Simplified geometrical adjustment of bioimpedance measured data to the complex plane with just three parameters

C A Gonzalez-Correa

Universidad de Caldas, Departamento de Ciencias Básicas de la Salud, Grupo de Investigación en Bio-Impedancia Eléctrica (GruBIE), Manizales-Caldas-Colombia-South America. Calle 65 No. 26-10, Edificio de Laboratorios, Oficina 502. Tel +57 6 8781500 Ext. 14160. E-mail: c.gonzalez@ucaldas.edu.co

Abstract. When measurements are made in the field of electrical bioimpedance spectroscopy (EBIS), it is common to fit the raw data to the Cole model. In theory, EBIS data graphed in the impedance locus (resistance \( R \) on the x axis or abscissa versus reactance \( X_c \) on the y axis or ordinate) is expected to form an arch of a circle with its center lying below the resistance axis. The fitting process is most commonly made using least square (LS) techniques to obtain the four parameters involved in the Cole model: resistance at zero frequency \( (R_0) \), resistance at infinite frequency \( (R_\infty) \), a time constant \( (\tau) \) and a dimensionless exponent \( (\alpha) \). In this article, the use of a geometrical approach to fit raw data to the expected arch is explored, where only three parameters are needed: the coordinates of the center in the Cartesian plane (named here as \( h \) for the abscissa, and \( k \) for the ordinate) and the length of the radius \( (r) \). These three parameters are obtained from the \( R \) and \( X_c \) values at three different frequencies. Data published in other literature was used to explain this approach, which is very simple and straightforward to use, while our own data was used to illustrate the performance of the method which, however, still needs thorough validation.

1. Introduction

When electrical impedance spectroscopy (EIS) measurements are taken from any biological tissue, the most appropriate way to handle them is to fit the raw, experimental data to a model, in order to obtain theoretical values for the corresponding model parameters. A physical model and its mathematical expression, with the corresponding parameters, are important as “…it is the only means of independently analyzing the individual components of a heterogeneous material system” [1] and they allow the explanation and interpretation of the data and, therefore, an understanding of tissue properties [2]. In human medicine, for instance, the measurements per se may be of interest for engineers and medical physicists, but, for clinicians, the interpretation of data in terms of physiological and anatomical events is what interest them [3]. In the field of electrical bioimpedance spectroscopy (EBIS), the current most accepted electrical and mathematical model of the material being studied (tissues, organs or whole organisms) is the Cole model, proposed by the American biophysicist Kenneth S Cole [4]. This is considered to be an improvement on the Debye model [5]. While the latter only uses three parameters \( (R_0, R_\infty \text{ and } \tau) \), the former introduced the dimensionless parameter alpha \( (\alpha) \), with values of between zero and one \( (0 < \alpha \leq 1) \). When \( \alpha = 1 \), the Cole model
equals the Debye model initially used in the (EBIS) field. In other words, the Debye model can be considered as an special case of the Cole model:

\[
Z = Z_e + \frac{R_0 - R_s}{1 + (j\omega\tau)^\alpha} \quad \text{(Cole)} \quad \text{becomes} \quad Z = Z_e + \frac{R_0 - R_s}{1 + (j\omega\tau)} \quad \text{(Debye) when } \alpha = 1.
\]

There are different approaches to carry out in order to fit EBIS data to the Cole model, but the one most frequently used is that of least squares (LS) [6, 7], a deterministic algorithm according to [2]. The Cole model can be represented either as an electric circuit, an equivalent equation or a plot in the bidimensional Cartesian coordinate system, the latter being named in different ways: impedance locus, Nyquist diagram or complex plot. When represented graphically, the Cole model gives the arc of a circle which, in the special case where \(\alpha = 1\) (Debye model), would be a complete semicircle, with its center lying on the x-axis (and, therefore, the ordinate or y value of that center being 0-zero). For this, cell membranes ought to act as perfect dielectrics (i.e., as perfect capacitors), which is not the case in real life. In any other case, the center of the circle is considered to be below the resistance axis [4] or “depressed”, giving a “suppressed” semicircle [8], with its center lying in quadrant IV of the bidimensional Cartesian system.

The spectrum of frequencies most commonly used in EBIS can be divided into three main regions: low, middle and high [7], although [9] subdivide these in the extremes into very high, high, low and very low. Cut off points for the regions can be either absolute (valid for any measurement) or relative (established for each measurement). In the first case, we would suggest accepting, for any measurement, those used by the SECA mBCA 525 Bioimpedance Analyzer: low frequencies would, then, be those \(\leq 5\) kHz, middle frequencies would be those \(> 5\) kHz and \(< 100\) kHz, and high frequencies would be those \(\geq 100\) kHz. If the characteristic frequency \(\omega_c\), or the frequency which gives the maximum \(X_c\), i.e., the frequency above the center of the circle) of a specific measurement is known, relative cut off points could be defined as \(< \omega_c/2, \leq \omega_c/2\) to \(< 2\omega_c\) and \(\geq 2\omega_c\), for low, middle and high frequencies, respectively, if the criteria for [9] is adopted, but without considering the subdivisions (or subregions) of very low and very high frequencies (i.e., they are included in the low and high regions, respectively). According to [3], deviations from the theoretical curve of measured EBIS data are minimal around \(\omega_s\), and, therefore, frequencies in the relative middle region (those near \(\omega_s\)) of the frequency spectrum would better represent the main dispersion of the raw data.

Although some authors consider that a minimum of four frequencies are required for a Cole fitting [8, 3], the appropriate number and range of frequencies to be used in EBIS have been subject of discussion and the companies producing commercial equipment have different approaches. For instance, while systems for the study of body composition (Bioelectrical Impedance Analysis, BIA) such as the ImpediMed SFB7 (Carlsbad, CA-USA) uses 267 frequencies in the range 4-1000 kHz; the old Xitron 4000B (San Diego, California) used up to 50 frequencies between 1 kHz and 1248 kHz, and the more recently launched SECA mBCA 525 (Hamburg, Germany) uses just 6 (1, 2, 5, 10, 20, 50, 100, 200 and 500 kHz). The last example suits our purpose very well, considering that: a) it has three frequencies in the low range, three in the middle range and 3 that can be considered as high, and b) because up to 500 kHz is the maximum recommended frequency for EBIS measurements [10], although some authors consider that EBIS for body composition works well up to only 100 kHz as, above this frequency, artifacts like the Hook effect may be present [10].

In their comparative study and using mathematical analysis, [8] Quien? proposed what they considered a novel fitting method by estimating the complex center and radius of the circle, which implies differentiation of the variance of the complex points to the calculated center of the circle. More recently, Gholami-Boroujeny & Bolic [6] mentioned the fact that data used to evaluate the performance of their algorithm are located exactly on a Cole plot with circle parameters given by them. In geometry, it is accepted that any three non-collinear points (i.e. points that do not lie in a straight line) can be considered as the vertices of a triangle and, as a cyclic polygon, this triangle has a unique circle that passes through all its vertices, which is known as the circumcircle. There are
different ways to calculate the center (circumcenter) and the radius (circumradius) of a triangle circumcircle.

In this article, data published by [1] are used to show how a very simple method for fitting raw EBIS data to an arch behaves, under the premise of accepting the following assumptions:

a. There is only one single dispersion embedded in the data
b. Ideally, data should adjust to a geometrical arch
c. Only any three points of a circle are needed to find the equation or parametric values of the circle to which the arch belongs (these parameters being named here as $h, k,$ and $r,$ where $h$ and $k$ are the $x$ and $y$ values of the circumcenter in the coordinate system, respectively, and $r$ is the length of the circumradius, according to the nomenclature being used in this article which will be explained later).

In this way, the results presented here can be considered a simple and basic explanation of the phenomenological behavior of bioimpedance measurements. Our own data was used to illustrate the performance of the proposed method, although thorough validation ought to be carried out later. The importance of searching for alternative methods for the extraction of impedance parameters is “… to reduce the number and cost of instruments for these measurements…” [7].

2. Methods
For this study, data calculated from information at the 9 above mentioned frequencies (1, 2, 5, 10, 20, 50, 100, 200 and 500 kHz) given by [1] were used. Among other data, they report impedance ($Z$) and phase angle ($\theta$) values for 21 frequencies in the range 1-1248 kHz measured in one subject, as well as their theoretical calculated values, along with those of the four Cole-Cole parameters. For our purposes, in each case, resistance ($R$) was calculated as impedance ($Z$) times cos($\theta$), reactance ($X_c$) as impedance times sen($\theta$), and the obtained values are shown in Table 1.

| Frequency kHz | Measured Data from [1] | Calculated | Corresponding values for $R$ & $X_c$ |
|--------------|------------------------|------------|------------------------------------|
| Z            | $\theta$               | $Z$        | $\theta$                          | $R$ | $X_c$ |
| $\Omega$     | Degrees                | $\Omega$  | Degrees                           | $\Omega$ | $\Omega$ |
| 1            | 561.5                  | 0.3        | 566.0                             | 1.5 | 565.8 | 14.8 | 561.5 | 2.9 |
| 2            | 557.7                  | 1.6        | 559.9                             | 2.4 | 559.4 | 23.4 | 557.5 | 15.6 |
| 5            | 546.1                  | 3.6        | 545.3                             | 4.0 | 544.0 | 38.0 | 545.0 | 34.3 |
| 10           | 528.9                  | 5.6        | 526.6                             | 5.7 | 524.0 | 52.3 | 526.4 | 51.6 |
| 20           | 499.5                  | 7.5        | 499.1                             | 7.3 | 495.1 | 63.4 | 495.2 | 65.2 |
| 50           | 451.6                  | 8.5        | 452.7                             | 8.6 | 447.6 | 67.7 | 446.6 | 66.8 |
| 100          | 417.8                  | 8.1        | 418.0                             | 8.3 | 413.6 | 60.3 | 413.6 | 58.9 |
| 200          | 391.8                  | 6.8        | 390.6                             | 6.9 | 387.8 | 46.9 | 389.0 | 46.4 |
| 500          | 366.4                  | 4.8        | 367.8                             | 4.6 | 366.6 | 29.5 | 365.1 | 30.7 |

There are different ways of calculating the parameters for the equation of the circle that passes through 3 non collinear points in a plane (circumcircle). This is a well known geometrical problem and, instead of presenting the steps for it, we chose to use one of the many free search engines available on the Internet. For this particular case we used the widget provided by WolframAlpha at: https://www.wolframalpha.com/input/?i=circle+thru+3+points.
The nomenclature that will be used through this article in relation to this aspect is as follows:

\[ P# = \text{point number (P1, P2 and P3), for the three different points used for calculating the circumcenter and the circumradius of a specific circumcircle} \]

\[ a = \text{x coordinate value (abscissa) for a point (equivalent to } R \text{ at a specific frequency)} \]

\[ b = \text{y coordinate value (ordinate) for a point (equivalent to } Xc \text{ at a specific frequency)} \]

\[ h = \text{x coordinate value (abscissa) for the circumcenter of the circumcircle} \]

\[ k = \text{y coordinate value (ordinate) for the circumcenter of the circumcircle} \]

\[ r = \text{length of the circumradius of the circumcircle}. \]

Figure 1 shows the screen seen in one of the calculations, as a graphical description of the geometrical explanation for the radius formula. It has four sections: a) circle: values of the three points (R and Xc) used for one of the models (see Table 2, model 5); b) visual representation of the circumcircle; c) corresponding equation for this circle, and d) properties (parameters) of the circumcircle.

In addition to the fitting used by [1], 8 more approaches to get the circumcircle parameters for the fitting arch were obtained, ending up with 9 different models as follows, according to the values being used to calculate them:

- **Model 1.** Those calculated (theoretical) from [1], using the data corresponding to frequencies 2, 20 and 200 kHz
- **Model 2.** Those of the lower range of frequencies (1, 2 and 5 kHz);
- **Model 3.** Those of the middle range of frequencies (10, 20 and 50 kHz);
Model 4. Those of the higher range of frequencies (100, 200 and 500 kHz);
Model 5. Those of the middle of the three above mentioned ranges (2, 20 and 200 kHz).
   Note: the values used in Model 1 at these same frequencies are those corresponding to the theoretical model given by the authors, while those used for this model correspond to the raw data);
Model 6. Averaging those corresponding to approaches 2, 3 and 4;
Model 7. Those of the two extreme frequencies (1 and 500 kHz) and the middle value of the middle range (20 kHz);
Model 8. Those of the two extreme frequencies (1 and 500 kHz) and those of the frequency with the highest value for \(X_c\) (50 kHz in this case);
Model 9. The same as for Model 5, but changing the value of \(r\) for the average of the distances from the raw data to its center.

Residuals for each model were calculated as the difference between the distance of each point to the center of the circumcircle minus the value of the respective calculated circumradius and, then, root mean square errors (RMSE) were calculated for each spectrum as a test of quality [3, 11]. A one way ANOVA was conducted in order to analyze the means of the residuals of the nine models, where the factor was the model and the residuals were the response variable. The null hypothesis \((H_0)\) was that the average of the residuals for the nine models could be considered as statistically equal. The significance level was taken as 0.05 and the Tukey test was used for post hoc analysis. In order to obtain the curves for each approach, we used the same values for \(R\) at the nine selected frequencies: 1, 2, 5, 10, 20, 50, 100, 200 and 500 kHz. For each model \(R_\infty\) and \(R_0\) were calculated using the Pythagorean equation as follows:

\[
R_\infty = h - (r^2 - k^2)^{0.5} \quad \text{and} \quad R_0 = h + (r^2 - k^2)^{0.5}
\]

3. Results
Table 2 shows: a) the values (a P1, b P1, a P2, b P2, a P3 and b P3) of the points used to calculate the parameters \((h, k \text{ and } r)\) of the circumcircle equation obtained for each of the nine models being considered; b) the circumcircle parameters themselves \((h, k \text{ and } r)\), and c) the calculated values for \(R_\infty, R_0\) and \(\alpha\) (obtained as the characteristic \(X_c\) divided by \(r\)). Figure 2 shows raw data published by [1] as well as the theoretical arch for each of the nine models obtained with the theoretical parameters derived from them.

| Variable | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  |
|----------|----|----|----|----|----|----|----|----|----|
| \(a\) P1 | 559.4 | 561.5 | 526.4 | 413.6 | 557.3 | 524.7 | 561.3 | 561.5 | 557.5 |
| \(b\) P1 | 23.4 | 2.9 | 31.6 | 58.9 | 15.6 | 17.6 | 2.9 | 2.9 | 15.6 |
| \(a\) P2 | 495.1 | 557.5 | 495.2 | 389.0 | 495.2 | 489.4 | 495.2 | 446.6 | 495.2 |
| \(b\) P2 | 63.1 | 15.6 | 65.2 | 65.2 | 61.2 | 65.2 | 66.8 | 65.2 |
| \(a\) P3 | 387.8 | 545.0 | 446.6 | 365.1 | 389.0 | 389.3 | 365.1 | 389.0 |
| \(b\) P3 | 46.9 | 34.3 | 66.8 | 30.7 | 46.4 | 45.3 | 30.7 | 46.4 |
| \(h\) | 459.9 | 505.2 | 467.4 | 515.8 | 459.7 | 457.0 | 454.6 | 452.8 | 459.7 |
| \(r\) | -64.9 | -7.9 | -41.2 | -172.6 | -43.4 | -58.0 | -44.4 | -57.3 | -43.4 |
| \(R_\infty\) | 133.0 | 57.4 | 110.0 | 253.0 | 114.2 | 122.5 | 116.9 | 124.2 | 114.3 |
| \(R_0\) | 342.8 | 448.4 | 365.4 | 330.7 | 354.0 | 348.0 | 346.5 | 342.6 | 353.9 |
| \(\alpha\) | 576.0 | 562.0 | 569.4 | 700.8 | 565.3 | 566.1 | 562.7 | 563.1 | 565.5 |

| Variable | \(a\) | \(b\) | \(c\) |
|----------|------|------|------|
| \(R_\infty\) | 0.51 | 0.66 | 0.63 |
| \(R_0\) | 0.32 | 0.62 | 0.53 |
| \(\alpha\) | 0.54 | 0.62 | 0.62 |

Table 2. a) Values for the points used for calculating the circumcircle parameters for each model considered in this study, b) values of the circumcircle parameters, and c) \(R_\infty, R_0\) and \(\alpha\), three of the 4 parameters for the Cole model.
Figure 2. Raw data (*) taken from [1] and arches drawn with the parameters ($h$, $k$ and $r$) obtained for each of the models (1-9) considered in the present study. All units are in $\Omega$.

The ANOVA gave a $P$ value of less than 0.05 ($1.95 \times 10^{-7}$) indicating that the mean of the residuals of at least one of the models was statistically different to the others and the Tukey post hoc analyses indicated that this was the case for models 2 and 4, with means 30.6 $\Omega$ and -24.8 $\Omega$, respectively. Therefore, these two models were not considered in further analysis and are not included in Figure 3, where the means and variances (given by the ANOVA) of the remaining seven models are represented.
Finally, in order to illustrate how the proposed method of fitting performs, we took 6 data sets from our archives and fitted the raw data to our calculated circumcircle, using the points at frequencies 10, 20 and 50 kHz. All data corresponds to whole body measurements taken on the right side of the body, 3 of them (a, b and c) with a mBCA 525 (SECA, Hamburg, Germany), while the remaining 3 (d, e and f) were taken with a Xitron 4000B (San Diego, California). All this is shown in Figure 4.

Figure 3. Means of the residuals, with their respective variances, for the seven models being considered (models 2 and 4 are excluded).

Figure 4. Six different examples of fitting real data (whole body measurements) with our proposed method: a), b) and c) are data taken with a mBCA 525 BIA analyzer from SECA (Hamburg, Germany) while d), e) and f) are data taken with a 4000B Bio-Impedance Analyser (BIA) from Xitron (San Diego, California). All units are in $\Omega$. 
4. Analysis

Six of the approaches (models) tried in this study give errors (residuals) comparable to those of the fitting values provided for the model used by [1]. Of these six models, numbers 5 and 9 seem to do better, as their means are closer to zero (0.104 Ω and 0.000 Ω, respectively) and their variances are among the lowest (7.5 Ω both). Actually, model 9 can be considered as a slightly improved version of model 5.

The results of this study suggest that data from the extremes of the frequency spectrum commonly used in EBIS (low and high frequencies), do not show well the data obtained with the whole spectrum [3], probably due to either artifacts (like the hook effect) or because there may be more than one dispersion, one of them probably with an inductive component [7]. In this article, a single dispersion was assumed. Data from frequencies in the middle range (between 10-50 kHz) better represent the whole spectrum. Nevertheless, under the assumptions taken in this study (especially that there is just one single dispersion), better parametrization is obtained when a point from each of the three regions (low, middle and high frequencies) is taken.

Another geometrical approach to calculate the parameters for the equation of a circle would be, for instance, if the resistance and the reactance of any given point of the arch ($R_a$ and $X_{ca}$), as well as the values for the resistance and the reactance at the characteristic frequency are known ($R_{ch}$ and $X_{ch}$, respectively). In this case, the circumradius ($r$) could be calculated with the formula:

\[ r = \frac{x^2}{8y} + \frac{y}{2} \]

where $x$ is the value of the chord and $y$ is the value of the sagitta or versina. To use this equation, $x$ would be equal to twice the absolute difference between the resistance of the point and that of the characteristic frequency, while $y$ would be equal to the reactance of the characteristic frequency minus the $Xc$ of the point being used for the calculations. Nevertheless, this would be a less straightforward solution as, even if there is a sweep of frequencies, it could still be uncertain which $Xc$ value corresponds to $f_c$, although one could still select the highest $Xc$ value of all obtained, assuming that the highest value for $Xc$ in the raw data is not that corresponding to the highest frequency (which would mean that the uncertainty would still remain).

The problem of noise interfering with the calculation of the parameters has to be considered, but this is an issue outside the scope of this study. One way of dealing with it could be a “denoising” procedure, as suggested by different authors [10, 12]. In terms of quality of the fitted parameters, though, it is considered that the mean square error of $Xc$ estimates the quality of both the noise and adjustment of the fitting [3, 11]. It is also worth mentioning that [11] also report, for their data, that the best fit was obtained with frequencies between 5 and 55 kHz.

5. Conclusions

Although the results reported here are very encouraging, a more thorough validation of the proposed method in this article is still to be done, before it can be confidently used. Nevertheless, it is worth highlighting that one of its main advantages is the ease to calculate the three parameters ($h$, $k$ and $r$) needed to fit the raw data to a theoretical arch. Another advantage is that practically anybody can calculate these parameters without the need for complicated mathematics or sophisticated algorithms. This could be especially useful for people in the biomedical field working with EBIS, as they do not have the required background to deal with analytical approaches and are not necessarily familiar with mathematical notations. Finally, only three points would be necessary for the fitting instead of the minimum 4 proposed by some other authors [8].

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References

[1] De Lorenzo A, Andreoli A, Matthie J and Withers P 1997 Predicting body cell mass with bioimpedance by using theoretical methods: a technological review J. Appl. Physiol. 82 1542-58

[2] Yousri DA, AbdelAty AM, Said LA, AboBakr A and Radwan AG 2017 Biological inspired optimization algorithms for cole-impedance parameters identification Int. J. Electron. Commun. (AEÜ) 78 79-89

[3] Ward LC, Essex T and Cornish BH 2006 Determination of Cole parameters in multiple frequency bioelectrical impedance analysis using only the measurement of impedances Physiol. Meas. 27 839-50

[4] Cole KS 1940 Permeability and impermeability of cell membranes for ions Cold Spring Harb. Symp. Quant. Biol. 8 pp 110-22

[5] Debye P 1929 Polar molecules (New York: Chemical Catalog Co, Inc) p 172

[6] Gholami-Boroujeny S and Bolic M 2016 Extraction of Cole parameters from the electrical bioimpedance spectrum using stochastic optimization algorithms Med. Biol. Eng. Comput. 54 643-651

[7] Freeborn TJ, Maundy B and Elwakil AS 2014 Extracting the parameters of the double dispersion Cole bioimpedance model from magnitude response measurements Med. Biol. Eng. Comput. 52 749-58

[8] Ayllón D, Seoane F and Gil-Pita R 2009 Cole equation and parameter estimation from electrical bioimpedance spectroscopy measurements - A comparative study Conf. Proc. IEEE. Eng. Med. Biol. Soc. 2009 3779-82

[9] Ayllón D, Gil-Pita and R Seoane F 2016 Detection and Classification of Measurement Errors in Bioimpedance Spectroscopy PLoS. One. 11 1-19

[10] Buendia R, Seoane F, Harris M, Caffarel J and Gil R 2010 Hook effect correction & resistance-based Cole fitting prior Cole model-based analysis: experimental validation Conf. Proc. IEEE. Eng. Med. Biol. Soc. 2010 6563-6

[11] Stroud DB, Cornish BH, Thomas BJ and Ward LC 1995 The use of Cole-Cole plots to compare two multifrequency bioimpedance instruments Clin. Nutr. 14 307-11

[12] Nejadgholi I, Caytak H, Bolic M, Batkin I and Shirmohammadi S 2015 Preprocessing and parameterizing bioimpedance spectroscopy measurements by singular value decomposition Physiol. Meas. 36 983-99