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Evaluation of algorithms for calculating bioimpedance phase angle values from measured whole-body impedance modulus

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Abstract

This paper addresses the problem of calculating the bioimpedance phase angle from measurements of impedance modulus. A complete impedance measurement was performed on altogether 20 healthy persons using a Solatron 1260/1294 system. The obtained impedance modulus (absolute impedance value) values were used to calculate the Cole parameters and from them the phase angles. In addition, the phase angles were also calculated using a Kramers–Kronig approach. A correlation analysis for all subjects at each frequency (5, 50, 100 and 200 kHz) for both methods gave R^2 values ranging from 0.7 to 0.96 for the Cole approach and from 0.83 to 0.96 for the Kramers–Kronig approach; thus, both methods gave good results compared with the complete measurement results. From further statistical significance testing of the absolute value of the difference between measured and calculated phase angles, it was found that the Cole equation method gave significantly better agreement for the 50 and 100 kHz frequencies. In addition, the Cole equation method gives the four Cole parameters (R_0, R_∞, τ_z and α) using measurements at frequencies up to 200 kHz while the Kramers–Kronig method used frequencies up to 500 kHz to reduce the effect of truncation on the calculated results. Both methods gave results that can be used for further bioimpedance calculations, thus improving the application potential of bioimpedance measurement results obtained using relatively inexpensive and portable measurement equipment.

Keywords: Bioimpedance, Kramers–Kronig relation, Cole equation, phase angle retrieval algorithms

(Some figures in this article are in colour only in the electronic version)

1. Introduction

Measured values of bioimpedance data are commonly used for calculating physiological data (Grimnes and Martinsen 2008, Kyle *et al* 2004), for instance in connection with sports and nutrition assessment. Other areas of use include surveyance of critical organ functions in connection with cardiovascular treatment (Bernstein 2010) and surveyance of the hydration process during haemodialysis treatment (Al-Surkhi *et al* 2007). Some of the measurement systems used do however only provide the impedance modulus while the applications of interest may require both the complete complex impedance and the Cole parameters. Methods that can provide more complete data from impedance modulus measurements are thus of great interest, and several approaches have been proposed and demonstrated like the Kramers (1926)–Kronig (1929) relation which provides a connection between the imaginary and real parts of a complex number, which is one possibility (Riu and Lapaz 1999). Another method is to anticipate that the Cole equation (Cole 1940, Grimnes and Martinsen 2005) is valid and use the measured impedance modulus at a minimum of four frequencies; we have used 5, 50, 100 and 200 kHz since these are the frequencies commonly used in calculations of physiological parameters (Kyle *et al* 2004), to find the Cole parameters and from them the bioimpedance phase angle (Kalvøy *et al* 2004, Nordbotten *et al* 2010). Investigations have indicated (Nordbotten *et al* 2010) that both methods give reliable results. The main intention of the present work is to perform measurements of both impedance modulus and phase angles on a number of healthy persons, and then calculate the phase angles from the obtained impedance modulus values. From this we can perform an evaluation of the Kramers–Kronig and Cole equation based methods by comparing calculated and measured values. The Cole equation method is using values for just four frequencies. For the Kramers–Kronig a large number of data points is being used for the summation and as a conclusion of Riu and Lapaz (1999) and Kalvøy *et al* (2004), 500 kHz has been chosen as the upper frequency for the summation. The intention is not to compare these two methods with the use of exactly the same dataset, but to compare the results obtained by the two methods when available data from a bioimpedance modulus measurement are used in the best way for the two methods for phase angle calculation.

2. Methods

In this section we will present the two methods to calculate the phase angle values from the impedance modulus and also the methods used for statistical analysis. We first present the two methods, the Cole equation based method and the Kramers–Kronig based approach, and then the statistical methods used.

2.1. The Cole equation model

An empirical model representing the impedance value of tissue within one dispersion has been given by Cole (1940) in the form

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

where R_0 and R_∞ are the resistance values at very low and very high frequencies, respectively. τ_Z is a characteristic time constant corresponding to a characteristic frequency

$$f_c = \frac{\omega_c}{2\pi} = \frac{1}{2\pi\tau_z}. \tag{2}$$

The constant α ($0 < \alpha \leqslant 1$) characterizes the distribution of the relaxation frequencies of the biomaterial. The normal procedure used for determining the four Cole parameters is to plot the circular arc representing the imaginary part of the impedance versus its real part. The Cole parameters are then found by geometrical interpretation. For the situation discussed here the measurements give only the modulus of the impedance for different frequencies. The main challenge with this commonly used measurement procedure is to obtain the Cole parameters and the phase angle which are required for many further calculations. These values can be calculated as follows. Introducing the relation

$$j^{\alpha} = \cos\left(\alpha\frac{\pi}{2}\right) + \mathrm{j}\sin\left(\alpha\frac{\pi}{2}\right) \tag{3}$$

into equation (1), the following expression is obtained for the modulus $|Z|$:

$$|Z| = \sqrt{\frac{k_1^{\alpha}R_{\infty}^2 + 2R_{\infty}k_1^{\alpha/2}k_2R_0 + R_0^2}{1 + 2k_1^{\alpha/2}k_2 + k_1^{\alpha}}}, \tag{4}$$

where the introduced abbreviations k_1 and k_2 are given by

$$k_1 = (2\pi f)^2\tau_Z = \omega^2\tau_Z^2$$
$$k_2 = \cos\left(\frac{\pi\alpha}{2}\right).$$

With a measured value $|Z|$ this is an equation with the four Cole parameters (R_0, R_{∞}, τ_z and α) as unknowns. By making measurements at four frequencies this can be solved using a nonlinear least-squares method. The real and imaginary parts of the impedance are then obtained by introducing these values into equation (1). The phase angle is then given by $\varphi = \arctan\frac{\mathrm{Im}(Z)}{\mathrm{Re}\,(Z)}$.

2.2. The Kramers–Kronig model

From the Kramers–Kronig theory (Kalvøy *et al* 2004) the imaginary part of a linear network can be calculated when the real part is known over the entire frequency range of interest. The phase angle at a given frequency ω_1 is then given by

$$\varphi(\omega_1) = \frac{2\omega_1}{\pi}\int_0^{\infty}\ln\frac{|Z(\omega)| - |Z(\omega_1)|}{\omega^2 - \omega_1^2}\delta\omega. \tag{5}$$

Since we need to use a numerical calculation we transfer this expression into a summation approximation:

$$\varphi(\omega_1) = \frac{2\omega_1}{\pi}\sum_{i=0}^{n}\frac{\ln(|Z(\omega_i)|) - \ln(|Z(\omega_1)|)}{\omega_i^2 - \omega_1^2}\Delta\omega. \tag{6}$$

The summation is limited to the frequency range of the measurement, which means that a truncation limiting the frequency range for the calculations is introduced. It has been shown that the relative error decreases fast when the upper summation limit is increased (Riu and Lapaz 1999) and it has been anticipated that the upper summation limit could be approximately 500 kHz (Kalvøy *et al* 2004). We used a step increment of 10 Hz and obtained the data points for the summation by performing a cubic-spline interpolation.

2.3. Statistical analysis

To compare the two phase angle estimation approaches, the differences between the estimated phase angles and the measured phase angles, $\Delta\varphi$, were calculated for each subject and grouped

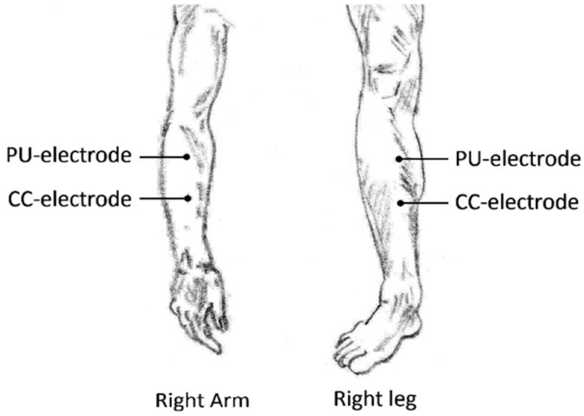

Figure 1. Sketch of electrode placement on right arm and right leg.

according to the four selected frequencies of 5, 50, 100 and 200 kHz and for both approaches. To assess which of the methods gave the best phase angle estimation, the absolute value of $\Delta\varphi$ was used in the comparison. $\Delta\varphi$ was used in favour of the percent-wise deviation from the measured phase angle due to a more equal variance among the groups for $\Delta\varphi$ based on the p-value of test for equal variance. Test for normality was done on each group by the Shapiro–Wilk test (Shapiro and Wilk 1965). Test for significance of the difference between the two approaches with $\alpha = 0.05$ was done for each frequency using the paired t-test when the normality test passed and the Wilcoxon signed rank (Wilcoxon 1945) test otherwise. To investigate whether $\Delta\varphi$ was dependent on either the phase angle or the measurement frequency, a multiple linear regression was done for both approaches using the phase angle and the frequency as independent variables and $\Delta\varphi$ as the dependent variable. This part of the statistics who done using SigmaPlot® v11.

The Excel function correl has been used for calculating the coefficient of determination R^2 between measured and calculated phase angle values.

2.4. Measurements

The whole body measurements were performed on 20 healthy persons in the age group 21–32 years using a Solatron 1260/1294 measurement system. The Solatron 1294 impedance interface has a specified accuracy of 1% up to 100 kHz, while above 100 kHz to 750 kHz it has a specified accuracy of 10%. The Solatron 1260 as such has an upper frequency of 32 MHz. A four electrode setup with two current-carrying (CC) and two pick-up (PU) electrodes was used. One pair of electrodes were placed 7 cm apart on the right leg and the other pair were placed in a similar way on the right arm as shown in figure 1.

The frequency was swept from 100 Hz to 500 kHz. The full measurement range was used for the Kramers–Kronig calculations to avoid further truncation, while the Cole equation approach used results up to 200 kHz only. For the Cole equation approach the frequencies 5, 50, 100 and 200 kHz commonly used in connection with measurements for calculations of body composition have been selected. The measurements were performed employing a signal amplitude of 800 mV AC. This amplitude was determined from a whole body measurement where the amplitude was varied from 80 mV to 2 V. The 800 mV amplitude was then chosen due to its optimal position well within the linear range.

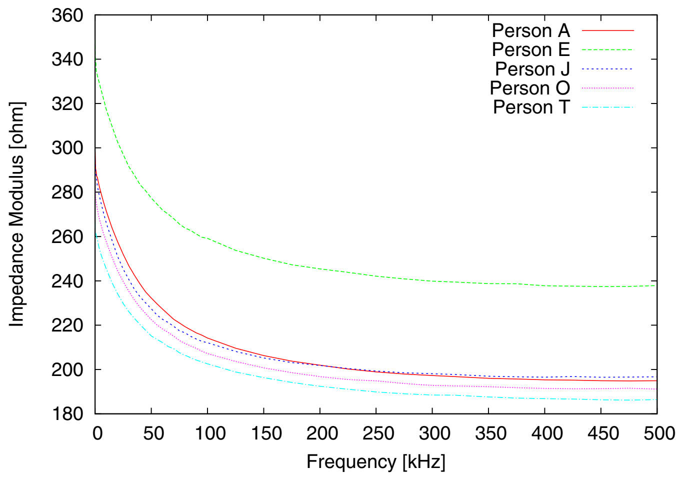

Figure 2. Plot of the measured impedance modulus on five different persons.

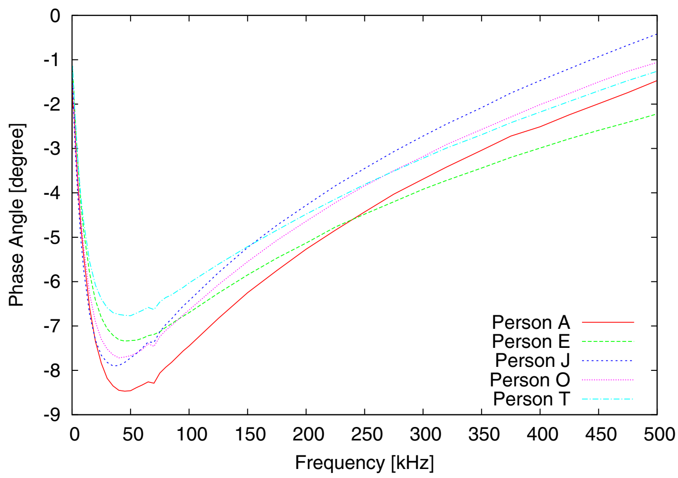

Figure 3. Plot of the measured phase angle for the five persons.

3. Results

A plot showing the measured impedance modulus for five different persons (A, E, J, O and T) is shown in figure 2. Most of the results for the different persons were closely grouped, and also varied within the range of expectation as illustrated by person E in the plot.

The complete set of measured impedance modulus results represented by figure 2 are used for calculating the corresponding phase angles while the corresponding measured phase angles as shown in figure 3 are used as reference for evaluation of the calculated values. The phase angle values show a more even spread than the impedance modulus values, but within an acceptable range for healthy persons of the age group considered (Barbosa-Silva *et al* 2005).

In figure 3 we observe a small notch in the phase angle at the 70 kHz range for all the persons; this is caused by the Solatron 1260 switching from using a digital lock-in amplifier

Table 1. Measurement result, with measured and calculated phase angles, where (M) is measured phase angle, (C) is the Cole approach and (K) is the Kramers–Kronig approach.

f (kHz)	5			50			100			200		
Persons	M (°)	C (°)	K (°)	M (°)	C (°)	K (°)	M (°)	C (°)	K (°)	M (°)	C (°)	K (°)
A	−3.8	−3.52	−3.57	−8.46	−8.63	−7.84	−7.45	−7.73	−6.9	−5.27	−5.83	−4.96
B	−3.83	−3.89	−3,65	−8.53	−8.66	−7.93	−7.49	−7.94	−6.83	−5.27	−6.25	−4.93
C	−4.69	−4.58	−4.71	−9.61	−10.28	−9.28	−8.47	−8.83	−7.89	−6.32	−6.43	−5.58
D	−3.83	−3.97	−3.62	−7.92	−7.86	−7.39	−6.9	−6.99	−6.27	−4.94	−5.41	−4.5
E	−3.34	−3.47	−3.16	−7.33	−7.4	−6.79	−6.7	−6.87	−5.8	−5.13	−5.54	−4.36
F	−3.71	−3.41	−3.48	−7.51	−7.58	−7.07	−6.64	−6.76	−6.08	−4.91	−4.92	−4.22
G	−3.88	−3.71	−3.86	−7.7	−7.88	−7.18	−6.8	−6.74	−6.16	−5.3	−4.93	−4.26
H	−3.9	−3.48	−3.78	−7.51	−8.05	−7.63	−6.23	−6.68	−5.94	−4.27	−4.67	−4.04
I	−3.31	−3.49	−3.12	−7.7	−7.53	−7.09	−6.95	−7.07	−5.79	−5.34	−5.75	−4.53
J	−4.08	−4	−3.91	−7.72	−7.92	−7.33	−6.43	−6.83	−5.95	−4.38	−5.11	−4.22
K	−3.74	−4.09	−3.56	−7.04	−7.61	−8.54	−6.75	−6.83	−5.89	−5.08	−5.4	−4.52
L	−3.86	−4.21	−3.52	−8.73	−8.74	−8.07	−7.85	−8.15	−7.1	−5.76	−6.62	−5.2
M	−3.8	−3.67	−3.68	−8.57	−8.75	−7.99	−7.49	−7.75	−6.81	−5.25	−5.79	−4.84
N	−2.49	−2.49	−2.43	−5.18	−5.14	−4.93	−4.52	−4.77	−4.06	−3.15	−3.85	−3.04
O	−3.71	−3.45	−3.55	−7.67	−7.82	−7.13	−6.64	−6.88	−6.11	−4.64	−5.15	−4.4
P	−3.54	−3.31	−3.31	−8.17	−8.29	−7.54	−7.26	−7.41	−6.55	−5.19	−5.54	−4.72
Q	−3.8	−3.81	−3.63	−8.12	−8.4	−7.59	−7.16	−7.57	−6.7	−5.02	5.84	−4.89
R	−3.83	−3.65	−3.85	−7.35	−7.56	−6.91	−6.25	−6.58	−5.84	−4.32	−4.92	−4.18
S	−3.5	−2.72	−2.98	−6.05	−7.45	−6.66	−5.87	−6.51	−5.81	−3.76	−4.68	−4.04
T	−3.28	−3.78	−3.23	−6.77	−6.83	−6.31	−6.03	−6.43	−5.58	−4.48	−5.41	−4.21

to an analog lock-in amplifier at 65.5 kHz. The measured and calculated phase angles are shown in table 1 for the frequencies 5, 50, 100 and 200 kHz. It is seen that the values obtained using the Cole method are scattered both above and below the measured phase angle, while the Kramers–Kronig phase angles are all well above the measured phase angle. This indicates that the truncation also at 500 kHz results in a systematic and high value of the calculated phase angle values.

Figures 5 and 6, which show measured and calculated phase angle values for persons I and R respectively, confirm this picture. It is however also observed that the greater the difference between the Kramers–Kronig approach and the measured phase angle the more negative is the phase angle value at 500 kHz.

The effect of truncation is further illustrated in figure 4 where the calculated phase angle is also shown for truncation at 225 kHz in comparison with the values obtained using frequencies up to 500 kHz.

As illustrated in figures 5 and 6, the smaller the Kramers–Kronig systematic error contribution the smaller is the measured phase angle at 500 kHz. Further investigations are however required to conclude this.

Table 2 shows the coefficient of determination R^2 for both Cole and Kramers–Kronig approaches for each frequency.

The results from the statistical analysis of the differences $\Delta\varphi$ between the estimated phase angles and the measured phase angles are shown in figures 7 and 8. Figure 7(a) shows the difference $\Delta\varphi$ where the line dividing the box represents the median value. The Kramers–Kronig $\Delta\varphi$'s are all positive with the truncation error contributing in this direction. The plots in figures 7(a) and (b) show a better result using the Cole approach except for the lowest frequency where they are almost equal.

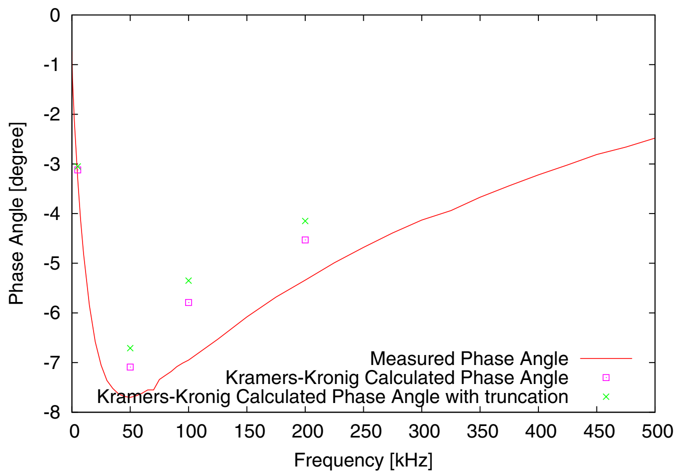

Figure 4. Plot of the effect of truncation when using the Kramers–Kronig approach for person I.

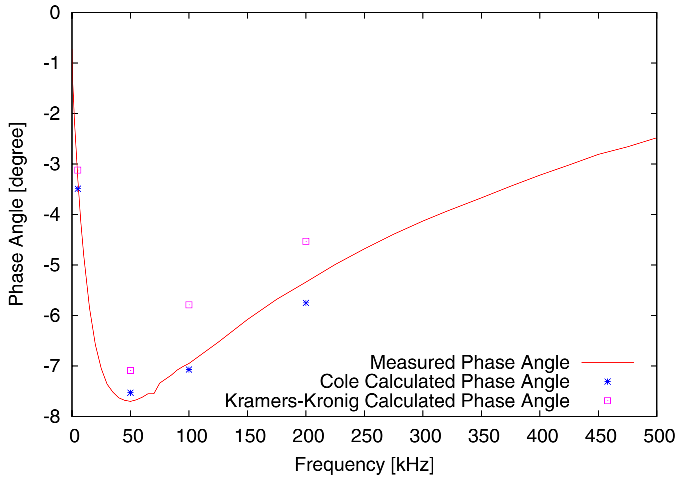

Figure 5. Plot of the measured phase angle, compared with the calculated phase angle using the Cole and Kramers–Kronig approach for person I.

Table 2. Coefficient of determination R^2 for both Cole and Kramers–Kronig (K–K) approach for each of the four frequencies 5, 50, 100 and 200 kHz.

Frequency (kHz)	R^2 for Cole	R^2 for K–K
5	0.70	0.96
50	0.96	0.96
100	0.96	0.92
200	0.77	0.83

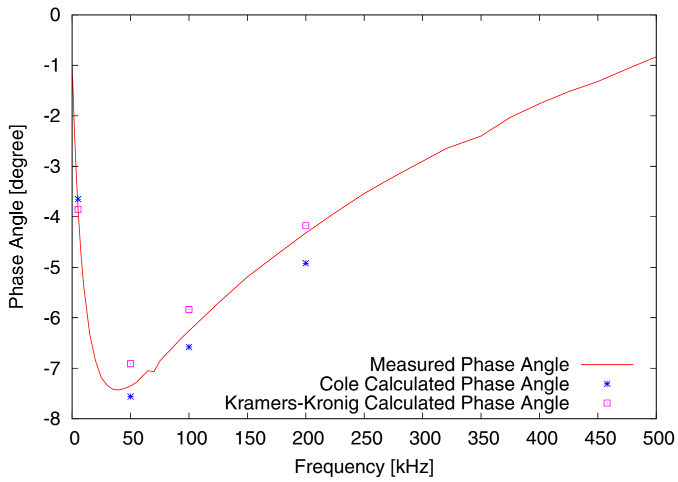

Figure 6. Plot of the measured phase angle, compared with the calculated phase angle using the Cole and Kramers–Kronig approach for person R.

4. Discussion

The average deviations between measured and calculated values obtained using the Cole equation approach are smaller than the corresponding averages from the Kramers–Kronig based calculations except for the values at 200 kHz where they are almost equal. For the standard deviation the situation is somewhat different, the values for the Kramers–Kronig method are smaller for the two lowest frequencies and more equal to those obtained by the Cole equation method for the two highest frequencies. This deviation can be explained by the systematic error contribution from the series truncation for the Kramers–Kronig method. The results obtained are however good for both calculation methods, with a preference for the results obtained by the Cole equation method. However, if a correction of 0.2°–0.3° could be used for the systematic error of the results from the Kramers–Kronig method, the picture would have changed.

From table 2 it is seen that the coefficient of determination R^2 gives generally high numbers for the Kramers–Kronig approach, while the Cole approach achieves a high coefficient of determination for the middle frequencies 50 and 100 kHz.

Figure 7 shows the comparison between the two approaches at each of the selected frequencies. As shown in figure 7(a), the Kramers–Kronig method tends to estimate with an offset on the negative side, significantly different from the Cole equation approach at the 50, 100 and 200 kHz frequencies. Comparing the approaches with respect to the absolute value of $\Delta\varphi$ as shown in figure 7(b), the Cole approach gives a significantly lower absolute deviation than the Kramers–Kronig approach for the 50 kHz and 100 kHz frequencies while the 5 kHz and 200 kHz yield no significant differences between the two approaches.

The multiple linear regression for the two approaches yielded a different dependence of $\Delta\varphi$ with respect to phase angle and frequency. The Cole $\Delta\varphi$ was significantly dependent on frequency ($p < 0.001$) as figure 7(a) indicates, but not on the phase angle ($p = 0.435$). The Kramers–Kronig $\Delta\varphi$ on the other hand was not significantly dependent on frequency ($p = 0.09$) but on the phase angle ($p < 0.001$).

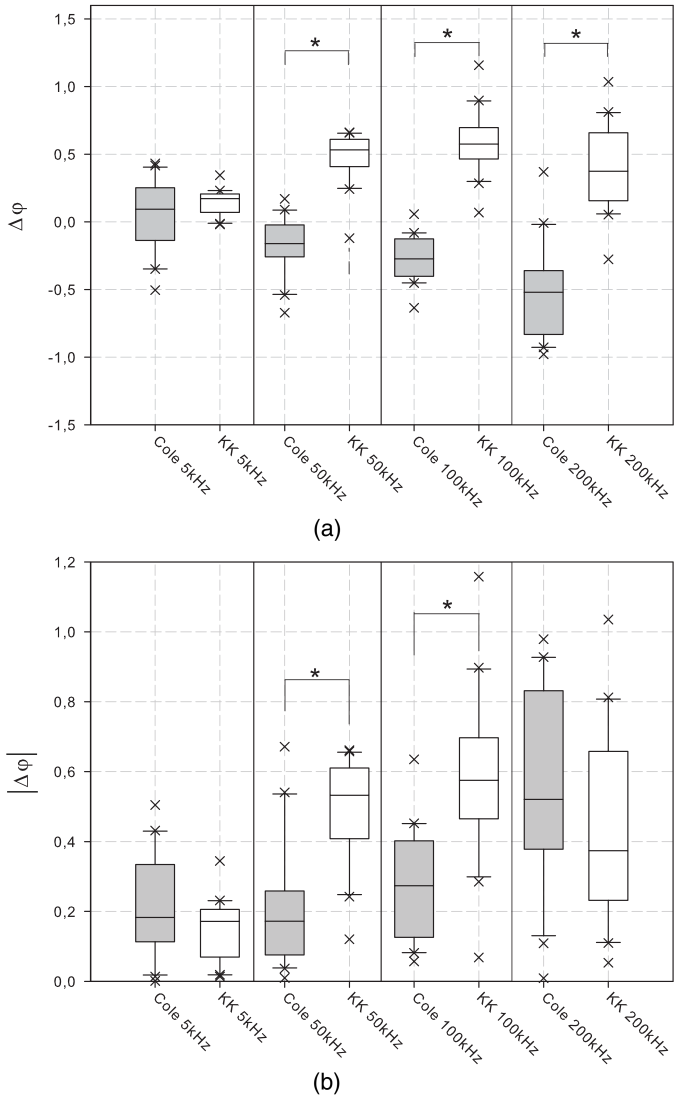

Figure 7. Boxplot for $\Delta\varphi$ in (*a*) and $|\Delta\varphi|$ in (*b*) for the Cole approach (gray boxes) and the Kramers–Kronig approach (white boxes) for each of the selected frequencies. $^*p < 0.05$.

Figure 8 shows $\Delta\varphi$ plotted against the mean phase angle values for all measurements. It is seen that the $\Delta\varphi$'s for the Kramers–Kronig approach show a significant dependence on the phase angle, while the Cole $\Delta\varphi$ looks more random.

The phase angle value gives important information on the health status represented by the barrier potential of the cell membranes. For healthy younger persons typical values at 50 kHz are around -8° for men and -7° for women (Barbosa-Silva *et al* 2005), with values decreasing with age. The phase angle has been found to be an indicator of survivability in several chronic conditions like HIV and lung cancer (Schwenk *et al* 2000, Toso *et al* 2005) to mention a few.

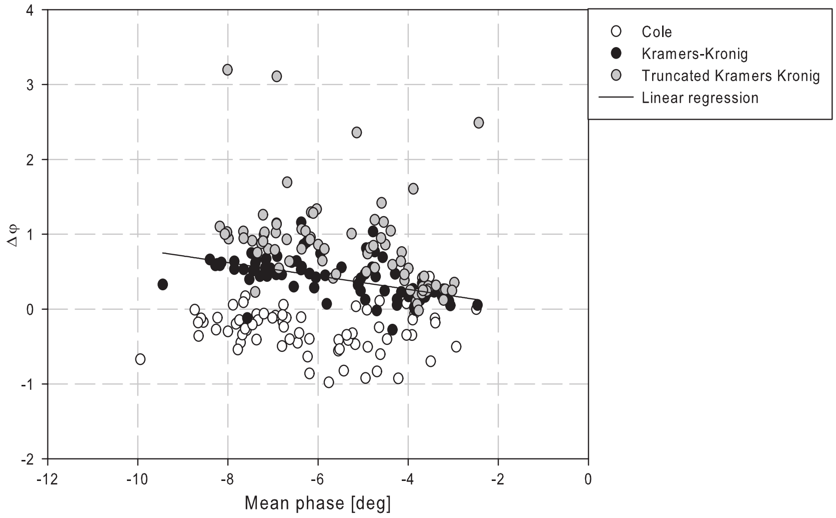

Figure 8. $\Delta\varphi$ for the Cole approach (white circles), the Kramers–Kronig approach (black circles) and the truncated Kramers–Kronig approach (gray circles) are plotted against the mean phase angle for all measurements. The Kramers–Kronig $\Delta\varphi$ was significantly dependent on the phase angle (multiple linear regression, $p < 0.001$). The straight line is a linear fit to the Kramers–Kronig $\Delta\varphi$.

5. Conclusions

It has been shown that the bioimpedance phase angle can be calculated from measured bioimpedance modulus values with good accuracy using both a Cole equation approach and a method based on the Kramers–Kronig relation. Comparing the calculated with the measured results and performing a statistical analysis involving all four frequencies it is found that the Cole equation method gives the most accurate results. This method also has the advantage that it requires measurements only at four frequencies (5, 50, 100 and 200 kHz). The Kramers–Kronig needs at least measurements up to 500 kHz to keep the truncation error contribution low. The Cole method also gives the four Cole parameters.

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