Solvation of Perfluorooctane and Octane in Water, Methanol, Acetonitrile, and Aqueous Mixtures of Methanol and Acetonitrile

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Molecular dynamics simulations are used to examine the local solvation structure of single octane and perfluorooctane molecules in liquid water, methanol, acetonitrile, and aqueous mixtures of methanol and acetonitrile. The motivation is to obtain baseline information about the solvation of perfluorooctane by liquids used as the mobile phase in liquid chromatography and how it differs from the solvation of octane. While octane is uniformly solvated by both water and the second component, perfluorooctane is solvated by methanol and acetonitrile with the exclusion of water from the first solvation layer when the solvent is a mixture.

Introduction

The use of fluorocarbon silica-based materials in reversedphase liquid chromatography (RPLC) has demonstrated an improved separation and molecular recognition of polar and halogenated compounds under highly aqueous mobile phase conditions ¹⁻⁵ in contrast to the often difficult separations that result on the more commonly used hydrocarbon phases. The interaction of solvent molecules with the fluorocarbon chains is anticipated to play a dynamic role in the overall mechanism of solute retention on these materials.⁶⁻¹¹ In this paper, we examine the solvation of a single perfluorooctane (C₈F₁₈) molecule as an initial model for a fluorocarbon-based chromatographic material in water, methanol, acetonitrile, and equimolar aqueous mixtures via molecular dynamics simulations. These results are directly compared with simulations of a single octane (C8H18) molecule in the same solvents to elucidate the influence of the fluoro substituents on the ordering of the solvent layer surrounding the molecules and its potential effect on the resultant octane and perfluorooctane chain structural conformation. Recnt molecular simulations of the local water structure around the small molecules CF 4 and C(CH 3) 4 have only small differences.¹² As shown below, this is not the case for the more extended solutes considered here.

Considerable differences in the thermodynamic behavior of a range of solutes have been observed between methanol and acetonitrile as organic modifiers in the aqueous mobile phase on monomeric-type hydrocarbon stationary phases.^{6,7,9,13} These differences have been largely attributed to the entropic effects promoted by the presence of acetonitrile clusters within the mobile phase.⁶ Evidence of microheterogeneity within acetonitrile-water mixtures has been elucidated by a wealth of experimental^{14–19} and molecular simulation ^{14–16,20–22} investigations. Furthermore, the formation of surface-adsorbed multilayers of organic modifiers on alkyl stationary phases has been demonstrated via adsorption isotherm experiments.^{23–26} Results are consistent with a relatively thick (1–2 nm) layer of acetonitrile adsorbed onto the hydrocarbon stationary phase surface for acetonitrile—water mixtures, in contrast to only a single methanol adsorbed layer for the methanol—water system. How these organic-rich interphases between the mobile phase and the stationary phase may influence solute retention processes under typical chromatographic conditions remains unclear.

The extent to which solvent molecules (including organic modifiers) can penetrate the stationary phase to form interfacial regions has been the subject of several molecular simulation investigations.²⁷⁻³³ Prior molecular dynamics simulations of n-C₁₈ stationary-phase models in methanol-water and acetonitrile-water mixtures have illustrated the preferential aggregation of organic solvent molecules toward the alkyl stationary phase.^{27,29,34,35} Recent Monte Carlo simulations^{32,36} have illustrated direct solvent partitioning into C₁₈ stationary-phase models with mobile phases of varying methanol-water concentrations. Solvent "bridge" aggregates from the bulk mobile phase to the surface silanols were observed for models containing 33%, 66%, and 100% methanol but were not readily observed for pure water systems.³² In addition, simulations of a single *n*-octadecane chain solvated in water-methanol³⁷ and water-acetonitrile38 mixtures were conducted to characterize the local solvent environment surrounding a chromatographically relevant alkyl chain. As a result, a local mole fraction enhancement of acetonitrile around the methylene segments of the chain was observed for the acetonitrile-water system, and was considerably more pronounced than observed for comparable methanol-water systems.

The local solvent environment for fluorocarbon-based chromatographic sorbents is also anticipated to play a predominant role in the retentive process. The influence of various organic modifiers (methanol, acetonitrile, and 2,2,2-trifluoroethanol (TFE)) on the chromatographic selectivity of two C₁₈ phases and one perfluorinated C₆ phase was previously investigated.³⁹ The most distinct selectivity was observed for the perfluorinated phase with TFE as a cosolvent and was attributed to potential adsorption of TFE on phase surface, stemming from prior observations of TFE clustering in aqueous mixtures from X-ray scattering⁴⁰ and molecular simulation studies.^{41–43} TFE is aslo commonly used as a cosolvent for protein solvation and is used to promote the formation of α -helical structures of peptides.⁴⁴ Although its mechanism of action is not entirely understood,⁴⁵

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the ability of TFE to promote helicogenicity in proteins is largely attributed to its aggregation around the peptide backbone and desolvation of specific peptide residues as observed through spectroscopic observations and molecular dynamics studies.^{46–48} Albeit less dramatic than TFE, other aliphatic alcohols (including methanol) have been shown to enhance the helical stability for poly- α -amino acids.⁴⁹

Together with the potential solvation effects that may exist between organic modifiers and the fluorocarbon substrate, the structural conformation of the fluorocarbon chain may also need to be considered. Perfluoroalkanes in the solid state have a helical conformation for 12 or more carbons and a planar zigzag conformation for eight or fewer carbons.^{50,51} It was also found in a prior molecular dynamics simulation study that it is necessary to have explicit electrostatics for the helical feature to develop.⁵¹ In contrast to the peptide literature, there is little, if any, information on how the fully solvated fluorocarbon chains are configured in aqueous solutions containing organic cosolvents.

We employ molecular dynamics simulations to examine the solvation of a single octane molecule (C_8H_{18}) and also a single perfluorooctane molecule (C_8F_{18}) with water (H_2O), methanol (MeOH), and acetonitrile (MeCN) and equimolar mixtures of water-methanol and water-acetonitrile as solvents. "Me" is used to represent a united atom representation of the CH₃ group in methanol and acetonitrile. For this study, we have focused on a detailed investigation of the two most commonly used RPLC cosolvents (MeOH and MeCN) but plan to extend our future investigations to other cosolvents of interest (e.g., TFE) that are employed with chromatographic sorbents. A methanolacetonitrile solvent system was not examined, as this mixture is not typical of a chromatographic system. The emphasis is on comparing how these fluids solvate the two solutes and to identify differences between them. The solvation structure found for the isolated molecules will differ from the corresponding structure for these molecules in a chromatographic environment. This has been found to be the case for water in contact with tethered n-C18 chains.33,34

The simulation methods used and the interaction models are described in the next section. This is followed by two sections containing the results of the simulations for each of the solvents. The paper concludes with a discussion and summary of the results.

Simulation Method

The solvation of the chain molecules was examined using molecular dynamics simulation of the mixtures at ambient conditions of temperature and pressure. Water is modeled using the rigid, three-site SPC/E model,52 methanol is modeled using the rigid, three-site model of van Leeuwen and Smit,⁵³ and acetonitrile is modeled using the rigid three-site model of Edwards, Madden, and McDonald.^{20,54-56} The CH₃ groups in these models are represented as single-site united atoms. Octane is modeled using the OPLS-AA (all atom) model,57 and perfluorooctane is modeled using the all-atom model of Watkins and Jorgensen.58 The atom-atom interactions in each of these models include Couloumb and Lennard-Jones potentials. The intermolecular potential parameters for the potentials are listed in the Appendix so that the reader has ready access to the charges on the atom sites of the molecules. The intramolecular potential parameters and molecular geometry of the models are found in the cited papers and are not repeated here. The internal degrees of freedom of the octane and perfluorooctane molecules are described using harmonic stretch and bend interactions, and the torsion potentials are represented by polynomials in the

 TABLE 1: Length, L, of the Simulation Cube Edge for the

 Various Solvents

solvent	<i>L</i> , Å	-
H ₂ O	28.2	-
MeOH	36.7	
MeCN	39.3	
H ₂ O-MeOH	32.6	
H ₂ O-MeCN	34.6	

cosines of the torsion angles. The unlike atom Lennard-Jones parameters are obtained using the Lorentz–Berthelot rules.⁵⁹ The long-range part of the Coulomb interactions are treated using the Ewald summation method.⁶⁰ The orientations of the rigid solvent molecules are described using quaternions.^{61–64} The equations of motion are integrated using a Velocity–Verlet-type algorithm⁶⁵ adapted to include the quaternions. The simulations were performed in the NVE ensemble with a time step of 1 fs.

Each of the simulated systems consist of 729 solvent molecules and one chain molecule. For liquids at ambient conditions in a cubic simulation cell, this is the smallest system where the fully extended chain in an all-*trans* configuration extends less than 1/2 the length of the cell edge for the highest density system, water. This avoids the undesirable feature of the chain interacting with itself as a result of periodic boundary conditions. For each of the 10 simulations discussed here, the temperature and volume of the system were adjusted so that the temperature was near 293 K and the pressure was within a few megapascals of zero. The cubic simulation cell sizes used are listed in Table 1. The same cell dimensions were used for both the octane and perfluorooctane solutes.

Once the temperature reached the desired value, several sequential runs of 100 ps duration were made to stabilize the system at the desired pressure by adjusting L. Stability was determined when the computed pressure did not change significantly from the results of the previous run. The distribution of molecules close to the chain is a particularly significant property. The number of stabilization runs was three or four except for the water—acetonitrile mixture. For that case, six runs were needed to develop the microheterogeneity present in the mixture.²⁹

Several quantities that probe the solvation of the chains are considered here. These include the time history of the torsion angles of the backbone of the chain molecule. We use the convention that a torsion angle ϕ close to zero corresponds to a *trans* configuration. There are five torsion angles describing rotation about the inner five carbon-carbon bonds. The other quantities are the site-site pair functions of the solvent sites with the hydrogen or fluorine sites of the chain molecule and some measures of the orientation of the solvent molecules around the chain. The solvent sites selected for the pair correlation functions are the oxygen site of water, the oxygen site of methanol, and the carbon site of acetonitrile.

The orientation measures for water and methanol are the distributions of cosines of the angle ψ between the vector from the oxygen site of the solvent to the hydrogen or fluorine site and some vectors, described below, that characterize the structure of the solvent molecule.⁶⁶ These distributions, $D(\cos \psi)$, are obtained as functions of the distance between the abovementioned selected sites of the solvent and the hydrogen or fluorine site. For water, the vectors characterizing the structure of the molecule are the dipole moment vector that bisects the angle formed by the OH bonds of the water molecule, the vector between the hydrogen sites, and the vector normal to the other Solvation of Perfluorooctane and Octane



Figure 1. The vectors used to discuss the orientation of water and methanol are shown here. For water (left side) these are the dipole moment vector (black), the vector between the hydrogen sites (red), and the cross product of these vectors (not shown). For methanol (right side) these are the vector along the methyl-oxygen bond (black), the vector along the methyl-hydrogen bond (red), and the cross product of these vectors (not shown).



Figure 2. The time development of the cosines of the torsion angles of the backbone of octane (upper plot) and perfluorooctane (lower plot) in methanol are shown over a 10 ns trajectory. The black, red, green, blue, and cyan lines are for the separate torsion angles starting from one end of the molecule. These histories are for block averages of 1 ps duration of the cosine of each angle.

two vectors. For methanol, the structure vectors lie along the oxygen-methyl group bond, the oxygen-hydrogen bond, and the vector normal to the other two. These vectors are indicated in Figure 1 for water and methanol.

The orientation measure for acetonitrile is the distribution of the cosine of the angle between the vector from the carbon site to the methyl site and the vector from the carbon site to the hydrogen or fluorine site on the chain. The cosines of the angles between the vector from the carbon site to the nitrogen site and the vector from the carbon site to the methyl site with the vector from the carbon site to a hydrogen or fluorine site are mirror images about $\pi/2$.

Initial results for the time history of the torsion angles, ϕ , suggested that transitions between *trans* and *gauche* conformations were rare events on the 100 ps time scale. This was checked and confirmed with a set of 10 ns duration runs for each of the systems examined. The rare transitions occur over intervals of 2 to 3 ps, suggesting that the transitions involve cooperative motion of the solvent molecules. For octane and perfluorooctane in methanol, the time history of the five cos ϕ 's are shown in Figure 2. Similar results are found for the other solvents and are not shown here.

The results for the conformation of octane in the solvents are summarized in Table 2, where the fraction of the time each of the five torsion angles were in the *gauche* conformation is

TABLE 2: Fraction of *Gauche* Defects Found for 10 ns Trajectories in Each of the Carbon Backbone Torsion Angles of Octane and the Fraction of the All-*Trans* Conformations for T = 290 K

solvent	1	2	3	4	5	all-trans
H ₂ O	0.0664	0.0875	0.0673	0.0440	0.0718	0.6925
MeOH	0.0556	0.0259	0.0302	0.0440	0.0586	0.7965
MeCN	0.0511	0.0530	0.0275	0.1120	0.0504	0.7221
H ₂ O-MeOH	0.0579	0.0320	0.0241	0.0593	0.0158	0.8305
H ₂ O-MeCN	0.0420	0.0598	0.0534	0.0793	0.0861	0.7046

TABLE 3: Fraction of *Gauche* Defects Found for 10 ns Trajectories in Each of the Carbon Backbone Torsion Angles of Perfluorooctane and the Fraction of the All-*Trans* Conformation for T = 500 K

solvent	1	2	3	4	5	all-trans
H ₂ O	0.0184	0.0087	0.0107	0.0181	0.0324	0.9149
MeOH	0.1048	0.0159	0.0010	0.0122	0.0064	0.9508
MeCN	0.0185	0.0169	0.0212	0.0208	0.0243	0.9012
H ₂ O-MeOH	0.0000	0.0000	0.0000	0.0000	0.0000	1.0000
H ₂ O-MeCN	0.0000	0.0033	0.0000	0.0000	0.0000	0.9967

listed along with the fraction of the time the molecule was in the all-*trans* conformation. Note that the sum of the fractions is only slightly larger that 1, indicating that the simultaneous presence of two *gauche* bends is a rare event.

For each of the solvents at 290 K, the perfluorooctane remained in the all-*trans* conformation for the entire 10 ns duration. As a check on the plausibility of this result, another set of 10 ns duration runs were made for perfluorooctane in each of the solvents at a temperature of 500 K at the same density. The results are summarized in Table 3. For the neat solvents, the fraction of the time the all-*trans* conformation is 0.9 to 0.95, so the molecule can develop *gauche* conformations at elevated temperatures. For the aqueous solvents, the barrier to forming *gauche* bends is quite high, as essentially no *gauche* conformations were found at 500 K.

Our conclusion from these long runs is that octane in these solvents at amibient conditions will exist in the all-*trans* conformation 70–80% of the time, while perfluorooctane only rarely develops *gauche* bends. The results presented below are averaged over the conformations sampled and are taken to be representative of these systems. The equilibrium distribution of *gauche* conformations is, in principle, obtainable using an appropriate Monte Carlo simulation method.^{37,38}

Results: Neat Solvents

The results for the individual solvents with octane and perfluorooctane are presented separately in this section. The first case is for water, the second is for methanol, and the third is for acetonitrile as the solvent. These cases provide a basis for a discussion of how the local environment changes when the solvent is an aqueous mixture.

Water. The various pair functions involving water and octane and water and perfluorooctane are shown in Figure 3. The upper panels are for the oxygen site of water and the sites of the solute, while the lower panel is for the hydrogen sites of water and the corresponding sites of the solute. The black lines are for the end-methyl carbon sites, the red lines are for the interiormethylene carbon sites, and the green lines are for the hydrogen or fluorine sites.

The features of these functions that occur at the smallest separations involve the hydrogen and fluorine sites of the solute. These are the green curves in Figure 3. For this reason, we next



Figure 3. The pair distribution functions, normalized to unity for large separations, are shown for water-octane (left panels) and for water-perfluorooctane (right panels). The upper panels are for the water-oxygen solute-hydrogen or -fluorine site pair functions, and the lower panels are for the water-hydrogen solute-hydrogen or -fluorine site pair functions. The lines are described in the text.



Figure 4. The cumulative number of solvent molecules, $\langle N(r) \rangle$, within a distance *r* of hydrogen and fluorine sites is displayed. The inset shows the average distance of closest approach, $\langle r_{\min} \rangle$, for each of the hydrogen and fluorine sites. The black lines are for water—octane, and the red lines are for water—perfluorooctane.

examine the orientation of water molecules "close" to the hydrogen and fluorine sites of the solutes.

The quantity $\langle N(r) \rangle$ is the cumulative number of solvent molecules within a distance *r* of a hydrogen or fluorine site. The average is over all sites and over the duration of a 10 ns run. We take "close" to be within the distance *R* where $\langle N(R) \rangle \approx 1$. *R* is used to characterize the first solvation shell. $\langle N(r) \rangle$ is shown in Figure 4. The inserts show the average distance of closest approach, $\langle r_{\min} \rangle$, for each of the 18 hydrogen or fluorine sites. For water-octane (black line), $R \approx 3$ Å, and for water-perfluorooctane (red line) $R \approx 3.3$ Å. Note that *R* is close to the mean value of the $\langle r_{\min} \rangle$ for the sites, but slightly larger. Also, *R* is significantly smaller than the distance on the order of 7 Å where pair functions approach unity.

An interesting feature is $D(\cos \phi)$, the distribution of angles between the dipole moment of the water and the vector from



Figure 5. The distribution of the cosines of the angles between the dipole moment vector of water and the oxygen-hydrogen or oxygen-fluorine site of the solute is shown. The lines are described in the text. The curves are normalized so that the integral over $\cos \psi$ equals the average number of molecules in the shell, as described in the text.

the oxygen site of the water to the hydrogen or fluorine site of the solute. These distributions are shown in Figure 5 for water molecules for shells of 0.5 Å thickness and inner radii of 2.5, 3.0, and 3.5 Å centered at a hydrogen or fluorine site of the solute. The distributions are averaged over all of the hydrogen or fluorine sites. The solid lines are for the shell of 2.5 Å radius, the dashed lines are for the next shell, and the dash-dot lines are for the third shell. The water-octane case is shown in the right panel, and the water-perfluorooctane case is shown in the left panel. The different amplitudes of the curves are related to the total average number of water molecules in the shells, as indicated in Figure 4.

The results in Figure 5 indicate that the water-oxygen site is preferentially oriented toward the hydrogen sites of octane. The opposite trend is found for water and perfluorooctane so that the water-oxygen site tends to point away from the fluorine sites. This is a consequence of the charges on the water-oxygen site (negative), octane-hydrogen sites (positive), and perfluorooctane-fluorine sites (negative). The explicit values of the charges are listed in the Appendix. This preferential orientation of water and the related features of the other systems show the importance of including the electrostatics explicitly in the octane and perfluorooctane models. This is not an example of "hydrogen bonding" between water and octane, as the sharp peak characteristic of hydrogen bonding between water molecules is not present in Figure 3.

The distributions for the angles made with the other two internal structure vectors for water are fairly uniformly distributed and are not considered further.

Methanol. There are nine site—site pair functions for the methanol—octane system. The one set described here is the most useful one for characterizing the immediate environment of the solute. The methanol—oxygen site and octane—hydrogen site functions are shown in the left panel of Figure 6 and the corresponding perfluorooctane-fluorine site functions are shown in right panel. The black lines are for the methyl—carbon sites of the solute, the red lines are for the methylene—carbon sites of the solute, and the green lines are for the hydrogen (or fluorine) sites of the solute.

The closest encounters are between the methanol-oxygen site and the hydrogen or fluorine sites of the solute. The quantities $\langle N(r) \rangle$ and $\langle r_{min} \rangle$ for methanol are shown in Figure 7. The black lines are for octane, and the red lines are for



Figure 6. The site—site pair functions for the methanol—oxygen site and the methyl—carbon sites (black line), methylene—carbon sites (red line) and the hydrogen (or fluorine) sites (green line) of the solute. These functions are normalized to unity at large separations. The left panel is for octane, and the right panel is for perfluorooctane.



Figure 7. The cumulative number of neighbors per site, $\langle N(r) \rangle$, and the average distance of closest approach, $\langle r_{\min} \rangle$, are shown for the oxygen site of methanol to the hydrogen sites of octane (black lines) and to the fluorine sites of perfluorooctane (red lines).

perfluorooctane. For octane, the solvation shell distance is $R \approx 3.5$ Å, and for perfluorooctane, $R \approx 4.4$ Å.

The orientation of methanol relative to the hydrogen and fluorine sites is indicated in Figure 8 for octane (left panels) and perfluorooctane (right panels). In these figures, the cosine of the angle, ψ , between the vector from the oxygen site to the hydrogen or fluorine site of the solvent and an internal structure vector described in Figure 1 is shown for three shells of thickness 0.5 Å and inner radius of 3.0, 3.5, and 4.0 Å reading from the top to bottom panels of the figures. The black lines are for the vector from the oxygen to the methyl site, and the red lines are for the vector from the oxygen to the hydrogen site of the methanol molecule.

Figure 7 indicates that the octane molecule is more closely solvated than the perfluorooctane molecule by methanol. Figure 8 indicates that the oxygen-to-methyl vector tends to be oriented in the direction of the octane hydrogen sites and more strongly so for the perfluorooctane fluorine sites.

Acetonitrile. The pair functions for octane (left panel) and for perfluorooctane (right panel) and the carbon site of acetonitrile are shown in Figure 9. As is the case with the other solvents, the hydrogen and fluorine sites are "closest" to the solvating fluid. Octane is a bit more closely solvated by acetonitrile than is perfluorooctane.

The closest encounters are between the acetonitrile-carbon site and the hydrogen or fluorine sites of the solute. The quantities $\langle N(r) \rangle$ and $\langle r_{\min} \rangle$ for acetonitrile are shown in Figure 10. The black lines are for octane, and the red lines are for perfluorooctane. For octane, the solvation shell distance is $R \approx 3.6$ Å, and for prefluorooctane, $R \approx 3.8$ Å.



Figure 8. The distribution of the cosines of the angles between the structure vectors described in Figure 1 and the vector connecting the methanol-oxygen site and the hydrogen site of octane (left panels) or the fluorine site of perfluorooctane (right panels). The lines are described in the text. The curves are normalized so that the integral over $\cos \psi$ equals the average number of molecules in the shell as described in the text.



Figure 9. The site-site pair functions for the acetonitrile-carbon site and the methyl-carbon sites (black line), methylene-carbon sites (red line), and the hydrogen sites (green line) of the octane (left panel) and for perfluorooctane (right panel) are shown here. These functions are normalized to unity at large separations.

Since acetonitrile is treated as a linear molecule in the united atom representation employed here, there is just one unique orientation measure. Even so, we show both of the distribution of cosines of the angles to illustrate the mirror symmetry about $\cos \psi = 0$.

The orientation measures for the acetonitrile—octane system (left panels) and for the acetonitrile—perfluorooctane system (right panels) are shown in Figure 11. There is a tendancy for the nitrogen site to be oriented in the direction of the octane—hydrogen sites and the methyl site to be oriented toware the perfluorooctane—fluorine sites. This is consistent with the negative charge on the nitrogen site and the positive charge on the methyl site of aceotnitrile.

Results: Mixed Solvents

In this section we examine the results for equimolar mixtures of water-methanol and of water-acetonitrile as solvents for octane and perfluorooctane. Of particular interest are features for the solvent components that are different from those of the neat solvent.

Water-Methanol. The solvent-chain pair correlation functions are shown in Figure 12. The most striking feature of these



Figure 10. The cumulative number of neighbors per site, $\langle N(r) \rangle$, and the average distance of closest approach, $\langle r_{\min} \rangle$, of the carbon site of acetonitrile to the hydrogen sites of octane (black lines) and the fluorine sites of perfluorooctane (red lines) are shown.



Figure 11. The distribution of the cosines of the angles between the structure vectors and the vector connecting the acetonitrile—carbon site and the hydrogen site of octane (left panel) and the fluorine site of perfluorooctane (right panels) are shown here. The black lines are for the carbon-to-methyl vector, and the red lines are for the carbon-to-nitrogen vector. The top panels are for the shell with inner radius 3.0 Å, the middle panels are for the shell with inner radius 3.5 Å, and the bottom panels are for the shell with inner radius 4.0 Å. The curves are normalized so that the integral over $\cos \psi$ equals the average number of molecules in the shell as indicated in Figure 10.

functions is that water is mostly excluded from the first layer of fluid solvating perfluorooctane. This is confirmed by the cumulative number of neighbors shown in Figure 13. The average minimum separations for the sites also reflect this.

The distribution functions related to the orientation of solvating molecules are shown in Figure 14. The upper panels are for the distribution of the dipole moments of water relative to the vector from the oxygen site of water to the hydrogen or fluorine sites of the solute. The lower panels show the distribution of the methanol structure vectors, described in Figure 1, relative to the vector from the oxygen site of methanol to the hydrogen and fluorine sites. The left panels are for octane,



Figure 12. The pair functions for the water oxygen and methanol oxygen sites with the hydrogen and fluorine sites of the solute are shown here. The octane functions are in the left panel, and the perfluorooctane functions are in the right panel. The solid lines are for water oxygen site, and the dashed lines are for the methanol oxygen site. The black lines are for the methyl carbon site, the red lines are for the methylene carbon site, and the green lines are for the hydrogen or fluorine sites of the solute.



Figure 13. The number of water and methanol molecules that are in the near vicinity of the hydrogen and fluorine sites of the solvent are shown. The average number, $\langle N(r) \rangle$ of water molecules within a distance *r* centered on hydrogen or fluorine sites are shown as solid lines, and the corresponding numbers for methanol molecules are shown as dashed lines. The black lines are for octane, and the red lines are for perfluorooctane. The same convention applies to the average minimum approach distance, $\langle r_{min} \rangle$.

and the right panels are for perfluorooctane. The shapes of these curves are similar to the corresponding curves for the neat solvent. Note the different vertical scale for the water-perfluorooctane plots due to the small number of water molecules solvating perfluorooctane. The methyl group of methanol is predominately oriented toward the fluorine site of perfluorooctane.

Water-Acetonitrile. The pair correlation functions for this system shown in Figure 15 reflect the microheterogeneous character of water-acetonitrile mixtures. Water solvates the octane with the exclusion of acetonitrile as indicated in the left panel. For perfluorooctane the situation is reversed, with water being exlcuded from the solvation shell. In both cases, the large distance limit is not reached within 10 Å and is characteristic of a microheterogeneous fluid.²⁰

If we use the criterion $R \approx 1$ for being fully solvated, Figure 16 indicates that octane is fully solvated by molecules within about 3.2 Å, while perfluorooctane has a solvation shell that extends outward from the fluorine sites by more than 5 Å that is primarily composed of acetonitrile.



Figure 14. The distribution of the vectors describing the orientation of water (upper panels) and of methanol (lower panels) are shown for octane (left panels) and perfluorooctane (right panels). The plots with increasing amplitude in each panel are for shells of inner radius 3.0, 3.5, and 4.0 Å, respectively. In the lower panels, the black lines are for the vector from the oxygen to the methyl site, and the red lines are for the vector from the oxygen to the hydrogen site of methanol.



Figure 15. The pair functions for the water—oxygen and acetonitrile—carbon sites with the hydrogen and fluorine sites of the solute are shown here. The octane functions are in the left panel, and the perfluorooctane functions are in the right panel. The solid lines are for water, and the dashed lines are for acetonitrile. The black lines are for the methyl carbon site, the red lines are for the methylene carbon site, and the green lines are for the hydrogen or fluorine sites of the solute.

The distributions of the orientation of the water and acetonitrile molecules shown in Figure 17 have shapes similar to the distributions for the neat solvents.

Discussion

Results of molecular dynamics simulations for determining the solvation structure around octane and perfluorooctane of several liquids used as the mobile phase in RPLC have been presented. The liquids are water, methanol, acetonitrile, and equimolar mixtures of water-methanol and water-acetonitrile.

The 10 ns duration simulations performed in this study provide different conformation distributions for octane and perfluorooctane in these solvents at ambient conditions. Octane is in the all-*trans* 70-80% of the time and has a single gauche bend the rest of the time. The transitions occur over time intervals of 2 ps or so and are distributed widely over the 10 ns interval as illustrated in Figure 2. Perfluorooctane remains in the all-*trans* conformation for the entire 10 ns interval. The



Figure 16. The number of water and acetonitrile molecules that are in the near vicinity of the hydrogen and fluorine sites of the solvent are shown. The cumulative number, $\langle N(r) \rangle$, of water molecules within a distance *r* centered on hydrogen or fluorine sites of octane are shown as solid lines, and the cumulative number of acetonitrile molecules are shown as dashed lines. The black lines are for octane, and the red lines are for perfluorooctane. The same scheme applies to the average distance of closest approach, $\langle r_{min} \rangle$.



Figure 17. The distribution of the vectors describing the orientation of water (upper panels) and of acetonitrile (lower panels) are shown for octane (left panels) and perfluorooctane (right panels). The plots with increasing amplitude in each panel are for shells of 0.5 Å thickness and inner radius 3.0, 3.5, and 4.0 Å, respectively. In the lower panels, the lines are for the vector from the carbon to the methyl site. Note the various vertical scales for these plots.

barrier to transitions is large, as demonstrated by the runs at 500 K summarized in Table 3. The barrier is larger for the aqueous mixtures than for the neat solvents. The basis for the large barrier to conformational change of perfluorooctane in these fluids is outside the scope of the current study.

The pair distribution functions provide a partial view of how these solutes are distributed about the chain molecules, but more refined measures provide a more detailed description. The orientation of the solvents can be described in terms of the orientation distribution of vectors that reflect the structure of the solvents as functions of distance of the solvent from the hydrogen or fluorine sites of the solutes. The local number of

TABLE 4: Potential Parameters for the Atom Types⁴

sites	ε, kJ∙mol ^{−1}	<i>σ</i> , Å	q, $ e $
H ₂ O			
O-O*	0.65	3.1657	-0.8476
$H - H^*$	0.0		0.4238
MeOH			
Me-Me	0.874	3.740	0.2650
0-0	0.7186	3.030	-0.7000
H-H	0.0		0.4350
MeCN			
Me-Me	1.5915	3.5999	0.2690
C-C	0.4166	3.40	0.1290
N-N	0.4166	3.29	-0.3980
C_8H_{18}			
$C_1 - C_1$	0.2761	3.50	-0.18
$C_2 - C_2$	0.2761	3.50	-0.12
H - H	0.1255	2.50	0.06
C_8F_{18}			
$C_1 - C_1$	0.2761	3.50	0.36
$C_2 - C_2$	0.2761	3.50	0.24
F-F	0.2218	2.95	-0.12

"The unlike pair parameters are obtained using the Lorentz-Berthelot mixing rule for the ε and σ parameters.⁵⁹ For octane and perfluorooctane, C_1 is the methyl carbon and C_2 is the methylene carbon.

first shell solvent molecules for the neat liquids is highest for water, intermediate for methanol, and lowest for acetonitrile. This is consistent with the ordering of the density of the liquids. This is not the case for the mixtures as will be discussed below.

The importance of including electrostatics in the interaction model is demonstrated by the orientation of water at small distances from the solutes.⁵¹ For octane, water is primarily orientated with the oxygen sites pointing toward the hydrogen sites of octane and pointing away from the fluorine sites of perfluorooctane. This is consistent with the negative charge on the water oxygen site and the positive charge on the octanehydrogen sites and the negative charge on the perfluorooctane fluorine sites. To a lesser extent, this behavior is found for acetonitrile where the methyl site has a positive charge and the nitrogen site has a negative charge.

For the mixture of water and methanol, the water molecules are partially excluded from the immediate vicinity of the perfluorooctane, while methanol is not excluded from octane. This sort of segregation is even more pronounced for the water-acetonitrile mixture. Actonitrile is slightly excluded from the octane, while water is almost totally excluded from closely approaching the perfluorooctane molecule. The adsorption on the perfluorooctane molecule by methanol and acetonitrile rather than water should have implications for how these mobile phase mixtures may adsorb on fluorinated stationary phase materials and hence influence separations in a chromatographic column. The thermodynamic properties of these systems is a topic for further study.

Appendix

The intermolecular potential parameters for the molecules used in this study are listed in this Appendix in Table 4.

References and Notes

(1) Danielson, N. D.; Beaver, L. G.; Wangsa, J. J. Chromatogr. 1991, 544. 187.

- (2) Dolfinger, R.; Locke, D. C. Anal. Chem. 2003, 75, 1355.
- (3) Jinno, K.; Nakamura, H. Chromatographia 1994, 39, 285.
- (4) Krafft, M. P.; Jeannaux, F.; Leblanc, M.; Reiss, J. G.; Berthod, A. Anal. Chem. 1988, 60, 1969
 - (5) Sadek, P. C.; Carr, P. W. J. Chromatogr. 1984, 288, 25.

- (6) Alvarezzepeda, A.; Barman, B. N.; Martire, D. E. Anal. Chem. 1992, 64, 1978.
- (7) Carr, P. W.; Doherty, R. M.; Kamlet, M. J.; Taft, R. W.; Melander, W.; Horvath, C. Anal. Chem. 1986, 58, 2674.

(8) Dorsey, J. G.; Dill, K. A. Chem. Rev. 1989, 89, 331.

- (9) Stalcup, A. M.; Martire, D. E.; Wise, S. A. J. Chrmoatogr. 1988, 442.1
- (10) Valko, K.; Snyder, L. R.; Glajch, J. L. J. Chromatogr. A 1993, 656, 501.

(11) Vailaya, A.; Horvath, C. J. Chromatogr. A 1998, 829, 1.

- (12) Asthagiri, D.; Ashbaugh, H. S.; Piryatinski, A.; Paulaitis, M. E.;
- Pratt, L. R. J. Am. Chem. Soc. 2007, 129, 10133.
 (13) Ying, P. T.; Dorsey, J. G.; Dill, K. A. Anal. Chem. 1989, 61, 2540. (14) Bako, I.; Megyes, T.; Palinkas, G. Chem. Phys. 2005, 316, 235.
- (15) Bako, I.; Megyes, T.; Grosz, T.; Palinkas, G.; Dore, J. J. Mol. Lig. 2006, 125, 174.
- (16) Kovacs, H.; Laaksonen, A. J. Am. Chem. Soc. 1991, 113, 5596. (17) Nishikawa, K.; Kasahara, Y.; Ichioka, T. J. Phys. Chem. B 2002,
- 106.693. (18) Shin, D. N.; Wijnen, J. W.; Engberts, J. B. F. N.; Wakisaka, A. J. Phys. Chem. B 2002, 106, 6014.

- (19) Takamuku, T.; Tabata, M.; Yamaguchi, A.; Nishimoto, J.; Kumamoto, M.; Wakita, H.; Yam-aguchi, T. J. Phys. Chem B 1998, 102, 8880.
 - (20) Mountain, R. D. J. Phys. Chem. A 1999, 103, 10744.
 - (21) Mountain, R. D. J. Phys. Chem. B 2001, 105, 6556.
- (22) Oldiges, C.; Wittler, K.; Tonsing, T.; Alijah, A. J. Phys. Chem. A 2002, 106, 7147.
 - (23) Gritti, F.; Guiochon, G. J. Chromatogr. A 2005, 1099, 1.
 - (24) Gritti, F.; Guiochon, G. Anal. Chem. 2005, 77, 4257.
- (25) Kazakevich, Y. V.; LoBrutto, R.; Chan, F.; Patel, T. J. Chromatogr. A 2001, 9/3, 75.
 - (26) Poplewska, I.; Antos, D. Chem. Eng. Sci. 2005, 60, 1411.
- (27) Beck, T. L.; Klatte, S. J. In Unified Chromatography; American Chemical Society: Washington, DC, 2000.
- (28) Klatte, S. J.; Beck, T. L. J. Phys. Chem. 1996, 100, 5931.
- (29) Schure, M. A. In Chemically Modified Surfaces; Society of Chemistry Information Services: Cambridge, U.K., 1994.
- (30) Slusher, J. T.; Mountain, R. D. J. Phys. Chem. B 1999, 103, 1354. (31) Zhang, L.; Sun, L.; Siepmann, J. I.; Schure, M. R. J. Chromatogr.
- A 2005, 1079, 127. (32) Zhang, L.; Rafferty, J. L.; Siepmann, J. I.; Chen, B.; Schure, M. R.
- J. Chromatogr. A 2006, 1126, 219. (33) Ashbaugh, H. S.; Pratt, L. R.; Paulaitis, M. E.; Clohecy, J.; Beck,
- T. L. J. Am. Chem. Soc. 2005, 127, 2808.
- (34) Beck, T. L.; Paulaitis, M. E.; Pratt, L. R. The Potential Distribution Theorem and Models of Molecular Solutions; Cambridge University Press: Cambridge, U.K., 2006).

(35) Fouqueau, A.; Meuwly, M.; Bemish, R. J. J. Phys. Chem. B 2007, 111, 10208.

- (36) Rafferty, J. L.; Zhang, L.; Siepmann, J. 1.; Schure, M. R. Anal. Chem. 2007, 79, 6551.
- (37) Sun, L.; Siepmann, J. I.; Schure, M. R. J. Phys. Chem. B 2006, 110, 10519
- (38) Sun, L.; Siepmann, J. I.; Schure, M. R. J. Chem. Theory Comput. 2007, 3, 350.
- (39) Valkó, K.; Espinosa, S.; Du, C. M.; Bosch, E.; amd, C.; Brevan, M. R.; Abraham, M. H. J. Chromatogr. A 2001, 933, 73.
- (40) Hong, D.; Hoshino, M.; Kuboi, R.; Goto, Y. J. Am. Chem. Soc. 1999, 121, 8427
- (41) Fioroni, M.; Burger, K.; Mark, A. E.; Roccatano, D. J. Phys. Chem. 2000, 104, 12347.
 - (42) Chitra, R.; Smith, P. E. J. Phys. Chem. B 2000, 104, 5854.
 - (43) Chitra, R.; Smith, P. E. J. Chem. Phys. 2001, 114, 426.
 - (44) Buck, M. Q. Rev. Biophys. 1998, 31, 297.

(45) Walgers, R.; Lee, T. C.; Cammers-Goodwin, A. J. Am. Chem. Soc. 1998, 120, 5073.

- (46) Roccatano, D.; Colombo, G.; Fioroni, M.; Mark, A. E. Proc. Natl. Acad. Sci. U.S.A. 2002, 99, 12179.
- (47) Fioroni, M.; Díaz, M. D.; Burger, K.; Berger, S. J. Am. Chem. Soc. 2002, 124, 7737
- (48) Díaz, M. D.; Fioroni, M.; Burger, K.; Berger, S. Chem.-Eur. J. 2002, 8, 1663.
 - (49) Conio, G.; Patrone, E.; Brighetti, S. J. Biol. Chem. 1970, 245, 3335.
- (50) Ellis, D. A.; Denkenberger, K. A.; Burrow, T. E.; Marbury, S. A. J. Phys. Chem. A 2004, 108, 10099.
- (51) Knochenhauer, G.; Reiche, J.; Brehmer, L.; Barberka, T.; Woolley, M.; Tredgold, R. J. Chem. Soc., Chem. Commun. 1995, 1619.
- (52) Berendsen, H. J. C.; Grigera, J. R.; Straatsma, T. P. J. Phys. Chem. 1987, 91, 6269.
 - (53) van Leeuwen, M. E.; Smit, B. J. Phys. Chem. 1995, 99, 1831.
- (54) Edwards, D. M. F.; Madden, P. A.; McDonald, I. R. Mol. Phys. 1984, 57, 1141.
 - (55) Mountain, R. D. J. Chem. Phys. 1997, 107, 3921.

(56) Gee, P. J.; Gunsteren, W. F. V. Mol. Phys. 2006, 104, 477.
(57) Jorgensen, W. L.; Maxwell, D. S.; Triado-Rives, J. J. Am. Chem. Soc. 1996, 118, 11225 Intermolecular potential parameters for the alkanes are found in supplemental material.

(58) Watkins, E. K.; Jorgensen, W. L. J. Phys. Chem. A 2001, 105, 4118.

(59) Allen, M. P.; Tildesley, D. J. Computer Simulation of Liquids; Clarendon Press: Oxford, 1987; p 21.

- (60) Sangster, M. J. L.; Dixon, M. Adv. Phys. 1976, 25, 247.
- (61) Evans, D. J.; Murad, S. Mol. Phys. 1977, 34, 327.

(62) Mackay, A. L. Acta Crystallogr. 1984, A40, 165.

- (63) Sonnenschein, R. J. Comput. Phys. 1985, 59, 347.
- (64) Rapaport, D. C. J. Comput. Phys. 1985, 60, 306.
- (65) Martys, N. S.; Mountain, R. D. Phys. Rev. E 1999, 59, 3733.

(66) Pártay, L.; Jedlovszky, P.; Vincze, Á.; Horvai, G. J. Phys. Chem. B 2005, 109, 20493.

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