


Supplementary Materials: Predicting the Solubility of Nonelectrolyte Solids using a Combination of Molecular Simulation with the Solubility Parameter Method MOSCED: Application to the Wastewater Contaminants Monuron, Diuron, Atrazine and Atenolol

Rachel C. Ollier¹, Thomas Nguyen¹, Hrithik Agarwal^{1,2}, Jeremy R. Phifer¹, Larissa Ferreira da Silva^{1,3}, Gabriel Gonçalves Nogueira^{1,3}, Ana Karolyne Pereira Barbosa^{1,4}, Ryan T. Ley¹, Elizabeth J. O'Loughlin¹, Brett T. Rygelski¹, Spencer J. Sabatino¹, and Andrew S. Paluch^{1,*} 

1. MOSCED's Association Term

As in UNIQUAC, the combinatorial term can readily be modeled using the athermal Flory-Huggins equation (or one of its various extensions) [1–3]. The residual term can be modeled using a solubility parameter based method. The original Scatchard-Hildebrand regular solution theory (RST) takes the form [1,2]:

$$\ln \gamma_2^{\infty, \text{RES}} = \frac{v_2}{RT} (\delta_1 - \delta_2)^2 \quad (1)$$

where R is the molar gas constant, v_2 is the molar volume of component 2, and δ_i is the solubility parameter of component $i = \{1, 2\}$, defined as the square root of the component's cohesive energy density. Unfortunately, for all cases we find that $\ln \gamma_2^{\infty, \text{RES}}$ is positive. This limitation stems from the fact that RST only accounts for dispersion interactions. Additional interactions may be taken into account by expanding the cohesive energy density as a sum of contributions (or partial solubility parameters) [2,4–6]. For example, the expansion used by the Hansen Solubility Parameter (HSP) method takes the form [5,7]:

$$\delta_i^2 = \delta_{i,D}^2 + \delta_{i,P}^2 + \delta_{i,H}^2 = \lambda_i^2 + \tau_i^2 + (\alpha_i \beta_i)^2 \quad (2)$$

where $\delta_{i,D}$, $\delta_{i,P}$, and $\delta_{i,H}$ correspond to the solubility parameter resulting from dispersion, polar, and association (or hydrogen bonding) interactions, respectively. We equivalently write our dispersion and polar solubility parameters as λ_i and τ_i , respectively, and write the association solubility parameter as the product of the contribution due to hydrogen bond acidity (α_i) and basicity (β_i). This results in:

$$\ln \gamma_2^{\infty, \text{RES}} = \frac{v_2}{RT} [(\lambda_1 - \lambda_2)^2 + (\tau_1 - \tau_2)^2 + (\alpha_1 \beta_1 - \alpha_2 \beta_2)^2] \quad (3)$$

While HSP offers an improvement in accuracy, unfortunately we again find that for all cases $\ln \gamma_2^{\infty, \text{RES}}$ is positive. Tijssen et al. [6] acknowledged the deficiency and suggested a splitting of the association term, leading to the following expression:

$$\ln \gamma_2^{\infty, \text{RES}} = \frac{v_2}{RT} [(\lambda_1 - \lambda_2)^2 + (\tau_1 - \tau_2)^2 + 2(\alpha_1 - \alpha_2)(\beta_1 - \beta_2)] \quad (4)$$

With this update, the association term can be positive or negative, allowing $\ln \gamma_2^{\infty, \text{RES}}$ to be positive or negative. We can re-write the association term to better understand its physical meaning as [8]:

$$(\alpha_1 - \alpha_2)(\beta_1 - \beta_2) = -(\alpha_1 \beta_2 + \alpha_2 \beta_1) + (\alpha_1 \beta_1 + \alpha_2 \beta_2) = -2(\bar{\alpha} \bar{\beta}_{\text{cross}} - \bar{\alpha} \bar{\beta}_{\text{self}}) \quad (5)$$

where we have defined $\bar{\alpha} \bar{\beta}_{\text{cross}}$ and $\bar{\alpha} \bar{\beta}_{\text{self}}$ to be the mean “cross” and “self” association term (or interaction energy), respectively:

$$\begin{aligned}\overline{\alpha\beta}_{\text{cross}} &= \frac{1}{2}(\alpha_1\beta_2 + \alpha_2\beta_1) \\ \overline{\alpha\beta}_{\text{self}} &= \frac{1}{2}(\alpha_1\beta_1 + \alpha_2\beta_2)\end{aligned}\quad (6)$$

If the system has favorable intermolecular cross-association interactions (relative to the self-association interactions), such that the two components would prefer to associate with each other, the association term will be negative. We therefore see that the limitation of HSP is that it compares only the self-association interaction of the two components (see eq. (3)). The split association term given by eq. (4) forms the basis of MOSCED, which has been shown to predict a range of phase-equilibrium with a high level of accuracy [8–15]. Interestingly, it has been suggested that HSP could be improved by likewise splitting the association term [16–19].

2. MOSCED's Asymmetry Terms

While empirical in nature, the inclusion of the asymmetry terms ψ_1 and ζ_1 are physically based and very important to modify the residual contribution for polar and hydrogen bonding interactions. The solubility parameters are solute descriptors. The same parameters used to characterize a solute may not be appropriate to characterize a solvent [20,21]. This disparity is accounted for (or corrected) by including ψ_1 and ζ_1 . These additional terms are not adjustable, but are a function of the solvent solubility parameters. The functional form has been optimized for numerical predictions. As emphasized by Park and Carr [22], the introduction of the asymmetry terms was a major advancement in improving the predictive accuracy of MOSCED over other solubility parameter methods.

3. MOSCED and Wilson's Equation

For a binary system we can compute the composition dependent activity coefficient of component 1 and 2, at mole fraction composition x_1 and $x_2 = 1 - x_1$ as:

$$\begin{aligned}\ln \gamma_{1,2} &= -\ln(x_1 + \Lambda_{12}x_2) + x_2 \left(\frac{\Lambda_{12}}{x_1 + \Lambda_{12}x_2} - \frac{\Lambda_{21}}{\Lambda_{21}x_1 + x_2} \right) \\ \ln \gamma_{2,1} &= -\ln(x_2 + \Lambda_{21}x_1) - x_1 \left(\frac{\Lambda_{12}}{x_1 + \Lambda_{12}x_2} - \frac{\Lambda_{21}}{\Lambda_{21}x_1 + x_2} \right)\end{aligned}\quad (7)$$

where Λ_{12} and Λ_{21} are adjustable parameters which may be related to the binary (inter-molecular) interaction parameters (BIPs) of the system (a_{12} and a_{21}):

$$\begin{aligned}\Lambda_{12} &= \frac{v_2}{v_1} \exp \left[-\frac{a_{12}}{RT} \right] \\ \Lambda_{21} &= \frac{v_1}{v_2} \exp \left[-\frac{a_{21}}{RT} \right]\end{aligned}\quad (8)$$

where v_1 and v_2 are the molar volume of pure component 1 and 2, respectively. At infinite dilution, eq. (7) reduces to:

$$\begin{aligned}\ln \gamma_{1,2}^\infty &= -\ln(\Lambda_{12}) + 1 - \Lambda_{21} \\ \ln \gamma_{2,1}^\infty &= -\ln(\Lambda_{21}) + 1 - \Lambda_{12}\end{aligned}\quad (9)$$

It follows that with knowledge of the limiting activity coefficient of each component in the binary mixture, eq. (9) reduces to a system of two equations with two unknowns that can be used to parameterize Wilson's equation. This would allow one to calculate composition dependent activity coefficients, and moreover this approach may readily be generalized to

multi-component systems. Wilson's equation has two binary parameters for each pair in a multi-components system, where limiting activity coefficients may be used to parameterize each binary pair [1].

4. Note on Solute Force Fields

The solute alkyl groups (CH_3 , CH_2 and CH) were modeled as a single united-atom pseudoatom as a result of the parameterization of the TraPPE-EH force field for *n*-alkanes which places the LJ site for a hydrogen atom at the center of the corresponding bond [23], and the complication of implementing such a model in a molecular dynamics framework. When generating intermolecular parameters using ANTECHAMBER, all sites were modeled explicitly. This ensured the atom types were properly identified. Once the final set of intramolecular parameters was obtained, intramolecular parameters involving alkyl hydrogens were removed. When computing CM4 partial atomic charges, the partial atomic charges computed for each alkyl group was summed together and placed at the center of the UA site. When using RESP, we are able to constrain the alkyl-H partial atomic charges to 0.

Additionally, note that TraPPE-EH does parameterize aniline in ref. 24. We chose not to use the N LJ parameters from aniline because it is a primary amine, and it was previously shown in ref. 25 that there is an appreciable change in LJ parameters in going from a primary to secondary amine. Also, in ref. 25, the primary amide LJ parameters are the same as the primary amine (i.e., only the charges change). Therefore, we took the secondary amide LJ parameters for N to be the same as for a secondary amine. The H has LJ parameters of 0 in primary and secondary amines and primary amides. The LJ parameters for H in a secondary amide were therefore taken to also be 0 in the present study.

1. Prausnitz, J.M.; Lichtenthaler, R.N.; de Azevedo, E.G. *Molecular Thermodynamics of Fluid-phase Equilibria*, 2nd ed.; Prentice-Hall, Inc.: Englewood Cliffs, NJ, 1986.
2. Hildebrand, J.H.; Prausnitz, J.M.; Scott, R.L. *Regular and Related Solutions*; Van Nostrand Reinhold Company: New York, NY, 1970.
3. Abrams, D.S.; Prausnitz, J.M. Statistical thermodynamics of liquid mixtures: A new expression for the excess Gibbs energy or partly or completely miscible systems. *AIChE J.* **1975**, *21*, 116–128.
4. Blanks, R.F.; Prausnitz, J.M. Thermodynamics of Polymer Solubility in Polar and Nonpolar Systems. *Ind. Eng. Chem. Fundam.* **1964**, *3*, 1–8.
5. Hansen, C.M. The Universality of the Solubility Parameter. *Ind. Eng. Chem. Prod. Res. Dev.* **1969**, *8*, 2–11.
6. Tijssen, R.; Billiet, H.A.H.; Schoenmakers, P.J. Use of the solubility parameter for predicting selectivity and retention in chromatography. *J. Chromatogr. A.* **1976**, *122*, 185–203.
7. Hansen Solubility Parameters. (accessed 16 October 2020).
8. Dhakal, P.; Roese, S.N.; Stalcup, E.M.; Paluch, A.S. Application of MOSCED to Predict Hydration Free Energies, Henry's Constants, Octanol/Water Partition Coefficients, and Isobaric Azeotropic Vapor-Liquid Equilibrium. *J. Chem. Eng. Data* **2018**, *63*, 352–364.
9. Lazzaroni, M.J.; Bush, D.; Eckert, C.A.; Frank, T.C.; Gupta, S.; Olson, J.D. Revision of MOSCED Parameters and Extension to Solid Solubility Calculations. *Ind. Eng. Chem. Res.* **2005**, *44*, 4075–4083.
10. Draucker, L.C.; Janakat, M.; Lazzaroni, M.J.; Bush, D.; C. A. Eckert, T.C.F.; Olson, J.D. Experimental determination and model prediction of solid solubility of multifunctional compounds in pure and mixed nonelectrolyte solvents. *Ind. Eng. Chem. Res.* **2007**, *46*, 2198–2204.
11. Frank, T.C.; Anderson, J.J.; Olson, J.D.; Eckert, C.A. Application of MOSCED and UNIFAC to screen hydrophobic solvents for extraction of hydrogen-bonding organics from aqueous solution. *Ind. Eng. Chem. Res.* **2007**, *46*, 4621–4625.
12. Dhakal, P.; Paluch, A.S. Assessment and Revision of the MOSCED Parameters for Water: Applicability to Limiting Activity Coefficients and Binary Liquid-Liquid Equilibrium. *Ind. Eng. Chem. Res.* **2018**, *57*, 1689–1695.
13. Dhakal, P.; Ouimet, J.A.; Roese, S.N.; Paluch, A.S. MOSCED parameters for 1-*n*-alkyl-3-methylimidazolium-based ionic liquids: Application to limiting activity coefficients and intuitive entrainer selection for extractive distillation processes. *J. Mol. Liq.* **2019**, *293*, 111552.
14. Dhakal, P.; Weise, A.R.; Fritsch, M.C.; O'Dell, C.M.; Paluch, A.S. Expanding the Solubility Parameter Method MOSCED to Pyridinium, Quinolinium, Pyrrolidinium, Piperidinium, Bicyclic, Morpholinium, Ammonium, Phosphonium, and Sulfonium Based Ionic Liquids. *ACS Omega* **2020**, *5*, 3863–3877.

15. Brouwer, T.; Schuur, B. Model Performances Evaluated for Infinite Dilution Activity Coefficients Prediction at 298.15 K. *Ind. Eng. Chem. Res.* **2019**, *58*, 8903–8914.
16. Panayiotou, C. Redefining solubility parameters: the partial solvation parameters. *Phys. Chem. Chem. Phys.* **2012**, *14*, 3882–3908.
17. Stefanis, E.; Panayiotou, C. A new expanded solubility parameter approach. *Int. J. Pharm* **2012**, *426*, 29–43.
18. Beerbower, A.; Wu, P.L.; Martin, A. Expanded Solubility Parameter Approach I: Naphthalene and Benzoic Acid in Individual Solvents. *J. Pharm. Sci.* **1984**, *73*, 179–188.
19. Louwerse, M.J.; Maldonado, A.; Rousseau, S.; Moreau-Masselon, C.; Roux, B.; Rothenberg, G. Revisiting Hansen Solubility Parameters by Including Thermodynamics. *ChemPhysChem* **2017**, *18*, 2999–3006.
20. Vitha, M.; Carr, P.W. The chemical interpretation and practice of linear solvation energy relationships in chromatography. *J. Chromatogr. A* **2006**, *1126*, 143–194.
21. Poe, R.B.; Rutan, S.C.; Hait, M.J.; Eckert, C.A.; Carr, P.W. Developing Models for Infinite Dilution Activity-Coefficients Using Factor-Analysis Methods. *Anal. Chim. Acta* **1993**, *277*, 223–238.
22. Park, J.H.; Carr, P.W. Predictive Ability of the MOSCED and UNIFAC Activity Coefficient Estimation Methods. *Anal. Chem.* **1987**, *59*, 2596–2602.
23. Chen, B.; Siepmann, J.I. Transferable Potentials for Phase Equilibria. 3. Explicit-Hydrogen Description of Normal Alkanes. *J. Phys. Chem. B* **1999**, *103*, 5370–5379.
24. Rai, N.; Bhatt, D.; Siepmann, J.I.; Fried, L.E. Monte Carlo simulations of 1,3,5-triamino-2,4,6-trinitrobenzene (TATB): Pressure and temperature effects for the solid phase and vapor-liquid phase equilibria. *J. Chem. Phys.* **2008**, *129*, 194510.
25. Wick, C.D.; Stubbs, J.M.; Rai, N.; Siepmann, J.I. Transferable Potentials for Phase Equilibria. 7. Primary, Secondary, and Tertiary Amines, Nitroalkanes and Nitrobenzene, Nitriles, Amides, Pyridine, and Pyrimidine. *J. Phys. Chem. B* **2005**, *109*, 18974–18982.