Translational Diffusion of Paramagnetic Tracers in Poly(1-vinylpyrrolidone) Hydrogel and Concentrated Aqueous Solutions by 1D Electron Spin Resonance Imaging

Jan Pilař,* Jiří Labský, Antonín Marek, and Čestmír Koňák

Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic, 162 06 Prague, Czech Republic

Shulamith Schlick

Department of Chemistry, University of Detroit Mercy, Detroit, Michigan 48219

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Introduction. Diffusion processes in polymer solutions and in swollen polymer networks (polymer gels) are of considerable importance for understanding of polymer dynamics and for numerous practical applications such as drug delivery systems and transport across membranes. Several papers have recently considered both the experimental and the theoretical aspects of diffusion processes in polymers.[1−6] The self-diffusion of solvents and polymers and diffusion of various tracers in polymer systems have been measured as a function of the molecular weight of the tracer, the molecular weight and concentration of the matrix polymer, and the temperature, and the results have been compared with the predictions of various models. In one of our previous papers we have shown that electron spin resonance imaging (ESRI) is a powerful tool for measuring macroscopic diffusion coefficients of paramagnetic tracers in polymer hydrogels.[7] Gels in the equilibrium swelling state have been studied in order to eliminate the contribution of the concentration gradient of the solvent to the driving force governing tracer diffusion. The dependence of the diffusion coefficients on molecular weight of the tracer and on the polymer content in the gel was in reasonable agreement with theoretical models.

A recent study by ESRI of the diffusion coefficient, D, of the low-molecular-weight paramagnetic tracer 4-oxo-3,3,5,5-[$^2H_4$]-2,2,6,6-tetra([$^2H_3$]methyl)piperidin-1-yloxyl **(IV)** revealed a significant difference between the D values determined in a polystyrene network (chemically cross-linked gel) swollen by toluene and in a toluene solution containing the same concentration of linear polystyrene.[8] This finding encouraged us to focus our attention on the investigation of the effect of presence and concentration of permanent chemical cross-links in gels on diffusion coefficients of tracers. These cross-links, which are responsible for the mechanical properties of gels, are present in the gel in addition to the temporary entanglements that exist in a solution containing the same polymer concentration as the gel. The preparation of well-defined gels and polymer solutions in the same solvent is the most important part of the intended research. In this Communication, we report the diffusion coefficients of various tracers in lightly cross-linked poly(1-vinylpyrrolidone) gel swollen at equilibrium with water and in the corresponding aqueous solution of the polymer. 1D ESRI was used for the determination of the D values.

Experimental Section. Materials. Commercial linear poly(1-vinylpyrrolidone) (PVP) **(I)** (Sigma, average molecular weight 360 000) was used to prepare the concentrated aqueous solutions. The PVP gel was prepared by polymerizing 2.4 mL of 1-vinylpyrrolidin-2-one (Fluka) in the presence of 0.3 g of 2,2′-azodi(propanimidamide)dihydrochloride **(II)** (Wako Chemicals USA, Inc.) and 30 mg of 1,1′-divinyl-3,3′-(ethane-1,1-diyl)di(pyrrolidin-2-one) **(III)** in 17.6 mL of deionized water under argon atmosphere in glass capillaries, i.d.≈1 mm (for ESRI experiments), or in glass ampules, i.d.≈ 1 cm (for DLS experiments), at 55 °C for 8 h. The amount of water added was the equilibrium content in the gel (88 wt %) determined gravimetrically in previous independent experiments. The syntheses of paramagnetic tracers 4-oxo-3,3,5,5-[$^2H_4$]-2,2,6,6-tetra([$^2H_3$]methyl)piperidin-1-yloxyl (**IV**), 4-acetylamino-3,3,4,5,5-[$^2H_5$]-2,2,6,6-tetra([$^2H_3$]methyl)piperidin-1-yloxyl **(V)**, 4-trimethylammonio-3,3,5,5-[$^2H_4$]-2,2,6,6-tetra([$^2H_3$]methyl)piperidin-1-yloxyl iodide **(VI)**, and spin-labeled poly(ethylene glycol), α-[(2,2,5,5-tetramethyl-1-ylooxy-2,5-dihydropyrrol-3-yl)carbonyl]poly(oxyethylene)-ω-{[(2,2,5,5-tetramethyl-1-ylooxy-2,5-dihydropyrrol-3-yl)carbonyl]oxy} (**VIIa**, $MW_{PEG} = 1500$; **VIIb**, $MW_{PEG} = 3000$), have been described.[7] The formulas of the polymer, cross-linker, initiator, and tracers are shown in Chart 1.

Dynamic Light Scattering (DLS). Polarized DLS measurements were performed at a scattering angle $\theta = 90°$ using a light-scattering apparatus equipped with an argon laser (514.5 nm) and an ALV 5000, multibit, multi-τ autocorrelator covering approximately 12 decades in the delay time. Both PVP concentrated solutions and gel were measured in sealed glass ampules of i.d. ≈1 cm. To avoid the effect of nonergodicity of gel samples on dynamic light-scattering results, the samples were rotated and autocorrelation functions obtained by averaging at least 10 measurements at different sample positions were used for analysis. The correlation functions were analyzed with the program REPES,[9,10] which targets the inverse Laplace transformation.

The collective (cooperative, gel mode) diffusion coefficients, D_c, of concentrated solutions and gel were calculated from the equation $D_c = 1/[\tau_c q^2(1 - \Phi)^2]$, where Φ is the polymer volume fraction ($\Phi = \bar{v}_2 c$, where $\bar{v}_2$ is the partial specific volume of PVP in water and c is the polymer concentration), τ_c is the mean characteristic decay time, $q = 4\pi n_o \sin(\theta/2)/\lambda_o$ is the magnitude of the scattering vector, n_o is the refractive index of the solvent, and λ_o is the wavelength of the incident light. The diffusion coefficients have been corrected for solvent backflow[11] by division with $(1 - \Phi)^2$. The concentrated solutions and gels have been characterized by the hydrodynamic correlation length, ξ_h, by using the Stokes−Einstein relation $\xi_h = kT/6\pi\eta D_c$, where T is the absolute temperature, k is the Boltzmann constant and η is the viscosity of the solvent.

Electron Spin Resonance Imaging (ESRI). Since ESRI was comprehensively reviewed,[12] new applications of 1D and 2D ESRI to the measurement of diffusion coefficients for paramagnetic tracers in various systems

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* Corresponding author. E-mail: pilar@imc.cas.cz.

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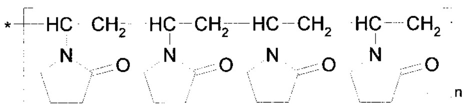
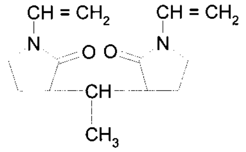
Chart 1



I



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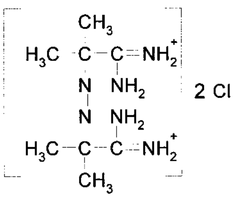
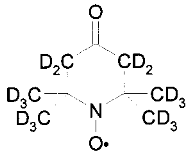
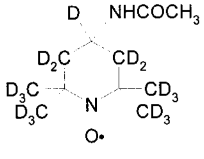


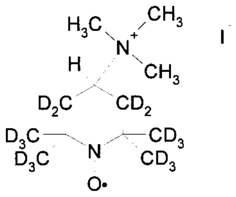
III



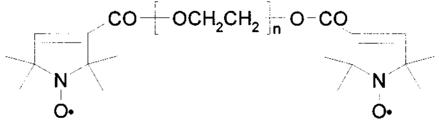
IV



V



VI



VIIa $MW_{PEG} = 1500$

VIIb $MW_{PEG} = 3000$

have been reported.[13-15] The 1D ESRI method enables faster and more precise determination of diffusion coefficients and, consequently, measurements of faster diffusion processes.[16] The diffusion coefficients can be deduced by simulating the ESR spectrum of the sample measured in the presence of a magnetic field gradient at a given time by convoluting the spectrum of the sample taken in the absence of the gradient with the concentration profile of the tracer in the sample calculated using a solution of Fick's equation for the particular sample geometry.[7,17,18] The starting values of the following parameters are needed for the simulations: C_0 (tracer concentration in the initial layer, in arbitrary units), D (macroscopic diffusion coefficient), l (length of sample), and h (thickness of the initial layer of tracer). In this study we employed a newly developed software that in the next steps performs a nonlinear least-squares fit to minimize the deviation between the experimental and calculated line shape by varying the initial parameters until the best fit is reached. The concentration profiles of the tracer in the sample at a given time (spatial scale) is part of the output. No correction for the sensitivity profile of the ESR cavity is needed for samples shorter than 5 mm. This method can be used only if the ESR line shape has no spatial dependence. The software will be described in more detail in a full paper.

The ESRI system in Detroit consists of a Bruker 200D ESR spectrometer with a new EMX console and equipped with two figure eight Lewis Coils and two regulated power supplies. Measurements were performed using a vertical gradient (perpendicular to the external magnetic field); $G_{\max} \approx 250$ G/cm. The instrumentation has been described in more details elsewhere.[7,8,16]

For ESR measurements, aqueous solutions of linear PVP were filled into glass capillaries of i.d. ≈1 mm and PVP gels were polymerized inside them. The lengths of the samples ranged from 3 to 5 mm. The samples were topped with 0.4 μL of a 10^{-2} M aqueous solution of the paramagnetic tracer, sealed by Parafilm, and positioned vertically, with the capillary axis parallel to the gradient direction, in the cavity of the ESR spectrometer. ESR spectra were measured at suitable time intervals in the presence and in the absence of the gradient. The effect of the gradient magnitude on the quality of the data was tested by using different gradients, 46.6 or 94.5 G/cm for most of the samples.

Results and Discussion. The hydrodynamic correlation length, ξ_h, measured by DLS was 2.82 ± 0.05 nm in the equilibrium-swollen PVP gel containing 88 wt % of water and 2.88 ± 0.05 nm in concentrated aqueous solution containing the same polymer volume fraction ($\Phi = 0.096$ for 12 wt % of PVP in water, calculated using $\bar{v}_2 = 0.8^{19}$). This result indicates that in this lightly cross-linked gel, the hydrodynamic correlation length is virtually the same as in corresponding solution and that presence of permanent cross-links, which makes the only difference between gel and solution matrices, plays only a negligible role. Similar conclusions have been derived for lightly cross-linked gels in numerous studies, for example by Candau et al.[20] The hydrodynamic correlation length is 1.59 ± 0.05 nm in a concentrated aqueous solution containing 24 wt % PVP. The concentrations of PVP in both solutions studied were by more than an order of magnitude higher than the crossover concentration, c^*, for the PVP used.

The D values for a given paramagnetic tracer can in principle be determined from one pair of projections (with and without the magnetic field gradient) taken after the start of the diffusion process. In practice many pairs of projections for a given sample were measured at various times, to check the reproducibility of the data and to estimate the standard deviation. Examples of the experimental and simulated projections together with concentration profiles of the paramagnetic tracer in the sample are shown in parts A and B of Figure 1. Analysis of the data indicated that the most precise data can be obtained once a measurable concentration of the tracer has reached the end of the sample. In such cases the sample length can be determined with high accuracy using the positions of the high-field features in the projection, as seen in parts A nad B of Figure 1. No measurable effect of the magnitude of the gradient on the accuracy of the diffusion coefficients was detected;

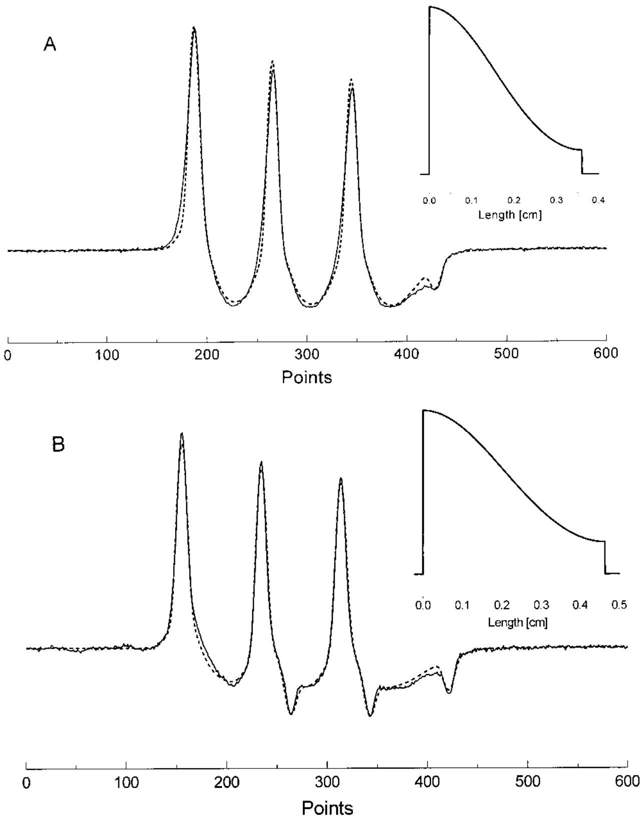


Figure 1. (A) Experimental (full line) ESR spectrum at time $t = 24\,960$ s after starting the diffusion of tracer **VIIb** in the PVP gel, measured with field gradient $G = 46.6$ G/cm, 4 scans, magnetic field sweep 120 G, and modulation amplitude 1.5 G. The simulated projection (dotted line) was calculated with $D = 0.48 \times 10^{-6}\text{cm}^2\ \text{s}^{-1}$, $h = 0.049$ cm, $C_0 = 18.1$, and $l = 0.361$ cm (see text). (B) Experimental (full line) ESR spectrum at time $t = 27\,480$ s after starting the diffusion of tracer **VIIb** in the 12 wt % PVP solution, measured with magnetic field gradient $G = 46.6$ G/cm, 9 scans, magnetic field sweep 120 G, and modulation amplitude 1.5 G. The simulated projection (dotted line) was calculated with $D = 0.83 \times 10^{-6}\text{cm}^2\ \text{s}^{-1}$, $h = 0.049$ cm, $C_0 = 42.9$, and $l = 0.464$ cm (see text). The external magnetic field increases from left to right. The values of the parameters were chosen by the nonlinear least-squares fit. The insets in A and B present the concentration profile of the tracer in the sample, with the top of the sample on the left.

some distortions of the projections due to nonplanarity of the top and bottom surfaces (the meniscus at the top of the samples) or to nonvertical sample positioning were found when high gradients (and resulting high spatial resolution of the technique), typically >80 G/cm, were applied.

The macroscopic diffusion coefficients determined by ESRI at 300 K for five paramagnetic tracers in the lightly cross-linked PVP gel containing in equilibrium 88 wt % of water and in the concentrated aqueous solution of the linear PVP containing the same polymer volume fraction are given in Table 1. The coefficients and the corresponding error limits resulted from the statistical analysis of a set of data determined by fitting projections taken at various times in the presence of various gradients for each sample. Table 1 is completed with diffusion coefficients of three of the tracers in aqueous solution containing a 2-fold concentration (24 wt %) of linear PVP. Presented data clearly show no significant difference between the diffusion coefficients of the first four small tracers (**IV**, **V**, **VI**, **VIIa**) in the lightly cross-linked gel and in the solution of linear PVP containing the same polymer volume fraction (12%). It follows that small concentration of permanent cross-links present in the gel in addition to the temporarily entanglements present in both gel and concentrated solution has no effect on the diffusion of the small tracers. Practically the same values of diffusion coefficients measured for each of small tracers in both 12% solution and gel correspond to the values of the hydrodynamic correlation length measured in both media by DLS that have been found equivalent within experimental error limits. The different molecular weights and possibly ionic character (**VI**) are responsible for the differences between the diffusion coefficients for particular tracers. In contrast to the behavior of the small tracers, nearly 100% difference was found between diffusion coefficients in the lightly cross-linked gel and in the corresponding solution for the bulkier paramagnetic tracer of molecular weight over 3000 (**VIIb**). According to our opinion this result indicates that even small concentration of permanent cross-links present in the gel is effective in slowing down diffusion of more voluminous tracer significantly regardless the same hydrodynamic correlation lengths measured in 12% PVP solution and in gel. When comparing both PVP aqueous solutions, slower diffusion has been observed in the solution containing the higher PVP concentration (24%) for all tracers studied in agreement with shorter hydrodynamic correlation length measured in the more concentrated solution by DLS.

An extension of this research to the 1D ESRI studies of macroscopic diffusion of similar and even bulkier paramagnetic tracers in set of gels containing higher concentrations of the cross-linker and in corresponding solutions of linear polymers is in progress.

Conclusions. The results demonstrated the high potential of the 1D ESRI technique and of the software developed for measurements of diffusion coefficients of paramagnetic tracers in polymer systems. The data clearly indicate that even small concentrations of permanent cross-links in the lightly cross-linked PVP gel are able to reduce the rate of transport of a bulky paramagnetic tracer to the value corresponding to 2-fold increase of linear PVP concentration in the solution where no chemically fixed obstacles (permanent cross-links) are present.

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Table 1. Diffusion Coefficients $D \times 10^6$ (cm^2 s^{-1}) for Selected Paramagnetic Probes in PVP Gel and PVP Aqueous Solutions Measured by 1D ESRI at 300 K

	tracer				
medium	**IV**	**V**	**VI**	**VIIa**	**VIIb**
PVP gel equilibrium−swollen with water (12 wt % PVP)	6.0 ± 0.7	6.4 ± 0.8	9.0 ± 1.0	1.4 ± 0.15	**0.50 ± 0.05**
12 wt % PVP solution in water	6.0 ± 0.6	6.6 ± 0.6	8.4 ± 0.7	1.3 ± 0.1	**0.87 ± 0.06**
24 wt % PVP solution in water		5.0 ± 0.5	6.2 ± 0.6		0.47 ± 0.05

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