

Solvent and polymer H/D isotope effects on miscibility in Poly(ethylene oxide)/Ethanol system



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HIGHLIGHTS

- SANS results from a series of PEO/ethanol solutions with various deuterated substitution are reported.
- Strong isotope effects on mixing/demixing characters are found when approaching the solubility limit upon cooling.
- Flip of the upper/lower critical solution temperature trends due to deuteration is observed.

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ABSTRACT

Various combinations between deuterated/nondeuterated poly(ethylene oxide) and (fully and partly) deuterated/nondeuterated ethanol solvents were investigated by small-angle neutron scattering. It was found that the deuteration process has strong effects on the polymer solution behavior when approaching the solubility limit upon cooling. Deuteration of the polymer and/or of the solvent can change the character of mixing/demixing and even 'flip' the upper/lower critical solution temperature trends in experimental temperature range.

1. Introduction

Deuteration, i.e., replacing hydrogen atoms by deuterium, is often used to enhance the contrast in neutron scattering. Deuteration is commonly performed either on macromolecules or on solvents. Some precautions must be taken with the use of deuterated polymers or deuterated solvents though, because the deuteration of molecules can change their chemical and physical properties significantly [1,2]. Deuteration on polymers has been shown to modify the temperature of phase transitions [3,4], vary the rate of crystallization [5], induce clustering in blends [6–8]. Hydrogen/deuterium exchange can also take place for macromolecules with labile protons when deuterated solvents are used, which thus significantly affects structures and phase behaviors of the studied objects [9–13].

Poly(ethylene oxide) (PEO), a quintessential biocompatible polymer, has been the subject of great many investigations, including the prevention of biofouling, controlled drug delivery, and tissue scaffolds. When dissolved in water, as a result of the hydrophilic interaction (hydrogen bonding of water molecules to the oxygen atoms on the polymers) and the hydrophobic interaction (the ethyl units repel water), PEO displays a closed loop phase diagram [14]. Small-angle

neutron scattering (SANS) measurements have shown strong isotope effects in PEO/water systems [15]: Solvent deuteration is seen to enhance the hydrophilic interaction while deuteration on the polymer chain is seen to enhance the hydrophobic interaction. The isotropic dependence of specific interactions is discordant, so the average polymer contrast match method which is typically used in the SANS technique by varying hydrogen/deuterium contents fails.

Here we note the work of Nystöm et al. [17], who carried out dynamic light scattering measurements of protonated PEO (H.PEO) in nondeuterated methanol (CH₃OH) and in (partly and fully) deuterated methanol (CH₃OD and CD₃OD) within the pressure range 1 bar–2500 bar. Nystöm et al. [17] observed strong solvent isotope effect in the pressure dependence of molecular cluster formation. Compared to H.PEO in CH₃OH solution, molecular association is enhanced when the solvent is switched to CH₃OD due to the changes in hydrogen bond strength, while molecular association is depressed when CD₃OD is used as solvent due to the difference in strength of the hydrophobic interactions between nonpolar groups. It is speculated that the molecular association might be related to the preliminary stage of a pressure induced solution crystallization process. In this context, we also note the work of Allen and Tanaka [7], who carried out SANS measurements

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on PEO crystals from melts in an attempt to obtain information on the conformation of individual molecules. They also found significant isotope effect on the crystallization behavior, probably related to a slight thermodynamic difference between protonated and deuterated species. For blends with the deuterated PEO (D.PEO) as a matrix, the added H.PEO species are evenly distributed between the crystalline and amorphous regions; For blends with H.PEO as a matrix, the solute D.PEO molecules form homogeneous local aggregates which further distribute in space in a non-random manner corresponding to the presence of inhomogeneous domains of large size.

In light of the above findings and the possibility of studying polymer and solvent isotope effects, the PEO/ethanol system seems to be important and interesting. That is because the repeating unit of PEO (–CH₂–CH₂–O–) resembles to ethanol (H–CH₂–CH₂–O–H). As a result of the similarity in the chemical structure at the monomer level, the solution property is subject to a delicate balance among solvent/polymer, polymer/polymer and solvent/solvent interactions. PEO molecularly disperses in ethanol and undergoes a crystallization process upon cooling to room temperature. A few years ago, Ho et al. [16] reported a SANS study of H.PEO dissolved in fully deuterated anhydrous ethanol (C₂D₅OD), in which the interference of a crystallization process with an upper critical solution temperature (UCST) phase diagram was observed. The research reported here focuses on isotope effects in PEO/ethanol systems. The scattering properties are investigated when the solutions, although remaining stable and homogeneous, are driven gradually close to the stability limit. Various combinations between deuterated/nondeuterated polymers (D.PEO, H.PEO) and (fully, partly) deuterated/nondeuterated solvents (C₂D₅OD, C₂H₅OD, C₂H₅OH) are investigated. The sensitivity to slight change in thermodynamic and/or hydrodynamic interaction due to deuteration when approaching crystallization and/or phase separation is reported.

2. Experimental section

2.1. Materials

The molecular weight of D.PEO used in this study is $M_n = 33,000$ g/mol (with $M_w/M_n = 1.1$), and that of H.PEO is $M_n = 37,000$ g/mol (with $M_w/M_n = 1.07$). Here, M_n is the number averaged molecular weight and M_w is the weight averaged molecular weight. Both polymers were purchased from Polymer Source. Both deuterated solvents, C₂D₅OD and C₂H₅OD, were purchased from Cambridge Isotope Labs. The undertreated solvent C₂H₅OH was purchased from Sigma-Aldrich Corporation. D.PEO or H.PEO or mixtures of the two polymers are dissolved in C₂D₅OD, C₂H₅OD, C₂H₅OH or mixtures of these solvents. All measured samples correspond to 8 wt % polymer in ethanol solvent, with compositions listed in Table 1.

S1 and S2 are designed to probe the effects of selective deuteration from the hydroxy group of solvent, since all other components in solutions are the same. S3 and S4 are designed to probe the effects of selective deuteration from the alkyl group of solvent, since all other components in solutions are the same. S2 and S3 are designed to probe

the effects of deuteration of polymer chain, since the solvent for two solutions is the same. S1 and S4 are designed to compare the results after switching the deuteration between polymers and solvents. Series S4, S5 and S6 are designed to consider the solution properties after part of the polymer is substituted by deuterated polymer. Series S5, S7 and S8 are designed to consider the effects after varying the solvent compositions which is a typical method to find zero-averaged contrast conditions. The ratio 68/32 between C₂D₅OD and C₂H₅OH for S8 is chosen based on theoretical calculation for zero-average contrast condition under random phase approximation. The discussion will go on a case by case basis mentioned here.

2.2. Small-angle neutron scattering measurement

The SANS measurements over a wave vector (Q) range of 0.0034–0.4054 Å⁻¹, were performed on the NGB-30 m SANS instrument at the NIST Center for Neutron Research. SANS data were reduced using standard methods to correct for empty cell and background scattering. Scattering data were scaled to an absolute cross section (units of cm⁻¹). Sample temperature was decreased from 55 °C down to 20 °C with 5 °C steps.

3. Data analysis

Solutions are visually all clear and transparent at 50 °C. Depending on compositions, solutions behave differently while cooling down, crystallization and/or phase separation is observed in some solutions. To show the different behaviors between solutions, three typical sets of SANS data at three temperatures are included in Fig. 1a, 1b and 1c corresponding to S1, S2 and S5, respectively. In these and other figures, statistical error bars correspond to one standard deviation.

For the D.PEO/C₂H₅OH solution (S1, Fig. 1a), different from the (H.PEO + D.PEO)/C₂D₅OD solution (Fig. 1c), the scattering curves share similar trends at 50 °C, 35 °C and 25 °C. Note that the coherent scattered intensity, $I(Q)$, gradually increases with decreasing temperature T (guided by the arrow) indicating that this solution is characterized by an UCST behavior; that is, the solution approaches the two-phase regime upon cooling if no other transitions (such as crystallization here) interrupts.

For the D.PEO/C₂H₅OD solution (S2, Fig. 1b), on the contrary, $I(Q)$ decreases with decreasing temperature T (guided by the arrow). It indicates that this solution possesses a lower critical solution temperature (LCST) behavior; that is, the polymer shows better solubility upon cooling. Another feature of this data set is that, in the steady-state, two main scattering regimes are clearly observed, one in the high- Q regime with a length scale of nm and the other in the low- Q regime with a length scale of sub-micron. The $I(Q)$ upturn seen at low- Q regime throughout 50 °C - 20 °C regime is due to the associated fluctuation of PEO through strong polymer-solvent interaction. This type of long-range correlated concentration fluctuation in semidilute solution has been observed in PEO/D₂O solution in which D₂O is a very good solvent [15], and generally observed in other systems with hydrogen-bonding

Table 1
Solution compositions reported in this study.

Solution ID	Polymer(s)	Solvent(s)
S1	D.PEO	C ₂ H ₅ OH
S2	D.PEO	C ₂ H ₅ OD
S3	H.PEO	C ₂ H ₅ OD
S4	H.PEO	C ₂ D ₅ OD
S5	H.PEO + D.PEO (50 wt % + 50 wt%)	C ₂ D ₅ OD
S6	H.PEO + D.PEO (20 wt% + 80 wt%)	C ₂ D ₅ OD
S7	H.PEO + D.PEO (50 wt % + 50 wt%)	C ₂ H ₅ OH
S8	H.PEO + D.PEO (50 wt % + 50 wt%)	C ₂ D ₅ OD + C ₂ H ₅ OH (68 vol % + 32 vol%)

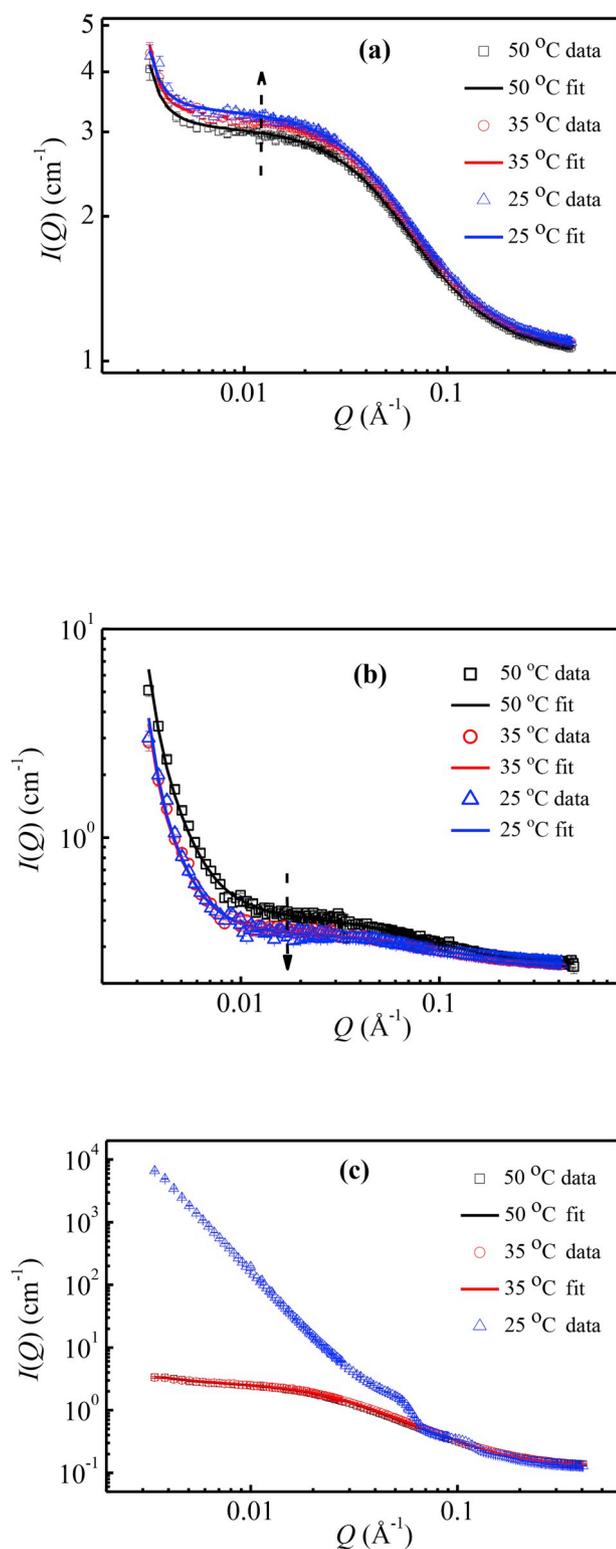


Fig. 1. SANS data from three solutions, S1 (a), S2 (b) and S5 (c). The solid lines correspond to fits to the correlation length model. The dashed lines with arrow provide a guide to the eyes for the intensity change with temperature decreasing.

interaction or electrostatic interaction, such as poly(*N*-isopropylacrylamide) (PNIPAM)/H₂O [19,20].

For the (H.PEO + D.PEO)/C₂D₅OD solution (S5, Fig. 1c), upon cooling, a sudden upturn at low-*Q* regime and peaks seen at

$Q > 0.03 \text{ \AA}^{-1}$ clearly demonstrate crystal formation at 25 °C. The crystals are on the order of micrometers, which can be also seen by the naked eye.

In order to reproduce the main common features of the scattering data, a fit to a power law plus the correlation length model with the following functional form is used:

$$I(Q) = A/Q^n + C/[1 + (Q\xi)^m] + B \quad (1)$$

The first term describes Porod scattering from clusters (low-*Q* feature), and the second term is a Lorentzian-like function describing scattering from polymer chains (high-*Q* feature). The constant *B* represents the incoherent background. The structure of crystal, which is tremendously different from random coil, is out of the interest of this study, therefore none of the data that include the crystallization feature will be quantitatively analyzed in this report. The low-*Q* feature for the amorphous samples will also not be discussed since only the tail of the low-*Q* feature is observed. The parameter ξ denotes the averaged correlation length between the polymer coils. The exponent *m* characterizes the polymer/solvent interactions which is related to the excluded volume parameter ν in Flory's mean-field theory by $m = 1/\nu$. Parameter *C* is referred to as the solvation intensity and used to infer mixing/demixing phase diagrams [18]. When solvation gets better, *C* decreases. When approaching phase separation, *C* increases due to increased composition fluctuations. By means of *C* and ξ , we are able to look into the solvation behaviors within the temperature range where the solutions can remain stable and homogeneous.

The solid lines in Fig. 1 are the corresponding nonlinear least-squares fits to the correlation lengths model for the entire *Q*-range window for various samples. This model reproduces the actual data very well. The range of uncertainty in each fitted parameter was determined by fixing that parameter at various values and allowing the other parameters to vary during the fitting within physically reasonable limits. In this way the maximum uncertainty of the fitted parameters was found to be approximately 10%.

4. Discussion

4.1. Deuteration effects from the hydroxy group of ethanol (Comparison between S1 and S2)

The differences in scattering patterns between D.PEO/C₂H₅OH (S1) and D.PEO/C₂H₅OD (S2), have been described above in Fig. 1a and 1b. It should be mentioned here that, phase transition is observed in the D.PEO/C₂H₅OH solution when the temperature is decreased from 25 °C to 20 °C, while such a transition is absent in the D.PEO/C₂H₅OD solution (Supplementary Information, Fig. s1).

The trends of the fitted *C* and ξ parameters as a function of temperature for four solutions with pure polymer dissolved in pure solvent (S1 – S4) are included in Fig. 2. The data pair under comparison here (S1 and S2) are in blue color. In D.PEO/C₂H₅OH (S1), *C* gradually increases with decreasing *T* characterizing a UCST behavior. When the hydroxy group of ethanol is deuterated, in D.PEO/C₂H₅OD (S2), *C* gradually decreases with decreasing temperature *T* characterizing a LCST behavior.

The solution behavior of D.PEO/C₂H₅OD is analogous to other well-known systems with LCST phase diagrams, such as PNIPAM/H₂O and (PEO-PPO-PEO)/H₂O, whereby one fast and one slow relaxation modes were observed in the semidilute regime by dynamics light scattering.^{19, 20} The slow mode is related to the associated fluctuation of transient polymer network (low-*Q* feature). The fast mode corresponds to fluctuation of chain segments inside each “blob” (high-*Q* feature) which becomes faster (shorter in length) as the solvent quality tend to be better with decreasing temperatures. For D.PEO/C₂H₅OD, from Fig. 2b, it is obvious that ξ (extracted from the high-*Q* feature) decreases with decreasing *T*. Better solubility at lower *T* gives a smaller correlation

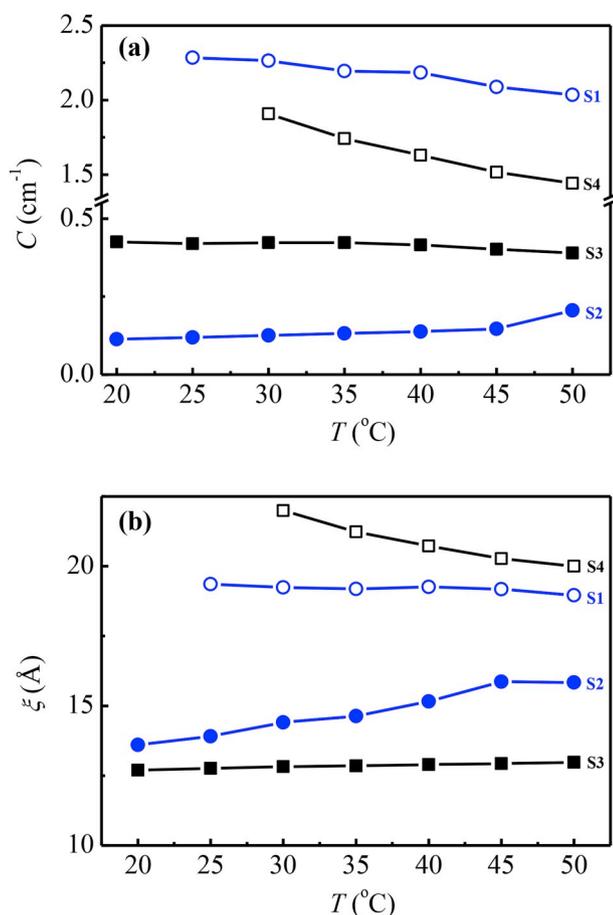


Fig. 2. Solvation intensity C (a) and correlation length ξ (b) as a function of temperature T for four solutions with pure polymer in pure solvent: S1 (—○—), S2 (—●—), S3 (—■—) and S4 (—□—).

length (“blob” size) due to a stronger screening effect. Furthermore, since the low- Q feature which originated from molecular association remains evident through 50 °C–20 °C, it is not a sign for crystallization process. Therefore, this type of long-range molecular association is not related to the preliminary stage of a temperature induced solution crystallization process.

In short, it can be concluded from the different solvation behaviors between D.PEO/C₂H₅OH and D.PEO/C₂H₅OD solutions that, selective deuteration of the hydroxy group of ethanol enhances the polymer/solvent interaction (due to stronger hydrogen bonding) which can even ‘flip’ the solvation behavior from a UCST behavior to a LCST behavior. Or say, the hydrophilicity/hydrophobicity of solvents causes the shift of phase diagram (which is probably a close loop as that in water) along the temperature axis. When a limited temperature window is focused, the observed flipping of solvation behavior between UCST and LCST is actually due to the shift of a close loop phase diagram, where we may be blind to either the LCST part or the UCST part.

4.2. Deuteration effects from the alkyl group of ethanol (Comparison between S3 and S4)

H.PEO in selectively deuterated ethanol C₂H₅OD (S3) is very stabilized, thus C is relatively insensitive to T throughout the experimental temperature regime. However, H.PEO in fully deuterated ethanol C₂D₅OD (S4) shows an obvious trend of demixing upon cooling, where C increases with decreasing T (Fig. 2a) and phase transition is observed when the temperature is decreased to 25 °C (Supplementary

Information, Fig. s2). These results indicate that deuteration on the alkyl group of ethanol depresses solubility.

This conclusion is also supported by values of ξ (Fig. 2b). It is known that polymer chains shrink as the solvent quality tends to be poor. For semidilute solutions of polymer chains with a finite length, the shrinkage results in fewer entanglement points and, consequently, a loose network with more defects or larger structural fluctuation. That is, larger values of ξ . Here, for the same polymer H.PEO with the same concentration 8 wt %, a better solubility in C₂H₅OD leads to smaller ξ while a relatively poor solvent (C₂D₅OD) results in larger ξ .

4.3. Deuteration effects from polymer chain (Comparison between S2 and S3)

When the scattering properties of D.PEO (S2) and H.PEO (S3) in the same solvent C₂H₅OD are compared (data with solid symbols, Fig. 2), it is seen that C and ξ of H.PEO/C₂H₅OD solution are less sensitive to T throughout the investigated temperature range. Therefore, H.PEO/C₂H₅OD is more further away from the thermodynamic phase transition boundary. This is probably related to a shorter CH \cdots HC distance, compared to CD \cdots DC distance. The hydrogen-hydrogen interactions along the H.PEO backbone are slightly more stable than deuterium-deuterium interactions along the D.PEO backbone.

4.4. Switch deuteration on both polymer and solvent (Comparison between S1 and S4)

From Fig. 2a, it is seen that, the solvation intensities for both D.PEO/C₂H₅OH (S1) and H.PEO/C₂D₅OD (S4) increase with decreasing T . It indicates that both solutions follow a UCST behavior. One apparent difference between these two solutions is in their crystallization temperatures. In D.PEO/C₂H₅OH, the crystallization transition is observed when the temperature falls from 25 °C to 20 °C (Supplementary Information, Fig. s1), while in H.PEO/C₂D₅OD, the transition is observed when temperature falls from 30 °C to 25 °C (Supplementary Information, Fig. s2). Apparently, switch of the deuteration between polymers and solvents influences the demixing thermodynamics. Solvent deuterated more significantly shifts the UCST to a higher temperature.

4.5. Nondeuterated/deuterated mixed polymers (Comparison among S4 – S6)

In SANS measurements, a sample can be generally made up of mixtures, in which a fraction of isotopically substituted molecules is dispersed. The C and ξ vs. T for four solutions with mixed polymers dissolved in pure or mixed solvents (S5 – S8) are included in Fig. 3. In this section, the effects whereby part of the polymer matrix is substituted by D.PEO are discussed. That is, the comparison is among S4, S5 and S6.

Note that, all measured samples correspond to 8 wt % polymer in ethanol, which is inside the semidilute regime. Compared to pure H.PEO in C₂D₅OD (S4, $\xi \approx 20$ Å), the apparent static correlation lengths are almost double when half of the polymer network is substituted by the deuterated component (S5, $\xi \approx 40$ Å), and the size is comparable to the mean radius of gyration R_g with further dilution (S6, $\xi \approx 42$ Å). D.PEO is barely distinguishable from C₂D₅OD by neutrons because of the similarity of their molecular structures implying a very low contrast, therefore this result is consistent with the scenario that the mesh size (average distance between entanglements) of the neutron-visible H.PEO network is wider as its concentration decreases.

If the thermodynamics of H.PEO and D.PEO in C₂D₅OD are the same, then any transitions (if there are any) should occur at exactly the same temperature regardless of the amount of deuterium substitution. The fact is, when the temperature falls from 35 °C to 30 °C, an upturn of

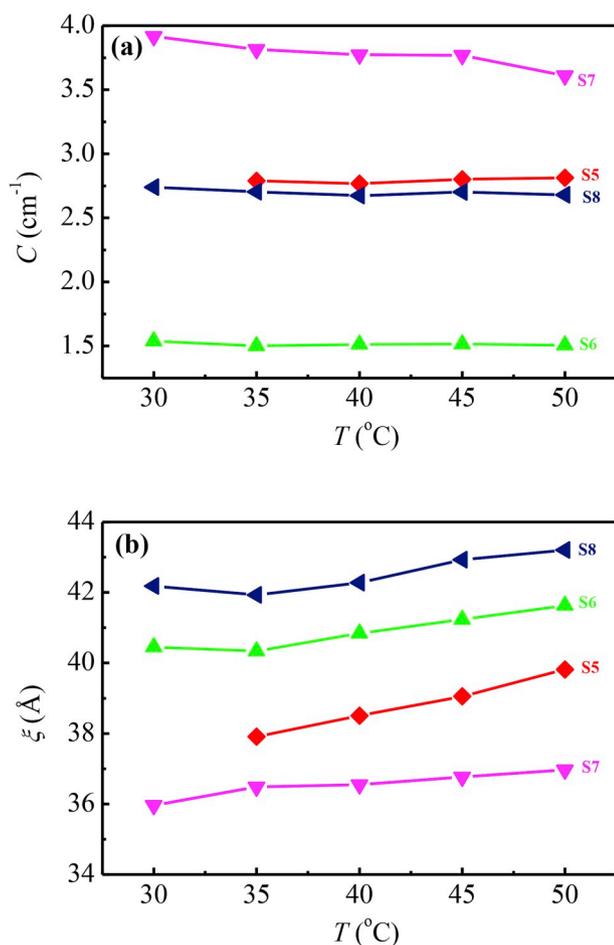


Fig. 3. Solvation intensity C (a) and correlation length ξ (b) as a function of temperature T for four solutions with mixed polymer dissolved in pure solvent or mixed solvents: S5 (—◆—), S6 (—▲—), S7 (—▼—), S8 (—◀—).

the scattering intensity in the low- Q regime indicating cluster formation is observed in solution with H/D polymer ratio of 50/50, while such a transition is not seen in solution with H/D polymer ratio of 20/80 (Supplementary Information, Fig. s3). From this observation, though we cannot tell the thermodynamics of D.PEO/ $\text{C}_2\text{D}_5\text{OD}$ directly due to very low contrast, we know that the thermodynamics of H.PEO and D.PEO in $\text{C}_2\text{D}_5\text{OD}$ are unsynchronized to temperature changes. It is possible that segregation happens between H.PEO and D.PEO upon cooling due to their slight difference in thermodynamics, which is consistent with what is observed in H.PEO/D.PEO blend [7].

4.6. Nondeuterated/deuterated mixed solvents (Comparison among S5, S7 and S8)

The interpretation of SANS results from multi-component solutions is complicated, due to the delicate interactions and a variety of scattering contrasts between polymer/polymer, polymer/solvent and solvent/solvent, consequently, the lack of simple clear meanings for the apparent parameters C and ξ . Here we look at solutions with the same mixed polymers (H/D = 50/50) as solute but in different solvents: pure $\text{C}_2\text{D}_5\text{OD}$ (S5), pure $\text{C}_2\text{H}_5\text{OH}$ (S7), and a mixed solvent with volume ratio between $\text{C}_2\text{D}_5\text{OD}$ and $\text{C}_2\text{H}_5\text{OH}$ of 68/32 (S8). If the pseudo-binary assumption, considering mixed polymers as one effective component and mixed solvents as another effective component, is applied to these ternary or quaternary mixtures (which we know from above it is not strictly correct for PEO/ethanol case), form C and ξ vs. T curves (Fig. 3),

one crude conclusion could be drawn is that the solvation behaviors are influenced by solvent composition. The values of apparent ξ strongly vary with solvent composition. Therefore, one should be prudent when applies the average polymer contrast match method, implying the random phase approximation, to PEO/ethanol system. To achieve further specific knowledge of these multi-component mixed systems, it requires more samples and more thorough data analysis schemes.

5. Conclusions

The main conclusion of this project is that the deuteration process has strong effects on the PEO/ethanol solution behavior when approaching to solubility limit. The interactions between polymer/polymer, polymer/solvent and solvent/solvent are so delicate that modification of any component by deuteration influences the solvation properties, therefore the discussion is made on a case by case basis. Deuteration of the polymer and/or of the solvent can change the character of mixing/demixing even flip the LCST/UCST trends in the experimental temperature zone, therefore it should be prudent when one applies the average polymer contrast match method to PEO/ethanol system. It is certain that selective deuteration of the hydroxy group of ethanol enhances the polymer/solvent interaction, while deuteration on the alkyl group of ethanol depresses solubility.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.polymer.2019.01.063>.

References

- [1] J.E. Campana, D.N. Heller, Deuterated Polymers: Chemical and Physical Properties and Future Prospects, NRL (Naval Research Laboratory), 1985 Report 8922.
- [2] G.D. Wignall, F.S. Bates, Applications and limitations of deuterium labeling methods to neutron scattering studies of polymers, *Makromol. Chem., Macromol. Symp.* 15 (1988) 105–122.
- [3] H. Yang, G. Hadziioannou, R.S. Stein, The effect of deuteration on the phase equilibrium of the polystyrene/poly(vinyl methyl ether) blend system, *J. Polym. Sci. Polym. Phys. Ed* 21 (1983) 159–162.
- [4] A. Sipsorska, J. Szydłowski, L.P.N. Rebelo, Solvent H/D isotope effects on miscibility and θ -temperature in the polystyrene-cyclohexane system, *Phys. Chem. Chem. Phys.* 5 (2003) 2996–3002.
- [5] F.C. Stehling, E. Ergos, L. Mandelkern, Phase separation in n-Hexatriacontane- d_{74} and polyethylene-poly(ethylene- d_4) systems, *Macromolecules* 4 (1971) 672–677.
- [6] J. Schelten, G.D. Wignall, D.G.H. Ballard, G.W. Longman, Small-angle neutron scattering studies of molecular clustering in mixtures of polyethylene and deuterated polyethylene, *Polymer* 18 (1977) 1111–1120.
- [7] G. Allen, T. Tanaka, A small-angle neutron scattering study on poly(ethylene oxide) crystals, *Polymer* 19 (1978) 271–276.
- [8] D.M. Sadler, A. Keller, Neutron scattering studies on the molecular trajectory in polyethylene crystallized from solution and melt, *Macromolecules* 10 (1977) 1128–1140.
- [9] C. Neylon, Small angle neutron and X-ray scattering in structural biology: recent examples from the literature, *Eur. Biophys. J.* 37 (2008) 531–541.
- [10] G. Makhatadze, G.M. Clore, A.M. Gronenborn, Solvent isotope effect and protein stability, *Nat. Struct. Biol.* 2 (1995) 852–855.
- [11] H.B. Stuhmann, Neutron small-angle scattering of biological macromolecules in solution, *J. Appl. Crystallogr.* 7 (1974) 173–178.
- [12] D.L. Price, L. Fu, F.J. Bermejo, F. Fernandez-Alonso, M.-L. Saboungi, Hydrogen/deuterium isotope effects in water and aqueous solutions of organic molecules and proteins, *Chem. Phys.* 424 (2013) 62–69.
- [13] A. Banc, C. Charbonneau, M. Dahesh, M.-S. Appavou, Z. Fu, M.-H. Morel, L. Ramos, Small angle neutron scattering contrast variation reveals heterogeneities of

- interactions in protein gels, *Soft Matter* 12 (2016) 5340–5352.
- [14] Y.C. Bae, S.M. Lambert, D.S. Soane, J.M. Prausnitz, Cloud-point curves of polymer solutions from thermo-optical measurements, *Macromolecules* 24 (1991) 4403–4407.
- [15] B. Hammouda, D. Ho, S. Kline, SANS from Poly(ethylene oxide)/water systems, *Macromolecules* 35 (2002) 8578–8585.
- [16] D. Ho, B. Hammouda, S. Kline, W.-R. Chen, Unusual phase behavior in mixtures of poly(ethylene oxide) and ethyl alcohol, *J. Polym. Sci. Polym. Phys. Ed* 44 (2006) 557–564.
- [17] B. Nyström, K. Olafsen, J. Roots, Effect of pressure on hydrodynamic properties of poly(ethylene oxide) in deuterated and in non-deuterated solvents, *Polymer* 32 (1991) 904–908.
- [18] B. Hammouda, Solvation characteristics of a model water-soluble polymer, *J. Polym. Sci. Polym. Phys. Ed* 44 (2006) 3195–3199.
- [19] G. Yuan, X. Wang, C.C. Han, C. Wu, Reexamination of slow dynamics in semidilute solutions: from correlated concentration fluctuation to collective diffusion, *Macromolecules* 39 (2006) 3642–3647.
- [20] G. Yuan, X. Wang, C.C. Han, C. Wu, Reexamination of slow dynamics in semidilute solutions: temperature and salt effects on semidilute poly(*N*-isopropylacrylamide) aqueous solutions, *Macromolecules* 39 (2006) 6207–6209.