Iterative method to obtain semi-circle variables from bioimpedance measurements for Cole's Modeling

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Abstract— **Bioimpedance Spectroscopy measurements and Cole-Cole models are commonly used to characterize biological systems. Cole-Cole model parameters may be obtained by fitting the measured bioimpedance data into a semicircle. This work proposes an iterative method to approximate a bioimpedance dataset to a Cole-Cole model analysis using only three points. The performance of the proposed method was compared against similar methods reported in a recent publication; our proposal presents greater efficiency (87.5%) and lower mean error (0.022) than the compared methods. The main contribution of the proposed method is that its performance does not rely on the user's technical knowledge, neither does it on the instrument used to perform the measurements, while the compared methods do.**

Clinical Relevance— **Our proposal is an efficient unsupervised iterative method to acquire the clinically-relevant parameters from a Cole-Cole analysis from a given bioimpedance spectroscopy dataset, eliminating the need for the user to have prior technical knowledge on bioimpedance, thus, furthering the use of bioimpedance technology in the clinical point-of-care.**

I.   INTRODUCTION

Bioimpedance is a physical parameter that quantifies the opposition that biological systems present to the flow of an alternating electrical current. This parameter allows the analysis of the electrical properties of a given biological system; common applications are in human beings [1], food [2] and agriculture [3]. In the biomedical field, it is applied to diagnose in a wide variety of systems such as respiratory [4], cardiac [5], metabolic [1], among others. Bioimpedance is frequency-dependent, meaning that each bioimpedance value corresponds to the frequency of the electrical signal applied to obtain the measurement. Each measure is expressed in a numeric complex value, therefore it has a binomial form (real and imaginary parts) and polar form (modulus and phase).

Bioimpedance applications are in the scope of interest of a variety of professionals like medics, physiatrists, engineers and physicists. As a consequence, the focus of each analysis is biased by the training of each specialist. However, there are commonly used models as the ones proposed by Fricke, Debye and Cole [6]. Moreover, since bioimpedance is about electrical impedance, analysis tools are taken from traditional circuit analysis such as the Nyquist diagram and Bode diagrams. One of the most used applications in the medical field is the

Bioelectrical Impedance Vector Analysis (BIVA), due to its easiness in the reading of the results for nontechnical users, because it considers the state of the patient from the modulus and phase of the bioimpedance phasor, as shown in Figure 1.

A common measurement used to characterize a biological system is bioimpedance spectroscopy, where bioimpedance measurements are taken in a defined range of frequencies and an impedance spectrum is constructed in the domain of the frequency. One way to represent these bioimpedance measurements is the complex plane in binomial form describing a flattened semicircle (see Figure 2).
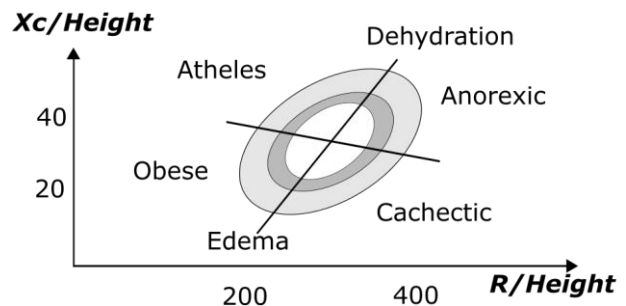

Figure 1. BIVA plot. The vector resulting from the bioimpedance measurement is located on a quadrant that defines the condition of the measured patient.

The Cole-Cole model [7] describes the electrical properties of this system with an equivalent circuit of three elements mathematically modeled by Equation (1). This model goes along with the Cole-Cole diagram [6], as seen in Figure 2.

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

From this diagram different parameters that characterize the biological system are obtained -the variables in Equation (1)- the resistance at zero frequency R_0, the resistance at infinite frequency R_∞, the theoretical constant α, and the time constant τ. From these parameters, the value of the critical frequency f_c , which is the frequency at which the reactance is the lowest (see Figure 2), can be obtained by calculating the inverse of the product of 2, π, and τ.

From a geometric and algebraic point of view, if 3 non-aligned points are given, represented as pairs of coordinates, from equation (2) a system of linear equations can be built to

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obtain the coordinates of the center (x_o, y_o) and the radius, R, of the circumference to which
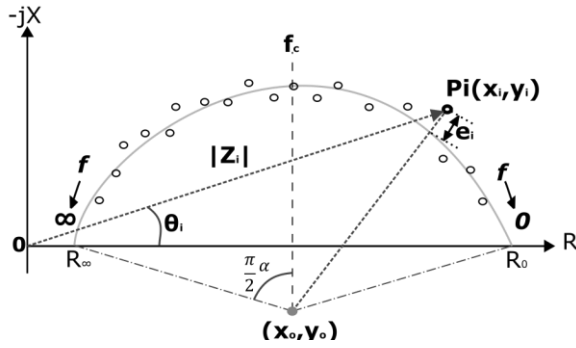

Figure 2. Cole Cole Plot. Empty circles represent bioimpedance measurement. $|Z_i|$ and Θ_i are module and phase and (x_i, y_i) are coordinates corresponds with the point Pi. Difference e_i is the error between Pi and represented semi circumference.

they belong. If this process is applied on a bioimpedance frequency sweep, a semicircle that models the variables in Cole's equation (1) can be obtained as well as the parameters of interest related to the biological system.

$$(x-x_o)^2 + (y-y_o)^2 = R^2 \qquad (2)$$

With the goal of providing a bioimpedance measurements analysis that offers the same ease in parameter reading for non-technical users as the BIVA, the present work proposes an iterative algorithm that takes bioimpedance measurements resulting from a frequency sweep as input and returns the characteristic Cole-Cole parameters of the processed measurements as output by generating a semicircle that represents the measurements with the lowest error. The aim of this work is to compare our proposed iterative method to those reported by González-Correa (international benchmark in the area of bioimpedance in medicine) in [8].

II. MATERIALS AND METHODS

A. Iterative method

The iterative algorithm was developed entirely in Python, making use of the data analysis library named Pandas and the scientific computing library Numpy. In summary the algorithm is as follows: (I) parsing dataset from file; (II) selection of all possible combinations of three points without repetition; (III) generate a circumference for each three points; (IV) calculation of the normal error of all points from the dataset in relation with the generated semicircle; (V) select the best circumference; and, (VI) calculation of the Cole-Cole model parameters.

I. Data is first loaded with the original format. Then it is parsed using a function from Pandas library to load into memory as a Numpy array with just the necessary columns for this work (Frequency, Imaginary part and Real part).

II. All possible combinations of point trios are generated using a nested triple for loop: the first one iterates over the n points, the second iterates over n-1 points and the third loop iterates over n-2 points. For each point trio steps (III), (IV) and (V) algorithms are executed.

At each iteration of the nested triple loop:

III. The point trio generated is used to build a square 3x3 matrix containing x_i, y_i, and 1 in its rows and a vector column with values $-(x_i^2 + y_i^2)$. Using the Numpy library functions, the linear system is solved and the semicircle containing the point trio center (x_o, y_o) and radius (R) are obtained. In case of throwing a singularity exception, those three points are discarded.

IV. Once the semicircle variables are obtained $(x_o, y_o$ and R), the distance between each point in the dataset and the center (C) coordinates is calculated as well as the respective error to all the dataset according to Equation (3), which represents the difference between each point of the dataset P_i and the semicircle arch as shown in Figure 2.

The error generated is normalized by dividing it by R to make it independent from the characteristic magnitudes of the measurements, then it is associated with each point trio. We will call this normal error.

$$normal\ error = \frac{1}{n}\sum_{i=0}^{n}\left|\frac{|P_i - C| - R}{R}\right| = \sum_{i=0}^{n}\left|\frac{e_i}{R}\right| \qquad (3)$$

V. If the generated circumference is the first one or its associated error is less than the already chosen as best circumference fit error, then it is set as the best circumference fit for this dataset.

VI. Once the best circumference is defined, the Cole-Cole model parameters, that intrinsically describe the bioimpedance measurements, are calculated according to Yuxiang Tang et al. [9].

B. Verification test

González-Correa [8] proposes 9 models using a dataset from DeLorenzo [10]. In each model, the author chooses 3 points to calculate the semicircle using commercial software (Wolfram Alpha©). Some models consisted in choosing three points in the low (model 2), medium (model 3) and high (model 4) frequency range. Other models choose the extreme values of the frequency spectrum (lowest and highest frequencies) and some intermediate point (in model 7 the midpoint of the entire spectrum and in model 8 the critical frequency). In the rest, the author heuristically averages points or combines his own models based on his experienced judgement. Our verification test consisted in inputting the author chosen points into our own algorithm and that of Wolfram Alpha© in order to evaluate and compare the traceability of the coordinates of the center and the radius obtained from each model.

C. Efficiency test

In order to compare the models proposed by González-Correa to our iterative algorithm proposal, the efficiency of each model was determined using the normal fitting error as the figure of merit. 128 bioimpedance measurement datasets were considered. The data used for the efficiency test were acquired using a commercial instrument (Solartron© 1287/1260) configured as frequency sweep over a biological phantom built of Agar-Agar with physiological solution and a bovine bone. A total of 126 different bioimpedance datasets with frequencies ranging from 1 Hz to 64 kHz were considered for this work, measurements were performed with different electrode's positions, thus in different sections of the phantom.

A detailed description of the measurement set-up is reported in a previous publication [11]. In addition, the 2 remaining bioimpedance datasets used in this work were taken from DeLorenzo (1 to 1248 kHz frequency range) and the subset of data selected by Gonzalez-Correa (1 to 500 kHz frequency range). Model 1 proposed by González-Correa was not implemented since it uses defined frequency points whose value was not exactly met by the Solartron© 1287/1260 (frequencies of 2, 20 and 200 kHz). For models 2 to 9, the frequency values where the points are chosen are not defined by the exact frequency value but for its relative position in the frequency range (e.g., the three lowest frequencies or the three highest frequencies), thus, it was possible to meet the point-choosing criteria. A total of 9 models (models 2 to 9 proposed by González-Correa and the one proposed in this work) were implemented using the 128 datasets to obtain the best semicircle that crosses the bioimpedance datapoints. The normal error of each model was calculated.

III. RESULTS

For the verification test, the Bland Altman graphic analysis was applied, in which the data obtained by our method and the Wolfram Alpha application for the point trios and for each model presented by Gonzalez-Correa [8] was processed. Figure 3 shows the graphs of the Bland Altman [12] analysis where all the parameters calculated by both methods fall within the 95% confidence interval.
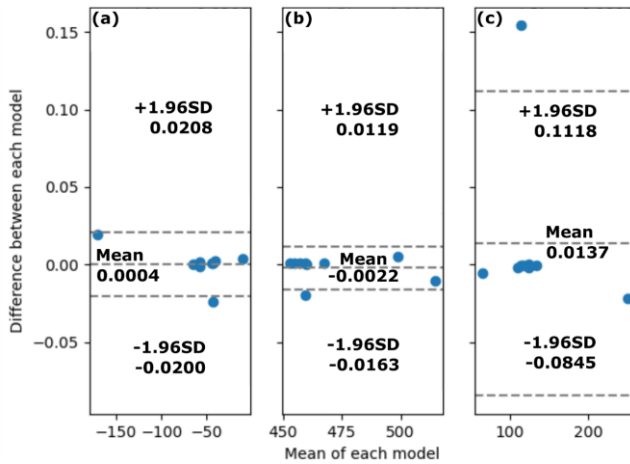

Figure 3. Bland Altman plots: (a) x_o, (b) y_o and (c) radius. Each circular point represents comparative analysis for each point trio for each model result between the iterative method and Wolfram Alpha resolution. Limit of interval is defined by +1.96SD and -1.96SD.

The efficiency test results show that in 87.5% of the total of cases, the proposed iterative method has the lowest associated normal error, model 3 reached 7.04%, model 7: 2.34%, model 6: 1.56%, models 2 and 8: 0.78%, while models 4, 5 and 9 did not have the lowest associated error in any case. Also, the mean error and standard deviation for each model/method is shown in Table 1.

The proposed iterative method has the highest efficiency and the lowest average error value (0.022 ± 0.027), it also has the lowest dispersion. In contrast, model 3 –second in efficiency percentage- has an average error of several orders of magnitude higher compared to the iterative method (5.556 ± 12.029). Models 5 and 9, without having been the best model for any processed dataset, have average errors and dispersions

among the smallest, which is consistent with what is stated in González-Correa's work. In the implementation of model 8, using the measurements taken by our working group, singularities are generated at the time of solving the system of linear equations. This occurs in 18 datasets (14.3% of the total) since in the choosing of the 3 points, it produces an overlap between one of the points and the point corresponding to the critical frequency, consequently, only two different points are taken from the three different ones that are needed, generating a singular matrix in the system to be solved.

TABLE I. MEANS OF FITTING ERROR AND SD OF EACH MODEL/METHOD

Model/Method	Mean error	S.D.
Model 2	8.175	19.945
Model 3	5.556	12.029
Model 4	54.610	85.178
Model 5	0.037	0.036
Model 6	0.036	0.034
Model 7	0.036	0.032
Model 8*	0.048	0.056
Model 9	0.039	0.036
Iterative	0.022	0.027

*Could not be applied to the totality of measurements.

Figure 4 shows different datasets plots with their respective semi-circle. Measurements have different bioimpedance magnitudes.
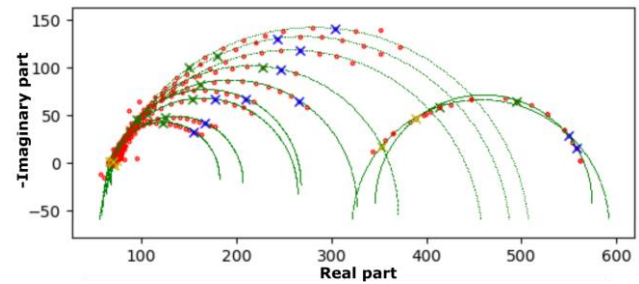

Figure 4. Right data set points correspond to [11]. Left data set points correspond to [8] and [10]. Crosses represents selected points for the iterative method in each case.

IV. DISCUSSION

From Table 1, it can be observed that for models 2, 3 and 4 the mean error and the standard deviation are substantially higher than those of the other models. This suggests that these models are not suitable for datasets with greater size than the applied in [8] since the entire fitting is conditioned to points highly dependent on their geometrical location.

The approximation of experimental bioimpedance measurement data with a circumference has been used in a wide range of published works employing different curve fitting techniques [6, 9, 13-15]. Nevertheless, only one author proposes defining the circumference with just three points in an attempt to estimate the Cole-Cole model parameters; this approach can in fact optimize execution time in the numeric processing. However, the point-selection criteria proposed by Gonzales-Correa in the 9 presented models [8] is biased by his experience in the bioimpedance area, his quickness in the analysis, and the frequency range in which the measurements are performed by his instruments: Xitron 4000B (USA) and Seca mBCA525 (Germany), becoming a particular analysis

for an individual solution. The present work aims to propose a method using a simple language (Python), eliminating the need of user's prior knowledge on bioimpedance, and making it independent on the measurement set-up of any equipment towards being implemented easily by even inexperienced users.

On the other hand, the iterative method executes a triple nested loop of algorithmic complexity $O(N^3)$, nowadays this is not a problem because of the actual processors and memories, although it is interesting to improve the search for all the different possible point trios inside the dataset.

V. CONCLUSION

In conclusion, the proposed iterative method presented the best performance after being tested with a total of 128 frequency sweep measurements, reaching the lowest error in 112 of the mentioned sets (87.5% of the cases) and having the lowest average normal error with less dispersion, which undoubtedly ponders it as an overcoming proposal. Besides, our method can be used with any bioimpedance dataset, no matter the frequency range performed by the measuring instrument, because it takes points in the complex plane (and not frequencies of particular interest), as long as it is a single dispersion measurement [6]; it is also free of singularities when solving the linear equation system since it always takes three different points in order to generate the semicircle. By not choosing the points at fixed frequencies to generate the circumference, we avoid taking data, a priori, altered with noise, a very common condition in bioimpedance measurements.

The aim of this work is to propose an iterative method to obtain an approximated circumference for the Cole-Cole analysis of bioimpedance datasets. We compared our method proposal to those proposed by González-Correa by contrasting the fitting error of the circumferences obtained by each method. The validation of the Cole-Cole parameters obtained by our method is beyond the scope of this work, although it would be valuable to do it with verified Cole-Cole parameters and its corresponding bioimpedance datasets, such as those published in [16], as well as extending the comparison of the proposed method with previous works to those of González-Correa [9, 17-19]. This work is a first approach aiming to develop a multi-device application (for any brand and model of commercial or home-made bioimpedance measurement equipment), in which the user can input the bioimpedance measurement dataset in the original format, which is provided by the device, and the application outputs the Cole-Cole parameters along with the Cole-Cole and Bode diagrams for the best possible interpretation. The purpose of this development is to provide verified and proven technical tools to non-technical users.

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