

INTERACTION OF ELECTROMAGNETIC FIELDS WITH BIOLOGICAL SYSTEMS AND DIELECTRIC PROPERTIES OF PROTEIN SOLUTIONS

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The effect of electromagnetic fields on specific rotational Brownian mobility is considered. A theory of dielectric relaxation of solutions of charged biopolymers is proposed. The theory includes such characteristics of macromolecules as charge, dipole moment, and concentration.

The importance of understanding the physical mechanisms of interaction of electromagnetic fields with biological objects is beyond question. The distinguishing features of the problem are as follows. First, interaction is observed in a very broad range of frequencies. In each wavelength region, distinction should be drawn between specific resonance and nonresonance absorption of radiation. Resonance absorption is studied by the nuclear magnetic resonance, nuclear quadrupole resonance, and electron paramagnetic resonance techniques. These techniques frequently employ high-power short radiofrequency pulses with the frequency spectra that cause simultaneous resonance transitions of the corresponding nuclear or electron spin systems. Magnetization variations with time are determined by the parameters that are related to correlation functions of particular molecular motions in the systems studied.

In solutions of such biologically important molecules as proteins, the rate of nuclear spin magnetization variations is determined by rotational diffusion of these macromolecules. The frequency spectrum of rotational diffusion extends from 0 to f_{\max} , where $f_{\max} = 1/\tau$, and τ is the correlation time of rotational motion [1-3].

Another effective method for studying diffusion processes in molecular solutions is the method of dielectric relaxation. Its use is based on the observation that in a wide frequency range, the frequency dependence of the complex permittivity of a system is determined by the spectral density of orientation motions of dipolar molecules. In the linear response theory, this dependence is written as

$$\epsilon^*(\omega) = \epsilon'(\omega) - i\epsilon''(\omega) = \epsilon_\infty + (kT)^{-1} \left\{ \langle M_z^2 \rangle - i\epsilon \int_0^\infty \langle M_z(0)M_z(t) \rangle \exp(-i\omega t) dt \right\}, \quad (1)$$

where ϵ' and ϵ'' are the real and imaginary parts of permittivity, respectively; ϵ_∞ is the permittivity value in the limit of high frequencies; M_z is the projection of the total dipole moment M of the system on the applied field direction (along the z axis).

According to current views, a part of solvent molecules form strong bonds with the surface of protein (the energy of these bonds exceeds kT). These molecules exchange protons with the other (free) solvent molecules. The exchange frequency of strongly bound molecules is well below the characteristic frequencies of motions of free solvent molecules. If we assume that transitions from the free to bound state and vice versa are accompanied by loss of orientation correlation of solvent molecules, and if the orientation correlation of macromolecules with each other is neglected, then general relation (1) leads to

$$\epsilon^*(\omega) = (1 - \Phi)\epsilon_s^*(\omega) + \Phi\epsilon_p^*(\omega). \quad (2)$$

Here Φ is the volume fraction of the solved protein, ϵ_p^* is the complex permittivity of the solvent, and $\Phi\epsilon_p^*$ is part of the dielectric permittivity determined by the presence of a protein in the solution. In the last term,

$$\epsilon_p^* = \epsilon_{p\infty} + \rho_p M_p^{-1} N_A (kT)^{-1} \left\{ \langle p_x^2 \rangle - i\omega \int_0^\infty \langle p_z(0)p_z(t) \rangle \exp\{-i\omega t\} dt \right\}, \quad (3)$$

where $\epsilon_{p\infty}$ is the high-frequency component, ρ_p is the density of the protein, M_p is the molar mass of the protein, N_A is Avogadro's number, and p is the dipole moment of a macromolecule including the total dipole moment of the hydration sheath formed by strongly bound solvent molecules.

It follows that for calculation purposes, we must determine the autocorrelation function for orientation of a separate macromolecule:

$$C_s(t) = \langle p_z(0)p_z(t) \rangle \langle p_z^2(0) \rangle^{-1} = \langle \cos \theta(0) \cos \theta(t) \rangle \langle \cos^2 \theta(0) \rangle^{-1}, \quad (4)$$

where $\theta(t)$ is the angle made by the external field direction and the dipole moment of the molecule. Equation (3) can then conveniently be written as

$$\epsilon_p^*(\omega) = \epsilon_{p\infty} + (\epsilon_p - \epsilon_{p\infty}) \left\{ 1 - i\omega \int_0^\infty C_s(t) \exp\{-i\omega t\} dt \right\}. \quad (5)$$

Here ϵ_p is the contribution of the protein component to the static permittivity of the solution, and $\epsilon_{p\infty}$ is the similar contribution at optical frequencies.

In solutions of biopolymers, the characteristic times of orientation relaxation of solvent molecules and macromolecules differ by several orders of magnitude. Therefore in the region of low-frequency dispersion, the frequency dependence is dominated by orientation motion of macromolecules. In infinitely dilute solutions, interaction of macromolecules can be ignored, and the correlation function of these macromolecules takes the traditional form

$$C_s(t) \exp\{-t/\tau_{0,l}\}, \quad \tau_{0,l} = [l(l+1)D_R]^{-1},$$

leading for $l = 1$ to the known relations

$$\begin{aligned} \epsilon_p'(\omega) &= \epsilon_{p\infty} + (\epsilon_p - \epsilon_{p\infty})(1 + \omega^2 \tau_{0,1}^2)^{-1}, \\ \epsilon_p''(\omega) &= (\epsilon_p - \epsilon_{p\infty})\omega \tau_{0,1}(1 + \omega^2 \tau_{0,1}^2)^{-1}, \end{aligned} \quad (6)$$

where D_R is the rotational diffusion coefficient of the macromolecule.

It is known that for solutions of biopolymers, experimental frequency dependences of ϵ' and ϵ'' are usually in rather poor agreement with Eqs. (6). This is explained using the hypothesis that there exists a spectrum of different correlation times. The physical reasons for the presence of such a spectrum, however, remain unclarified.

The theory of dielectric relaxation of a system of Brownian particles in a solution described in this work suggests a simple explanation of the observed patterns. Specifically, it is shown that the character of experimental frequency dependences and the degree of their deviation from dependences (6) are determined by such system parameters as the charge and dipole moment of Brownian particles and their concentration.

The special features of molecular motion in solutions of biopolymers are determined by abnormally high, of 10^2 – 10^3 D, dipole moments of charged protein macromolecules.

This is the reason why even at low (5% or less) protein concentrations, the energy of dipole-dipole interaction is on the order of kT . Interaction of particles causes significant deviations of the spectral density of orientation motion of macromolecules from the Lorentzian function and, therefore, results in dispersion relations different from Eq. (6).

Rotational Brownian motion of a macromolecule can be described by the Langevin equation [4], which, in addition to the usual moment of forces exerted by the solvent particles, includes the moment of forces exerted by other Brownian particles on the macromolecule:

$$d[I\Omega_i(t)]/dt + \hat{\zeta}I\Omega_i(t) = M_i^f(t) + M_i^{el}(t). \quad (7)$$

Here Ω_i is the angular rotation frequency of the i th Brownian particle, I is the moment of inertia of this particle, $\hat{\zeta}$ is the friction coefficient for rotational motion, M_i^f is the moment of random forces exerted by the solvent molecules, and $M_i^{e'l}$ is the moment of forces exerted by other Brownian particles. The value of the latter moment of forces is determined by the sum of dipole-dipole and charge-dipole interactions:

$$\begin{aligned} M_i^{e'l} &= [p_i(t)E_i(t)], \\ E_i(t) &= \sum \{Qr_{ij}/\varepsilon r_{ij}^* + [3(p_j r_{ij})r_{ij} - r_{ij}^2 p_j]/\varepsilon r_{ij}^5\}, \end{aligned} \quad (8)$$

where p is the dipole moment of the macromolecule with its hydration sheath, Q is the charge of the macromolecule, ε is the permittivity of the pure solvent (at the given frequencies), and r is the radius vector between the centers of the i th and j th Brownian particles.

For the moment of random forces M_i^f we have

$$\langle M_i^f(t)M_i^f(t + \Delta t) \rangle = 3kT\zeta\delta(t). \quad (9)$$

Note that Langevin equation (7) and Eq. (9) for the moment of random forces can be obtained from the dynamical equations for a system of charged Brownian particles. For simplicity, particles are taken to be symmetrical in Eq. (7), and the hydrodynamic interaction through the medium is assumed to be negligible compared with the Coulomb interaction. Equations (7) and (9) can be used to write the correlation function for the angular velocity of a Brownian particle through the correlation function for the moment of Coulomb forces acting on the macromolecule.

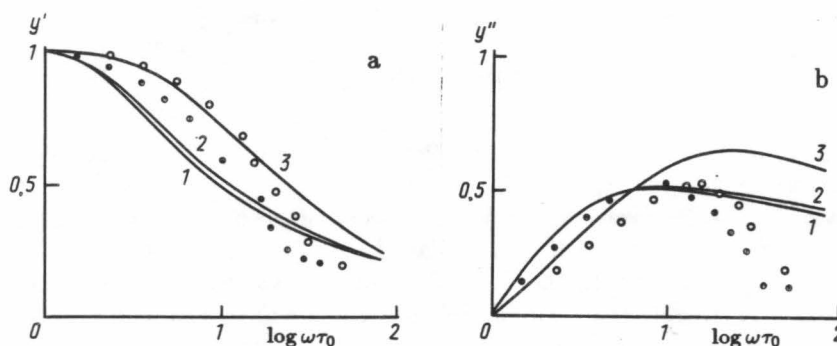


Fig. 1

The normalized values of the real part $y' = (\varepsilon'_p(\omega) - \varepsilon_{p\infty})/(\varepsilon_p(0) - \varepsilon_{p\infty})$ (a) and the imaginary part $y'' = \varepsilon''_p/(\varepsilon_p(0) - \varepsilon_{p\infty})$ (b) of the permittivity as functions of $\omega\tau_{0,1}$ in semilogarithmic coordinates. Calculated dependences: (1) $Q = 0$, $p = 0$, and $\Phi = 0$ (the Debye function); (2) $Q = 4$, $p = 500$ D, and $\Phi = 0.1$; (3) $Q = 12$, $p = 500$ D, and $\Phi = 0.1$. Experimental data: pH 5.5, $Q = 4$, $\Phi = 0.1$ (solid circles) and pH 7, $Q = 12$, $\Phi = 0.1$ (open circles).

We eventually obtain

$$\varepsilon'_p(\omega) = \varepsilon_{p\infty} + (\varepsilon_p - \varepsilon_{p\infty}) - \left[1 - \frac{\omega\tau_{0,1}(\omega\tau_{0,1} - A_1\chi_2 - A_2\chi_4)}{(1 + A_1\chi_1 + A_2\chi_3)^2 + (\omega\tau_{0,1} - A_1\chi_2 - A_2\chi_4)^2} \right], \quad (10)$$

$$\varepsilon''_p(\omega) = (\varepsilon_p - \varepsilon_{p\infty}) - \left[\frac{\omega\tau_{0,1}(1 + A_1\chi_1 + A_2\chi_3)}{(1 + A_1\chi_1 + A_2\chi_3)^2 + (\omega\tau_{0,1} - A_1\chi_2 - A_2\chi_4)^2} \right], \quad (11)$$

$$A_1 = p^4\Phi/(6\varepsilon^2(kT)^2R^6), \quad (12)$$

$$A_2 = p^2Q^2\Phi/(12\varepsilon^2(kT)^2R^4),$$

where R is the radius of Brownian particles, Φ is the volume fraction of these particles, and the χ_1 , χ_2 , χ_3 , and χ_4 functions are

$$\chi_1 = \operatorname{Re} \chi_s(i\omega\tau_{0,1}), \quad \chi_2 = \operatorname{Im} \chi_s(i\omega\tau_{0,1}), \quad (13)$$

$$\chi_3 = \operatorname{Re} \chi_Q(i\omega\sigma_{0,1}), \quad \chi_4 = \operatorname{Im} \chi_Q(i\omega\tau_{0,1}), \quad (14)$$

$$\chi_s = 1/[3(2+x)] - [C^2(2+x) - 1 + \exp\{-2C(2+x)^{0.5}\} - (C(2+x)^{0.5} + 1)^2]/[2C^3(1+x)^{2.5}], \quad (15)$$

$$\chi_Q = 1/(1+x) - [1 - \exp\{-2C(1+x)^{0.5}\}]/[2C(1+x)^{1.5}], \quad (16)$$

$$C = 2R/(2D_t\tau_{0,1})^{0.5}; \quad x = \omega\tau_{0,1}, \quad (17)$$

where D_t is the translational diffusion coefficient.

In Eqs. (10) through (17), $\tau_{0,1}$ is the orientation correlation time for noninteracting macromolecules (in the limit of $\Phi \rightarrow 0$). Calculations by these equations showed that consideration for the charged particles considerably changes the form of the frequency dependence of solution permittivity compared with the ordinary Lorentzian dependences. At a constant protein solution concentration, as the charge and dipole moment of a charged protein macromolecule increase, the maximum of the dependence shifts to higher frequencies and becomes sharper.

The calculated frequency dependences for a solution of biopolymers (serum albumin) at various values of the parameters are shown in Fig. 1 together with the experimental values and a Lorentzian dependence (the Debye function).

As regards more complex molecular systems, such as cells and tissues of living organisms, there exists no completed theory of their dielectric properties. Certain model approaches have been developed in a number of laboratories, of which Schwan's and Pliquett's laboratories should be mentioned first [5-7]. Frequency dispersions for such systems range from 10 Hz to 10 GHz and exhibit several absorption maxima. Most often, the action of electromagnetic radiation on biological objects is explained by thermal effects [8].

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