Activity of Complex Multifunctional Organic Compounds in Common Solvents

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Juergen Rarey
Deresh Ramjugernath
Overview

- Motivation
- Current Methods
- Plan of Action
- Applications
- Future Work
Project Motivation

- Solute activity required for:
  - Design of separation equipment
  - Partitioning between compartments
  - Dispensing of drugs
  - …
Some Current Methods

- Group contribution methods
  - UNIFAC, Mod. UNIFAC (Do)
- Quantum chemical methods
  - COSMO-RS/SAC
- Molecular simulation
- Problems …
Proposed Plan of Action

- Reference solvents

  - Dispersive e.g. Hexane
  - H-bonding e.g. Water
  - Dispersive & H-bonding e.g. Alcohols
Simplify the Problem

\[ \gamma = f(x, T, P, \text{solvent}, \text{solute}) \]

- Solvent
  - Reference solvents
- Concentration
  - Solid solubility data mainly of interest
  - Infinite dilution \((x < 0.01)\)
- Pressure
  - Small at low to moderate pressures
- Temperature
  - Non-trivial
  - 298 K
Simplify the Problem

\[ \gamma_{298K,\text{solvent}}^\infty = f(\text{solute}) \]

- Pure component property

\[
\ln \gamma_{\text{solute in solvent}}^\infty = \sum_i v_i C_i + \frac{1}{2} \sum_i \sum_j \frac{G_{i-j}}{n(m)}
\]

- Trained to data for a single solvent

- Group Contributions
  
- Group Interactions

\[ v_i \rightarrow \text{group frequency} \]

\[ C_i \rightarrow \text{group contribution} \]

\[ G_{i-j} \rightarrow \text{interaction contribution} \]

\[ n \rightarrow \text{number of non-H atoms} \]

\[ m \rightarrow \text{number of interaction groups} \]
Available Data

- Most frequent solvents in the $\gamma^\infty$ DDB
  - Water
  - Others ???

<table>
<thead>
<tr>
<th>Solvent</th>
<th>No. Solutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>585</td>
</tr>
<tr>
<td>Squalane</td>
<td>207</td>
</tr>
<tr>
<td>Hexadecane</td>
<td>198</td>
</tr>
<tr>
<td>Sulfolane</td>
<td>137</td>
</tr>
<tr>
<td>1-Octanol</td>
<td>128</td>
</tr>
<tr>
<td>Phthalic acid dinonyl ester</td>
<td>126</td>
</tr>
<tr>
<td>Heptane</td>
<td>116</td>
</tr>
<tr>
<td>N-Methyl-2-pyrrolidone</td>
<td>115</td>
</tr>
<tr>
<td>Octadecane</td>
<td>103</td>
</tr>
<tr>
<td>19,24-Dioctadecyldotetracontane</td>
<td>99</td>
</tr>
</tbody>
</table>
Results for Infinite Dilution Activity Coefficients in Water @ 298 K

<table>
<thead>
<tr>
<th>Name</th>
<th>This Work</th>
<th>UNIFAC*</th>
<th>Mod. UNIFAC*</th>
<th>COSMO-RS(OL)**</th>
<th>COSMO-SAC**</th>
</tr>
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<tbody>
<tr>
<td>All compounds</td>
<td>7.3^{630}</td>
<td>23.7^{442}</td>
<td>14.9^{396}</td>
<td>23.4^{295}</td>
<td>30.0^{295}</td>
</tr>
</tbody>
</table>

- Significantly lower relative mean deviation (%) in lnγ^∞
- Typically 2nd best, far superior to the other literature methods
- More generally applicable (greater number of compounds)

* Consortium version 2008
** Based on B3LYP-6-311G(d,p)
Available Data

- Most frequent solvents in the $\gamma^\infty$ DDB
  - Water
  - Others ???

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alkane

water
Reduction to a Common Solvent - Hexane

- Combinatorial and residual contribution
- Solution of groups concept

\[ \gamma_{1,\text{hexane}}^\infty = \gamma_{1,\text{hexane}}^{R,\infty} \times \gamma_{1,\text{hexane}}^{C,\infty} \]

\[ \gamma_{1,\text{squalane}}^\infty = \gamma_{1,\text{squalane}}^{R,\infty} \times \gamma_{1,\text{squalane}}^{C,\infty} \]
Reduction to a Common Solvent - Hexane

- Combinatorial and residual contribution
- Solution of groups concept

\[ \gamma_{1,\text{hexane}}^\infty = \gamma_{1,\text{squalane}}^\infty \]

\[ \gamma_{1,\text{hexane}}^{R,\infty} \times \gamma_{1,\text{squalane}}^{C,\infty} = \gamma_{1,\text{squalane}}^{R,\infty} \times \gamma_{1,\text{squalane}}^{C,\infty} \]
Reduction to a Common Solvent - Hexane

- Combinatorial and residual contribution
- Solution of groups concept

\[ \gamma_{1,\text{hexane}} = \frac{\gamma_{1,\text{hexane}}^{\infty}}{\gamma_{1,\text{reference}}^{\infty}} \]
Performance of Combinatorial Expressions

- Ethanol (2) in alkanes (1) ...
Performance of Combinatorial Expressions

- Ethylcyclohexane (2) in alkanes (1) …

Error starts to become noticeable when $q_1/q_2 < 0.8$
Performance of Combinatorial Expressions

Infinite dilution activity coefficient data

Big solutes in small solvents

- <0.5: 11.9%
- 0.5-0.8: 46.4%
- 0.8-1.2: 18.5%
- 1.2-1.5: 9.0%
- >1.5: 14.1%
New Combinatorial Expression

- Modified the FV expression as follows:

\[ \gamma_{C,\infty}^2 = \exp \left( 1 - \frac{V_{i}^{FV}}{V_{1}^{FV}} + \ln \left( \frac{V_2^{FV}}{V_1^{FV}} \right) - 5q_2 \left( 1 - \frac{r_2}{r_1} + \ln \left( \frac{r_2}{q_2} \right) \right) \right) \]

\[ V_{i}^{FV} = \left( V_i \right)^{2/3} - \left( V_i^* \right)^{2/3} \]

\( V_i \) – Molar volume (cm\(^3\)/mol)

\( V_i^* \) - van der Waals Volume (cm\(^3\)/mol)

\( q_i \) – UNIQUAC surface area

\( r_i \) – UNIQUAC volume
Performance of the New Combinatorial Expression

- Ethylcyclohexane (2) in alkanes (1) …
Performance of the New Combinatorial Expression

- Exp. Data
- UNIFAC
- Mod. UNIFAC
- FV
- New Expression

Chemical Structures:
- hexane
- hexadecane (ref.)
- N'-(4-Chlorophenyl)-N,N-dimethyl-urea
Results for Infinite Dilution Activity Coefficients in Hexane

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<th>UNIFAC*</th>
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<th>COSMO-RS(OL)**</th>
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<tr>
<td>All compounds</td>
<td>25.9\textsuperscript{202}</td>
<td>47.6\textsuperscript{176}</td>
<td>37.7\textsuperscript{170}</td>
<td>48.1\textsuperscript{156}</td>
<td>54.5\textsuperscript{156}</td>
</tr>
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- Lowest relative mean deviation (%) in $\ln \gamma^\infty$
- More generally applicable (greater number of compounds)
- Typically 2\textsuperscript{nd} best

* Consortium version 2008
** Based on B3LYP-6-311G(d,p)
Interpolation between Water and Hexane

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{OH} \\
\text{H}_2 & & \text{H}_2 & & \text{H}_2
\end{align*}
\]

\[a_i,\text{CH}_2\quad a_i,\text{OH}\]
Applications

<table>
<thead>
<tr>
<th>Solvent</th>
<th>$a_{OH}$</th>
<th>$a_{CH_3}$</th>
<th>$\gamma^{\exp.}$</th>
<th>$\gamma^{\pred.}$</th>
<th>RMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>1.8</td>
<td>0</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethanol</td>
<td>0.296</td>
<td>0.704</td>
<td>16.53</td>
<td>15.8</td>
<td>4.5%</td>
</tr>
<tr>
<td>Hexane</td>
<td>0</td>
<td>2</td>
<td>764</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Paracetamol
Applications

\begin{center}
\includegraphics[width=\textwidth]{chart.png}
\end{center}

\textbf{9H-Fluorene}

- tert-pentanol
- ethanol
- methanol

\textbf{γ prediction}

\textbf{γ∞ experimental}

- This work
- UNIFAC
- Mod. UNIFAC
- Ideal fit line
Future Work

- Add a polar solvent?

- Other approaches?
Conclusion

Initial problem

Solvent Extrapolation

Interpolate to alcohols

Pure component property

Water / Hexane
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  - Prof. J. Rarey

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  - Prof. J. Gmehling
  - Prof. D. Ramjugernath

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  - DDBST GmbH

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