Micro-particle Electrical Conduction through Human Blood

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ABSTRACT

The electric properties of human blood is vital. This is normal because this viable fluid have huge quantity of unexplored domains about its properties. For example, only few authors have examined the correlation between the electrode polarization and the dielectric alpha dispersion of micro-dipoles present in bio-fluids such as human blood. Even, there is no other authors have reported the presence of alpha dispersion in blood. After the application of ac- field, it is shown that in addition to the presence of electrode polarization; alpha, beta and gamma dispersions are present and can carry out the energy through blood. A model is presented in which different micro-components through blood play an essential role in transferring the energy between the electrodes. The electrode polarization through blood can completely mask the alpha dispersion which may explain why this latter has never been detected through blood. The presented model has successfully fitted to some recent published experimental results that confirm the micro-particle electric conduction and show the presence of alpha dispersion in blood. This will improve diagnostic-medical applications of metallic electrodes as micro biosensors and potential different therapeutic-medical applications.

Keywords: blood, electrode polarization, alpha dispersion, permittivity- Human Blood – Complex permittivity.

1 INTRODUCTION

Although the dielectric properties of human blood have been explored since more than 100 years [1], research into this domain is still producing new scientific facts till now [2, 3]. Dielectric measurements are non-invasive method that is applicable to biological cells for characterization. However, the accurate calculation of the dielectric properties of a highly heterogeneous system, such as human blood (representative of highly conductive biological cell suspension), is a difficult issue because of two factors: First, the dielectric response of such highly conductive materials depends on the way how one can model these materials. Second, there is high screening effect around the metallic electrodes due to high charges distribution near the electrodes which leads to electrode polarization effect. In general, remarkable dielectric responses attributed to interfacial polarization have been observed in the frequency region of the beta dispersion for a cell suspension [4, 5]. Previous published dielectric measurements data have shown, for example, different properties between normal lymphocytes and leukemia cells [6] and the change of dielectric response for human erythrocytes with glucose concentration in an extracellular medium [7, 8]. Therefore, dielectric measurements are promising technique for cell diagnostic applications, monitoring of blood glucose level and other fundamental and applied studies. However, analysis of dielectric measurements data according to the majority of published models [9- 11] are limited to bulk measurements with minimizing the electrode polarization effect. Also, some studies completely ignore the electrode polarization effect. Only approximate or relative changes in these measurements can be estimated for correct measurements in particular at low frequency range. Low frequency or dc-measurements for conductive materials such as human blood can appear to have unusually low electrical conductivity when the incorrect model is used to explain the properties of complex conductivity through the conductive fluid. This phenomenon is due to electrode polarization which is ubiquitous phenomenon that takes place at the interface between a metallic and ionic conductor. It shows a characteristic signature in the net dielectric response of the blood in dependence on frequency and applied electric field, temperature, concentration of charges around the electrodes and the distance between electrodes [12- 15].

In another work [2], we have shown that the relaxation of white blood cells (WBCs) results in alpha dispersion through blood. In the literature, the effect of alpha dispersion through blood has never been reported because as we will see in this work, it is superimposed by the effect of electrode polarization. The relaxation time of these WBCs under the application of low-frequency applied field is 6.8×10^{-4} seconds [2] which corresponds to frequency of 234 Hz. This frequency lies entirely in the low frequency range. A better way to characterize the electrode polarization parameters is to fit the full expression for electrodes polarization and the effective dielectric alpha, beta and gamma- dispersions to some raw experimental data (different published data) over the whole frequency range investigated, without the need to make privilege choice that might be ambiguous. The results give further support to the analysis of dielectric spectra by means of combination of a fractal model of electrode polarization described by scaling-law frequency dependence and a typical relaxation function model, over the whole frequency range investigated.

The objectives of the present paper is: 1- to elucidate the role played by micro particle in electrical conduction through blood; and in producing electrical double layer near the metallic contacts (electrodes) 2- to demonstrate the applicability of the distribution RC circuits for the modeling of electrode polarization effect to explain the electrical conduction through blood (micro-particle electric conduction) and 3- to provide evidence to the presence of alpha dispersion in human blood which has never been reported before by other authors.

2 THEORETICAL MODEL

To know the effect of microscopic mechanism (s) of electrode polarization on charge transfer, one can ask about the signature of electrode polarization in the complex dielectric function with respect to the complex conductivity. Other questions may come into scope: What is the most suitable model to describe electrode polarization that can fit well the experimental data? The effect of the electrode material is, also, an essential parameter. Moreover, it is worthy to know about the plausible quantitative information that can be deduced from the proposed (electrode polarization)-model. Experimentally, electrode polarization results in a large and sometimes uncontrollable error (s) in the measured charge transfer phenomenon and in particular dielectric parameters. This prevents the use of low-frequency (up to 1 MHz) in monitoring the dielectric properties of biological systems, particularly biological cell suspension (such as human blood). The greater the

ionic conductivity of the cell suspension will produce greater electrode polarization effect [16, 17] that, in some cases, may completely obscure the dielectric properties of the material. In the present work, one considers the behavior of different micro-particles that suspended through blood, under the influence of an external alternating field, one develops, here, the previously presented model [8, 9, 18- 20] for the complex permittivity taking into account the effect of electrode polarization. Such a model has already been presented for the case of oscillating white blood cells which are responsible for the alpha dispersion in blood [2]. In this last reference, we have considered ionic conduction through blood. The charge carriers for ionic conduction through the fluid are the charged micro particles which are intrinsically charged or extrinsically charged: For example Lay and Burton [21 have reported that the electrical potential difference across the human red blood cell membrane is negative potential - 8.0 ± 0.21 mv, the inside being negative with respect to outside. i.e. negative 8 mV on each RBC whether there is an external electric field or not [21]; moreover, all free radicals in the blood are positively charged, for example "hydro-water" free radical has the highest potential which about 2300 mV [41] while iron free radical (Fe++) has about +120 mV [22]. Free radicals are generated as by-product of normal cellular metabolism; however, several conditions are known to disturb the balance between the reactive oxygen spices production and cellular defense mechanisms. Free radicals are formed disproportionately in diabetes by glucose auto-oxidation, polyol and non-enzymatic glycation of proteins[23]. Moreover, when applying an external electric field, micro particles will be charged by mirror images. Water molecules (in plasma) are also principal source of charges and they play a stimulating role to keep micro particles permanently charged as follows: The electric conduction through blood involves the transport of micro particles which have a mass like their surroundings. A charged micro particle through blood will polarize its surroundings. As a result, the polarized micro particles (or even nano-particles in blood) will rearrange themselves to form mobile dipoles, providing a screening effect on the ions. Since the polarization of surroundings reduces the electrostatic energy of the charged micro particle, the particles rearrange themselves always to have the minimum electrostatic energy. In addition, a micro particle not only polarizes the surroundings but is also polarized by the opposite charges of the surroundings dipoles as it moves past them.

The positively charged free radicals moving toward the cathode and the negatively charged micro particles moving toward the anode under an applied electric field will create hetero-space charges near the electrodes. If the charges of micro particles are not neutralized at the electrodes, they will accumulate there. These hetero-space charged micro particles form finally at the thermo-dynamic equilibrium what is called electric double layer, EDL around the electrodes. The formation of this EDL may alter the interface behavior at the metal/blood contacts. Furthermore, because of the formation of EDL, the field distribution between electrodes becomes highly disturbed which will change the spatial distribution of the dielectric properties, resulting in the formation of multilayer capacitor. Based on the presented model, the behavior of such capacitor under ac fields has been analyzed. Blood contains micro- and nano cells, such a biological cell suspension will suffer different electrical conduction (electrical losses), if it will be subjected to an ac-electric field. Different micro-particles (with different masses) have their characteristic frequency. For example, white blood cells will have f0WBCs, red blood cells will have f0rBCs and light micro particles will have f_0 LMPs [2]. The electric losses obtained are due to the resonance between the oscillations of the applied electric field and the natural frequency of these three sorts of micro particles.

This reduction of relaxation time inhibits the electric conduction leading to feeble values of the electrical conductivity. To calculate this latter with the effect of electrode polarization, a new term that counts for the electrode polarization should be added we will describe the electrical conductivity of the whole blood combined with the effect of the electrode polarization using our previous relations [18- 20]:

$$\sigma = \sum_{Nw}[\sigma_{dc}]_w + \omega^2[\tau\frac{\sigma_\infty - \sigma_{dc}}{1+(\omega\tau)^2}]_w + \sum_{Nr}[\sigma_{dc}]_r + \omega^2[\tau\frac{\sigma_\infty - \sigma_{dc}}{1+(\omega\tau)^2}]_r + \sum_{NL}[\sigma_{dc}]_L + \omega^2[\tau\frac{\sigma_\infty - \sigma_{dc}}{1+(\omega\tau)^2}]_L + \sum_{NEP}[\sigma_{dc}]_{EP} + \omega^2[\tau\frac{\sigma_\infty - \sigma_{dc}}{1+(\omega\tau)^2}]_{EP} \quad (1)$$

$$\varepsilon' = \sum_{Nw}[\varepsilon_\infty]_w + [\frac{\varepsilon_{dc} - \varepsilon_\infty}{1+(\omega\tau)^2}]_w + \sum_{Nr}[\varepsilon_\infty]_r + [\frac{\varepsilon_{dc} - \varepsilon_\infty}{1+(\omega\tau)^2}]_r + \sum_{NL}[\varepsilon_\infty]_L + [\frac{\varepsilon_{dc} - \varepsilon_\infty}{1+(\omega\tau)^2}]_L + \sum_{NEP}[\varepsilon_\infty]_{EP} + [\frac{\varepsilon_{dc} - \varepsilon_\infty}{1+(\omega\tau)^2}]_{EP} \quad (2)$$

$$\varepsilon'' = \sum_{Nw}\omega[\tau\frac{\varepsilon_{dc} - \varepsilon_\infty}{1+(\omega\tau)^2}]_w + \sum_{Nr}\omega[\tau\frac{\varepsilon_{dc} - \varepsilon_\infty}{1+(\omega\tau)^2}]_r + \sum_{NL}\omega[\tau\frac{\varepsilon_{dc} - \varepsilon_\infty}{1+(\omega\tau)^2}]_L + \sum_{NEP}\omega[\tau\frac{\varepsilon_{dc} - \varepsilon_\infty}{1+(\omega\tau)^2}]_{EP} \quad (3)$$

where ε_∞ is the dielectric constant at very high frequencies: f is much higher than $1/(2\pi\tau)$, ε_{dc} is the dc-current, static, or very low frequency dielectric constant and τ_p is the relaxation time for any particle of the above mentioned three types. It should be noted that the relaxation time τ_p lies in the range:

$$[\frac{\varepsilon_0\varepsilon_S}{\sigma_S}]_p > \tau_p > [\frac{\varepsilon_0\varepsilon_\infty}{\sigma_\infty}]_p \quad (4)$$

each type of these micro particles are characterized by relaxation time constant: For WBCs, τ_w; for RBCs; τ_r and For LMPs; τ_L; and dc-conductivity: For WBCs, $[\sigma_{dc}]_w$; for RBCs; $[\sigma_{dc}]_r$ and For LMPs; $[\sigma_{dc}]_L$. We have used the same notations as in reference [2].

3 RESULTS AND DISCUSSIONS

3.1 Electrical conductivity of blood with different hematocrit rates as a function of frequency

Fig. 1 shows the experimental data of the electrical conductivity σ at different rates of Hct as a function of frequency, at 310K. At Hct = 0.86 two net step-like increases are seen in the σ as a function of f curve; one in the frequency range near 240 Hz and the other at about $1x10^6$ Hz. The experimental values of σ as a function of f have been well fitted with the fitting parameters

shown in table (1). Moreover, conductivities of other curves with different Hct rates have, also, good fit with Eq. (11) as seen in Fig. (1): The solid black line(s) stands for calculated values after Eq. (11) while symbols are for experimental values. One can notice that the magnitude of step-like increases with Hct.

The step-like increase which is illustrated in FIG. 1 near 1 x 10^9 Hz is clearly diminishes with decreasing Hct. For example, the electrical conductivity of blood (Hct = 0.23) as a function of the applied frequency is illustrated in Fig. 2 which shows that the step-like increase shown by the arrow is weaker than that shown in Fig. 1. From Fig. 2, one can notice also that the step-like increase moves towards higher frequency.

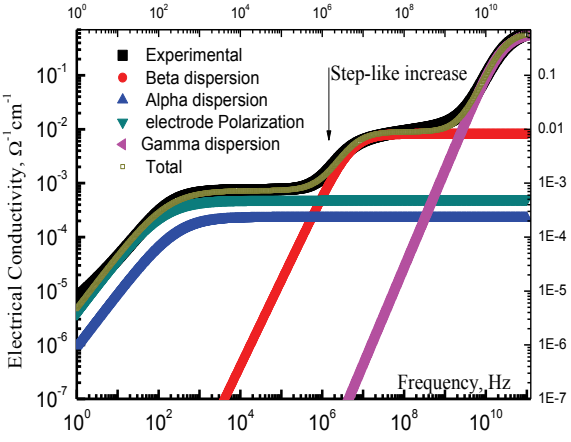

Figure 1: The electrical conductivity of blood (Hct = 0.86) as a function of the applied frequency. Black squares stand for experimental values after Wolf et al [44]. Green triangles represent the effect of electrode polarization calculated after Eq. (11). Blue triangles for alpha dispersion and solid red circles are for beta dispersion calculated after Eq. (11). Pink triangles represent gamma dispersion calculated values. One notice that the step-like increase shown by the arrow is stronger than that shown in FIG. 2 of blood (Hct = 0.23) because micro particles have weaker density.

Moreover, the electrical conductivity, σ mes-plasma of plasma (where the hematocrit rate, Hct = 0) is presented in Fig. 3. at 310 K. σ mes-plasma exhibits a steep continuous increase in the low frequency range 1Hz < f < 1x102 Hz, followed by a plateau (0.0175 $\Omega^{-1}cm^{-1}$) in vast range of frequency 1x10^3 Hz < f < 1x10^9 Hz, followed by a strong increase of σ mes-plasma with f at high frequency near 1x10^9 Hz.

1.1 Careful comparison between the conductivity in Figs. 1, 2 and 3 shows clearly that the elimination of these micro-particles in plasma leads to elimination of the two step-like increases in the plasma conductivity curve.

The elimination of the two step-like increases in the plasma curve means that micro particles in blood are responsible for these two step-like increases. Moreover, the increases of the magnitude step-like increases with hematocrit ratio stand for the first estimation that the electrical conduction through blood is carried out by micro-particles.

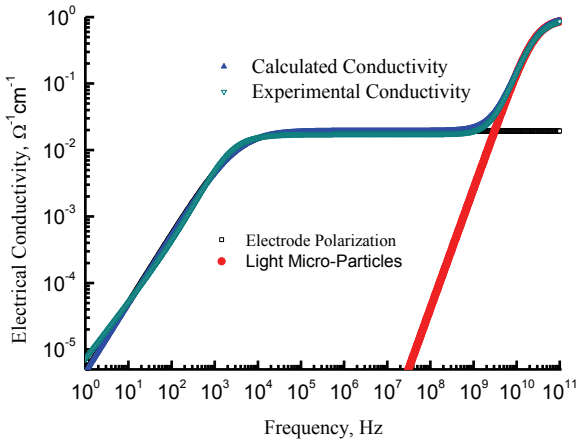

Figure 2: The electrical conductivity of plasma (Hct = 0) as a function of the applied frequency: Green triangles stand for experimental values after Wolf et al [44]. Black squares represent the effect of electrode polarization calculated after Eq. (11) and solid red circles are for light micro-particles calculated after Eq. (11). Experimental points are so close that they appear as line and they coincide with the calculated values. One notices that the step-like increase shown by the arrow in FIGs. 1 and 2 are completely eliminated because there are no more micro-particles in plasma.

However, at very low and very high frequency, σ becomes insensitive to Hct. This can be explained in the light of the presented model as follows: At very low frequency, the dipoles accumulate near the electrodes forming EDL with high density of charges in small region which screens the effect of any more charges [24]. At high frequency range, light micro-particles and nano-particles relax with very short relaxation time and the micro-particles will be too heavy to respond to the electric field at so high frequencies.

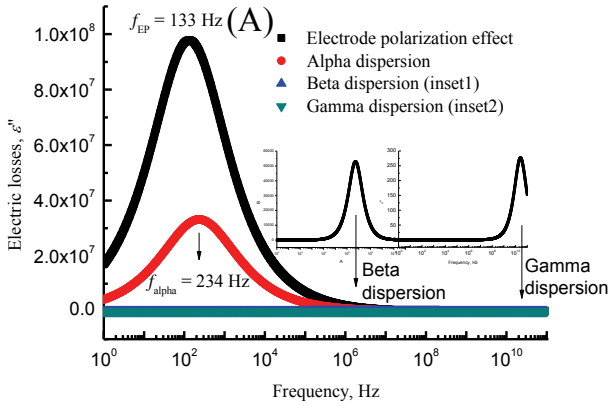

Figure 3: The dependence of ε'' as a function of f when Hct = 0.86 which is characterized by *four* well manifested peaks. At the frequencies $f_{EP} \approx 133$ Hz, $f_{alpha} \approx 234$ Hz, $f_{Beta} \approx 2.3 \times 10^6$ Hz and the fourth at high frequency range about $f_{LMP} \approx 2.65 \times 10^{10}$ Hz. The magnitude of beta-dispersion and gamma-dispersion is by far smaller than the magnitude of alpha-dispersion; these dispersions are presented in two insets in figur3.

3.2 Electric Losses (Dielectric Dispersion): Frequency Dependence

Now, to obtain the exact values of the relaxation times for all types of micro-particles, we plot the electric losses ε" as a function of f curve for different Hct rates. We fit Eq. (13) to the experimental data of ε" obtained as follows:

$$\left(\varepsilon''\right)_p = \left(\frac{\sigma_{meas} - \sigma_0}{\omega}\right)_p \qquad (14)$$

where σ_{meas} is the measured ac-conductivity, ω is the angular frequency and σ_0 is low frequency conductivity. First, when Hct = 0.86 (case of maximum density of micro-particles in our study), the variation of ε" as a function of f is characterized by *four* well manifested peaks (Fig. 6) one at low frequency $f_{EP} \approx 133$ Hz, $f_{alpha} \approx 234$ Hz, $f_{Beta} \approx 2.3 \times 10^6$ Hz and the fourth at high frequency range about $f_{LMP} \approx 2.65 \times 10^{10}$ Hz.

In reference [2], we have reported two values which are in agreement with the present's work values: $f_{alpha} \approx 239$ Hz (present work) and $f_{WBCs} \approx 234$ Hz (Ref [2]), also $f_{Beta} \approx 1.25 \times 10^6$ Hz (present work) and $f_{RBCs} \approx 1.33 \times 10^6$ Hz (Ref [2]). These values stand for the assumption that has been proposed in reference[8] that RBCs are responsible for the alpha dispersion. We will see in the next section that the other two peaks lay at $f_{EP} \approx 133$ Hz and $f_L \approx 2.65 \times 10^{10}$ Hz are due to the effect of electrode polarization and light micro-particles, respectively. Second, for other Hct rates: 0.57, 0.39 and 0.23, the above mentioned four peaks are present but their magnitude decrease with the Hct rate. Not only the decrease of ε" with Hct but also, these peaks move towards lower frequencies with Hct as it can be seen in Fig. 3. Not only the frequency varies with frequency and Hct, but also the magnitudes of varies in wide range over several decades: 4 Hz < ε"< 2.65 x 10^{10} Hz. The presentation is standardized to the electrode polarization effect as shown in Fig. 3. On this Figure, one can see that the polarization effect and alpha dispersion are so close that fine experimental results should be carried out to distinguish between the two phenomena. Some considerations have been taken into account in the presented model: 1- In micro-particle suspended solutions (like blood), the electrical conductivity is the sum of the conductivities of all the conducting micro-particles because the majority of these particles are charged and can act as current carrier and/or dipole oscillator. When a charged micro-particle (such as red blood cell or white blood cell) is immersed in an electrolyte medium (such as blood-plasma) it attracts a cloud of counter ions, forming a layer of charges on the outer surface of the cell membrane. An electric potential will be established due to the presence of this layer. 2- The charged particle will experience a force when an electric field is applied to the medium and acquires a net mobility through the electrolyte (plasma). The particle velocity will strongly depends upon the applied electric field strength, the dielectric constant of both particle and medium and viscosity of the medium; in addition to the created potential on the particle itself. The measurement of the terminal velocity is the usual mean to obtain the established electric potential. 3- In blood, the micro-particles that freely suspended in plasma have intrinsic property: They permanently oscillate with natural frequency, f_0. Every type of micro-particles has his own natural frequency [8, 19], for example RBCs have a most probable frequency $(f_0)_{RBC}$ and WBCs have a most probable frequency $(f_0)_{WBC}$. 4- In another work, we have shown that the natural frequencies of all RBCs are distributed in a Gaussian manner through the blood. The width of the Gaussian distribution is correlated with the Cole factor [18]. 5- The regular addition of glucose rate to blood shift the natural relaxation time of RBCs towards lower values [3]. The last reference shows that the natural relaxation time, $(f_0)_{RBC}$ decreases exponentially with glucose rate. 6- At the metal-electrode/ blood interface is surrounded with double layer charges EDL [24]. Although these charges have their own natural frequency when they are freely suspended in blood, but under the presence of other near electric charges and external electric field, their frequency will be highly reduced to $(f_0)_{EP}$. Thus, one can expect that the relaxation time of charged micro-particles bounded in the EDL region is lower than the same charged micro-particles which are freely suspended in blood. One can write $(f_0)_{EP} < (f_0)_w < (f_0)_r < (f_0)_{MLP}$ and we will see that frequencies will correspond the frequency of bound charges near the electrodes which are smaller than the frequency of alpha dispersion, smaller than the frequency of beta dispersion, etc. One can write: $(f_0)_{EP} < (f_0)_{alpha} < (f_0)_{beta} < (f_0)_{gamma}$.

4 CONCLUSIONS

The resonance oscillations of micro-particles suspended through blood affect the charge transfer and electric conduction through the human blood. When the frequency of the ac-applied field matches with the natural frequency of the suspended micro-particles maximum electric loss will appear as a peak of the frequency curve. This demonstrates that dielectric measurements are promising technique for cell diagnostic applications, monitoring of blood glucose level and other fundamental and applied studies.

REFERENCES

[1] G.N. Stewart, J. of Physiol., xxiv, (1899) 356- 377
[2] S. Abdalla, IEEE Trans on Nano-bioscience, 10, (2) (2011) 113- 120.
[3] S. Abdalla, AIP Advances 1, 012104, (2011) 1- 11.
[4] S. Takashima, Electrical Properties of Biophysics and Membranes Adam Hilger, Bristol, (1989) 181.
[5] P.-Y., Hsiao, Y.-F. and H. –C Chang, soft matter, 7, (2011) 1207- 1213.
[6] Y. Polevava, I. Ermolina, M. Schlesinger, B.-Z Ginzburg, Y. Feldman, Biochim. Biophys. Acta 1419, (1999) 257- 271.
[7] A. Caduff, L. Livshits, Y. Hayashi, Y. Feldman, J. Phys. Chem. B 108, (2004) 13827- 1330.
[8] L. Livshits, A. Caduff, M. S. Talary, Y. Feldman, J. Phys. D: Appl. Phys. 40, (1), (2007) 15- 19.
[9] P. Lunkenheimer, V. Bobnar, A. Pronin, A. Ritus, A. Volkov, A. Loidl, Phys. Rev. B, 22, 152105 (2002) 3158- 3168.
[10] J. C. Maxwell, A treatise of electricity and magnetism, part 2, chapter 10, Oxford University Press, London, (1873) 101.
[11] K. W. Wagner, Erklarung der dielektrischen Nachwirkungsvorgangeauf Grund Maxellescher Vorstellungen, Arch. Elektrotech. 2, (1914) 371-387.
[12] A. R. Minerick, R. Zhou, Pavlo Takhistov, H. –C Chang, Electrophoresis, 24, (2003) 3703- 3717
[13] K. Asami, Meas. Sci. Tech., 22, 8, (2011) 085801- 085808
[14] S. Basuray and H. –C Chang, Phys. Rev. E 75, (2007) 060501- 060504
[15] S. Basuray and H. –C Chang, Biomicrofluidcs 4, 013205 (2010) 022801-022807.
[16] P.A. Cirkel, J.P.M. Van der Ploeg, G.J.M. Koper, Physica A, 235, (1997) 1-2.
[17] L.Y. Yeo, D. Hou, S. Maheshswari, H. –C. Chang, Appl. Phys. Lett., 88, 233512 (2006) 269- 278.
[18] S. Abdalla, Physica B: Condensed Matter, 403, 3, (2011) 584- 587.
[19] S. Abdalla, Journal of Molecular Liquids, 160, 3, (2011) 130- 135.
[20] S. Abdalla, S. S. Al-ameer, and S. H. Al-Magaishi, Electrical properties with relaxation through human blood, Biomicrofluidics 4, September (2010) 034101-034116.
[21] A. W. Lay and A. C. Burton, Biophys. J., 9, 2, (1969) 115- 121.
[22] G. R. Buettner, Radiation Research, 145, (1996) 532- 541.
[23] I. G. Obrosova, C. Vanlteysen, L. Fathallah, X. Cao, D. A. Greene, M. J. Stevens, FASEB J., 16, (2005) 123- 125.
[24] Z. Gagnon, and H. –C Chang, Electrophoresis, 26, (2005) 3725- 3737.