cell membrane allows the accumulation of charges, which gives rise to the most noticeable dielectric properties of the cell.

The dielectric properties of tissues are given by the dielectric behaviour not only of the cell membrane and the surrounding ionic fluids. Also in the intra- and extracellular spaces there are polar molecules, proteins and macromolecules that are too large to move in the presence of an electrical field. However, these particles can rotate and align the dipole along the gradient of the electrical field. Thus, the low frequency properties of biological tissue and the electrical behaviour exhibited at higher frequencies make biological tissue to be considered as an ionic dielectric conductor.

2.1.1 Frequency Dispersions

The passive dielectric properties of biological tissue are conductivity and permittivity. Conductivity [\(\sigma\)] is a magnitude used to indicate the ease with which free charges move through a medium; it is related to the conductance, i.e., the real part of the inverse of the impedance. Permittivity [\(\varepsilon\)] is the ability of bounded charges to be polarised inside the medium; it is related to the susceptance, i.e., the imaginary part of the inverse of the impedance. Because of the composition and structure of biological tissue, their values are frequency dependent. The relationships between frequency and the conductivity (\(\text{S/m}\)) and relative permittivity of a muscular tissue are shown in Figure 2.1.
The dispersion windows share the spectrum based on the conductivity and permittivity of the tissue at different frequencies. There are four windows in different regions of the spectrum (H.P. Schwan, 1994), which can be observed in Figure 2.1.

\[ \text{Muscular Tissue} \]

\[ \begin{align*}
\alpha & \quad \beta \\
\delta & \quad \gamma
\end{align*} \]

\[ \text{Figure 2.1 Plot of the frequency dependence of the electrical properties of muscular tissue} \]

\( \alpha \)-dispersion

The \( \alpha \)-dispersion window dominates at low frequencies ranging between a few Hz to a few kHz. The mechanisms contributing to this dispersion window are not clear (H. P. Schwan et al., 1993). Three of the mechanisms which are well established are the effect of the endoplasmic reticulum, the channel proteins inside the plasma membrane affecting the conductivity, and the relaxation of counter-ions on the charged cellular surface.

\( \beta \)-dispersion

The plasma membrane is the main contributor to this dispersion window because of its capacitive properties. The membranes of the organelles inside the cell also contribute. The window ranges from approximately a few kHz to hundreds of kHz.

\( \delta \)-dispersion

The \( \delta \)-dispersion is a small, nondominating dispersion that appears between \( \beta \) and \( \gamma \); it is caused by proteins and amino acids and range from hundreds of MHz to a few GHz.

\( \gamma \)-dispersion

The molecules of water in the intra and extracellular medium cause this dispersion. The dielectric properties of biological tissue are determined by the molecules of water, which have a relaxation frequency of 20 GHz. However, tissue water due to the presence of proteins and other components set a dispersion window that occupies a wide band in the spectrum, from hundreds of MHz to several GHz.
## 2.2 Electrical Bioimpedance

Electrical bioimpedance is the opposite to the flow of electrical current presented by biological material when an external electric field is applied. Biological tissue is composed of cells, which contain and are surrounded by conductive fluids. Therefore, it is widely accepted to model biological tissue dielectric behaviour as a suspension of cells in conductive fluids. Admittance is the inverse of impedance, and immittance is a neutral term that refers to any of them.

The immittance of a material depends on its passive electrical properties, conductivity and permittivity; other factors affecting the immittance are the shape and the volume. The immittance can only be measured by applying external energy to the material. The conductivity of a cell is a function of the specific conductivity of the medium, the ion concentration and the organelles, as well as the shape and the volume of the cell.

This approximation to a suspension of cells, in spite of its simplicity and full acknowledgement that it is far from reality, is the basis of the Fricke’s model (H Fricke, 1924; H. Fricke et al., 1925), see Figure 2.2, which has been widely accepted and used for a long period of time with acceptable results.

In a Fricke-based model, the resistive components are associated with the extra and intracellular fluids, while the capacitor is associated with the cell membrane. The total impedance of the tissue is represented by two resistors \( R_e, R_i \), which represent the extra- and intracellular resistances, respectively. A resistor \( R_m \) in parallel with a capacitor \( C_m \) models the cell membrane as an imperfect capacitor; however, \( R_m \) is very big, and therefore, it can be neglected, as shown in Figure 2.2. According to the model, ionic current can flow around the cell using the extracellular compartment as well as into the cell through the ionic channels across the lipid bilayer.

![Figure 2.2 Fricke’s electrical model and the circuit representation. The membrane conductance usually is very small; thus, it is considered to be negligible](image-url)
As Fricke’s model suggests, the ionic current flowing through biological tissue follows different paths at different frequencies. As shown in Figure 2.3, the current flowing at very low frequencies does not pass through the cells; instead, current flows through the extracellular medium. However, as the frequency increases in the β dispersion frequency range, the cell membrane capacitor charges and discharges the current at the frequency rate. Thus, the charge displacement in the cell membrane becomes significant, and current flows through the cell membrane by displacement in both the extra- and intracellular fluid. At very high frequencies, i.e., the high part of the β dispersion window, the charge-discharge process is so fast that the cell membrane effect is very small, and nearly all the current passes through the cell in the same way as outside the cell.

### 2.3 Electrical Bioimpedance Measurements

Electrical Bioimpedance (EBI) is based on the passive electrical properties of tissue. Therefore, an external stimulus is required to excite the passive tissue and to observe the response of the tissue to such a stimulus. In EBI, the stimulus comes in the form of electrical energy, voltage or current, which is applied to the tissue under study. The stimulus generates a response in the form of either current or voltage, which is then measured. Thus, the EBI is obtained through deflection, i.e., by applying electrical energy and observing the response (Pallàs-Areny et al.; Woo et al., 1992). The stimulation and the response sensing are obtained using electrodes. Usually, when measuring EBI, an amperometric approach is used in which current is injected and the resulting voltage is sensed. Note that voltammetric approaches are also used when performing EBI measurements.

EBI measurements can be used in several applications, but the following descriptions are specifically focused on Body Composition Assessment (BCA).
2.3.1 Single Frequency and Spectroscopy Measurements

In the history of EBI single frequency has been used the longest to monitor changes such as those caused by breathing or produced by cardiac activity in impedance cardiography. Single frequency electrical bioimpedance (SF-EBI) measurements at 50 kHz have also been used for TBC, giving rise to single frequency bioimpedance analysis (SF-BIA), which is a widely used method. These measurements can be accomplished with wrist-to-ankle configurations or body segments.

EBIS measurements require information for the whole spectrum or at least enough frequencies to perform spectroscopy analysis. Thus, the term spectroscopy (Kuhlmann et al., 2005) is used. Until now, the most accepted applications of EBIS measurements are skin cancer screening (Aberg et al., 2005; Aberg et al., 2004) and BCA. The measured frequencies for BCA and all the applications related to body composition and hydration status typically range from a few kHz to upper frequencies in the range of hundreds of kHz or up to 1 MHz. In BCA, EBIS measurements allow direct differentiation between intra-extracellular water compartments, which allows ECW and ICW to be estimated. EBIS is a commonly used method for the early detection of several diseases when hydration monitoring is used.

2.3.2 Two- and Four-Electrode Measurements

The number of electrodes used to perform an EBI measurement has an important influence on the final value of the measurement. There are several measurement techniques using two, three or four electrodes (S Grimnes et al., 2000), but in this section, only two and four-electrode techniques are examined.

When using two electrodes to measure the EBI of a tissue, both are used for sensing and stimulating simultaneously, as can be observed in the measurement model shown in Figure 2.4. The ideal differential amplifier measures the voltage caused by the current flowing through the tissue and, in addition, the voltage created by the current flowing through the electrode. Thus, it is not able to differentiate between the electrode impedance and the tissue impedance, where the impedance measured $Z_{\text{meas}}$ is the sum of $Z_{\text{Tissue}}$ and both electrode polarisation impedances, $Z_{\text{ep}}$, which is the impedance that the interface skin electrode presents. Equations 2.1-2.4 can be reviewed for a better understanding.

Two-electrode measurements are useful for single frequency applications based on detection of changes of impedance with time, e.g., impedance cardiography and respiration function monitoring. Otherwise, they are not in use for applications used to identify or assess tissue condition.

\begin{align*}
Z_m &= \frac{V_m}{I_m} \quad \text{Equation 2.1} \\
V_{\text{ep}} &= I_{\text{ep}} Z_{\text{ep}} \quad \text{Equation 2.2} \\
V_m &= V_{\text{ep}} + V_{\text{TUS}} + V_{\text{ep}} = V_{\text{TUS}} + 2V_{\text{ep}} \quad \text{Equation 2.3} \\
Z_m &= \frac{V_{\text{TUS}} + 2V_{\text{ep}}}{I_m} = Z_{\text{TUS}} + 2Z_{\text{ep}} \quad \text{Equation 2.4}
\end{align*}
In the four-electrode technique shown in Figure 2.5, in an amperometric approach, the current is applied through two electrodes, while the voltage sensing is done by two different electrodes. A voltammetric approach can be implemented by applying a voltage and sensing electrical current instead.

This technique can, in an ideal case, eliminate the effect of the electrodes on the measurement if $Z_{ep}$ is sufficiently small when compared with the input impedance of the circuit used to detect the voltage. In Figure 2.5, if the operational amplifier $Z_{in}$ is sufficiently large to consider $I_{ep}$ negligible, $V_{ep}$ can be considered null, and thus $Z_{meas} = Z_{Tissue}$, see Equation 2.5. However, the four-electrode approach does not prevent the effect of stray capacitances.

$$Z_m = \frac{V_{TUS} + 2V_{ep}}{I_m} = Z_{TUS} \quad \text{Equation 2.5}$$

### 2.4 Cole Function

More than 70 years ago, Kenneth S. Cole (Cole, 1940) presented the Cole function, shown in Equation 2.6 as a mathematical equation that experimentally fits EBIS data. Since then, in EBI applications, the function and its parameters have been widely used to represent EBIS measurement data on the impedance plane. For the last 25 years, the Cole function has also been
used for data analysis in EBI applications.

The Cole function, see Equation 2.6, is a complex nonlinear function of frequency, which fits experimental EBIS data from the β dispersion window. Such function are built up by 4 parameters $R_0$, $R_\infty$, $\alpha$ and $\tau$, where the natural frequency ($\omega$) is the independent variable.

$$Z(\omega) = R_\infty + \frac{R_0 - R_\infty}{1 + (j\omega)^\alpha}$$  \hspace{1cm} \text{Equation 2.6}

The Cole function is quasi-compatible with Fricke’s model. Therefore, in cells in suspension in a conductive fluid, as represented in Figure 2.3, the cell membranes behave as capacitors, $C_m$. Thus, at zero frequency, it becomes an open circuit, impeding electrical current from flowing through the interior of the cells. Otherwise, at high frequencies, near $\infty$, the impedance of the $C_m$ becomes short-circuited, allowing the current to flow through the intracellular space as well. In the frequency range from 1 kHz to 100 MHz, the $C_m$ charge and discharge at the rate of the frequency.

Thus, at low frequency, the impedance of the suspension is close to $R_0$, and contains information about the conductivity of the ECF. At $\infty$ frequency, the impedance of the suspension is purely resistive, $R_\infty$, and the resistance contains information about the conductivity of both the ECW and ICW. All these phenomena occur inside the β-dispersion window. At very low and very high frequencies inside the β-dispersion range, the effect of the $C_m$ is very small; however, at the characteristic frequency $f_c$, the effect is maximum, which is why at this frequency the value of the reactance is maximum.

The representation of the Cole equation in the impedance plane is a depressed semicircle Cole plot, which is shown in Figure 2.6. Observing the Cole plot, the reactance is null at zero and at infinite frequency. Because measuring at zero or infinite frequency is not possible, the measurements are collected within the β-dispersion frequency limits, the values for $R_0$ and $R_\infty$ are extrapolated until reaching zero reactance. $\tau$ is the time constant and the inverse of the characteristic natural frequency, as in Equation 2.7. The parameter $\alpha$ is responsible for the observed depression of the semicircle; $\alpha$ takes values between 0 and 1.

$$\tau = (\omega_c)^{-1}$$  \hspace{1cm} \text{Equation 2.7}

\subsection*{2.5 Cole Fitting}

The analysis of the Cole parameters forms the basis for most EBIS applications. To obtain the four parameters, the EBIS data from the spectral measurement are fitted to the Cole function.
The Cole equation is a complex nonlinear function of frequency that can be represented in the impedance plane, which is perpendicular to the frequency plane. Therefore, the equation is fit to the experimental data using iterative methods either in the frequency domain or the impedance domain. When the curve fitting is complete in the impedance plane, the circular characteristics of the Cole function are used to simplify the process. In most cases, such methods are based on numerical approximations to obtain the minimum of the least square error of a cost function using an iterative gradient.

Complex least square fitting methods for fitting EBIS data were introduced by MacDonald (1987). The nonlinear least square (NLLS) method to fit the Cole function as a semicircle in the impedance plane to EBIS data was proposed by Kun & Peura (1999). To fit the data to a circle, the centre and the radius are estimated in an iterative procedure that minimises the summed square of the error of the equation of a circle, as expressed in Equation 2.8.

\[ F(x_0, y_0, r) = \sum_{i=1}^{N} (\sqrt{(x_i-x_0)^2 + (y_i-y_0)^2} - r)^2 \]  \hspace{1cm} \text{Equation 2.8} 

This fitting approach may be good for the estimation of \( R_0 \), \( R_\infty \) and \( \alpha \) because they can be calculated analytically from the parameters of the circle. However, the approach does not account for the frequency, and therefore, the estimation of \( \tau \) will not be accurate, especially if the data are noisy or contain artefacts.

2.6 Nonlinear least square curve fitting

Iterative fitting through the Nonlinear Least Square (NLLS) method is intended to obtain the best coefficients for a given model that fits the experimental data. The method given by Equation 2.9 minimises the summed squared of the error between the measured data value and
the modelled value. In Equation 2.9, N is the number of frequencies, e is the error, X is the data, and $\bar{X}$ is the model.

$$\min \sum_{i=1}^{N} e_i^2 = \min \sum_{i=1}^{N} (|X_i| - |\bar{X}_i|)^2 \quad \text{Equation 2.9}$$

Recently, the use of the NLLS method has increased when EBIS data are fitted to the Cole function, but the immittance spectrum (Ayllón et al., 2009; R. Buendia et al., 2011; Nordbotten et al., 2011) has been used instead of a semicircle in the impedance plane. In this approach, the frequency information is used to find the best fit, and the four Cole parameters are estimated simultaneously instead of sequentially, as is usually the case in semi-circular fittings.

### 2.7 Electrodes and Textrodes

Electrodes are instruments providing an interface between the tissue and the measurement electronic device by conducting current across the interface. Textrodes are being developed and used in different scenarios such as ECG monitoring (Habetha, 2006), EEG (Lofhede et al., 2010) or bioimpedance spectroscopy measurements (J. C. Marquez, 2011; Vuorela, 2011).

Medrano determined (G. Medrano, 2011) that textrodes as a material are a viable alternative to standard EBIS electrodes. The transduction function in EBIS measurements depends on the skin-electrode contact and the humidity of the interface. Moreover, other parameters, such as conductivity of the textile material, smoothness, moisture absorption, ability to stretch and washability, might influence the performance of a Textrode and should be considered when choosing one.

The feasibility of using Textrodes in EBIS applications has been widely demonstrated in recent studies (J. C. Marquez, 2011; Vuorela, 2011) and the research activities performed in the MyHeart and the Heart Cycle projects. There are a handful of novel and emerging applications that could benefit from the use of textrodes, especially in the field of home healthcare and personalise health monitoring systems. However, the use of textrodes often produces EBI measurements with higher variability than EBI measurements obtained with conventional Ag/AgCl gel electrodes, especially when the skin-textrode interface is poorly established.
Chapter 3

Background to the performed studies

There are many applications of EBIS, and all of them are susceptible to stray capacitances. Those obtained with textrodes are particularly vulnerable because a poor skin-electrode contact is more likely to occur with this kind of electrode; those obtained in an electrically noisy environment, such as an intensive care unit, are also vulnerable. Most EBIS applications are based on Cole parameter analysis, and therefore, the approaches to avoid the effect of stray capacitances can be used in the cole parameter estimation.

An example of the importance of overcoming the effect of stray capacitances is the MyHeart project. Most of the EBIS measurements contained in this project deviate from the spectrum produced by stray capacitances (Publication 3). These measurements are thoracic measurements taken with textile electrodes integrated in a vest designed by Phillips Research Medical Signal Processing group; the vest can be observed in Figure 3.1.

In the following sections, an overview of the applications relevant to the work presented in this licentiate job is presented.

Figure 3.1 Vest with an integrated EBIS measurement system used in the MyHeart project (Source: Philips)
3.1 Assessment of Body Composition

Currently, the fluid distribution is assessed from estimates of the BCA parameters: total body water (TBW), extracellular water (ECW) and intracellular water (ICW). ECW is related to Fat Free Mass (FFM) (Lukaski et al., 1985), which is especially significant in nutrition. ICW and ECW form the basis for the hydration status assessment. Such parameters can be quickly obtained from EBI measurements in a noninvasive procedure.

Several Single Frequency EBI (SF-EBI) measurement approaches have been proposed and widely used, but all of them have drawbacks. Nonmodelling multifrequency methods also have drawbacks (Matthie, 2008). Cole function fitting to the EBIS data and Cole-based analysis methods appear to be the most appropriate approaches to estimate BCA parameters (Matthie, 2008).

3.1.1 Total Body Composition

Wrist-to-ankle four-electrode measurements are the most widespread approach used for Total Body Composition (TBC) assessment. This method is appropriate, easy to employ and accurate under most conditions. An intuitive example of the measurement set-up and the results can be found at Figure 3.2.

The primary criticism of this method is that the trunk represents approximately 60% of the body mass but represents less than 10% of the wrist-to-ankle impedance measurement; thus, it contributes little to the water volume prediction. To overcome this error, segmental measurements are applied to obtain a more uniform measured volume related geometry. However, the TBC assessment results from segmented measurements have not proven to be better than those from wrist-to-ankle measurements (Matthie, 2008).

Cole parameters are the basis for TBC parameter estimation. The BCA parameters estimates from Cole-based analysis methods are determined using the resistances at DC and infinite frequency, $R_0$ and $R_\infty$, respectively, from the Cole function (Cole 1940); see Section 2.4.

![Figure 3.2 Wrist to ankle RS EBI measurements set-up](image-url)
of this report. This approach is motivated by Fricke’s model which was explained in Section 2.2. $R_0$ is assimilated into the extracellular resistance $R_e$, and $R_i$ is assimilated into the equivalent resistance calculated from neglecting the capacitor $C_m$ and leaving a parallel combination $R_e//R_i$, i.e., the resistance of the extra- and intracellular spaces.

For TBC, the following approximation considers the whole body to be built of 5 cylinders, where $k_b$ is a shape factor in Equation 3.1,

$$R = \frac{k_b \rho H^2}{V_{Body}} \quad \text{Equation 3.1}$$

where $V_{Body}$ is the body volume, $H$ is the high and $\rho$ is the resistivity; moreover, the value of $k_b$ was set to 4.3 (Van Loan et al., 1993).

According to Fricke’s model, at low frequencies only information from the extracellular space can be obtained, the information about the intracellular space will be obtained at higher frequencies by applying Hanai’s mixture theory (Hanai, 1968) because the impedance information contains a contribution from both the intracellular and extracellular spaces. Thus, the apparent resistivity ($\rho_{ae}$) is obtained through Equation 3.2, where $V_{ECW}$ is the ECW volume

$$\rho_{ae} = \rho_e \left(\frac{V_{Body}}{V_{ECW}}\right)^{3/2} \quad \text{Equation 3.2}$$

Thus, the ECW resistance results are expressed in Equation 3.3

$$R_e = k_b H^2 V_{Body}^{1/2} \rho_e V_{ECW}^{-3/2} \quad \text{Equation 3.3}$$

If $V_{Body}$ is the ratio of body weight $W$ and density $D_b$, the $V_{ECW}$ could be expressed as in Equation 3.4

$$V_{ECW} = \frac{1}{100} \sqrt[3]{\frac{k_b^2 \rho_b^2}{D_b} \cdot \frac{H^4 W}{R_0^5}} \quad \text{Equation 3.4}$$

and the ICW volume is calculated as proposed by (De Lorenzo et al., 1997) and expressed in Equation 3.5, which cannot be solved analytically

$$\left(1 + \frac{V_{ICW}}{V_{ECW}}\right)^{5/2} = \left(\frac{R_0}{R_{\infty}}\right) \left(1 + \frac{\rho_i V_{ICW}}{\rho_e V_{ECW}}\right). \quad \text{Equation 3.5}$$

After obtaining the ECW and ICW volumes, the TBW volume is simply their sum.

### 3.1.2 Dry weight determination for dialysis patients

Dry weight is the targeted optimal body weight of the patient, achieved through the removal of excess water during dialysis (Kuhlmann et al., 2005). Three methods have been proposed to determine the dry weight of dialysis patients:
The normovolemia/hypervolemia slope method uses EBIS wrist-to-ankle measurements to estimate pre and postdialysis ECV. The ECV when dry weight is achieved should be the same as that of healthy subjects. In predialysis, the patient is overhydrated and the excess water is removed by ultrafiltration. When the ECV of the patient reaches the ECV level of a healthy subject with the same physical characteristics, the dry weight is reached.

The continuous intradialytic calf impedance method uses EBIS segmental calf measurements to determine ECV. During hemodialysis, the calf will be the last region of the body from which the excess water will be removed because excess water is present because of gravity.

Measurements of extracellular resistance are taken at a distance of 10 cm across the lateral side of one calf because volume and size are well defined. EBIS are monitored during hemodialysis. When the extracellular resistance remains stable for approximately 20 min despite ongoing ultrafiltration, the dry weight is reached.

The VIVA method was introduced by Piccoli et. al. (1994). SF-EBI 50 kHz measurements are taken, normalised with the high of the subject and plotted against each other in a graph. The location of the vector point in relation to gender specific reference distribution areas obtained from normally hydrated healthy individuals (indicated by a dotted ellipse) is representative of the hydration status of the individual patient. Normal hydration is defined as the range of impedance vectors falling within the 75% tolerance interval of the reference group. The vector distribution area of healthy individuals is influenced by gender, race or ethnicity, body mass index and age (Piccoli et al., 2002).

### 3.2 Detection of Cardiogenic Pulmonary Oedema

Cardiogenic pulmonary oedema is one of the symptoms of decompensation in heart failure patients. Different EBI approaches based on SF-EBI, Electrical Impedance Tomography (EIT) and EBIS have been proposed for this purpose.

There is a lack of consensus in SF-EBI approaches because they differ in the frequency used. Nevertheless, the development of these approaches confirms that the thoracic impedance changes at several frequencies during decompensation. The commercial product ZOE uses an Impedance Cardiography (ICG) approach to measure the thoracic impedance at a single frequency (Milzman et al., 2009; Peacock et al., 2000). ZOE uses 100 kHz instead than the typical 20 or 50 kHz.

Among the EIT approaches Pulmotrace is a remarkable tool that is commercially available (Freimark et al., 2007; Radai et al., 2008). Pulmotrace uses low frequencies 10-20 kHz and multi-channel measurements to estimate the internal conductivity of each lung. The conductivity is obtained with relatively good accuracy, which may make this approach attractive.

The first study that can be found using EBIS for this purpose is by (Mayer et al., 2005). Subsequently, Lisa Beckman et al. in (Beckmann et al., 2007) proposed EBIS as a good candidate to detect cardiogenic pulmonary oedema at an early stage. Their work is based on the usefulness of EBIS for detecting body water shifts. They also propose optimal locations for the electrodes and the optimal frequency range in the same work.
Habetha (2008) states that impedance can be reliably measured with textile-enabled instrumentation and that thoracic bioimpedance might be a good approach to detect a de-compensating patient because of fluid accumulation in the lungs at an early stage. This finding is the basis for the use of a textile-enable EBIS measurement system for early diagnosis of cardiogenic pulmonary oedema in the European projects *MyHeart* and *Heart Cycle*. In these projects, noninvasive bio-impedance measurements on the thorax are proposed to detect the amount of water in the lungs of patients for the management of chronic heart failure (Reiter et al., 2011)
Chapter 4

Analysis of the Effect of Stray Capacitances in EBIS

4.1 Deviation of the EBI Spectrum

EBIS measurements sometimes have a hook-alike deviation, especially at high frequencies. This observed frequency dependence does not arise from the passive electrical properties of the measured biological tissue and must be considered a measurement artefact, which taints the EBIS measurement. Fitting EBIS data containing this artefact to the Cole model would produce an incorrect estimation of the Cole parameters, which would affect the estimation of the Cole parameters, mainly to the estimation of $R_\infty$ and $f_c$.

As a consequence of these data deviations, any subsequent analysis of the EBIS data based on the value of the Cole parameters would be tainted and would lead to incorrect conclusions. Because most of the applications of EBIS measurements are based on the use of the Cole parameters, the influence of such artefacts on the Cole parameter estimation process must be eliminated through correction, minimisation or avoidance.

Originally, this hook-alike deviation was attributed to time delays in the measured signals (De Lorenzo et al., 1997). In De Lorenzo’s work, the deviation is justified by a time delay ($T_d$), which is produced mainly by the length of the measurement leads and models other effects that might cause a linear phase shift with frequency. However, while differences in time delays only modify the phase, leaving the magnitude of the impedance unaltered, parasitic capacitances affect the whole complex EBI data. It is precisely the deviation observed in the modulus of the impedance measurement that indicates a capacitive leakage effect rather than a $T_d$ as the origin of the hook-alike deviation in EBIS measurements (Bolton et al., 1998; Scharfetter et al., 1998).

4.2 Capacitive leakage effect

Given the initial models of artefacts in EBI measurements proposed by Scharfetter (Scharfetter et al., 1998) and Bolton (Bolton et al., 1998) to the latest proposed by Mirtaheri (Mirtaheri et al., 2004) and then simplifying them, it is possible to obtain a simple electrical model equivalent (R Buendia et al., 2010) based on a parasitic capacitance. The obtained model is a current divider, and it is depicted in Figure 4.1.
The parasitic capacitance, $C_{par}$, expresses all the parasitic capacitances that create an alternative pathway for the current to leak away from the tissue. Therefore, the current flowing through the tissue is smaller than the reference measurement current, which produces an underestimate of the impedance of the tissue being measured ($Z_{TUS}(\omega)$). The admittance created by the capacitance decreases with frequency, and consequently, $I_{\text{leak}}$ increases with frequency, which accentuates the underestimation.

In Figure 4.2, the modulus and phase, as well as the resistance and reactance of the model in Figure 4.1, are shown. In the blue trace, the spectra of the impedance of the tissue are plotted. $Z_{TUS}$ is based on a Cole impedance built with Cole parameter extracted from a right side wrist-to-ankle measurement, the parameters value are: $R_0=450$ Ω, $R_\infty=297$, $f_c=30.2$ kHz and $\alpha=0.72$. In the red trace, it is possible to observe the spectra obtained when the impedance is estimated from the voltage created by the current divider between $Z_{TUS}(\omega)$ and a $C_{\text{par}}$ with a value of 50 pF.

![Figure 4.1 Capacitive leakage artefact model](image)

![Figure 4.2 Impedance spectra of the capacitive leakage artefact model presented in Figure 4.1, considering a parasitic capacitance of 50 pF: Modulus A), Phase B), Resistance C) and Reactance D).](image)
From Figure 4.2, it is evident that the capacitive leakage effect is much greater in the phase and the reactance than in the modulus and the resistance and increases, in every case, with frequency.

### 4.3 Artefact vulnerability of EBIS data obtained with textile-enabled instrumentation

The main limitation of textile electrodes is the risk of establishing a poor skin-textrode interface, which would generate a large $Z_{ep}$ that can accentuate the capacitive leakage effect or create electrode mismatch effects.

Because the capacitive leakage effect occurs because part of the injected current leaks away from the load due to the existence of alternative pathways, whether there is a large impedance in series with the measurement load, the alternative pathways are more attractive for the current to leak away, increasing the effect of capacitive leakage on the EBIS measurement.

The mismatch of electrodes occurs when there is a large difference between the $Z_{ep}$ of the electrodes used in the EBIS measurement. With electrodes that present very low $Z_{ep}$, the possibility of a noticeable mismatch is small because the difference between the minimum $Z_{ep}$ of one and the maximum $Z_{ep}$ of another electrode cannot be very large. With textrodes, the value for $Z_{ep}$ can be very high, especially when using dry electrodes. In this case, the probability of obtaining an electrode mismatch effect is larger. The mismatch effect produces data deviations that are very noticeable at high frequencies (Bogómez-Franco et al., 2009).

### 4.4 Robustness of the Fitting Process in the presence of Stray Capacitances

To overcome the effects of capacitive leakage on the spectra of EBIS measurements and to calculate a reliable estimate of the Cole parameters, Scharfetter et al. (1998) recommended avoiding the use of high frequency values for the curve fitting process by setting an upper limit of 500 kHz. Because the admittance of stray capacitances in parallel with the load increases with frequency, decreasing the upper frequency limit would improve the robustness of the Cole fitting approach.

In addition, because the phase and the reactance are significantly affected by capacitive leakage, avoiding any of these immittance magnitudes in the data would also significantly improve the robustness of the fitting process.

Often, EBI spectrometers present larger measurement error in the phase than in the module, and such errors in the phase increase with the measurement frequency; Ferreira et al. (2011) provide a practical example. This increase provides an additional reason to avoid the phase data in the Cole fitting approach.

The significant effect of stray capacitances on the phase and the reactance, especially at high frequencies, has a negative effect on the widespread EBIS data fit to a depressed circle in the impedance plane. As a result, the semicircular shape of the EBIS data in the impedance plane is not preserved. Therefore, when fitting the measurement to a circle, the accuracy of the fitting is
poorer, and the elevated reactance values cause the radius of the fitted circle to increase significantly. This increase in the radius makes the value of $R_\infty$ to decrease significantly, which leads to an inaccurate estimate of the value of the Cole parameter $\tau$. $\tau$ is usually calculated as the middle point of the circle, i.e., the point with the largest reactance. The value of $\tau$ can be determined by evaluating the distance of the cathetus of the triangle formed between the highest point of the reactance and both intersections of the circle with the resistance axis. The frequency of the value at which both distances are equal is the characteristic frequency. Additionally, an increase in the $R_0$-$R_\infty$ segment also contributes to an inaccurate estimate of the centre of the circle and the radius of the best-fit circle. These inaccurate estimations would most definitely contribute to an inaccurate estimate of the value of $\alpha$.

Any curve fitting process depends on the number of points to fit, the accuracy of the model and the reliability of the information contained in the measurement points. In EBIS, it is possible to obtain the 4 Cole parameters with just 4 measurement points. Ward et al (2004; 2006) suggested that using 16 frequency points to estimate the Cole parameters from EBIS would improve the results significantly. Therefore, decreasing the number of frequencies from the commonly used 50 or 256 may be not only possible but also beneficial, especially when the upper frequency limit is lowered as well.

### 4.5 Critique of Td Compensation

Currently, the most widespread approach to correcting deviations is the well known Td compensation postulated by De Lorenzo in 1997 (De Lorenzo et al., 1997). It has been widely used by the commercial EBI spectrometers manufactured by Xitron Technologies, Impedimed Ltd. and Fresenius Medical Care AG. The high frequency deviation is attenuated by multiplying the measured impedance $Z_{\text{meas}}(\omega)$ by an imaginary exponential factor, as shown in Equation 4.1.

$$Z_{\text{comp}}(\omega) = Z_{\text{meas}}(\omega) \cdot e^{-j\omega T_d} \quad \text{Equation 4.1}$$

However, as stated in (Bolton et al., 1998) “The observed phase shift with frequency or time delay (Td) used in the Xitron modelling software appears to be the result of a time constant caused by stray capacitance and so is unlikely to have any biological meaning.”

The $T_d$ compensation approach is also known as fitting to the Extended Cole Model, and it was introduced in this way by Scharfetter et al. in 1998 (Scharfetter et al., 1998). In their work, Scharfetter et al. validated the $T_d$ compensation approach with a model containing stray capacitances and producing a capacitive leakage effect. As a result, the EBIS data are fitted to the Cole model and are multiplied by the same factor as that in the $T_d$ compensation, $e^{-j\omega T_d}$; see Equation 4.2.

$$Z_{\text{meas}}(\omega) = Z_{\text{Cole}}(\omega) \cdot e^{-j\omega T_d} \quad \text{Equation 4.2}$$

It is evident from Equation 4.1 that because the exponential is just imaginary, the $T_d$ compensation approach only modifies the phase. Therefore, because the deviation occurs in both the module and the phase, the $T_d$ compensation approach can never properly address the observed deviation.
Moreover, the phase change introduced by the $T_d$ compensation is linear, while the deviation in the phase is not. Nevertheless, the phase compensation seems to be acceptable in most cases.

This approach is still in use because the capacitive leakage effect affects the phase much more than the magnitude. It might appear to be acceptable to compensate for the deviation, but underestimating the value of the modulus of the impedance at high frequencies leads to underestimating $R_\infty$, which leads to incorrect conclusions in posterior analysis, e.g., estimating the intracellular volume when assessing body composition.

More scientifically solid ways to overcome the hook-like deviation in EBIS measurements must be proposed as alternatives to $T_d$ compensation. In this thesis, three approaches to reliably obtain the Cole parameters from EBIS data contaminated with capacitive leakage effect are presented.
Chapter 5

Overcoming the Effect of Stray Capacitances

As indicated in the previous section, because $T_d$ Compensation is a limited approach, alternatives must be sought. Potential alternatives should focus on correcting, avoiding or minimising the influence of capacitive leakage on the measurement or the estimation of the Cole parameters.

5.1 Preprocessing the EBIS Tainted Data: Correction Function

The $C_{par}$ Correction approach identifies a capacitive behaviour from the susceptance of the measurement to estimate the value of $C_{par}$. Then, the influence of the capacitive leakage is removed from the measurement. In this approach, both the modulus and phase of the impedance are modified and corrected.

Considering the capacitive leakage model of section 4.2 in which the obtained $Z_{meas}(\omega)$ is the parallel of $Z_{TUS}(\omega)$ and the reactance of a parasitic capacitance $C_{par}$ and to remove the influence of $C_{par}$ from the EBIS measurement and obtain $Z_{Corr}(\omega)=Z_{TUS}(\omega)$ from $Z_{meas}(\omega)$, Equation 5.1 can be applied.

$$Z_{Corr}(\omega) = Z_{meas}(\omega) \cdot \frac{1}{1-z_{meas}(\omega) j \omega C_{par}} \quad \text{Equation 5.1}$$

Note that Equation 5.1 can be rewritten in exponential form to obtain a similar formula to that used in $T_d$ compensation; however, instead of using $T_d$ as a scalar, a complex function of frequency is used, i.e., the correction function. This function modifies both the modulus and phase of the impedance measurement to correct the deviation produced by the capacitive leakage. The correction function in Equation 5.2 is just used for explanatory comparison purposes because it resembles $T_d$ Compensation.

$$Z_{Corr}(\omega) = Z_{meas}(\omega) e^{-\log(1-z_{meas}(\omega)) j \omega C_{par}} \quad \text{Equation 5.2}$$

5.1.1 Parasitic Capacitance Estimation

The susceptance of Cole impedance increases with frequency until it reaches its maximum value. Then, it decreases with frequency and tends to null at infinite frequency. A $C_{par}$ in parallel with the measurement load, makes the susceptance of the measurement different than null at very high frequencies but equal to the susceptance created by a capacitance with the value $j \omega C_{par}$, see Figure 5.1. Thus, the susceptance value of the measurement increases linearly with frequency and has a slope equal to $C_{par}$. Therefore, by estimating the slope of the susceptance
from the EBIS measurements at frequency values at which the Cole susceptance can be neglected, the value of $C_{\text{par}}$ can be determined and applied in Equation 5.1. The correction method corrects the capacitive leakage effect in the EBIS measurement.

The accuracy of the $C_{\text{par}}$ estimate depends on the maximum frequency measured and the value of $C_{\text{par}}$; the estimate improves as both increase. Therefore, it may not be possible to accurately estimate small values of $C_{\text{par}}$ at typical frequency ranges in EBIS. Despite this limitation, the method is reliable because the capacitive leakage effect with small values of $C_{\text{par}}$ or at medium frequencies only slightly affects the measurement.

5.2 Bioconductance NLLS Fitting

Because only the susceptance contains the artefactual data caused by the capacitive leakage, by using the spectrum of the conductance to estimate the Cole parameters, the influence of the capacitive leakage can be avoided in the Cole parameter estimates.

By analysing the capacitive leakage model of Figure 4.1 in the admittance domain the model of Figure 5.2 is obtained. Equations 5.3-5.6 indicate that $C_{\text{par}}$ affects the susceptance of the EBIS measurement and leaves the conductance free from capacitive leakage, independent of the capacitance. Therefore, when the EBIS data is fit to the Cole model in the conductance, see Equation 5.6, the capacitive leakage effect is avoided.

$$Y_{\text{meas}} = Y_{\text{cole}} + jS_{\text{cpar}} \quad \text{Equation 5.3}$$

$$Y_{\text{meas}} = G_{\text{meas}} + jS_{\text{meas}} \quad \text{Equation 5.4}$$

$$Y_{\text{meas}} = G_{\text{cole}} + j(S_{\text{cole}} + S_{\text{cpar}}) \quad \text{Equation 5.5}$$
When $Z_{ep}$ has a high value, the capacitive leakage effect may also affect the conductance. In that case, this approach may not be accurate.

5.3 *Minimising the influence of stray capacitances in the Curve fitting process*

From the analysis of the robustness of the fitting process in the presence of stray capacitances, it is found that using the Modulus of the impedance or the resistance, which has a small contribution from the susceptance, reduces the influence of the data deviation in the curve fit. In addition, because the effect of the artefact remarkably increases with frequency, when the upper limit of the frequency range containing the EBIS data is reduced, the influence of the deviated data is further reduced.

This approach is valid independent of the value of $Z_{ep}$ and $C_{par}$; however, a small error may still exist.
Chapter 6

Experimental Validation

6.1 Correction Function Approach Validation

The correction function introduced in section 5.1 was applied for wrist-to-ankle RS, segmental arm and segmental trunk EBIS measurements, and the estimated $C_{par}$ had a mean of 0.94 pF and a SD of 1.9 pF; a mean of 120.29 pF and a SD of 1.9 pF; and a mean of 683.23 pF and a SD of 26.08 pF, respectively (Publication 1).

The EBIS measurements were performed with the SFB7 bioimpedance spectrometer manufactured by Impedimed Ltd. using repositionable Red Dot Ag/AgCl electrodes manufactured by 3M in the frequency range from 3.096 to 1000 kHz; 100 measurements were taken for each configuration.

An example of the performance of the correction is shown in Figure 6.1 for the segmental arm case.

The correction function was also applied on thoracic measurements taken with textile

![Graphs showing impedance, reactance, susceptance, and estimated capacitance results.]

Figure 6.1 Experimental results obtained from the segmental arm EBI measurements
electrodes integrated in a vest designed by Phillips Research Medical Signal Processing group as a part of MyHeart project (Habetha J, 2006). Most of the measurements considered in this project show the deviation introduced in section 4.1 (Publication 3).

In this paper, the estimates of the Cole parameters for the fit to the extended Cole model and the fit to the Cole model after applying the Correction Function are compared. The results are similar for both approaches, but the extended Cole model approach indicates a smaller value of deviation. While the estimates of $R_0$ and $R_\infty$ produce similar values in both approaches, the estimates of $f_c$ differ because the first fitting approach used the equation of a circle and therefore did not account for frequency information, while the second approach used the modulus of the Cole function to account for the frequency information.

Marquez et al. (2010) compared textile electrodes with red dot electrodes in wrist-to-ankle RS measurements performed on three healthy volunteers; the measurements with textile electrodes were corrected with the correction function.

6.2 Bioconductance fitting validation

The hypothesis that the measured conductance is free from the capacitive leakage effect was experimentally proven with synthetic data using the Cole impedance with modelled noise added. The experimental noise was extracted from wrist-to-ankle measurements, and it is characterised by determining the mean, standard deviation and spectral components (Publication 2).

NLLS fitting was applied to the Cole conductance and to a depressed semicircle. The conductance-based fitting produced the same results independent of $C_{par}$. Otherwise, the fit to a depressed circle is significantly affected by $C_{par}$, even though that 15 pF is a small value. Figure 6.2 is an example of the observed results.

![Impedance Plot]

Figure 6.2 Generated EBI data and the results from the performed curve fittings on the impedance plane and the conductance domain with and without a capacitance of 15 pF in parallel.
6.3 Modulus Fitting Validation

The Cole parameters obtained by fitting the EBIS data to the modulus of the impedance were calculated from wrist-to-ankle RS measurements. This Cole parameter estimation produced practically the same estimates of the BCA parameters as that obtained by applying the commercially available, widely used software *Bioimp*; see the correlation plots in Figure 6.3 (Publication 5).

![Figure 6.3 TBC Correlation results](image)

6.4 Influence of the Upper Limit and Number of Frequencies on the Cole Parameter Estimates

In Publication 4, it was shown that the number of frequencies and the upper limit of the maximum frequency used when fitting the data to the Cole function could be reduced significantly while producing accurate estimates of the Cole parameters. Reducing the maximum frequency from 1000 kHz to 256 kHz and then to 16 frequencies, produced a Mean Absolute Percentage Error (MAPE) smaller than 1% compared with the original Parameters. Synthetic data such as those introduced in section 6.2 were utilised.
Chapter 7

Discussion & Conclusions

7.1 Discussion

The $T_d$ compensation does not have sufficient scientific grounds to fully compensate for the measurement artefact created by stray capacitances. However, it has been widely used for more than a decade because capacitive leakage does not have a remarkable effect on the modulus of the impedance; moreover, $T_d$ compensation can effectively adjust the phase. However, $T_d$ compensation is linear with frequency, and the phase deviation caused by capacitive leakage is not linear; when the upper limit of the measurement is below 500 kHz, the obtained phase compensation is considered to be acceptable in most cases.

$C_{par}$ correction is proposed as a scientifically based approach that may fully correct the capacitive leakage effect in EBIS measurements. However, a limitation is found when estimating the value of $C_{par}$ from the susceptance of the measurement. When the value of the stray capacitance is very small, its contribution to the susceptance of the measurement is very small. Consequently, very high frequencies are required to obtain a reliable estimation of $C_{par}$ from the slope of measured susceptance. Moreover, in this work, the potential influence of $Z_{ep}$ has been disregarded.

Performing the fitting in the conductance spectrum may be a promising way to avoid the influence of capacitive leakage on the estimates of the Cole parameters. However, its robustness to capacitive leakage in cases with large $Z_{ep}$ has not been fully investigated.

Reducing the upper frequency limit and the number of frequencies seems to be a valid option to improve the accuracy of the Cole parameter estimates. From the theory and simulations with synthetic data in wrist-to-ankle RS measurements, the limits of 250 kHz and 16 frequencies seems to be sufficient. However, the effect of the upper limit and the number of frequencies on the Cole parameters estimation should be validated with many experimental measurements.

Currently, fitting the EBIS data to a depressed semicircle is a wide spread approach to estimating the Cole parameters. This fitting approach is vulnerable to the effect of capacitive leakage artefacts because the tainted EBIS data no longer resemble a semicircle. Because the artefact has a quasi-negligible effect on the resistance and modulus of the impedance, NLLS curve fittings performed on the resistance or modulus should be much more robust to the capacitive leakage effect, which has been proven experimentally.

Reducing the upper frequency limit and the amount of frequencies can be an accurate method for estimating the Cole parameters, and it is an approach compatible with NLLS curve fittings to the resistance or modulus of the impedance spectra, as well as to the conductance spectrum in the admittance domain.
The most appropriate practice may be to perform NLLS fitting on a reduced conductance spectrum. Reducing the upper limit and, only in the case of a non-noisy signal, the number of frequencies; in the presence of noise, it is important to have more measurements because some of them will have to be neglected.

In applications in which a very high $f_c$ can be found, such as brain impedance, the upper limit cannot be reduced because the frequencies around $f_c$ have the most information. In these cases, fitting the whole spectrum of the conductance may be the best option.

When using an EBIS measurement device that does not provide phase measurements or presents a significant error in the phase, NLLS fitting can be performed in a reduced modulus spectrum instead of the conductance spectrum.

When spectral analysis of the EBIS measurement without Cole modelling is required, function correction is the only valid approach among those proposed in this thesis.

The dry interface of a textrode may produce larger $Z_{ep}$ than gel electrodes, which would create or worsen the influence of measurement artefacts. In addition, the potentially large difference in the value of $Z_{ep}$ makes textile-enabled EBIS measurements vulnerable to electrode mismatch. This effect should be studied in depth. Nevertheless, because textrodes fabrics allow the implementation of measurement garments, it is possible, with the help of more ergonomic designs, to implement textrodes with very large contact area. A large contact area improves the skin-electrode interface and, therefore, minimises the presence of artefacts in the measurements.

EBIS measurements obtained with textile-enabled instrumentation are often tainted by the effect of stray capacitances. The different approaches presented in this work may significantly improve the reliability of the Cole parameter estimates and, consequently, improve any subsequent analysis from tainted EBIS measurements.

### 7.2 Future work

When analysing the capacitive leakage effect in EBIS data, it is usually possible to neglect the influence of $Z_{ep}$. However, when approaching measurements obtained from textiles, it may be convenient to take it in account because $Z_{ep}$ may have a large value. The measurement model including $Z_{ep}$ can be observed in Figure 7.1, and its mathematical expression is given in Equation 7.1. The model has an equivalent impedance to that introduced by Mirtaheri (Mirtaheri et al., 2004), which was originally proposed as admittance. Taking into account $Z_{ep}$ would affect the $C_{par}$ correction approach as well as the conductance fitting approach.

$$Z_{meas}(\omega) = \frac{Z_{tus}}{1+j\omega C_{par}(Z_{tus}+Z_{ep})}$$

Equation 7.1

The effect of frequency reduction in the fitting process to estimate the Cole parameters should be validated with many experimental EBIS measurements.

Additionally, the dependency of electrode mismatch and textile electrodes should be studied in depth. Specific experimental tests should be implemented, and a deep analytical study should be performed to determine the exact source of the measurement artefacts.
A large validation of all the approaches on experimental measurements of TBC with reference BCA parameters would be an appropriate step to further this line of research. The BCA parameters obtained by reference methods such as DEXA or dilution methods together with EBIS measurements could be used to verify most of the methods presented in this work. This verification is currently in progress.

7.3 Conclusions

In this thesis, methods for improving robustness to measurement artefacts emanating from capacitances have been presented and validated with synthetic EBIS data and experimental measurements.

These methods can be combined, and the best combinations, depending on the circumstances, have been discussed.

In the course of this study, several new research questions have arisen, and there is also a general need for method verification with large data sets of experimental measurements. New studies targeting these new research issues, as well as method verification on a set of hundreds of EBIS measurements with reference BCA parameters, are scheduled for 2012.

![Figure 7.1 Capacitive leakage effect model accounting with Z_{ep}](image)

Figure 7.1 Capacitive leakage effect model accounting with $Z_{ep}$
REFERENCES


SUMMARY OF APPENDED PAPERS

Paper 1


In this paper, the deviation of the EBI spectrum described was introduced in addition to the capacitive leakage effect, including the current divider model with a parasitic capacitance in parallel with the load. Subsequently, the Td compensation method was revisited, and the Correction Function, including the approach used to estimate the parasitic capacitance, was proposed. Finally, the Correction Function was validated on wrist-to-ankle, segmental arm and segmental trunk experimental measurements.

Paper 2


In this paper, the NLLS fitting performed on the conductance of EBIS measurements was proposed. The hypothesis that the bioconductance is free from the capacitive leakage effect was proven with synthetic data using the Cole impedance with added modelled noise. Estimating the Cole parameters from the conductance was also found to be feasible.

Paper 3


In this paper, the need of to overcome the capacitive leakage effect was demonstrated. EBIS measurements contained in the MyHeart project were utilised. These measurements were obtained with a wearable measurement system integrated in a vest. Most of the measurements exhibit the deviation of the EBI spectrum. In this paper, the Cole parameter estimates from the fitting to the extended Cole model and the fitting to the Cole model after applying the Correction Function were compared.

Paper 4


In this paper, the NLLS fitting was performed after reducing the upper frequency and the number of frequencies. It was shown how significantly reducing the number of frequencies and the upper limit the error obtained was non-significant.
**Paper 5**


In this paper, the BCA parameters obtained from Cole parameters that were calculated with 2 approaches, circular fitting on the impedance plane and NLLS modulus fitting, were compared. The feasibility of the NLLS modulus fitting was proven. In addition, the drawbacks of circular fitting were introduced.