Self-Diffusion Studies of Water and Poly(ethylene glycol) in Solutions and Gels of Selected Hydrophilic Polymers

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Received February 16, 1999

ABSTRACT: To test the effect of the matrix polymer on diffusion, we have measured the self-diffusion coefficients of water and poly(ethylene glycol) of a molecular weight of 600 (PEG-600) in aqueous systems of selected polymers using the pulsed-gradient spin-echo NMR technique. The polymers used in this study include poly(vinyl alcohol) (PVA), hydroxypropyl methyl cellulose (HPMC), poly(*N*,*N*-diethylacrylamide) (PNNDEA), and poly(*N*-isopropylacrylamide) (PNIPA). The polymer concentrations varied from 0 to 0.38 g/mL. The effect of the polymer network on the self-diffusion coefficients of the solvent (water) and a solute (PEG-600) was investigated by analyzing the diffusion data with the use of the free volume model of Yasuda et al. [Yasuda, H.; Lamaze, C. E.; Ikenberry, L. D. *Makromol. Chem.* **1968**, *118*, 19], the diffusion model proposed by Phillies [Phillies, G. D. J. *Macromolecules* **1986**, *19*, 2367], and the model of Petit et al. [Petit, J.-M.; Roux, B.; Zhu, X. X.; Macdonald, P. M. *Macromolecules* **1996**, *29*, 6031]. The results obtained with PVA, HPMC, PNNDEA, and PNIPA are used to evaluate the applicability of these models in polymer−water−solute ternary systems. The physical significance of the parameters used in the models is discussed.

Introduction

The study of the diffusion of solvents and solutes in polymer solutions and gels has attracted much research interest because of its importance related to the use of polymer materials. For example, diffusion studies can be used to obtain information on the mixing of polymers,[1] the diffusion of a plasticizer in a polyelectrolyte,[2] the characterization of polymer microstructures,[3,4] intermolecular interactions,[5] and more recently the controlled release of drugs in biomedical and pharmaceutical applications of polymers.[6] The polymer carriers used for the controlled release of drugs are usually hydrophilic and can swell in water. They include poly(vinyl alcohol) (PVA) and hydroxypropyl methyl cellulose (HPMC).[7] PVA is also used in many other applications,[8] and the degree of hydrolysis of the acetic groups of poly(vinyl acetate) determines the solubility of PVA in water.[9] Recently, the use of thermosensitive polymers in biomedical fields has also been studied.[10]

We have already studied the self-diffusion of diffusants of various sizes in PVA aqueous solutions and gels.[11−13] In the study of self-diffusion of solutes probes with different functional groups (alcohol, amine, ammonium salt, amide, acid) in PVA solutions and gels, we found that the diffusion behavior is primarily influenced by the size of the diffusant and secondarily by the chemical functions.[11] The self-diffusion of a series of linear oligo- and poly(ethylene glycol)s in PVA solutions and gels was also studied.[13] It was found that the molecular size of the diffusant plays the most important part in the diffusion process.[11,13] In the present study, we would like to examine the effect of different polymer matrices on the diffusion of the solvent, water, and a solute, poly(ethylene glycol) (PEG), in different ternary polymer−water−PEG systems. The polymers used include PVA, HPMC, poly(*N*,*N*-diethylacrylamide) (PNNDEA), and poly(*N*-isopropylacrylamide) (PNIPA). PVAs with various molecular weights and degrees of hydrolysis were selected in order to investigate the effect of the chain length and structure of the matrix polymer on the self-diffusion of the solvent and the solute. For a better understanding of the diffusion in polymers, we have used the pertinent physical models of diffusion in the analysis of the experimental data obtained.

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Theoretical Background

A number of physical models of diffusion have been proposed.[14−26] They are based on different physical concepts, such as the obstruction effect, the hydrodynamic interactions, and the free volume concept in polymers. Recently, Amsden[27] reviewed some of these models and indicated their usefulness and limitations.

In the diffusion models based on the obstruction effect, the polymer chains are considered as motionless and impenetrable objects that increase the root-mean-square displacement of the diffusants. These models usually work well in the treatment of self-diffusion data of small diffusants, but not for those of large diffusants.[11,17,19,27−29]

The free volume theory considers the diffusion process as a succession of jumps in voids created by the thermal motion of the species present in solution.[22] In a binary system (solvent−polymer) or in a ternary system (solvent−polymer−solute) where the solute is present in low concentration, the contribution to the free volume is mainly from the solvent. The diffusion of all the species in the system would slow down with increasing polymer concentration. The free volume model of Fujita[22] does not apply to aqueous systems, and the model of Vrentas-Duda[25,26] is difficult to be used in ternary systems because of the numerous physical parameters needed. The model of Yasuda et al.,[23] however, can be used to describe diffusion in aqueous systems

$$D = D_0 \exp\left[\frac{B_s}{f_w}\left(1 - \frac{1}{1-\varphi}\right)\right] \qquad (1)$$

10.1021/ma990211s CCC: $18.00
Published on Web 06/11/1999

where D is the self-diffusion coefficient of the solute in the polymer−solvent mixture, D_0 is the self-diffusion coefficient of the solute in the same solvent but in the absence of the polymer, B_s is the minimum hole size required for diffusant displacement, f_w is the free volume of the solvent in the polymer−water system, and φ is the volume fraction of the matrix polymer.

The hydrodynamic models take into account the interactions between the solvent and the polymer.[17] Among them, the model proposed by Phillies[30] is often used since it provides generally good fits of the experimental data. This model was proposed to describe the self-diffusion of one macromolecule (polymers and proteins) in another over a wide range of concentrations.[30] The polymer chains are considered mobile and can be described by spheres joined by rods that can rotate as defined by Kirkwood.[31] The stretched exponential equation proposed by Phillies is written as

$$D = D_0 \exp(-\alpha c^{\nu}) \tag{2}$$

where c is the polymer concentration and α and ν are the scaling parameters. Phillies also developed theoretical arguments for eq 2[32,33] and provided physical interpretations of the parameters α and ν. According to Phillies, α depends strongly on the molecular weight ($\alpha \sim M^{0.9\pm0.1}$) for macromolecular diffusants, whereas it depends on the hydrodynamic radius ($\alpha \sim R_h/a_0$, where a_0 is defined as the distance of closest approach) for smaller diffusants.[32−35] Park et al.[36] and Gibbs and Johnsson[37] reported empirical relationships of $\alpha = 3.03R_h^{0.59}$ and $\alpha = 3.2R_h^{0.53}$, respectively. The parameter ν should scale between 1 for low molecular weight diffusants and 0.5 for high molecular weight diffusants and inside these limits it scales according to $\nu \sim M^{-1/4}$.[34] Equation 2 can provide good fits to the experimental data in many polymer systems.[30,32−34] However, disagreements still remain on the dependence and physical meaning of the parameters.[38,39]

The diffusion model of Petit et al.[12] was elaborated in the treatment of the diffusion data of molecules with various sizes and functional groups in ternary PVA−aqueous−solute systems and binary poly(methyl methacrylate)−organic solvent systems.[12,13,40] The diffusion is considered to be a succession of jumps of the diffusant from one cavity to another in the polymer matrix. The following equation was given to describe the self-diffusion coefficient

$$D = \frac{D_0}{1 + \alpha c^{2\nu}} \tag{3}$$

where $a = D_0/k\beta^2$, and $k\beta^2$ and ν are the parameters of the model. The parameter ν depends on the quality of the solvent and should be a constant for a given system. β should be a constant and independent of the concentration or molecular weight of the matrix.[12] k is the jump frequency, which varies with the molecular weight or size of the diffusant, temperature, and the concentration of the matrix polymer. However, k is considered as a constant within a certain polymer concentration range, even though the polymer concentration influences the size of the cavity.[12] In the treatment of the diffusion data of both small and macromolecular probes, the parameters of the model were determined.[13] The parameter ν, which depends on the solvent quality, was found to be a constant equal to 0.58 for the PVA−water system. $k\beta^2$ was found to depend on the hydrodynamic radius (R_h) of the diffusant.[13]

Table 1. Physical Characteristics of the Polymers Used

sample	deg of hydrolysis[a] (%)	M_w[b] (10^3 g/mol)	M_w/M_n[b]	M_w[c] (10^3 g/mol)
PVA-1	80	8.4	1.42	18 ± 1
PVA-2	88	15.4	1.76	21 ± 1
PVA-3	99	20.3	1.63	17 ± 2
PVA-4	99	52.8	2.09	52 ± 4
PVA-5	88	124.7	2.46	130 ± 9
PVA-6	99	131.5	2.26	136 ± 9
HPMC-1		10.7	4.14	
HPMC-2		231.0	2.98	
PNIPA		105.0	2.95	
PNNDEA		69.8	3.13	

[a] Given by the supplier (Aldrich). [b] Determined by SEC. [c] Determined by static light scattering.

Experimental Section

Materials. PEG with a molecular weight of 600 (PEG-600), PVA, and HPMC (see Table 1 for more details) as well as *N*-isopropylacrylamide, 2,2′-azobis(isobutyronitrile) (AIBN), and sodium thiocyanate (NaSCN) used in this study were purchased from Aldrich (Milwaukee, WI). D_2O was purchased from C.I.L. (Andover, MA). PNNDEA and PNIPA were synthesized in this laboratory.

Synthesis of Polymers.[41] The monomer *N,N*-diethylacrylamide was synthesized by reacting acryloyl chloride with diethylamine in dichloromethane in an ice bath under a flow of dry nitrogen. After the removal of diethylammonium chloride salt and the evaporation of the solvent, the product was purified by vacuum distillation (bp 30−35 °C at 0.01 mmHg). *N,N*-Diethylacrylamide was then polymerized in toluene with AIBN as the initiator. The starting temperature at 40 °C was gradually raised to 70 °C for 1 h and maintained for ca. 3 h. After removing toluene on a rotary evaporator, poly(*N,N*-diethylacrylamide) was redissolved in acetone, precipitated by adding hexane, and dried. Poly(*N*-isopropylacrylamide) was synthesized similarly.[41]

Molecular Weight Determination. Size exclusion chromatography (SEC) was carried out on a Waters 600 controller system equipped with a Waters 410 differential refractometer and two Ultrahydrogel columns of nominal porosity of 10 and 6 μm (Ultrahydrogel 500 and 120), respectively. Poly(ethylene glycol)s and poly(ethylene oxide) (PEO) standards (Polymer Standards Service-USA, Inc., MD) were used for the calibration. The polymers were solubilized in deionized water (Milli-Q), and sodium thiocyanate was added in a salt/polymer mass ratio of 1.5 to 1 to avoid the aggregation of the polymers.[8] The polymer solutions (5 mg/mL) were filtered through 0.45 μm filters (Sarstedt, NJ) before injection. The flow rate of the eluent was at 0.6 mL/min. The columns and detector were equilibrated at 32 and 35 °C, respectively.

For light scattering measurements, sets of five concentrations (0.3−3 wt %) were obtained by dilution of the stock solutions (3 wt %) containing 0.5 M of NaSCN. The dilute solutions were filtered five times through 0.2 μm Anotop 25 filters (Whatman, NJ) directly in scintillation vials, which were previously treated with sulfochromic acid and washed thoroughly with distilled water and methanol to prevent spurious scatterers in the solutions. Static light scattering measurements were performed on Dawn-B instrument (Wyatt Technology Corp., Santa Barbara, CA)[42] with a helium−neon laser operating at 632.8 nm at room temperature. An incremental refractive index of 0.159 mL/g was used. The weight-average molecular weights of our samples were derived by the Zimm double-extrapolation method using the Aurora routine.[43,44]

Pulsed-Gradient Spin-Echo (PGSE) NMR Measurements. The measurements of the self-diffusion coefficients

were carried out on a Bruker Avance AMX-300 NMR spectrometer operating at 300.13 MHz for protons. The temperature was set at 25 °C. The PGSE pulse sequence developed by Stejskal and Tanner[45] was used. A Bruker magnetic resonance imaging probe (Micro 2.5 Probe) coupled with a gradient amplifier (BAFPA-40) was used. Gradient pulses were applied only in the *z*-direction. The gradient strength was calibrated by doing one-dimensional imaging experiment along the axis, using a solution of doped water (with $CuSO_4$) in a 10 mm NMR tube in which a well-defined object was contained. The NMR image profile was compared to the dimension of the object. The daily calibration was accomplished with a sample of known self-diffusion coefficient such as 1 vol % HDO in D_2O ($D_{HDO} = 1.9 \times 10^{-9}$ m^2/s).[46] The gradient strengths, G, used in this study ranged between 0.1 and 1 T/m. The other parameters were kept constant, and their values are those noted in parentheses depending on the experiments: δ (1−5 ms), Δ (40−150 ms), recycle delay (15−60 s), number of acquisitions (1−16), 90° pulse (23−29 μs), spectral width (3−8 kHz), line broadening (5−10 Hz).

Results and Discussion

Characterization of the Polymers. The polymers (PVA, HPMC, PNNDEA, and PNIPA) used as the matrix were analyzed by SEC and light scattering experiments to determine their molecular weights and polydispersity, and the results are listed in Table 1.

The first SEC experiments were carried out 3 days after sample preparation, which corresponds to the same delay for the PGSE NMR measurements. SEC measurements of PVA and HPMC can be significantly affected by the formation of aggregates in water. The aggregation of PVA in solutions and gels is due to inter- and intramolecular hydrogen bonding.[9] In fact, the PVA aggregates appear as separated peaks corresponding to higher molar masses on the chromatograms (Figure 1). In the case of PVA-1, no such aggregation was observed for the freshly prepared solution. The same solutions were injected 4 days later, the peaks of the aggregated PVAs became more intense (Figure 1), and the aggregation for PVA-1 also became apparent. Therefore, the aggregation of PVA is time-dependent and is affected by the degree of hydrolysis of PVA. PVA-1 has the lowest molecular weight and lowest degree of hydrolysis among all the PVA samples. Stephans and Foster[9] showed by the magnetization-transfer NMR technique that completely hydrolyzed PVA chains form a gel more rapidly than PVA with a lower degree of hydrolysis, which seems to confirm the difference between PVA-1 and other PVAs observed in this study. To overcome this problem, we have prepared polymer solutions with NaSCN.[8] Addition of the salt prevented the aggregation as shown in Figure 1A. The molecular weights reported in Table 1 are obtained from SEC measurements with added NaSCN. Very broad peaks were observed with HPMCs as a result of aggregation, but the addition of sodium thiocyanate did not change the appearance of the peaks.

The aggregation of PVAs and HPMCs in water caused saturation of the detectors in the light scattering experiments. The weight-average molecular weights of PVAs were determined with PVA solutions in water in the presence of NaSCN, and the results are reported in Table 1. These values are mostly comparable with those determined by SEC. Due to the presence of aggregates, light scattering measurements of HPMC solutions were not possible even after the addition of NaSCN.

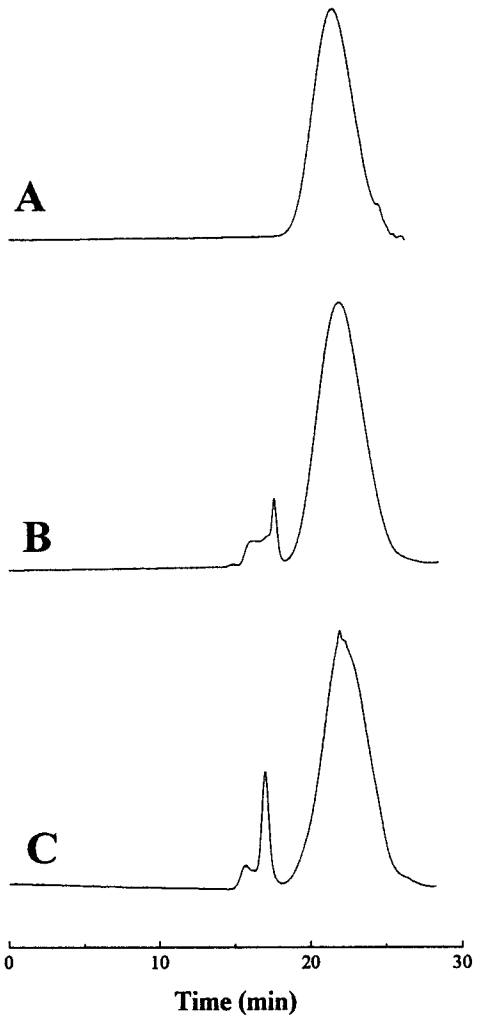

Figure 1. Size exclusion chromatograms obtained for PVA-4 (A) dissolved in an aqueous solution of NaSCN (salt/polymer weight ratio = 1.5:1), (B) dissolved in water and injected 3 days after preparation, and (C) the same water solution as (B) but injected after 7 days. Chromatogram A shows that the salt NaSCN can prevent the aggregation of PVA. Comparison of chromatograms B and C indicates that the aggregation of PVA is time-dependent.

Analysis of the Diffusion Data with the Model of Yasuda et al. Equation 1 can be rewritten as

$$\ln D = \ln D_0 - \frac{B_f}{f_w}\left(\frac{\varphi}{1-\varphi}\right) \tag{4}$$

Therefore, the free volume parameters can be obtained by linear regression of the data. The logarithms of the self-diffusion coefficients of water and PEG-600 are plotted as a function of $\varphi/(1-\varphi)$ as shown in Figure 2 for PVA-2. The dashed lines are fits of the linear parts of the data to eq 4. The fitting parameters are listed in Table 2. For small molecules, such as water, a very good fit can be obtained. For larger molecules such as PEG-600 the linearity over the entire range is rather poor. Petit et al.[11] observed a gradual deterioration of the fits with increasing diffusant size. The same observation can be made here which illustrates the limitation of the model. Similar results and limitations were obtained for the diffusion of water and PEG-600 in the other hydrophilic polymers (PVA, HPMC, PNNDEA, and PNIPA). The deviations at higher polymer volume fractions are due to the approximation that the total free volume of

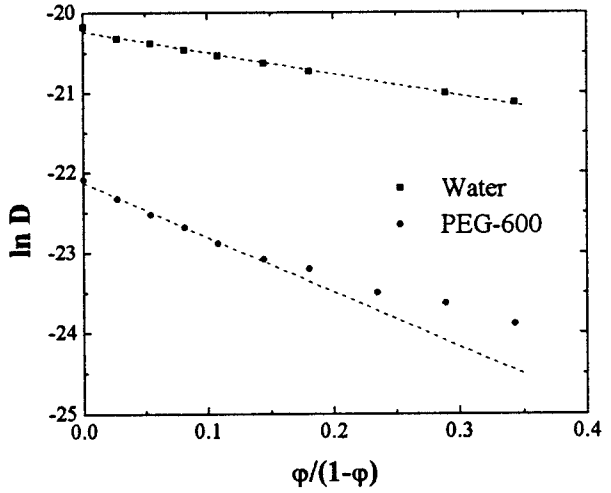

Figure 2. Semilogarithmic plot of the self-diffusion coefficient of water and PEG-600 in PVA-2 as a function of $\varphi/(1-\varphi)$. Dashed lines are the best fits to eq 4. For PEG-600, the deviation from the linearity at high polymer concentrations is shown.

Table 2. D_0 and B_s/f_w as Free Parameters Obtained from Fits to Eq 4 with the Experimental Diffusion Data Obtained for PVA, HPMC, PNNDEA, and PNIPA Aqueous Systems

	parameters for PEG-600		parameters for water	
polymer	$D_0 \times 10^{10}$ (m^2/s)	B_s/f_w	$D_0 \times 10^{9}$ (m^2/s)	B_s/f_w
PVA-1	2.49	6.81	1.69	2.66
PVA-2	2.46	6.48	1.64	2.50
PVA-3	2.48	6.48	1.63	2.88
PVA-4	2.40	6.76	1.65	2.42
PVA-5	2.43	6.49	1.66	2.59
PVA-6	2.42	6.55	1.64	2.52
HPMC-1	2.42	7.53	1.63	2.29
HPMC-2	2.43	8.21	1.62	3.02
PNNDEA	2.50	5.21	1.70	2.31
PNIPA	2.52	6.08	1.64	2.78

the system is only contributed by the solvent (water), i.e., $f_{total} = f_w$.[23] This approximation is no longer valid in concentrated polymer systems where the free volume contribution from the polymer is no longer negligible. We have attempted to fit the diffusion data of PEG-600 only for the low polymer concentrations as shown in Figure 2.

The measured D_0 values for PEG-600 and water are 2.56×10^{-10} and 1.73×10^{-9} m^2/s, respectively. We tried to use D_0 and B_s/f_w all as free parameters in the fitting to eq 4. The D_0 values obtained for PEG-600 and water from the fits are systematically lower than the measured D_0 values in all the polymer matrices studied here (Table 2). The parameter B_s/f_w obtained for PEG-600 is more or less a constant for a given polymer system. Average values of 6.59, 7.87, and 5.64 were found for PVA, HPMC, and PNNDEA−PNIPA, respectively. When the diffusant (only 1 wt % solution in water) does not affect the properties of the solvent, f_w should remain constant. Consequently, the variation of the parameter B_s/f_w should reflect the variation of the minimum hole size required for diffusant displacement, B_s. The average value obtained for B_s/f_w increases from PNNDEA−PNIPA to PVA and HPMC. This suggests that the minimum hole size required for diffusant displacement increases with the ease of formation of hydrogen bonds in the polymer matrix. The values of B_s/f_w obtained for water are similar for all polymer systems, which indicates that the minimum hole size required for solvent

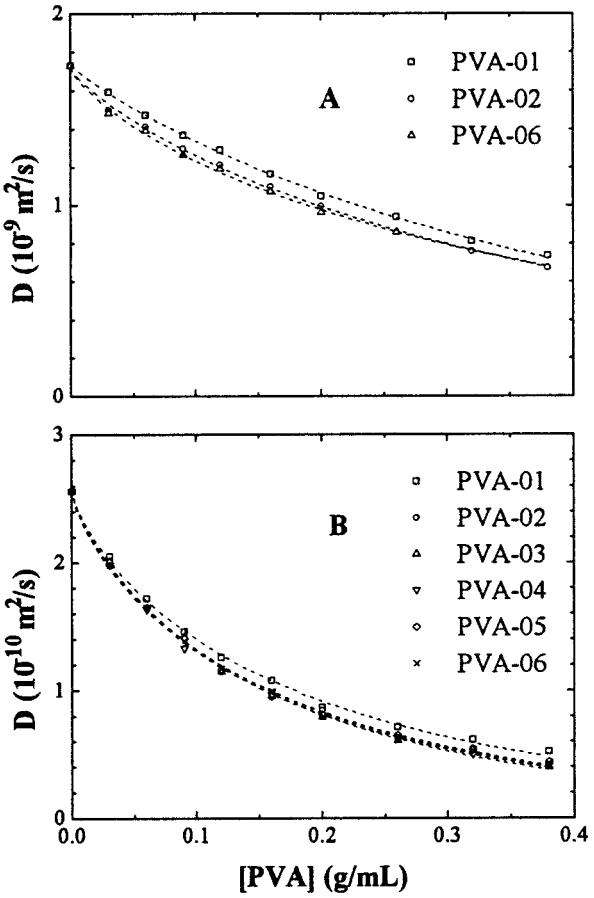

Figure 3. Plot of the self-diffusion coefficient of water (A) and PEG-600 (B) as a function of the PVA concentration for various PVA matrices at 25 °C. Dashed lines are fits to eq 2.

displacement remains a constant. This is logical and agrees with the results of Gao and Fagerness,[6] who studied water self-diffusion in HPMC solutions and gels. They reported that the degree of polymerization of the polymer matrix does not affect the diffusion of the solvent.[6] We have also fitted the experimental data after fixing D_0 to the experimental value. In this case, the B_s/f_w values are generally higher.

Analysis of the Diffusion Data with the Model of Phillies. Figure 3 shows the self-diffusion coefficient of water and PEG-600 plotted as a function of PVA concentration for PVA−water−PEG ternary systems. Good agreement is observed between the fits with eq 2 and the experimental data for both water and PEG-600 over the entire range of polymer concentrations. Very good agreements are also obtained for the other hydrophilic polymers (HPMC, PNNDEA, and PNIPA). The fitting parameters are listed in Table 3. Even when D_0 is allowed to vary freely in all the fittings, it remained a constant for a given diffusant in all the polymer systems.

According to Phillies, the scaling parameter ν should scale between 0.5 for high molecular weight diffusant and 1 for low molecular weight diffusants.[34] All the ν values obtained (Table 3) lie between these limits. In this study, the diffusant is kept constant and the matrix is changed. The ν values obtained for PEG-600 are found to be unique for a given polymer−water system. Average values of 0.77, 0.71, and 0.89 are found for the diffusion of PEG-600 in PVA, HMPC, and PNNDEA−PNIPA, respectively. Therefore, the results tend to indicate that the scaling parameter ν is a constant for a given polymer

Table 3. D_0, α, and ν as Free Parameters Obtained from Fits to Eq 2 with the Experimental Diffusion Data Obtained for PVA, HPMC, PNNDEA, and PNIPA Aqueous Systems

	parameters for PEG-600			parameters for water		
polymer	$D_0 \times 10^{10}$ (m^2/s)	α	ν	$D_0 \times 10^{9}$ (m^2/s)	α	ν
PVA-1	2.57	3.51	0.76	1.73	2.10	0.91
PVA-2	2.57	3.92	0.77	1.72	2.08	0.83
PVA-3	2.57	4.13	0.79	1.73	1.82	0.78
PVA-4	2.57	3.91	0.76	1.72	2.00	0.83
PVA-5	2.57	3.80	0.76	1.73	2.00	0.85
PVA-6	2.57	3.85	0.76	1.72	2.04	0.79
HPMC-1	2.56	3.75	0.71	1.71	1.71	0.78
HPMC-2	2.56	3.96	0.71	1.72	1.93	0.72
PNNDEA	2.57	3.83	0.88	1.73	1.95	0.91
PNIPA	2.56	4.48	0.89	1.73	2.06	0.79

system, independent of the molecular weight of the polymer matrix. Distinct average ν values are also observed for water, ca. 0.83, 0.75, and 0.85 for PVA, HPMC, and PNNDEA−PNIPA, respectively. Therefore, the scaling parameter ν may reflect the quality of the solvent for a given polymer. No significant dependence on the molecular weight of the matrix polymer was observed.

The scaling parameter α is found to be more or less a constant for water and PEG-600 as shown in Table 3. Average α values of 3.85 and 3.86 are found for PEG-600 diffusion in PVA and HPMC, respectively. But the α values in PNNDEA and PNIPA are quite different. Average α values of 2.00, 1.82, and 2.00 are found for water diffusion in PVA, HPMC, and PNNDEA−PNIPA, respectively. The hydrodynamic radii of water and PEG-600 can be calculated from the self-diffusion coefficients with the Stokes−Einstein equation, corresponding to 13.95 and 1.30 Å for PEG-600 and water, respectively. With these values, the relationship of Park et al.[36] would give α values of 14.4 and 3.54 for PEG-600 and water, respectively, and the relationship of Gibbs and Johnson[37] would provide α values of 13.0 and 3.68 for PEG-600 and water, respectively. These α values are higher than the values obtained from the fits (Table 3). In a previous work,[13] we have studied the self-diffusion of a series of oligo- and poly(ethylene glycol)s in PVA solutions and gels by PGSE NMR spectroscopy. The dependence of the parameter α and the molecular weight of the diffusants did not show any simple mathematical dependence. The parameter α seems to depend on the size of the diffusant, but no significant dependence is observed in these hydrophilic systems.

Analysis of the Diffusion Data with the Model of Petit et al. Diffusion data of water and PEG-600 in PVA solutions and gels and the fits with eq 3 are shown in Figure 4. The fits for both water and PEG-600 are very good in all the PVA systems over the entire range of polymer concentrations. The fitting parameters are listed in Table 4. D_0, as a free fitting parameter, remained a constant for both diffusants, close to the experimental value. The ν values obtained for PEG-600 are found to be close to the value of 0.58 as reported previously.[13] This result confirms that ν depends on the solvent quality, which should be similar for the PVA−water systems. $k\beta^2$ remains also more or less a constant for a diffusant in the PVA systems as shown in Table 4. This implies that the jump frequency of a given diffusant is similar for all the PVA systems used here. The ν values obtained for the solvent water as diffusant

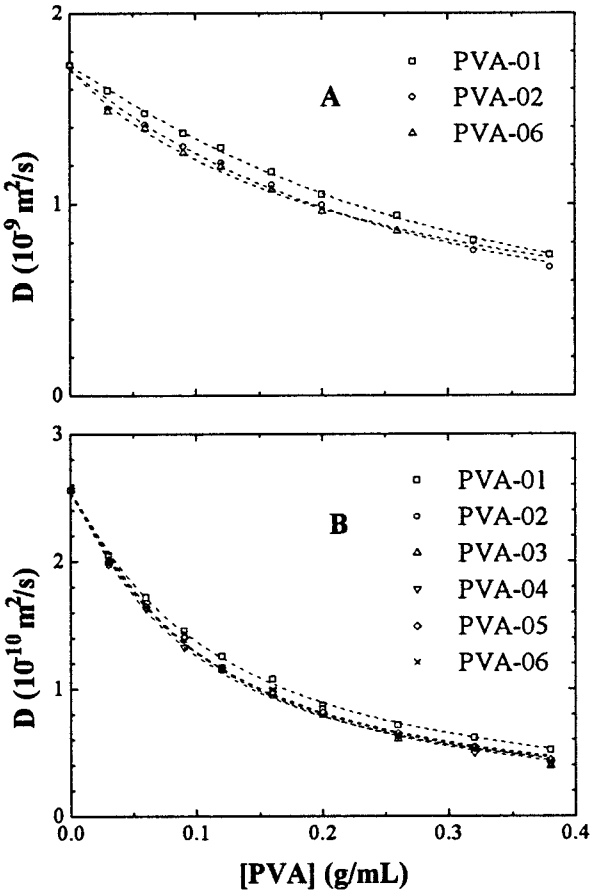

Figure 4. Plot of the self-diffusion coefficient of water (A) and PEG-600 (B) as a function of the PVA concentration for various PVA matrices at 25 °C. Dashed lines are fits to eq 3.

Table 4. D_0, $k\beta^2$, and ν as Free Parameters Obtained from Fits to Eq 3 with the Experimental Diffusion Data Obtained for PVA, HPMC, PNNDEA, and PNIPA Aqueous Systems

	parameters for PEG-600			parameters for water		
polymer	$D_0 \times 10^{10}$ (m^2/s)	$k\beta^2 \times 10^{10}$	ν	$D_0 \times 10^{9}$ (m^2/s)	$k\beta^2 \times 10^{10}$	ν
PVA-1	2.54	0.228	0.56	1.72	4.30	0.58
PVA-2	2.54	0.181	0.58	1.70	4.18	0.53
PVA-3	2.54	0.166	0.60	1.72	5.07	0.50
PVA-4	2.55	0.184	0.57	1.71	4.57	0.52
PVA-5	2.54	0.194	0.56	1.72	4.55	0.53
PVA-6	2.54	0.190	0.57	1.71	4.28	0.51
HPMC-1	2.54	0.192	0.53	1.71	5.64	0.48
HPMC-2	2.55	0.197	0.51	1.72	5.04	0.44
PNNDEA	2.53	0.211	0.63	1.73	4.83	0.56
PNIPA	2.54	0.170	0.64	1.73	4.47	0.50

are also quite constant (0.53) and slightly lower than the ν value for the solute (ca. 0.58). $k\beta^2$ remains also quite constant, but the values are much higher than those determined for PEG-600. This is reasonable since the jump frequency of water should be higher than that of PEG-600. This result is in good agreement with the prediction of the model of Petit et al. that considers k dependent on the molecular weight or the size of the diffusant.[12,13,40]

For the PVA systems, the measured self-diffusion coefficients for a given diffusant, either water or PEG-600, are quite similar over the entire range of polymer concentrations. The diffusion data are almost superposed as shown in Figure 4, which indicate that the microstructures (porosity and mesh size) of the PVAs

are rather similar. At a given PVA concentration, the diffusion of PEG-600 does not seem to vary to any significant extent with the molecular weight or degree of hydrolysis of PVA. However, the self-diffusion coefficients of PEG-600 are slightly but systematically higher in PVA-1 than in the other PVA solutions, indicating less obstruction in this polymer network. The PVA microstructure in water depends mainly on the intra- and intermolecular associations via hydrogen bonds, which should be related to the degree of hydrolysis of the polymer.[9] Therefore, PVA-1 may differ as a result of its lower degree of hydrolysis. This is also seen in the $k\beta^2$ values for PEG-600, which are quite constant for the PVAs, with the exception of PVA-1. A small difference is also observed for the self-diffusion coefficients of water in PVA-1 and in the other PVAs (Figure 4A). PVA-1 may be less hydrated than the other PVAs due to its lower degree of hydrolysis. Therefore, the solvent molecules on average are freer to diffuse in PVA-1 than in the other PVAs. The existence of several states of water in PVA solutions and gels due to interactions was often noted in the literature.[47−49] The intermolecular interactions between PVA and solvent may also depend on the microtacticity of PVA. The PVAs used in this study, however, are atactic polymers as shown in the NMR characterization of the polymers in water. The result for an example of the PVAs (PVA-4) has been reported earlier.[50]

Matsukawa and Ando[5] showed that PEG-4250 can form complexes with poly(acrylic acid) (PAA) through intermolecular hydrogen bonds. The self-diffusion coefficient of PEG-4250 was found to be lower in PAA gels than in PNNDEA gels. Furthermore, the authors have also studied the self-diffusion coefficient of PEG-4250 in PAA−PNNDEA copolymers. The self-diffusion coefficient of PEG-4250 in a copolymer with a PAA molar fraction higher than 0.9 is much smaller than that in a copolymer with a PAA molar fraction lower than 0.5. We have found that PVA-4 can also form complexes with diffusants such as ethylene glycol and even poly(ethylene glycol)s by hydrogen bonding. In this study, PVA-1 has a lower degree of hydrolysis (ca. 80%) and thus fewer hydroxyl groups. Therefore, we can assume that this polymer will form fewer intra- or intermolecular hydrogen bonds than the other PVAs used, which may explain the higher D values observed.

Figure 5 shows the diffusion data for water and PEG-600 in HPMC solutions and gels and the fits to eq 3. The fitting parameters are listed in Table 4. The ν values determined from the fits of PEG-600 are similar for both HPMCs with an average value of 0.52. This value is somewhat lower than the average value determined for PVAs systems, indicating that it is characteristic of the system. The $k\beta^2$ values determined from the fittings are similar to those determined for PVAs, which indicates that the diffusant PEG-600 in HPMC solutions and gels may have similar jump frequencies as in PVAs. The ν values determined from the fittings for water seem to be lower than those obtained for PVAs, whereas the $k\beta^2$ values are higher. As shown in Figure 5B, the D values of PEG-600 decrease with increasing polymer concentration, and the data are almost superimposed for both polymers. As in the case of PVA, the molecular weight of HPMC does not have any significant effect on the diffusion of PEG-600. Recently, Gao and Fagerness studied the self-diffusion of adinazolam in HPMC gels by PGSE NMR spectroscopy.[6] They used HPMCs with different viscosity grades (i.e., different molecular weights) and also found similar D values for adinazolam in all the HPMCs used.

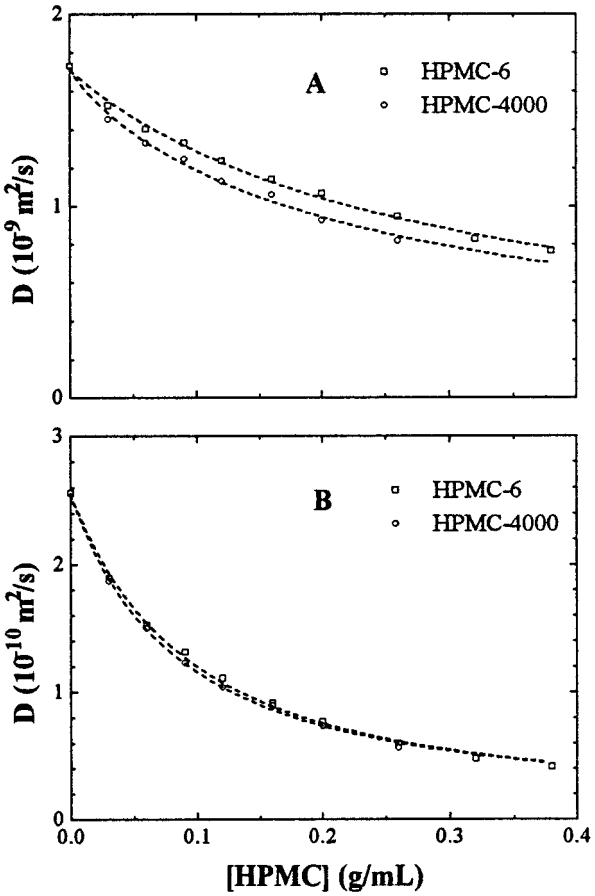

Figure 5. Plot of the self-diffusion coefficient of water (A) and PEG-600 (B) as a function of the HPMC concentration for the two HPMC matrices at 25 °C. Dashed lines are fits to eq 3.

As shown in Figure 5A, the self-diffusion coefficient of water decreases when the molecular weight of the matrix is increased. This indicates that the root-mean-square displacements of water molecules in the two HPMC systems are not quite the same. Water molecules experienced a larger obstruction effect in HPMC-2. The existence of different states of water in HPMC is well-known,[51−53] and it depends on the methoxy/hydroxypropoxy substitution ratio.[54,55] HPMCs used in this study have the same percentage of methoxy and hydroxypropoxy groups but different molecular weights. Gao et al. have studied the effects of HPMC/lactose ratio and of HPMC molecular weight on solute release and swelling of HPMC matrix tablets.[56] They found that drug release rates observed with low viscosity grade HPMC are greater than those observed with high viscosity grade HPMC due to inhomogeneous gel swelling. The difference in D values of water may also be due to inhomogeneous gel swelling.

Figure 6 shows the self-diffusion data of water and PEG-600 in PNNDEA and PNIPA systems. The fits of the experimental data to eq 3 are very good for water and PEG-600 in both polymers. Although the measured D values are different in PNIPA and PNNDEA for both water and PEG-600, the ν values obtained from the fittings of PEG-600 are very close. The average value, 0.64, is higher than the values obtained in PVAs and

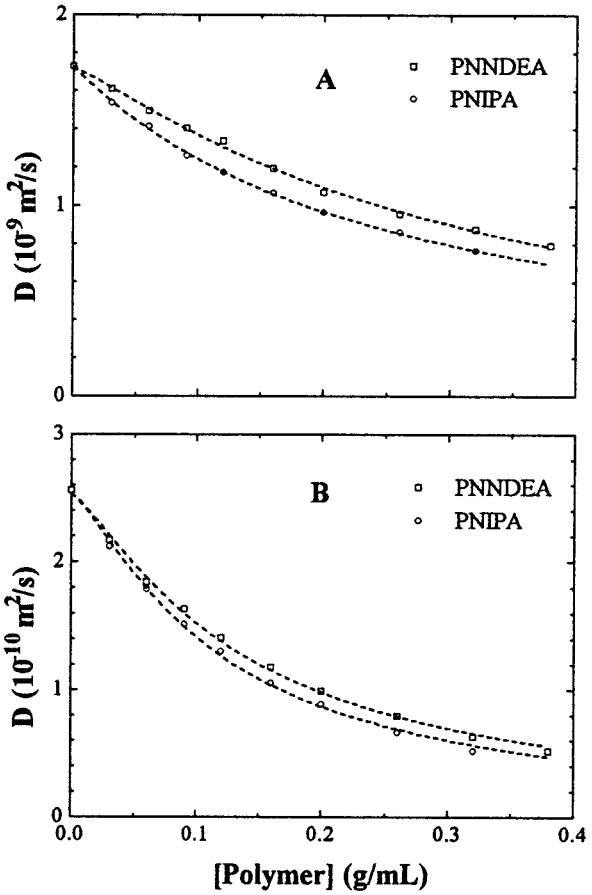

Figure 6. Plot of the self-diffusion coefficient of water (A) and PEG-600 (B) as a function of the polymer (PNNDEA and PNIPA) concentration for at 25 °C. Dashed lines are fits to eq 3.

HPMCs. In PNIPA and PNNDEA, the formation of hydrogen bonds is not as easy as in PVAs and HPMCs. Therefore, the variations in the diffusion data should be attributed to the quality of the solvent. The $k\beta^2$ value obtained for PEG-600 in PNNDEA is higher than the $k\beta^2$ value obtained in PNIPA. This means that the jump frequency of PEG-600 is higher in PNNDEA than in PNIPA, which is in concordance with the relative D values. The difference observed for the self-diffusion of PEG-600 between the two polymers may be attributed to the hydration of the polymer chains. PNIPA should be more hydrated since its amide group is both a proton donor and acceptor in the formation of hydrogen bonds. The difference of the $k\beta^2$ values for water can be explained similarly. The diffusion of both water and PEG-600 in PNNDEA is faster than that in PNIPA.

Concluding Remarks

We have studied the self-diffusion of water and PEG-600 in different hydrophilic polymer systems, including different polymers as well the same polymer with different molecular weight or different degree of hydrolysis. The diffusion of both water and PEG-600 in the same class of polymers is rather similar and does not vary significantly with the molecular weight or small variations in the degree of hydrolysis of the polymer matrix used. It seems that diffusion in these hydrophilic polymers is mostly affected by the facility in the formation of hydrogen bonds as exemplified by the differences observed for PNNDEA and PNIPA.

The diffusion data have been also analyzed with several pertinent physical models in the literature. The free volume model of Yasuda et al. can be used in the description of the diffusion of small molecules, such as the solvent water in this case. Significant deviations from the model were observed for the diffusion data of larger diffusants in polymer solutions and gels. The universal equation proposed by Phillies provided good fits to the diffusion data over the whole range of polymer concentrations, for all the diffusants and matrix polymers. The parameter ν was found to be a constant for a given class of polymers and for a given diffusant. In general, the parameter α was also found to increase somewhat with increasing size of the diffusant (from water to PEG-600). The diffusion data of both water and PEG-600 in all these polymer systems all fitted very well to the diffusion model of Petit et al. The parameter ν was found to be constant for a given polymer system and depends on the quality of the solvent. The parameter $k\beta^2$ was found to be a measure of the jump frequency of the diffusant which depends mostly on the size of the diffusant. To a less extent, it also depends on the interaction of the diffusant with the matrix polymer as shown by the differences for PVA-1 and between PNNDEA and PNIPA.

Acknowledgment. Financial support from Natural Sciences and Engineering Research Council (NSERC) of Canada and from the Quebec Government (Fonds FCAR) is gratefully acknowledged. The authors thank Professor A. Eisenberg and Mr. C. Bartels of McGill University for their help in the light scattering experiments.

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MA990211S