

Some Observations on Dynamical Modeling of Electrical Impedance Implemented to Human Skin

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Abstract.

Bio-electrical impedance spectroscopy (*EIS*) electrical signals of low power of human tissue, relatively low frequencies (up to 1 MHz), as well as non-invasive method is important to distinguish the physiological state of organisms. Modelling of electrical properties of human skin in the standard laboratory conditions is an open theoretical, practical and clinical problem. The purpose of this study is twofold: 1) The analysis and decision on possible options under the new biophysical models of its electric characteristics, based on discrete-continuous model of frequency scaling; 2) From the literature known concept of frequency dependent negative dynamic electrical resistance as used in the case of high frequency $\omega \rightarrow \infty$, bringing the total model considerably improves. Both objectives have in common that they stem from a dynamic approach to modeling material. To measure bioimpedance of the human skin was used instrument *1255* Frequency Response Analyser in combination with Solartron *1286* Pstat/Gstat, with suitable additional equipment. Due to the inadequacy of the software package *ZView*® for Windows in this case, for fitting data was used *Levmar*. Both packages are based on the Levenberg-Marquardt's nonlinear least squares algorithm. Mathematical and biophysical model presented as a unified continuous-discrete Cole - equation for impedance of the material. Measurements were done on human skin of the forearm, as the test system. The applied voltage is 1 V , interval of the source frequency is $[0.1\text{ Hz}, 100\text{ kHz}]$ and electrode diameters are 0.25 cm and 2 cm . In the paper shows that the standard continuous two- and three-component model of Cole bioimpedance human skin is fitted better than their discretized version, in all scales, for all the selected frequency steps. Assuming a negative value of active high-frequency electrical resistance, we have improved fit of the continuum model as compared to the previous continuous model about 10%. For here introduced the dynamic properties of the model, it is necessary to carry out as many new bio-medical and clinical analysis of different tissues.

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1. Introduction

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Electric models of human skin, based on *BEIS* can be conditionally divided into those low frequencies (up to 1 MHz) and at those high frequencies (above 1 MHz). These types of models are qualitatively different properties [1]. First works for *BEIS* of the human skin dating from the seventies and eighties [2], [3]. The importance of bioimpedance of the human skin can be seen from some works dedicated to this problem. With *BEIS* carry out research of normal and pathological conditions [4], [5], [6].

In the area of frequencies below 1 MHz , for the low voltage, human skin characterized by α - and β - dispersion [1]. From the standpoint of biophysics, it is understood as a passive, linear complex electrical element. The first of the above, α - dispersion, characteristic for the counterion effects (perpendicular or lateral) near the membrane surfaces, active cell membrane effects and gated channels, intracellular structures, ionic diffusion, dielectric losses for all membranes.

Second, β - dispersion, described properties of intracellular organelle membranes, passive cell membrane capacitance, Maxwell–Wagner effects, protein molecule response. Typical conductivity in the above frequency range of human skin 10^{-5} S/m , while the phase angle between current and voltage mainly around 30° .

Basic electrical models of human skin based on the Cole equation for impedance [2], [7], i.e. for weak ionic conductor, based on the element of constant phase *CPE* [1], on their generalization[8]⁸ and the memristor element in parallel with a *CPE* [9]. In the first on two cases (weak ionic conductor) have characteristic that there are two basic types of relaxation time: relaxation time charge carrier drift and relaxation time of the electric field in the material. The first time constant of the material is much smaller than the other, which means that the electric field remains longer in this poor electrical conductor, i.e., it has at least paraelectric characteristics. Memristor model the electrical behavior of the human skin, unlike the previous ones, nonlinear, and analysis by *BEIS* very difficult to implement. In addition, it is known that the electrical behavior of the biosystem significantly different from person to person [10]. That is why the possible two basic types of experiments; respectively, when the skin is understood as a test system for a model, and in groups, where on the basis of the parameters of this model analyzes the properties part of the population.

This paper proposes a procedure for testing a new model, based on the precepts of Hilger's timescales calculus [11]. The basic idea in this sense has that the frequency of the alternating current may be discretized-atomized, and to the degree a function of the frequency which is characterized by *CPE* replace factorial function. This factorial type function in some cases depending on time is the natural for biological / medical systems, such as growth or tumor cell populations [11], [12], but has not been studied variable step, except in the special case, theoretically, in the physics [13]. Also, this paper considers the possibility that he exists negative value of active high-frequency linear electrical resistance, which has not been the case. This conditions when it is possible to see in a book [14]. Both types of analysis, the one based on Hilger model, and one which is based on possibility of a negative active resistance, represent a dynamic characterization of the material. The first model is dynamic because of the description

of sudden changes. Second model also dynamic due to possible time dependence of appropriate frequency step.

2. Methods

When for describing the impedance used a new type of Fourier transformation, analogous to books Bochner [15] which is applied to the constitutive equations as in [8] (Eq. (44)). The time scale of this work is continuous, but frequency scale is discrete. Because generalized exponential function for this transformation does not have the classic characteristics [16], terms of generalized Fourier's sum or Fourier transformation, scalar product in an appropriate Hilbert's space are not mathematically based, and therefore can not be used results from [8] .

The standard model used for *BEIS* in the frequency range up to *1 MHz* – model of Serial connections of more Cole electrical components. The process of fitting is determined that other electrical schemes have a much higher values of mean nonlinear least squares (or, Mean squared error - *MSE*). The model discussed in this paper is described by the following equation

$$\underline{Z} = R_{\infty} + (R_0 - R_{\infty}) \cdot \sum_{k=1}^n \frac{p(\alpha_k)}{1 + (j\tau_{\alpha_k})^{\alpha_k} \omega_h^{(\alpha_k)}} \quad (1)$$

where: $R_0 = \lim_{\omega \rightarrow 0} R(\omega)$ is a static resistance: $R_0 \geq 0$; $R_{\infty} = \lim_{\omega \rightarrow \infty} R(\omega)$ is a high frequency active resistance, for which the following applies $R_{\infty} \in \mathbb{R}$; τ_{α_k} , $p(\alpha_k)$ is, respectively, the characteristic relaxation time of the material and the partial contribution of electrical resistance $R_0 - R_{\infty}$, for which the following conditions satisfied $\sum_{k=1}^n p(\alpha_k) = 1$ and $p(\alpha_k), \tau_{\alpha_k} \geq 0$; j - imaginary unit: $j^2 = -1$, while $\omega_h^{(\alpha_k)}$ is a factorial function of frequency of sources voltage ω step h and degree α_k , $k = 1, \dots, n$. We standard assume that $\alpha_k \in (0, 1]$. Function $\omega_h^{(\alpha)}$ is defined as follows

$$\omega_h^{(\alpha)} := h^{\alpha} \cdot \frac{\Gamma\left(\frac{\omega}{h} + 1\right)}{\Gamma\left(\frac{\omega}{h} + 1 - \alpha\right)}, \quad \alpha \in (0, 1]. \quad (2)$$

In the previous equation $\Gamma(\cdot)$ is Euler Gamma function. Also, important the following relations: $\omega_h^{(1)} = \omega$ and $\lim_{h \rightarrow 0^+} \omega_h^{(\alpha)} = \omega^\alpha$. Because of validity of past relation, frequency step satisfy $h \in [0, \infty)$. The case when $h \rightarrow 0^+$ defined a continuous variable $\omega \in (0, \infty)$, whereas for $h > 0$, $\omega_h^{(1)} \in h \cdot \mathbb{N}_0$ defined discrete frequency scale, with provided that $\omega_h^{(\alpha)}$ the function over her. Case when $h \rightarrow 0^+$ in (1) presents well-known continuous model of Serial connections of more Cole elements [7]. For $n=1$ he described one Cole element for that material, while $n=2,3$ corresponds, respectively, Serial connection with two and three Cole elements. Frequency step determined feature of materials which may be associated with some the living process in him. In the interval of the considered frequencies, we expected that in this case the procedure of finding the value of h makes sense. Step h check, along with the description model system, quality of laboratory conditions - the impact of equipment, radiation fields, temperature, humidity etc. In this paper, we discuss cases $n=2,3$ in Eq. (1) for following values of step h : $h \rightarrow 0^+$, $h=0.01, 0.1, 1, 10, 100$. Besides, the in the consideration of electrical to its impedance, and introducing $R_\infty \in \mathbb{R}$ a novelty. So far, it was considered that the $R_0, R_\infty \geq 0$ [1], [2].

Measurements of *BEIS* were of human skin performed at University of Belgrade, on upper arm of volunteer, with Solartron 1255 Frequency Response Analyzer in combination with Solartron 1286 Pstat/Gstat [18]. All devices are regularly calibrated. Experiments were done in shielded Faraday caged room. The linearity of all measurements with both electrode sizes was endorsed by testing the system with Solartron Schlumberger 12861 test module. The electrodes were made of stainless steel. We have used two types of electrodes: with diameter of 0.25 cm and 2.0 cm. The distance between outer edges of two electrodes was 5 cm (Fig.1.). The electrodes was completely covered of highly conductive cream (3.3 S/m) Grass EC33 obtained from Grass technologies. Total required time for the frequency sweep measurement was about 10 minutes at 22 °C and 50% relative humidity, thus, minimalizing artifacts production during measurements due to long cream exposure or cream penetration to skin, as well as sweating. Error of measurements was 0.1%. Twenty series of measurements were taken at each of the 61 different frequencies ranging between 0.1 Hz and 100.0 KHz: $\omega = 10^{v \cdot l}$ Hz, $l \in \{-10, -9, \dots, -1, 0, 1, \dots, 9, 10, 11, \dots, 49, 50\}$ and $v = 0.1$. Frequency uncertainty for devices is 100 ppm [8], [18]. Measured uncertainty devices is fixed, and, small steps values of h for low frequencies invisible for those of more. In other hand, the greater value of h , is a roughness for propound experimental conditions.

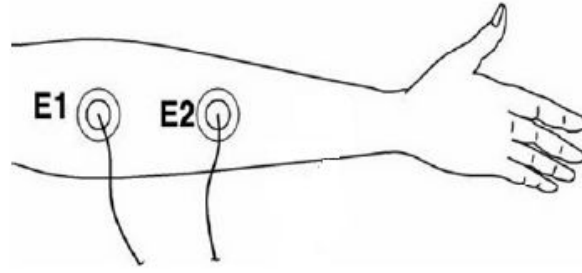


Fig. 1. Two-electrode system for *BEIS* human skin used in the experiments.

Levenberg-Marquardt algorithm (*LMA*) of nonlinear least squares L_2 , based on the use of L_2 norm in the propagation of errors, was used for fitting of experimental data. Precisely, was used Levmar package in Octave programming environment [19]. Without complications or this fitting calculation, we could use maximally 10 parameters. This restriction encourages the implementation of *LAPACK* libraries in *C/C++*. The main feature of this package is that with its use can determine the interval in which the values of each parameter. In practice, instead of an exact Jacobian \mathbf{J} -gradient, for *LMA* usually used iterative approximate formula for his computing, which significantly slows down computer functioning. The most common criteria for stopping this algorithm are: 1) *MSE*, for $\chi^2(\mathbf{p})$ less than a some positive number: $\chi^2(\mathbf{p})/(n-m+1) < \varepsilon_1$, n – number of data points, m – number of parameters; 2) parametric: $\max(h_j/p_j) < \varepsilon_2$; 3) gradient terminated: $|\mathbf{J}^T \mathbf{W}(\mathbf{y} - \hat{\mathbf{y}}(\mathbf{p}))| < \varepsilon_3$, ε_1 , ε_2 i ε_3 are the predetermined positive numbers (\mathbf{W} -diagonal matrix of weights - standard deviations; \mathbf{y} - vector of measured values, $\hat{\mathbf{y}}(\mathbf{p})$ - vector of values calculated on the basis of a parametric model of a certain parameter vector \mathbf{p}). In this work, of the above, we used the second criterion. In addition, due to the uncertainty of the absolute impedance measurement errors, the default is assumed $w_i = 1$ in \mathbf{W} , while the criterion of quality of fit sum of squares of deviations corrected by $1/(n-m+1)$. For different frequency scales do not have to be the same number of experimental points, nor the same $\chi^2(\mathbf{p})/(n-m+1)$. For higher values of h is possible to lower the values of the adjusted *MSE*. For each frequency step h - for defined scale, performed comparison between continuous and corresponding model. When we use greater values of h for the given data, this resulting mainly coarser scale and a smaller number of measurement results and lower quality modeling. Then $\chi^2(\mathbf{p})/(n-m+1)$ is generally not adequate measure of quality of fit.

3. Results and discussion

In the analysis of experimental data started to the analysis feature of the software. After that, all numerical procedures were first pilot-tested. In both cases, the two circular electrodes with a 0.25 cm diameter and 2.0 cm in the case of a serial connection of two elements Cole, was

compared Levmar and well-known software package ZView® for Windows [20] and achieved practically equal fitting result, where the relative differences in the parameter values were below $1 \cdot 10^{-6}$. Subsequently, in further analyzes, exclusively used Levmar.

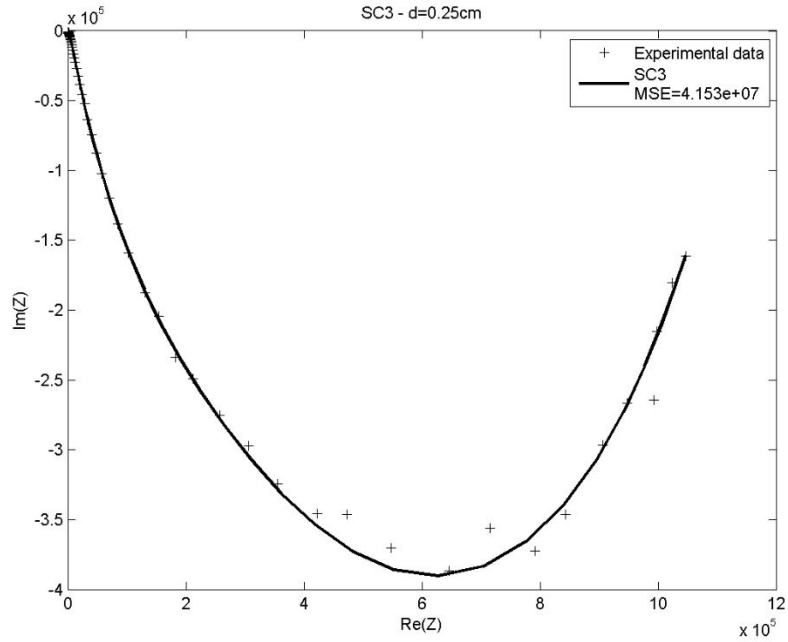


Fig.2. SC3, the best fitting function, for $d = 0.25 \text{ cm}$.

In the continuous case, the electrode diameter with a 0.25 cm and 2.0 cm , respectively, were the best fits in the case of a Serial connection of three elements Cole (SC3) and a Serial connection of two elements Cole - SC2 (see Fig.2. and Fig.3.).

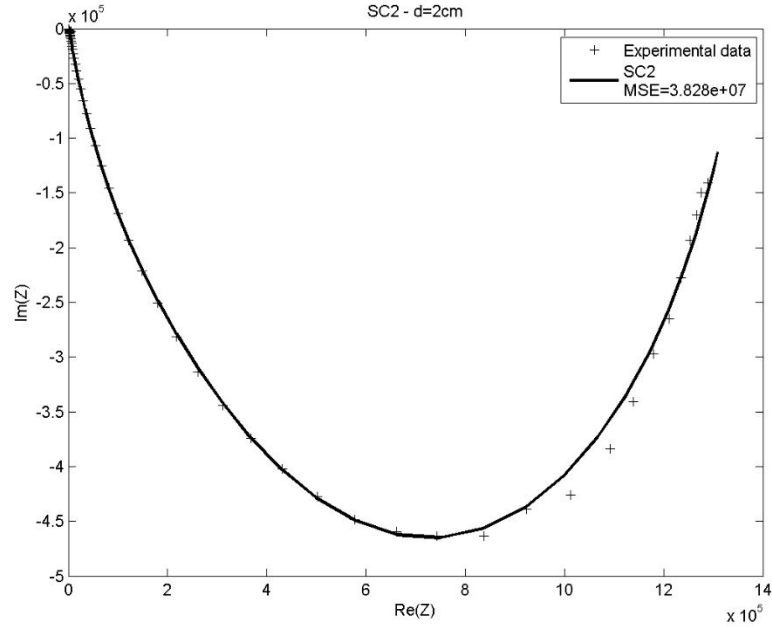


Fig.3. SC2, the best fitting function, for $d = 2.0 \text{ cm}$.

For the measurement results for the first electrode is characterized by the fact that, in case a better fit, the value of active resistance is negative: $R_{\infty} = -195 \Omega$ (Table 1). From the above follows that, there is a value of the frequency for which is $\text{Re}(Z) = 0 \Omega$. The values of the parameters accepted fit, for the second measurement electrode are standard.

Table 1

LMA Fitted Parameters for Impedance Models SC2, SC3

| 1.0 V, d = 0.25 cm | | | | 1.0 V, d = 2.0 cm | | | |
|----------------------------|-------|----------------------------|--------|----------------------------|-------|----------------------------|-------|
| Parameters | SC2 | Parameters | SC3 | Parameters | SC2 | Parameters | SC3 |
| R_0 (M Ω) | 1.118 | R_0 (M Ω) | 1.119 | R_0 (M Ω) | 1.352 | R_0 (M Ω) | 1.353 |
| R_{∞} (k Ω) | 1.911 | R_{∞} (k Ω) | -0.195 | R_{∞} (k Ω) | 1.718 | R_{∞} (k Ω) | 1.936 |
| α_1 | 0.743 | α_1 | 0.395 | α_1 | 0.784 | α_1 | 0.826 |
| τ_1 (s) | 0.266 | τ_1 (s) | 47.15 | τ_1 (s) | 0.110 | τ_1 (s) | 0.647 |
| $p(\alpha_1)$ | 0.267 | $p(\alpha_1)$ | 0.261 | $p(\alpha_1)$ | 0.200 | $p(\alpha_1)$ | 0.878 |
| α_2 | 0.851 | α_2 | 0.948 | α_2 | 0.831 | α_2 | 1.252 |

| | | | | | | | |
|---|-------|---------------|-------|---------------|-------|---------------|-------|
| τ_2 (s) | 1.414 | τ_2 (s) | 1.471 | τ_2 (s) | 0.687 | τ_2 (s) | 0.113 |
| $p(\alpha_2)$ | 0.733 | $p(\alpha_2)$ | 0.461 | $p(\alpha_2)$ | 0.800 | $p(\alpha_2)$ | 0.027 |
| | | α_3 | 0.807 | | | α_3 | 0.813 |
| | | $p(\alpha_3)$ | 0.278 | | | $p(\alpha_3)$ | 0.101 |
| | | τ_3 (s) | 0.295 | | | τ_3 (s) | 0.051 |
| Mean least sum of squared errors ($\cdot 10^7$) | 4.410 | | 4.153 | | 3.828 | | 3.829 |

Results comparing the corresponding continuous and discrete Cole - models for the various steps are reported in Table 2. Mean least sum of squared errors in all cases are underlined. The main feature of these comparisons is that in all cases continuous models have a lower value of that sums.

Table 2

Mean least sum of squared errors for Impedance Models SC2, SCDF2, SC3, SCDF3 for different frequency steps h

| 1.0 V, d = 0.25 cm | | | | | 1.0 V, d = 2.0 cm | | | |
|---|---------------|-------|--------------|-------|-------------------|-------|--------------|-------|
| Mean least sum of squared errors ($\cdot 10^7$) | | | | | | | | |
| h | SC2 | SC2DF | SC3 | SCDF3 | SC2 | SCDF2 | SC3 | SCDF3 |
| 0.001 | <u>4.410</u> | 6.708 | 4.153 | 4.330 | <u>3.828</u> | 5.166 | 3.829 | 3.986 |
| 0.01 | <u>4.410</u> | 6.573 | 4.153 | 31.27 | <u>3.828</u> | 4.272 | 3.829 | 607.1 |
| 0.1 | 13.75 | 7.248 | <u>4.636</u> | 39.03 | 332.0 | 5.468 | <u>1.414</u> | 384.2 |
| 1 | <u>0.2536</u> | 4.836 | 2.185 | 1.832 | 45.36 | 72.40 | <u>0.058</u> | 199.0 |
| 10 | 0.027 | 5.796 | <u>0.017</u> | 1.061 | <u>0.048</u> | 32.33 | 0.050 | 33.81 |
| 100 | <u>0.016</u> | 0.266 | 0.017 | 0.072 | 0.057 | 1.196 | <u>0.051</u> | 1.774 |

Even the original Cole's work [7] in the equation (1) is, in the case of a single Cole element ($n = 1$), when the frequency scale for alternating current is continuous, for the cell membrane

assumed instead $R_\infty - Z_\infty$ (complex number), in the first place, but not elsewhere, on the other side of equation. From the analogy of the Cole-Cole equation for the dispersion of the dielectric constant, for R_∞ is allowed to still be a positive number. In principle, it would be more precise to write in both sides Z_∞ , and then on the basis of established analogies, for the selenium semiconductor diode, allowing positive value of R_∞ , which means that the materials at higher frequencies have only conductive properties. The aforementioned statement is basically correct. However, since the nature of this resistance is such that he can have a real value, it is necessary to clarify what this actually means at this point. The solution for the previous problem, regardless of the type of model, when viewed microscopically, given system more complicated than the above semiconductor [21]. The main conclusion in that regard is: exists is an internal dynamic voltage sources in certain cells of the human skin, which, in this case, the induced AC power. Their nature is not known.

Also, regardless of the different biophysical explanation of constant $\alpha_1 = \alpha$ [1], relation (2), in relation to a continuous the degree function ω^α ($h = 0$), formally represented to deviation from the scaling properties of impedance in the frequency range, characteristic for CPE . Practically, this means for that the frequency scale, then the material was inhomogeneous, and has a lowest characteristic, atomic frequency. However, there is still a possibility and that type of model depends on the step h , for a given material. This means that for different minimal frequency "atoms" of the measuring instrument (or, for more or less accurate devices), models are changing. Just described function of changes is the characteristics of the material. For human skin is characteristic that the impedance models may vary depending on h , but all remain continuous. There is another feature of the skin that can be monitored, and it's a sign of electrical resistance R_∞ for optimal models in the Table 2. For the electrode diameter $d = 0.25$ cm, when for $h = 1, 10, 100$, these resistances are negative, order of magnitude $k\Omega$, whereas, for the second electrode, when the R_∞ negative resistance, her order of magnitude is $c\Omega$.

4. Conclusions

Dynamic effects of electromagnetic fields passing through human tissue possess significant complexity. In the area of small alternating voltage of the human skin, that is, in this case, is reflected in existence of the high frequency negative resistance for adequate continuous models, which appears in different frequency sources coarsened. This also establishes the possibility of the existence of internal active power source. These results can be the basis for a new characterization of the physiological state of the human skin in different conditions.

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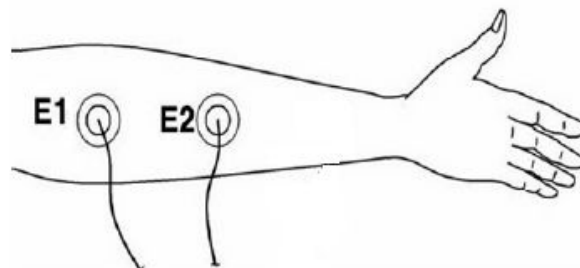
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Fig. 1. Two-electrode system for *BEIS* human skin used in the experiments.

Fig.2. *SC3*, the best fitting function, for $d = 0.25$ cm.

Fig.3. *SC2*, the best fitting function, for $d = 2.0$ cm.



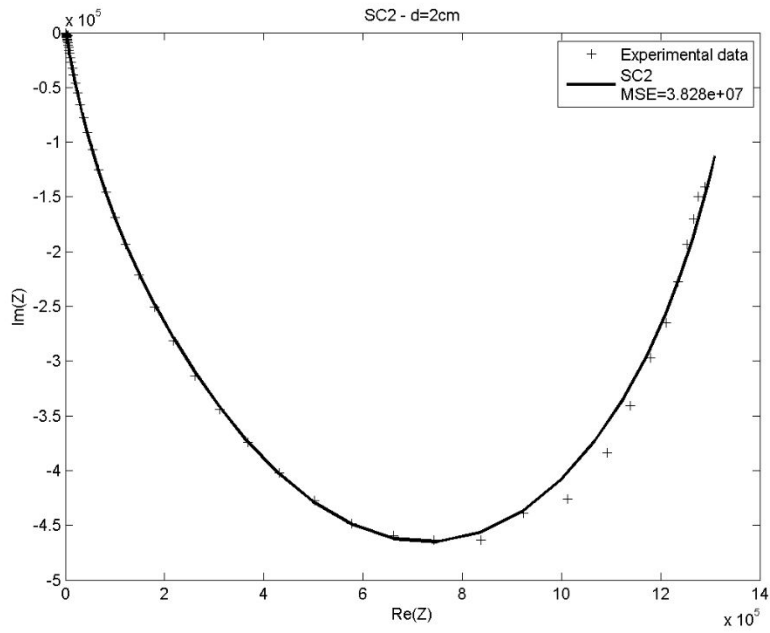
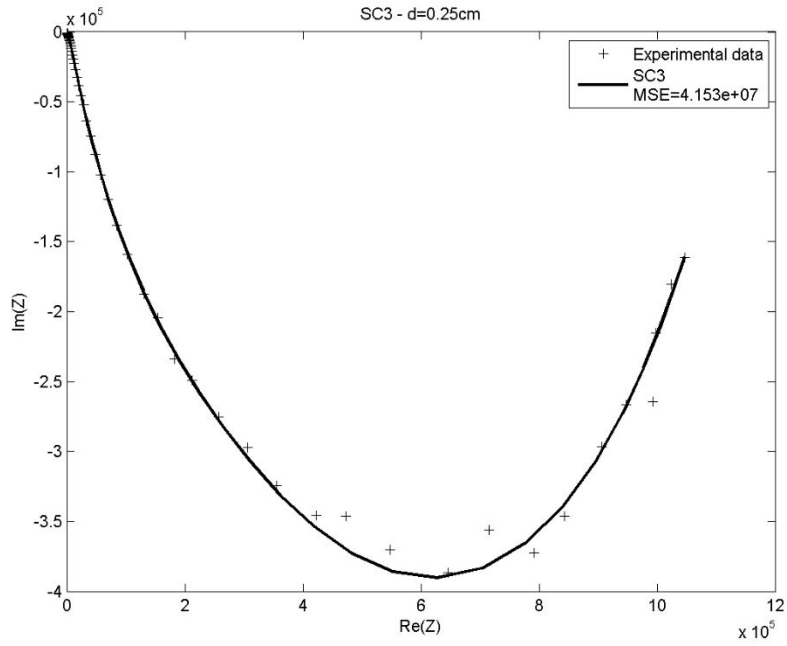


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| 1 | <u>0.2536</u> | 4.836 | 2.185 | 1.832 | 45.36 | 72.40 | <u>0.058</u> | 199.0 |
| 10 | 0.027 | 5.796 | <u>0.017</u> | 1.061 | <u>0.048</u> | 32.33 | 0.050 | 33.81 |
| 100 | <u>0.016</u> | 0.266 | 0.017 | 0.072 | 0.057 | 1.196 | <u>0.051</u> | 1.774 |