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Cellular absorption of electric field energy: influence of molecular properties of the cytoplasm

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Abstract

Molecular dispersions may significantly alter the frequency dependence of structural polarizations. Consequently, the molecular properties cannot be neglected when the energy absorption is calculated with a subcellular resolution. Our example presents calculations that explain the absorption in single human red blood cells. The molecular properties of the cytoplasm have been derived from literature data on the impedance of Hb suspensions. The resulting cell properties were then compared to own data obtained by single cell dielectric spectroscopy. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

1.1. Energy absorption of biological cells

Biological cells, their compartments and the adjacent media absorb energy when exposed to electromagnetic fields. The volume specific absorption (P_v) is proportional to *Joule's heating* given by the square of the effective local field strength (E_{eff}) and the specific conductivity (σ) of the medium

$$P_v = E_{eff}^2 \sigma \quad (1)$$

Field distribution is frequently calculated assuming electrically homogeneous, isotropic properties for the cytoplasmic and membranous compartments as well as for the external medium. A medium (index k) would possess a frequency-independent permittivity (ε_k) and conductivity (σ_k). However, molecular dispersions may result in frequency-dependent permittivities and conductivities, which in turn are of importance for the frequency-dependent local field and energy absorption [1–3]. In this paper, we consider dispersions of the cytoplasm of human red blood cells (Fig. 1).

1.2. The model

The calculations are based on the model proposed by Gimsa and Wachner [4] and which was recently extended to the general ellipsoidal shape. The model consists of three RC pairs in series, representing the very special geometry of

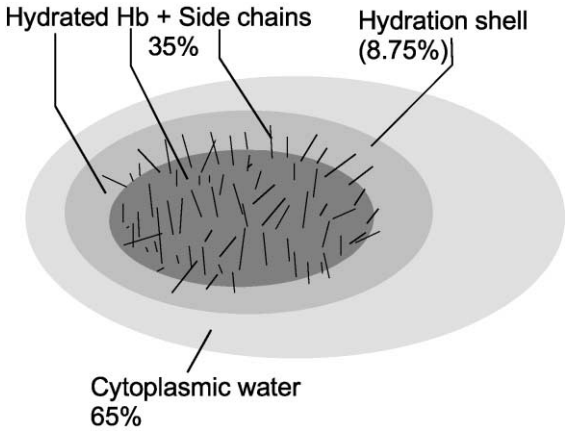

Fig. 1. Schematic drawing of the cytoplasmic content of human red blood cells. The concentrations of the compartments are given in vol%.

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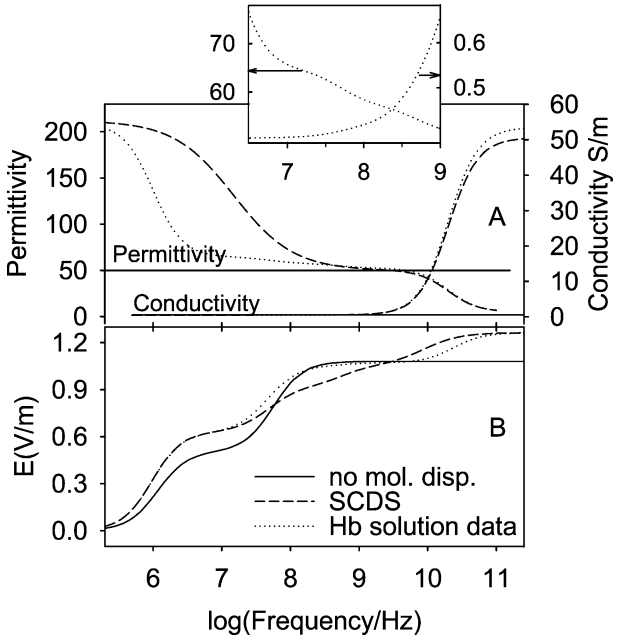

Fig. 2. Frequency-dependence of the cytoplasmic permittivities, conductivities and field strengths (V/m) for a single shell model, with or without molecular dispersions. For cell parameters, see Table 1. The model cell is assumed to be orientated with the symmetry axis perpendicular to the external field.

a finite element ansatz that corresponds to the Laplace solution. Accordingly, the electrical properties of the external (e), membrane (m) and cytoplasmic (i) media are correctly reflected by the well-known expression for the complex, specific conductivity σ^*

$$\sigma_k^* = \sigma_k + j\varepsilon_k\varepsilon_0\omega, \quad \text{with k = e, m, i} \tag{2}$$

where ε_0 stands for the absolute permittivity of vacuum. The model allows for the introduction of molecular dispersions by replacing σ_k and ε_k in Eq. (2) by (see Refs. [2,3] and references cited therein)

$$\varepsilon_k(\omega) = \varepsilon_k^{\infty} + \sum \frac{1}{1+(\omega\tau_j)^{2(1-\alpha_j)}}\Delta\varepsilon_j,$$

$$\sigma_k(\omega) = \sigma_k^0 + \varepsilon_0 \sum \frac{(\omega^2\tau_j)^{(1-\alpha_j)}}{1+(\omega\tau_j)^{2(1-\alpha_j)}}\Delta\varepsilon_j \tag{3}$$

where ω, $\varepsilon_k{}^{\infty}$, $\sigma_k{}^0$ are the circular field frequency, the permittivity at infinite frequency and the static conductivity, respectively. τ_j, $\Delta\varepsilon_j$ and α_j are the time constant, the dielectric decrement and the frequency distribution of a certain molecular dispersion, j. Starting from the assumptions in Ref. [5], an equation for the homogeneous effective cytoplasmic field can be derived

$$E_i = \frac{E}{(1-n)(1+\frac{d}{r}\frac{\sigma_i^*}{\sigma_m^*}) + n\frac{\sigma_i^*}{\sigma_e^*}} \tag{4}$$

where E, n, d and r are the external field strength, the depolarizing factor *for the axis oriented in field direction*, the membrane thickness and the cell radius, respectively.

Table 1
Electrical properties of the exterior, membrane and cytoplasm used in the model calculations

Human red blood cells, standard model		
Medium, k	Permittivity (ε_k)	Conductivity (σ_k/S m^{-1})
Exterior, e	80	0.12
Membrane, m	9.04 @ 8 nm thickness [3]	10^{-6} [3]
Cytoplasm, i	50 [6]	0.53 [6]

Frequency dependent cytoplasmic properties

Cytoplasmic compartments	f_j (MHz)	$\Delta\varepsilon$ for different volume contributions (%) of a compartment		Extrapolated data for physiological concentrations: ε and σ (S m^{-1})				Single cell dielectric spectroscopy: f_j (MHz), ε and σ (S m^{-1})				
				$\Delta\varepsilon$	$\Delta\sigma$	$\varepsilon_k(\omega)$	$\sigma_k(\omega)$	f_j	$\Delta\varepsilon$	$\Delta\sigma$	$\varepsilon_k(\omega)$	$\sigma_k(\omega)$
Hb	1	15% 63 [9]	22% 89 [7]	35% 145	0.01	203.8	0.4	(1.13) 15 α=0.5 [3]	162	0.14 [3]	(1.12) 212	0.4 [3]
Hb side chains	50	22% Hb 4.5 [7]	26.6% Hb 5.4 [7]	35% Hb 7	0.02	58.8	0.41				50	0.54 [6] (1.15)
Hydration shell (0.25 g/g Hb)	500	100% 55 [7]		8.75% 4.8	0.27	51.8 47	0.43 0.7					
"Bulk" water	20,000	85% 55 [9]		65% 42	52.7	5 [8]	53.4	20,000	45	49.9	5 [8]	50.4

Three sources of data, corresponding to the three curves in Figs. 2 and 3, were used (see explanations in the text). The dispersions of the cytoplasmic properties are described by dielectric decrements ($\Delta\varepsilon_j$) and the resulting increments ($\Delta\sigma_j$) in the cytoplasmic conductivity, occurring around specific relaxation frequencies (f_j) with a distribution parameter (α_j) of 0, if not otherwise stated.

1.3. Dielectric parameters

For red blood cells, the cytoplasmic properties are mainly determined by the most abundant components, i.e. hemoglobin (Hb) and cytoplasmic water.

The distinct dispersions below 500 MHz are related to the polar nature of Hb, the internal vibrations of Hb side chains and to the dielectric properties of the protein-bound water (Fig. 2, insert). These dispersions have been extensively studied in Hb solutions at different concentrations and temperatures [6,7]. Information on the cytoplasmic properties can be also obtained under more physiological conditions by single cell dielectric spectroscopy (SCDS) [3]. However, the latter experiments suggested a single broad relaxation ($\alpha = 0.5$), centered at 15 MHz, with a dielectric decrement of 162. The dispersions observed at frequencies above 500 MHz must be assigned to small molecular component, e.g. free water. Nevertheless, in the cytoplasm much of the water is structured by the high protein and ion concentration, suggesting modified dielectric properties [8,9].

Table 1 presents literature data and model parameters used to calculate the curves in Figs. 2 and 3.

The standard model of human red cells assumes 3.3, 3.3 and 1.65 μm for the semi-axes and frequency-independent properties [3]. For a description of the frequency-dependent cytoplasmic properties, data from dielectric spectroscopy (DS) on Hb suspensions and SCDS were used. The latter data could directly be taken from the literature [3]. However, since SCDS measurements in the medium GHz range were limited technically, an additional dispersion corresponding to the cytoplasmic bulk water was introduced in order to cover the frequency range to 30 GHz. This dispersion was adjusted to give a relative permittivity of 5 at frequencies higher than 50 GHz [8]. For the DS parameter set, the dielectric decrements of the Hb compartments were extrapolated to their physiological volume concentrations:

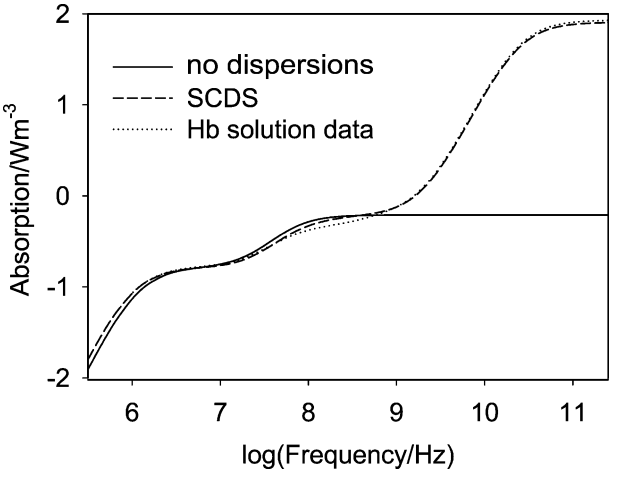

Fig. 3. Frequency-dependence of the cytoplasmic power absorption (W/m^3), with or without molecular dispersions. The absorption is normalized to an external field strength of 1 V/m.

hydrated Hb (35%), hydration shell (or bound water, 8.75%) and cytoplasmic water (or bulk water, 65%) ([6], Fig. 1). Starting at a relative permittivity value of 5 [8] and summing up the decrements of all compartments a DC value of 203.8 has been obtained. For both parameter sets the related conductivity steps were calculated from Eq. (3). A conductivity of 0.54 S/m measured at 250 MHz [6] was used as a reference to estimate the absolute values of the conductivity plateaus for SCDS.

2. Results and discussion

The DS and SCDS methods are based on different principles. DS, which has been applied on Hb solutions is an impedance technique, registering the integrative electric response of a population of objects and the suspension medium. The distributions in size and shape, in the orientation of nonspherical objects and even in the physiological status of biological objects cause a scatter in the response. The contributions of the various effects are hard to distinguish and thus hard to evaluate. Therefore, DS calls for monodisperse systems. Monodispersity is not necessary in SCDS, where the response of the individual object is based on the difference in the polarizabilities of object and medium. This differential principle leads to a much higher parameter resolution at the single cell level. Nevertheless, the resolution of DS on molecular suspensions can hardly be obtained on complete cells, even not by SCDS. This coincides with Schwan's notion of the molecular dispersions in cells as hidden by the much stronger structural dispersions [10].

Interestingly, a comparison between the parameter sets from Table 1 reveals a fairly good quantitative agreement in the overall dielectric decrements obtained on Hb solutions and cells by DS and SCDS, respectively. This is true, although SCDS does not resolve the dispersion steps obtained by DS.

For a precise model of cellular absorption, it will be of great interest to re-introduce the frequency dependence of the properties of molecular suspensions into a cell model which can be tested by SCDS. Although Schwan et al. dealt intensively with the properties of red blood cells [6] and later on with those of Hb suspensions [7,8], such a complex cell model has never been established, partly due to the inability of the impedance technique to prove it (H. Schwan, personal information, Oslo, 2001).

The extraordinary height of the conductivity step (around 50 S/m) in the GHz region is mainly due to the high dispersion frequency of the cytoplasmic water (Fig. 2A, compare to Eq. (3)). The cytoplasmic fields in the models with and without molecular dispersions are not significantly different (Fig. 2B). However, the molecular dispersions, and consequently the molecular absorption, strongly modulate the overall cytoplasmic absorption.

The value of 0.5–0.6 W/m^3 obtained for frequency independent properties, at an external field strength of 1

V/M, is exceeded by a factor of 140, resulting in an absorption of around 80–85 W/m^3. Introduction of the molecular properties results in a strong difference between the two models, especially above 100 MHz, where the molecular properties induce a significant increase in the cytoplasmic conductivity (see Eq. (1)).

The SCDS frequency range has recently been extended into the low GHz-range. Our future goal is to verify the cytoplasmic properties by SCDS—the only technique that allows for a high parameter resolution under physiological conditions. Here, individual human red blood cells are a well-established model system for dielectric investigations. Knowledge of the actual cytoplasmic properties will contribute to the understanding of the interaction mechanisms of cells and electromagnetic fields.

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