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UCRL-JRNL-228620

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March 4, 2007

Fluid Phase Equilibria

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# Prediction of the bubble point pressure for the binary mixture of ethanol and 1,1,1,2,3,3,3-heptafluoropropane from Gibbs ensemble Monte Carlo simulations using the TraPPE force field

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## Abstract

Configurational-bias Monte Carlo simulations in the Gibbs ensemble using the TraPPE force field were carried out to predict the pressure–composition diagrams for the binary mixture of ethanol and 1,1,1,2,3,3,3-heptafluoropropane at 283.17 and 343.13 K. A new approach is introduced that allows to scale predictions at one temperature based on the differences in Gibbs free energies of transfer between experiment and simulation obtained at another temperature. A detailed analysis of the molecular structure and hydrogen bonding for this fluid mixture is provided.

## 1 Introduction

The ability to predict phase equilibria and other thermophysical properties for binary and multicomponent systems is of great importance to the chemical and pharmaceutical industry. The design of process equipment depends largely on the accuracy of the available thermophysical data. With advances in the efficiency of sampling schemes (Monte Carlo or molecular dynamics), the accuracy of force fields, and the increase in computer speeds, molecular simulations are increasingly being used to compute phase equilibria and other thermophysical properties. Most important, the utility of molecular simulations extends far beyond thermophysical property prediction because molecular simulation can provide unique understanding on molecular-level details of complex chemical systems. This molecular-based knowledge is essential for the development of novel processes, while accurate thermophysical data are needed for incremental improvements to existing technologies.

Hydrofluorocarbons (HFCs) are finding many applications including propellants in metered dose inhalers (MDIs),<sup>1–3</sup> cleaning solutions,<sup>4,5</sup> and refrigerants.<sup>4</sup> HFCs have largely replaced ozone depleting chlorofluorocarbons (CFCs) in industrial and pharmaceutical formulations.

The work presented here is in response to the State Conditions Transferability problem of the 2006 Industrial Fluid Properties Simulation Challenge, IFPSC (<http://fluidproperties.org/challenge/third/challenge.html>). The task is to predict the bubble point pressure of the binary mixtures of ethanol and 1,1,1,2,3,3,3-heptafluoropropane (HFC-227ea) at 343.13 K for various liquid mole fractions, where one is supposed to utilize experimental data for the bubble point pressures of this mixture at 283.17 K. The main tools used in this work are the TraPPE force field and the Gibbs ensemble Monte Carlo approach. The next sections describe the force field and simulation details. This is followed by the presentation of the simulation results for the pressure–composition diagram and of a novel scaling approach. Thereafter, a detailed analysis of molecular structure and hydrogen bonding is given.

## 2 Force Field

The TraPPE (transferable force field for phase equilibria) force field has been very successful in predicting thermophysical properties of organic compounds such as alkanes, alkenes, arenes, alcohols, ethers, ketones, aldehydes, thiols and thioethers.<sup>6–14</sup> This force field derives its strength from the functional simplicity and transferability. To this extent, the parameterization follows a stepwise approach during which the interaction parameters for a given site are determined from fits to experimental vapor–liquid coexistence curves (spanning usually the entire liquid range). In special cases, not only vapor–liquid equilibria for neat systems are considered, but also fluid phase equilibria for binary mixtures and solid–fluid equilibria are included.<sup>15</sup> There are two representations for CH<sub>x</sub> segments available in the TraPPE force field: united-atom (UA) and explicit-hydrogen (EH) models. In the united-atom version, an entire CH<sub>x</sub> segment is represented by a single interaction site located at the position of the carbon atom. This reduction in the number of interaction sites results in substantial savings of computer time. In the case of the TraPPE-EH force field, additional interaction sites are placed at the C–H bond centers.<sup>8</sup> For both the UA and EH models, polar hydrogens are always treated explicitly with an interaction site located at hydrogen’s atomic position.

Table 1: TraPPE parameters for non-bonded interactions of HFC-227ea and ethanol

Interaction site	$\sigma$ (Å)	$\epsilon/k_B$ (K)	$q$ (e)	source
C (CF <sub>3</sub> )	3.55	36.0	+0.256	this work
C (CFH)	3.60	46.5	+0.068	this work
F (CF <sub>3</sub> )	2.95	24.3	-0.090	this work
F (CFH)	2.95	24.3	-0.124	this work
H (CFH)	2.40	18.5	+0.084	this work
CH <sub>3</sub>	3.73	98.0	-	6
CH <sub>2</sub>	3.95	46.0	+0.265	10
O (OH)	3.20	93.0	-0.700	10
H (OH)	-	-	+0.435	10

The TraPPE-UA and TraPPE-EH force fields divide the total potential energy into pairwise additive non-bonded interactions and bonded terms for pairs of atoms separated by one, two, or three bonds. The non-bonded interactions are represented by Lennard-Jones (LJ) and Coulomb potentials

$$U(r_{ij}) = 4\epsilon_{ij} \left[ \left( \frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left( \frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] + \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}, \quad (1)$$

where  $r_{ij}$ ,  $\sigma_{ij}$ ,  $\epsilon_{ij}$ ,  $q_i$ ,  $q_j$ , and  $\epsilon_0$  are the distance between two interaction sites, the LJ diameter and well depth for this pair of sites, the partial atomic charges on sites  $i$  and  $j$ , and the permittivity of the vacuum, respectively. If the two interaction sites are of different types, then the Lorentz-Berthelot<sup>16,17</sup> combining rules are used to compute the unlike LJ parameters:

$$\sigma_{ij} = \frac{(\sigma_{ii} + \sigma_{jj})}{2} \quad (2)$$

$$\epsilon_{ij} = \sqrt{\epsilon_{ii}\epsilon_{jj}}. \quad (3)$$

The non-bonded LJ parameters and charges for the ethanol and HFC-227ea are listed in Table 1.

In the TraPPE force field, molecules are treated as semiflexible chains. The bond lengths (1-2 interactions) are fixed at experimentally observed values or at those obtained from electronic structure calculations. However, if it is desirable for computational convenience (e.g., in molecular dynamics simulations) to use flexible bond lengths, then the bond stretching force constants from other common force fields may be used because it has been shown that fluid phase equilibria are insensitive to the small fluctuations encountered when bond stretching is treated by harmonic potentials<sup>18</sup> (as long as the nonbonded interactions do not cause a shift of the bond length from the equilibrium position of the harmonic potential). Bond angle bending is governed by harmonic potentials and torsional flexibility is controlled by one of two cosine series for a given dihedral angle

$$U^{\text{bend}}(\theta) = \frac{1}{2}k_\theta [\theta - \theta_0]^2, \quad (4)$$

$$U^{\text{tors}}(\phi) = c_1[1 + \cos(\phi + A)] + c_2(1 - \cos[2(\phi + A)]) + c_3(1 + \cos[3(\phi + A)]) \quad (5)$$

$$U^{\text{tors}}(\phi) = c_0 + \sum_{i=1}^6 c_i \cos[i(\phi + A)] \quad (6)$$

where  $\theta$ ,  $k_\theta$ ,  $\phi$ ,  $C_i$ , and  $A$  are the bond angle, the associated harmonic force constant, the dihedral angle (with the trans conformer considered to have a dihedral angle of zero), the constants for the cosine series, and an offset for the dihedral angle, respectively. The interaction sites involved in any of the bonded interaction are excluded for the non-bonded interactions. Hence, 1-2, 1-3 and 1-4 interactions are excluded when computing LJ and Coulomb energies.

Table 2: TraPPE bond lengths for HFC-227ea and ethanol

bond type	length (Å)	source
(CF <sub>3</sub> ) <sub>2</sub> FC–H	1.08	this work
(CF <sub>3</sub> )–CFH	1.54	this work
C–F	1.33	this work
CH <sub>3</sub> –CH <sub>2</sub>	1.54	19
CH <sub>2</sub> –O	1.43	20
O–H	0.945	20

Table 3: TraPPE bending parameters for HFC-227 and ethanol

bend type	$\theta_0$ (deg)	source	$k_\theta/2k_B$ (K/rad <sup>2</sup> )	source
C–C–C	115.90	this work	31250	21
C–C–F	109.50	this work	25150	22
C–CF–H	108.30	this work	20120	22
F–C–F	109.47	this work	38731	22
F–C–H	109.60	this work	20120	22
CH <sub>3</sub> –CH <sub>2</sub> –O	109.47	20	25200	23
CH <sub>2</sub> –O–H	108.50	20	27729	23

The TraPPE parameters for bond lengths, bond bending and torsional degrees for freedom needed for HFC-227ea and ethanol are listed in Tables 2, 3, and 4, respectively.

For the ethanol, the existing TraPPE–UA force field<sup>10</sup> was used without any modification. Previous applications of the TraPPE–UA alcohol force field include calculations of octanol–water partition constants,<sup>24</sup> an investigation of the vapor–liquid interfacial properties of mutually saturated 1-butanol/water solutions,<sup>25</sup> an exploration of vapor–liquid nucleation in ethanol/water mixtures,<sup>26</sup> the computation of Henry’s law constants of small gas molecules in ethanol,<sup>27</sup> and a detailed analysis of the structure of a reversed-phase liquid chromatography system for mobile phases with various methanol/water compositions.<sup>28</sup>

TraPPE parameters were not available for HFC-227ea, and a new force field was developed in accordance with the TraPPE philosophy of parameterization. Since HFC-227ea contains potentially five different types of interaction sites, it is not possible to fit all parameters uniquely from a comparison with only the vapor–liquid coexistence of HFC-227ea. Thus, exploratory simulations were carried for tetrafluoromethane and hexafluoroethane to find suitable LJ parameters for a carbon atom that is bonded to three fluorine and one other carbon atom, and for a fluorine atom that is bonded to this type of carbon atom.

Bond lengths and bending angles for HFC-227ea were obtained from the gas-phase optimized geometry (but keeping already existing C–C and C–H bond lengths because these were close to those found in the optimized structure). The bending constants were taken from the OPLS-AA force field.<sup>22</sup> The torsional parameters were obtained from *ab initio* calculations with Gaussian 03 package.<sup>29</sup> The MP2/6-311+G\*\*//HF/6-311G\*\* level of theory/basis sets were used for single point energy calculations (torsional potential) and geometry optimization (bond lengths, angles and relax other degrees of freedom during the torsional potential energy scan).

The (fixed) partial atomic charges for the HFC-227ea molecule were obtained from an electronic structure calculation (B3P86 functional with 6-311G\* basis set) in an implicit solvation model; specifically, the partial charges are the CM4 atomic charges computed for the Cramer-Truhlar solvation model<sup>6,30</sup> in an implicit 1-octanol solvent (the “universal” solvent used for the development of the TraPPE model<sup>31</sup>) using the Minnesota Gaussian solvation module.<sup>32</sup> Experimental saturated liquid densities and vapor pressures for pure HFC-227ea<sup>33</sup> were used to determine the LJ parameters for the central carbon and the hydrogen atoms while keeping the LJ parameters for the fluorine atom fixed. (It should be noted that this does not result in a unique parameter fit because a single vapor–liquid coexistence

Table 4: TraPPE torsional parameters (in units of K) for HFC-227 and ethanol

Torsion type	eq.	$c_0/k_B$	$c_1/k_B$	$c_2/k_B$	$c_3/k_B$	$c_4/k_B$	$c_5/k_B$	$c_6/k_B$	$A$	source
F-C-C-F	5	2543.4	1.3	-8.6	-1261.6				$\pi$	this work
F-C-C-C	5	1985.6	-0.2	4.1	-992.5				$\pi$	this work
F-C-C-H	6	819.0	-6.2	-43.9	895.4	42.4	-16.1	87.3	$\pi$	this work
CH <sub>3</sub> -CH <sub>2</sub> -O-H	5	0.0	209.8	-29.2	187.9				0	<sup>20</sup>

curve is used for two different atom types.)

### 3 Simulation Details

#### 3.1 Force Field Development

We employed coupled-decoupled configurational-bias Monte Carlo (CBMC) simulations<sup>7,34</sup> in the constant-volume Gibbs ensemble<sup>35,36</sup> to compute the vapor-liquid coexistence curve for neat HFC-227ea. Simulations were carried out at five temperatures (spanning the range from 250 to 350 K). The simulated system consisted of 250 HFC-227ea molecules which is sufficient to maintain a box length larger than twice the cut-off distance ( $r_{\text{cut}} = 14 \text{ \AA}$ ) used for the LJ potential and the real space part of Ewald summation. The total volume for the two phases was adjusted to allow for approximately 40 to 60 molecules in the vapor phase. Analytical tail corrections<sup>37</sup> were used to account for the LJ interactions beyond  $r_{\text{cut}}$ . An Ewald summation<sup>37,38</sup> with tin foil boundary condition was used to calculate the Coulombic interactions. The Ewald sum convergence parameter was obtained using the equation  $\kappa = 3.2/r_{\text{cutchg}}$ , where  $r_{\text{cutchg}}$  is the charge-charge interaction cutoff for the real space part of the Ewald summation, which is set equal to  $r_{\text{cut}}$ . For the reciprocal space, the upper bound for the number of lattice vectors,  $\mathbf{K}_{\text{max}}$ , was set to 10.

Constant-volume Gibbs ensemble Monte Carlo simulations employ five different kinds of Monte Carlo moves to sample the configurational part of the phase space: translations of the center of mass, rotations around the center of mass, conformational changes using CBMC, volume exchanges between the two simulation boxes, and CBMC particle swaps between the two boxes. The maximum displacements for translational, rotational, and volume moves were adjusted to achieve about 50% acceptance. To increase the efficiency of sampling the configurational space, different maximum displacements were used for the vapor box and the liquid box. Simulations were started with placing the molecules on a lattice, then 1000 Monte Carlo cycles (where a cycle consists of  $N = 250$  randomly selected trial moves) at high temperature were used to melt the initial crystalline lattice. Another 5000 Monte Carlo cycles at a temperature close to the critical temperature were used to cool the system. During the melting and cooling stages, only translational, rotational and conformation change moves were employed. After cooling, the system was equilibrated at the desired simulation temperature for at least 50000 Monte Carlo cycles using all five move types. The probabilities for volume and swap moves were adjusted to yield at least one accepted move of each kind every 10 to 50 Monte Carlo cycles. The production periods consisted of 50000 Monte Carlo cycles. The standard deviation for a given property was estimated by dividing the production run in 5 blocks.

The critical temperature and density of HFC-227ea were estimated from weighted linear fits of sub-critical simulation data to the density scaling law<sup>39</sup> for the critical temperature

$$\rho_{\text{liq}} - \rho_{\text{vap}} = B(T - T_c)^\beta \quad (7)$$

and to the law of rectilinear diameters<sup>40</sup> for the critical density

$$\frac{1}{2}(\rho_{\text{liq}} + \rho_{\text{vap}}) = \rho_c + A(T - T_c) \quad (8)$$

and for the critical pressure, the Reidel equation<sup>41</sup> is used

$$\ln P = A + \frac{B}{T} + C \ln T + DT^2 \quad (9)$$

where  $\beta$ ,  $A$ ,  $B$ ,  $C$  and  $D$  are the universal Ising critical exponent and fitting constants, respectively.

Table 5: Numerical data for the vapor–liquid coexistence curve of neat HFC-227ea calculated for the TraPPE force field: saturated vapor pressure, vapor density, liquid density and their respective standard deviations, and heat of vaporization.

$T$ (K)	$P^{\text{sat}}$ (kPa)	$\rho_{\text{vap}}$ (kg/m <sup>3</sup> )	$\rho_{\text{liq}}$ (kg/m <sup>3</sup> )	$\Delta H_{\text{vap}}$ (kJ/mol)
250.0	98.5 ± 9.3	8.3 ± 0.8	1565 ± 6	22.1
275.0	234 ± 22	19.1 ± 1.8	1472 ± 9	20.3
300.0	581 ± 43	47.1 ± 4.8	1381 ± 5	18.1
325.0	973 ± 49	77.3 ± 5.3	1253 ± 2	15.6
350.0	1830 ± 120	167 ± 30	1099 ± 34	11.7

### 3.2 Binary system of HFC–227ea and ethanol

The simulation set up for the binary mixture of ethanol and HFC–227ea was very similar to the one used for the force field development. Again, we used the constant-volume version of the Gibbs ensemble because it is substantially easier to adjust the total volume to yield a satisfactory phase ratio for a given overall composition, then to adjust the overall composition for a given pressure. Long-range LJ and Coulombic interactions were accounted for using tail corrections and Ewald summations, respectively, with the same parameter as for the neat HFC-227ea simulations. The binary systems consisted of a total of 600 molecules, of which approximately 200-250 molecules were in the vapor phase. The initial systems were set up with varying mole fractions for the binary system. Simulations were started by randomly placing ethanol and HFC-227ea molecules on a lattice the in liquid and vapor phase. 5000 Monte Carlo cycles at 1000 K were used to melt the initial structure in the condensed phase box. Melting was followed by 10000 Monte Carlo cycles of cooling at 400 K. The systems were further equilibrated at the temperatures of interest, namely 283.17 and 343.13 K, for 20000 Monte Carlo cycles. During melting and thermal equilibration only translational, rotational, and CBMC moves were employed. At this stage volume and swap moves were turned on and an additional  $10^5$  Monte Carlo cycles were used to equilibrate the system. During the swap moves, molecule types were randomly selected with equal probability. The probabilities for the volume, swap, CBMC regrowth, translational, and rotational moves were set to 0.001, 0.199, 0.2, 0.3, and 0.3, respectively.

## 4 Results and Discussions

### 4.1 Neat HFC-227ea

The vapor–liquid coexistence curve and Clausius–Clapeyron plot for neat HFC-227ea calculated for the TraPPE force field are compared to experimental data<sup>33</sup> in Figures 1 and 2, respectively. From Figure 1, it clear that the force field developed here can accurately describe the saturated liquid densities for neat HFC-227ea over a wide temperature range. It is evident from Figure 2 that the saturated vapor pressures are slightly overestimated at the lower temperatures. Table 5 lists the numerical values of the saturated vapor pressures, saturated vapor densities, saturated liquid densities, and heats of vaporization obtained for the TraPPE force field.

A comparison of the experimental critical temperature, pressure and density, and normal boiling point of neat HFC-227ea<sup>33</sup> and those computed for the TraPPE force field is given in Table 6. The TraPPE force field yields excellent results with errors of 1.1%, 1.5%, 8%, and 1.6% for the  $T_c$ ,  $\rho_c$ ,  $P_c$ , and  $T_b$ , respectively. For  $\rho_c$  and  $P_c$ , the experimental data lie within one standard deviation of the predicted data. As mentioned above, the saturated vapor pressures at lower temperatures are slightly overestimated, which leads to an underestimation of  $T_b$  by 4 K.

### 4.2 Vapor–liquid Equilibria for the Binary Mixture of Ethanol and HFC-227ea

#### 4.2.1 Predictions at 283.17 K

The constant-volume Gibbs ensemble approach allows the user to specify the total mole fraction and the total volume for the simulated two-phase system, but not to constrain the liquid-phase mole fraction. Thus, it is not possible to carry out Gibbs ensemble simulations that yield exactly the liquid-phase mole fractions specified in the Challenge task. Hence, to provide a good sweep of the isothermal pressure–composition diagram, simulations were carried out for 14 and 24 different mole fractions (see Tables 7 and 8) at 283.17 and at 343.13 K, respectively.

Figure 3 shows the pressure–composition diagrams at  $T = 283.17$  K measured experimentally (<http://fluidproperties.org/challenge/third/2006state.html>), obtained from simulations with the TraPPE force field, and

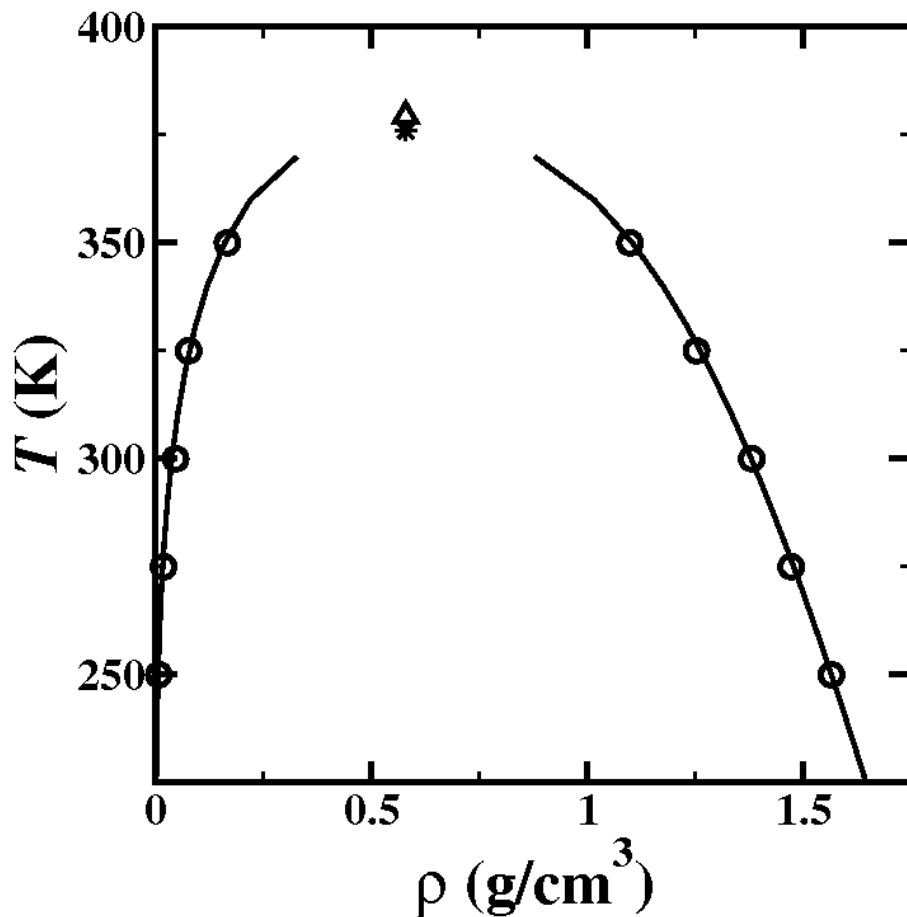


Figure 1: Vapor–liquid coexistence curve for HFC-227ea. Solid lines and asterisk represent experimental coexistence data and critical point,<sup>33</sup> while circles and triangle are the corresponding results obtained for the TraPPE model, respectively. Standard deviations for the computed coexistence densities are smaller than the symbol size.

Table 6: Critical constants and normal boiling of neat HFC-227ea as measured experimentally<sup>33</sup> and calculated for the TraPPE force field.

Property	Expt.	Sim.
$T_c$ (K)	374.83	$379 \pm 2$
$\rho_c$ (kg/m <sup>3</sup> )	588	$579 \pm 9$
$P_c$ (kPa)	2911.6	$3068 \pm 567$
$T_b$ (K)	255.0	$251 \pm 1$



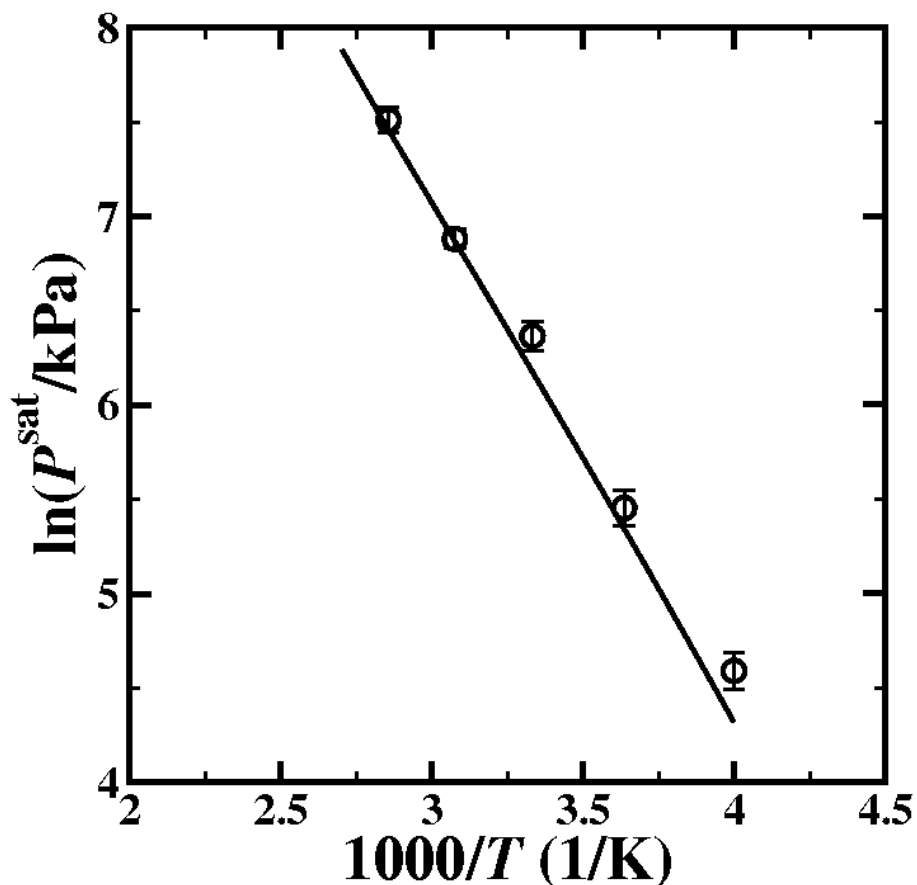


Figure 2: Clausius–Clapeyron plot for HFC-227ea. Solid line and circles depict the experimental data<sup>33</sup> and simulation results, respectively.

calculated using the COSMOtherm/C2.1 thermodynamics software and sigma profiles released with this software<sup>42</sup> which is an efficient implementation of the COSMO-RS method<sup>43,44,48</sup>. The numerical values of the simulation data are listed in Table 7. The TraPPE force field yields an excellent prediction for the saturated pressures of the neat ethanol and HFC-227-*ea* with the experimental data falling into the uncertainty range of the simulation results. However, the TraPPE force field is not able to reproduce the initial dip in the bubble point pressure observed experimentally, i.e., whereas the experimental bubble point pressure decreases by about 4% upon addition of about 5% ethanol, the bubble point pressure obtained for the TraPPE model is essentially unchanged. Thus, it appears that the TraPPE force field underestimates the ethanol–HFC-227*ea* interactions at low ethanol mole fraction in the liquid phase. At this point, one may speculate that, at very low ethanol mole fractions, weak hydrogen bonds are formed between ethanol and HFC-227*ea* molecules, whereas ethanol might self-aggregate as its concentration reaches a certain threshold. A detailed analysis of hydrogen bonding and aggregation will be provided in section 4.3.

For comparison, the COSMOtherm/C2.1<sup>42</sup> calculations yield an underestimation of the neat HFC-227*ea* vapor pressure by about 28% (that for ethanol agrees very well with experiment) and a bubble pressure curve that appears close to Raoult’s law behavior<sup>41</sup> in contrast to the rather non-ideal behavior found for the experimental and TraPPE data. Thus, the COSMOtherm/C2.1 calculations point to a liquid phase which is relatively homogeneous and does not exhibit preferential enhancements of local compositions.

Here it should be emphasized that Klamt and Eckert<sup>46,47</sup> obtained significantly better predictions using the COSMO-RS model and an earlier parametrization, BP\_TZVP\_C11\_0101.<sup>44,45</sup> The C2.1 parametrization used here allows for hydrogen bonding to the polar hydrogen in HFC-227*ea*, but the BP\_TZVP\_C11\_0101 parametrization sets its hydrogen bond capability to zero.<sup>46</sup> In their submission to this challenge, Klamt and Eckert<sup>47</sup> explicitly considered fine-tuning of the hydrogen bond capability for the HFC-227*ea* hydrogen and would undoubtedly find that the standard value in the C2.1 parametrization need to be adjusted. Thus, with this fine-tuning one may expect that

Table 7: Simulation details and pressure–composition data for simulations with the TraPPE force field of the binary mixture of ethanol and HFC-227ea at 283.17 K: numbers ethanol and HFC-227ea molecules, liquid and vapor-phase mole fractions, and bubble point pressures.

$N_{\text{ethanol}}$	$N_{\text{HFC}}$	$x_{\text{ethanol}}$	$y_{\text{ethanol}}$	$P$ (kPa)
0	600	0.0	0.0	$284 \pm 12$
20	580	$0.061 \pm 0.001$	$0.0039 \pm 0.0005$	$288 \pm 5$
50	550	$0.151 \pm 0.003$	$0.0061 \pm 0.0004$	$278 \pm 5$
50	550	$0.157 \pm 0.001$	$0.0058 \pm 0.0001$	$288 \pm 1$
200	400	$0.373 \pm 0.001$	$0.0069 \pm 0.0011$	$270 \pm 7$
155	445	$0.428 \pm 0.008$	$0.0071 \pm 0.0012$	$243 \pm 6$
250	350	$0.475 \pm 0.002$	$0.0082 \pm 0.0007$	$245 \pm 8$
200	400	$0.520 \pm 0.007$	$0.0090 \pm 0.0014$	$221 \pm 6$
350	250	$0.667 \pm 0.003$	$0.0105 \pm 0.0016$	$192 \pm 6$
355	245	$0.709 \pm 0.004$	$0.0106 \pm 0.0036$	$197 \pm 5$
300	300	$0.716 \pm 0.009$	$0.0129 \pm 0.0014$	$188 \pm 5$
455	145	$0.837 \pm 0.006$	$0.0197 \pm 0.0005$	$116 \pm 9$
450	150	$0.886 \pm 0.007$	$0.0283 \pm 0.0034$	$100 \pm 5$
600	0	1.0	1.0	$3.1 \pm 0.2$

the results for C2.1 would achieve a similar accuracy as reported for the BP\_TZVP\_C11\_0101 parametrization.

In addition to the liquid-phase composition, the vapor-phase mole fractions calculated for the TraPPE force field are also depicted in Figure 3. Unfortunately, experimental data are not available for comparison. As one should expect from the large difference in the neat vapor pressures for ethanol and HFC-227ea, the vapor phase is predominantly populated by HFC-227ea molecules. That is, even as the liquid-phase concentration approaches 90% ethanol, its concentration in the vapor phase only reaches about 3%. The fact that the vapor phase composition remains in a narrow range up to very high ethanol mole fractions in the liquid phase, will be later exploited for estimating the inaccuracies in the Gibbs free energies of transfer found for the TraPPE force field.

Since the Challenge task requires the prediction of bubble point pressures for specific (liquid-phase) ethanol mole fractions, we employed an unweighted 5th order polynomial fit of the form

$$P^{\text{tot}}(x_1) = P_2^{\text{sat}} * (1 - x_1) * (1 + a_0 * x_1 + a_1 * x_1^2 + a_2 * x_1^3 + a_3 * x_1^4 + a_4 * x_1^5) + P_1^{\text{sat}} * x_1 \quad (10)$$

where  $P^{\text{tot}}$ ,  $P_2^{\text{sat}}$ ,  $P_1^{\text{sat}}$ ,  $x_1$ , and  $a_i$  are the bubble point pressure, saturated vapor pressure of component 2 (HFC-227ea), saturated vapor pressure of component 1 (ethanol), ethanol mole fraction, and the five constants (determined by fitting the bubble point pressure curve), respectively. This form of polynomial ensures that the saturated vapor pressures for the two neat compounds ( $x_1$  is either 0 or 1) are exactly reproduced. For validation, we applied this polynomial to the experimental bubble pressure curve and found that the data are fitted with a deviation of less than 1% over the entire composition range (see Figure 3). The polynomial also yields an acceptable fit to the simulation data, albeit it should be noted that there is significant scatter in the simulation data. The uncertainty range for the polynomial is obtained by fitting additional polynomials through the upper and lower bounds (as determined by the standard deviations) of the simulation data.

#### 4.2.2 A Novel Scaling Approach

As mentioned above, the TraPPE force field appears to underestimate the strength of the ethanol–HFC-227ea interactions at low ethanol mole fractions in the liquid phase. This might not come as a surprise because an ethanol molecule can strongly polarize a neighboring HFC-227ea molecule. To remedy this situation, one could develop polarizable

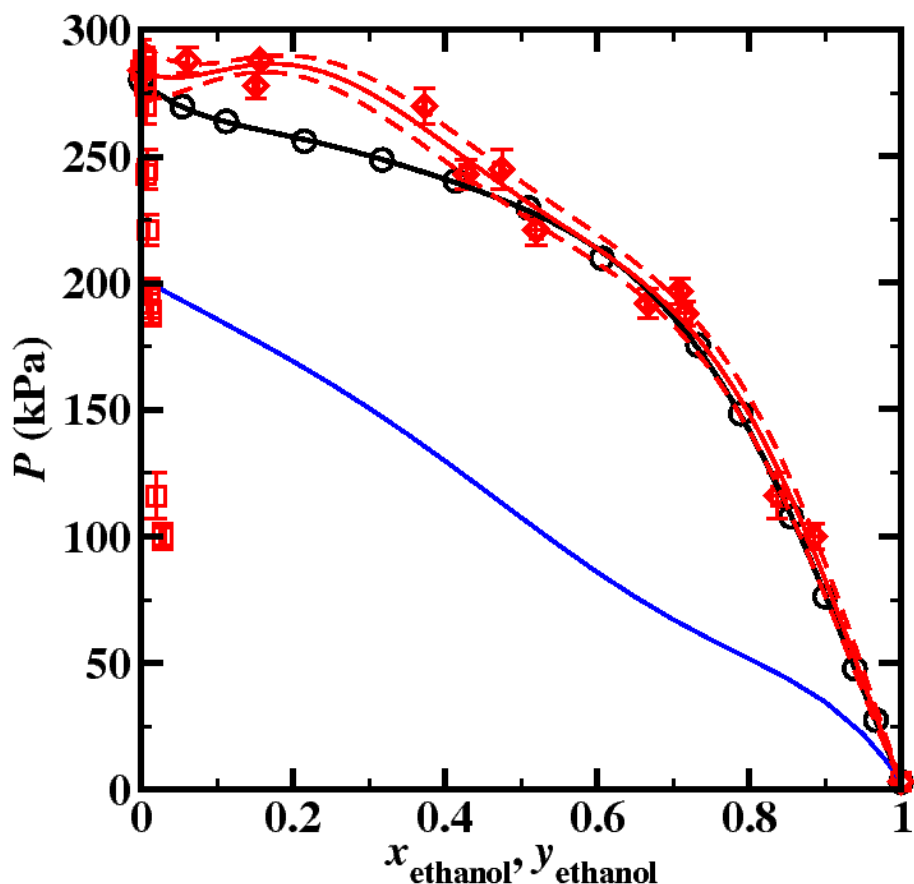


Figure 3: Pressure composition diagram for the binary mixture of ethanol and HFC-227ea at 283.17 K. The black circles, red diamonds, and red squares depict the experimental bubble point pressures (<http://fluidproperties.org/challenge/third/2006state.html>), and the liquid and vapor phase compositions for the TraPPE model, respectively. The black, red, and blue solid lines show the polynomial fits to the experimental and predicted TraPPE bubble point pressures and the bubble point pressures predicted with COSMOtherm/C2.1.<sup>42</sup> The red dashed lines give the uncertainty range (see text) for the polynomial fit to the TraPPE data.

force fields for these molecules or try to adjust the fixed charges (most likely on HFC-227ea) to yield improve binary vapor–liquid equilibria.<sup>14</sup> [It should be noted that binary data were not used in the parameterization of neither ethanol<sup>10</sup> nor HFC-227ea.] However, both of these approaches would require a very significant effort.

Since the Challenge description explicitly states that this task should involve “to use mixture phase equilibria information obtained at one isotherm () and extrapolate to state conditions at other temperatures,” (<http://fluidproperties.org/challenge/third/2006state.html>) it appears opportune to make use of the experimental bubble point pressures for this mixture at 283.17 K and of the saturated vapor pressures for the neat compounds at 343.13 K which were provided with this Challenge problem.

In order to utilize these data in conjunction with predictions obtained from Gibbs ensemble (or grand canonical ensemble) simulations, we propose a novel scaling approach that makes use of composition-dependent scaling free energies.

The simulations do not only provide the liquid- and vapor-phase coexistence compositions and the bubble point pressure, but also the number densities for the two species in the liquid and vapor phases. From these number densities, one can evaluate the Gibbs free energies for the vapor–to–liquid transfer.<sup>49,50</sup> If the number densities or the corresponding Gibbs free energies of transfer for the same binary system have been determined experimentally, then one can find a composition-dependent scaling free energy as follows

$$\Delta\Delta G_i^1(x_1, T_1) = -RT_1 \ln \left( \frac{\rho_{\text{vap},i}^{\text{sim}}(x_1)\rho_{\text{liq},i}^{\text{exp}}(x_1)}{\rho_{\text{liq},i}^{\text{sim}}(x_1)\rho_{\text{vap},i}^{\text{exp}}(x_1)} \right) \quad (11)$$

where  $\rho_{\text{vap},i}^{\text{sim}}(x_1)$ ,  $\rho_{\text{liq},i}^{\text{sim}}(x_1)$ ,  $\rho_{\text{vap},i}^{\text{exp}}(x_1)$ , and  $\rho_{\text{liq},i}^{\text{exp}}(x_1)$  are the number density of component  $i$  in the vapor or liquid phase at a specified liquid phase composition obtained either from simulation or experiment. Assuming that the difference in the liquid-phase number densities between experiment and simulation is negligible (most force fields predict liquid densities with much, much higher accuracy than saturated vapor densities), then the liquid-phase number densities cancel and the equation for the scaling free energy simplifies to

$$\Delta\Delta G_i^1(x_1, T_1) = -RT_1 \ln \left( \frac{\rho_{\text{vap},i}^{\text{sim}}(x_1)}{\rho_{\text{vap},i}^{\text{exp}}(x_1)} \right) \quad (12)$$

Unfortunately, these vapor phase number densities (or Gibbs free energies of transfer) are rarely available for experimental measurements. Thus, we have to make further approximations to convert the equation for the scaling free energy that can be used with knowledge of only the experimental bubble point pressures.

First, let us assume that the vapor phase is an ideal gas (or that the fugacities are known), then one can replace the vapor-phase number densities with partial pressures. This is certainly a very good approximation at the lower temperature investigated here. Second, since the vapor-phase composition is not provided here, one needs to assume that the difference in vapor-phase composition between experiment and simulation is negligible. Again, this should be a rather good approximation for the specific case investigated here because the vapor phase consists of predominantly HFC-227ea ( $y_2 \approx 1$ ) over a vast range of the liquid composition. In this case, the same scaling free energy can be applied to both components, that is

$$\Delta\Delta G_i^1(x_1, T_1) = -RT_1 \ln \left( \frac{P_{\text{tot}}^{\text{sim}}(x_1)}{P_{\text{tot}}^{\text{exp}}(x_1)} \right) \quad (13)$$

where  $P_{\text{tot}}^{\text{sim}}(x_1)$  and  $P_{\text{tot}}^{\text{exp}}(x_1)$  are the bubble point pressures obtained from simulation and experiment, respectively.

If one assumes that the scaling free energy mostly originates from an inability of the force field to yield the correct enthalpy of transfer, then one can directly apply this scaling free energy to correct bubble point pressures at a different temperature.

Finally, if experimental neat vapor pressures are available at this second temperature, then one may want to use them to further improve the scaling free energies. That is, the neat vapor pressures obtained directly from the simulations at the second temperature are initially adjusted by the scaling free energies obtained from the first temperature. These scaled vapor pressures for the neat compounds can then be compared to the experimental data and additional scaling free energy can be determined from

$$\Delta\Delta G_i^2(T_2) = -RT_2 \ln \left( \frac{(P'_i)^{\text{sim}}}{P_i^{\text{exp}}} \right) \quad (14)$$

where  $(P'_i)^{\text{sim}}$  is the vapor pressure of neat compound  $i$  adjusted by the scaling free energy obtained at  $T_1$ . Since only the experimental pressures for the neat compounds are available, the additional scaling free energy for intermediate compositions needs to be determined from a straight line between the two end points. The bubble point pressures computed directly from the simulations at the second temperature can now be scaled by the combined (composition-dependent) scaling free energies.

Figure 4 depicts the first, second, and combined scaling free energies for the binary mixture of ethanol and HFC-227ea that are calculated from comparison of the 5th order polynomial fits to the experimental data and the simulation results for the TraPPE force field. It should be noted that the first scaling free energy was determined using the 5th order polynomial fit to the TraPPE results because simulation data are not available for precisely the same liquid-phase mole fractions. The uncertainty in the combined scaling free energy is obtained by propagating the errors from the first and second scaling free energies.

Here we would like to emphasize that the magnitude of the scaling free energies is quite small (less than 0.3 kJ/mol in magnitude) which demonstrate that the TraPPE force field by itself already performs rather well. In particular, the vapor pressures of the neat ethanol and HFC-227ea at 343.13 K require almost no scaling (see below). The fact that the scaling free energies, in particular at low (liquid-phase) ethanol mole fractions, are negative indicates that the favorable unlike interactions are underestimated.

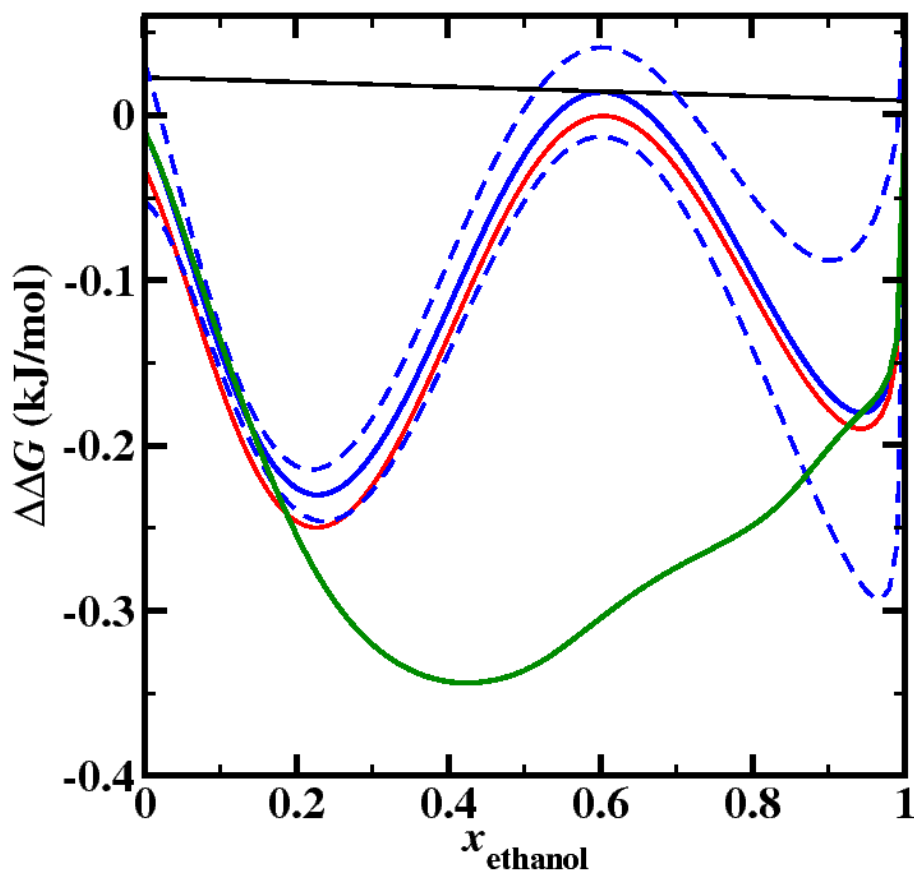


Figure 4: Scaling approach to Gibbs free energies of transfer. The red line shows the scaling free energies of transfer (difference between experimental and TraPPE vapor-to-liquid free energies of transfer) obtained from polynomial fits to the simulation and experimental data at  $T = 283.17$  K. The black lines show the additional scaling free energies that are required to match the experimental vapor pressures for the neat compounds at  $T = 343.13$  K. The blue line depicts the final scaling free energies (sum of the other two scaling free energies) applied to the polynomial fit of the simulation data at  $T = 343.13$  K. The dashed lines give the uncertainty range (see text). The green line shows the “perfect” scaling free energy that would be required to match the simulation data at  $T = 343.15$  K to the experimental benchmark data at this temperature.

Furthermore, it should be noted that the uncertainties in the scaling free energies are considerable. This demonstrates that extremely long simulations for large systems would be required to allow for optimization of the TraPPE force field parameters for this specific mixture.

In Figure 5, a comparison is shown between the scaled TraPPE bubble point pressures at  $T = 283.17$  K and those calculated with the COSMOtherm/C2.1 software when the experimental vapor pressures for the neat compounds and the predicted activities are used ( $P^{\text{tot}} = P_1^{\text{exp}} x_1 \gamma_1 + P_2^{\text{exp}} x_2 \gamma_2$ ).<sup>42,45</sup> By definition, the curve for the scaled TraPPE bubble point pressures overlaps with the experimental data (because the first scaling free energy is computed at this state point). Use of the experimental neat vapor pressures greatly improves the overall fit for COSMOtherm/C2.1 but does not remedy the Raoult’s law behavior for intermediate compositions. Again, it should be noted that better predictions are obtained with the BP\_TZVP\_C11\_0101 parametrization<sup>47</sup> or could be obtained by fine-tuning the hydrogen-bond parameter for parametrization C2.1.<sup>46</sup>

### 4.2.3 Predictions at 343.13 K

Figure 6 shows the pressure–composition diagrams at  $T = 343.13$  K measured experimentally (only for the neat compounds) (<http://fluidproperties.org/challenge/third/2006state.html>), obtained from simulations with the TraPPE force field, and calculated using the COSMOtherm/C2.1 thermodynamics software and sigma profiles released with

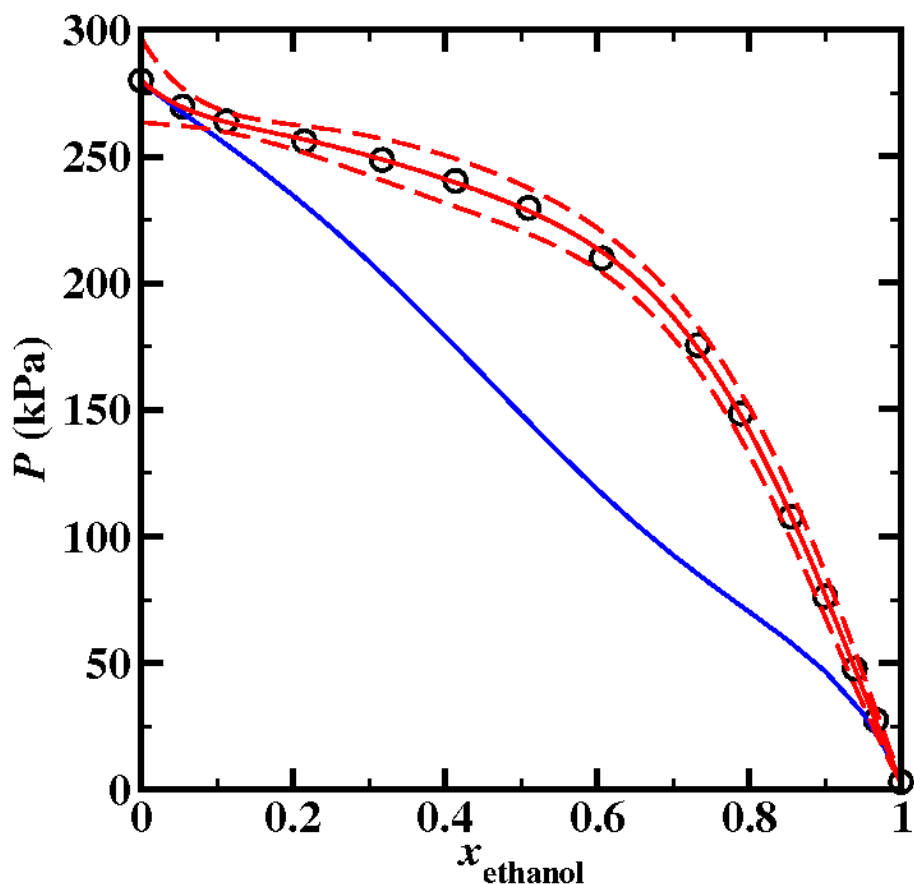


Figure 5: Pressure composition diagram for the binary mixture of ethanol and HFC-227ea at 283.17 K. The black circles depict the experimental bubble point pressures (<http://fluidproperties.org/challenge/third/2006state.html>). The red and blue lines show the scaled TraPPE bubble point pressures and the COSMOtherm/C2.1 bubble point pressures using the experimental values for the endpoints and computed activities for intermediate compositions.<sup>42</sup> The red dashed lines give the uncertainty range (see text) for the scaled polynomial fit to the TraPPE data.

this software.<sup>42,48</sup> The numerical values of the simulation data are listed in Table 8. As at the lower temperature, the TraPPE force field yields an excellent prediction for the saturated pressures of the neat ethanol and HFC-227-*ea* with the experimental data falling into the uncertainty range of the simulation results. Compared to the simulation data for the lower temperature (see Figure 3), the TraPPE model now predicts a decrease of the bubble point pressure for  $x_{\text{ethanol}} < 0.15$ , i.e. the deviation of the bubble point pressure from Raoult's law behavior is not as extensive, and one would expect the local structure to be more homogeneous (see below).

For comparison, the COSMOtherm/C2.1 calculations yield an underestimation of the neat HFC-227*ea* vapor pressure by about 25% (that for ethanol agrees very well with experiment) and a bubble pressure curve that is fairly linear with liquid phase composition up to  $x_{\text{ethanol}} \approx 0.9$ . Again, much better predictions were obtained by Klamt and Eckert with the BP\_TZVP\_C11\_0101 parametrization.<sup>47</sup>

In Figure 7, a comparison is shown between the scaled TraPPE bubble point pressures at  $T = 343.13$  K and those calculated with the COSMOtherm/C2.1 software when the experimental vapor pressures for the neat compounds and the predicted activities are used.<sup>42,45</sup> As at the lower temperature, the curve for the scaled TraPPE data shows two inflection points. The numerical data at the 7 liquid-phase mole fractions specified in the Challenge task are given in Table 9 for the bubble point pressures predicted directly from simulations with the TraPPE force field and for those obtained from using the scaling free energy approach to the TraPPE data. The latter numbers constitute our entry for this Challenge problem.

A comparison with the experimental benchmark data (<http://fluidproperties.org/Files/VLEBenchmark2006.pdf>) shows that the scaled TraPPE bubble point pressure curve yields excellent agreement for  $x_{\text{ethanol}} < 0.2$  and  $x_{\text{ethanol}} <$

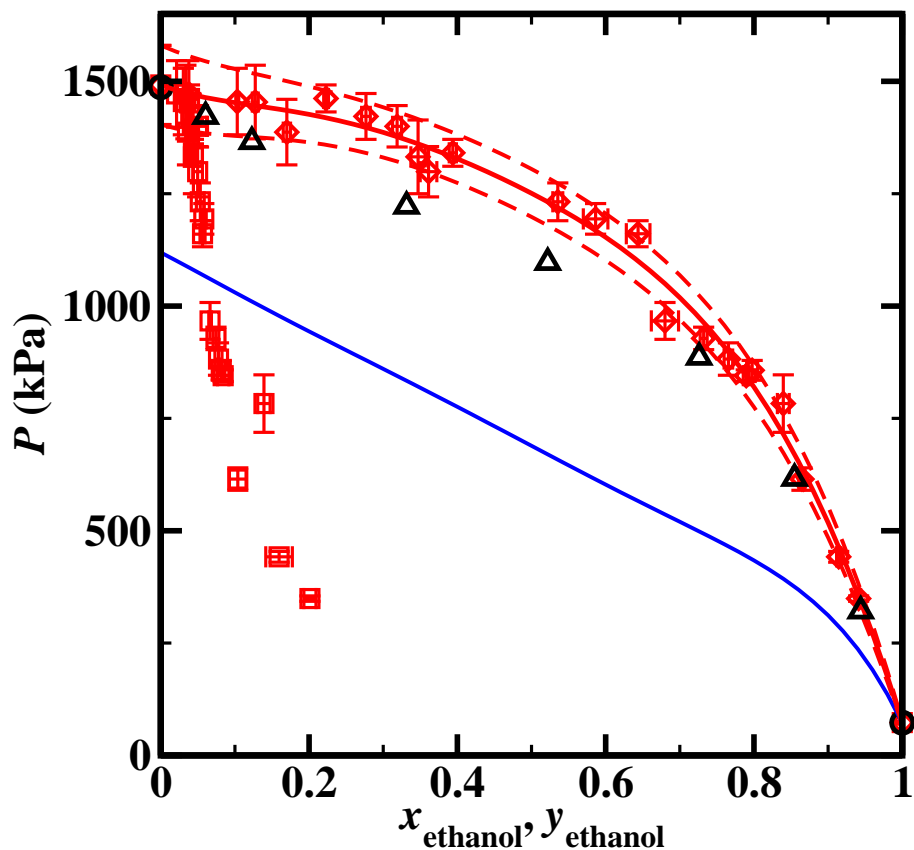


Figure 6: Pressure composition diagram for the binary mixture of ethanol and HFC-227ea at 343.13 K. The black circles, black triangles, red diamonds, and red squares depict the experimental pressures for the neat compounds (<http://fluidproperties.org/challenge/third/2006state.html>), the experimental benchmark data for the mixture (<http://fluidproperties.org/Files/VLEBenchmark2006.pdf>), and the liquid and vapor phase compositions for the TraPPE model, respectively. The red and blue solid lines show the polynomial fits to the predicted TraPPE bubble point pressures and the bubble point pressures predicted with COSMOtherm/C2.1.<sup>42</sup> The red dashed lines give the uncertainty range (see text) for the polynomial fit to the TraPPE data.

0.8, whereas the bubble point pressure is somewhat overestimated at intermediate liquid-phase compositions with the largest error of about 12% for  $x_{\text{ethanol}} = 0.5219$ . Overall, the mean unsigned percent error is 4.3% for the scaled TraPPE values and a large value of 8.4% for the direct polynomial fit to the TraPPE simulation data, i.e. the scaling procedure reduced the MUPE by about a factor of 2. With hindsight, it appears that the simulation data obtained at  $T = 283.17$  K and  $x_{\text{ethanol}} = 0.520$  and  $0.667$  that yield bubble point pressures below the experimental data and below the polynomial fit to the simulation data, resulted in a scaling free energy that is not sufficiently negative in this intermediate concentration region. For comparison, the “perfect” scaling free energy that would scale the simulation data at  $T = 343.13$  K to the benchmark data is also shown in Figure 4.

### 4.3 Structural Analysis for the Binary Mixture of Ethanol and HFC-227ea

Based on the previous discussion, the structural question that should be answered first, is whether there are any (weak) hydrogen bonds formed between ethanol and HFC-227ea molecules. Figure 8 shows the radial distribution functions (RDFs) and the corresponding number integrals (NIs) for oxygen atoms of ethanol being surrounded by hydrogen atoms of HFC-227ea and for hydrogen atoms of ethanol being surrounded by fluorine atoms of HFC-227ea for four compositions at both temperatures. The oxygen–hydrogen RDFs for the unlike species shows a fairly weak peak at a separation of about  $2.7$  Å, substantially larger than the  $1.8$  Å found in strongly hydrogen-bonding systems (see below). Nevertheless, the corresponding NIs give a value of about 0.5 at the lowest ethanol mole fractions. The hydrogen–fluorine RDFs for the unlike species do not give any indication for specific (hydrogen-bond like) interactions. It

Table 8: Simulation details and pressure–composition data for simulations with the TraPPE force field of the binary mixture of ethanol and HFC-227ea at 343.13 K: numbers ethanol and HFC-227ea molecules, liquid and vapor-phase mole fractions, and bubble point pressures.

$N_{\text{ethanol}}$	$N_{\text{HFC}}$	$x_{\text{ethanol}}$	$y_{\text{ethanol}}$	$P$ (kPa)
0	600	0.0	0.0	1492 ± 88
20	580	0.0379 ± 0.0007	0.0213 ± 0.0012	1472 ± 74
50	550	0.1032 ± 0.0020	0.0304 ± 0.0012	1455 ± 74
60	540	0.1275 ± 0.0040	0.0339 ± 0.0028	1454 ± 82
80	520	0.1700 ± 0.0049	0.0359 ± 0.0023	1387 ± 73
100	500	0.2229 ± 0.0032	0.0387 ± 0.0018	1462 ± 30
125	475	0.2767 ± 0.0059	0.0404 ± 0.0032	1422 ± 51
150	450	0.3187 ± 0.0061	0.051 ± 0.011	1400 ± 46
160	440	0.3470 ± 0.0097	0.0440 ± 0.0019	1332 ± 82
155	445	0.361 ± 0.011	0.0497 ± 0.0065	1299 ± 56
180	420	0.3939 ± 0.0049	0.0439 ± 0.0040	1341 ± 30
250	350	0.5354 ± 0.0068	0.0533 ± 0.0053	1232 ± 42
200	400	0.587 ± 0.017	0.0580 ± 0.0032	1194 ± 34
225	375	0.644 ± 0.016	0.0563 ± 0.0034	1161 ± 29
275	325	0.680 ± 0.018	0.0665 ± 0.0018	967 ± 41
275	325	0.7322 ± 0.0047	0.0744 ± 0.0039	928 ± 25
350	250	0.7655 ± 0.0059	0.0778 ± 0.0048	882 ± 36
400	200	0.7896 ± 0.0040	0.0841 ± 0.0078	845 ± 13
300	300	0.7976 ± 0.0075	0.0816 ± 0.0049	857 ± 22
355	245	0.8396 ± 0.0080	0.1391 ± 0.0084	783 ± 64
450	150	0.8647 ± 0.0042	0.104 ± 0.012	615 ± 25
500	100	0.9143 ± 0.0029	0.156 ± 0.018	442 ± 12
455	145	0.9412 ± 0.0027	0.2011 ± 0.0081	349 ± 6
600	0	1.00	1.00	73 ± 3

Table 9: Bubble point pressures at  $T = 343.13$  K as obtained from a 5th order polynomial fit to the TraPPE simulation data and estimated from the scaling approach. For comparison the experimental benchmark data (<http://fluidproperties.org/Files/VLEBenchmark2006.pdf>) and the mean unsigned percent error are also listed.

$x_{\text{ethanol}}$	$P_{\text{tot}}$	$P_{\text{tot}}^{\text{scaled}}$	$P_{\text{exp}}$
0.0604	1464±80	1420±83	1422±3
0.1228	1447±71	1364±68	1366±3
0.3314	1370±55	1286±61	1222±2
0.5219	1232±54	1227±63	1097±2
0.7260	975±49	963±58	885.9±1.8
0.8547	670±42	638±57	616.5±1.2
0.9440	342±26	322±40	321.5±0.6
MUPE	8.4%	4.3%	



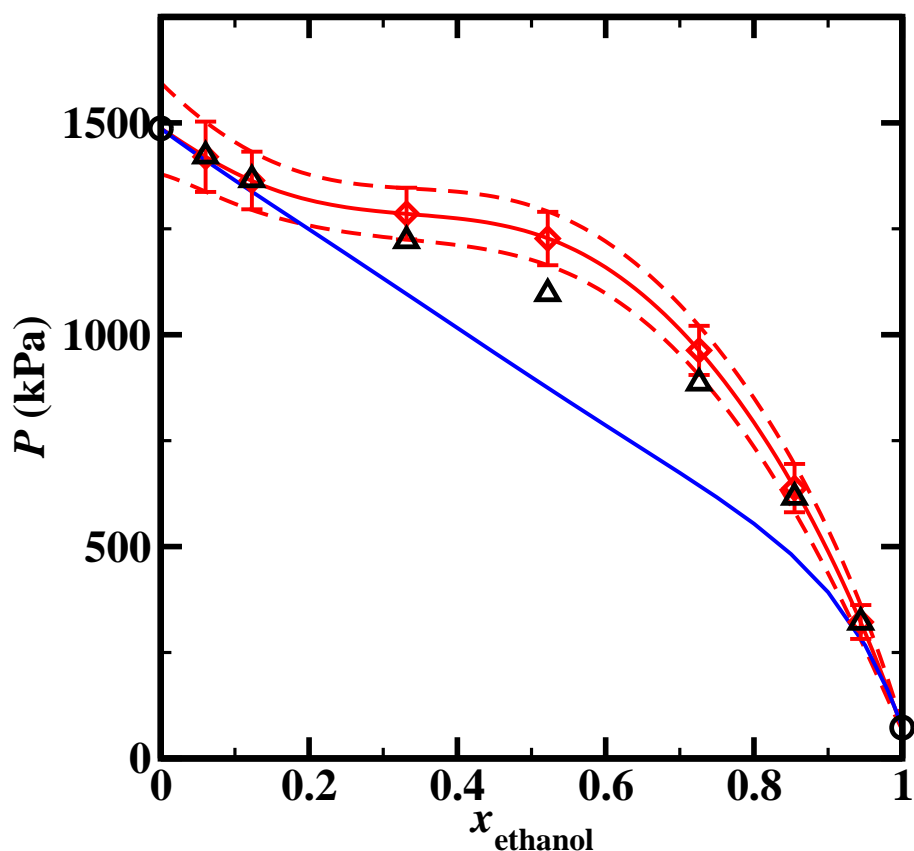


Figure 7: Pressure composition diagram for the binary mixture of ethanol and HFC-227ea at 343.13 K. The black circles, black triangles, and red diamonds depict the the experimental pressures for the neat compounds (<http://fluidproperties.org/challenge/third/2006state.html>), the experimental benchmark data for the mixture (<http://fluidproperties.org/Files/VLEBenchmark2006.pdf>), and the TraPPE estimates (scaled polynomial fit) for the liquid compositions stated in the Challenge task, respectively. The red and blue lines show the scaled TraPPE bubble point pressures and the COSMOtherm/C2.1 bubble point pressures using the experimental values for the endpoints and computed activities for intermediate compositions.<sup>42</sup> The red dashed lines give the uncertainty range (see text) for the scaled TraPPE data.

should be noted that neither the oxygen–hydrogen nor hydrogen–fluorine RDFs for the unlike species exhibit at strong composition dependence.

The oxygen–hydrogen and oxygen–oxygen RDFs and NIs for ethanol pairs are shown for five compositions at both temperatures in Figure 9. These exhibit the typical behavior for strongly hydrogen bonding system with preferential aggregation.<sup>51–53</sup> The oxygen–hydrogen and oxygen–oxygen RDFs have pronounced and sharp peaks at the hydrogen bonding distances of 1.8 and 2.8 Å, respectively. The RDFs also shown strong second peaks. The peak heights for the RDFs increase with decreasing ethanol concentration; this is indicative of strong preferential solvation and the formation of aggregates. In contrast to the RDFs, the plateau values found for all NIs show little composition dependence, i.e. the significant aggregation is found for all concentrations and the majority of ethanol molecules are involved in the formation of at least one hydrogen bond.

The distribution of ethanol–ethanol head group pair energies (obtained by computing the 9 site-site interactions involving the hydroxyl hydrogen and oxygen atoms, and the  $\alpha$  methylene group). The peak position for hydrogen-bonded pairs is independent of composition with values of  $-25$  and  $-24$  kJ/mol at 283.17 and 343.13 K, respectively. The strong composition dependence of the peak height does not indicate that a larger fraction of ethanol molecules is involved in hydrogen bonds at lower concentration, it simply is the outcome of the increasing number of ethanol molecules with increasing concentration. (Since an ethanol molecule can at most be involved in three hydrogen bonds, all other molecules,  $N - 4$  can not show the same favorable pair energy with a given ethanol molecule.)

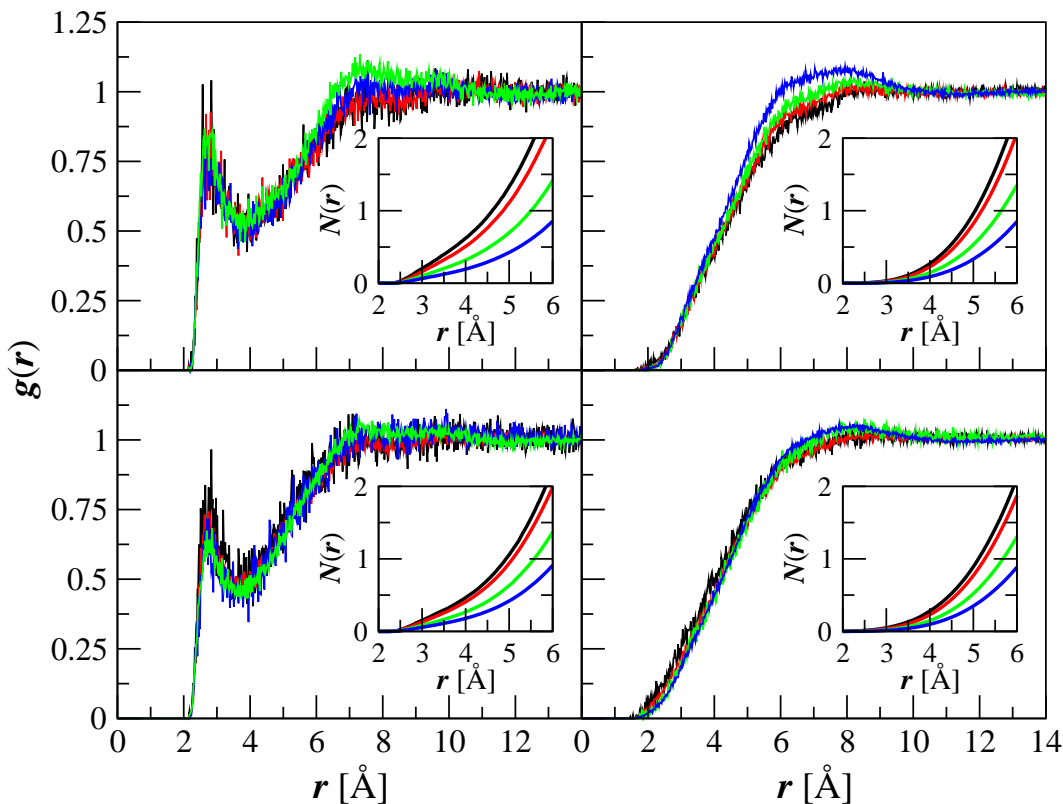


Figure 8: Oxygen (ethanol)–hydrogen (HFC-227ea) (left column) and hydrogen (ethanol)–fluorine (HFC-227ea) (right column) radial distribution functions and number integrals at 283.17 K (top row) and 343.17 K (bottom row). The black, red, green, and blue lines show data for the four binary mixtures (excluding the lowest concentration) listed in Table 10 in order of increasing ethanol mole fraction.

Further structural insight for this binary mixture can be gleaned from an analysis of hydrogen bonds. Based on the similarities in the RDFs, head group energies, and distributions of hydrogen bond angles (not shown), we employed the same set of criteria to define a hydrogen bond as in a previous investigation of 1-hexanol in *n*-hexane mixtures.<sup>51,54</sup> This is a combined distance/angle/energy metric and a hydrogen bond exists when a pair of molecules satisfies the following criteria:  $r_{OO} \leq 3.3 \text{ \AA}$ ,  $r_{OH} \leq 2.5 \text{ \AA}$ ,  $\cos \theta_{OH\dots OL} \leq -0.1$ , and  $u_{\text{head}} \leq -13 \text{ kJ/mol}$ , where  $r_{OO}$ ,  $r_{OH}$ ,  $\cos \theta_{OH\dots OL}$ , and  $u_{\text{head}}$  are the oxygen–oxygen distance, the oxygen–hydrogen distance, the angle between the OH bond vector on the donating molecule and the oxygen–lone pair vector on the accepting molecule, and the potential energy between the two  $-\text{CH}_2\text{OH}$  head groups, respectively.

The numbers of hydrogen bonds per ethanol molecule in the liquid and vapor phases calculated for six compositions at the two temperatures are listed in Table 10. With the exception of  $x_{\text{ethanol}} = 0.038$  at  $T = 343.13 \text{ K}$ , the average liquid-phase ethanol molecule is involved in the formation of more than one hydrogen bond. Hydrogen bonding is significantly more pronounced in the liquid phase at 283.17 K than at 343.13 K. At the lower temperature, the number of hydrogen bonds per ethanol molecule at  $x_{\text{ethanol}} = 0.061$  has already reached more than 80% of the value found for neat ethanol. Thus, the ethanol molecules strongly aggregate with each other even at this low concentration. This strong self-aggregation of ethanol molecules is most likely responsible for the small composition dependence found for the TraPPE bubble point pressure at low ethanol concentration, i.e. there is minimal aggregation with HFC-227ea molecules and the bubble point pressure remains close to the value for neat HFC-227ea. At the higher temperature, we find that the number of hydrogen bonds per ethanol molecule at  $x_{\text{ethanol}} = 0.038$  is less than one and free ethanol molecules will at least weakly bond to surrounding HFC-227ea molecules. Indeed, the TraPPE simulations at the higher temperature yield a decrease of the bubble point pressure at low  $x_{\text{ethanol}}$ , albeit not as pronounced as for the experimental data at the lower temperature.

At the lower temperature, we do not find significant clustering of ethanol molecules in the vapor phase for all

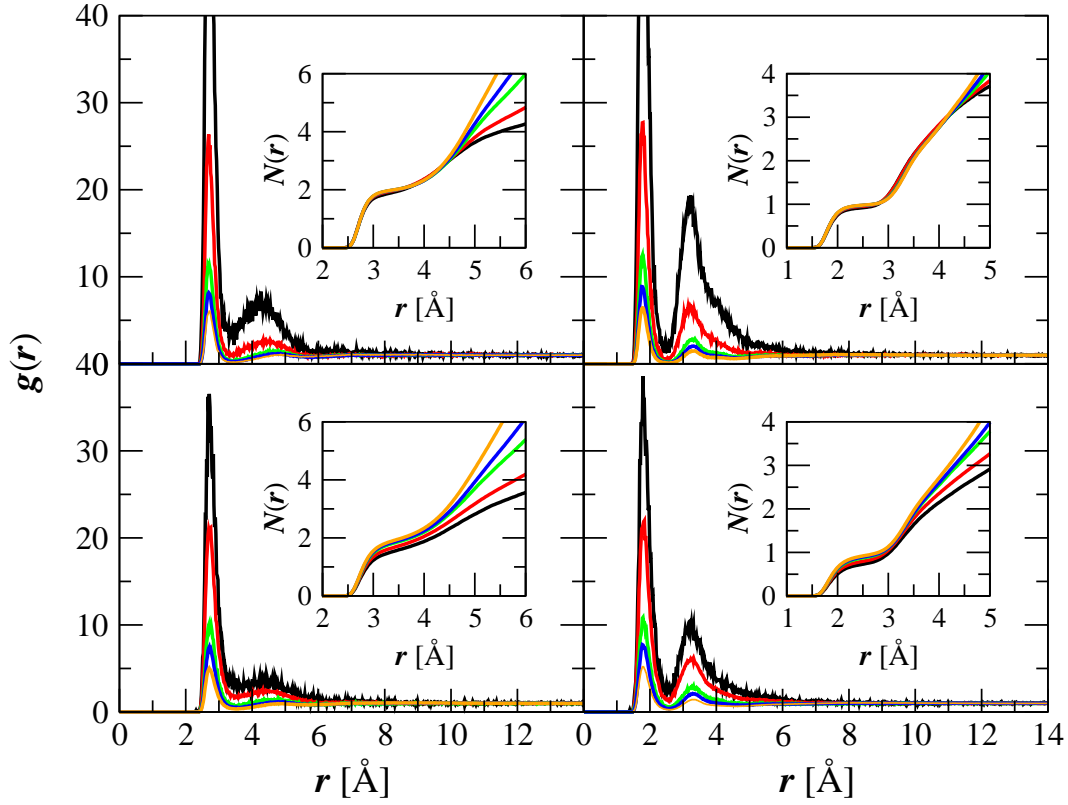


Figure 9: Oxygen–oxygen (left column) and oxygen–hydrogen (right column) radial distribution functions and number integrals for ethanol pairs at 283.17 K (top row) and 343.17 K (bottom row). The black, red, green, blue, and orange lines show data for the four binary mixtures (excluding the lowest concentration) and neat ethanol listed in Table 10 in order of increasing ethanol mole fraction.

Table 10: Number of hydrogen bonds per ethanol molecule in the liquid and vapor phases.

$x_{\text{ethanol}}$	283.17 K		343.13 K		
	$N_{\text{liquid}}$	$N_{\text{vapor}}$	$x_{\text{ethanol}}$	$N_{\text{liquid}}$	$N_{\text{vapor}}$
0.061	1.58	0.00	0.038	0.62	0.02
0.151	1.76	0.01	0.223	1.36	0.09
0.373	1.84	< 0.01	0.361	1.48	0.08
0.667	1.87	< 0.01	0.680	1.66	0.07
0.837	1.87	0.01	0.840	1.65	0.09
1.000	1.88	0.01	1.000	1.69	0.16

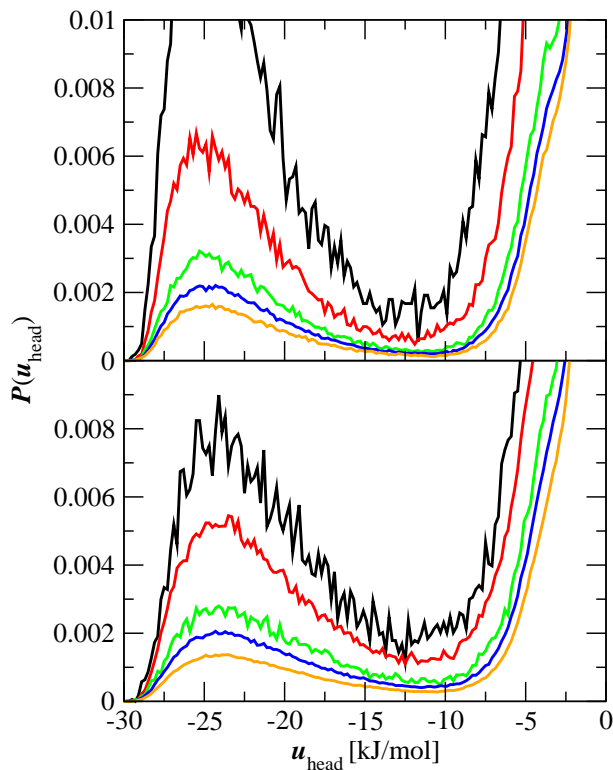


Figure 10: Distribution of ethanol–ethanol head group pair energies at 283.17 K (top) and 343.17 K (bottom). Line styles as in Figure 9.

compositions. Here one should recall that we assumed that the vapor phase is ideal to derive the scaling free energy curve at 283.17 K. In contrast to the lower temperature, the number densities of ethanol molecules in the vapor phase at 343.13 K are sufficiently high to allow for some hydrogen bonding.

The distribution of ethanol molecules over (hydrogen-bonded) aggregate sizes is given in Table 4.3. Again, the liquid phase at  $x_{\text{ethanol}} = 0.038$  and  $T = 343.13$  K stands out in the sense that the majority (65%) of ethanol molecules are found as free monomers. On the opposite side, about half of the ethanol molecules at  $x_{\text{ethanol}} = 1.0$  and  $T = 283.17$  K are found in aggregates containing at least 10 ethanol molecules. At the lower temperature, less than 20% of the ethanol molecules were found to be free monomers even at the lowest ethanol concentration studied here. For this case and for  $x_{\text{ethanol}} = 0.151$  and  $0.373$ , the ethanol molecules appear to prefer aggregate consisting of four or five molecules; an observation that has also been made for other hydrogen-bonding molecules in non-polar solvents.<sup>51,52</sup>

## 5 Conclusions

Configurational-bias Monte Carlo simulations in the Gibbs ensemble and the TraPPE force field were employed to predict the pressure–composition diagrams and to explore the liquid-phase structures for the binary mixture of ethanol and HFC-227ea at two temperatures. The TraPPE force field yields excellent predictions for the saturated vapor pressures of the neat compounds at both temperatures. However, the TraPPE force field yields bubble point pressures that are too high at low ethanol concentrations for  $T = 283.17$  K. The structural analysis demonstrates that ethanol molecules strongly self-aggregate at this temperature even at low ethanol concentrations and that there is little specific binding for unlike species. To remedy the overprediction of the bubble point pressures, a scaling approach is introduced that makes use of composition-dependent free energies of transfer. Comparison with the experimental benchmark data yields mean unsigned percent errors of 8.4% and 4.3% for the TraPPE simulations data and the scaled simulation data, respectively, at  $T = 343.13$  K.

Future work will explore whether addition of a short-range potential that mimics the increased strength of ethanol–HFC-227ea hydrogen bonding, will change the aggregation threshold to higher ethanol mole fractions. This would allow us to demonstrate that stronger ethanol–HFC-227ea interactions are required to yield the initial dip in

Table 11: Fraction of ethanol molecules belonging to hydrogen bonded-aggregates of a given size in the liquid phase.

283.17 K										
$x_{\text{ethanol}}$	1	2	3	4	5	6	7	8	9	$\geq 10$
0.061	0.19	0.13	0.10	0.26	0.07	0.08	0.03	0.02	0.01	< 0.01
0.151	0.08	0.09	0.07	0.21	0.30	0.13	0.04	0.02	0.04	0.01
0.373	0.03	0.08	0.07	0.19	0.22	0.10	0.06	0.03	0.03	0.20
0.667	0.01	0.07	0.07	0.11	0.12	0.09	0.05	0.05	0.04	0.39
0.837	0.02	0.08	0.07	0.09	0.09	0.07	0.06	0.04	0.04	0.44
1.000	0.02	0.07	0.07	0.07	0.07	0.06	0.06	0.05	0.05	0.49
343.13 K										
$x_{\text{ethanol}}$	1	2	3	4	5	6	7	8	9	$\geq 10$
0.038	0.65	0.16	0.07	0.09	0.03	< 0.01	–	–	–	–
0.223	0.24	0.19	0.13	0.17	0.13	0.06	0.04	0.02	0.01	0.01
0.361	0.18	0.18	0.14	0.17	0.13	0.08	0.04	0.03	0.02	0.04
0.680	0.14	0.16	0.14	0.15	0.13	0.09	0.06	0.05	0.04	0.05
0.840	0.09	0.16	0.14	0.13	0.12	0.08	0.06	0.05	0.04	0.13
1.000	0.08	0.15	0.13	0.13	0.11	0.08	0.07	0.05	0.04	0.17

bubble point pressure observed experimentally for  $x_{\text{ethanol}} < 0.05$  and to validate that a monomer-to-aggregate transition causes the inflection point at  $x_{\text{ethanol}} \approx 0.2$ .

**Acknowledgements.** Financial support from the National Science Foundation (CTS-0553911) and a Graduate School and an Owens Fellowships (J.L.R.) are gratefully acknowledged. Part of this work was performed under the auspices of the U.S. Department of Energy by the University of California Lawrence Livermore National Laboratory (LLNL) under contract No. W-7405-Eng-48. Part of the computer resources were provided by the Minnesota Supercomputing Institute.

## References

- [1] Blondino, F. E.; Byron, P. R. *Drug Development and Industrial Pharmacy* **1998**, *24*(10), 935–945.
- [2] Meier, M.; Fischer, F. X.; Keller, M.; Halfmann, H. J. *Pharmazeutische Industrie* **1996**, *58*, 78–82.
- [3] Pishtiak, A. H. *Chimica OGGI-Chemistry Today* **2002**, *20*, 14.
- [4] United States Patent 5064559.
- [5] Zhang, L.; Siepmann, J. I. *Langmuir* **2007**, *23*, in preparation.
- [6] Martin, M. G.; Siepmann, J. I. *J. Chem. Phys.* **1998**, *102*, 2569–2577.
- [7] Martin, M. G.; Siepmann, J. I. *J. Phys. Chem. B* **1999**, *103*, 4508–4517.
- [8] Chen, B.; Siepmann, J. I. *J. Phys. Chem. B* **1999**, *103*, 5370–5379.
- [9] Wick, C. D.; Martin, M. G.; Siepmann, J. I. *J. Phys. Chem. B* **2000**, *104*, 8008–8016.
- [10] Chen, B.; Potoff, J. J.; Siepmann, J. I. *J. Phys. Chem. B* **2001**, *105*, 3093–3104.
- [11] Stubbs, J. M.; Pottoff, J. J.; Siepmann, J. I. *J. Phys. Chem. B* **2004**, *108*, in press.
- [12] Wick, C. D.; Stubbs, J. M. ; Rai, N.; Siepmann, J. I. *J. Phys. Chem. B* **2005**, *104*, 18974–18982.
- [13] Lubna, N.; Kamath, G.; Potoff, J. J.; Rai, N.; Siepmann, J. I. *J. Phys. Chem. B* **2005**, *109*, 24100–24107.
- [14] Potoff, J. J.; Siepmann, J. I. *AIChE J.* **2001**, *47*, 1676–1682.
- [15] J. I. Siepmann, Challenges in the development of transferable force fields for phase equilibria calculations, in "Forum 2000: Fluid Properties for New Technologies, Connecting Virtual Design with Physical Reality," NIST Special Publications 975, pp. 110-112, eds. J.C. Rainwater, D.G. Friend, H.H.J.M. Hanley, A.H. Harvey, C.D. Holcomb, A. Laesecke, J. Magee, and C. Muzny (NIST, Boulder, 2001).
- [16] Lorentz, H. A. *Ann. Phys.* **1881**, *12*, 127.
- [17] Berthelot, D. C. R. *Hebd. Seanc. Acad. Sci. Paris* **1898**, *126*, 1703.
- [18] Mundy, C. J.; Siepmann, J. I.; Klein, M. L. *J. Chem. Phys.* **1995**, *102*, 3376–3380.
- [19] Siepmann, J. I.; Karaborni, S.; Smit, B. *Nature* **1993**, *365*, 330–332.
- [20] Jorgensen, W. L. *J. Phys. Chem.* **1986**, *90*, 1276–1284.
- [21] van der Ploeg, P.; Berendsen, H. J. C. *J. Chem. Phys.* **1982**, *76*, 3271–3276.
- [22] Watkins, E. K.; Jorgensen, W. L. *J. Phys. Chem. A* **2001**, *105*, 4118–4125.
- [23] Cornell, W. D.; Cieplak, P.; Bayly, C. I.; I. R. Gould and K. M. Merz, J.; Ferguson, D. M.; Spellmeyer, D. C.; Fox, T.; Caldwell, J. W.; Kollman, P. A. *J. Am. Chem. Soc.* **1995**, *117*, 5179–5197.
- [24] Chen, B.; Siepmann, J. I. *J. Phys. Chem. B* **2006**, *110*, 3555–3563.
- [25] Chen, B.; Siepmann, J. I.; Klein, M. L. *J. Am. Chem. Soc.* **2002**, *124*, 12232–12237.
- [26] Chen, B.; Siepmann, J. I.; Klein, M. L. *J. Am. Chem. Soc.* **2003**, *125*, 3113–3118.
- [27] Zhang, L.; Siepmann, J. I. *Theor. Chem. Acc.* **2006**, *115*, 391–397.
- [28] Zhang, L.; Rafferty, J. L.; Siepmann, J. I.; Chen, B.; Schure, M. R. *J. Chromatogr. A* **2006**, *222*.

- [29] Gaussian 03, Revision C.02. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A.
- [30] Kelly, C. P.; Cramer, C. J.; Truhlar, D. G. *J. Theor. Comput. Chem.* **2005**, *1*, 1133–1152.
- [31] Rai, N.; Siepmann, J. I.; manuscript in preparation.
- [32] Chamberlin, A. C.; Kelly, C. P.; Thompson, J. D.; Xidos, J. d.; Li, J.; Hawkins, Winget, P. D.; G. D.; Zhu, T.; Rinaldi, D.; Liotard, D. A.; Cramer, C. J.; Truhlar, D. G.; Frisch, M. J. *MN-GSM*, version 6.0, University of Minnesota, Minneapolis, MN 55455-0431, 2006 .
- [33] E.W. Lemmon, M.O. McLinden, and D.G. Friend, Thermophysical Properties of Fluid Systems, NIST Chemistry WebBook, NIST Standard Reference Database Number 69, Eds. P.J. Linstrom and W.G. Mallard, June 2005, National Institute of Standards and Technology, Gaithersburg MD, 20899 (<http://webbook.nist.gov>).
- [34] Siepmann, J. I.; Frenkel, D. *Mol. Phys.* **1992**, *75*, 59–70.
- [35] Panagiotopoulos, A. Z. *Mol. Phys.* **1987**, *61*, 813–826.
- [36] Panagiotopoulos, A. Z.; Quirke, N.; Stapleton, M.; Tildesley, D. J. *Mol. Phys.* **1988**, *63*, 527–545.
- [37] Allen, M. P.; Tildesley, D. J. *Computer Simulation of Liquids*; Clarendon Press: Oxford, 1987.
- [38] Frenkel, D.; Smit, B. *Understanding Molecular Simulation: From Algorithms to Applications*; Academic Press: San Diego, 1996.
- [39] Rowlinson, J. S.; Widom, B. *Molecular Theory of Capillarity*; Oxford University Press, New York, 1989.
- [40] Rowlinson, J. S.; Swinton, F. L. *Liquids and Liquid Mixtures*; Butterworth, London, 1982.
- [41] Reidel, L.; *Chem. Eng. Tech.* **1954**, *26*, 83-89
- [42] Eckert, F.; Klamt, A.; COSMOTHERM, Version C2.1, Release 01.05; COSMOlogic GmbH & Co. KG, Germany, 2005.
- [43] Klamt, A. *J. Phys. Chem.* **1995**, *99*, 2224.
- [44] Eckert, F.; Klamt, A. *AICHE J.* **2002**, *48*, 369-385.
- [45] Klamt, A.; Eckert, F.; *Fluid Phase Equil.* **2004**, *217*, 53-57.
- [46] Klamt, A.; private communication.
- [47] Klamt, A. ; Eckert, F.; *Fluid Phase Equil.* **2007**, submitted for publication.
- [48] Klamt, A. *COSMO-RS: From Quantum Chemistry to Fluid Phase Thermodynamics and Drug Design*; Elsevier, Amsterdam, 2005.
- [49] Naim, A. B. *Statistical Thermodynamics for Chemists and Biochemists*; Plenum Press: New York, 1992.
- [50] Martin, M. G.; Siepmann, J. I. *Theo. Chem. Acc.* **1998**, *99*, 347–350.
- [51] Stubbs, J. M.; Siepmann, J. I. *J. Am. Chem. Soc.* **2005**, *127*, 4722–4729.

- [52] Stubbs, J. M.; Siepmann, J. I. *J. Phys. Chem. B* **2002**, *106*, 3968–3978.
- [53] Stubbs, J. M.; Siepmann, J. I. *J. Chem. Phys.* **2004**, *121*, 1525–1534.
- [54] Stubbs, J. M.; Siepmann, J. I. *J. Phys. Chem. B* **2007**, *111*, in preparation.