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Cole Equation and Parameter Estimation from Electrical Bioimpedance Spectroscopy Measurements - A Comparative Study

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***Abstract*— Since there are several applications of Electrical Bioimpedance (EBI) that use the Cole parameters as base of the analysis, to fit EBI measured data onto the Cole equation is a very common practice within Multifrequency-EBI and spectroscopy. The aim of this paper is to compare different fitting methods for EBI data in order to evaluate their suitability to fit the Cole equation and estimate the Cole parameters. Three of the studied fittings are based on the use of Non-Linear Least Squares on the Cole model, one using the real part only, a second using the imaginary part and the third using the complex impedance. Furthermore, a novel fitting method done on the Impedance plane, without using any frequency information has been implemented and included in the comparison. Results show that the four methods perform relatively well but the best fitting in terms of Standard Error of Estimate is the fitting obtained from the resistance only. The results support the possibility of measuring only the resistive part of the bioimpedance to accurately fit Cole equation and estimate the Cole parameters, with entailed advantages.**

I. Introduction

During the last decades the applications of measurements of Electrical Bioimpedance (EBI) to assess on tissue contents or tissue status have proliferated, especially applying Multi-Frequency analysis known as (MF-EBI) and spectroscopy known as EBIS.

From the initial application of EBIS to body composition already in 1992 [1], the use of EBIS has proliferated to the application areas of tissue characterization like skin cancer detection [2].

Fitting the EBI measured data to the Cole equation is a very common practice within MF-EBI and EBIS, well for data visualization through the Cole plot or for data analysis through the Cole parameters [3].

In this work two different approaches for Cole fitting are tested. The performance and wellness of the fitting in both the frequency and the impedance domain are compared. In the case of the frequency domain, the performance of the model fitting is studied and compared for the cases when the fitting is done from complex EBI data or the fitting is done only on resistance or reactance.

II. Methods

EBI data has been obtained from a biological-based Cole model with added measurement noise. Different Cole fitting methods have been applied on the EBI data, and the obtained performance to fit the curve and to recover the original Cole parameters have been studied in terms of Standard Error of Estimate (SEE).

A. Cole Equation

In 1940 Cole [4], introduced a mathematical equation that fitted the experimentally obtained EBI measurements (1). This equation is not only commonly used to represent but also to analyze the EBI data. The analysis is based on the four parameters contained in the Cole equation R_0, R_∞, α and τ, **i.e.** the inverse of characteristic frequency ω_C.

$$Z(\omega) = R_\infty + \frac{R_0 - R_\infty}{1+(j\omega\tau)^\alpha} \tag{1}$$

The value generated by the Cole equation is a complex value, the impedance, with a non-linear relationship with the frequency that generates in the impedance plane a suppressed semi-circle. Through the relationship in (2) it is possible to decompose Z in (1) into resistance R and reactance X, in (3) and (4) respectively.

$$j^\alpha = \cos(\alpha\pi/2) + j\sin(\alpha\pi/2) \tag{2}$$

$$R(\omega) = R\infty + \frac{(R_0 - R\infty)\left(1+(\omega\tau)^\alpha \cos(\alpha\frac{\pi}{2})\right)}{1+2(\omega\tau)^\alpha\cos(\alpha\frac{\pi}{2})+(\omega\tau)^{2\alpha}} \tag{3}$$

$$X(\omega) = -j\frac{(R_0 - R\infty)(\omega\tau)^\alpha \sin(\alpha\frac{\pi}{2})}{1+2(\omega\tau)^\alpha\cos(\alpha\frac{\pi}{2})+(\omega\tau)^{2\alpha}} \tag{4}$$

B. Non-Linear Least Squares Fitting

This method obtains the best coefficients for a given model that fits the curve, the method aims to minimize the summed squared of the error between the data point and the fitted model (5).

$$\min\sum_{i=1}^{N} e_i^2 = \min\sum_{i=1}^{N}(y_i - \bar{y}_i)^2 \tag{5}$$

where N is the number of data points included in the fit.

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This method can be implemented in Matlab® with the function *fit* that provides an estimation of one curve that fits a given measurement as input data, to a non-linear real parametric model with coefficients. The *fit* function has been evaluated with three different models, $R(\omega)$, $jX(\omega)$ and $R(\omega) + jX(\omega)$, according to (3) and (4), using the natural frequency ω as independent variable for estimating the Cole parameters as the model coefficients.

C. Impedance Plane Fitting

Another possibility to estimate the Cole parameters is by fitting the EBI data to the Cole plot in the impedance plane [5].

Since the Cole plot is a perfect semicircle with the centre depressed below the resistance axis, a novel method that estimates the complex centre and radius of the Cole plot is introduced. The methods is based in the fact that from a circular shaped set of points it is possible to obtain the value of the centre of that circle so that the variance of its squared distance to each point is minimum. See Appendix.

D. Cole Fitting and Error Analysis

According to the approaches previously described, four different methods for curve fitting have been employed to estimate R_0, R_∞, α and τ. Three of the curve fittings have been done in the frequency domain and another in the impedance plane.

The goodness of the fitting for the different methods has been assessed by studying the SEE on the following estimations: $R(\omega)$, $jX(\omega)$, $|Z(\omega)|$ and the Cole plot in the impedance plane. For the fitting done in the frequency domain, the SEE has been calculated as follows in (6), and (7) has been used to calculate the SEE obtained when fitting the Cole plot.

$$SEE_M = \sqrt{\frac{\sum\left((M-\overline{M})\right)^2}{N}} \tag{6}$$

where N is the number of estimations and M is the magnitude under study i.e. $R(\omega)$, $jX(\omega)$ *and module of* $Z(\omega)$.

$$SEE_Z = \sqrt{\frac{\sum\left(R-\overline{R}\right)^2}{N}} + \sqrt{\frac{\sum\left(X-\overline{X}\right)^2}{N}} \tag{7}$$

E. EBI data generation

To simulate the data, a Cole equation extracted from a wrist-to-ankle 4-electrode EBI measurement has been used with the following Cole parameter values: $R_0 = 750$, $R_\infty = 560$, $\alpha = 0.68$ and $\tau = 3.55\text{e-}6$. The impedance spectrum has been created with values of frequency spaced logarithmically as suggested in [6].

F. Noise model

Measurement noise has been characterized by mean, Standard Deviation and spectral components obtained from 100 measurements of complex EBI from the wrist-to-ankle. The measurements were performed with the 4-electrode method and the use of the SFB7 impedance spectrometer manufactured by Impedimed. The experimentally estimated noise has been added to the simulated EBI data.

III. Results

A. Frequency based estimation

Table 1 contains the Standard Error of Estimate and Fig. 1 the obtained fitting for each estimation and method.

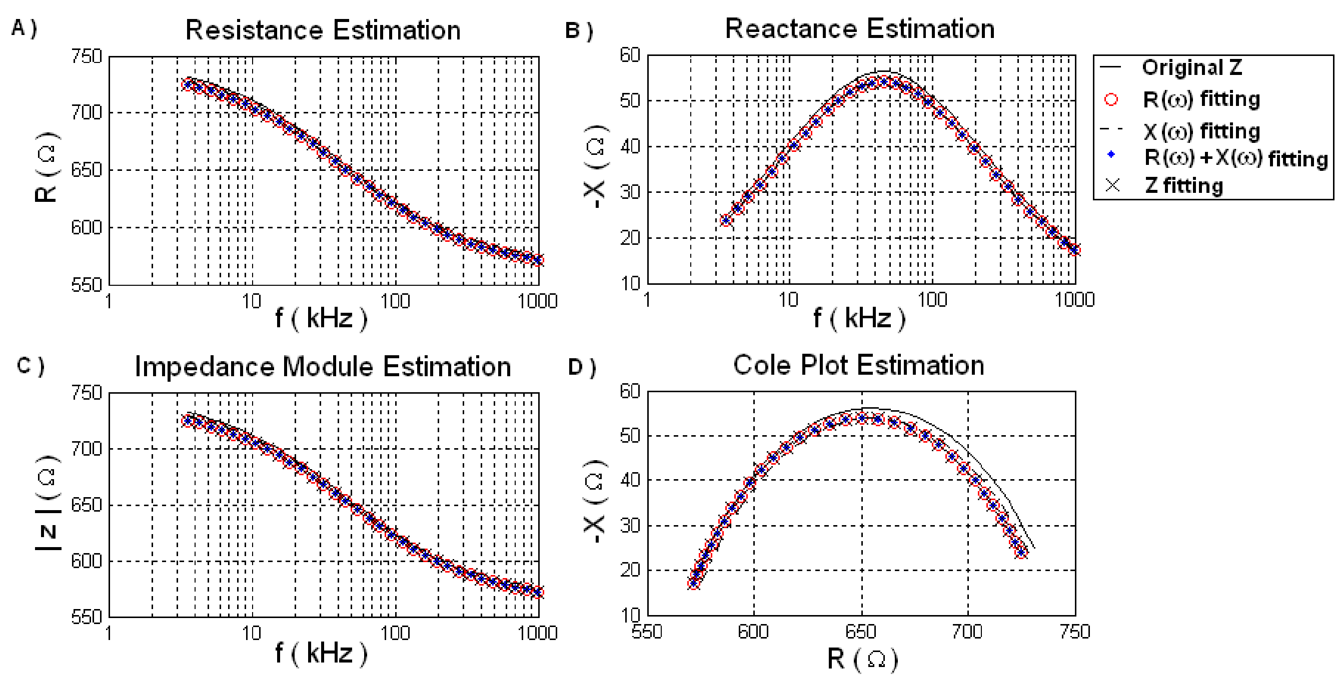

Fig. 1.Curve fitting for each of the estimations $R(\omega)$, $jX(\omega)$, $|Z(\omega)|$and the Cole Plot in A), B), C), D) respectively for each of the four fittings compared with the original curve labeled Original Z. Each fitted curve contains values obtained from the average value from 100 performed fitting.

TABLE I
STANDARD ERROR OF ESTIMATE (SSE) FOR THE CURVE FITTING OF THE RESISTANCE, REACTANCE, IMPEDANCE MODULE AND COLE PLOT FROM *R(W)* ,*X(W)*, *R(W)+jX(W)* & Z PLANE

	$R(\omega)$	$X(\omega)$	$R(\omega)+jX(\omega)$	*Z plane*
SEE_R	0.117	3.570	0.153	0.152
SEE_X	0.151	0.120	0.153	0.129
$SEE_{\|Z\|}$	0.117	3.562	0.150	0.153
$SEE_{\text{Cole Plot}}$	0.191	3.572	0.217	0.200

From them it is possible to observe that the best fitting for the resistance spectrum and the impedance module, $|Z(\omega)|$ is obtained from $R(\omega)$, see Fig 1.A) and Fig 1.C) respectively, while the best fitting for the reactance spectrum is obtained from $X(\omega)$, see Fig 2.B).

The fitting method using $X(\omega)$ performs very badly for all fittings except for the estimation of the reactance spectrum, see Fig1. A), C) & D). When using $R(\omega)$ *or* $R(\omega) + jX(\omega)$, the fitting method performs very well for all the fittings; including the Cole Plot fitting, see Fig 1.A), B), C) & D). However, using $R(\omega)$ for the fitting of the of reactance spectrum and the Cole fitting, the error is lower.

B. *Impedance Plane estimation*

According to Table 1 and Fig.1, this method obtains the best estimation when fitting the reactance spectrum and produces the second best fitting of the Cole plot, while for the impedance module $|Z(\omega)|$ and the resistance spectrum the obtained fittings provide slightly larger values of SSE than the best obtained curve fittings.

C. *Cole Parameters*

Fig. 2 shows that all the fitting methods provide very good estimations for the Cole parameters. Nevertheless, the estimations of f_C, for $R(\omega)$ and $R(\omega) + jX(\omega)$ see Fig 2.C), present a slightly higher dispersion of values

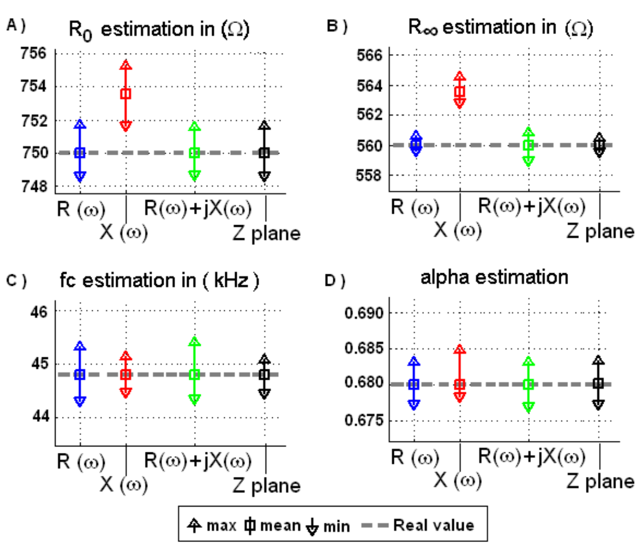

Fig. 2. Cole parameters estimation from the 4 different performed curve fittings.

that results in a maximum deviation slightly over 1%.

From Fig. 2.A) & B) is possible observe that the estimation done from $X(\omega)$ for R_0 and R_∞ is slightly worse than for the rest. However the maximum observed deviations are still below 0.8%.

IV. DISCUSSION

All the methods performed relatively well for all the curve fittings with the exception of the Non-Linear Least Square (NLLS) method using $X(\omega)$, which performs the best curve fitting for the reactance spectrum, as it could be expected, but produces a relatively large SEE for all the rest of curve fittings.

The slightly lower performance exhibited by the NLLS method when using $X(\omega)$ influences in the ability of the method to estimate the Cole parameters R_0 and R_∞. Nevertheless the observed differences are exceptionally small.

The exceptional performance of the NLLS method to fit each curve from the corresponding source is should not be a surprise due to the non-linear nature of the three models $R(\omega)$, $jX(\omega)$ and $R(\omega) + jX(\omega)$.

What is more surprising is the observed good performance of the proposed method of fitting a circle to the Cole plot, besides not making use of the frequency. This relatively good performance is unexpected, especially for the estimation of f_C, since we expected that neglecting the frequency information would have more remarkable negative impact on the curve fitting as well as on the estimation of the characteristic frequency.

The observed relatively good performance of both approaches might be due to the level of noise used in the fitting. Despite that the noise was modeled from experimental measurements, the obtained noise level was very low. In order to fully evaluate the performance of the methods a noise sensitivity test should be performed.

To space the frequencies logarithmically might help to improve the curve fitting as well [6] but this may hold only for measurement with the characteristic frequency in the lower part of the frequency scale.

The distribution of the measurement frequencies and in combination with the curve fitting method might have a strong influence on the performance of the curve fitting. To study such relationship is important in order to fully understand the factors influencing the performance of methods for fitting the Cole equation.

V. CONCLUSION

In general, all the studied methods perform relatively well, but the NLLS method using $R(\omega)$ exhibits a superior performance. Performing measurements of resistance is quite different than performing measurements of complex impedance and it has important repercussions, especially in the electronic instrumentation of the measurement system. To be able to estimate accurately the full Cole equation from only resistance measurements would influence significantly several applications of MF-EBI and EBIS that are based on the proper estimation of the Cole parameters, like body composition assessment [7, 8].

Since the answer to the question of how many frequencies to use in MF-EBI has been answered by ward and Cornish [9] and in theory a Cole fitting only requires 4 measurement points. We intend to investigate further the effect of noise and the frequency scaling on the performance of the fitting methods presented in this paper not only to fully validate the NLLS on $R(\omega)$ method but also to find which is the best distribution of frequencies for measuring EBI. We also aim to increase the generalization of future results by increasing the number Cole models used for the fittings with more application-based models like impedance cardiography, respiration rate or skin cancer detection.

APPENDIX

Let us assume we have N complex points:

$$Z_n = X_n + jY_n,\ n = 1,\cdots,N \tag{A.1}$$

The distance R_n from the centre $C = x + jy$ to the impedance $Z_n = X_n + jY_n$ is expressed as:

$$R_n{}^2 = \left|C - Z_n\right|^2 = (x - X_n)^2 + (y - Y_n)^2 \tag{A.2}$$

The objective is to find x and y so that the variance of R_n is minimum. It can be demonstrated that the variance is:

$$Var\left\{R_n{}^2\right\} = \frac{1}{N}\sum_{n=1}^{N}\left(R_n{}^2 - \frac{1}{N}\sum_{m=1}^{N}R_m{}^2\right)^2 \tag{A.3}$$

So differentiating the variance with respect to x and y, equalling both expressions to zero and solving the system of equations, the centre of the Cole curve is obtained:

$$\begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} 2\sum_{n=1}^{N} Xc_n{}^2 & 2\sum_{n=1}^{N} Xc_n Yc_n \\ 2\sum_{n=1}^{N} Xc_n Yc_n & 2\sum_{n=1}^{N} Yc_n{}^2 \end{pmatrix}^{-1} \begin{pmatrix} \sum_{n=1}^{N}\left(X2c_n + Y2c_n\right)Xc_n \\ \sum_{n=1}^{N}\left(X2c_n + Y2c_n\right)Yc_n \end{pmatrix} \tag{A.4}$$

where

$$Xc_n = X_n - \frac{1}{N}\sum_{n=1}^{N}X_n \quad \text{(A.5)} \qquad Yc_n = Y_n - \frac{1}{N}\sum_{n=1}^{N}Y_n \quad \text{(A.6)}$$

and

$$X2c_n = X_n{}^2 - \frac{1}{N}\sum_{n=1}^{N}X_n{}^2 \quad \text{(A.7)} \qquad Y2c_n = Y_n{}^2 - \frac{1}{N}\sum_{n=1}^{N}Y_n{}^2 \quad \text{(A.8)}$$

From the Cole equation is deduced that the centre of the circle and the radius are

$$\Re\{C\} = \frac{R_0 + R_\infty}{2} \quad \text{(A.9)} \qquad \Im\{C\} = \frac{R_0 - R_\infty}{2}\frac{\cos(\alpha\pi/2)}{\sin(\alpha\pi/2)} \quad \text{(A.10)}$$

$$R = \frac{R_0 - R_\infty}{2\sin(\alpha\pi/2)} \tag{A.11}$$

From the last result and combining with (3) and (4), R_0 and R_∞ are estimated as

$$R_\infty = \Re\{C\} - \sqrt{R^2 - \Im\{C\}^2} \tag{A.12}$$

$$R_0 = \Re\{C\} + \sqrt{R^2 - \Im\{C\}^2} \tag{A.13}$$

α can be obtained from the slope that $C - R_\infty$ has $\forall\ \alpha \le 1$

$$\alpha = 1 \pm \frac{2}{\pi}\phi\{C - R_\infty\}$$

$$\Rightarrow \alpha = 1 \pm \frac{2}{\pi}\arctan\left\{\left(\sqrt{\left(\frac{R}{\Im\{C\}}\right)^2 - 1}\right)^{-1/2}\right\} \tag{A.14}$$

From alpha and solving directly the Cole equation for τ the value of f_C can be estimated.

REFERENCES

[1] J. R. Matthie, P. O. Withers, et al., "Development of a commercial complex bio-impedance spectroscopic (CBIS) system for determining intracellular water (ICW) and extracellular water (ECW) volumes," in Proceedings of 8th International Conference on Electrical Bio-impedance, Kuopio, Finland, University of Kuopio,, 1992, pp. 203–205.

[2] P. Aberg, I. Nicander, et al., "Skin cancer identification using multifrequency electrical impedance – A potential screening tool," IEEE Trans. Bio. Med. Eng., vol. 51, pp. 2097-2102, 2004.

[3] R. Gudivaka, D. A. Schoeller, et al., "Single- and multifrequency models for bioelectrical impedance analysis of body water compartments," J Appl Physiol, vol. 87, pp. 1087-96, Sep 1999.

[4] K. S. Cole, "Permeability and impermeability of cell membranes for ions.," Quant. Biol., vol. 8, pp. 110–122, 1940.

[5] B. H. Cornish, B. J. Thomas, and L. C. Ward, "Improved prediction of extracellular and total body water using impedance loci generated by multiple frequency bioelectrical impedance analysis," Phys. Med. Biol., vol. 38, pp. 337-346, 1993.

[6] A. De Lorenzo, A. Andreoli, et al., "Predicting body cell mass with bioimpedance by using theoretical methods: a technological review," J Appl Physiol, vol. 82, pp. 1542-58, May 1997.

[7] U. G. Kyle, I. Bosaeus, et al., "Bioelectrical impedance analysis--part I: review of principles and methods," Clin Nutr, vol. 23, pp. 1226-43, Oct 2004.

[8] U. G. Kyle, I. Bosaeus, et al., "Bioelectrical impedance analysis-part II: utilization in clinical practice," Clin Nutr, vol. 23, pp. 1430-53, Dec 2004.

[9] L. C. Ward and B. H. Cornish, "Multiple Frequency Bielectrical Impedance Analysis how many Frequencies to use?," in XII ICEBI Conference, Gdansk, Poland, 2004, pp. 321-324.