

## The Fifth Industrial Fluid Properties Simulation Challenge †

Fiona H. Case <sup>a</sup>, Anne Chaka <sup>b</sup>, Jonathan D. Moore <sup>c</sup>, Raymond D. Mountain <sup>d\*</sup>, James D. Olson <sup>e</sup>, Richard B. Ross <sup>f</sup>, Martin Schiller <sup>g</sup>, Vincent K. Shen <sup>d</sup> and Eric A. Stahlberg <sup>h</sup>

<sup>a</sup> Case Scientific, Essex Junction, VT 05452, USA

<sup>b</sup> National Institute of Standards and Technology (NIST), 100 Bureau Drive Stop 8443, Gaithersburg, MD 20899-8440, USA

<sup>c</sup> The Dow Chemical Company, Midland, MI, USA

<sup>d</sup> National Institute of Standards and Technology, 100 Bureau Drive Stop 8320, Gaithersburg, MD 20899-8320, USA

<sup>e</sup> The Dow Chemical Company, S. Charleston, WV 25303, USA

<sup>f</sup> 3M Company, St. Paul, MN, USA

<sup>g</sup> Du Pont de Nemours (Deutschland) GmbH, Germany

<sup>h</sup> Ohio Supercomputer Center, Columbus, OH, USA

\* Corresponding author. Tel.: +1 301 975 2484; fax: +1 301 869 4020.

E-mail address: [Raymond.Mountain@nist.gov](mailto:Raymond.Mountain@nist.gov) (R.D. Mountain).

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### Abstract

The fifth industrial fluid properties simulation challenge was held in 2008. In it the contestants were challenged to predict specific, industrially relevant, properties of fluid systems, namely the 1-octanol/water partition coefficient and the infinite dilution activity coefficient in water of 1-ethylpropylamine and 3-methyl-1-pentanol at specified state conditions. The focus of this challenge was on evaluating methods that could be applied to more difficult liquid-liquid equilibrium problems where a third component is present at a high enough concentration to influence the mutual solubilities of the two main components. Four groups accepted the challenge and used a variety of molecular simulation methods.

Keywords: 1-octanol/water partition coefficient, activity coefficient, industrial fluid properties simulation challenge, 1-ethylpropylamine, 3-methyl-1-pentanol, molecular simulation

### 1. Introduction

In recent years, a series of simulation challenges has been organized to demonstrate the capabilities of modern molecular simulation methods, especially molecular dynamics and Monte Carlo methods, to provide useful predictions of thermophysical properties of

fluids that are industrially relevant. Another important aspect of these simulation challenges is the identification of areas in which molecular simulation requires further development.

The first four challenges are described in earlier issues of this journal. [1-4] The background and history of the challenges has been described earlier [4] and will not be repeated in detail here. In summary, the simulation challenge is aligned with the vision of the Industrial Fluid Properties Simulation Collective:

A robust, accurate, and easy-to-use set of modeling tools will be widely available for the prediction of physical properties of fluids and obtaining insight into the connections between molecular structure and properties. As a part of this tool set, molecular simulation will become a breakthrough technology that is widely accepted in the chemical industry and applied in conjunction with other predictive methods to meet the industry's evolving fluid property data needs. Through an international collaboration (IFPSC) between industry, academia, and national labs (coordinated by the National Institute of Standards and Technology), we will develop Standard Reference Simulations, validation of methods, quantification of uncertainty, force field and simulation databases, communication standards between computer programs, and recommendations regarding the use of other predictive methods, thus enabling users to select the appropriate tools to achieve results with requisite accuracy and insight.

Though progress has been made, this vision remains mostly unrealized in the chemical industry as was noted recently. [5]

Multi-component phase equilibrium is deeply rooted in all aspects of science, technology, and industry. Key quantities that are often required to make these calculations in practical settings are partition (distribution) coefficients and infinite-dilution activity coefficients, both of which describe the solubility of a solute in a solvent(s). In particular, the partition coefficient quantifies the relative solubility of a solute in two different, usually immiscible, solvents. The activity coefficient describes the solubility of a given solute in a specific solvent. For some solution models, knowledge of the infinite-dilution activity coefficient can be used to predict the solubility over a significant range of conditions. [6]

The objective of the Fifth Challenge was to test the ability of computer modeling (any molecular simulation method) to predict the 1-octanol/water partition coefficient,  $K_{OW}$ , and infinite dilution activity coefficient ( $\gamma_{\infty}$ ) in water for two compounds, 1-ethylpropylamine (CAS# 616-24-0) and 3-methyl-1-pentanol (CAS# 589-35-5). The specific states are listed in the following section. The prediction of 1-octanol/water partition coefficients, which have been widely studied by non-molecular simulation methods, is viewed as a stepping stone to more difficult liquid-liquid-equilibrium (LLE) problems, such as the situation where a third component is present at a high enough level to influence the mutual solubilities of the other two components. Molecular dynamics and Monte Carlo simulation methods have been used in conjunction with free energy

determinations to determine  $K_{ow}$  for compounds where the experimental values are known. [7-9] For this Challenge, the solutes were chosen in part because the experimental values of the partition coefficient were not available.

The structures of the solute molecules for this challenge are shown in Figure. 1

## 2. The Challenge

The Challenge consisted of two parts for each of the molecules, 1-ethylpropylamine and 3-methyl-1-pentanol. The first part was to compute the 1-octanol/water partition coefficient (in mole fraction units assuming neutral species) at 300 K and 101.325 kPa. The second part was to compute the infinite-dilution activity coefficient (mole fraction units with Lewis and Randall reference state [10]) for the molecules in water at 325 K and 13.5 kPa.

Four groups accepted the challenge and submitted valid entries. A group of simulation experts, who did not enter the challenge and were external to the organizing committee, examined the entries to see that the rules of the competition were followed and that the work was valid. The rules of the challenge can be found on the organizing committee's web site. [11] The work of the first three groups is discussed in separate papers in this special issue. [12-14] The fourth group chose to not submit a paper.

The first entry by C-M. Hsieh and S-T. Lin, used the Peng-Robinson equation of state with the parameters in the equation of state determined using a solvation model developed on first principle COSMO calculations to make their predictions. [12] The second entry from A. Klamt, F. Eckert, and M. Diedenhofen used the COSMO-RS theory (Conductor-like Screening Model with extension to Real Solvents). [13] The third entry from Y. Liu, X. Li, L. Wang, and H. Sun used molecular dynamics and thermodynamic integration to calculate the residual chemical potentials of the solutes in the appropriate solvents. [14] The fourth entry from J. R. Elliott used a second order perturbation theory approach parameterized using data for a small set of related molecules.

## 3. Results

The predicted values for the partition coefficients and activity coefficients are compared with the experimental values in Figures 2 and 3. The experimental values were determined at Dow Chemical, as described in the paper following this one, [15] and the values were not available until after the closing date for submission of entries was past.

The entries were ranked using two metrics, a quantitative accuracy metric and a relative accuracy metric, with a maximum point total of 100. These metrics were structured to indicate how industrial modelers would value the worth of the predictions.

The first metric is a Quantitative Accuracy Metric (60%). For each property, full credit was awarded for predictions within the uncertainty limit of 5% of the experimental value. A linear interpolation of partial credit was awarded for predictions with an absolute deviation above the minimum threshold and a maximum of 40%. No points were awarded for prediction above the maximum deviation.

The second metric is a Relative Accuracy - Relative Ranking Metric (40%). The computed 1-octanol/water partition coefficient and the infinite-dilution activity coefficient of each molecule were compared to the respective experimental values. The molecule that was in best agreement to experiment was used as a normalization to determine relative coefficients (ie: (coefficient worst predicted)/(coefficient best)). The relative ratios were compared to the corresponding normalized ratios using the experimental data. The quantity (coefficient/coefficient-ref) predicted received full credit if it was within 5% of the corresponding quantity (coefficient/coefficient-ref) from experiment. As in the quantitative accuracy section, similar partial credit was awarded on a sliding scale.

Using these metrics, entry 1 was found to have the best score. Entry 3 received special recognition as the best molecular dynamics simulation entry.

#### 4. Discussion

This section contains some additional comments/observations about the entries that may be of interest to the industrial modeling community. The entries earning the highest point totals, entries 1 and 2, focused primarily on modeling the electrostatic interactions. Both made use of specific prior knowledge of parameters based on comparisons of properties of a substantial set of fluid properties for “related” molecules. In this sense, it is the parameterization of interactions in these approaches that is different from the type used to determine explicit intermolecular and intramolecular interaction parameters used in molecular dynamics (and Monte Carlo) simulations.

One aspect of the molecular simulation results that was not included in the ranking metrics was the inherent uncertainty of the simulation results for the specific models (i.e., forcefield) used. How to include this in the ranking is not clear to us and suggestions from the simulation community would be most welcome for inclusion in future Challenges.

Each of the simulation-based entries used a free energy based approach to determine the 1-octanol/water partition coefficient, which is related to the ratio of fugacities in the two phases. An alternative that was not followed, for good reason, would be the direct simulation of some molecules of the solute partitioned between the phases. The reason for not attempting this direct approach is that the sampling problems are severe. An indication of the nature of the sampling issues is contained in a recent simulation of 1-octanol/water. [16]

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## Symbols

$K_{OW}$  1-octanol/water partition coefficient

Greek letters

$\gamma_{\infty}$  infinite dilution activity coefficient

## References

- [1] F. Case, A. Chaka, D. G. Friend, D. Frurip, J. Golab, R. Johnson, J. Moore, R. D. Mountain, J. Olson, M. Schiller, J. Storer, *Fluid Phase Equilibr.* 217 (2004) 1-10.
- [2] F. Case, A. Chaka, D. G. Friend, D. Frurip, J. Golab, P. Gordon, R. Johnson, P. Kolar, J. Moore, R. D. Mountain, J. Olson, R. Ross, M. Schiller, *Fluid. Phase. Equilibr.* 236 (2005) 1-14.
- [3] F. H. Case, J. Brennan, A. Chaka, K. D. Dobbs, D. G. Friend, D. Frurip, P. A. Gordon, J. Moore, R. D. Mountain, J. Olson, R. B. Ross, M. Schiller, V. K. Shen, *Fluid Phase Equilibr.* 260 (2007) 153-163.
- [4] F. H. Case, J. Brennan, A. Chaka, K. D. Dobbs, D. G. Friend, P. A. Gordon, J. D. Moore, R. D. Mountain, J. D. Olson, R. B. Ross, M. Schiller, V. K. Shen, E. A. Stahlberg, *Fluid Phase Equilibr.* 274 (2008) 2-9.
- [5] E. J. Maginn, *AIChE J.* 55 (2009) 1304-1310.
- [6] J. M. Prausnitz, R. N. Lichtenthaler, and E. G. de Azevedo, *Molecular Thermodynamics of Fluid-Phase Equilibria*, Prentice Hall (1998) 804-807.
- [7] E. M. Duffy, W. L. Jorgensen, *J. Am. Chem. Soc.* 122 (2000) 2878-2888.
- [8] A. P. Lyubartsev, S. P. Jacobsson, G. Sundholm, A. Laaksonen, *J. Phys. Chem. B.* 105 (2001) 7775-7782.
- [9] C. A. F. De Oliveira, C. R. W. Guimarães, H. De Mello, A. Echevarria, R. B. De Alencastro, *Intl. J. Quantum Chem.* 102 (2005) 542-553.
- [10] J. M. Prausnitz, R. N. Lichtenthaler, and E. G. de Azevedo, *Molecular Thermodynamics of Fluid-Phase Equilibria*, Prentice Hall (1998) 20-23, 222-225.
- [11] <http://fluidproperties.org>
- [12] C-M. Hsieh, S-T. Lin, *Fluid Phase Equilibr.* (this issue)
- [13] A. Klamt, F. Eckert, M. Diedenhofen, *Fluid Phase Equilibr.* (this issue)
- [14] Y. Liu, X. Li, L. Wand, H. Sun, *Fluid Phase Equilibr.* (this issue).
- [15] J. D. Olson, *Fluid Phase Equilibr.* (this issue).
- [16] B. Chen, J. I. Siepmann, *J. Phys. Chem. B* 110 (2006) 3555-3565.

Figure 1. The structure of the solute molecules.

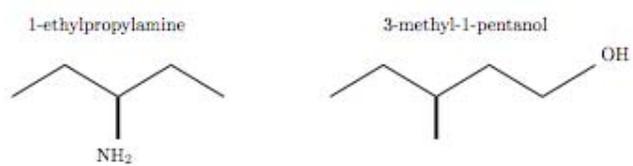


Figure 2. The results for the 1-octanol/water partition coefficient. Entry #0 is the experimental values while entries 1-4 are for the groups listed. The circles are for 1-ethylpropylamine and the squares are for 3-methyl-1-pentanol.

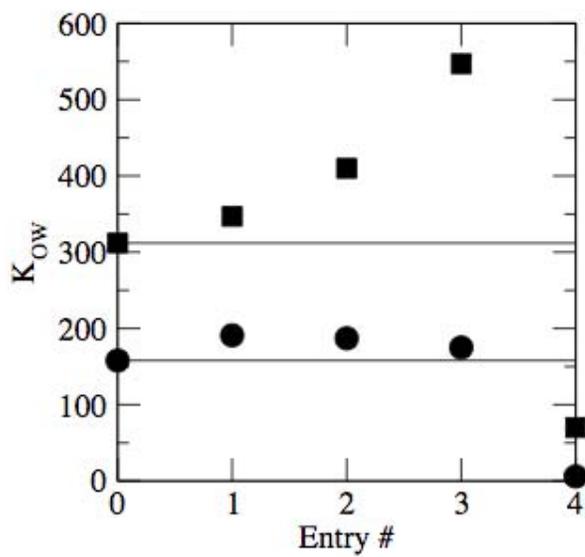


Figure 3. The results for the infinite dilution activity coefficients. The symbols are the same as for Figure 2.

