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Modeling of Bioimpedance for Human Skin Based on Fractional Distributed-Order Modified Cole Model

Electrical impedance measurement data and fractional calculus have been utilized for modeling bioimpedance properties of human skin. We introduced and proposed revisited Cole model using modified distributed-order operator based on the Caputo-Weyl fractional derivatives. Our proposed model presents essentially modified single-dispersion Cole model, since it introduces a new parameters k and σ in single-dispersion Cole impedance equation. These parameters characterize the width of interval around fractional index α and they are important for more accurate describing bioimpedance properties of human skin. The impedance spectrum was measured in a finite frequency range up to 100 kHz. Our proposed modified Cole model fits much better to experimental curve in a given frequency range compared to existing Cole models. The fitting is done using the Levenberg-Marquardt nonlinear least squares.

Keywords: *human skin, fractional calculus, Cole model, frequency analysis, electric impedance.*

1. INTRODUCTION

Bioelectro-physical properties of human skin tissue, like most other soft tissues, exhibit electrical behavior [1],[2]. To obtain complete information about the electrical behavior of human skin, it is also necessary to have experimental data over a wide range of time scales.

If electricity is applied from an external source outside the living organism, we can measure bio-impedance. To analyze the skin impedance effectively, it is very desirable to introduce the skin impedance model. Also, the complex modulus concept is a powerful and widely used tool for characterizing the electrical behavior of materials in the frequency domain. In this case, according to the proposed concept, bioimpendance moduli can be regarded as complex quantities [3]. In the *BIS* technique impedance, measurements are done at each frequency, and then plotted forming a circular arc [3]. Using electrical modeling mathematics, the points on a circular arc can be transformed into an equivalent electrical model where the values correspond to specific compositional elements.

On the other hand, the theory of fractional calculus is a well-adapted tool to the modelling of many physical phenomena, allowing the description to take into account some peculiarities that classical integer-order model simply neglect. The importance of fractional order mathematical models is that they can be used to produce a more accurate description, and so give a deeper insight into the physical processes underlying long range memory behaviors. From mathematical point of view, the fractional integro-differential operators (*fractional calculus)* [3],[4],[5],[6], are a generalization of integration and derivation to non-integer order (fractional) operators.

Particularly, a memory function equation, scaling relationships and structural–fractal behavior of biomaterials and mathematical model based on fractional calculus, were used for the physical interpretation of the Cole-Cole (Cole) exponents [1],[3],[7]. As it is a well-known, three expressions for the impedance allow one to describe a wide range of experimental data: Cole–Cole function, Cole–Davidson function and Havriliak–Negami function [1],[2],[8],[9].

According to literature data, the skin is usually observed as a relative simple structure, and equivalent electrical model of skin doesn't include tissue lamination. Such relaxation processes occur because the epidermis is a mosaic in which layers of laminated, inhomogeneous cell structure pile up on top of one another. Frequency-dependent components such as *CPE* (constant phase element), that exists in the single-dispersion Cole model, can be considered as composed of an infinite number of lumped components. Based on this fact, some authors [10] have replaced the ideal capacitor in the Debey model by the *CPE* in modeling the layers of the stratum corneum. Cole impedance model was used to analyze human and rabbit irritated skin [9]. Not only the Cole distribution, but also any log normal distribution of relaxation times will produce curves which are indistinguishable from depressed circular arcs [14]. Measured data may represent contributions from electrode polarization, stratum corneum, sweat ducts and deeper tissue, and furthermore several dispersions of some of these components. Only one-dispersion Cole impedance equation is shown for the electrode polarization although two dispersions have been found in some studies [15]. The stratum corneum is dominated by one

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broad dispersion [16] and the sweat ducts may exhibit dispersion due to countering relaxation [17]. In [18] different Cole impedance behavior of materials models are described: layer models (series layer model, parallel layer model, brick layer model, …) and effective medium models. In relation to our experimental in vivo conditions, structure and complexity of the considered system - human skin, we decided to have its electrical behavior described by the series layer Cole model. In this paper, we propose the skin structure as a more complex system, consisting of several layers. We obtain the mathematical model of skin structure applying fractional calculus, which describes a series of structures via new generalizing the Cole impedance equation. According to this model and experimental data of the skin bioimpedance measurements, one may predict more complex equivalent electrical circuit. In approximation, the new interval single-dispersion Cole model, better describes electrical behavior of human skin in the sense as a one-dispersion Cole model. In addition, it best describes the electrical properties of human skin to high-frequency source of alternating current.

2. CONTINUOUS FRACTIONAL DERIVATIVE MODEL OF HUMAN SKIN

2.1 Some Basic Results Related to Cole and Cole-Cole equation

In paper [19], it was showed that the capacitive component of the polarization admittance–dielectric information is the proper electrical component to monitor the material as an insulator or semiconductor. The electrical impedance method was used as a quantitative technique for evaluating changes in the skin. Dielectric information, in general, may be presented in a number of equivalent ways and it is important to use the most appropriate form of presentation to suit particular requirements. The following principal dielectric functions may be defined:

(a) the complex permittivity $\varepsilon^*(\omega)$ and susceptibility $\chi^*(\omega)$, for frequency $\omega \in (0,\infty)$,

$$\chi^*(\omega) = \frac{\left[\varepsilon^*(\omega) - \varepsilon_\infty\right]}{\varepsilon_0} = \chi'(\omega) - j\chi''(\omega),\ j^2 = -1 \quad (1)$$

where ε_0 is the permittivity of free space, and ε_∞ is a suitable high-frequency permittivity contributing to the real and imaginary components of the polarization.

So, Debye, Cole–Cole, Cole-Davidson and Havriliak–Negami functions are presented as follows:

$$\chi^*(\omega)\big|_{\mathrm{D}} = \frac{\chi_0}{1 + j\cdot\omega/\omega_p}$$

$$\chi^*(\omega)\big|_{\mathrm{C\text{-}C}} = \frac{\chi_0}{1 + \left(j\cdot\omega/\omega_p\right)^\alpha} \quad (2)$$

$$\chi^*(\omega)\big|_{\mathrm{C\text{-}D}} = \frac{\chi_0}{\left(1 + j\cdot\omega/\omega_p\right)^\nu}$$

$$\chi^*(\omega)\big|_{\mathrm{G\text{-}N}} = \frac{\chi_0}{\left(1 + \left(j\cdot\omega/\omega_p\right)^\alpha\right)^\nu}$$

Here, χ_0 is constant, $\omega_p = 1/\tau_\alpha \geq 0$ is the loss peak frequency, τ_α denotes characteristic damped time, $0 < \alpha,\nu \leq 1$.

The experimental data show that α and ν are strictly dependent on temperature, structure, composition and other controlled physical parameters [19]. The α and ν were discussed as the parameters of the distribution of the relaxation times or mentioned as broadening parameters without further discussion.

For $\alpha = 1$ in the Cole-Cole function one can obtain the Debye function (2). The Cole-Cole equation described by means of permittivity [20] is

$$\varepsilon^* = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + \left(j\cdot\omega\cdot\tau_{1-\alpha}\right)^{1-\alpha}} \quad (3)$$

where ε_s is the static permittivity of material. The above equation for human skin is discussed in [21] for interval of frequencies below 100 Hz. One of them, the Cole impedance model (for the specific electrical resistance) was introduced in its final form [22], by introducing *CPE*. In [3], *CPE* is shown in the equivalent fractional circuit diagrams (Fig. 1).

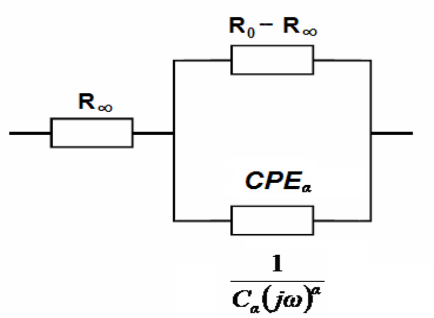

Figure 1. Equivalent circuit single-dispersion fractional Cole model

The papers [2],[7] present the circuit which was used to model the skin, and after some adaptation it will be applied for this study. A complex impedance of the system is (Cole equation for single-dispersion model)

$$\underline{Z}_\alpha(\omega) = R_\infty + \frac{R_0 - R_\infty}{1 + \left(j\cdot\omega\cdot\tau_\alpha\right)^\alpha} \quad (4)$$

where R_0 denotes a low-frequency resistor and R_∞ is a high-frequency resistor, $\alpha \in (0,1]$ is fractional *CPE* exponent-index. For $\alpha \to 0$, $\underline{Z}_\alpha(\omega) \to R_0$. In [3] equation for τ_α is (C_α is a fractional order capacitance)

$$\tau_\alpha = \sqrt[\alpha]{\left(R_0 - R_\infty\right)\cdot C_\alpha} \quad (5)$$

This constant represents relaxation time constant. Fig. 2 shows the equivalent circuit for the impedance of general dispersion model (called “non-Cole” model) presented in [2] and [10].

G_{var} means the added conductor causes the locus to be circular arc with a characteristic time constant τ_Z and frequency ω_c corresponding to the apex of the arc (similar to ω_p).

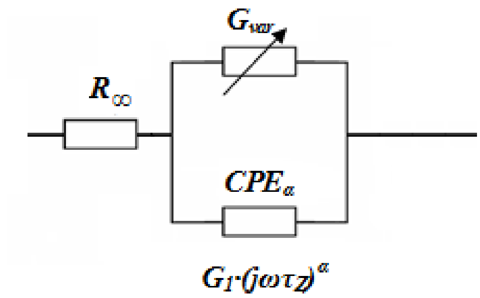

Figure 2. Dispersion model in accordance with relaxation theory (6), impedance model

In presented model $G_{\text{var}} = (R_0 - R_\infty)^{-1}$, G_1 is a conductivity at $\omega \cdot \tau_Z = 1$ in $G_{CPE} = G_1 \cdot (\omega \cdot \tau_Z)^\alpha$ for augment the Fricke circuit element CPE_F to a CPE_F corresponding to a given dispersion model. Equation for this empirical model is

$$\underline{Z}_\alpha(\omega) = R_\infty + \frac{1}{G_{\text{var}} + G_1 \cdot (\text{j} \cdot \omega \cdot \tau_Z)^\alpha} \tag{6}$$

If $G_1 = G_{\text{var}}$, (6) is equivalent to (4) and $\tau_\alpha = \tau_Z$ in (5). Otherwise

$$\frac{1}{C_\alpha \cdot (\text{j} \cdot \omega)^\alpha} = \frac{1}{G_1 \cdot (\text{j} \cdot \omega \cdot \tau_Z)^\alpha} \tag{7}$$

valid from

$$\begin{aligned} \tau_Z &= \sqrt[\alpha]{\frac{C_\alpha}{G_1}} \\ \tau_\alpha &= \tau_Z \cdot \sqrt[\alpha]{\frac{G_1}{G_{\text{var}}}} = \sqrt[\alpha]{\frac{C_\alpha}{G_{\text{var}}}} \end{aligned} \tag{8}$$

The second relation in (8) corresponds to expression (5). Both models are equivalent and they are given by (4) and (6). Dielectric and conductive properties of the material, described respectively by single-dispersion Cole-Cole and Cole model are in some sense mutually dual. The first model is described in literature [2],[3] by using a electrical circuit *2C-1R*, while the other is described by *2R-1C*. Single-dispersion Cole-Cole model, and serial based on this models, however, is much more studied. In this paper it will be used single-dispersion Cole model, where (4) is the basis for considering more complex models.

2.2 Distributed-order Cole model

The idea of fractional calculus has been known since the development of the regular calculus, with the first reference probably being associated with Leibniz and L'Hospital in 1695. Only in the last few decades scientists and engineers have realized that such fractional differential equations provided a natural framework for the discussion of various kinds of questions modelled by fractional differential equations and fractional integrals, i.e. they provide more accurate models of systems under considerations. Fractional derivatives provide an excellent instrument for the description of hereditary properties of various materials and processes [3],[4],[5]. At first, one can generalize the differential and integral operators into one fundamental ${}_{t_0}\text{D}_t^\alpha$ operator which is known as fractional calculus [4]:

$${}_{t_0}\text{D}_t^\alpha = \begin{cases} \dfrac{\text{d}^\alpha}{\text{d}t^\alpha}, & \alpha > 0 \\ 1, & \alpha = 0 \\ \int_{t_0}^{t} (\text{d}\tau)^{-\alpha}, & \alpha < 0 \end{cases} \tag{9}$$

Let $f \in L([t_0, t_1])$ and α>0 [6], behalf, in left Riemann-Liouville integral of *f(t)* of fractional order α which is:

$${}^{RL}_{t_0}\text{I}_t^\alpha f(t) := \frac{1}{\Gamma(\alpha)} \int_{t_0}^{t} (t - t')^{\alpha - 1} f(t')\text{d}t' \tag{10}$$

where $\Gamma(.)$ is the well known Euler's gamma function. For the initial moments $t_0 = -\infty$ usually refers to integral as *a left Weyl fractional integral* of order $\alpha \in (0,1]$. Also, *left Riemann-Liouville* and *Caputo derivative* of $f(t)$ of order α, can be presented as follows, $\alpha \in [0,1)$:

$$\begin{aligned} {}^{RL}_{t_0}\text{D}_t^\alpha f(t) &= \frac{\text{d}}{\text{d}t}\left({}^{RL}_{t_0}\text{I}_t^{1-\alpha} f(t) \right) \\ &= \frac{1}{\Gamma(1-\alpha)} \frac{\text{d}}{\text{d}t} \int_{t_0}^{t} (t - t')^{-\alpha} f(t')\text{d}t' \end{aligned} \tag{11}$$

$${}^{C}_{t_0}\text{D}_t^\alpha (f(t)) := {}_{t_0}\text{I}_t^{1-\alpha} f'(t) \tag{12}$$

In the case $t_0 = -\infty$, expression (12) represents *a left Weyl fractional derivative* (in turn, *Riemann-Liouville-Weyl* and *Caputo-Weyl derivative*). Beside linearity and derivative of the constant is zero, a left Caputo-Weyl fractional derivative has following characteristics [5], which are used in this paper $f(t) = C \cdot \exp(s \cdot t)$, $\Re(s) = 0$, $s = \text{j} \cdot \omega$

$${}^{CW}_{-\infty}\text{D}_t^\alpha f(t) = (s)^\alpha \cdot f(t) \tag{13}$$

In addition [6],

$${}^{CW}_{-\infty}\text{D}_t^0 f(t) = f(t) \tag{14}$$

Also, the initial conditions problems of fractional differential equations which were compared to the given fractional derivatives, were considered in paper [23]. In line with recent work, if the input or output system known as in our case, it is possible to calculate physically acceptable initialization function.

The Caputo derivative was used as the initial moment $t_0 = 0$, but was not usable for distant initial moments t_0=-∞, as Caputo-Weyl's, which was used to describe harmonic processes in this work.

In terms of single frequency electrical circuits in *BIS*, the Cole equation determines behavior of the biological tissue [9], [24] especially for some points of the human skin [25]. The parameters of impedance were obtained from an electrical impedance system based on current response to a voltage step excitation. If we connected the complex alternating - oscillating voltage to the same electric circuit in the shape of $V(t) = V_0 \cdot \exp(\mathrm{j} \cdot \omega \cdot t + \theta)$, Caputo-Weyl derivative can be used, (V_0 is the voltage amplitude, ω is the source frequency, θ is the phase angle between the voltage and the current on time). Then, if the depending of the electric current of amplitude i_0 and is introduced as $i(t) = i_0 \cdot \exp(\mathrm{j} \cdot \omega \cdot t)$, it yields (the sign "||" for the parallel connection of complex resistance)

$$\underline{Z}_\alpha(\omega) = R_\infty + (R_0 - R_\infty) \,||\, \frac{1}{(\mathrm{j} \cdot \omega)^\alpha \cdot C_\alpha} \tag{15}$$

Then (6) which describes the electric Cole circuit which is influenced by the aforementioned alterating voltage, actually modells the system consisting of orderly connection of resistance R_∞ and reduced Cole element $(R_0 - R_\infty)||C_\alpha (\mathrm{j}\omega)^\alpha$, for the given dispersion model. Knowing that, according to (13) behavior of fractional Caputo-Weyl derivatives

$$V(t) = \widehat{\underline{Z}}_\alpha i(t) \tag{16}$$

Cole operator $\widehat{\underline{Z}}_\alpha$ it is

$$\widehat{\underline{Z}}_\alpha = R_\infty + \frac{(R_0 - R_\infty)}{1 + (\tau_\alpha)^\alpha \cdot \left({}_{-\infty}^{CW}\mathrm{D}_t^\alpha \right)} \tag{17}$$

It's action is described by the equation

$$\left(1 + (\tau_\alpha)^\alpha \cdot \left({}_{-\infty}^{CW}\mathrm{D}_t^\alpha \right)\right) V(t) = \left(R_\infty \cdot (\tau_\alpha)^\alpha \cdot \left({}_{-\infty}^{CW}\mathrm{D}_t^\alpha \right) + R_0 \right) i(t) \tag{18}$$

In this paper it is suggested the generalization of the previous Cole model based on (6) in skin case. The basic suppositions for which this generalization is done are that there are neither inductive resistances, nor active or nonlinear elements, serially or parallely connected. In that case, the skin is, in the electric sense, taken as serially continually many connected non-interactive, linear, reduced Cole elements $p(\alpha)\cdot(R_0 - R_\infty) ||C_\alpha(\mathrm{j}\cdot\omega)^\alpha$ and one R_∞ (Fig. 3). Resistance $p(\alpha)\cdot(R_0 - R_\infty)$ characterized each individual reduced Cole element, where $p(\alpha)$ is a real non-negative function; $\tau_\alpha, 0 < \alpha \le 1$ are corresponding time relaxation constants, as a non-negative function of α: $\tau_\alpha = \left(C_\alpha \cdot p(\alpha) \cdot (R_0 - R_\infty)\right)^{1/\alpha}$. The equivalent total impedance $\underline{Z}_C(\omega)$ of this new electric circuit is given by the equation

$$\underline{Z}_C(\omega) = R_\infty + (R_0 - R_\infty) \cdot \int_{0^+}^{1} \frac{p(\alpha) \cdot \mathrm{d}\alpha}{1 + (\mathrm{j} \cdot \omega \cdot \tau_\alpha)^\alpha} \tag{19}$$

or, this expression (19) is the *continuous generalization of the Cole equation.*

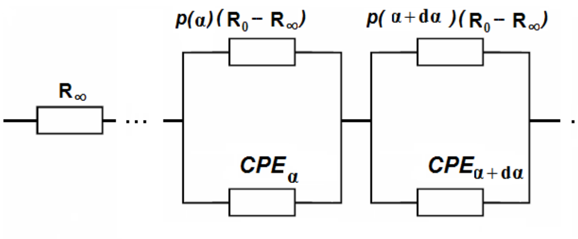

Figure 3. Electrical continuum model of the skin, based on the Cole equation, p(α) is a fraction of (R_0 - R_∞).

For $\omega \to 0^+$, condition of normalization of non-negative function $p(\alpha)$ is

$$\int_{0^+}^{1} p(\alpha) \cdot \mathrm{d}\alpha = 1 \tag{20}$$

Mathematically speaking, (19) corresponds to the application of continually many derivatives in general sense, which have distributed-order model, [26]. If we define the normalized Cole operator

$$\widehat{\underline{Z}}_{\alpha,N} = \frac{\widehat{\underline{Z}}_\alpha - R_\infty}{R_0 - R_\infty} = \frac{1}{1 + (\tau_\alpha)^\alpha \cdot \left({}_{-\infty}^{CW}\mathrm{D}_t^\alpha \right)} \tag{21}$$

Acting on the function and *i(t)*, so that the result of the function *V(t)*

$$V(t) = R_\infty \cdot i(t) + (R_0 - R_\infty) \cdot \widehat{\underline{Z}}_{\alpha,N} i(t) \tag{22}$$

If

$$\left(1 + (\tau_\alpha)^\alpha \cdot \left({}_{-\infty}^{CW}\mathrm{D}_t^\alpha \right)\right) V(t) = \left(R_\infty \cdot (\tau_\alpha)^\alpha \cdot \left({}_{-\infty}^{CW}\mathrm{D}_t^\alpha \right) + R_0 \right) i(t) \tag{23}$$

Then (19) corresponds to the operator

$$\widehat{\underline{Z}}_c = R_\infty + (R_0 - R_\infty) \cdot \int_{0^+}^{1} p(\alpha) \cdot \widehat{\underline{Z}}_{\alpha,N} \cdot \mathrm{d}\alpha \tag{24}$$

acting in a manner analogous described by (16). On other hand, assuming

$$\frac{p(\alpha)}{1 + (j \cdot \omega \cdot \tau_\alpha)^\alpha} \to \sum_{i=1}^{n} \frac{p(\alpha_i)}{1 + \left(\mathrm{j} \cdot \omega \cdot \tau_{\alpha_i}\right)^\alpha} \cdot \delta(\alpha - \alpha_i) \tag{25}$$

(19) reduces to

$$\underline{Z}(\omega) = R_\infty + (R_0 - R_\infty) \sum_{i=1}^{n} \frac{p(\alpha_i)}{1 + \left(\mathrm{j} \cdot \omega \cdot \tau_{\alpha_i}\right)^{\alpha_i}} \tag{26}$$

and represent discrete series of reduced Cole elements and R_∞.

2.3 Discrete approximation of a distributed-order Cole model

One of the main difficulties when using the distributed model is the large number and functionality of the distribution of material constants depending on the fractional index in relation to the number of experimental data. Some of the major solutions to this problem are given in advance of their functional dependence of the fractional indices and/or approximation of the integral of the operator based on fractional derivatives its integral sum. In this paper proposes a new approach based on approximation of linear combinations of delta by disjunct intervals $p_\delta(\alpha)$ - $p_\delta(\alpha) \to p_{\delta;appr}(\alpha)$ in (25) and its application in the (19). Parameters σ_i, $i \in \{1,...,n\}$, define the length of each disjoint intervals $U_{\alpha i}(\sigma_i) \subset (0,1]$ ($\alpha_i \in U_{\alpha i}(\sigma_i)$) and k_i points their position in relation to an fractional indices $\alpha_i^* \in U_{\alpha i}(\sigma_i)$.

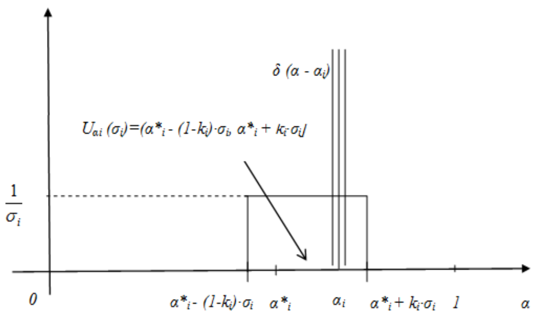

Figure 4. Approximation (25) and (26)

The value of the integral (19) outside these intervals is equal to zero. Within these intervals assumes that existing of a common value, due to their connection, of $p\left(\alpha_i^*\right)$ and $\tau_{\alpha^*_i}$. Explicitly

$$\frac{p(\alpha)}{1+(\mathrm{j}\cdot\omega\cdot\tau_\alpha)^\alpha}\cdot\delta(\alpha-\alpha_i)|_{U_{\alpha_i}(\sigma_i)} \to$$

$$\frac{1}{\sigma_i}\frac{p\left(\alpha_i^*\right)}{1+\left(\mathrm{j}\cdot\omega\cdot\tau_{\alpha_i^*}\right)^\alpha}|_{U_{\alpha_i}(\sigma_i)}, \; p\left(\alpha_i^*\right)\geq 0$$

$$U_{\alpha_i}(\sigma_i)= \tag{27}$$

$$\left(\alpha_i^*-(1-k_i)\cdot\sigma_i,\alpha_i^*+k_i\cdot\sigma_i\right]\subset(0,1], k_i\in[0,1], \sigma_i>0$$

$$\tau_{\alpha_i^*}=\left(C_{\alpha_i^*}\cdot p_{\alpha_i^*}\cdot(R_0-R_\infty)\right)^{1/\alpha_i^*}$$

Altogether (28)

$$\underline{Z}_{c;appr}(\omega)=R_\infty+(R_0-R_\infty)\cdot$$

$$\sum_{i=1}^{n} p(\alpha_i^*)\cdot\left(1-\frac{1}{\sigma_i\cdot\ln\left(\mathrm{j}\cdot\omega\cdot\tau_{\alpha_i^*}\right)}\cdot\ln\left(\frac{1+\left(\mathrm{j}\cdot\omega\cdot\tau_{\alpha_i^*}\right)^{\alpha_i^*+k_i\cdot\sigma_i}}{1+\left(\mathrm{j}\cdot\omega\cdot\tau_{\alpha_i^*}\right)^{\alpha_i^*-(1-k_i)\cdot\sigma_i}}\right)\right)$$

is multiple dispersion approximation (modification) of distributed-order of the Cole equation, and beside condition $\omega\to 0^+$

$$\sum_{i=1}^{n} p\left(\alpha_i^*\right)=1 \tag{29}$$

In (28), if $(\forall i)(\sigma_i \to 0)$ then $p_{\delta;appr}(\alpha)\to p_\delta(\alpha)$.

The meaning of parameters σ_i and k_i is that if the intervals are short length, the better the approximation of discrete Cole element in relation to the type of distributed model. Eq. (28) described a model for the finite number of material constants in the experiment may, in principle, decide on the type of model and approximated in the case of continuous approximation, the size and position of interval fractional indices. Within a specified interval index $U_{\alpha_i}(\sigma_i)$ is possible simultaneous existence of Cole model discrete and distributed type.

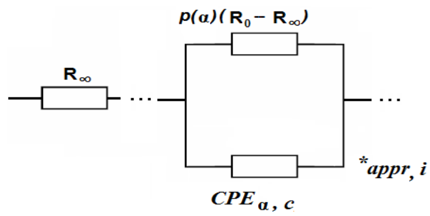

Figure 5. Modified electrical continuum model of the skin, based on Cole equation, $p\left(\alpha_i^*\right)$ is a fraction of (R_0-R_∞)

The model described by (28) is determined by the system of series complex elements and resistance R_∞. Each of these elements is a complex combination compared to a parallel connection between the $CPE_{\alpha_i^*}$ and $p_{\alpha_i^*}(R_0-R_\infty)$. Complex elements are, in mathematical terms, a consequence of approximation of continuous Cole model. Analogously, (24) is

$$\widehat{\underline{Z}}_{c,appr}=R_\infty+(R_0-R_\infty)\cdot\sum_{i=1}^{n} p\left(\alpha_i^*\right)\cdot\widehat{\underline{Z}}_{\alpha_i^*,appr,N} \tag{30}$$

with

$$\widehat{\underline{Z}}_{\alpha_i^*,appr,N}=1-$$

$$\frac{1}{\sigma_i\cdot\ln\left(\tau_{\alpha_i^*}\cdot{}^{CW}_{-\infty}\mathrm{D}_t^1\right)}\cdot\ln\left(\frac{1+\left(\tau_{\alpha_i^*}\right)^{\alpha_i^*+k_i\cdot\sigma_i}\cdot{}^{CW}_{-\infty}\mathrm{D}_t^{\alpha_i^*+k_i\cdot\sigma_i}}{1+\left(\tau_{\alpha_i^*}\right)^{\alpha_i^*-(1-k_i)\cdot\sigma_i}\cdot{}^{CW}_{-\infty}\mathrm{D}_t^{\alpha_i^*-(1-k_i)\cdot\sigma_i}}\right) \tag{31}$$

This operator is not linear, and its effect on the respective function is reduced to the application of (28). Analogously, it can describe the dielectric properties of materials.

3. MATERIALS AND METHODS

The proposed experimental method uses a two-electrode technique with a constant amplitude sinusoidal voltage. The skin of the upper arm impedance mesaurement was carried out in twenty healthy young men under laboratory conditions. The electrodes were made of stainless steel, diameter 2.0cm and the distance betwen the electrodes was 5.0cm. The electrode paste used was

a cream (*EC* 33 skin conductance). The measuring system Solartron 1255 Frequency Response Analyser in combination with Solartron 1286 Pstat/Gstat was used for measuring the components of impedance and charactericts frequency of the skin in the frequency range of 0.1 Hz to 100.0 kHz. Measurements were taken at 61 different frequencies betwen 0.1 Hz and 100.0 kHz and the applied voltage amplitude was 1.0 V.
Total required time for the frequency sweep measurement twenty times, was about 10 minutes.

The fitting method used in this paper, in the Octave programming environment are well known Levenberg-Marquardt nonlinear least squares algorithms L2 (L_2-norm) - further marked with LM [27],[28],(Fig.6). The largest number of parameters in this calculation can be used without complications was ten. This restriction encourages the implementation of LAPACK libraries in *C/C++*. So, to the single-dispersion Cole (n=1 in (26)) model was adequate, the expected boundary value of new parameter σ should be very small compared to α for single-dispersion interval Cole model (n=1 in (28)). Also, for smaller values of σ from a boundary all the other parameters should be approximately equal to the corresponding parameters. Otherwise, when the available distributed-order Cole model (19) or discrete model (n>1 in (26)), for larger values of σ from the boundary, the values of other parameters should be approximately equal to the corresponding parameters and the numerical value of the sum of squares of absolute values of difference fitting and experimental values is smaller than the corresponding values in the single-dispersion Cole model.

4. RESULTS AND DISCUSSION

One of the main issues bioimpedance current at frequencies below 500 kHz is that the Cole model adequate to describe the electrical characteristics of the system, [29]. However, in the literature there are models that describe the bioelectrical properties of the skin with two or more of Cole elements in the serial connection. In [7], for human skin dielectric, one fractional index is 0.82 (single-dispersion Cole-Cole model for small frequencies). Single-dispersion Cole impedance model was used to analyze human and rabbit irritated skin [6]. In [16], two orderly connected impedance *CPE*s with indices of about 0.71 and relaxation times of 0.001s were observed. In [15], obtained, for normal skin and acupuncture points, approximately the same *CPE* index, for non-Cole model, the value of which was 0.80. However, the general conclusion on the number of electrical elements of Cole, if they are seen in serial connection, not yet final.

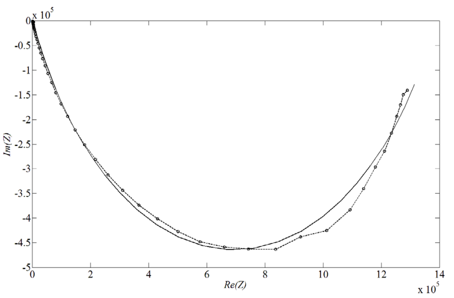

Figure 6. Graph fit of proposed LM algorithm for modified single-dispersion Cole model

The aim of the paper is determining the adequacy of single-dispersion Cole model, provided that the use of the serial model is adequate. Three models are presented: single, modified single and two-dispersion Cole model. Equations for the single and two-dispersion Cole model (n=1 and n=2 in (26)) is

$$\underline{Z}_{\alpha_1}(\omega)= R_\infty+\frac{p(\alpha_1)\cdot(R_0-R_\infty)}{1+\left(\mathrm{j}\cdot\omega\cdot\tau_{\alpha_1}\right)^{\alpha_1}},\ p(\alpha_1)=1, 0<\alpha_1\le 1,$$

$$\underline{Z}_{\alpha_2}(\omega)=R_\infty+(R_0-R_\infty)\cdot \left(\frac{p(\alpha_1)}{1+\left(\mathrm{j}\cdot\omega\cdot\tau_{\alpha_1}\right)^{\alpha_1}}+\frac{p(\alpha_2)}{1+\left(j\cdot\omega\cdot\tau_{\alpha_2}\right)^{\alpha_2}}\right), \quad (32)$$

$$p(\alpha_1)+p(\alpha_2)=1,\ 0<\alpha_1,\alpha_2\le 1$$

For the modified single dispersion Cole model (n=1 in (28)) equation is

$$\underline{Z}_{c;appr}(\omega)=R_\infty+(R_0-R_\infty)\cdot p(\alpha_1^*)\cdot\left(1-\frac{1}{\sigma_1\cdot\ln\left(\mathrm{j}\cdot\omega\cdot\tau_{\alpha_1^*}\right)}\cdot\ln\left(\frac{1+\left(\mathrm{j}\cdot\omega\cdot\tau_{\alpha_1^*}\right)^{\alpha_1^*+k_1\cdot\sigma_1}}{1+\left(\mathrm{j}\cdot\omega\cdot\tau_{\alpha_1^*}\right)^{\alpha_1^*-(1-k_1)\cdot\sigma_1}}\right)\right), \quad (33)$$

$$0<\alpha_1^*\le 1,\ p(\alpha_1^*)=1$$

The best model is the one with smallest sum of squared deviations. The results of fitting, shown in Table 1, show the quality of fit for modified single-dispersion Cole model. Fitting three-Cole dispersion model gave a non-physical result for a one fractional index alpha.

Table 1. Parameters for three presented Cole models

Parameters	LM Cole-1	LM Cole-1 modified	LM Cole-2
R_0 (MΩ)	1.387000	1.386960	1.352500
R_∞ (kΩ)	1.859950	1.859390	1.717720
α_1	0.748690	0.631482	0.783799
τ_1 (s)	0.529495	0.979852	0.110119
$p(\alpha_1)$	1.0	1.0	0.200180
α_2			0.831377
τ_2 (s)			0.686758
$p(\alpha_2)$			0.799820
σ		0.246225	
k		0.979851	
The sum of squares ($\cdot 10^9$)	8.054574	7.708689	4.439905

Size parameter σ reflects the fact that the value of fractional index is not concentrated in one point. Also, given the initial values of parameters of single-dispersion Cole model as a starting, it was determined that there are not another interval or subinterval within a given interval.

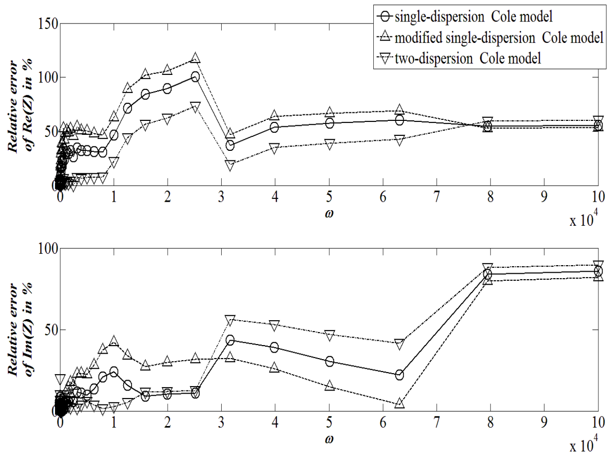

Figure 7. The relative error of fitting the real and imaginary part of impedance against frequency

Properties of fitting for three presented models are given in the Fig. 7. The relative error of the corresponding values are given by equations

$$\delta_{\%}\left(\mathrm{Re}(Z)\right)=\left|\frac{\mathrm{Re}\left(Z_{fitt}\right)-\mathrm{Re}\left(Z_{\exp}\right)}{\mathrm{Re}\left(Z_{\exp}\right)}\right|\cdot 100\%,$$
$$\delta_{\%}\left(\mathrm{Im}(Z)\right)=\left|\frac{\mathrm{Im}\left(Z_{fitt}\right)-\mathrm{Im}\left(Z_{\exp}\right)}{\mathrm{Im}\left(Z_{\exp}\right)}\right|\cdot 100\%, \quad (34)$$

The quality of fitting for the modified single-dispersion Cole model based on Fig. 7, is the best for high frequencies. For medium and lower frequencies best fitted two Cole dispersion model. At low frequencies the modified single-dispersion dispersion Cole better fitted by a single-dispersion Cole model. On the other hand, under other conditions, in [2], [15], [16], [22] values for the parameters α_i are in the specified interval, although the (33) is approximate. Therefore, the parameters k and σ probably could be understood as a material constants. This inter alia means that, they can be and diagnostic parameters. In addition, to these approximations δ-functions can have other, perhaps more appropriate and more complex.

On the other hand, if we consider the anharmonic functions, operators are defined based on the fractional derivatives, as described (16), (21), (24) and (31) generally have complex features and difficult to apply.

5. CONCLUSION

In this paper, we proposed the skin structure as a more complex system, consisting of several layers. We obtained the mathematical model of skin structure which describes series of structures of skin via new generalizing the Cole impedance equation applying fractional calculus modified distributed-order Caputo-Weyl fractional derivatives. In the case analyzed here, it is introduced continuous (distributed-order) Cole model as well as its approximation modified single-dispersion Cole model. The above approximation, in addition to defining the area where they should be fractional indices, in the range of high frequencies, may better describe the electrical properties of the system. The main conclusion of this paper is that the electrical properties of skin can be modelled better using a more discrete Cole impedance element rather than one discrete Cole impedance element. Moreover, these considerations could be applied to other frequency bioimpedance scales, in theories viscoelasticity, dielectrics, superparamagnetics and bioengineering.

APPENDIX

In the case that $R_0 \to \infty$ (perfect insulator) assuming that (17) is valid, (16) transforms into

$$\widehat{\underline{Z}}_{\alpha}=R_{\infty}+\left(C_{\alpha}\cdot {}_{-\infty}^{CW}\mathrm{D}_t^{\alpha}\right)^{-1} \quad (35)$$

Taking into account (18) it follows

$$C_{\alpha}\cdot {}_{-\infty}^{CW}\mathrm{D}_t^{\alpha}V(t)=\left(R_{\infty}\cdot C_{\alpha}\cdot {}_{-\infty}^{CW}\mathrm{D}_t^{\alpha}+1\right)i(t) \quad (36)$$

Continuous generalization of the previous relationship then describes the distributed derivatives, (see [17])

$$\int_{0^+}^{1}\mathrm{d}\alpha\cdot\left(C_{\alpha}\cdot {}_{-\infty}^{CW}\mathrm{D}_t^{\alpha}\right)V(t)=\left(R_{\infty}\cdot\int_{0^+}^{1}\mathrm{d}\alpha'\cdot\left(C_{\alpha'}\cdot {}_{-\infty}^{CW}\mathrm{D}_t^{\alpha'}\right)+1\right)i(t) \quad (37)$$

Under these assumptions, therefore, action of $\widehat{\underline{Z}}_c$ in (24) implies (36).

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МОДЕЛОВАЊЕ БИОИМПЕДАНСЕ ЉУДСКЕ КОЖЕ ПРИМЕНОМ ДИСТРИБУИРАНОГ НЕЦЕЛОГ РЕДА МОДИФИКОВАНОГ КОЛЕ МОДЕЛА

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Експериментални подаци отпорности и рачуна нецелобројног реда користе се за моделирање биоимпедансних особина људске коже. Увели смо и предложили модификовани Коле модел користећи при том оператор дистрибуираног нецелог реда који је заснован на Caputo-Weyl –овим изводима нецелог реда.Наш предложени модел представља измењен једно-дисперзијски Коле модел, јер уводи нове параметре k и σ у једно-дисперзијској Коле импедансној једначини. Ови параметри карактеришу ширину интервала око фракционог индекса α и они су важни за прецизнији опис биоимпедансних особина људске коже. Предложени модификовани Коле модел много боље даје фитовање дате експерименталне криве у датом фреквентном опсегу у поређењу са са постојећим Коле моделима. Фитовање је урађено применом Levenberg-Marquardt алгоритма нелинеарних најмањих квадрата.