Supporting Information: Prediction of Aqueous Free Energies of Solvation Using Coupled QM and MM Explicit Solvent Simulations

Daniel Sadowsky*,†,‡ and J. Samuel Arey†,¶

†*Environmental Chemistry Modeling Laboratory, École Polytechnique Fédérale de Lausanne (EPFL), GR C2 544, Station 2, 1015 Lausanne, Vaud, Switzerland*

‡*Division of Physical and Computational Sciences, The University of Pittsburgh at Bradford, 300 Campus Drive, Bradford, Pennsylvania 16701, United States*

¶*Current address: ExxonMobil Biomedical Sciences, Inc., Annandale, New Jersey 08801, United States*

E-mail: sadowsky@pitt.edu

Phone: 1-814-362-0982

S.1.1 Methodology

Table S.1: Values of the equilibrium length of the unit cell, a_{eq} (Å), density, ρ_{eq} ($g \cdot mL^{-3}$), and molar concentration, c (M), predicted by MM simulations in the NPT ensemble with a prescribed equilibrium temperature of 298.15 K and equilibrium pressure of 1.01325 bar.

solute	a_{eq}	ρ_{eq}	c [M]
none	12.3625	[a]0.9972	
argon	12.4509	1.0105	0.8603
methanol	12.4846	1.0058	0.8534
acetonitrile	12.5278	0.9929	0.8446
trans-1,2-dichloroethene	12.5944	1.0229	0.8312

[a] The experimental value at these conditions is 0.9970.

S.1.2 Predictions of MM Free Energies of Solvation

The predictions reported by Shivakumar et al.[7] for the four organic solutes in the test set are reproduced in Table S.2, together with the $\Delta_{solv}G^{MM}$ values predicted by this work and the previously reported experimental values. Shivakumar et al. found that for 239 neutral solutes, the predictions of free energies of aqueous solvation with the best agreement with experiment were those based on AM1 charges.

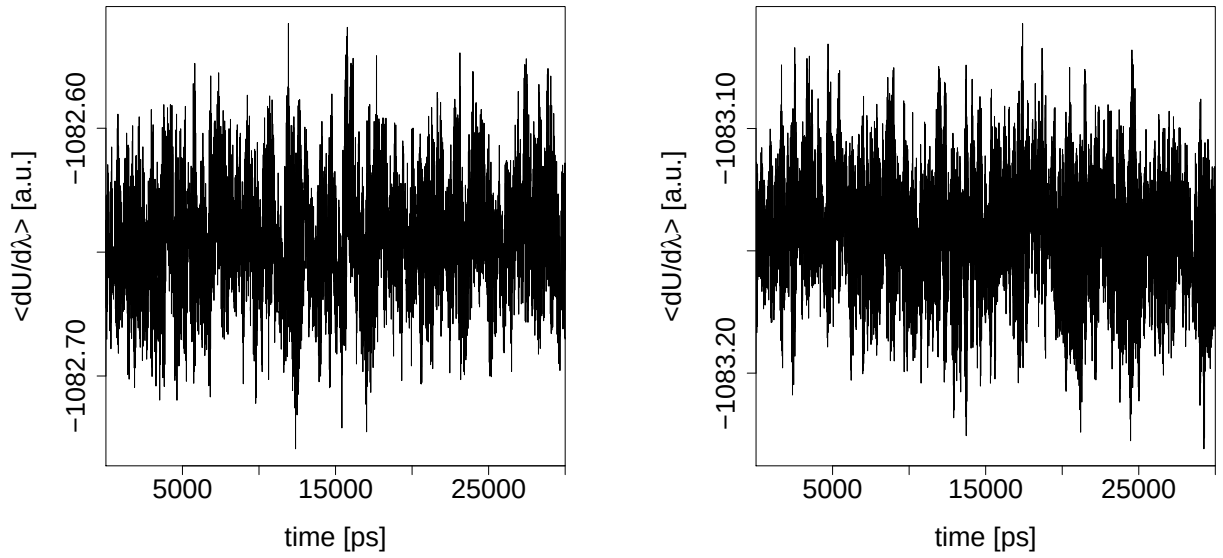
Table S.2: The free energies of aqueous solvation predicted by Shivakumar et al., the MM method in this work, and by experiment ($kJ \cdot mol^{-1}$).

solute	[a]GAFF/RESP	[a]GAFF/ChelpG	[a]GAFF/AM1	This work (MM)	experiment
methanol	-15.86	-15.52	-12.05	[b]-9.7 ± 0.2	-21.3 ± 0.2 [13]
acetonitrile	-12.22	-12.18	-7.20	[c]-17.2 ± 0.2	-17.7 ± 0.1 [15]
trans-1,2-dichloroethene	4.14	5.82	4.10	[b]10.7 ± 0.2	-2.36 ± 0.02[14]

[a]Taken from ref. 7.
[b]Parameters from GAFF/CM5 method.
[c]Parameters from ref. 20.

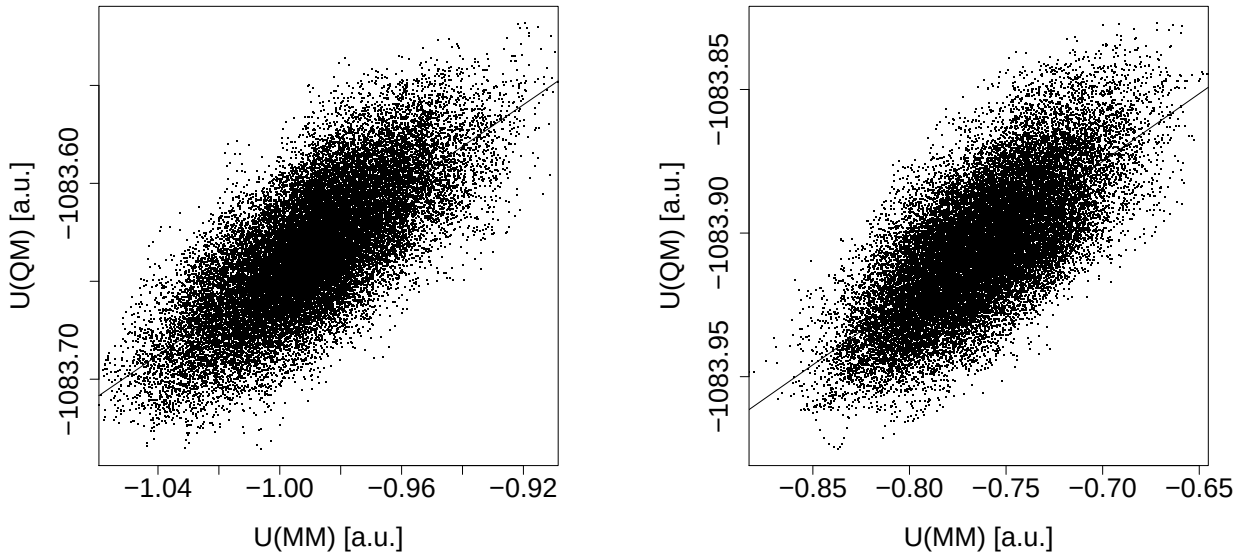
S.1.3 Predictions of Free Energies of Model Chemistry Transfer

Figure S.1: Time evolution of $< dU/d\lambda' >$ for 63 water molecules when $\lambda' = 0$ (a) and $\lambda' = 1$ (b).



(a) (b)

Figure S.2: Correlation between U^{QM} and U^{MM} for 63 water molecules when $\lambda' = 0$ (a) and $\lambda' = 1$ (b). The coefficients of determination (R^2) for the linear regressions are 0.538 (a) and 0.495 (b).



(a) (b)

Figure S.3: The thermodynamic integration of $\Delta_{MM\rightarrow QM}\mathrm{G}(v)$.