Electrostatic and Excluded Volume Effects on the Transport of Electrolytes in Poly(ethylene glycol)−Water "Mixed Solvents"

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Received: January 28, 2003; In Final Form: July 29, 2003

The transport properties of NaCl in poly(ethylene glycol)−water (PEG−water) mixtures are presented, with special regard to the dielectric and hydrodynamic effects. We report experimental data of mutual diffusion, viscosity, and conductivity for the aqueous ternary system containing PEG with an average molecular weight of 2000 a.m.u. (PEG2000, component 1) and sodium chloride (NaCl, component 2). Both PEG2000 and NaCl are used extensively as protein-crystallizing agents. The four diffusion coefficients (D_{11}, D_{12}, D_{21}, and D_{22}) that are required to describe the diffusive properties of a ternary system correctly were determined by the precise Gouy interferometric method. We also report measurements of the dielectric constant for several aqueous binary systems containing PEG with three different molecular weights (200, 400, and 2000 a.m.u.), which significantly decreases the dielectric constant of aqueous solutions. The experimental values of the four diffusion coefficients are discussed in terms of obstruction, excluded volume, and dielectric effects. The dependence of the PEG main-term diffusion coefficient, D_{11}, on the salt concentration is quantitatively described by the corresponding change of viscosity. The cross-term diffusion coefficients, D_{12} and D_{21}, are described in terms of excluded volume effects and PEG−salt nonpreferential interactions. The dependence of the salt main term diffusion coefficient, D_{22}, on PEG concentration is essentially due to obstruction effects. Moreover, a remarkable agreement between D_{22} and the salt equivalent conductivity has been determined. This correlation suggests that, even though the dielectric constant significantly changes in the presence of PEG, the electrostatic ion−ion interactions (the summation of the extent of ion-pairing and electrophoretic contributions) are not significantly modified by the polymer. This analysis of the diffusive and conductivity properties of electrolytes in the presence of PEG have allowed us to clarify important aspects of the electrostatic properties of aqueous PEG−salt systems and supplies valuable information for salt properties in "mixed solvents". A useful classification of mixed solvents is proposed, distinguishing between "viscous" and "dielectric" mixed solvents.

Introduction

Poly(ethylene glycol) (PEG) is a nonionic polymer, widely used in relation to several biotechnological, pharmacological, and industrial applications. The extensive practical use of this polymer is justified by its complete miscibility with water. Because of the broad use of this hydrophilic polymer, PEG−water binary systems have been investigated experimentally and theoretically from the thermodynamic and transport points of view.[1−4] Moreover, because PEG does not essentially interfere with the biological and structural properties of biomolecules,[5,6] this polymer is considered to be the most universal crystallizing agent for proteins.[5] The action of PEG in aqueous solutions is often interpreted in terms of macromolecular crowding, i.e., the increase of the effective concentration of other macromolecules in solution.[5−14]

However, bio-macromolecular systems are usually complex matrixes, in which other small inorganic and organic components are present.[5] For instance, PEG is used in conjunction with salts, buffers, and small organic molecules in several protein crystallization protocols. Salts are usually indispensable, because they effectively reduce the electrostatic repulsive interactions between the charged proteins, promoting the attractive hydrophobic interactions responsible for protein crystallization.[15]

It is important to remark that PEG, similar to many other organic molecules, can significantly reduce the dielectric constant of aqueous solutions.[13] In the case of water−organic-solvent−salt mixtures, it has been observed that the decrease of the dielectric constant (ϵ) caused by the presence of the organic solvent enhances the ionic electrostatic interactions and promotes the formation of ion pairs.[16] Thus, the efficacy of the salt electrostatic screening in these complex protein solutions may significantly depend on the PEG concentration.

To understand the combined role of PEG and salt in aqueous solutions, we have performed measurements of the transport properties (i.e., diffusion coefficients, viscosities, and equivalent conductivities) on the PEG−NaCl−H_2O ternary systems. Transport properties are not only important for probing molecular interactions,[13,17,18] but they also have a crucial role in many biological and biotechnological processes. For instance, diffusion and viscosity are directly involved in the nucleation and growth of protein crystals.[19−22]

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10.1021/jp034223y CCC: $25.00 © 2003 American Chemical Society
Published on Web 10/15/2003

TABLE 1: Diffusion Coefficients D_{11}, D_{12}, D_{21}, and D_{22} for the PEG2000(1)−NaCl(2)−H_2O System at 298.15 K

Concentration (mol dm^{-3})		Diffusion Coefficients ($\times 10^9$ m^2 s^{-1})			
c_1	c_2	D_{11}	D_{12}	D_{21}	D_{22}
0.1250	0.2500	0.242 ± 0.007	0.0156 ± 0.0010	0.51 ± 0.05	0.671 ± 0.027
0.1250	0.7497	0.236 ± 0.002	0.0143 ± 0.0006	1.96 ± 0.16	0.668 ± 0.022
0.1250	1.2485	0.230 ± 0.001	0.0132 ± 0.0003	3.49 ± 0.09	0.654 ± 0.007

We have previously reported measurements of multicomponent diffusion coefficients for the PEG400−NaCl−H_2O ternary system.[23] This work was centered on the analysis and predictability of the behavior of the four diffusion coefficients required for the description of a ternary system. In a second work, we have reported measurements of multicomponent diffusion coefficients for the PEG4−NaCl−H_2O ternary system (where PEG4 is an abbreviation for tetraethylene glycol).[24] This paper highlights the strong correlation between the transport and thermodynamic properties of the PEG−salt−H_2O ternary mixtures. Although the analysis of the PEG−NaCl coupled diffusion have allowed us to describe several aspects related to PEG diffusion, the role of PEG on the salt transport properties remains still unclear.

Herein, we present measurements of multicomponent diffusion coefficients for the PEG2000−NaCl−H_2O ternary system at 298.15 K, along with measurements of the ϵ values for the PEG4−H_2O, PEG400−H_2O, and PEG2000−H_2O binary systems, which show how PEG significantly modifies the dielectric properties of the medium. To clarify the role of PEG in the salt electrostatic interactions, we also report measurements of the viscosity and conductivity for the PEG−NaCl−H_2O ternary systems.

The mutual diffusion coefficients of salts in the presence of one solvent are described extensively in the literature, and equations that take the ion−ion interactions into consideration have been proposed and tested with the experiments. The Nernst−Hartley equations[25] describe electrolyte diffusion at an infinite dilution of salt in the presence of one solvent. The Onsager−Fuoss[26] and Pikal[27] theories respectively account for the effect of the ion−ion electrostatic interactions and ion-pair formation on the salt diffusion at finite salt concentration. Only a few papers have been devoted to studying electrolyte diffusion in "mixed solvents".[28,29] Most of them inaccurately describe these multicomponent mixtures as binary salt−solvent systems, reporting only one pseudo-binary diffusion coefficient.[29] However, to correctly consider all the components in the system and how they interact with each other, a matrix of multicomponent diffusion coefficients is mandatory.[30−33] Ultimately, our measurements of multicomponent diffusion coefficients, together with our conductivity and viscosity data, will supply useful and unique information on the transport properties of salts in mixed solvents.

A tentative classification is also proposed to guide the evaluation of the dominant contribution on the electrolyte transport properties of mixed solvents.

Experimental Section

Materials and Solution Preparation. Poly(ethylene glycol) with average molecular weight of 2000 a.m.u. (PEG2000) was purchased from Aldrich and used without further purification. (The company supplied the following information for the PEG2000: lot 06423HZ, number-average molar mass of 1919 g/mol, weight-average molar mass of 2034 g/mol, and polydispersity index of 1.06.[34]) The weight-average molar mass was used to calculate the molar concentration from the polymer weight. Sodium chloride (NaCl) was purchased from Aldrich (purity listed as 99.9%) and used without further purification. NaCl samples were dried by heating the samples at 450 °C, as described by Rard.[35] The molar mass value, 58.443 g/mol, was used to calculate the NaCl molar concentration. Deionized water was distilled two times for all the experiments. All solutions were prepared by weight, using a Mettler Toledo model AT400 electrobalance. To determine the molar concentration of the solutions, density measurements are required. All density measurements were performed using a Mettler-Paar model 602 densitometer thermostated with water at a temperature of 298.15 ± 0.01 K. The densitometer was calibrated with respect to the densities of water (0.997044 g cm^{-3} at 298.15 K) and air (calculated at 298.15 K, using ambient pressure and humidity).

Dielectric Constant Measurements. The measurements of the static dielectric constant (ϵ) of aqueous PEG2000 solutions were performed at 298.1 ± 0.1 K, using a commercial apparatus (DIEM) that was operating at 1 MHz and 0.6 V. The instrument was calibrated using three reference solvents of known dielectric constant: cyclohexanol (ϵ = 15.00), dimethylsulfoxide (ϵ = 46.68), and water (ϵ = 78.39).

Viscosity Measurements. The viscosity measurements reported here were performed using an Ubbelhode viscometer thermostated with water at 298.15 ± 0.01 K. The viscometer was calibrated using the water viscosity at 298.15 K (η = 0.8937 cP) as a reference.

Free-Diffusion Measurements. The diffusion measurements reported here were performed using the Gouy interferometric technique. Interferometric methods provide measurements of the diffusion coefficients matrix with the highest precision and accuracy. Both experimental procedure and data analysis are described elsewhere in detail.[36−39]

Conductivity Measurements. The conductivity measurements were performed at 298.15 ± 0.01 K, using a conductimeter (YSI model 3200) with a conductivity cell (YSI model 3256). The cell was calibrated using two standard solutions with known conductivities (a solution purchased from Hanna Instrument, with a conductivity of 1.413 μS/cm, and a solution purchased from Orion, with a conductivity of 12.900 μS/cm). The equivalent conductivity, Λ, is defined as the ratio of the salt conductivity to the stoichiometric salt concentration.

Results and Discussion

Diffusion Coefficients of PEG2000−NaCl−Water Ternary Systems. The diffusion coefficients for a ternary system are defined by the following Fick's first law:[25]

$$\begin{cases} -J_1 = D_{11}\nabla c_1 + D_{12}\nabla c_2 \\ -J_2 = D_{21}\nabla c_1 + D_{22}\nabla c_2 \end{cases} \quad (1)$$

The main-term diffusion coefficients, D_{ii} (with i = 1 or 2), give the flux of solute i, J_i, induced by its own concentration gradient, ∇c_i. The cross-term diffusion coefficients, D_{ij} (with $i \neq j$), give the flux of solute i, J_i, induced by the concentration gradient of the other solute, ∇c_j. Herein, the subscript "1" refers to PEG2000, whereas the subscript "2" refers to NaCl.

In Table 1, we report the values of diffusion coefficients obtained for the PEG2000−NaCl−H_2O ternary systems. Under

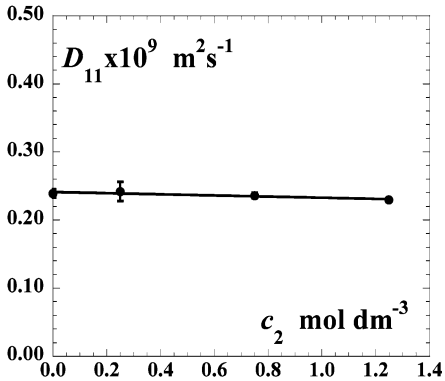

Figure 1. Ternary diffusion coefficient, D_{11}, as a function of the NaCl concentration, c_2, for the PEG2000−NaCl−H_2O system (●) at c_1 = 0.125 mol dm^{-3} and 298.15 K. In the figure, the binary diffusion coefficient for the system PEG2000−H_2O (○) is also reported. Error bars are reported, and the solid line is a linear fit to the experimental data.

TABLE 2: Relative Viscosities, η^r_{12}, for the PEG2000−NaCl−H_2O System at 298.15 K and Ratio of the Ternary and Binary Diffusion Coefficients

Concentration (mol dm^{-3})						
c_1	c_2	η^r_{12}	η^r_1/η^r_{12}	D_{11}/D_1	η^r_2/η^r_{12}	D_{22}/D_2
0.1250	0.2500	6.98	0.996	1.01 ± 0.03	0.147	0.456
0.1250	0.7497	7.03	0.989	0.98 ± 0.01	0.153	0.452
0.1250	1.2485	7.08	0.982	0.96 ± 0.01	0.159	0.440

all the investigated conditions, the PEG2000 molar concentration, c_1, was kept equal to c_1 = 0.1250 mol dm^{-3} (a PEG2000 mass concentration of $w_1 \approx$ 250 g dm^{-3}). On the other hand, the NaCl molar concentration, c_2, was increased from 0.2500 mol dm^{-3} to 1.2500 mol dm^{-3}. At this temperature, no spinodal composition is expected for our system; therefore, although the determinant of the diffusion matrix decreases as the value of c_2 increases, it is never expected to go to zero.

PEG Diffusion due to Its Own Gradient: D_{11}. In Figure 1, we report D_{11} as a function of salt concentration. We also include the value of D_{11} at $c_2 = 0$ ($D_{11} = 0.2391 \times 10^{-9}$ m^2 s^{-1}), i.e., the binary diffusion coefficient corresponding to the PEG2000−H_2O system. D_{11} decreases as the salt concentration increases, and at the highest salt concentration, D_{11} is ∼4% smaller than the corresponding binary diffusion coefficient value. In Table 2, we report the relative viscosity values (i.e., the ratio of the solution viscosity to the water viscosity), η^r_{12}, obtained for the PEG2000−NaCl−H_2O ternary systems at c_1 = 0.1250 mol dm^{-3} as a function of c_2. In Table 1, we report the values of D_{11}/D_1 and η^r_1/η^r_{12} where η^r_1 is the relative viscosity corresponding to the binary PEG2000−H_2O system. We observe that the change of D_{11}, as a function of the salt concentration, is consistent with the corresponding change of the solution viscosity.

The theory of Brownian motion[25,40] shows that the diffusion coefficient of a particle is inversely proportional to the viscosity of the system. This microscopic theory assumes that the diffusing particle is significantly larger than the solvent molecules, which implies that the solvent can be treated as a continuum medium. The theory also assumes that particle−particle interactions are negligible, i.e., the condition of infinite dilution must be respected. Our results show that the dependence of the PEG main diffusion coefficient, D_{11}, on the salt concentration can be quantitatively described by the change of

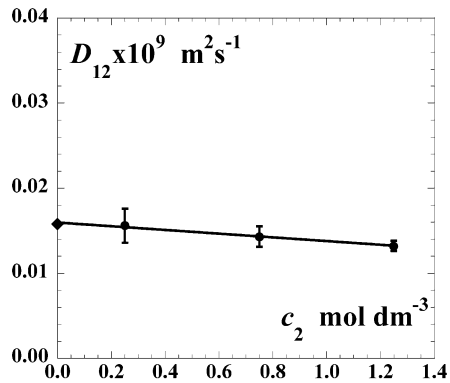

Figure 2. Ternary diffusion coefficient, D_{12}, as a function of the NaCl concentration, c_2, for the PEG2000−NaCl−H_2O system (●) at c_1 = 0.125 mol dm^{-3} and 298.15 K. In the figure, the value extrapolated to $c_2 = 0$ (○) is also reported. Error bars are reported, and the solid line is a linear fit to the experimental data.

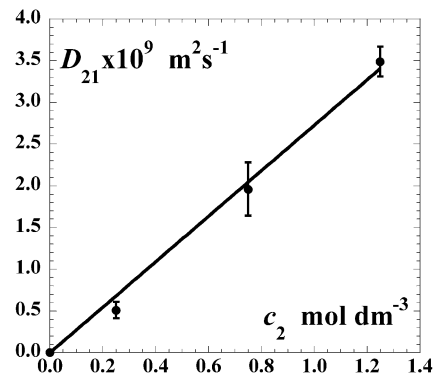

Figure 3. Ternary diffusion coefficient (D_{21}), as a function of the NaCl concentration (c_2) for the PEG2000−NaCl−H_2O system at c_1 = 0.125 mol dm^{-3} and 298.15 K. Error bars are reported, and the solid line is a linear fit to the experimental data.

the medium viscosity, as it is expected by this theory. The agreement between theory and experiment is consistent with the size of the molecules; indeed, NaCl ions and water are significantly smaller than PEG molecules and can be treated as a continuum. However, because the concentration of PEG2000 is very high (a concentration of 0.125 mol dm^{-3} corresponds to ∼25 wt %), polymer−polymer interactions are significant. Thus, the observed experimental correlation between the dependence of D_{11} and η^r_{12} on salt concentration would conclude that high salt concentrations essentially do not modify the polymer−polymer interactions.

Coupled Diffusion: D_{12} and D_{21}. In Figure 2, we report D_{12} as a function of salt concentration, along with its extrapolated value at $c_2 = 0$ ($D_{12} = 0.039 \times 10^{-9}$ m^2 s^{-1}). We observe that D_{12} is positive and slightly decreases as the salt concentration increases. In Figure 3, we report D_{21} as a function of salt concentration. At $c_2 = 0$, a gradient of the PEG2000 concentration (∇c_1) cannot induce a flow of NaCl (J_2) and, hence, D_{21} = 0. We observe that D_{21} is positive and directly proportional to the salt concentration.

The behavior of the cross-diffusion coefficients is consistent with the behavior observed for the other PEG−NaCl−H_2O systems.[23,24] The cross-term diffusion coefficient, D_{12}, describes the effect of a salt gradient on the flow of PEG. D_{12} is positive; therefore, PEG diffuses from high to low salt concentration. This dynamic behavior suggests that PEG molecules prefer to minimize the interactions with the ions and, correspondingly, maximize the interaction with water molecules.

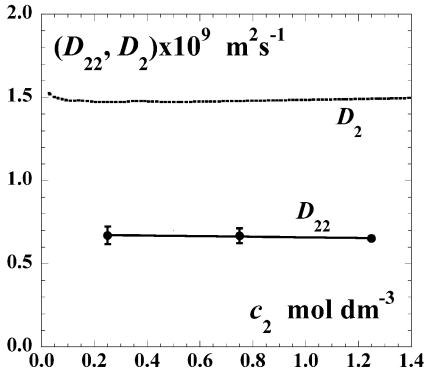

Figure 4. Ternary diffusion coefficient (D_{22}), as a function of the NaCl concentration (c_2) for the PEG2000−NaCl−H_2O system at $c_1 = 0.125$ mol dm^{-3} and 298.15 K. In the figure, the binary diffusion coefficients for the NaCl−H_2O system (dashed line) are also reported. Error bars are reported, and the solid line is a linear fit to the experimental data.

D_{21} is positive and linearly increases with salt concentration. The behavior of this cross-diffusion coefficient can be described in terms of excluded volume effects.[23,41−44] Because the volume occupied by the large PEG molecules is excluded to the salt ions, the presence of a gradient of the PEG concentration produces a gradient of "interstitial" salt concentration, which results in a correspondingly larger flow of the ions. The following equation for D_{21}, which is based on this excluded volume interpretation, has been reported in ref 23:

$$D_{21} \approx D_{22}\frac{c_2 V_1}{(1 - c_1 V_1)^2} \tag{2}$$

where V_1 is the volume excluded to the salt by 1 mol of PEG. From eq 2, D_{21} is expected to be a linear function of the salt concentration, as observed experimentally. The excluded volume, $V_1 \approx 2.2$ dm^3 mol^{-1}, obtained by fitting our experimental values with eq 2, is larger than the partial molar volume, $\bar{V}_1 = 1.68$ dm^3 mol^{-1} (obtained from our density measurements), and substantially equal to the PEG hydrodynamic volume, $V_1^h \approx 2.2$ dm^3 mol^{-1}.[23] The difference between the larger $V_1 \approx V_1^h$ and the smaller $\bar{V}_1$ indicates that the concentration of salt around the PEG molecules is depleted, i.e., PEG is preferentially surrounded by water.

Salt Diffusion due to Its Own Gradient: D_{22}. In Figure 4, we report D_{22} as a function of salt concentration (data points). In the same figure, the binary diffusion coefficient, D_2 (denoted by the dashed line), as a function of the salt concentration for the NaCl−H_2O binary system ($c_1 = 0$), is also included. From Table 1 and Figure 4, we can see that D_{22}/D_2 is essentially constant within the experimental domain. However, it is important to remark that the value of the ternary diffusion coefficient D_{22} is ∼50% smaller than the corresponding binary value, D_2. As we can see from Table 2, the change of viscosity quantitatively fails to describe the difference between the ternary and binary salt diffusion coefficients. In fact, the decrease of salt mobility caused by the presence of PEG molecules cannot be simply rationalized by considering the PEG−water mixed solvent as a continuum. In this case, the effect of PEG on the NaCl diffusion properties is better described by the obstruction of the motion of the ions caused by quasi-localized large particles, and only a qualitative agreement between viscosity and diffusion is expected. Moreover, the PEG−water dielectric constant decreases as PEG concentration increases. In Table 3, we report the values of the dielectric constant, ϵ, for the PEG2000−H_2O binary system as a function of the PEG2000 mass concentration, w_1 (in units of g dm^{-3}). For comparison, we also include our measurements relative to the PEG400−H_2O and PEG4−H_2O binary systems.[23,24] The table shows that, in all cases, the value of ϵ decreases as a function of the PEG concentration; the effect is greater for the higher PEG molecular weights. It is important to remark that, in the case of the PEG2000−H_2O system at $w_1 = 250$ g dm^{-3} ($c_1 = 0.1250$ mol dm^{-3}), the value of ϵ is ∼50% smaller than that corresponding to pure water. Thus, PEG might promote strong ion−ion electrostatic interactions. Strong electrostatic interactions can even induce the formation of neutral ion pairs.[16] Therefore, in principle, both steric obstruction and electrostatic effects are expected to determine the dependence of D_{22} on the salt and PEG concentrations.

TABLE 3: Relative Dielectric Constant (ϵ) for the PEG2000−H_2O, PEG400−H_2O, and PEG4−H_2O Systems at 298.15 K

PEG2000(1)−water		PEG400(1)−water		PEG4(1)−water	
c_1 (mol dm^{-3})	ϵ	c_1 (mol dm^{-3})	ϵ	c_1 (mol dm^{-3})	ϵ
0.0000	78.39	0.0000	78.39	0.0000	78.39
0.0459	68.67	0.0500	77.28	0.2500	75.98
0.0484	67.07	0.1000	75.74	0.5000	73.67
0.0534	65.41	0.1500	74.32	0.8759	70.33
0.0752	60.89	0.2500	71.70	1.0000	69.26
0.0848	55.25	0.3000	70.48	1.3090	66.64
0.1041	53.75	0.3500	69.80	1.6898	63.47
0.1063	48.50	0.4000	68.39	2.0000	60.90
0.1134	48.00			2.1238	59.87
0.1275	44.65			2.7549	54.49
				2.9982	52.32

To evaluate the electrostatic effect on the NaCl diffusion coefficients, we have considered a hypothetical pure solvent that has the same dielectric constant and viscosity as those of the binary system PEG2000(1)−water at $c_1 = 0.1250$ mol dm^{-3}. We can then estimate how the so-called electrophoretic effect and the ion-pair formation could affect the electrolyte diffusion.[26,45] The Onsager−Fuoss theory[26] has been used to estimate the contribution of the electrophoretic effect to the D_{22} value. This electrophoretic term ($\Delta_1 + \Delta_2$ in the Onsager−Fuoss equation; see Appendix A)[26] is directly proportional to ϵ and inversely proportional to the viscosity of the medium. We estimate that the presence of PEG2000 at $c_1 = 0.1250$ mol dm^{-3} would cause a decrease of ∼4% in the salt diffusion coefficient, with respect to the NaCl−water binary system. We believe that, in the case of PEG, the large viscosity value of the corresponding aqueous solutions is responsible for such a small $\Delta_1 + \Delta_2$ contribution. Yet, it is important to note that this is not a general case. There are many co-solvents, such as alcohols with small carbon chains, for which a significant decrease of the value of ϵ does not correspond to a considerable increase of the viscosity. In this case, the change of the salt diffusion coefficient, with respect to water, is essentially due to the variation in ϵ. Indeed, we can divide the binary mixture of water and inorganic solvents into two categories: the "viscous solvents" and the "dielectric solvents" (see Figure 5).

Let us now consider the case of ion-pair formation. The formation of Na−Cl neutral ion pairs, which is caused by small ϵ values, is described by the following mass-action equilibrium:

$$K = \frac{c_{\mathrm{NaCl}}}{c_{\pm}^2} \tag{3}$$

where $c_{\pm}$ and c_{NaCl} are, respectively, the concentrations of dissociated and associated salt, and K is the equilibrium constant, which is a function of ϵ or, equivalently, of c_1. Although eq 3

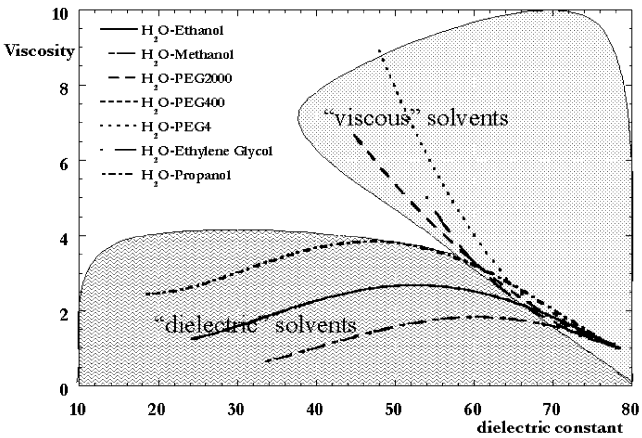

Figure 5. Viscosity and dielectric constant of several binary water−co-solvent systems. This graph allows a qualitative classification of solvents in "viscous" solvents (with a high viscosity and high dielectric constant) and "dielectric" solvents (with a low viscosity and low dielectric constants).

assumes that the activities may be replaced by the corresponding concentrations of the single species, this equation provides some important general insights on the dependence of the diffusion coefficient on salt concentration. By applying a mass balance, in the case of the formation of ion pairs, we can obtain (see Appendix B)

$$D_{22} = \frac{1}{1 + 2\sqrt{Kc_{\mathrm{NaCl}}}} D_{\pm} + \frac{2\sqrt{Kc_{\mathrm{NaCl}}}}{1 + 2\sqrt{Kc_{\mathrm{NaCl}}}} D_{\mathrm{NaCl}} \qquad (4)$$

where $D_{\pm}$ is the mutual diffusion coefficient of the dissociated salt and D_{NaCl} is the mutual diffusion coefficient of the ion pair. Equation 4 is general and also applies for $c_1 = 0$, i.e., for the binary NaCl−water system. If $K = 0$ (strong electrolyte conditions), then $D_{22} = D_{\pm}$. If K is significantly large, the mobility of the ion pairs will affect the dependence of D_{22} on c_2.

The effect of chemical association on the behavior of the diffusion coefficient has been investigated in several studies.[46−50] If the difference between the mobilities of associated and dissociated species is very large, chemical association effectively shapes the concentration dependence of the diffusion coefficients.[46,47] Indeed, measurements of diffusion coefficients can be used to successfully estimate association constants for host−guest and micellar systems.[47,49]

The diffusion coefficient of the Na−Cl ion pair in water was estimated to be equal to 0.86×10^{-9} m^2 s^{-1}, which is approximately half the value of $D_{\pm}$.[51] If K is a function of the PEG concentration, eq 4 would suggest the ratio D_{22}/D_2 to be a function of c_2. This is not supported by the experimental values reported in Table 2. This result indicates that either K is not a function of c_1 or eq 4 is not accurate enough for our purposes, because the difference between $D_{\pm}$ and D_{NaCl} is not sufficiently large. To understand the role of PEG on the electrolyte properties better, we performed measurements of equivalent conductivities.

Equivalent Conductivity of Sodium Chloride in PEG−NaCl−Water Ternary Systems. We report in Table 4 the values of the NaCl equivalent conductivities, Λ_{12}, obtained for the PEG2000−NaCl−H_2O and ternary systems at $c_1 = 0.1250$ mol dm^{-3}, as a function of c_2; Table 4 also lists the NaCl equivalent conductivities obtained for the PEG4−NaCl−H_2O and PEG400−NaCl−H_2O ternary systems at the same concentrations where measurements of diffusion coefficients were previously performed.[23,24] In the same table, we also include

TABLE 4: Equivalent Conductivities in the Ternary System (Λ_{12}) for the PEG2000−NaCl−H_2O, PEG400−NaCl−H_2O, and PEG4−NaCl−H_2O Systems at 298.15 K[a]

Sodium Concentration (mol dm^{-3})				
c_1	c_2	Λ_{12} (Ω cm^2 mol^{-1})	Λ_{12}/Λ_2	D_{22}/D_2
	PEG2000−NaCl−H_2O			
0.1250	0.2500	48.13	0.481	0.456
0.1250	0.5000	44.09	0.476	
0.1250	0.7497	41.30	0.468	0.452
0.1250	1.2485	37.42	0.445	0.440
	PEG400−NaCl−H_2O			
0.2579	0.2501	76.93	0.770	0.786
0.2578	0.7735	67.53	0.761	0.784
0.2623	1.2718	61.28	0.744	0.785
	PEG4−NaCl−H_2O			
0.2500	0.4997	83.70	0.904	0.889
0.5000	0.4997	71.88	0.776	0.788
1.0000	0.5000	57.36	0.620	0.606
2.0000	0.5000	31.18	0.337	0.331
2.9921	0.4988	14.50	0.157	0.157

[a] The ratio between the ternary equivalent conductivity (Λ_{12}) and binary equivalent conductivity (Λ_2) is also reported.

the ratio Λ_{12}/Λ_2, where Λ_2 is the NaCl equivalent conductivity of the NaCl−H_2O binary system.[52] The Λ_{12} values decrease as a function of both the PEG and salt concentrations. As c_2 increases, the ratio Λ_{12}/Λ_2 changes from 0.48 to 0.45 for PEG2000 ($c_1 = 0.1250$ mol dm^{-3}), whereas it changes from 0.77 to 0.74 for PEG400 ($c_1 = 0.2600$ mol dm^{-3}). In the case of PEG4, we have performed conductivity measurements at a constant salt concentration and observed that the ratio Λ_{12}/Λ_2 decreases from 0.89 to 0.16 as c_1 increases. From the inspection of the values of Λ_{12}/Λ_2 and D_{22}/D_2 reported in Table 4, we observe that Λ_{12}/Λ_2 is practically equal to D_{22}/D_2.

Let us now first consider the dependence of the equivalent conductivity, Λ_{12}, on c_1 and c_2. The dependence of Λ_{12} on the PEG concentration is influenced by both obstruction and electrostatic effects.[45] Both the conductivity and diffusion of electrolytes depend on the mobility of the single ionic species (see Appendix A);[53] therefore, we expect that the obstruction effect, which is caused by the large and neutral PEG molecules, affects these two properties in the same way. On the other hand, ion−ion electrostatic interactions produce opposite effects on the behavior of these two transport quantities.[45,53] If an external electric field is applied, the oppositely charged ions migrate in opposite directions, whereas if a concentration gradient is present, all the ions diffuse in the same direction, to preserve the electroneutrality of the electrolyte solution. This implies that, as the salt concentration increases, the electrophoretic effect increases the diffusion coefficient and decreases the equivalent conductivity. Moreover, in the case of the equivalent conductivity, the so-called relaxation effect, which is caused by the external electric field, provides an additional negative contribution to the value of the equivalent conductivity.[45,53]

Ion-pair formation has also a different effect on the diffusion and equivalent conductivity, because the neutral ion pair does not migrate in the presence of the external electric field. Because the electric conductivity is only caused by the motion of the single ions, the behavior of the "stoichiometric" equivalent conductivity in the ternary system, Λ_{12}, is described by the following equation:

$$\Lambda_{12} = \Lambda_{\pm}\frac{c_{\pm}}{c_2} = \frac{\Lambda_{\pm}}{1 + \sqrt{Kc_{\mathrm{NaCl}}}} \qquad (5)$$

where $\Lambda_{\pm}$ is the equivalent conductivity of the dissociated salt.

If K depends on the PEG concentration, eq 5 would suggest that the ratio Λ_{12}/Λ_2 is a function of c_2. The equivalent conductivity of the neutral ion pair is zero; therefore, we expect conductivity to be more sensitive than diffusion to the ion-pair formation. Again, this is not supported by the experimental values reported in Table 4. These results strongly support the hypothesis that PEG does not induce ion-pair formation.

Yet, the most impressive result is the experimental evidence that D_{22}/D_2 is practically equal to Λ_{12}/Λ_2. We can therefore conclude that the effect of PEG on both diffusion and equivalent conductivity is the same. Our findings clearly imply that the dependence of Λ_{12} on the PEG concentration is entirely due to obstruction effects. The tight correlation between D_{22}/D_2 and Λ_{12}/Λ_2 does indicate that the presence of a large amount of PEG does not sensitively affect the electrostatic interaction between Na^+ and Cl^-. This conclusion is consistent with a corresponding molecular picture in which Na^+ and Cl^- ions are preferentially surrounded by water molecules.

Summary and Conclusions

We have characterized the transport properties of the PEG−NaCl−water system. We have found that the dependence of the PEG main term diffusion coefficient, D_{11}, on the salt concentration can be quantitatively described by the change of the system viscosity. We have also found that the dependence of the salt main term diffusion coefficient, D_{22}, on both the salt and PEG concentration is strongly correlated to the change of the salt equivalent conductivity. The remarkable and unexpected concordance between salt conductivity and salt diffusion implies that the ion−ion electrostatic interactions are not substantially modified by high PEG concentrations. These experimental evidences are consistent with a molecular configuration where both PEG and salt are preferentially surrounded by water molecules. The behavior of the cross-term diffusion coefficients provides additional support for this microscopic interpretation. In particular, the behavior of the cross-term diffusion coefficient, D_{21}, can be simply associated with excluded volume PEG−salt interactions.

Appendix A

In this appendix, we review how the electrostatic interactions are taken into consideration in the case of the diffusion coefficient and the equivalent conductance of an electrolyte solution.

At infinite dilution, the following relations hold for the diffusion coefficient of a univalent electrolyte:

$$D_\pm^\infty = \frac{2D_+^\infty D_-^\infty}{D_+^\infty + D_-^\infty} \quad \text{(Nernst−Hartley equation)} \tag{A1}$$

$$D_\pm^\infty = \frac{KT}{6\pi(r_+ + r_-)\eta_0} = \frac{KT}{6\pi r_\pm \eta_0} \text{ (Stokes−Einstein equation)} \tag{A2}$$

where D_+^∞ and D_-^∞ are the respective diffusion coefficients of the cation and anion, r_+ and r_- are the respective radii of the cation and anion, and η_0 is the solvent viscosity.[25]

In a dilute electrolyte solution, where the viscosity effect can be neglected, the salt diffusion coefficient, $D_\pm$, can be described by the Onsager−Fuoss equation:[25,26]

$$D_\pm = (D_\pm^\infty + \Delta_1 + \Delta_2)\left(1 + \frac{\partial \ln y_\pm}{\partial \ln c_\pm}\right) \tag{A3}$$

where $y_\pm$ is the salt activity coefficient in the molar scale, whereas Δ_1 and Δ_2 are the Onsager−Fuoss parameters, which are functions of the dielectric constant ϵ.[25,26] The Δ_1 and Δ_2 terms are opposite in sign and their values are at least 1 order of magnitude smaller than the value of the diffusion coefficient at infinite dilution. These two parameters are positive (i.e., the electrolyte diffusion is enhanced) and take the so-called "electrophoretic effect" into consideration.[25,26,45]

In more-concentrated solutions, the "medium" viscosity effect must be taken into consideration. The Gordon equation states[25,45]

$$D_\pm = (D_\pm^0 + \Delta_1 + \Delta_2)\left(1 + \frac{\partial \ln y_\pm}{\partial \ln c_\pm}\right)\frac{\eta_0}{\eta_\pm} \tag{A4}$$

where η_0 is the solvent viscosity and $\eta_\pm$ is the viscosity of the electrolyte solution. The viscosity correction is an extension of the Stokes−Einstein equation to finite concentration.

Let us now consider the equivalent conductance. At infinite dilution, the equivalent conductance can be written as

$$\Lambda_\pm^\infty = \lambda_+^\infty + \lambda_-^\infty \tag{A5}$$

$$\Lambda_\pm^\infty = \frac{eF}{6\pi\eta_0}\left(\frac{1}{r_+} + \frac{1}{r_-}\right) \tag{A6}$$

where λ_+^∞ and λ_-^∞ are the ionic equivalent conductances at infinite dilution, r_+ and r_- are the ionic radii, e is the electron charge, F is the Faraday constant, and η_0 is the solvent viscosity. Equations A5 and A6 are the Walden equations.[45] At increasing salt concentrations, the decrease of the equivalent conductance of strong electrolytes can be attributed to the electrophoretic effect, the time relaxation effect, and "medium viscosity".[25,45]

Appendix B

We now derive eq 4. In the presence of Na−Cl ion pairs, the total salt concentration is the sum of two contributions:

$$c_2 = c_\pm + c_{NaCl} \tag{B1}$$

The total flux of salt (J_2) is the sum of the flux related to the dissociated salt ($J_\pm$) and the flux related to the ion pairs (J_{NaCl}):

$$J_2 = J_\pm + J_{NaCl} \tag{B2}$$

with

$$J_\pm = -D_\pm \nabla c_\pm \tag{B3a}$$

and

$$J_{NaCl} = -D_{NaCl}\nabla c_{NaCl} \tag{B3b}$$

Applying eqs B2 and B3, we derive the following relation:

$$-J_2 = D_\pm \nabla c_\pm + D_{NaCl}\nabla c_{NaCl} = \left(D_\pm \frac{\partial c_\pm}{\partial c_2} + D_{NaCl}\frac{\partial c_{NaCl}}{\partial c_2}\right)\nabla c_2 = D_{22}\nabla c_2 \tag{B4}$$

An expression for the two partial derivatives, $\partial c_\pm/\partial c_2$ and $\partial c_{NaCl}/\partial c_2$, can be obtained by considering the condition of chemical equilibrium expressed by eq 3:

$$\frac{\partial c_\pm}{\partial c_2} = \frac{1}{1 + 2\sqrt{Kc_{NaCl}}} \tag{B5a}$$

$$\frac{\partial c_{\mathrm{NaCl}}}{\partial c_2} = 1 - \frac{\partial c_{\pm}}{\partial c_2} = \frac{2\sqrt{Kc_{\mathrm{NaCl}}}}{1 + 2\sqrt{Kc_{\mathrm{NaCl}}}} \qquad \text{(B5b)}$$

Using eqs B4 and B5, we obtain the expression for D_{22}:

$$D_{22} = \frac{1}{1 + 2\sqrt{Kc_{\mathrm{NaCl}}}} D_{\pm} + \frac{2\sqrt{Kc_{\mathrm{NaCl}}}}{1 + 2\sqrt{Kc_{\mathrm{NaCl}}}} D_{\mathrm{NaCl}} \qquad \text{(B6)}$$

Acknowledgment. We acknowledge the Italian Space Agency (ASI) for financial support.

References and Notes

(1) Vergara, A.; Paduano, L.; Vitagliano, V.; Sartorio, R. *Phys. Chem. Chem. Phys.* **1999**, *1*, 5377.
(2) Paduano, L.; Sartorio, R.; D'Errico, G.; Vitagliano, V. *J. Chem. Soc., Faraday Trans.* **1998**, *94*, 2571.
(3) Ninni, L.; Camargo, M. S.; Meirelles, A. J. A. *Thermochim. Acta* **1999**, *329*, 169.
(4) Herskowitz, M.; Gottlieb, M. *J. Chem. Eng. Data* **1985**, *30*, 233.
(5) McPherson, A. *Crystallization of Biological Macromolecules*; Cold Spring Harbor Laboratory Press: Plainview, NY, 1999.
(6) Albertsson, P. A. *Partition of Cell Particles and Macromolecules*; Wiley: New York, 1986.
(7) Asakura, S.; Oosawa, F. *J. Chem. Phys.* **1954**, *22*, 1255.
(8) Lekkerkerker, H. N. W.; Poon, W. C. K.: Pusey, P. N. Stroobants; A.; Warren, P. B. *Europhys. Lett.* **1992**, *20*, 559.
(9) Atha, D. H.; Ingham, K. C. *J. Biol. Chem.* **1981**, *256*, 12108.
(10) Arakawa, T.; Timasheff, S. N. *Biochemistry* **1985**, *24*, 6756.
(11) Kulkarni, A. M.; Chatterjee, A. P.; Schweizer, K. S.; Zukoski, C. F. *J. Chem. Phys.* **2000**, *113*, 9863.
(12) Finet, S.; Tardieu, A. *J. Crys. Growth* **2001**, *232*, 40.
(13) Vergara, A.; Paduano, L.; Sartorio, R. *Macromolecules* **2002**, *35*, 1389.
(14) Annunziata, O.; Asherie, N.; Lomakin, A.; Pande, J.; Ogun, O.; Benedek, G. B. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 14165.
(15) Rosenberger, F.; Vekilov, P. G.; Muschol, M.; Thomas, B. R. *J. Cryst. Growth* **1996**, *168*, 1.
(16) Hefter, G.; Marcus, Y.; Waghorne, W. E. *Chem. Rev.* **2002**, *102*, 2773.
(17) Annunziata, O.; Paduano, L.; Pearlstein, A. J.; Miller, D. G.; Albright, J. G. *J. Am. Chem. Soc.* **2000**, *122*, 5916.
(18) Fine, B. M.; Lomakin, A.; Ogun, O.; Benedek, G. B. *J. Chem. Phys.* **1996**, *104*, 326.
(19) Kashchiev, D. *Nucleation: Basic Theory with Applications*; Butterworth−Heinemann: Oxford, U.K., 2000.
(20) Lin, H.; Rosenberger, F.; Alexander, J. I. D.; Nadarajah, A. *J. Cryst. Growth* **1995**, *151*, 153.
(21) Castagnolo, D.; Vergara, A.; Paduano, L.; Sartorio, R.; Annunziata, O. *Acta Crystallogr., Sect. D: Biol. Crystallogr.* **2002**, *58*, 138.
(22) Annunziata, O.; Albright, J. G. *Ann. N.Y. Acad. Sci.* **2002**, *974*, 610.
(23) Vergara, A.; Paduano, L.; Vitagliano, V.; Sartorio, R. *Macromolecules* **2001**, *34*, 991.
(24) Vergara, A.; Paduano, L.; Sartorio, R.; Annunziata, O.; Miller, D. J.; Albright, J. G. Multicomponent Diffusion in Crowded Solutions. 2. Mutual Diffusion in the Ternary System Tetra(ethylene glycol)−NaCl−Water, submitted to *J. Phys. Chem. B.*
(25) Tyrrell, H. J. V.; Harris, K. R. *Diffusion in Liquids*; Butterworth: London, 1984.
(26) Onsager, L.; Fuoss, R. *J. Phys. Chem.* **1932**, *36*, 2689.
(27) Pikal, M. J. *J. Phys. Chem.* **1971**, *75*, 663.
(28) Havenga, E.; Leaist, D. G. *J. Chem. Soc., Faraday Trans.* **1998**, *94*, 3353.
(29) Leaist, D. G.; Lyons, P. A. *J. Solution Chem.* **1981**, *10*, 95.
(30) Onsager, L. *Ann. N.Y. Acad. Sci.* **1945**, *46*, 241.
(31) Gosting, L. J. In *Advances in Protein Chemistry*; Anson, M. L., Bailey, K., Edsall, J. T., Eds.; Academic Press: New York, 1956; Vol. XI, p 429.
(32) Miller, D. G.; Albright, J. G. In *Measurement of the Transport Properties of Fluids*: *Experimental Thermodynamics*; Wakeham, W. A., Nagashima, A., Sengers, J. V., Eds.; Blackwell Scientific Publications: Oxford, U.K., 1991; p 272.
(33) Vitagliano, V. *Pure Appl. Chem.* **1991**, *63*, 1441.
(34) Albright, J. G.; Paduano, L.; Vergara, A.; Vitagliano, V.; Sartorio, R. *J. Chem. Eng. Data* **2001**, *46*, 1283.
(35) Rard, J. A. *J. Chem. Thermodyn.* **1996**, *28*, 83.
(36) Kegeles, G.; Gosting, L. J. *J. Am. Chem. Soc.* **1947**, *69*, 2516.
(37) Fujita, H.; Gosting, L. J. *J. Phys. Chem.* **1956**, *78*, 1099.
(38) Fujita, H.; Gosting, L. J. *J. Phys. Chem.* **1960**, *64*, 1256.
(39) Albright, J. G.; Miller, D. G. *J. Phys. Chem.* **1989**, *93*, 2169.
(40) Einstein, A. *Investigation on the Theory of Brownian Movement*; Methuen: London, 1926.
(41) Vergara, A.; Paduano, L.; Sartorio, R. *J. Phys. Chem. B* **2001**, *105*, 328.
(42) Vergara, A.; Paduano, L.; Vitagliano, V.; Sartorio, R. *J. Phys. Chem. B* **2000**, *104*, 8068.
(43) Vergara, A.; Paduano, L.; Vitagliano, V.; Sartorio, R. *Mater. Chem. Phys.* **2000**, *66*, 126.
(44) Albright, J. G.; Annunziata, O.; Miller, D. G.; Paduano, L.; Pearlstein, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 3256.
(45) Robinson, R. A.; Stokes, R. H. *Electrolyte Solutions*; Butterworth: London, 1970.
(46) Leaist, D. G. *J. Colloid Interface Sci.* **1986**, *111*, 230.
(47) Annunziata, O.; Constantino, L.; D'Errico, G.; Paduano, L.; Vitagliano, V. *J. Colloid Interface Sci.* **1999**, *216*, 8.
(48) Paduano, L.; Sartorio, R.; Vitagliano, V.; Albright, J. G.; Miller, D. G.; Mitchell, J. *J. Phys. Chem.* **1990**, *94*, 6885.
(49) Paduano, L.; Vergara, A.; Sartorio, R.; Vitagliano, V. *Trends Phys. Chem.* **1999**, *7*, 209.
(50) Leaist, D. G. *J. Solution Chem.* **1992**, *21*, 1035.
(51) Johnson, K. S. *Mar. Chem.* **1981**, *10*, 195.
(52) Lobo, V. M. M. *Electrolyte Solutions: Literature Data on Thermodynamic and Transport Properties*; University of Coimbra: Coimbra, Portugal, 1975.
(53) Miller, D. G. *J. Phys. Chem.* **1966**, *70*, 2639.