Dielectric spectra broadening as a signature for dipole-matrix interaction. IV. Water in amino acids solutions

Evgeniya Levy, Silvina Cervený, Irina Ermolina, Alexander Puzenko, and Yuri Feldman

Citation: *The Journal of Chemical Physics* **140**, 135104 (2014); doi: 10.1063/1.4869542

View online: <http://dx.doi.org/10.1063/1.4869542>

View Table of Contents: <http://scitation.aip.org/content/aip/journal/jcp/140/13?ver=pdfcov>

Published by the [AIP Publishing](#)

Articles you may be interested in

Stokes shift dynamics of ionic liquids: Solute probe dependence, and effects of self-motion, dielectric relaxation frequency window, and collective intermolecular solvent modes

J. Chem. Phys. **139**, 164503 (2013); 10.1063/1.4825195

Terahertz absorption of dilute aqueous solutions

J. Chem. Phys. **137**, 235103 (2012); 10.1063/1.4772000

Dielectric spectra broadening as the signature of dipole-matrix interaction. I. Water in nonionic solutions

J. Chem. Phys. **136**, 114502 (2012); 10.1063/1.3687914

Surface and confinement effects on the dielectric relaxation of a monohydroxy alcohol

J. Chem. Phys. **135**, 174510 (2011); 10.1063/1.3655356

Composition-dependent dynamical structures of 1-propanol–water mixtures determined by dynamical dielectric properties

J. Chem. Phys. **113**, 9748 (2000); 10.1063/1.1321767

AIP | Applied Physics
Letters

is pleased to announce **Reuben Collins**
as its new Editor-in-Chief

Dielectric spectra broadening as a signature for dipole-matrix interaction.

IV. Water in amino acids solutions

Evgeniya Levy,¹ Silvina Cervený,^{2,3} Irina Ermolina,⁴ Alexander Puzenko,¹
and Yuri Feldman^{1,a)}

¹Department of Applied Physics, The Hebrew University of Jerusalem, Givat Ram, Jerusalem 91904, Israel

²Centro de Física de Materiales - Material Physics Center (MPC), CSIC - UPV/EHU,
San Sebastian 20018, Spain

³Donostia International Physics Center, San Sebastian 20018, Spain

⁴De Montfort University, School of Pharmacy, Faculty of Health and Life Sciences,
The Gateway, Leicester LE1 9BH, United Kingdom

(Received 24 December 2013; accepted 13 March 2014; published online 7 April 2014)

In this paper, the fourth one of our series on the dielectric spectrum symmetrical broadening of water, we consider amino acid (AA) aqueous solutions. The developed 3D-trajectory is applied here to the variety of zwitterion amino acids representing both the hydrophobic and hydrophilic nature of their residues. The dipole moment of amino acids due to their zwitterion determines their interaction with the solvent and reflects mostly the dipole-matrix interactions described in our Paper I [E. Levy *et al.*, J. Chem. Phys. **136**, 114502 (2012)]. It is also shown that in the case of charged AAs at high concentrations, the shape of the 3D trajectory transforms to the pattern typical of the dipole-charge interactions that were described in our Paper III [A. Puzenko *et al.*, J. Chem. Phys. **137**, 194502 (2012)]. © 2014 AIP Publishing LLC. [<http://dx.doi.org/10.1063/1.4869542>]

I. INTRODUCTION

Amino acids (AAs) are important organic molecules since they play a very significant role in living systems. They are the main components of proteins and as such, determine their variety in properties and functions. The typical structure of AAs, presented in Fig. 1, consists of an amine ($-\text{NH}_2$) and a carboxylic acid ($-\text{COOH}$) functional group and a side-chain group (R) that is specific for each amino acid.¹ AAs are classified according to the side-chain group properties that are described as charged and polar (hydrophilic), non-polar (hydrophobic), and as a special case (i.e., absent side group or secondary amine group). At neutral pH, the AAs in aqueous solution are represented as zwitterions due to a positive charge at the amine group, a negative charge at the carboxylic group and a positive or negative charge on the side-chain group (for charged AAs). The majority of AAs (15 of 20) are not charged at any pH, but some of them have a side-chain group that is polar, i.e., it possesses a distribution of partial charges due to different electro-negativities of the atoms. The isoelectric point (pI) for non-charged AAs is usually about 5.5–6 and significantly varies for charged ones: two AAs have an acidic pI ~ 3 , two AAs have a basic pI ~ 10 –11, and one amino acid (His) has a pI at a neutral pH (i.e., 7.5). The polar nature of amino acids determines their behavior in aqueous solutions and allows studying their dynamics and structure using broad-band dielectric spectroscopy.^{2–16}

Two processes have been recorded in these solutions in a frequency range from hundreds of Megahertz to tens of Gigahertz that were confirmed by a recent systematic study (see Fig. 2).¹⁷ The low frequency process is assigned to the ro-

tation of the AA molecule in solution and the high frequency process is ascribed to the main dielectric relaxation of the solvent, respectively. The latter reveals the broadening of the water peak described by the phenomenological Cole-Cole⁵ (CC) spectral function,¹⁷ in agreement with our initial hypothesis that whenever water interacts with another dipolar or charged entity, a broadening of the dielectric relaxation peak occurs.¹⁷ Following our phenomenological approach (see Appendix A and Papers I–III),^{20–22} it is natural to speculate about a physical concept underlying the CC broadening in AA aqueous solutions. The chosen research approach, based on the use of 3D trajectories constructed from all the parameters of the CC spectra, was used previously to describe the state of water interacting in non-ionic,²⁰ ionic,²¹ and nucleotide solutions.²² In this paper, aqueous solutions of six AAs will be analyzed in terms of water-matrix interactions. The amino acids considered in this work represent typical types of the whole family of AA residues (non-polar, polar and charged). The 3D trajectory approach is applied in this case to calculate the dynamic and structural characteristics of the solvent.

II. RESULTS AND DISCUSSION

The dielectric spectra for different concentrations of six AA aqueous solutions are measured at 22 °C in a wide frequency band 0.2–35 GHz.¹⁷ Using Datama,²³ a program designed in-house, the full experimental spectra were fitted based on the sum of the Havriliak-Negami (HN)²⁴ and CC¹⁸ functions (the routine was applied for both real and imaginary parts of the complex dielectric permittivity simultaneously):

$$\varepsilon^*(\omega) = \varepsilon_\infty + \frac{\Delta\varepsilon_1}{[1 + (i\omega\tau_1)^{\alpha_1}]^{\beta_1}} + \frac{\Delta\varepsilon_2}{1 + (i\omega\tau_2)^{\alpha_2}}, \quad (1)$$

^{a)} Author to whom correspondence should be addressed. Electronic mail: yurif@mail.huji.ac.il

FIG. 1. Typical structure of an AA, where R is a side chain group.

where $i^2 = -1$, $\omega = 2\pi\nu$, ε_{sk} and $\varepsilon_{\infty k}$ ($k = 1, 2$) are the extrapolated low- and high-frequency permittivity, respectively, $\Delta\varepsilon_k = \varepsilon_{sk} - \varepsilon_{\infty k}$ is the dielectric strength, and τ_k is the relaxation time. β_1 is the asymmetry parameter for the first process ($0 < \beta_1 \leq 1$) and α_k ($0 < \alpha_k \leq 1$) indicates the peak broadening. Note that for the charged AAs Arginine and Lysine, a conductivity term $-i\sigma/\omega\varepsilon_0$ was added to the fitting function Eq. (1) ($\varepsilon_0 = 8.85 \times 10^{-12}$ F/m). The typical fitting parameters for one of AA solution at different concentrations is presented in Table I in Appendix B. Below we will focus only on the high frequency CC process, omitting the index “2”.

Following the protocol of Papers I–III of the series^{20–22} and using the CC parameters obtained from the fitting routine, the 3D trajectories for 3 main types of AAs (non-polar, polar, and charged) are plotted in Fig. 3. We also present here the 3D trajectory for the special amino acid, Proline. It is unique among the 20 protein-forming amino acids in that, unlike all the others, the amine nitrogen is bound to the amino group, leading to the formation of a pyrrolidine ring with the R-carbon.¹ The specific 3D space is defined by the rectangular coordinates $X = \ln B$, $Y = \ln \tau$, and $Z = \alpha$, where B is Froehlich’s function²⁵ at the temperature T :

$$B = \Delta\varepsilon \frac{2\varepsilon_s + \varepsilon_\infty}{3\varepsilon_s} T. \quad (2)$$

It is clear that the 3D trajectories depict the specificity of the AA molecular structure and the type of interaction with the

solvent. However, the understanding of the kinetics, structure, and hydration process in solutions can be expanded by considering various 2D projections. A detailed analysis of the different dependences of α upon the variable $x = \ln \tau$ shows that all of them can be summarized by one universal function, Eq. (A4):

$$\alpha = A + \frac{G}{x - x_0}. \quad (3)$$

Equation (3) describes four hyperbolic curves bounded by two asymptotes (see Appendix A). At low concentrations of the amino acid, $\alpha(\ln \tau)$ dependences are located in the first quadrant ($\tau > \tau_c$; $\alpha > A$) (see Figs. 3 and 4) for all AAs and depict the dipole nature of solute molecules.^{20,22} However, at high concentrations the charged amino acid Arginine demonstrates dipole–charge interactions corresponding to the second quadrant: ($\tau < \tau_c$; $\alpha > A$) (see Fig. 4(b)). Note that the charged amino acid Lysine, even at high concentrations, does not make this transition due to the high isoelectric point. Applying the fitting function (3) to the experimental pattern $\alpha(\ln \tau)$ and substituting the fitting parameters A , G , and x_0 into the model Eqs. (A2) and (A4)

$$N_\tau = N_{0\tau} \left(\frac{\tau}{\tau_c} \right)^A, \quad N_{0\tau} = \exp(G), \quad \tau_c = \exp(x_0), \quad (4)$$

we can calculate the following parameters: cutoff relaxation time τ_c ; the number, $N_{0\tau}$, of the elementary relaxation acts during this time, and N_τ , the number of the relaxation acts during the experimental relaxation time τ . Unlike the case of monosaccharide aqueous solutions,²⁰ the cutoff relaxation time τ_c is much longer than 1 ps (reorientation time of a single water molecule in the bulk) and is close to the relaxation time of the bulk solvent at the same temperature (~ 8.9 ps at 22 °C). Moreover, the AAs present a value of $N_{0\tau} = 1$, similar to that of nucleotides,²² which indicates only one minimal cooperative relaxation event during around 8–9 ps. The only exclusion to this is the special amino acid Proline that was mentioned above, which has quite an unusual zwitterion form ($\tau_c \sim 5.8$ ps).

In order to evaluate information about the structure of the solution from 3D trajectories, Froehlich’s function B from Eq. (2) can be presented in terms of the fluctuating macroscopic dipole moment M :

$$B = \frac{1}{3\varepsilon_0 k V} \langle M^2 \rangle. \quad (5)$$

Here k is the Boltzmann constant, T is the absolute temperature, V is a volume with N microscopic cells that contains some dipoles (charges), $M = \sum_{i=1}^N m_i$, where m_i is the average dipole moment of the i th cell, and the brackets $\langle \dots \rangle$ indicate a statistical averaging over all possible cell configurations. The description of the cell dipole moments and an additional assumptions used in the averaging value $\langle M^2 \rangle$ are presented in Appendix C.

FIG. 2. Real $\varepsilon'(\nu)$ and imaginary $\varepsilon''(\nu)$ parts of the complex permittivity of aqueous solutions of Alanine at different concentrations at 22 °C. Data for bulk water are also shown (dash line).¹⁷

FIG. 3. 3D trajectories of CC relaxation processes of 4 AA aqueous solutions at 22 °C driven by solution concentration: (a) Alanine, (b) Proline, (c) Threonine, and (d) Arginine.

By substitution of Eq. (C11) into Froehlich's function (5), we get

$$B = \frac{1}{3\epsilon_0 k V} \{ N_w \mu_w^2 g_w + 2 N_{aa} \mu_w \langle M^a \rangle N_{wn} \langle \cos \theta_{wn} \rangle + N_{aa} \langle M^a \rangle^2 \}. \quad (6)$$

It is more convenient to normalize both sides of Eq. (6) using the Froehlich function $B(0)$ for the bulk water at zero concentration of the solute:²²

$$B(0) = \frac{N_w(0) \mu_w^2 g_w}{3\epsilon_0 k V}, \quad N_w(0) = N_w|_{\text{bulk water}}. \quad (7)$$

We then obtain

$$\frac{B}{B(0)} = \frac{N_w}{N_w(0)} + 2 \frac{N_{aa}}{N_w(0)} \frac{\langle M^a \rangle}{\mu_w g_w} N_{wn} \langle \cos \theta_{wn} \rangle + \frac{N_{aa}}{N_w(0)} \frac{\langle M^a \rangle^2}{\mu_w^2 g_w}. \quad (8)$$

Let us consider an effective water cluster that we presented earlier²⁰⁻²² (N_{cl} is equal to the effective number of the water molecules perturbed by one AA molecule). This number can be estimated from Eq. (8) as follows:

$$N_{cl} = \left[\frac{B}{B(0)} - \frac{N_w}{N_w(0)} \right] \frac{N_w(0) g_w}{N_{aa}}, \quad (9)$$

FIG. 4. The $\alpha(\ln \tau)$ dependences for AA aqueous solutions at 22 °C. Solid lines are the fitting curves using Eq. (3).

FIG. 5. The concentration dependence of the effective number of water molecules N_{cl} perturbed by one AA molecule at 22 °C.

where

$$N_{cl} = N_d |F|, \quad N_d = \frac{\langle M^a \rangle^2}{\mu_w^2}, \quad F = 1 + 2 \frac{\mu_w}{\langle M^a \rangle} N_{wn} \langle \cos \theta_{wn} \rangle. \quad (10)$$

Here N_{cl} is the multiplication of the two unknown functions N_d and F . Although these functions cannot be determined from the same equation, each of them has a clear physical meaning. The value N_d is the number of non-correlated water dipoles, by which the average dipole moment of amino acid hydration shell can be constructed. At the same time, function F describes the interaction of the bulk water molecules with the hydration shell. Note that as discussed earlier,²² F contains $\langle \cos \theta_{wn} \rangle$ and can be negative and for this reason we use the absolute value of the F factor in Eq. (10). The numbers of water molecules associated with one amino acid are presented in Fig. 5, where the weak concentration and structural dependence of N_{cl} for all AAs except Proline is observed.

The large amount of water molecules interacted with Proline could be probably explained by the specific structure of the amino acid residue. Moreover, the data presented in Fig. 5 show that the N_{cl} for most of the amino acids exceeds the effective hydration number per one amino acid obtained in a recent study.¹⁷ There, the number of “frozen” (i.e., irrotationally bound) water molecules by a solute molecule was evaluated and found to be in agreement with the spread of the hydrodynamic radius of the amino acid rotational diffusion. Thus, the concept of a dipole-matrix interaction associated with a CC relaxation process, together with the proposed 3D trajectories, allowed to evaluate the dynamic character and the effective number of water molecules perturbed by one AA molecule in only the high frequency CC process related to the main relaxation peak of the solvent. These findings confirm our early results obtained for variable matrices (solvent) that have different chemical and electric properties (monosaccharides,²⁰ ions,²¹ and nucleotides²²).

III. CONCLUSIONS

In this contribution, we have applied the dipole-matrix interaction approach to the aqueous solutions of 6 amino acids. Due to their zwitterion nature, the CC broadening of the dielectric peak of the solvent is similar to that of the aqueous solutions of nucleotides. However, in contrast to AMP/ATP solutions, the role of charges in the case of AAs is weak and its influence is observed only in the case of the Arginine solution. The consideration of the structural events in terms of the B function allowed us to calculate the number N_{cl} of water dipoles perturbed by one amino acid molecule. These results have made it possible to unravel the mechanisms governing the role of water in protein hydration.

ACKNOWLEDGMENTS

This work has been supported by an ISF grant 465/11 (E.L., A.P., and Y.F.). The authors are grateful to Professor Vladimir Rozenshtein and Dr. Paul Ben Ishai for helpful discussion. S.C. acknowledges project MAT2012-31088 and SAIOTEK Program No. S-PE13IV001.

APPENDIX A: THE MODEL OF $\alpha(\ln \tau)$ DEPENDENCE

The phenomenological CC^{18} spectral function can be represented by a frequency dependent complex dielectric permittivity $\varepsilon^*(\omega)$:²⁶

$$\varepsilon^*(\omega) = \varepsilon_\infty + \frac{\Delta\varepsilon}{1 + (i\omega\tau)^\alpha}. \quad (A1)$$

It has been found experimentally that the parameters α , τ , and $\Delta\varepsilon$ are strictly dependent on temperature, sample structure, composition, pressure, and other physical quantities.²⁷ The fractional Fokker-Planck equation, coupled with the memory function in the Mori-Zwanzig projection formalism has been found to be a very effective mathematical tool for understanding the fractal nature and cooperative behavior of the underlying CC relaxation process.^{28–33} It was shown that the broadening parameter α , which is controlled by macroscopic physical quantities, reflects the rate of interactions of the dipole relaxation units with their surroundings:

$$\alpha = \frac{\ln N_\tau}{\ln(\tau/\tau_c)}. \quad (A2)$$

In the dimensionless time interval $\xi = \tau/\tau_c$, this rate leads to the average number of discrete interactions N_τ , which can be described by following recursive fractal:^{19–22}

$$N_\tau = N_{0\tau} \left(\frac{\tau}{\tau_c} \right)^A, \quad (A3)$$

where the mass fractal dimension A adopts values in the range $0 < A \leq 1$ and τ_c is a cutoff time that defines the time scaling. According to (A3), $N_\tau = N_{0\tau}$ if $\xi = 1$, i.e., factor $N_{0\tau}$ is defined as an average number of elementary relaxation acts happening during the period τ_c . All experimental dependences of α versus the variable $x = \ln \tau$ can be summarized in one

function as follows:¹⁹

$$\alpha = A + \frac{G}{x - x_0}, \quad (\text{A4})$$

where $x_0 = \ln \tau_c$ and the parameters of function Eq. (A4) are connected to the fractal model Eq. (A3) by the relationships:

$$N_{0\tau} = \exp(G), \quad \tau_c = \exp(x_0). \quad (\text{A5})$$

The constant A , representing the asymptotic value of the parameter α divides the plane of parameters α , x along the α -axis into two half-planes: $\alpha > A$ and $\alpha < A$. Parameter x_0 refers to the asymptotic value of x that divides the whole plane α , x along the x -axis into two half-planes: $x > x_0$ and $x < x_0$ (i.e., correspondingly $\tau > \tau_c$ and $\tau < \tau_c$) (see Fig. 6). Thus, Eq. (A4) describes the four hyperbolic curves bounded by two asymptotes (see Fig. 6). Water in complex system represents the dipole subsystem,^{19,27} while others components may be defined as a matrix.

FIG. 6. The four hyperbolic branches of the function defined by Eq. (A4). Reprinted with permission from A. Puzenko, P. Ben Ishai, and Yu. Feldman, Phys. Rev. Lett. **105**, 037601 (2010). Copyright 2010 by the American Physical Society.

APPENDIX B: THE FITTING PARAMETERS OF THE AA SOLUTIONS

TABLE I. The typical dielectric relaxation parameters for Alanine solution at various concentrations and 22 °C.^a

Alanine							
c , mol/L	$\Delta\epsilon_1 \pm 1\%$	τ_1 , ps $\pm 2\%$	$\alpha_1 \pm 0.5\%$	$\beta \pm 0.5\%$	$\Delta\epsilon_2 \pm 1\%$	τ_2 , ps $\pm 2\%$	$\alpha_2 \pm 0.5\%$
0.195	6.58	47.5	0.944	1	72.5	8.42	0.979
0.391	13.2	52.9	1	0.990	70.2	8.44	0.975
0.579	20.0	54.0	1	1	68.0	8.49	0.969
0.791	26.9	59.2	1	1	65.8	8.55	0.964
1.165	40.3	68.7	0.997	0.946	61.1	8.68	0.960
1.526	54.4	75.9	0.986	0.965	56.8	8.84	0.957

^aNote that following the protocol of Paper II,²¹ we fixed $\epsilon_\infty = \epsilon_{\infty 2} = 4.24$ (we set $\epsilon_{\infty 1} = 0$).

APPENDIX C: EVALUATION OF $\langle M^2 \rangle$

The random realization of the macroscopic dipole moment $\mathbf{M}$ of the solution volume V can be represented as follows:

$$\mathbf{M} = \sum_{i=1}^{\tilde{N}_w} \boldsymbol{\mu}_{wi} + \sum_{l=1}^{N_{aa}} \mathbf{M}_l^a. \quad (\text{C1})$$

Here $\boldsymbol{\mu}_{wi}$ is the dipole moment of the i th water molecule in the liquid state ($|\boldsymbol{\mu}_{wi}| = 3.84 D$),^{25,34} N_{aa} is the number of the AA molecules in the volume V , $\mathbf{M}_l^a$ is the total dipole moment of the AA molecule together with the hydrated shell (hydrated shell-amino acid complex), $\tilde{N}_w$ is the number of water molecules in the same volume V except those within all hydration shells. The mean square of the dipole moment is

$$\langle M^2 \rangle = S_{11} + 2S_{12} + S_{22}. \quad (\text{C2})$$

The term S_{11} takes into account the interactions between the water dipoles and can be expressed via the Kirkwood correla-

tion factor g_w .²¹

$$S_{11} = \sum_{i=1}^{\tilde{N}_w} \sum_{k=1}^{\tilde{N}_w} \langle \boldsymbol{\mu}_{wi} \boldsymbol{\mu}_{wk} \rangle = \tilde{N}_w \boldsymbol{\mu}_w^2 g_w. \quad (\text{C3})$$

The interaction of bulk water molecules with the hydrated shells is described by the second term of Eq. (C2)

$$S_{12} = \sum_{i=1}^{\tilde{N}_w} \sum_{j=1}^{N_{aa}} \langle \boldsymbol{\mu}_{wi} \mathbf{M}_j^a \rangle. \quad (\text{C4})$$

Note that for dilute solutions, condition $N_{aa}/\tilde{N}_w \ll 1$ is valid and under the assumption that $|\mathbf{M}_j^a|$ is the same for any complex, i.e.,

$$|\mathbf{M}_j^a| \cong M^a. \quad (\text{C5})$$

The double sum (C2) can be represented as follows:

$$S_{12} \cong N_{aa} N_{wn} \mu_w \langle M^a \cos \theta_{wn} \rangle, \quad (\text{C6})$$

where the N_{wn} is the number of the closest to hydrated shell water molecules and θ_{wn} is the angle between the dipole

moment of the closest bulk water molecules and the dipole moment of the water-acid complex.

Due to the diluted solution in the term S_{22} , we can neglect the interaction between complexes and also assume that $\langle (\mathbf{M}_i^a)^2 \rangle$ is independent of i :

$$S_{22} = \sum_{i=1}^{N_{aa}} \sum_{j=1}^{N_{aa}} \langle \mathbf{M}_i^a \mathbf{M}_j^a \rangle \cong \sum_{i=1}^{N_{aa}} \langle (\mathbf{M}_i^a)^2 \rangle \cong N_{aa} \langle (\mathbf{M}^a)^2 \rangle. \quad (\text{C7})$$

For further simplification, we assume that the fluctuations $\delta \mathbf{M}^a$ of $\mathbf{M}^a$ are small:

$$\mathbf{M}^a = \langle \mathbf{M}^a \rangle + \delta \mathbf{M}^a, \quad \frac{\langle (\delta \mathbf{M}^a)^2 \rangle}{\langle \mathbf{M}^{a2} \rangle} \ll 1, \quad (\text{C8})$$

i.e.,

$$\langle (\mathbf{M}^a)^2 \rangle \cong \langle (\mathbf{M}^a)^2 \rangle. \quad (\text{C9})$$

Taking into account (C8), we obtain

$$\langle \mathbf{M}^a \cos \theta_{wn} \rangle \cong \langle \mathbf{M}^a \rangle \langle \cos \theta_{wn} \rangle. \quad (\text{C10})$$

For the dilute solutions, the number $\tilde{N}_w$ in Eq. (C3) can be replaced by the total number of the water molecules N_w in the volume V and finally, the mean square of the dipole moment can be written as follows:

$$\langle \mathbf{M}^2 \rangle = N_w \mu_w^2 g_w + 2N_{aa} \mu_w \langle \mathbf{M}^a \rangle N_{wn} \langle \cos \theta_{wn} \rangle + N_{aa} \langle \mathbf{M}^a \rangle^2. \quad (\text{C11})$$

¹H. Lodish, D. Baltimore, A. Berk, S. L. Zipursky, P. Matsudaira, and J. Darnell, *Molecular Cell Biology*, 3rd ed. (Scientific American Books Inc., New York, 1995).

²J. G. Kirkwood, *J. Chem. Phys.* **2**, 351 (1934).

³J. Wyman and T. L. Meekin, *J. Am. Chem. Soc.* **55**, 915 (1933).

⁴J. Wyman, *J. Am. Chem. Soc.* **56**, 536 (1934).

⁵S. T. Bayley, *Trans. Faraday Soc.* **47**, 509 (1951).

⁶M. W. Aaron and E. H. Grant, *Trans. Faraday Soc.* **63**, 2177 (1967).

⁷M. Kumazaki and S. Sugai, *J. Phys. Soc. Jpn.* **32**, 785 (1972).

⁸J. B. Bateman, C. Gabriel, and E. H. Grant, *J. Chem. Soc. Faraday Trans.* **86**, 3577 (1990).

⁹E. H. Grant, R. J. Sheppard, and G. P. South, *Dielectric Behaviour of Biological Molecules in Solution* (Clarendon, Oxford, 1978).

¹⁰Y. A. Gusev, N. V. Sedyh, Yu. D. Feldman, and A. A. Gusev, *Naukova Dumka, Kiev* **6**, 24 (1974).

¹¹T. Sato, R. Buchner, S. Fernandez, A. Chiba, and W. Kunz, *J. Mol. Liq.* **117**, 93 (2005).

¹²X. Liao, G. S. V. Raghavan, G. Wu, and V. A. Yaylayan, *J. Mol. Liq.* **107**, 15 (2003).

¹³M. Suzuki, J. Shigematsu, Y. Fukunishi, and T. Kodama, *J. Phys. Chem. B* **101**, 3839 (1997).

¹⁴F. Bordin, C. Cametti, and G. Paradossi, *Biopolymers* **53**, 129 (2000).

¹⁵F. Bordin, C. Cametti, and A. Motta, *Macromolecules* **33**, 1910 (2000).

¹⁶F. Bordin, C. Cametti, and A. Motta, *J. Polym. Sci., Part B: Polym. Phys.* **37**, 3123 (1999).

¹⁷I. Rodríguez-Arteche, S. Cervený, A. Alegría, and J. Colmenero, *Phys. Chem. Chem. Phys.* **14**, 11352 (2012).

¹⁸K. S. Cole and R. H. Cole, *J. Chem. Phys.* **9**, 341 (1941).

¹⁹A. Puzenko, P. Ben Ishai, and Yu. Feldman, *Phys. Rev. Lett.* **105**, 037601 (2010).

²⁰E. Levy, A. Puzenko, U. Kaatz, P. Ben Ishai, and Yu. Feldman, *J. Chem. Phys.* **136**, 114502 (2012).

²¹E. Levy, A. Puzenko, U. Kaatz, P. Ben Ishai, and Yu. Feldman, *J. Chem. Phys.* **136**, 114503 (2012).

²²A. Puzenko, E. Levy, A. Shendrik, M. S. Talary, A. Caduff, and Yu. Feldman, *J. Chem. Phys.* **137**, 194502 (2012).

²³N. Axelrod, E. Axelrod, A. Gutina, A. Puzenko, P. Ben Ishai, and Yu. Feldman, *Meas. Sci. Technol.* **15**, 755 (2004).

²⁴S. Havriliak and S. Negami, *J. Pol. Sci.: Part C* **14**, 99 (1966).

²⁵H. Frölich, *Theory of Dielectrics* (Clarendon, Oxford, 1958).

²⁶Yu. Feldman, A. Puzenko, P. Ben Ishai, and E. Levy, in *Recent Advances in Broad Band Dielectric Spectroscopy*, edited by Y. P. Kalmykov (Springer, Perpignan, France, 2013), p. 1.

²⁷Yu. Feldman, A. Puzenko, and Ya. Ryabov, in *Advances in Chemical Physics*, edited by Y. P. Kalmykov, W. T. Coffey, and S. A. Rice (Wiley, New York, 2006), Vol. 133, p. 1.

²⁸R. Metzler and J. Klafter, *Phys. Rep.* **339**, 1 (2000).

²⁹R. Hilfer, *Fractals* **03**, 549 (1995).

³⁰R. Hilfer, in *Applications of Fractional Calculus in Physics*, edited by R. Hilfer (World Scientific, Singapore, 2000), p. 87.

³¹R. Hilfer, *Chem. Phys.* **284**, 399 (2002).

³²W. T. Coffey, Yu. P. Kalmykov, and S. V. Titov, *J. Chem. Phys.* **116**, 6422 (2002).

³³W. T. Coffey, Yu. P. Kalmykov, and S. V. Titov, in *Fractals, Diffusion, and Relaxation in Complex Disordered Systems*, a special volume of *Advances in Chemical Physics*, Vol. 133, edited by W. T. Coffey and Yu. P. Kalmykov (Wiley, New York, 2006), p. 285.

³⁴K. Fuchs and U. Kaatz, *J. Phys. Chem. B* **105**, 2036 (2001).