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Effect of structure of HEMA–DEGMA hydrogel matrix on diffusion coefficients of PEG tracers. Variation of hydrogel crosslink density by change of polymer concentration

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ABSTRACT

Dependence of diffusion coefficients of spin-labeled poly(ethylene glycol)s (PEGs, $M_w = 1500$, 3000, and 6000) determined by One-Dimensional Electron Spin Resonance Imaging (1D ESRI) on the properties of hydrogel matrices prepared by photopolymerization of 2-hydroxyethyl methacrylate (HEMA) and 2-(2′-hydroxyethoxy)ethyl methacrylate (DEGMA) was studied. The hydrogels were characterized by degree of crosslinking, ν_{gel}, by hydrodynamic correlation length, ξ_{gel}, and by self-diffusion coefficient of water, D_{H_2O}. The tracer diffusion coefficients were analyzed in the frame of scaling reptation and hydrodynamic models. Molecular weight dependence of the tracer diffusion coefficients follow expression $D \sim M_w^x$ with exponent $x = -1.2 \pm 0.1$ which excludes contribution of reptation to the diffusion. Steep decrease of the tracer diffusion coefficients with increasing polymer concentration was observed. Decrease of the tracer diffusion coefficients with increasing ratio of the hydrodynamic radius of the tracer to the hydrodynamic correlation length of the hydrogel matrix, R_H/ξ_{gel}, was well fitted with predicted stretched exponential expression. Dependence of the tracer diffusion coefficients on the degree of crosslinking ν_{gel} suggested as a new scaling variable was found to closely follow empiric stretched exponential dependence in the whole ν_{gel} range studied.

1. Introduction

Diffusion processes in swollen crosslinked polymer networks (polymer gels) that have direct impact on numerous practical applications such as drug delivery systems and transport across membranes have been reviewed recently [1,2]. Polymer gels swollen with water (polymer hydrogels) are compounds of soft and rubbery-like consistency that have the ability to retain substantial amounts of water. Various techniques have been used for diffusion measurements. Classical concentration-gradient methods and dynamic light scattering (DLS) are examples of techniques used to determine mutual-diffusion coefficients whereas the pulsed-field-gradient nuclear magnetic resonance (PGSE) and radioactive tracer methods are used to determine self-diffusion coefficients [3]. These coefficients are in general different. The self-diffusion coefficient of a particle is directly related to the velocity autocorrelation function of the particle and on the other hand, the mutual-diffusion coefficient is a transport quantity associated with relaxation of solute density fluctuation [4].

Amsden [1] reviewed various models, hydrodynamic, free volume, obstruction, and their combinations, derived to explain and predict solute diffusion in hydrogels, and tested them against literature data. He concluded that of those used to describe solute diffusion in hydrogels composed of flexible polymer chains (homogeneous hydrogels) the model most consistent with the data and with physical parameters of the hydrogels was the hydrodynamic scaling model of Cukier [5] resulting in equation:

$$D/D_0 = \exp(-\kappa R) \tag{1}$$

where D and D_0 are the diffusion coefficients of the tracer in the gel matrix and in the pure solvent in absence of the gel network, respectively, R is radius of a tracer, and κ is an inverse hydrodynamic screening length of polymer chain forming the matrix. According to Cukier [5] the inverse hydrodynamic screening length κ, in semidilute polymer solutions, has a power law dependence on the concentration of polymer matrix c, $\kappa = A'c^n$. After substitution Eq. (1) becomes the stretched exponential function

$$D/D_0 = \exp(-Bc^n) \tag{2}$$

where $B = A'R$. Real gels have permanent networks of crosslinks responsible for their mechanical properties. The crosslinks are

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present in gels in addition to polymer chain entanglements existing as the only obstacles in semidilute solution and polymer gel matrices may exhibit different barriers to tracer diffusion than polymer semidilute solutions do. The inverse hydrodynamic screening length κ is taken to be comparable to the hydrodynamic correlation length ξ which can be measured in gels by DLS and another modification of the Cukier Eq. (1) with R/ξ as scaling variable, stretched exponential $D/D_0 = \exp(-H(R/\xi)^m)$ has been applied [6].

Basic scaling and reptation theory [7,8] leads to the dependence of the macroscopic translational diffusion coefficient D of the tracer on its molecular weight M_w and on concentration of the polymer matrix c given by

$$\mathrm{D} \sim M_\mathrm{w}{}^x \mathrm{c}^k \tag{3}$$

where the exponents $x = -2$ and $k = -1.75$ in good solvents and $k = -3$ in θ solvents.

Rotstein and Lodge [9] studied with DLS diffusion of linear polystyrene tracers in poly(vinyl methyl ether) gels swollen with nearly isorefractive solvent toluene. Polystyrene tracers of molecular weight M_w ranged from 3.2×10^4 to 1.05×10^6 were incorporated in the pregel solution before polymerization at concentration well below their coil overlap concentration. Significantly stronger dependence of diffusion coefficients of the tracers on their molecular weights M_w than the reptation model $D \sim M_\mathrm{w}^{-2}$ predicts characterized by the exponents -2.7 and -2.8 for $c = 0.200$ and 0.235 g/mL, respectively, was determined. They also concluded that the gel retards tracer diffusion in the same manner as the solution containing the same concentration of the high molecular weight polymer ($P = 1.3 \times 10^6$). Besides the reptation model also alternative analysis of basic features of the measured data using Eq. (1), considered as the antithesis to reptation in that the mechanism of diffusion is the same as for a hard sphere, has been performed. Experimental data have been well fitted by Eq. (1) when reasonable approximations based on experimental data determined earlier for D_0 and other parameters, $R = R_\mathrm{G}$ (gyration radii of the polystyrene tracers), $R_\mathrm{G} = 0.03\ M_\mathrm{w}^{0.5}$ [in nm], and $\kappa^{-1} = 2$ nm close to estimated $\xi = 2$ nm has been used.

Park et al. [6] studied diffusion of benzospiropyran dye (SP) and labeled bovine serum albumin (BSA) tracers in polyacrylamide (PA) gels with holographic relaxation spectroscopy. Concentration of the gels ranged from 0.025 to 0.38 g/mL and the mesh size ξ of each gel was calculated from the collective diffusion coefficient determined by photon correlation spectroscopy. The concentration dependence of the mesh size of the gels $\xi = 12.6c^{-0.64}$ [in Å] and concentration dependence of the diffusion coefficients characterized by stretched exponential function Eq. (2) with exponents $n = 0.93$ and 0.92 for SP and BSA tracers, respectively, was found. On the basis of the data analysis the combination $R_\mathrm{H}c/\xi$ has been suggested as a new scaling variable for diffusion in PA gels described by a new universal stretched exponential equation $D/D_0 = \exp(-\alpha\ (R_\mathrm{H}c/\xi)^q)$.

Recently Seiffert and Oppermann [10] measured diffusion of linear polyacrylamides and spherical particles as tracers in semidilute polyacrylamide solutions and polyacrylamide networks using fluorescence recovery after photobleaching (FRAP) technique. They found negligible dependence of the linear tracer diffusion coefficients on the degree of crosslinking of the low concentrated matrices (20–80 g/L) similarly as was concluded in some other quoted papers. Comparability of the degrees of crosslinking presented in the paper is complicated by differences in definitions and techniques of determination of these values.

In addition to the mentioned techniques One-Dimensional X-band Electron Spin Resonance Imaging (1D ESRI) has developed as a powerful tool for measuring coefficients of diffusion of paramagnetic tracers in various matrices at presence of concentration gradient of the tracer. If the concentration gradient of the tracer coincides with the direction of magnetic field gradient applied to the sample in addition to the external magnetic field, an experimental concentration profile of the paramagnetic tracer along the gradient direction at particular time after the start of diffusion can be determined from ESRI experimental data by a deconvolution procedure [11–15]. By fitting a theoretical concentration profile expressed as a solution of Fick's equation for proper sample configuration to the experimental profile the diffusion coefficient as one of the parameters of the fit can be deduced [16].

Using ESRI technique we have shown that even small concentration of permanent crosslinks in the lightly crosslinked poly(1-vinyl-2-pyrrolidinone) (PVP) hydrogel (equilibrium water content 88 wt%) was able to reduce the rate of transport of a bulky paramagnetic tracer to the value corresponding to two-fold volume fraction of linear PVP in solution [17]. Similarly, measurements of diffusion coefficients of paramagnetic tracers in crosslinked HEMA gels swollen with methanol close to equilibrium and in polyHEMA methanolic solutions confirmed [18] slower diffusion of the tracers in HEMA gels compared with the solution containing the same concentration of polyHEMA and even with the solution characterized by the same hydrodynamic correlation length.

To clarify diffusion process in polymer gels we have focused on getting more information on the way by which diffusion of tracers is affected by structural properties of the gels. Copolymer HEMA–DEGMA hydrogels in the state close to equilibrium swelling prepared by photopolymerizing pregel aqueous solution containing predetermined monomer mixture at various concentrations were selected as matrices for diffusion. The hydrogels were characterized by concentration of elastically active network chains (degree of crosslinking), ν_gel, determined by force-deflection measurement of elastic moduli, by hydrodynamic correlation length (mean distance between adjacent crosslinks), ξ_gel, determined by dynamic light scattering (DLS), and by self-diffusion coefficient of water in hydrogels determined by pulsed-gradient stimulated NMR spin-echo (PGSTE).

2. Experimental

2.1. Preparation of hydrogel matrices

HEMA–DEGMA hydrogels I (Fig. 1) were prepared by polymerizing a mixture of 2-hydroxyethyl methacrylate (HEMA, Fluka) containing a non-removable amount of 0.12 wt% of ethylene dimethacrylate crosslinker as determined by gas chromatography, 2-(2′-hydroxyethoxy)ethyl methacrylate (diethyleneglycol methacrylate) (DEGMA), crosslinker 2,3-dihydroxybutane-1,4-diyl dimethacrylate [19], water in proper proportions (Table 1), and initiator 2-hydroxy-2-methyl-1-phenylpropan-1-one (DAROCUR® 1173, Ciba) at amount 10 μL per 1 mL of the pregel solution.

After 10 min bubbling with argon the pregel solution was filled into glass sample tubes, sealed up and the reaction mixture was photo-polymerized (UVB irradiation, 20 W) at room temperature for 30 min. Experimental techniques used for diffusion measurement and characterization of the hydrogels require preparation of samples in sample tubes of various diameters within each series (for particular composition of the pregel solution); capillaries of o.d. 1 mm for ESRI, tubes of o.d. 4 mm for PGSTE, and tubes of o.d. 10 mm for DLS, swelling experiments, or measurement of elastic moduli. Lengths of the hydrogel samples prepared in capillaries for ESRI diffusion experiment ranged from 3 to 6 mm. The hydrogels A1—A4 in the state close to equilibrium swelling were prepared by polymerizing reaction mixtures composition of which (see Table 1)

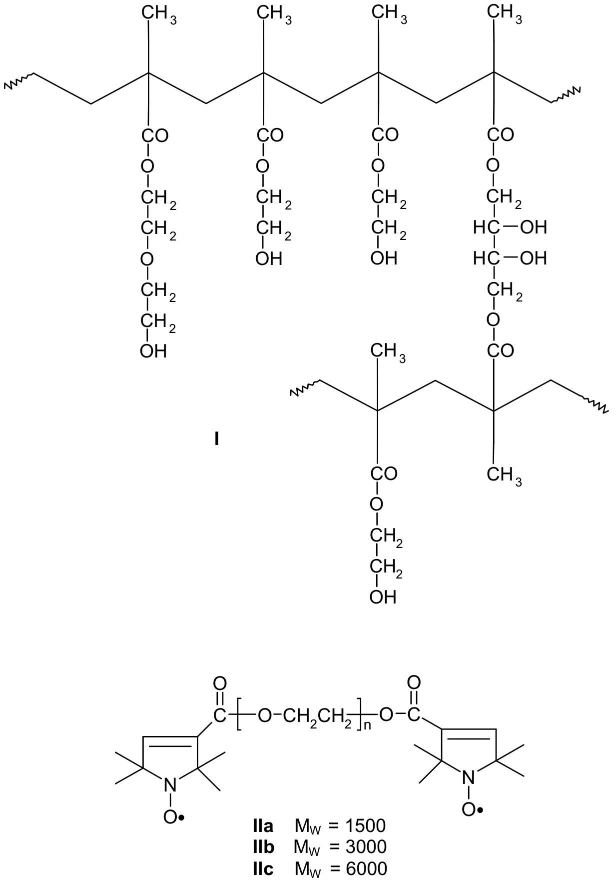

Fig. 1. Structures of HEMA–DEGMA copolymer hydrogel matrix (I) and of paramagnetic PEG tracers (II).

was determined by iterative procedure during preliminary swelling experiments.

2.2. Materials

DEGMA was synthesized in this Institute from Fluka products by re-esterification of methyl methacrylate by diethylene glycol. Product of syntheses was subsequently purified by shaking and distillation [20,21]. Resulting analyses (gas chromatography and Fisher method of water content determination) show very good quality of monomer with small amount of typical impurities (diethylene glycol dimethacrylate crosslinker 0.2 wt%, diethylene glycol 8.1 wt%, water 0.12 wt%).

Table 1
Characterization of hydrogels used as matrices for tracer diffusion studied in this work.

Composition of monomer mixture: 55 mol% HEMA/45 mol% DEGMA	Hydrogel			
	A1	A2	A3	A4
Added crosslinker concentration in monomer [mol/t]	21.1			
Over all crosslinker concentration in monomer, C_s [mol/m^3]	37.8			
Polymer volume fraction in swollen gel, Φ	0.34	0.37	0.40	0.44
Polymer concentration in swollen gel, c, [g/mL]	0.43	0.47	0.51	0.56
Change of water content in gel during swelling test [wt%]	+5	+9	+10	+23
Degree of crosslinking in swollen gel, ν_{gel}, [mol/m^3]	10	13	20	46
Correlation length in gel, ξ_{gel}, [nm]	3.7	2.7	2.1	1.3

Paramagnetic tracers IIa–IIc (Fig. 1) were prepared by spin labeling poly(ethylene glycol) (PEG) standards 1500, 3000, and 6000 (Fluka) and their molecular weights, M_w, 1840, 2920, and 6510, respectively, were determined by MALDI-TOF mass spectrometry as described earlier [18].

2.3. Characterization of hydrogels

2.3.1. Swelling experiments

State of swelling of the hydrogels was checked gravimetrically in long-term swelling experiments. A part of thicker (o.d. 10 mm) samples from each series was subjected to swelling test to check deviation from equilibrium swelling. The hydrogels were removed from the glass tube, immersed in water and their swelling was monitored gravimetrically till equilibrium was reached.

2.3.2. DLS experiments

The DLS instrument consists of an ALV CGE photogoniometer equipped with a Uniphase 22 mW HeNe laser, an ALV6010 correlator and a pair of avalanche photodiodes operated in a pseudo-crosscorrelation mode using an optical fiber splitter. Data were measured at various angles in the range 30–150°, at a temperature of 25 °C controlled by a thermostat. The measured intensity correlation function $g^2(t)$ was analyzed using the program REPES [22] performing the inverse Laplace transformation yielding the distribution of relaxation times $A(\tau)$ which in the numerical calculations is represented by the set of amplitudes A_i corresponding to the relaxation times τ_i. In graphs with logarithmic scale on the relaxation time axis, the distributions are shown in the equal area representation [23] $\tau A(\tau)$ versus $log(\tau)$. The collective (cooperative) diffusion coefficients of gels, D_c, were calculated in standard way from the mean characteristic decay times using the expression $D_c = 1/\tau_c q^2(1-\Phi)^2$, where 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. A correction for solvent back-flow, division by $(1-\Phi)^2$ [24], is included in this expression. There Φ is the polymer volume fraction, $\Phi = v_2 c$, v_2 is the partial specific volume of the copolymer, we used the value $v_2 = 0.785$ cm^3 g^{-1} determined for polyHEMA [25], and c [g/mL], is the polymer concentration. D_c for gels was further corrected by the heterodyne method introduced by Geissler [24]. Then the gels were characterized by the dynamic correlation length (mean distance between adjacent crosslinks or hydrodynamic blob size), $\xi_{gel,}$ by using the Stokes–Einstein relation, $\xi_{gel} = k_B T/6\pi\eta D_c$, where T is the absolute temperature, k_B is the Boltzmann constant, and η the viscosity of the solvent. In the case of polymer gels, the DLS technique is not able to resolve contribution of the polymer chain entanglements and permanent crosslinks to ξ_{gel}.

Hydrodynamic radii, R_H, of both diamagnetic and paramagnetic PEG tracers (PEG standards and their spin labeled derivatives) were automatically measured at the scattering angle $\theta = 173°$ on a Zetasizer Nano-ZS instrument, model ZEN3600 (Malvern Instruments, UK).

2.3.3. Force-deflection dependences

Force-deflection dependences in uniaxial compression were measured using Advanced Rheometr Extended System (ARES, Scientific Rheometrics) on cylindrical gel specimens. Elastic moduli, G, of the gels were obtained and processed using the affine Gaussian rubber elasticity theory [26]. Concentration of elastically active network chains in moles per unit volume of the swollen gel network $\nu_{gel} = G/RT$, where R is gas constant and T the absolute temperature. Concentration of elastically active network chains per unit volume of the dry network $\nu_{\text{dry}} = \nu_{\text{gel}}/\Phi$. Concentration of elastically active network chains is often shortly called network density or degree of crosslinking. In a series of gels prepared at a constant Φ, the experimental dependences of degree of crosslinking on crosslinker concentration, C_S, are found to be of the type $\nu_{\text{dry}} = 2E + 2k_C C_S$, where E can be interpreted as a concentration of physical crosslinks (polymer chain entanglements permanently trapped between chemical crosslinks) and k_C as an efficiency of the crosslinker for the formation of chemical crosslinks. With increasing fraction of solvent during polymerization (i.e., with decreasing Φ), both E and k_C are found to diminish. This effect can be ascribed to a partial disentanglement of polymer chains due to dilution of the system and to a partial wastage of crosslinker due to the formation of elastically inactive cycles and to incomplete reaction of its double bonds.

2.3.4. PGSTE experiments

PGSTE experiments were used to determine self-diffusion coefficients of H_2O in the swollen hydrogels and self-diffusion coefficients of diamagnetic derivatives of the tracers (PEGs without paramagnetic nitroxides attached) in aqueous solutions. Also attempts to determine self-diffusion coefficients of the tracers in the swollen hydrogels were made. Measurements were performed with an upgraded Bruker Avance DPX 300 NMR spectrometer using a water-cooled z-gradient diffusion probe connected to a Bruker BGU2 gradient unit. A Tanner pulsed-field-gradient stimulated echo sequence with incremented gradient power (0—650 G/cm, pulse length $\delta = 1$ ms) was used. The diffusion time Δ was usually 20 ms, in some experiments it was prolonged to 100 ms without apparent change of the diffusion coefficient obtained. In all cases, mono-exponential decays and thus mono-component diffusion times were obtained.

2.4. Measurements of tracer diffusion coefficients by ESRI

2.4.1. Sample preparation and ESRI measurement

ESRI experiments were performed using a Bruker ELEXSYS E—540 X-band ESRI spectrometer equipped with a pair of eight-shaped Lewis gradient coils delivered by George Associates (Berkeley, USA) that are able to produce vertical gradient perpendicular to the external magnetic field $G_{\text{max}} \sim 320$ G/cm. After polymerization the capillaries with the hydrogel samples for ESRI were opened, the hydrogel surface was topped with approximately 2 μL of aqueous solution of the paramagnetic tracer (5×10^{-2} mol/L) and sealed again. We called this experimental arrangement "from-top-to-bottom" [18]. The capillary was then placed, with its axis parallel to the gradient direction, in the cavity of the ESR spectrometer (Fig. 2). ESR spectra without magnetic field gradient and projections at presence of the magnetic field gradient were measured at suitable time intervals Δt after the diffusion start for each of the samples to get estimate of experimental error and to disclose possible effects of non-Fickian processes typically characterized by time-dependence of diffusion coefficients. At least two samples for each combination hydrogel-tracer were studied. Measurements were performed at two values of the magnetic field gradient (120 and 280 G/cm) to test an effect of the gradient magnitude on the quality of the data. All the measurements were performed at room temperature (298 ± 2 K) and the samples were kept at the same temperature when outside the cavity.

2.4.2. ESRI data processing

The projection measured in the presence of the gradient could be expressed as a superposition of the spectra of all individual tracers at various positions inside the sample (i.e. at various effective external magnetic fields) (Fig. 3) weighted by the spectrometer sensitivity at particular position [11]. Projection measured at the gradient-on could be mathematically expressed as a convolution of the spectrum measured at the gradient-off and the concentration profile of the tracer inside the sample providing that there is no lineshape variation in the tracer ESR spectrum throughout the sample. In order to get the concentration profile, the reverse deconvolution process must be performed, i.e. the spectrum at the gradient-off must be deconvoluted out of the projection measured at the gradient-on (Fig. 3). If the spatial region of the diffusion is wide (>5 mm in our experimental arrangement), it is necessary to divide the result of the deconvolution by the spectrometer spatial sensitivity function that could be readily determined by measuring concentration profile in the sample with homogenous tracer distribution. Deconvolution of the experimental data was performed using software developed in this laboratory as described in the previous paper [18] using the Fourier method in the first step. The result was used as the starting point for the Monte Carlo method, which was used as a feedback to assure the reverse validity of the convolution relation between the measured spectra and tracer concentration profile. An example of 2D ESRI spectral-spatial image was reconstructed from the ESRI data using software described in Marek's thesis [27].

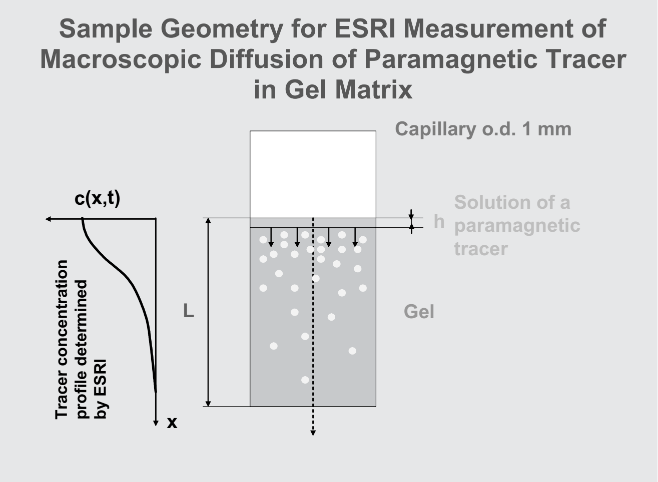

Fig. 2. Experimental arrangement of ESRI experiment.

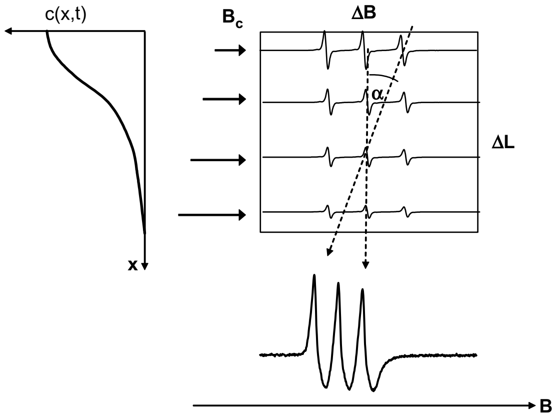

Fig. 3. Origin of lineshape of ESRI projection of a sample containing inhomogeneous distribution of a nitroxide probe characterized by the concentration profile $c(x,t)$ along the direction of the gradient of the magnetic field B_c applied to the sample in addition to the static external magnetic field B.

2.4.3. Determination of diffusion coefficients of paramagnetic tracers

On the assumptions that the concentration of the tracer inside the sample is low enough so that the translational diffusion obeys Fick's law, that the diffusion in cylinder along the capillary axis strongly predominates over those in other directions, that the tracer is initially confined in the in the region $0 < x < h$ and diffuses into a finite system of length l between the top and bottom walls, and at boundary conditions that at $t = t_0$ $C = C_0$ for $x \leq h$ and $C = 0$ for $x > h$, and $\partial C/\partial x = 0$ at $x = l$, we may use for our sample geometry the solution of the Fick's equation [16,27]

$$C(x,t) = ½C_0 \sum \left\{ \mathrm{erf}[(h + 2nl - x)/2\sqrt{(Dt)}] + \mathrm{erf}[(h - 2nl + x)/2\sqrt{(Dt)}] \right\} \tag{4}$$

where $C(x,t)$ is 1D spatial and time dependence of the tracer concentration in the sample, x is the space coordinate measured normal to the cylinder section, D is the diffusion coefficient, and $\mathrm{erf}(x) = (2/\sqrt{\pi}) \int \exp(-\xi^2)\,\mathrm{d}\xi$ is error function.

Diffusion coefficient $D_{\Delta t}$ can be determined as one of the parameters of the fit of this equation to the experimental concentration profile determined after time interval Δt since the diffusion start. Nonplanarity of the top sample surface due to the meniscus at the hydrogel surface when performing "from-top-to-bottom" diffusion makes the real top wall not sharp as assumed, which implies that the real 1D concentration profile does not begin by a jump change at the top of the sample but rather by a gradual increase. The position of the reflection wall is one of the parameters of the simple fitting procedure and the minimization procedure tries to place the edge of the theoretical concentration profile somewhere in the middle of the broadened slope of the wall of the experimental concentration profile which decreases the quality of the simple fit. To overcome this problem including of the symmetrization procedure into the process of fitting the experimental concentration profiles of the tracer was suggested in the previous paper [18]. As this procedure uses experimentally determined initial profile, it is advantageous to use various combinations of the particular concentration profile determined at time interval Δt after the diffusion start with some of the profiles measured before taken as initial profile. If the diffusion follows Fick's law, combinations of different pairs of the concentration profiles should give the same diffusion coefficient $D_{\Delta t}$. The symmetrization procedure must be performed with both the final and the initial concentration profile. Resulting nearly Gaussian symmetrized profiles can be fitted with a substantially higher correlation comparing with the simple fitting process. The plot of $D_{\Delta t} \times \Delta t$ versus Δt could be fitted with a straight line crossing the origin, and its slope gives tracer diffusion coefficient D. For deconvolution and fitting procedures we used above mentioned software under the Matlab environment [18,27].

3. Results and discussion

3.1. Characterization of hydrogel matrices

All data characterizing copolymer HEMA–DEGMA hydrogels used as matrices in diffusion experiments are given in Table 1. Molar ratio of HEMA to DEGMA monomers and weight ratio of crosslinker to monomer mixture was kept constant in all hydrogels. Polymer concentration was varied to meet state of equilibrium swelling as close as possible in order to eliminate contribution of the concentration gradient of the solvent to the driving force governing the tracer diffusion. Described procedure of sample preparation was adopted because the technique of ESRI diffusion experiment does not allow any additional manipulation with the prepared hydrogels (washing, swelling or deswelling). Equilibrium swelling requirement restricted the accessible concentration range of suitable hydrogels. State of swelling of the hydrogels was checked gravimetrically in long-term swelling experiments before diffusion measurements. No measurable amount of components of pregel solution was found in water after long term swelling. Deviation from equilibrium swelling at amount of 10% of water content or smaller was found in the hydrogels A1–A3, larger additional swelling 20% was observed in the hydrogel A4.

Thorough characterization of the gels is necessary condition for trustworthy interpretation of the experimental data. Dynamic correlation length, ξ_{gel}, determined in hydrogels by DLS presented in double logarithmic plot in Fig. 4a decreases with increasing polymer concentration in the hydrogels and follows scaling prediction $\xi_{\mathrm{gel}} = Ac^p$. The best fit of the experimental data by this expression calculated for $p = -3.9$ is presented by solid line. Absolute value of this exponent is significantly higher than that of the exponent $p = -0.64$ determined in polyacrylamide gels by Park et al. [6].

The degree of crosslinking, ν_{gel}, determined by measurement of the elastic moduli of the gels increases with increasing polymer

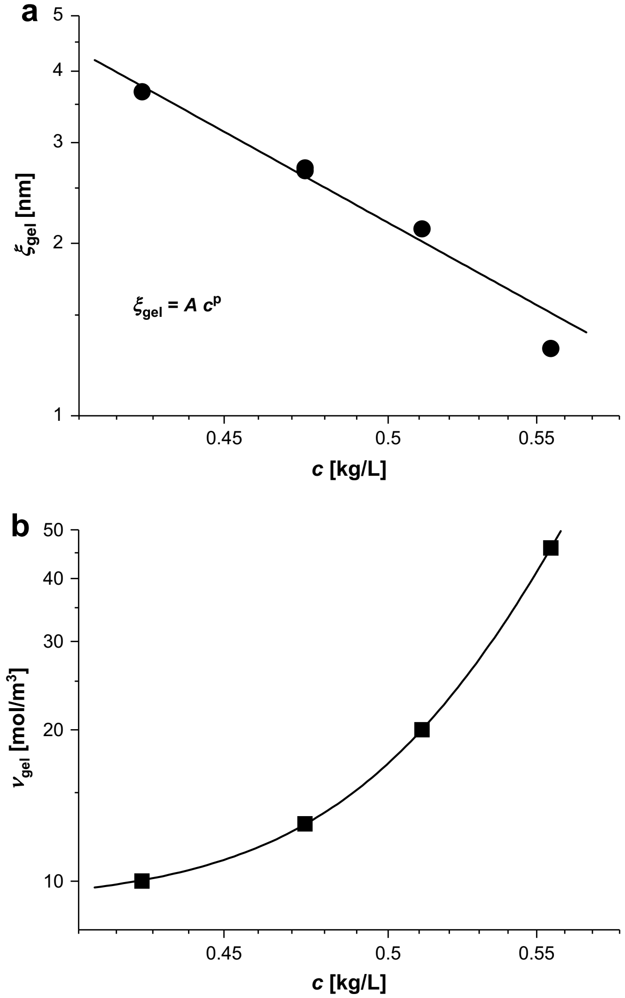

Fig. 4. Double logarithmic plots of the dependences of the dynamic correlation length ξ_{gel} (●) determined in the hydrogels by DLS (a) and of the degree of crosslinking of the hydrogels ν_{gel} (■) calculated from elastic moduli of the hydrogels determined by force-deflection measurements (b) on polymer concentration in hydrogels c. Solid line in (a) represents the best fit of the predicted expression $\xi_{\mathrm{gel}} = Ac^p$ to the experimental data characterized by $A = 0.19$ and $p = -3.5$.

concentration in hydrogel (Fig. 4b). The degree of crosslinking comprises contribution from both polymer chain entanglements, concentration of which depends on polymer concentration in the gel, and on the concentration of permanent crosslinks controlled by the concentration of the crosslinker. It follows that considering the same concentration of the crosslinker in monomer mixtures presence of the same concentration of permanent crosslinks in all the gels prepared for this study is reasonable expectation. Variation of the concentration of entanglements is responsible for changing properties of the hydrogel matrices then. We attempted to use degree of crosslinking of the hydrogels, ν_{gel}, as a new scaling parameter characterizing the hydrogel.

Self-diffusion coefficients of H_2O in hydrogels, D_{H_2O}, determined in the hydrogels by PGSTE were corrected for decrease due to the exchange interaction of water with OH groups present in the hydrogel by division by the factor $[H_2O]/(2[H_2O]+[OH])$ where the concentrations are molar and [OH] are all labile hydrogens present in hydrogel accessible to water. The corrected values of the self-diffusion coefficients D_{H_2O} are plotted in Fig. 10. Slight decrease of the diffusion coefficient D_{H_2O} with degree of crosslinking increasing follows from the presented data.

3.2. Hydrodynamic radii of the PEG tracers

Hydrodynamic radii are important parameters characterizing tracers applied in studies of diffusion properties of various matrices. Hydrodynamic radii of the paramagnetic PEG tracers in dilute aqueous solutions ($\sim$1 wt%) used in the paper for calculation of D_0 measured by Zetasizer are plotted in Fig. 5. Hydrodynamic radii of the diamagnetic PEG tracers (PEGs without nitroxides attached) determined by various techniques are given in Fig. 5 for comparison. Under the same experimental conditions the smaller radii for the diamagnetic PEGs comparing with the paramagnetic ones were measured by Zetasizer as expected. Hydrodynamic radii of the diamagnetic PEGs can also be calculated using the Stokes–Einstein relation, $R_H = k_BT/6\pi\eta D_s$ from their self-diffusion coefficients D_s determined by PGSTE technique. This technique is unfortunately not applicable to paramagnetic compounds. Molecular weight dependence of the radii calculated from the diffusion coefficients determined by Masaro et al. [28] are in close agreement with the data calculated from our PGSTE measurements in 5 wt% aqueous solutions. Higher PEGs concentration in the aqueous solutions is probably responsible for the higher values of the radii determined from the PGSTE measurements when comparing with the Zetasizer measurement. Significantly lower values of the hydrodynamic radii were calculated from the diffusion coefficients of tracer amounts of radioactive PEGs determined by radioactive tracer method in water [29]. The very low PEG concentrations are probably responsible for this difference. The plot is completed with cross section of poly(tetramethylene glycol) determined by quantum chemical calculation [30]. The cross section fits well the data determined by radioactive tracer method. The fact that self-diffusion coefficients are determined by PGSTE and radioactive tracer methods whereas mutual diffusion coefficients are determined by light scattering and concentration gradient methods [3] should be taken in consideration.

3.3. Diffusion coefficients of paramagnetic tracers in hydrogel matrices

Time intervals Δt after the diffusion start at which ESRI measurements were performed were selected considering speed of the diffusion process. The intervals ranged from 10 h in the case of PEG 1500 in the less concentrated hydrogel A1 to several weeks in the case of PEG 6000 in the hydrogel A4. The diffusion process was followed till the homogeneous distribution of the tracer in the gel sample was reached. The period ranged from one week in the case of the fastest diffusions to several months in the case of the slowest ones.

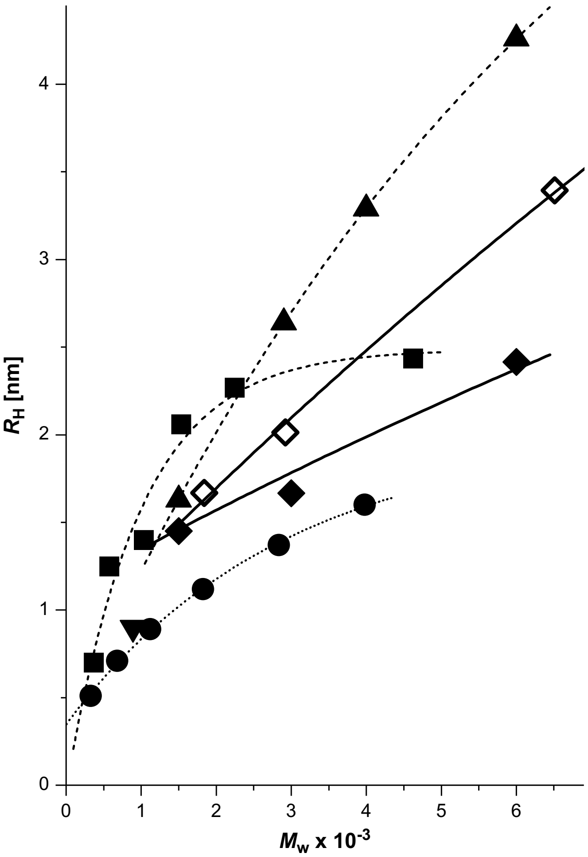

Fig. 5. Molecular weight dependence of hydrodynamic radii of the PEG tracers calculated from diffusion coefficients of the tracers determined by our PGSTE measurements in 5 wt% aqueous solution (▲), calculated from diffusion coefficients of the tracers in aqueous solution determined by PGSTE measurements performed by Masaro et. al. [28] (■), calculated from the diffusion coefficients of tracer amounts of radioactive PEGs determined by radioactive tracer method in water [29] (●), determined by our Zetasizer measurement in 1 wt% aqueous solution (◆ ◇), and determined by quantum chemical calculation for polytetramethylene glycol [30] (▼). Data determined for diamagnetic PEGs without nitroxides attached are given by full symbols, data determined for paramagnetic spin labeled PEG tracers by Zetasizer, used in the paper for determination of D_0, are presented by empty symbols.

An independence of the tracer spectral lineshape of the position along the magnetic field gradient direction in the sample is one of the conditions for applicability of the deconvolution procedure described above. An example of 2D ESRI image of the A2 hydrogel sample containing homogeneously distributed tracer IIa taken when the macroscopic diffusion process was practically completed (Fig. 6) confirms accomplishment of this condition. The same conclusion is valid for all studied systems.

The tracer diffusion coefficients, D, of the paramagnetic PEG tracers in hydrogel matrices A1–A4 were determined by fitting process characterized by correlation coefficient typically better than 0.97. Due to decreasing sensitivity of the shape of the calculated profile to the value of the tracer diffusion coefficient accuracy of determination of the diffusion coefficient by the fitting process decreases when tracer approaches homogeneous distribution in the sample. Such profiles were excluded from the evaluation process. The tracer diffusion coefficients, D, or their normalized values D/D_0, are presented in Figs. 7–10. Differences in the diffusion coefficients of particular tracer in various gel samples prepared by

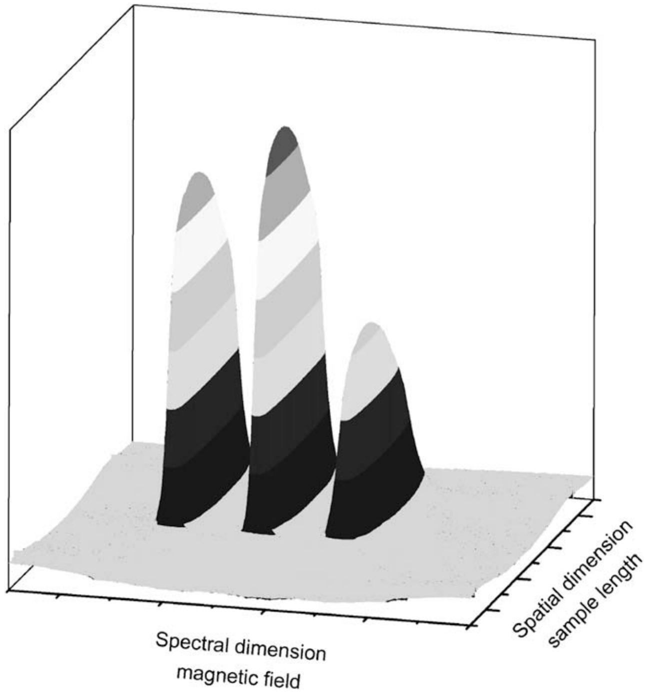

Fig. 6. 2D ESRI spectral-spatial image of the hydrogel sample A2 containing practically homogeneous distribution of the paramagnetic tracer PEG 1500 (IIa) taken at the end of the diffusion experiment. Absence of any change of the tracer ESR lineshape with position inside sample is clearly visible.

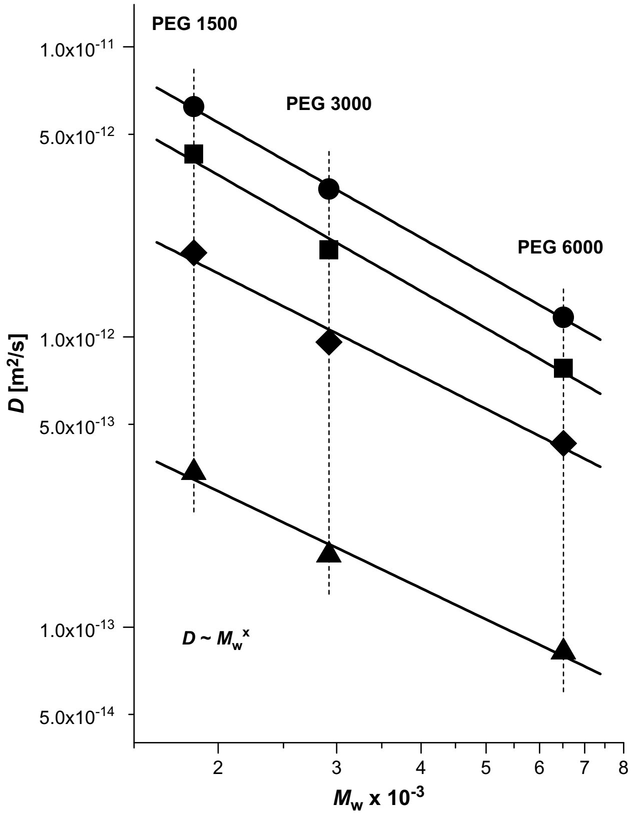

Fig. 7. Double logarithmic plots of the dependences of the diffusion coefficients D of the paramagnetic tracers IIa–IIc determined in hydrogel matrices A1 (●), A2 (■), A3 (◆), A4 (▲) by ESRI on the molecular weight of the tracer. Solid lines represent the best fits of the experimental data by the expression $D \sim M_w^x$ found for exponents $x = -1.2 \pm 0.1$.

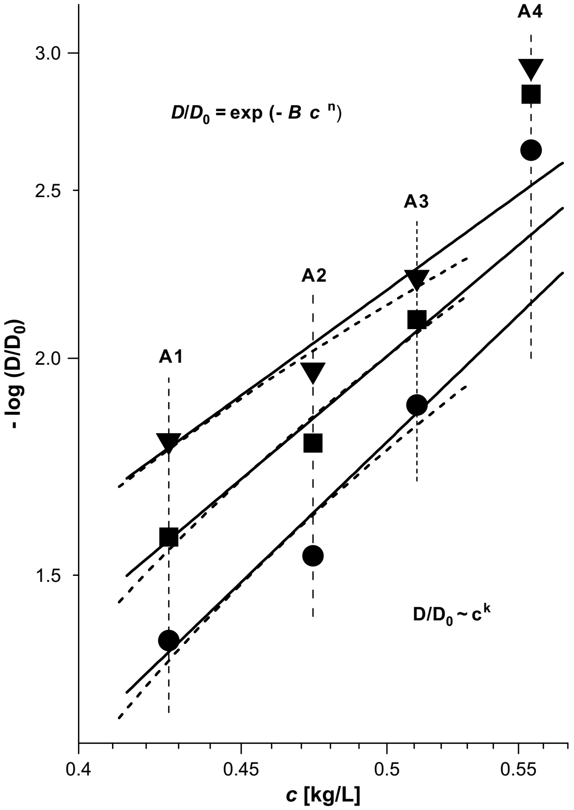

Fig. 8. Log log versus log plots of the dependences of the logarithm of the normalized diffusion coefficients D/D_0 of paramagnetic tracers IIa (●), IIb (■), and IIc (▼) determined in the hydrogel matrices A1–A4 by ESRI on the polymer concentration in the hydrogel matrices c. D_0 are the diffusion coefficients calculated from the hydrodynamic radii of the paramagnetic tracers measured in 1% aqueous solution by Zetasizer (Fig. 5). Solid lines represent the best fits of the experimental data by the stretched exponential $D/D_0 = \exp(-B\,c^n)$ found for $B = 13.4 \pm 0.7$ and $n = 1.6 \pm 0.2$. Dashed lines represent the best fits of the experimental data determined in the three less concentrated hydrogel matrices A1–A3 by the expression $D/D_0 \sim c^k$ found for $k = -6 \pm 0.5$.

polymerizing identical pregel solution do not exceed 5%. Two sets of A1 and A2 gel samples were prepared by polymerizing two different pregel solutions of the same composition. The diffusion coefficients determined in both sets of gel samples agree within experimental error smaller than 10%. It means that experimental error limits of determination of the diffusion coefficients are comparable to the size of symbols used in the plots.

Dependences of the tracer diffusion coefficient, D, on the tracer molecular weight M_w are presented in double logarithmic scale in Fig. 7. The best fits of the presented data to the $D \sim M_w^x$ expression were found for exponent values $x = -1.2 \pm 0.1$ in all four hydrogels (−1.32, −1.33, −1.17, and −1.11 in the hydrogels A1, A2, A3, and A4, respectively). This value indicates that reptation does not affect the diffusion process. This conclusion can be well understood considering that hydrodynamic radii R_H of the paramagnetic PEG tracers plotted in Fig. 5 are comparable to the hydrodynamic correlation lengths ξ_{gel} presented in Fig. 4a. The situation is in this respect similar to the diffusion in entangled solutions [31].

Log log versus log plots of the dependences of the logarithm of the normalized diffusion coefficients D/D_0 of paramagnetic tracers determined in the hydrogel matrices A1—A4 by ESRI on the polymer concentration in the hydrogel matrices c are given in Fig. 8. D_0 are diffusion coefficients of the paramagnetic PEG tracers in pure water solvent calculated from the hydrodynamic radii of the paramagnetic tracers measured in 1% aqueous solution by Zetasizer (Fig. 5). Solid lines represent the best fits of the experimental data

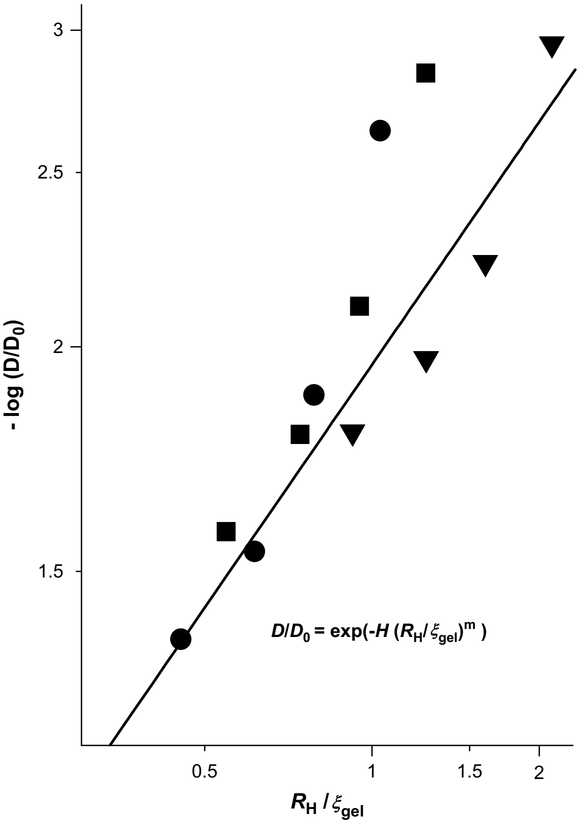

Fig. 9. Log log versus log plot of the dependence of the logarithm of the normalized diffusion coefficients D/D_0 of paramagnetic tracers IIa (●), IIb (■), and IIc (▼) determined in the hydrogel matrices A1—A4 by ESRI (for D_0 see the caption to Fig. 8) on the ratio of the tracer hydrodynamic radius to the hydrodynamic correlation length of the hydrogel matrix. Solid line represents the best fit of the experimental data by the stretched exponential $D/D_0 = \exp(-H(R_H/\xi_{gel})^m)$ found for $H = 4.5 \pm 0.2$ and $m = 0.45 \pm 0.06$.

by the stretched exponential (2) found for $B = 13.4 \pm 0.7$ and $n = 1.6 \pm 0.2$. The expression (2) fits well the data determined for all three tracers in the three less concentrated hydrogel matrices A1–A3 but predicts faster diffusion in the matrix A4. Park et al. [6] found exponents $n \sim 0.9$ when analyzing diffusion coefficients of benzospiropyran dye and labeled bovine serum albumin in polyacrylamide gels in the concentration range 0.025–0.380 g/mL.

Dashed lines in Fig. 8 represent the best fits of the experimental data determined in the three less concentrated hydrogel matrices A1–A3 by the expression $D/D_0 \sim c^k$ found for $k = -6 \pm 0.5$. Also this expression is not able to predict diffusion coefficients in the hydrogel matrix A4 correctly. Similarly in the study of diffusion of linear polystyrenes in poly(vinyl methyl ether) solutions [31] at the highest concentration studied (~300 kg/L) the slope of the concentration dependence of the normalized diffusivity close to -3.3 was reported. Our data indicate slope corresponding to ~ -6 in the concentration range 400–500 kg/L and much steeper concentration dependence at higher polymer concentrations of the crosslinked HEMA–DEGMA matrices. Increasing concentration of the polymer chain entanglements in the hydrogel matrices is probably responsible for the observed steep c dependence of the tracer diffusion coefficients.

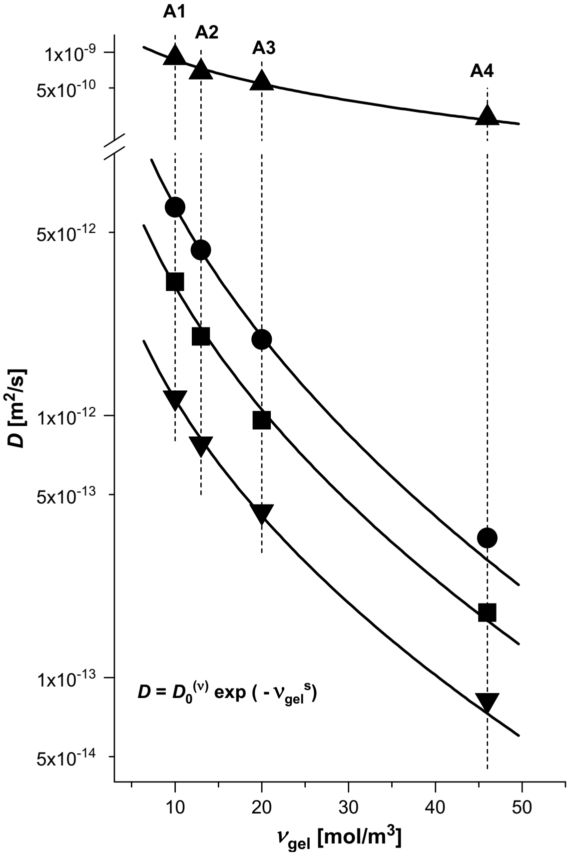

Fig. 10. Logarithmic plot of the dependence of diffusion coefficients of paramagnetic tracers IIa (●), IIb (■), and IIc (▼) determined by ESRI on the crosslink density ν_{gel} calculated from the elastic moduli determined in the hydrogels A1–A4 by force-deflection measurements. Solid curves represent the best fits of the data by the stretched exponential $D = D_0^{(\nu)}\exp(-\nu_{gel}{}^s)$ found calculated with $s = 0.45 \pm 0.02$ for all three tracers and with $D_0^{(\nu)} = 12$, 5.6, and 1.9×10^{-11} for the tracers IIa, IIb, and IIc, respectively. Self-diffusion coefficients of H_2O in hydrogel matrices determined by PGSTE (▲) are given in the plot for comparison, the best fit was calculated with $s = 0.30$ and $D_0^{(\nu)} = 6 \times 10^{-9}$.

Log log versus log plot presented in Fig. 9 shows dependence of the logarithm of the normalized diffusion coefficients D/D_0 of paramagnetic tracers determined in the hydrogel matrices on the ratio R_H/ξ_{gel} selected as a scaling variable. The hydrodynamic radii of the paramagnetic PEG tracers were measured by Zetasizer and hydrodynamic correlation lengths in the hydrogel matrices were determined by DLS. The corresponding stretched exponential expression $D/D_0 = \exp(-H\,(R/\xi)^m)$ fits the experimental values D/D_0 for all three tracers in all four hydrogels well with the best fit parameters $H = 4.5 \pm 0.2$ and $m = 0.46 \pm 0.06$. Quality of the fit decreases with increasing both polymer concentration in the gel matrix and molecular weight of the tracer. Park et al. [6] found the higher exponent $m = 1.48 \pm 0.06$ characterizing slopes of dependences of normalized diffusion coefficients of five various tracers in polyacrylamide gels. We observed no improvement of the quality of the fit when using the ratio R_Hc/ξ_{gel} as a scaling variable in the expression $D/D_0 = \exp(-\alpha\,(R_Hc/\xi)^b)$.

Dependence of the tracer diffusion coefficients on the degree of crosslinking ν_{gel} that we have introduced as another measurable scaling parameter characterizing hydrogels as matrices for diffusion is presented in Fig. 10. Empiric stretched exponential expression $D = D_0^{(\nu)}\exp(-\nu_{gel}{}^s)$ fits experimental dependences of the tracer diffusion coefficients on this parameter very well in the whole ν_{gel} range studied. The fits presented by solid lines in Fig. 10 were calculated with the best fit values $s = 0.45 \pm 0.02$ for all three tracers and with $D_0^{(\nu)} = (12, 5.6, \text{and } 1.9) \times 10^{-11}$ for the PEG 1500, 3000, and 6000, respectively. This parameter should be related to the diffusion coefficient of the particular tracer in the non-crosslinked matrix ($\nu_{gel} = 0$) containing the same polymer components as the corresponding hydrogel.

PGSTE offers an opportunity to measure self-diffusion coefficients of tracers homogeneously distributed in the hydrogel matrices prepared for ESRI measurements. We followed Rotstein and Lodge [9] and prepared hydrogel samples by polymerizing the pregel solution containing 5 wt% of diamagnetic derivatives of the tracers. Unfortunately, PGSTE have shown that the hydrogels prepared in this way are not homogeneous, especially in the case of more voluminous tracers IIb and IIc. In attempt to overcome this problem we try to create homogeneous distribution of sufficient concentration of the tracers inside hydrogel samples by allowing the tracers to diffuse into the swollen hydrogel from concentrated aqueous solutions similarly as in the case of samples subjected to the ESRI study. Experiments in this direction and experiments in the hydrogels containing various concentration of the crosslinker are in progress.

4. Conclusions

Four HEMA–DEGMA hydrogels swollen close to equilibrium were prepared by photopolymerizing pregel aqueous solution containing predetermined monomer mixture at various concentrations. Diffusion coefficients of paramagnetic tracers in the hydrogel matrices at presence of the tracer concentration gradient were determined using ESRI technique. Their dependences on the classical scaling parameters (tracer molecular weight, polymer concentration in hydrogel, and ratio of the hydrodynamic radius of the tracer to the hydrodynamic correlation length of the hydrogel matrix) have been found to follow expressions resulting from the theoretical predictions of the hydrodynamic scaling model in medium concentrated hydrogels (up to ∼500 kg/L). These expressions predict faster diffusion in the most concentrated hydrogel matrix than observed. “Harder” character of the HEMA–DEGMA hydrogels used in this study (concentration range 0.42—0.56 kg/L) is probably responsible for the steeper concentration dependences of the tracer diffusion coefficients found when comparing with e.g. polyacrylamide gels. Empirical stretched exponential expression describing dependence of the tracer diffusion coefficients on the degree of crosslinking that was selected as a new scaling parameter is able to fit tracer diffusion coefficients in the whole range of degree of crosslinking of the matrices studied.

Acknowledgments

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