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Role of erythrocytes and leucocytes in charge transfer through human blood

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ABSTRACT

One of the rare subjects that is still keeping its scientific importance for a long time are the electric and dielectric properties of human blood. However, this viable fluid has a huge quantity of unexplored domains. For example, despite the wide applications of metallic electrodes in biophysics, 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 more, no other authors have reported the presence of alpha dispersion in blood. A theoretical model is presented in which different micro-components through blood (for example red and white blood cells) play an essential role in transferring the electric energy between two metallic electrodes. After the application of ac-electric field to blood, it is shown that in addition to the presence of electrode polarization; alpha, beta and gamma dispersions are present and can carry out the electric energy through blood. It has been demonstrated that 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 confirms the micro-particle electric conduction and shows 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.

1. Introduction

Among last year's number of considerable studies have published concerning dielectric measurements of human blood [1–6]. This scientific subject has been studied since the beginning of the last century [7] and it is still keeping its scientific momentum up to the present. In fact, more than 100 years of research into the dielectric properties of human blood is still producing new scientific facts till now [8,9]. Dielectric measurements are a label-free, 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 [10,11]. Previous published dielectric measurements data have shown, for example, different properties between normal lymphocytes and leukemia cells [12] and the change of dielectric response for human erythrocytes with glucose concentration in an extracellular medium [13,14].

Therefore, dielectric measurements are a 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 [15–17] is 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 a 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 [18–21]. In addition, it is known [22] that electrode polarization is highly affected by the nature of the metallic electrodes where an insulating boundary layer is formed around the electrodes because of the formation of an electrochemical potential barrier which inhibits the flow of current from one electrode to another. Furthermore, local inhomogeneities at the electrode surface enhance the formation of a chemical thin layer [22], in particular an oxide layer that formed at the electrode surface [23]; for example nickel electrodes,

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immersed in blood, oxidize ethanol comparably to glucose as demonstrated in a number of papers [24–26], that resist the flow of the charges and resist the flow of electric current through the fluid. In ac-complex conductivity measurements, one often is concerned with situations where the electrodes effects are not the main trunk of the study but still cannot be ignored. Sometimes, these electrode effects are more important than the intrinsic (bulk) property and they can even mask it; for example, the dielectric alpha relaxation through blood has totally disappeared because of the effects of metallic electrodes polarization [8].

The direct modeling of electrode polarization has used a common principal explanation: Equivalent circuits or a so-called constant phase element [6,27–29]. The equivalent circuits are assumed to be connected in series to the intrinsic bulk contribution of the sample. The most common ones are parallel resistance-capacitance RC circuit [30–32]. In our study, this approach has certain drawbacks when analyzing ac-complex conductivity measurements where contributions from electrode polarization are observed only in the low frequency region. Moreover, we will see that this model will be applied: Once for a distributed RC equivalent circuit, based on a Cole–Cole distribution of relaxation times [33,34] to describe electrode polarization while the other will describe the phenomenon in the bulk (alpha dispersion). This is true not only for blood but also for such different materials as aqueous solutions, biological systems, solid-state electrolytes, ionic liquids, and all kinds of electronic conductors. Moreover, Basuray and Chang [20] have used the parallel resistance-capacitance RC circuit and they have shown that the characteristic relaxation frequency of induced nano-dipoles by dielectrophoresis is inversely proportional to the charging and discharging of the diffuse-layer capacitance in micro-fluids, which affects both the electrical and mechanical properties of blood [9].

In another work [8], 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}s [8] which corresponds to a 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.

The term human blood, in the present work will be simply abbreviated as blood (it means normal blood without any disorders or diseases) and in the whole text, the subscript p denotes particle (white blood cell WBC, red blood cell RBC or micro light particle MLP). These micro light particles may be different substances like proteins, glucose, vitamins, hormones, macromolecules and antibodies [35]. They have very light masses and they are by far lighter than RBCs and WBCs.

2. Model and analysis

The electrode polarization is an indispensable parameter which should be taken into account when explaining the mechanisms of charges transfer through biomaterial whether it is solid or liquid. 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 [36,37] 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 [8,9,34,38,39] 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 [8]. 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 et al. [40] 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 [40]; 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 [41]. 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 [42]. 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. This opposes the mobility of micro particles and causes an increase of the resistivity of blood. Due to electrolysis reactions at the electrodes, Minerick et al. [4] have shown that red blood cells move due to gradient in pH values between electrodes which alter the local chemical potential and RBCs can thus flow under the electro-endoosmotic effect.

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.