Journal of Molecular Structure 972 (2010) 81–86

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

On the behaviour of water hydrogen bonds at biomolecular sites: Dependences on temperature and on network dimensionality

Daniela Russo [a,*], John R.D. Copley [b], Jacques Ollivier [c], José Teixeira [d]

[a] CNR-INFM & CRS/Soft, c/o Institut Laue Langevin, 6 rue J. Horowitz BP156, F-38042 Grenoble, France
[b] National Institute of Standards and Technology, Gaithersburg, MD 20899-6102, USA
[c] Institut Laue Langevin, 6 rue J. Horowitz BP156, F-38042 Grenoble, France
[d] Laboratoire Léon Brillouin (CEA/CNRS), Saclay CEA, 91191 Gif-sur Yvette Cedex, France

ARTICLE INFO

Article history:
Received 5 November 2009
Received in revised form 3 December 2009
Accepted 5 December 2009
Available online 8 January 2010

Keywords:
Hydration water dynamics
Hydrophobic interaction
Hydrophilic interaction
Protein dynamics
Neutron scattering
Hydrogen bond network

ABSTRACT

Neutron scattering experiments have been used to investigate the effects of temperature and network dimensionality (from hydrated powders to highly concentrated solutions) on the hydrogen bond dynamics of hydration water molecules at specific sites in selected biomolecules. With this aim in view, the evolution of hydration water dynamics of a prototypical hydrophobic amino acid with polar backbone, *N*-acetyl-leucine-methylamide (NALMA), and a hydrophilic amino acid, *N*-acetyl-glycine-methylamide (NAGMA), has been investigated as a function of temperature.

We show that the temperature dependence of the diffusive dynamics of water molecules is the same for both hydrophilic and hydrophobic peptides. A comparison between hydrated powders and high concentrated solutions reveals a similar behaviour, particularly for the hydrophobic peptide. On the other hand we find a distinct difference in the behaviour with temperature of the hydrogen bond lifetime in solutions and hydrated powders. Whereas at room temperature the hydrogen bond lifetime is longer in solution than in the hydrated powder, the reverse situation obtains at low temperatures. This result suggests a change in the *plasticity* of the hydrogen bond network depending on its extension. Differences in the densities of states lend support to this concept.

1. Introduction

Most of the literature on hydration of biomolecules focus on the structure and dynamics of the first layer of hydrated powders [1–4], "first layer" means the collection of water molecules required in order to cover the exposed surface of the biomolecule. In such cases, the role of hydrophilic sites is generally dominant so that most of the water molecules of the first layer form relatively stable bonds with the substrate, limiting their translational diffusion and influencing the structure and dynamics of the biomolecules. More detailed studies [5–8] can better discriminate between the behaviour of individual water molecules at the vicinity of specific hydrophilic sites or hydrophobic regions of the surface of biomolecules, as well as between, translational diffusion, molecular rotations and hydrogen bond lifetime effects. In a sense such studies may be interpreted within the context of other general studies of water under confinement.

To a large extent it has been demonstrated that the dynamics of biomolecules depends on the hydration level of the molecule. Both the details of the water binding sites and the extension of the hydration water network influence the intrinsic motions as has been observed by Zanotti and coworkers [9] for myoglobin and lysozyme proteins, by Zaccai and coworkers for human hemoglobin and macromolecules in *Escherichia coli* [10,11] and by Russo and coworkers [12,13] on small bio model peptides. Despite the fact that the dynamic time scale of water molecules at the biomolecular interface remains comparable to the dynamics of supercooled water [3,7,8,14,15], both in hydrated powders and in highly concentrated solutions, distinct patterns of biomolecular dynamical behaviour can be observed. This is probably due to the fact that in solution the hydration water molecules interact not only with the biomolecular interface but with other water molecules within an extended hydrogen bond network. Thus the interaction among water molecules takes place in an extended three-dimensional space. In contrast, the hydration water of hydrated powders interacts almost exclusively with the biomolecular interface, given the small number of neighbouring water molecules (probably none at low hydration levels), so the interaction range is limited to a surface and the first hydration layer is probably less structured than in solutions. Since the ultimate goal of hydration studies in biology is an understanding of relatively concentrated aqueous solutions, as close as possible to the situation of living cells, it seems necessary to establish a connection between studies

* Corresponding author.
E-mail address: russo@ill.fr (D. Russo).

0022-2860/$ - see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.molstruc.2009.12.020

of hydrated powders and studies of aqueous solutions. Within this general picture, it is important to finally shed light on the question whether fully hydrated biomolecular powders properly represent the dynamics intrinsic to proteins in their natural environment, necessary for biological function. To this goal, Russo and coworkers [12,13] and Zaccai and coworkers [10,11], using different approaches, gave a contribution to elucidate this new aspect of the complex world of protein–water dynamics.

In this work, we report an investigation of the change of the hydrogen bond dynamics of hydration water molecules at biomolecular sites, due to temperature and hydrogen bond network extension. We analyse quasielastic neutron scattering (QENS) experiments to study, from highly hydrated powder to highly concentrated solution, the evolution of hydration water dynamics in the same simplified protein model interface. We examine the temperature dependence of picosecond dynamics of two fully hydrated powders, of (a) *N*-acetyl-leucine-methylamide (NALMA), which comprises a *hydrophobic* amino acid side chain, $(CH_3)_2$–CH–CH_2, attached to the C_α atom of a polar blocked polypeptide backbone with CH_3 end-caps, (CH_3–CO–NH–C_αH–CO–NH–CH_3) and (b) *N*-acetyl-glycine-methylamide (NAGMA) which comprises the polar blocked backbone and a hydrogen atom attached to the C_α atom.

The investigation performed with the fully deuterated peptide enabled a *unique* study of hydration water dynamics in the vicinity of biomolecules. A complementary investigation on the completely hydrogenated peptides, from powder to solution, which allowed probing the dynamics of the molecule itself, has been already been published [13].

With this work we provide experimental confirmation of changes in the *plasticity* of the hydrogen bond network, depending on its extension and on the hydrophilicity/hydrophobicity of the interface.

2. Materials and methods

2.1. Sample preparation

Perdeuterated *N*-acetyl(d_3)-leucine(d_{10})-methylamide(d_3) (d-NALMA) and perdeuterated *N*-acetyl(d_3)-glycine(d_2)-methylamide(d_3) (d-NAGMA) were purchased from CDN Isotopes, Canada. After total de-hydration achieved placing the sample under vacuum in presence of silica salts for at least two days, water (H_2O) was added in well controlled amounts [7]. The total amount of added hydration water was determined from the change in mass of the samples. These two peptides were chosen because their chemical compositions are similar but NALMA is more hydrophobic than NAGMA because of the hydrophobic chain in the leucine amino acid.

The neutron measurements on powders were performed at 60% hydration level for the d-NALMA peptide (7 molecules of water per molecule of peptide) and 50% for the d-NAGMA sample (4 molecules of water per molecule of peptide) what corresponds to full hydration in both cases. The dry peptides were also measured. Roughly 100 mg of deuterated peptide were used for each of the measurements.

2.2. Experimental procedure

Quasielastic and inelastic incoherent neutron scattering experiments were performed at the NIST Center for Neutron Research, using the Disk Chopper time-of-flight Spectrometer (DCS) [16] with an incident neutron wavelength of 7.5 Å, which corresponds to an elastic wave vector transfer (Q) range from 0.15 to 1.57 $Å^{-1}$ and an energy resolution of 35 μeV (correlation time ≈ 20 ps) at full width half maximum (FWHM). We collected quasielastic neutron scattering (QENS) spectra at 200, 270 and 300 K for the d-NALMA and d-NAGMA peptides in both hydrated and dry conformations. Samples were loaded into slab containers 0.1 mm tick. Typical data collection times were of the order of 8 h per sample. All spectra were corrected for scattering by the sample container, and detector efficiencies and the elastic energy resolution were determined using a standard vanadium target. The data were reduced and analyzed using the NCNR's DAVE software package [17].

For comparison purposes we shall also present previously reported results, obtained with the same instrumental resolution, for the dynamics of hydration water molecules attached to the same peptides at low hydration [8] and for highly concentrated solutions (3 M NAGMA at room temperature and 2 M NALMA as a function of temperature) [18–20].

2.3. Experimental analysis

The principal contribution to the scattering from the water–peptide samples studied in the present work derives from the incoherent scattering by the protons in the hydration water molecules. The incoherent scattering from the peptide molecules is considered negligible as compared with the scattering from the surrounding water molecules.

Quasielastic intensities measured at different angles using the DCS were summed to improve counting statistics, and qualitative analyses of the temperature and water content dependence were performed. Fig. 1 shows a typical example of data obtained with 50% hydrated d-NAGMA at three temperatures. The fits assume either one or three components, i.e. an elastic line or an elastic line plus two Lorentzians. The elastic line represents all motions that are too slow to be observed given the instrumental resolution, together with elastic coherent scattering contributions. The two Lorentzians represent contributions from rotational and translational diffusion, characterized by distinct relaxation times and different dependences on Q [21]. This model is not totally exhaustive, indeed other models have been proposed to describe the reorientational dynamics of water molecules [22,23], but it allows a simple qualitative description of the dynamics of the hydration water molecules.

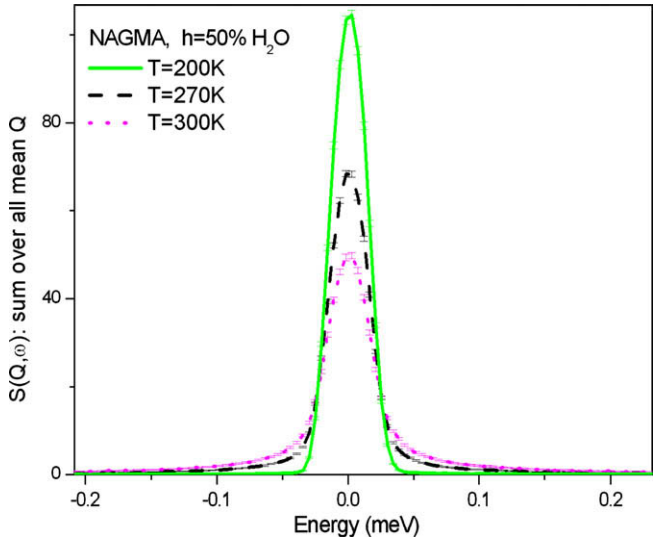

Fig. 1. Incoherent scattering function, summed over all mean Q, for 50% hydrated d-NAGMA as a function of temperature: 200 K (straight line), 270 K (dotted line), and 300 K (dashed line). The 200 K data represent the instrumental resolution function. In this figure and in later figures the error bars represent standard uncertainties (plus or minus 1 standard deviation).

We write:

$$I(\omega) = [A + B\delta(\omega) + CL_1(\omega) + DL_2(\omega)] \otimes R(\omega) \quad (1)$$

where A, B, C and D are constants, ω is the exchanged frequency, $\delta(\omega)$ is the Dirac delta function and $L_i(\omega)$ are normalized Lorentzian functions centered at $\omega = 0$. The symbol $\otimes$ means convolution, $R(\omega)$ is the experimental resolution.

Despite the relatively small amount of water in the samples, of the order of a few percent by weight, Fig. 1 clearly shows peak broadening that increases with increasing temperature. While the 200 K dataset can be considered representative of the resolution function (the fit to the data only requires a delta function), the 270 and 300 K datasets show clear quasielastic scattering fingerprints.

The density of states (DOS) has been calculated using the expression [24]:

$$\mathrm{DOS} \cong \frac{d^2\sigma}{d\Omega dE_f}\frac{k_i}{k_f}\frac{\omega}{Q^2}\left\{1 - \exp\left(-\frac{\hbar\omega}{k_B T}\right)\right\} \quad (2)$$

where T is the temperature, k_i and k_f are the initial and final wave vectors, $\frac{d^2\sigma}{d\Omega dE_f}$ is the double differential neutron scattering cross-section per unit solid angle and final energy E_f. The calculation ignores corrections such as for multiphonon and multiple scattering.

3. Results and discussion

The first purpose of this communication is the analysis of the hydrogen bond network dynamics in highly hydrated powders of fully deuterated peptides as a function of temperature. In both cases the level of hydration was the highest possible without going into the liquid state. It is worth noting that hydration levels should not be compared directly according to their magnitude because the global behaviour for the same level of hydration varies greatly, depending on the degree of hydrophilicity/hydrophobicity of the peptide.

Our second purpose is to investigate the influence of the hydrogen bond network's extent on the hydration water dynamics by comparing, as a function of temperature, the highly hydrated powder with the highly concentrated solution, where solute molecules have only enough water to share one water hydration layer [18–20]. We shall compare a network that comprises a small number of water molecules (4–7 molecules), which interact almost exclusively with the bio-interface, with a more extended network (of order 25 water molecules per solute molecule, corresponding to a hydration layer of ~4 Å thickness), where the interactions among water molecules take place in an extended space, rather than at an interface. We have previously observed [8,19] that at room temperature, in both cases, the dynamic time scale of the water molecules remains comparable to that of water molecules in the supercooled state.

Fig. 2 compares the scattering function, $S(Q, \omega)$, at room temperature, for the highly concentrated solution and the hydrated powder for d-NAGMA (panel A) and d-NALMA (panel B). In order to compare quasielastic widths for the two sets of experiments each spectrum has been normalized to the same peak intensity (so that the comparison is independent of the amount of sample). We immediately observe that in both peptides the FWHM for the solution is larger than that of the hydrated powder, in particular for the completely hydrophilic peptide (NAGMA). A more detailed comparison of the data for the different systems has been achieved by fitting the spectra using Eq. (1) and examining the behaviours of fitting parameters such as the amplitudes and widths of the Lorentzian functions.

Again we stress the concept that the degree of hydrophilicity/hydrophobicity of the peptide quantitatively modifies the dynamics of the hydration water molecules. In Fig. 3 we show the quasielastic intensity fraction $(C + D)/(B + C + D)$ of hydration water for all the samples, both dry and fully hydrated, as a function of temperature. To relate this temperature dependence to the previously observed behaviour as a function of hydration level [8], we also plot the room temperature intensity fraction for the two low hydration biomolecules. As was already observed as a function of hydration, the quasielastic intensity fraction for the fully hydrated hydrophobic d-NALMA peptide is systematically higher than for the hydrophilic d-NAGMA for temperatures above 200 K (at which temperature the dry and hydrated peptides do not show any QENS signal). This result again confirms that the more hydrophobic the peptide, the easier the onset of diffusion. We also remark that not only the intensity is different between the two distinct environments but also their dependence on temperature seems to be different: linear for d-NALMA but faster for d-NAGMA. This distinct difference in behaviour appears to depend on the different struc-

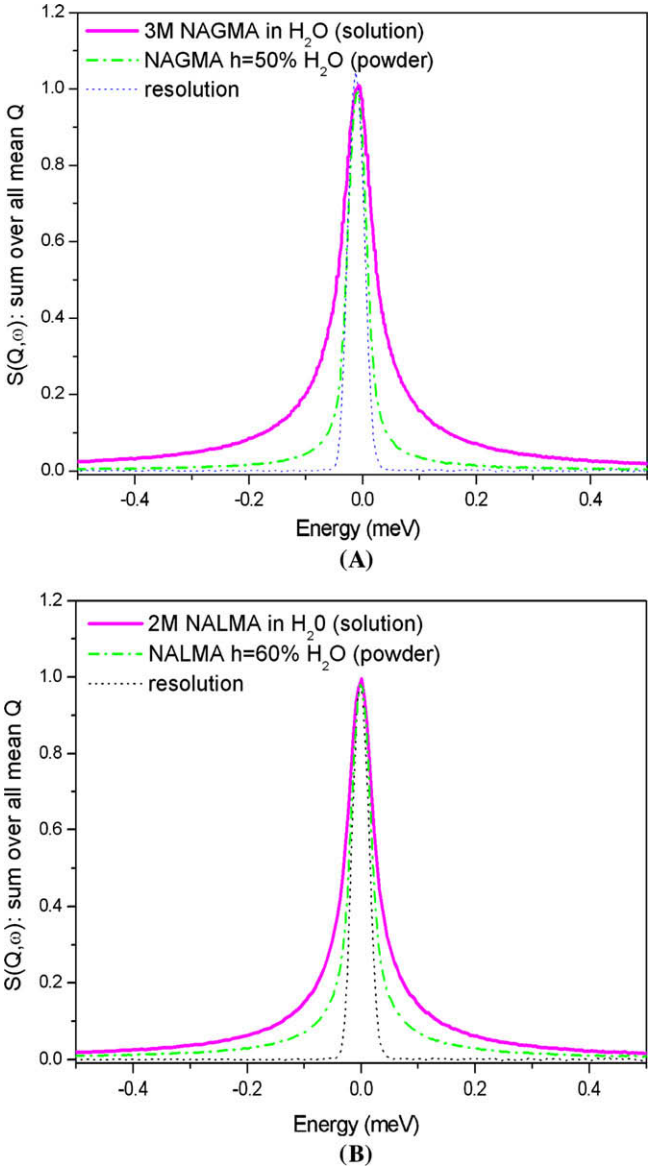

Fig. 2. A comparison of the room temperature incoherent scattering function, summed over Q, in highly hydrated powders (dash-dotted lines) and highly concentrated solutions (full lines), for d-NAGMA (panel A) and d-NALMA (panel B). The dotted lines represent the resolution function. Each spectrum is normalized to unit peak intensity. The resolution function is represented by a dotted line.

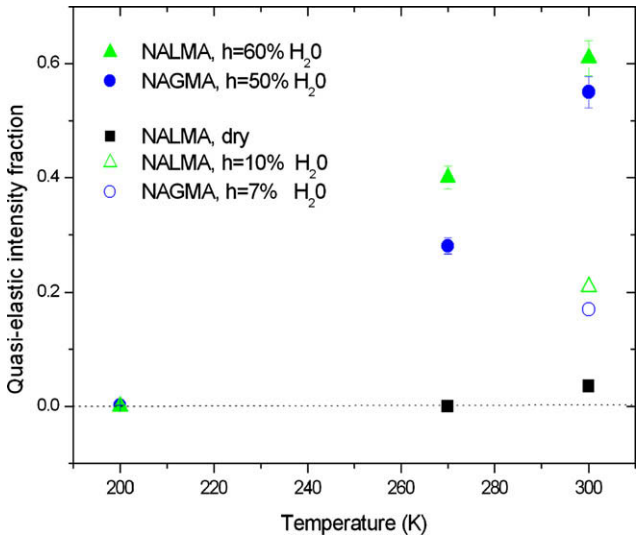

Fig. 3. Quasielastic intensity fractions for dry and hydrated d-NALMA (squares and triangles), and for hydrated d-NAGMA (circles) as functions of temperature. Filled circles and triangles correspond to high hydration levels whereas empty symbols correspond to low hydration levels. (The reported values are taken from Ref. [8]) The dotted line is a guide to the eye.

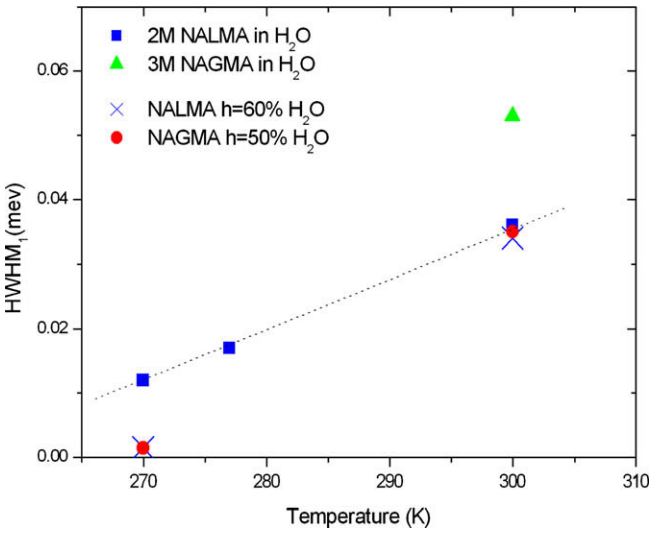

Fig. 4. Averaged half widths at half maximum for the Lorentzian functions $HWHM_1$, plotted versus temperature, for d-NALMA and d-NAGMA hydrated powder peptides (crosses and circles) and highly concentrated solutions (squares and triangles). The dotted line is a guide to the eye.

tural organization of the water molecules and of the hydrogen bonding networks around the two peptides. It is also possible that, at 270 K, the dynamics of water molecules forming hydrogen bonds with hydrophilic sites are restricted to more local motions in contrast with the situation in a hydrophobic environment.

As reported in the experimental analysis section we decided to perform a type of analysis where the scattering at different angles was summed to improve statistics. Another reason that justifies our choice of analysis method is the difficulty associated with a detailed study of the Q dependence, due to the small quasielastic fraction at low temperatures (Fig. 3). The significance of the different linewidths and their interpretation are supported by a comparison with previous published work on hydration water, where detailed analyses as a function of Q were performed [7,18–20,25]. In every case two distinct linewidths have been extracted from the data: the narrower component corresponds to the slow diffusion of water molecules on the surface of the peptide whereas the broader component is attributed to large amplitude motions of the hydrogen atoms associated with the dynamics of the bonds.

Fig. 4 depicts the half widths at half maximum (HWHMs) of the narrower Lorentzian components, designated $HWHM_1$, for highly hydrated powders and highly concentrated solutions, as functions of temperature. As proposed in our previous work [8], the narrower component can be identified with slow translational diffusive motions of water molecules on the surface of the peptide. We remember that the 200 K measurements for both hydrated powders revealed that the elastic component was sufficient to fit the data, suggesting a lack of discernible motion within the experimental time window.

An interesting result is that at each of the two measurement temperatures, 270 and 300 K, the HWHM is identical for the hydrophilic and hydrophobic hydrated powders.

The observed equivalent intensities, for the two distinct hydrated peptides, could suggest that the time scale of the diffusive motion of those highly confined hydration molecules of water depends not only on the type of the interface but also on the curvature of the hydrogen bonding network that is starting to build up around the peptides.

Comparing the results obtained for powders with the averaged linewidths obtained for hydration water molecules in solution (2 M NALMA and 3 M NAGMA) we find a difference in the temperature dependence. At room temperature a difference in behaviour in solution was previously observed for the hydrophilic and hydrophobic peptides [18–20].

In solutions, in particular for the 2 M d-NALMA in H_2O, the network is more extended, but not relaxed (as in the case of dilute solutions or bulk water), because of the strong influence of the hydrophobic side chain. Consequently, the effect of temperature on the dynamics of the hydration shell is larger than in powders. Actually, for powders there is no extended three-dimensional network and the water molecules are strongly attached to the binding sites of the interface. In this context it is worth pointing out that the hydration water does not crystallize at 270 K, neither in powders nor in solutions. Consequently, the observed differences in the linewidths are meaningful. On the other hand, it is also meaningful that at room temperature the average HWHM of the 2 M d-NALMA coincides with that of the two hydrated peptides whereas for the highly concentrated hydrophilic solution the dynamics is “faster”. We explain the difference between the two highly concentrated solutions through the spatial heterogeneity of the water dynamics [18,19]. This spatial heterogeneity in the water dynamics is in turn due to the heterogeneity of the NALMA chemical composition, namely the presence of a hydrophobic side chain on a hydrophilic backbone. As we reported in Ref. [20] for simulations of NALMA hydration dynamics under ambient conditions, and as has been observed in other simulation studies of model peptides [26], the average residence times for labeled water near the hydrophobic side chain are shorter and the corresponding orientational correlation times are shorter as compared with that of water molecules near the hydrophilic backbone. The results of the experimental study in solution suggest that there is spatial heterogeneity in the water dynamics in highly hydrated powders where water is highly confined, but in this case the heterogeneity is present at the atomic level. The loss of distinct heterogeneity results in a hydration dynamics signature that looks more like normal diffusion.

In Fig. 5 we report HWHMs for the broader Lorentzian component (panel A) and the corresponding relaxation time associated with the hydrogen bond lifetime (panel B) for both hydrated powder and high concentrated solutions [20].

The HWHM of the Lorentzian function of the hydrophilic and hydrophobic hydrated powders at 270 K has an average value of 0.05 meV which, in our hypothesis, corresponds to a very slow

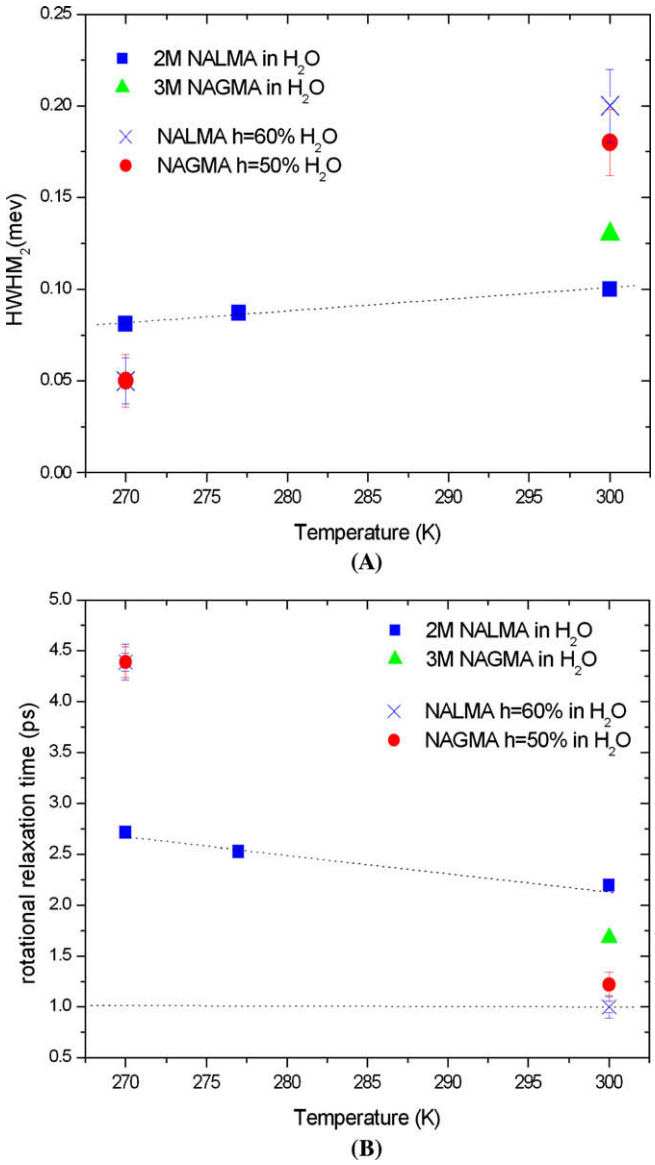

Fig. 5. (A) Averaged half widths at half maximum for the Lorentzian functions $HWHM_2$, plotted versus temperature, for d-NALMA and d-NAGMA hydrated powder peptides (crosses and circles) and highly concentrated solutions (squares and triangles). The dotted lines are guides to the eye. (B) Rotational relaxation time inferred from the HWHMs of the Lorentzian functions, Γ_2, plotted versus temperature, for d-NALMA and d-NAGMA hydrated powder peptides (crosses and circles) and highly concentrated solutions (squares and triangles). The dotted lines are guides to the eye.

relaxation time of the hydrogen bond (~4 ps). The same value was found, at room temperature, for the intrinsic water of the dry d-NALMA sample. As previously discussed [8], the 300 K HWHM of the hydrated d-NAGMA hydration water seems to be slightly smaller than that of d-NALMA suggesting a more stable hydrogen bonding network around the hydrophilic peptide. The large hydrophobic side chain that distinguishes the two peptides slightly perturbs the water environment inducing the bonds to break more frequently. The opposite behaviour is observed for the more extended network of the highly concentrated solution, where the rotational timescale for 3 M d-NAGMA is faster than for 2 M d-NALMA, or in other words closer to bulk water behaviour. We consider these experimental results as evidence of the fact that the hydrogen bond extension is a critical parameter in the properties of hydration water.

For the narrow linewidths, and also in this case, on comparing hydrated powders to highly concentrated solutions, we find a different behaviour with temperature. In terms of the activation energy required to break a bond [21] it seems that a higher energy is required for the powder than for the solution, where the hydration water network is *less structured* and water molecules interact mostly with the interface. A difference in the *plasticity* of the hydrogen bond network as a function of its extension is also confirmed by the different patterns of the corresponding densities of states.

In Fig. 6 we plot the low energy part of the vibrational density of states for the fully hydrated powders and for a concentrated solution of the hydrophobic peptide, NALMA. The peak at 7 meV is currently attributed to the inter-molecular O–O–O bending. In bulk water, it shifts to higher energy transfer with decreasing temperature [27].

The measured densities of states of hydrated powders show significant shifts of the peak position to higher energy and a decrease of the amplitude which corresponds to an apparent lower temperature as compared with bulk water. Both effects are more pronounced for the hydrophilic peptide, which confirms that the dynamics of hydration water is similar to that of bulk water at lower temperatures and that the "plasticity" of the hydrogen bond is larger in hydrophobic environments.

4. Conclusions

Our study of the dynamics of hydration water in two peptides as a function of temperature elucidates the main processes of interaction of the molecules with the interface and the dynamics of hydrogen bonds. The comparison with studies of the same peptides in concentrated solutions shows important differences that may be mainly explained as due to differences in the dimensionality of the space available to the water molecules. Only in solutions, the exchange of water molecules with external layers in a 3D space is possible. In contrast, in hydrated powders most of the water molecules are isolated and interact solely with the surface of the peptide.

An important conclusion from our study is that the onset of diffusion is easier in the vicinity of hydrophobic regions. This is due to the absence of bonds between water and the substrate. When the

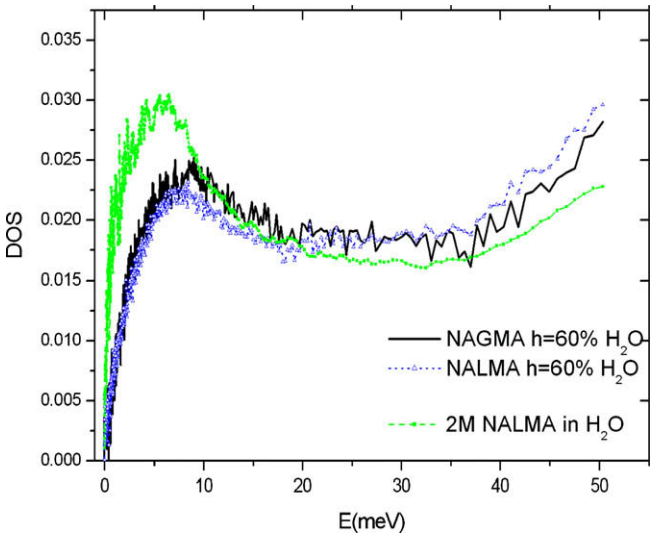

Fig. 6. Low energy densities of states of hydration water in fully hydrated NAGMA and NALMA powders, compared with that of a saturated solution of NALMA. For comparison purposes the densities of states were normalized to their integral between 0 and 50 meV.

hydrophobic region is large enough, which is the case with our NALMA sample, a structured network of water molecules is formed at low temperatures. This network suddenly generates mobility at a well defined temperature as shown in our previous studies. In addition the residence time of water molecules is shorter near hydrophobic environments.

The hydrogen bond dynamics is less dependent on the hydrophobicity of the substrate but is very different between hydrated powders and concentrated solutions. As expected, room temperature hydrogen bond relaxation times are longer for solutions because of the additional bonds established with neighbouring water molecules. Times at lower temperatures are very long for molecules forming bonds with hydrophilic sites.

This detailed study of hydration water dynamics in two peptides that only differ in the presence of a hydrophobic lateral chain show a large variety of behaviours. Nevertheless some general features have been established and can be understood qualitatively. These conclusions may furnish a framework for the prediction of the dynamics of water in more complex situations, namely large biomolecules.

Acknowledgments

This work utilized facilities supported in part by the National Science Foundation under Agreement No. DMR-0454672. "Certain commercial materials are identified in this paper to foster understanding. Such identification does not imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it imply that the materials identified are necessarily the best available for the purpose."

References

[1] N. Smolin, R. Winter, J. Phys. Chem. B 108 (2004) 15928.
[2] A. Paciaroni, A. Orecchini, E. Cornicchi, M. Marconi, C. Petrillo, M. Haertlein, M. Moulin, H. Schober, M. Tarek, F. Sacchetti, Phys. Rev. Lett. 101 (2008) 148104.
[3] M.-C. Bellissent-Funel, J. Teixeira, K.F. Bradley, S.H. Chen, J. Phys. I (France) 2 (1992) 995.
[4] I. Brovchenko, A. Krukau, A. Oleinikova, A.K. Mazur, J. Phys. Chem. 111 (2007) 3258.
[5] B. Born, H. Weingartner, E. Brundermann, M. Havenith, J. Am. Chem. Soc. 131 (2009) 3752.
[6] J. Qvist, B. Halle, J. Am. Chem. Soc. 130 (2008) 10345.
[7] D. Russo, P. Baglioni, E. Peroni, J. Teixeira, Chem. Phys. 292 (2003) 235.
[8] D. Russo, J. Ollivier, J. Teixeira, PCCP 10 (2008) 4968.
[9] J. Perez, J.M. Zanotti, D. Durand, Biophys. J. 77 (1999) 454.
[10] A.M. Stadler, I. Digel, J.P. Embs, T. Unruh, M. Tehei, G. Zaccai, G. Buldt, G.M. Artmann, Biophys. J. 96 (2009) 5073.
[11] M. Jasnin, M. Moulin, H. Haerlein, G. Zaccai, M. Tehei, Biophys. J. 95 (2008) 857.
[12] D. Russo, G. Hura, J.R.D. Copley, Phys. Rev. E 75 (2007) 1.
[13] D. Russo, J. Teixeira, J. Ollivier, J. Chem. Phys. 130 (2009) 235101.
[14] E. Persson, B. Halle, PNAS 105 (2008) 6266.
[15] A. Frolich, F. Gabel, M. Jasnin, U. Lehnert, D. Oesterhelt, A.M. Stadler, M. Tehei, M. Weik, K. Wood, G. Zaccai, Faraday Discuss. 141 (2009) 117.
[16] J.R.D. Copley, J.C. Cook, Chem. Phys. 292 (2003) 477.
[17] R.T. Azuah, L.R. Kneller, Y. Qiu, P.L.W. Tregenna-Piggott, C.M. Brown, J.R.D. Copley, R.M. Dimeo, J. Res. Nat. Inst. Stand. Technol. 114 (2009) 341.
[18] D. Russo, R.K. Murarka, G. Hura, E. Verschell, J.R.D. Copley, T. Head-Gordon, J. Phys. Chem. B 108 (2004) 19885.
[19] D. Russo, R.K. Murarka, J.R.D. Copley, T. Head-Gordon, J. Phys. Chem. B 109 (2005) 12966.
[20] D. Russo, G. Hura, T. Head Gordon, Biophys. J. 86 (2004) 1852.
[21] J. Teixeira, M.-C. Bellissent-Funel, S.-H. Chen, A.J. Dianoux, Phys. Rev. A 31 (1985) 1913.
[22] D. Laage, J.T. Hynes, Science 311 (2006) 832.
[23] D. Laage, J. Phys. Chem. B Lett. 113 (2009) 2684.
[24] G.L. Squires, Introduction to the Theory of Thermal Neutron Scattering, Cambridge University Press, 1978 (Chapter 3, Eq. (3.136)).
[25] M.-C. Bellissent-Funel, S.-H. Chen, J.M. Zanotti, Phys. Rev. E 51 (1995) 4558.
[26] D.A.C. Beck, D.O.V. Alonso, V. Daggett, Biophys. Chem. 221 (2003) 100.
[27] S. Krishnamurthy, R. Bansil, J. Wiafe-Akenten, J. Chem. Phys. 79 (1983) 5863.