

Supercooled Water in PVA Matrixes: I. An Incoherent Quasi-Elastic Neutron Scattering (QENS) Study

Gaio Paradossi,^{*,‡} Francesca Cavalieri,[‡] Ester Chiessi,[‡] and Mark T. F. Telling[†]

*Dipartimento di Scienze e Tecnologie Chimiche and INFM, Sezione B, Università di Roma "Tor Vergata",
Via della Ricerca Scientifica, 00133 Roma, Italy and Rutherford Appleton Laboratory, Chilton Didcot,
Oxfordshire OX11 0QX, United Kingdom*

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The incoherent quasi-elastic neutron scattering study of poly(vinyl alcohol) based hydrogels was carried out to elucidate the dynamic state of water caged in polymeric matrixes with different degree of cross-linking and nature of the cross-linking agent. This investigation focuses on the determination of the relationship occurring between the diffusional parameters of water and the polymer network architecture. Analyzing the broadening factor of the dynamic structure factor, a marked supercooling of water was detected in all the matrixes under consideration. In all cases, the activation energies were about 4 kcal/mol indicating a hydrogen bond regime governing the matrix–solvent interaction. In some favorable cases, an insight on the polymer dynamics was also possible. The q -dependence of the broadening factor of polymer relaxation component revealed a behavior compatible with a bound random jump dynamics and concerning segmental motions of the chain coupled with the interaction with water.

Introduction

Hydrogels are achieving growing importance in material science. Some of their properties, that is, swelling, liquid and solid-state dual behavior, and responsiveness to environmental characteristics changes, are often unique.¹ Biomedicine is the field where these systems are already widely used, in particular, as soft transducers,² tissutal substitutes,³ devices for controlled drug delivery,⁴ and scaffolds for tissue engineering.⁵ These applications impose strict requirements in terms of biocompatibility, surface morphology, interfacial properties, and diffusivity of solute. In any of these items, gel behavior is characterized by key parameters concerning the polymer moiety such as cross-link density, chemical or physical nature of the cross-links, hydrophobicity, and polymer chain flexibility. These aspects are intertwined with the dynamic behavior of water in confined media and the reason to study the water state in such matrixes stems from the following considerations:

(i) The unusual properties of water⁶ such as the temperature dependence of equilibrium and nonequilibrium variables in the liquid and in the supercooled state, that is, density, dielectric relaxation, and diffusion coefficient, have been studied in the vicinity of the glass transition in experimental and theoretical works.^{7–11} In particular, it seems established that the water behavior in the vicinity of the glass transition is influenced by tri- and bidimensional confinement.^{12,13} In this respect, organic and inorganic structured assemblies can be used as confinement agents to allow the study of supercooled water properties in a temperature range where bulk water is subjected to ill-defined phase transformations.

(ii) Most of the water participating in processes relevant for the life cycle is in many cases a confined one, with static and dynamic peculiarities such as supercooling.

With these motivations, several studies on water in confined systems have been carried out focusing on mesoscopic 2D and 3D geometries where the confinements were accomplished using different matrixes. Sorption of water in zeolites¹⁴ resulted in a slowing down of the rotational motion of the solvent with an activation energy of reorientation of 7.35 kJ·mol^{−1}, comparable with the value for bulk water. A two-dimensional confinement was obtained by adsorbing water in vermiculite clay layers. In this study,¹⁵ the dielectric and QENS studies on the fully hydrated system in the 130–215 K temperature range showed a complex dielectric behavior for the double H₂O layer with three different dispersions.

The present work deals with the characterization of water in novel soft materials for biomedical applications. In particular, poly(vinyl alcohol), PVA, can be considered a polymer material with good potentialities because of its chemical versatility.¹⁶ Usually, chemical hydrogels are obtained by a chemical networking reaction of a polymeric moiety with a cross-linking agent. Often, the cross-linker is not biocompatible. As pointed out in our former papers,^{17,18} the hydroxylic moiety and the presence of head-to-head sequences in the PVA chain allow for the synthesis of a chemical hydrogel without the addition of a chemically different, external, cross-linking agent, such as glutaraldehyde, which could deplete the hydrogel biocompatibility. To achieve this goal, we have nicked the head-to-head sequences of the PVA chains by means of the specific oxidative reaction with the metaperiodate ions. The reactive aldehydic functionalities produced by this reaction are placed at the ends of the nicked PVA chains and can be further used to self-cross-link by means of an acetalization reaction with the hydroxylic moiety of the chains. The resulting PVA network does not contain any external cross-linking agent that could impinge the biocompatibility of the starting polymer material.

To study the release properties of these matrixes, a knowledge of the dynamic and equilibrium characteristics of solvent medium is necessary as the diffusivity of drug molecules in

* Corresponding author. E-mail: paradossi@stc.uniroma2.it.

[‡] Università di Roma "Tor Vergata".

[†] Rutherford Appleton Laboratory.

hydrogels are regulated by the dynamics of water engulfing the network. A suitable approach to the study of the diffusive modes of the solvent in the matrix is the incoherent quasi-elastic neutron scattering,¹⁹ QENS, since the parameters obtainable by this method describe the dynamic behavior of the solvent at molecular scale distances and at picosecond time scale.²⁰ Therefore, this approach opens a clue on the possibility to relate the macroscopic observations concerning the drug release with the molecular processes involved and furthermore makes accessible the direct comparison between the experimental evaluation of diffusion parameters such as diffusion coefficients and average characteristic times with the molecular dynamics simulations of the process. In this respect, molecular dynamics simulations have become an established tool in the study of biomolecules, complementary to experimental methodologies.²¹

Despite the increasing number of applications of this computational approach to complex systems, molecular dynamics studies of aqueous solutions of synthetic polymer and hydrogels are less frequently encountered in the literature. Computer simulation studies of physical hydrogels are reported for poly(acrylamide),²² poly(vinyl alcohol),^{23–26} poly(vinyl methyl ether),^{23,24} and poly(*N*-isopropylacrylamide)^{23,24} but, to our knowledge, molecular dynamics has not yet been applied to models of chemical hydrogels.

In a future MD investigation on hydrogels from this laboratory, a particular interest will be devoted to the analysis of the polymer-induced modification of water properties. Our experimental findings will be compared with a molecular dynamics study of chemical hydrogels of PVA, with the aim to explore at a molecular level the dynamics of the hydrogen-bonded water molecules inside the chemical network of the polymer. The results of this investigation will be reported in a following paper. Accordingly to the experimental findings here described, we expect to reveal a supercooled water behavior, in terms of diffusion coefficient, radial distribution functions, and hydrogen bonding.

We have formerly reported on the water diffusivity on a PVA hydrogel cross-linked by glutaraldehyde by means of QENS approach.²⁷ The contribution to the broadening of the scattering peak because of the diffusional behavior of water was found to strictly correlate to water diffusivity parameters, that is, diffusion coefficient and correlation times. Evidence for water supercooling in this matrix was gathered together with a characterization of a diffusivity described in terms of a confined random-jump model. In the present work, we have extended the investigation to a set of PVA-glutaraldehyde, hereafter PVA-G, and telechelic PVA hydrogels to evaluate the influence of the chemical characteristics of the network on the solvent diffusion and to obtain a more general view on the key factors responsible for the diffusion processes in PVA gels.

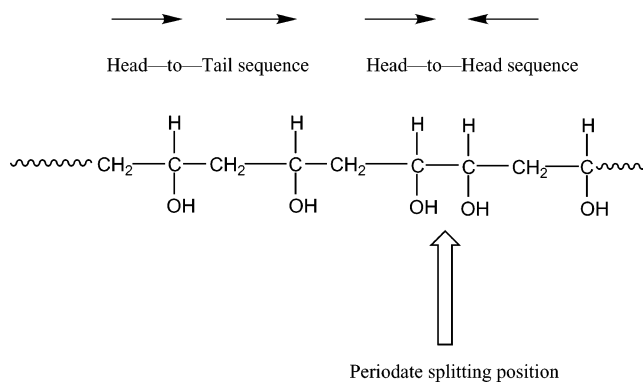
The main structural difference between the PVA-G and the telechelic PVA hydrogels is the length of the cross-linker. In the former type, the coupling agent responsible for the cross-linking is the glutaraldehyde molecule, whereas in the latter the cross-linker used is a macromer consisting in a PVA bearing two aldehydic end groups reacting with the hydroxylic moiety of the PVA backbone.

Experimental Section

Samples Preparation. (a) *Telechelic PVA Networks.* The obtainment of the telechelic PVA is related to the sequencing of the repeating units occurring in the PVA chains (see Chart 1).

A description of the method for the obtainment of the telechelic PVA has been given in a recent paper.¹⁶ The

CHART 1: Repeating Unit Sequences in PVA Chains



prevailing arrangement of the repeating units in the PVA chain is a head-to-tail type, whereas the head-to-tail sequence can be considered as a randomly distributed defect along the chain. In commercial PVA samples, its amount is around 1.5% of the total. The telechelic PVA molecules are the product of the splitting reaction between the PVA chains with metaperiodate, the oxidizing agent which is known to cleave specifically vicinal diols of the type found in the head-to-head sequences of the PVA chain. The length of this molecule is determined by the relative amount of splitting agent, that is, periodate, with respect to the number of PVA head-to-head sequences. In the present study, we have cleaved all these sequences, obtaining the shortest allowed telechelic chains. The number-average molecular weight can be evaluated as 2000 g/mol¹⁷ corresponding to 45 repeating units, much longer if compared with the other cross-linker used in this study, that is, glutaraldehyde, having a molecular weight of 100 g/mol. As a consequence, the geometry of the network obtained from the acetalization reaction of the telechelic PVA is therefore different from the PVA-G one. Operating at the same cross-linker/polymer repeating unit molar ratio, in the case of the self-cross-linking of telechelic PVA, the network meshes will be wider than those obtainable using glutaraldehyde as cross-linking agent.

Telechelic PVA membranes were prepared following the general procedure already described in a previous paper.¹⁷ A commercial sample of PVA (Sigma) containing 1.5% of head-to-head sequences, as determined by microcalorimetric titration,¹⁸ was dissolved in water to a concentration of 20% (w/v). A slight molar excess of sodium metaperiodate (Carlo Erba) with respect to the fraction of head-to-head sequences was added to quantitatively split these units in the PVA chains. Addition of HCl (Carlo Erba) 0.1 M started the condensation of the PVA diols with the aldehydic end groups of the telechelic PVA. Before the system reached the gel point, it was poured on a flat Teflon surface and allowed to set overnight. The obtained gel slabs were washed against MilliQ water repeatedly for a week to deplete the membranes from residual reagents.

Deuterated telechelic PVA hydrogels for neutron scattering experiments were obtained by equilibrating the swollen membranes described above in a large excess of D₂O (99.98% abundance, Isotech Inc.) in closed containers and replacing the external heavy water several times.

(b) *PVA-Glutaraldehyde Networks.* Aqueous PVA solutions at a concentration of 20% (w/v) were added with different amounts of glutaraldehyde (Sigma) to obtain a cross-linking degree of 0.02, 0.05, and 0.1 with respect to the polymer repeating units. To initiate the cross-linking reaction, a HCl concentration of 0.01 M is required. These hydrogels were labeled PVA-G 0.02, 0.05, and 0.1, respectively.

The mixture was transferred on a flat Teflon surface and was uniformly spread. After 8 h, the membranes were detached from the Teflon and were washed exhaustively against MilliQ water.

Dynamic Mechanical Thermal Analysis. Network structures are usually characterized in terms of cross-linking density, ρ , the number-average molecular weight between cross-links, M_c , and the mesh size, ξ . These parameters are interrelated and experimentally accessible by means of dynamic mechanical thermal analysis.

The viscoelastic properties of the cross-linked polymers were tested by dynamic mechanical analysis (Perkin-Elmer DMA-7) working in tensile mode. Elastic moduli, E' , of samples PVA-G 0.05 and PVA-G 0.1 were determined in tension experiments carried out at the frequency of 1 Hz, at 1% dynamic strain, over a temperature range of 298–353 K on dry membranes (4 mm in width, 5 mm in length, and 200–300 μ m in thickness). The elastic compression modulus measurements of swollen telechelic PVA hydrogels were performed on slabs (20 mm in diameter and 2–4 mm in thickness) by applying a dynamic strain of 0.2% at the frequency of 1 Hz. The equilibrium stress–strain dependence of the elastomeric networks in the region of low elongation and compression were elaborated on the basis of the Gaussian rubber elasticity theory^{28,29} assuming the deformation affine. The cross-link densities, ρ , and the average molecular weight between cross-links, M_c , of PVA-G 0.05 and 0.1 were calculated according to eqs 1.1 and 1.2, accounting for network imperfections resulting from chains ends

$$\rho = \frac{E}{3RT} \quad (1.1)$$

$$M_c = \frac{d_p}{\rho + \frac{d_p}{M_n}} \quad (1.2)$$

where E is elastic modulus, d_p is the polymer density equal to 1.269 g/cm³, and M_n is the number-average molecular weight of PVA. For telechelic network, measurements were performed in the swollen state and evaluation of ρ requires the use of eq 2.1 which takes into account the polymer volume fraction of the network before and after swelling, ϕ_0 and ϕ_2 , respectively. Because of the terminal position of the reactive groups of telechelic PVA, the determination of M_c was carried out without dangling chain ends correction according to eq 2.2:

$$\rho = \frac{E}{3RT} \phi_0^{-2/3} \phi_2^{-1/3} \quad (2.1)$$

$$M_c = \frac{3\rho RT}{E} \quad (2.2)$$

The results are reported in Table 1. The average mesh size, ξ , of different PVA hydrogels can be evaluated in the approximation that the chains of the swelled networks are in a Gaussian conformational regime. In this case, ξ is related to M_c by²⁹

$$\xi = \phi_2^{-1/3} (C_\infty M_c \langle M_r \rangle)^{1/2} l \quad (2.3)$$

where the number of repeating units $\langle M_r \rangle$ is the mass of the average repeating unit between two cross-links and C_∞ is the characteristic ratio of the PVA chain with a carbon–carbon bond length, l .

TABLE 1: Structural Parameters for PVA Based Networks from Dynamic Mechanical Measurements

network	$\rho \cdot 10^4$ (mol/cm ³)	M_c (g/mol)	ϕ_2	ξ (Å)
telechelic PVA	3.7	3000	0.12	77
PVA-G 0.05	41	350	0.25	20
PVA-G 0.1	45	280	0.25	18

As expected, the M_c value and consequently the pore size is smaller for hydrogel PVA-G 0.1 with higher cross-linking degree whereas telechelic PVA exhibits a very large pore size.

QENS Experiments. Incoherent QENS measurements were performed at ISIS pulsed neutron facility (Rutherford Appleton Laboratory, Chilton, United Kingdom) using the time-of-flight inverted-geometry spectrometer IRIS³⁰ and employing the 002 reflection of pyrolytic graphite for the near-backscattering crystal analyzer configuration. The gel slabs of a thickness of about 0.2 mm were placed in a measuring cell made of two bolted aluminum plates sealed with an Indium wire. Four temperatures were explored, that is, 291, 303, 313, and 523 K, by putting a heater in a notch between the plates of the cell. A typical measurement was carried out for 5 h under vacuum in a temperature environment equipped with a CCR unit.

A full width at half-maximum (FWHM) instrumental energy resolution of 15 μ eV was determined by using vanadium slabs in the measuring cell. Fifty channels covering an energy transfer window, $\hbar(\omega)$, from -0.4 to 0.9 meV and corresponding to momentum transfer values, q , $q = 4\pi/\lambda \sin \theta$, accessible at the elastic line and ranging from 0.44 to 1.55 Å⁻¹ were binned to have equally spaced spectra with respect to the q scale. Corrections for multiple scattering were not applied as the membrane thicknesses were always smaller than 0.3 mm.

Raw data were corrected for absorption and background using the standard software package GUIDE available from ISIS.

Theoretical Background

The double differential cross section,¹⁹ $\partial^2\sigma/\partial\Omega\partial\omega$, is the quantity governing the neutron scattering, and it relates to the probability to find in a solid angle portion $d\Omega$ a neutron with an energy exchange between $\hbar\omega$ and $\hbar(\omega + d\omega)$. The spatial and time correlation are extracted from the coherent and incoherent contributions to the nuclei cross sections, σ , as a function of the energy and of the momentum transferred, respectively.

In highly hydrated systems, such as hydrogels, the prevailing contribution to the double differential cross section comes mainly from the presence of a large amount of water protons and secondarily from the protons of the polymer network.²⁰ With an incoherent cross section about 40 times larger than the corresponding coherent part¹⁹ and because of the dominance on the cross sections of the other elements present in the gel, protons are the nuclei contributing almost exclusively to the double differential cross section. According to eq 3,¹⁹ the double differential cross section is linked to the coherent and incoherent scattering laws, S_{coh} and S_{inc} by

$$\frac{\partial^2\sigma}{\partial\Omega\partial\omega} = \frac{1}{4\pi N k_0} [\sigma_{\text{coh}} \cdot S_{\text{coh}}(q, \omega) + \sigma_{\text{inc}} \cdot S_{\text{inc}}(q, \omega)] \quad (3)$$

In eq 3, the scattering vector, \vec{q} , is the difference vector of the scattered wave vector, \vec{k} , and the incident wave vector, \vec{k}_0 .

For hydrogel systems where hydrogen abundance prevails, the double differential cross section is dominated by the observed incoherent scattering law, $S_{\text{inc}}^{\text{obs}}(q, \omega)$, which is the result of the convolution integral of the dynamic structural factor,

$S_{\text{inc}}(q, \omega)$, of the system with the resolution of the instrument determined by an independent measurement of the scattering of vanadium.

The model function used to describe the $S_{\text{inc}}(q, \omega)$ scattering law of the hydrogel, eq 4, normalized by a factor A , is composed by two contributions relative to the system components, that is, the polymer network and the water entrapped in it.²⁷

$$S_{\text{inc}}(q, \omega) = \frac{1}{A} \{ p[A_0(q)\delta(\omega) + (1 - A_0)L_p(q, \omega)] + (1 - p)[w_n L_n(q, \omega) + (1 - w_n)L_b(q, \omega)] \} + \text{bkg} \quad (4)$$

The weights of the linear combination in eq 4, p , and $(1 - p)$, are the molar fraction of protons of the polymer and of the solvent, respectively. The terms in square brackets describe the static and dynamic behavior of the polymer moiety and of water. The contribution of the network consists of an elastic term, $A_0\delta(\omega)$, and of an inelastic Lorentzian term, $(1 - A_0)L_p$, where A_0 is the incoherent static structure factor (EISF) and L_p represents the relaxation function of the polymer network. Both these terms refer to the segmental motions of the polymer chains and as in the model, a term dealing with translations of the center-of-mass is lacking because of the presence of the chemical junctions holding in place the polymer chains and allowing only for segmental motions. A representation made of a linear combination of elastic and quasi-elastic contributions refers to a dynamics occurring in a confined space, a scenario closely resembling our real hydrogel systems. The assumptions implied in this model are the separation between the translational and roto-vibrational contributions of the dynamic structure factors and the description of the diffusive and rotational motions of water molecules as isotropic processes.²⁰

The quasi-elastic contribution of water to $S_{\text{inc}}(q, \omega)$, second term in eq 4, consists of two weighted terms to account for the main features of the dynamic behavior of confined water: a slow relaxing Lorentzian component, $L_n(q, \omega)$, with weight w_n relative to the diffusive processes of water in the polymeric matrix and a fast relaxing Lorentzian component, $L_b(q, \omega)$, with weight $(1 - w_n)$ accounting for roto-vibrational motions of the molecule.²⁷ Finally an offset, bkg , is placed in the model (see eq 4) for a proper leveling of the model function in the fitting procedure.

The Lorentzian functions used in the function model for the relaxations of the polymer component and for the diffusive process of water are characterized by half width at half-maximum (HWHM), Γ_p and Γ_n , respectively. The use of Lorentzians for the description of the relaxation processes in eq 4 comes from the available models for diffusion and constrained motions (see below). The dependence of the Lorentzian width from q can be analyzed in terms of different diffusion models that we will briefly review here.

Diffusion Models. Fickian diffusivity holds also at microscopic level if Brownian motion can be assumed and if the quadratic mean free distance and the time between two collisions are very small. If these conditions are met, the diffusion coefficient of the second Fick equation can be interpreted as the ratio between the quadratic mean free distance and 6 times the time elapsing between two collisions.¹⁹

The structural dynamic scattering factor, S_{inc} , is obtained by Fourier transforming twice the Gaussian space–time correlation function obtained from the integration of the Fick equation:¹⁹

$$S_{\text{inc}}(q, \omega) = \frac{1}{\pi} \frac{Dq^2}{\omega^2 + (Dq^2)^2} \quad (5)$$

where the HWHM width of the Lorentzian relaxation function is $\Gamma(q) = Dq^2$.

The HWHM, $\Gamma(q)$, will show a linear dependence from q^2 , having a slope equal to the diffusion coefficient. At small q values, the distance probed is large and the linear dependence of $\Gamma(q)$ is generally observed and the diffusion can be considered a continuous process. For high values of q , deviations from Fickian behavior can be expected, as continuous diffusion phenomenon on short distance scale cannot be treated anymore according to Fick's laws. It is therefore necessary to consider alternative models as the "random jump" model.³¹

In this case, the diffusion is described as a sequence of jumps from one equilibrium site to another, residing in each site a time τ_0 much longer than the time needed for jumping to another site. In this model, the distribution probability of the jumps is Gaussian and the dependence of the HWHM, $\Gamma(q)$, on q is expressed by eq 6:

$$\Gamma(q) = \frac{Dq^2}{1 + D\tau_0 q^2} \quad (6)$$

This model, introduced by Singwi and Sjolander,³¹ has been used in several studies concerning the translation dynamics of H-bonded liquids, in particular for bulk water³² and for water contained in physical gels³³ where a clear deviation from the Fickian behavior has been observed at large q .

The behavior of this model at small q converges with the prediction of the classical Fickian diffusion. On the contrary, the "random jump" model shows at large q an asymptotic behavior by which the residence time, τ_0 , can be extracted. Other models³⁴ differ from the Singwi and Sjolander one in the formulation of the distribution probability function but the difference in behavior of the HWHM, $\Gamma(q)$, with q is within the errors of the experimental observations.

Results and Discussion

PVA-G Hydrogels. Incoherent quasi-elastic neutron scattering (QENS) is an established methodology for the study of the dynamics of confined water. In this study, observations were made on PVA chemical hydrogels cross-linked by glutaraldehyde, PVA-G, and used as reference system for further studies on PVA hydrogels more relevant as potential biocompatible material for applications in biomedicine. In this respect, the QENS experiments on PVA-G and on telechelic PVA hydrogels were carried out at temperatures relevant for biomedical applications, ranging from 291 to 323 K.

As the main emphasis of this work is on the dynamical behavior of water, the results obtained for PVA-G 0.02, 0.05, and 0.1 hydrogels will be presented first, followed by the analysis of the results on the telechelic PVA hydrogels both in H_2O and in D_2O . A section concerning the information obtained on the segmental dynamics of the polymer component will be in order.

In Figure 1, a representative example of the observed scattering law at a q value of 1.222 \AA^{-1} and at the lowest explored T , that is, $T = 291 \text{ K}$, for PVA-G 0.05 is reported together with the deconvoluted components according to the model equation (eq 4).

The adequacy of the model to this system is assessed by the analysis of the deviation between the observed and theoretical scattering laws (see lower part of Figure 1). According to the adopted model, the analysis of the water dynamics in the explored transferred momentum range shows the presence of a narrow Lorentzian relative to the translational relaxation motions

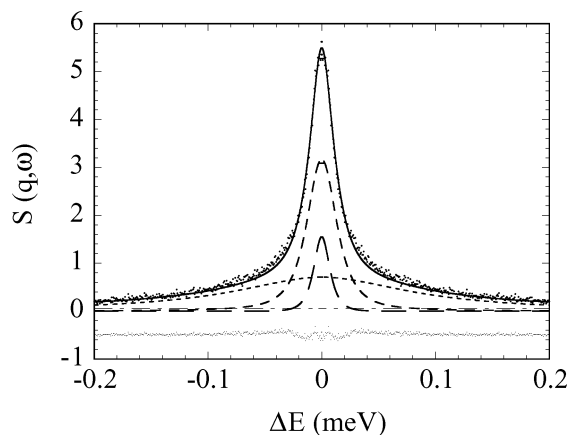


Figure 1. Example of the QENS scattering law of the hydrogel PVA-G 0.05 at $T = 291$ K and $q = 1.222 \text{ \AA}^{-1}$. Dots are the experimental scattering law, and solid line represents the total fit; the elastic contribution (---), the quasi-elastic contribution (—) for polymer, and the narrow (---) and broad (— · —) contributions of water are also shown. In the lower part of the plot it is shown the difference between the experimental values and the fit.

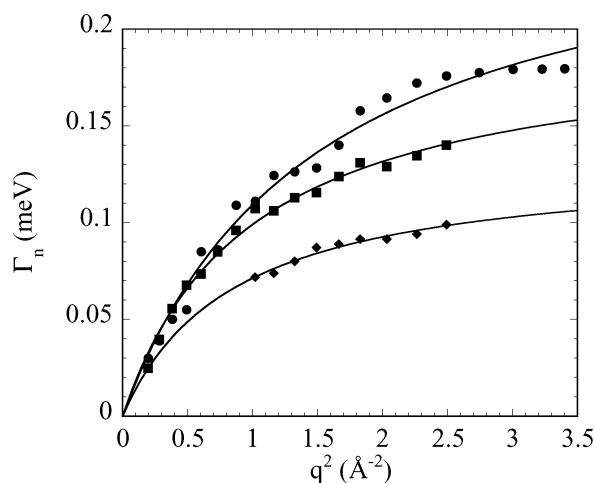


Figure 2. Broadening factor of the narrow Lorentzian relaxations, Γ_n , as a function of q^2 for PVA-G hydrogels at 303 K. (●) $R = 0.02$, (■) $R = 0.05$, (◆) $R = 0.1$. Solid lines represent the random jump fit of Γ_n according to eq 6.

of the solvent molecules and of a Lorentzian with a broadness of about 1.8 meV attributed to the roto-vibrational modes of the water molecules. The HWHM, Γ_n , relative to the diffusive motion inside the hydrogels meshes has a q^2 dependence well described by the random jump diffusion model (eq 6). The analysis of the observed scattering laws in the three PVA-G hydrogels at different cross-linking degrees showed an analogous behavior for all the PVA-G systems. The dynamic behavior of water was always characterized by the presence of a narrow and of a broad Lorentzian with different dependence from the scattering vector. In Figure 2, the trend of Γ_n as a function of the squared scattering vector at the temperature of 303 K is analyzed in terms of the random jump diffusion model for the three PVA-G hydrogels.

In Table 2, an overview of the diffusion coefficient and residence time parameters is given. Combination of these parameters according to the Einstein's relationship $\langle r^2_0 \rangle = 6D \cdot \tau_0$ allows the evaluation of the mean square length of a jump, $\langle r^2_0 \rangle$.

For an increase of the cross-linking degree (from 0.02–0.05 to 0.1), the diffusion coefficient decreases and correspondingly there is an increase in the residence time. In analogy with

TABLE 2: Diffusion Parameters^a of Water in PVA-G Hydrogels at $T = 303$ K

R	$D (\text{cm}^2/\text{s}) \cdot 10^5$	$\tau_0 (\text{ps})$	$\langle r^2_0 \rangle^{1/2} (\text{\AA})$
0.02	1.8	3.7	2.0
0.05	2.0	5.1	2.5
0.1	1.5	7.6	2.6

^a Errors of D and τ_0 within 10%.

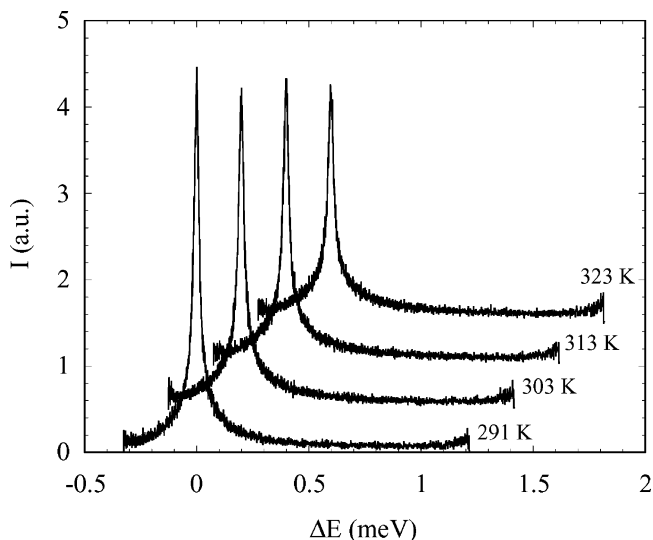


Figure 3. Peak broadening dependence of PVA-G 0.05 from the temperature at $q = 1.505 \text{ \AA}^{-1}$ for the temperatures indicated.

polysaccharidic physical hydrogels,³³ a more marked influence of R on τ_0 than on D was found. It should be stressed that physical and chemical hydrogels are inherently heterogeneous in the distribution of the cross-linking and pore size, PVA gels making no exception to this rule. The reported diffusion parameters are therefore average properties of these hydrogels. The question whether QENS approach is sensitive to heterogeneities and in what extent has been recently addressed by our group in the study of a series of hydrogels with narrowly dispersed pore size and results are under scrutiny.

The temperature-dependence study was carried out at temperatures ranging from 291 to 323 K for the PVA-G hydrogels with a cross-linking degree, R , of 0.05 and 0.1, whereas a broader range of temperatures was explored for the hydrogel with R equal to 0.02. The coarse effect on the observed scattering laws of these PVA-G for an increase of temperature is a remarkable broadening due to the increased mobility of the polymeric component and of water. As an example, in Figure 3, it is reported the behavior of the observed $S(q, \omega)$ for PVA-G with $R = 0.05$ with the temperature at a q value of 1.505 \AA^{-1} . The q^2 trend of the broadening factors, Γ_n , characterizing the diffusive behavior of water in the three PVA-G hydrogels is well reproduced by the "random jump" model³¹ for the whole range of temperatures investigated. It was therefore possible to obtain the temperature behavior of the diffusive properties of water that will be discussed in comparison with the thermal behavior of the other type of PVA based chemical hydrogel considered in this study, that is, the telechelic PVA hydrogels.

In some favorable cases, the segmental dynamics of PVA chains in the PVA-G hydrogels was evaluated from the observed scattering laws.

The connectivity of a macroscopic gel network is due to the junction points. The dynamic structure factor of the polymeric moiety, according to eq 4, is described by an elastic incoherent

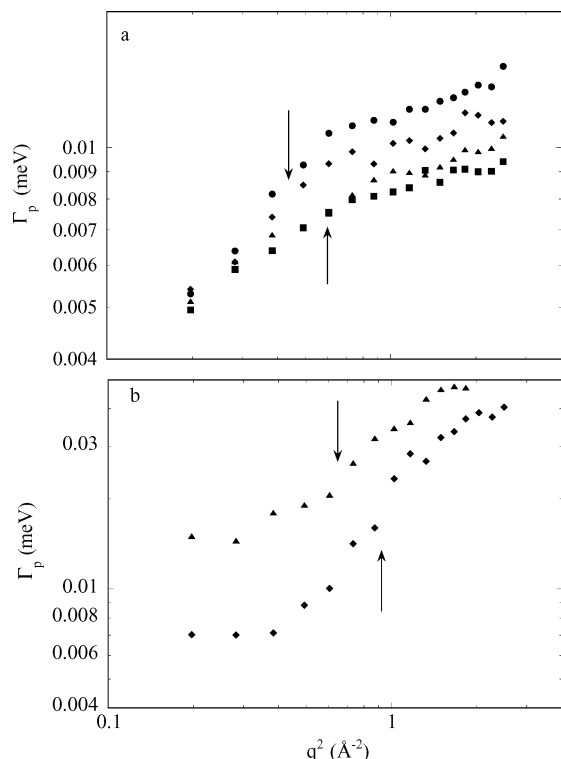


Figure 4. Broadening factor of the quasi-elastic polymer component, Γ_p , in the system PVA-G 0.05 (a) and PVA-G 0.02 (b) as a function of q^2 at different temperatures: (a) (■) $T = 291$ K, (▲) $T = 303$ K, (◆) $T = 313$ K, (●) $T = 323$ K; (b) (◆) $T = 330$ K, (▲) $T = 350$ K. Arrows indicate the $(q^*)^2$ crossover values of the scattering vector (see text).

term and by a Lorentzian, L_p . In these systems, the network mobility is limited by the junctions and only the chain segments between cross-links can contribute with their localized motions to the polymer scattering law. In this respect, the network scattering law can be treated in terms of the bound random jump diffusion model.^{31,34}

In this model, the incoherent scattering law is given by

$$S_{\text{inc}}(q, \omega) = A_0(q) \delta(\omega) + \frac{1}{\pi} \sum_{n=1}^{\infty} A_n(q) \frac{\Delta\omega_n}{\Delta\omega_n^2 + \omega^2} \quad (7)$$

where the incoherent elastic term is represented by $A_0 \delta(\omega)$ and the relaxation dynamics is an infinite series of Lorentzian relaxations with amplitudes A_n ($n \geq 1$) and widths $\Delta\omega_n$. It should be stressed that the $A_n(q)$ terms are rapidly decaying as $1/n^4$ and that only the $\Delta\omega_n$ terms with low n will effectively contribute to the observed broadening, Γ_p , as they decay exponentially according to the relationship:^{34,35}

$$\Delta\omega_n = \frac{1}{\tau} \left\{ 1 - \exp \left[-\frac{1}{2} (n\pi r_0/l)^2 \right] \right\} \quad (8)$$

The log–log plot of the overall quasi-elastic broadening as a function of q^2 shows a transition from a spatially limited continuous diffusion regime, at low q values, to an unbound “random jump” diffusion regime at high q ’s.³⁴

In practice, the analysis is usually carried out on some relevant parts of the dependence of the HWHW, Γ_p , from q^2 , as it is shown in Figure 4a and 4b. In our experiments, the HWHM, Γ_p , of the Lorentzian relaxation because of the polymer moiety showed a q^2 behavior interpretable in terms of this model and in agreement with the findings obtained in a previous work

where only PVA-G 0.02 was examined.²⁷ In Figure 4a and 4b, the experimental behavior of the polymer contribution to the HWHM line broadening, Γ_p , is reported for PVA-G 0.05 and 0.02, respectively. At high transferred momentum, the trend is analogous to the free random jump diffusion, whereas only for PVA-G 0.02 (Figure 4b) the available dynamic region allows the observation of a clear plateau at low q .

In PVA-G 0.05 (Figure 4a), the line width values are considerably smaller even for higher temperatures, as expected for a polymer network with higher cross-linking degree and with a more impeded polymer local dynamics. In this case, the corresponding plateau at low q is not fully reached because of the limitations in the available momentum and energy-transfer regions.

The crossover value of the scattering vector, q^* , between the behaviors at low and high q regions gives an estimate of the characteristic dimension of the boundary of the well.

The trend of Γ_p at small q is diagnostic of a polymer local diffusivity relative to the molecular motion of the chain segments, but it does not allow quantitative estimation of the diffusion coefficient in the well because of the spectrometer configuration suitable for the study of water dynamics. More informative is the q^* threshold value, where the polymer scattering law broadening is well above the instrumental resolution, thus giving a reliable estimation of the well dimension. According to the Ross and Hall model,³⁴ the linear dimension of the well with infinite potential walls, L , is given by

$$L = \frac{2\pi}{q^*} \quad (9)$$

In Figure 4a and 4b, it is possible to note a shift of the threshold points, q^* , toward lower value of the scattering vector as the temperature increases. A q^* value of 0.6 \AA^{-1} is evaluated for the PVA-G 0.05, at 313 and 323 K which corresponds to a confinement dimension, L , of 10.3 \AA . At the lowest two temperatures, the dimension of the confinement is about 8 \AA , a length that seems to be characteristic of the segmental motion for several different systems, such as proteins³⁶ and synthetic polymers.³⁷ As it is shown in Figure 4a, for the high q region where shorter distances are probed and line widths follow the jump diffusion behavior, the leveling off of the asymptotic values of Γ_p for the PVA-G 0.05 hydrogels ranges from 9 to $13 \mu\text{eV}$ for increasing temperatures from 291 to 323 K. These values correspond to residence times, τ , of several hundreds of ps. In the network PVA-G 0.02, the asymptotic value of the Γ_p versus q^2 curves at 330 and 350 K, see Figure 4b, the residence times range around 90 ps. Although the evaluation of these parameters is semiquantitative because of the unfavorable instrumental configuration and because of the large hydration degree of the systems, it allows an insight in the segmental dynamics of the polymer mediated by the interaction with the solvent. QENS studies on bulk polymer melts^{38–40} report values of residence times comparable with the ones found in this work and attributed to local motions involving more than few bonds in the chains.³⁸

To substantiate this picture we analyzed, an example is given in Figure 5, the elastic incoherent structure factors, EISF, for PVA-G ($R = 0.05$). The fit was carried out according to the confined diffusion model already mentioned:^{31,37}

$$F_{\text{EISF}}(q) = n \cdot [a_0(q) - 1] + 1 \quad (10)$$

where n is the proton fraction involved in the polymer local

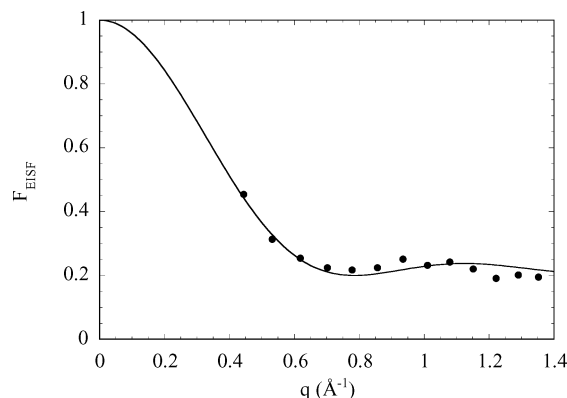


Figure 5. q^2 dependence of the function F_{EISF} for PVA-G 0.05 at $T = 291$ K. The solid line represents the fit according to eqs 10 and 11.

motion and a_0 represents the zero-order spherical Bessel function:

$$a_0(q) = j_0^2\left(\frac{qL}{2}\right) \quad (11)$$

An asymptotic value of F_{EISF} equal to 0.2 was found in the investigated temperatures with all the PVA-G hydrogels in the cases when it was possible to determine the relaxation of the polymer moiety, that is, for R equal to 0.02 and 0.05, indicating that about 80% of the protons participate to the segmental motions.

It is not possible to extract detailed information on the dynamics of the polymer chains, as it is usually done in incoherent quasi-elastic neutron scattering studies on bulk polymers, since in these hydrogels only 15% of the total proton number belongs to the polymer. Despite this unfavorable situation, the results of the fit indicate a characteristic confined displacement, L , of about 10 Å, in agreement with the findings coming from the analysis of the quasi-elastic scattering function of the polymer component.

Telechelic PVA Hydrogels. The structural features of this type of hydrogels have deep influence on the neutron scattering behavior. In the telechelic PVA hydrogels, the distinction between cross-linking agent and polymer chain is not applicable anymore. The internal architecture of these systems is built exclusively by macromolecular species capable to accommodate a large number of water molecules.

A result of this structural difference if compared to the PVA-G hydrogels is a marked broadening of the observed scattering laws, as it is shown in Figure 6a. In this case, the study of the dynamics of the polymer moiety is unfeasible. We decided therefore to extend the analysis to samples of telechelic PVA hydrogels where water was completely replaced by heavy water, see Figure 6b. In this system, the model equation has been modified as the substitution of water and of the polymer exchangeable protons with D_2O and deuterium atoms, respectively, causes a large decrease of the intensity of the scattering peak because of the reduced cross-section of deuterium compared to protons. Moreover, only the nonexchangeable polymer protons contribute to the overall scattering.

Taking into account these considerations, the scattering law representing this model is

$$S_{\text{inc}}(q, \omega) = \frac{1}{A} \{ p[A_0(q) \cdot \delta(\omega) + (1 - A_0(q)) \cdot L_p] + (1 - p)L_D \} + \text{bkg} \quad (12)$$

where A is the normalization factor, p is the molar fraction of

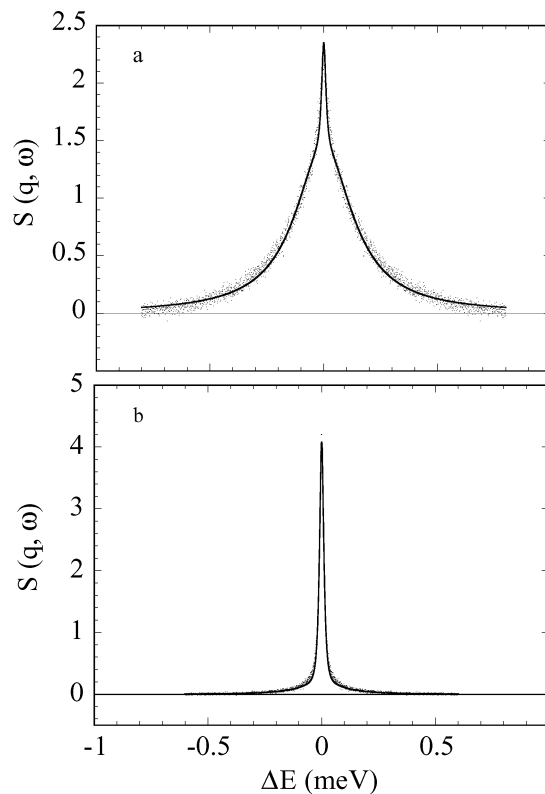


Figure 6. Comparison between the structure dynamic scattering factor, $S(q, \omega)$, of telechelic PVA hydrogels in water (a) and in D_2O (b), $q = 1.222 \text{ Å}^{-1}$ and $T = 303$ K. Dots and solid line represent the experimental scattering law and the total fit according to eq 12.

the hydrogen of the polymeric matrix, and $(1 - p)$ is the molar fraction of the deuterium contained in the solvent. In analogy with the first model, the local dynamics of the polymer chains is described by an elastic term $\delta(\omega)$ weighted by the incoherent elastic structure factor, A_0 , and by a quasi-elastic term, L_p , characterized by a HWHM, Γ_p , weighted by the factor $(1 - A_0)$ complementing the elastic factor, while the L_D contribution accounts for the quasi-elastic behavior of heavy water. In the background term, bkg, are cumulated all the contributions from which is impossible to extract any structural and dynamic information. The quite limited contribution of the polymer elastic part and of D_2O quasi-elastic part does not allow to get any structural dynamic information. On the other hand, the informative part of the equation model is the HWHM of the deuterated polymer relaxation function L_p . In analogy with the findings obtained for the polymer moiety of the PVA-G hydrogels, the features of Γ_p as a function of q^2 indicate a constrained diffusion regime interpretable according to the model of Ross and Hall.³⁴ A q^* threshold of about 0.8 Å^{-1} is found corresponding to a characteristic well dimension of 9 Å, as it is shown in Figure 7. Inspection of the asymptotic values of Γ_p in the high q^2 region and their temperature dependence gives indication of a characteristic time or residence time, τ , of an average chain segment in a local conformation. The corresponding values of τ are characteristic of localized chain relaxation modes involving several repeating units in analogy with the results reported on polymer melts³⁸ and indicating that also some short-range translational motion is performed by the chain segments. An activation energy of about 4 kcal/mol, determined by the Arrhenius analysis showed in the insert of Figure 7, is required to perform a jump between two segmental configurations.

The relatively large average dimension of the potential well and of the activation energy characterizing this type of motion

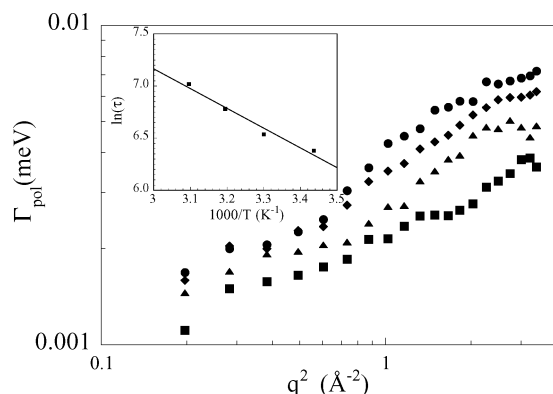


Figure 7. Broadening factor of the quasi-elastic polymer component, Γ_p , in the telechelic PVA hydrogel in D_2O as a function of q^2 at different temperatures: (■) $T = 291$ K, (▲) $T = 303$ K, (◆) $T = 313$ K, (●) $T = 323$ K. Insert: Corresponding Arrhenius plot.

TABLE 3: Diffusion Parameters^a of Water in Telechelic PVA Hydrogels as a Function of Temperature

T (K)	D (cm ² /s)·10 ⁵	τ_0 (ps)	$\langle r^2_0 \rangle^{1/2}$ (Å)
291	1.2	3.3	1.5
303	1.7	3.0	1.7
313	2.2	2.8	1.9
323	2.5	2.4	2.0

^a Errors of D and τ_0 within 10%.

are indicative of a coupling with heavy water dynamics. This picture can be taken only as an indication of a strong involvement of the solvent molecules with the polymer units. Only an ad hoc study on the internal motion of the polymer moiety in hydrogels, implemented with molecular dynamics simulations, can supply complete information on the short-range polymer dynamics.

The study of the telechelic PVA hydrogel in water was carried out according to the equation model eq 4, using the elastic and quasi-elastic Lorentzian relaxation components for the description of the polymeric part obtained in the QENS study of the same hydrogel in D_2O . In this situation, the structural and dynamic parameters characterizing the diffusive behavior of caged water were determined as the only unknown part of the scattering law for this system. The behavior of the HWHM, Γ_n , the broadening factor of the slow relaxing diffusive mechanism for water has again the features proper of an unbound random jump as found for the same component of the PVA-G hydrogels. One of the features to consider in this case is the dramatic decrease in the relative weight of the telechelic polymer contribution (see eq 3), p , to the overall $S(q, \omega)$ if compared with the value obtained in the case of PVA-G hydrogels. This is diagnostic of a larger mesh size of the telechelic PVA network with an enhanced swelling process.

In Table 3, the diffusion coefficient, the mean residence time, and the average free length between two jumps describing the diffusive properties of water are reported.

From an inspection of such values, it can be noted that water is less impeded in the diffusion process, in particular for τ_0 . This is attributable to a larger mesh size of the pores of the telechelic PVA hydrogel.

Arrhenius Behavior of the Diffusion Parameters of Water Caged in Different Hydrogels. Finally, here we present a comparative evaluation of the parameters characterizing the diffusion behavior of water in the hydrogels studied in this work. In particular, a comparative outlook of these parameters can be used in deciding whether the structural differences characterizing the two types of gels can cause a change in the activation of

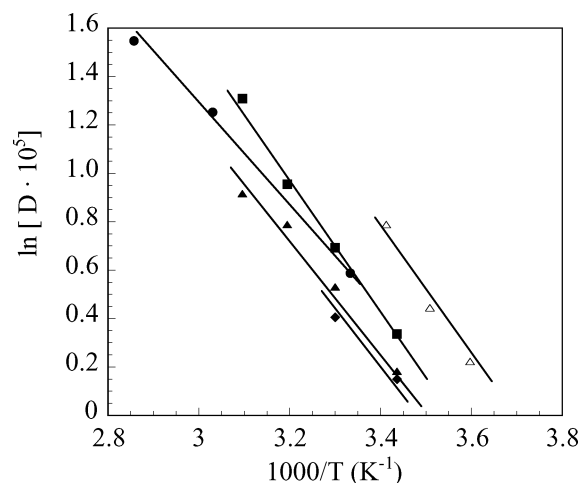


Figure 8. Arrhenius plot of the diffusion coefficient of water in the studied hydrogels: (●) PVA-G 0.02, (■) PVA-G 0.05, (◆) PVA-G 0.1, (▲) telechelic PVA, (△) bulk water.³²

diffusive motion of water. In Figure 8, we report the temperature dependence of the water diffusion coefficient of the investigated hydrogels as Arrhenius plot.

Comparison with the diffusion coefficient of bulk water³² in a comparable temperature range, as it is shown in Figure 8, reveals that in the studied systems water is supercooled. The slowing down of water dynamics demonstrates that water inside the hydrogels is confined even if the mesh size is order of magnitudes larger than the average distances characterizing the elementary diffusion step, that is, a jump. The trends are almost parallel for all the gels indicating similar activation energy in the diffusion process and its value is 4.0 ± 0.6 kcal/mol for all the investigated gels (the differences are within the experimental errors). These findings show that water diffusion remains an H-bonding governed mechanism although its diffusivity is profoundly influenced by a reduced mobility when it is caged in the polymeric matrix.

Concluding Remarks

The understanding of the role of water in biological environments and in soft matter devices for biomedical applications requires the knowledge of the dynamic behavior of water in confining media. In this paper, we have presented the results of a comparative study on the state of water in PVA based hydrogels. The aim of this project is to rationalize how the structural features of the polymer network influence the diffusive properties of the solvent as this issue is of paramount importance for polymer matrixes design in controlled drug delivery. This QENS study reveals a strong coupling of water with the hydrophilic network in all the investigated hydrogels at the maximum swelling degree. According to our model, the relaxation responsible for the line broadening was mainly attributed to translational motions of the water molecules. The diffusion coefficient dependence on the mesh size of the network was evidenced in this study, indicating the possibility of tuning the diffusivity of solvent by changing the degree of cross-linking of the matrix. The comparison of the diffusion coefficients and the residence time between two elementary diffusion steps shows that the main effect of the polymer–water interaction is a remarkable lowering of both dynamic parameters. This effect opens the possibility to effectively regulate the diffusion of water by using these biocompatible matrixes as release devices. Moreover, water confinement by polymer networks can be envisaged as a way to study dynamic properties of liquid water

in range of temperatures where bulk water usually crystallizes. Activation energy barriers for the diffusion process evaluated in the temperature study of the QENS spectra show a common value for all the systems studied in this work. A value of about 4 kcal/mol was measured in agreement with previous reported measurements²⁷ and with other hydroxylated systems,^{20,33} clearly indicating a hydrogen-bonding regime regulating the interaction of water with the matrix. Another relevant factor governing the mobility of water within the hydrogel is the polymer chain mobility, that is, the stiffer the polymer matrix the stronger the confinement of water to narrow diffusion pathways whereas even in uncharged polymer networks the dynamics of solvent appears to be strongly influenced. Open questions, such as sensitivity of QENS approach to heterogeneities in the distribution of gel cross-links, have been recently addressed by our group in a QENS study of hydrophilic gels with well-characterized pore size distribution.

The dynamics of the polymeric moieties present in the different examined hydrogels was described in terms of a constrained random jump model. The polymer dynamic structure factor showed that segmental chain motions are present and span distances of about 10 Å, probably resembling the swinging of a cord between two junction zones and involving water molecules in the hydration shell. At this stage, general conclusions cannot be drawn because of the relative paucity in the literature of QENS study of the dynamics of solvent in gels covering a wide range of physical and chemical characteristics.

This scenario will be the basis of a computer simulation of the solvent and of the polymer moiety dynamics at the same time scale. The comparison of these approaches should give a better understanding of the main features of the gel phase.

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