Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.


# Supplementary Information

## Energy-Entropy Method with Multiscale Cell Correlation to Predict Toluene-Water logP in the SAMPL9 Challenge.

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**Table S1.** Entropy Components (J $K^{-1}$ $mol^{-1}$) of Pure Water and of the Solute and Averaged Over All Solvent for Each Aqueous Solution

| Drug | Solute | | | | | | Solvent | | |
|---|---|---|---|---|---|---|---|---|---|
| | $S_{M}^{transvib}$ | $S_{M}^{rovib}$ | $S_{M}^{or}$ | $S_{UA}^{transvib}$ | $S_{UA}^{rovib}$ | $S_{UA}^{conf}$ | $S_{wat,UA}^{transvib}$ | $S_{wat,UA}^{rovib}$ | $S_{wat,UA}^{or}$ |
| - | - | - | - | - | - | - | 47.1 | 21.0 | 10.0 |
| 1 | 86.9 | 82.6 | 21.6 | 498.8 | 174.1 | 26.8 | 47.5 | 21.4 | 9.3 |
| 2 | 87.1 | 83.4 | 19.5 | 519.7 | 269.2 | 44.0 | 47.5 | 21.4 | 9.5 |
| 3 | 89.5 | 85.5 | 22.5 | 571.9 | 258.2 | 28.8 | 47.6 | 21.4 | 9.4 |
| 4 | 89.8 | 84.9 | 19.0 | 656.7 | 216.1 | 35.7 | 47.7 | 21.5 | 9.4 |
| 5 | 89.6 | 85.8 | 23.5 | 535.9 | 213.0 | 35.8 | 47.6 | 21.3 | 9.4 |
| 6 | 81.9 | 74.8 | 21.2 | 341.3 | 163.4 | 17.1 | 47.3 | 21.5 | 9.9 |
| 7 | 90.5 | 87.4 | 19.6 | 909.4 | 283.1 | 59.1 | 47.5 | 21.3 | 9.1 |
| 8 | 88.9 | 87.4 | 15.9 | 1048.9 | 319.1 | 80.0 | 47.4 | 21.3 | 9.0 |
| 9 | 89.1 | 85.1 | 23.0 | 571.4 | 265.4 | 38.0 | 47.5 | 21.4 | 9.2 |
| 10 | 86.0 | 80.9 | 20.5 | 515.8 | 169.2 | 32.9 | 47.6 | 21.4 | 9.3 |
| 11 | 87.3 | 82.5 | 21.3 | 446.5 | 143.0 | 17.8 | 47.6 | 21.3 | 9.1 |
| 12 | 82.9 | 75.4 | 21.2 | 268.8 | 114.1 | 9.2 | 47.5 | 21.4 | 9.8 |
| 13 | 86.1 | 82.4 | 19.6 | 497.5 | 236.7 | 28.8 | 47.5 | 21.3 | 9.5 |
| 14 | 88.4 | 86.0 | 19.2 | 696.0 | 271.4 | 20.3 | 47.6 | 21.4 | 9.2 |
| 15 | 85.2 | 79.9 | 21.3 | 542.1 | 179.0 | 25.6 | 47.3 | 21.4 | 9.4 |
| 16 | 89.4 | 87.8 | 18.1 | 763.8 | 238.4 | 45.6 | 47.4 | 21.3 | 9.1 |

**Table S2.** Entropy Components (J $K^{-1}$ $mol^{-1}$) of Pure Toluene and of the Solute and Averaged Over All Solvent for Each Toluene Solution

| Drug | Solute | | | | | | Solvent | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $S_{M}^{transvib}$ | $S_{M}^{rovib}$ | $S_{M}^{or}$ | $S_{UA}^{transvib}$ | $S_{UA}^{rovib}$ | $S_{UA}^{conf}$ | $S_{tol,M}^{transvib}$ | $S_{tol,M}^{rovib}$ | $S_{tol,M}^{or}$ | $S_{tol,UA}^{transvib}$ | $S_{tol,UA}^{rovib}$ |
| - | - | - | - | - | - | - | 72.4 | 59.9 | 23.8 | 36.6 | 28.0 |
| 1 | 91.3 | 84.2 | 26.2 | 500.9 | 175.1 | 24.5 | 72.4 | 59.9 | 23.6 | 36.6 | 28.1 |
| 2 | 90.5 | 85.6 | 25.7 | 522.6 | 269.2 | 41.1 | 72.4 | 59.9 | 24.1 | 36.6 | 28.0 |
| 3 | 91.1 | 86.7 | 28.1 | 572.6 | 258.3 | 30.4 | 72.4 | 59.9 | 24.5 | 36.6 | 28.0 |
| 4 | 91.7 | 86.7 | 26.7 | 657.4 | 215.6 | 36.0 | 72.4 | 59.9 | 24.0 | 36.6 | 28.1 |
| 5 | 91.6 | 87.9 | 27.6 | 536.3 | 212.8 | 36.1 | 72.4 | 59.9 | 24.4 | 36.6 | 28.0 |
| 6 | 90.4 | 84.8 | 27.2 | 339.9 | 167.2 | 17.8 | 72.4 | 59.9 | 24.2 | 36.6 | 28.0 |
| 7 | 93.1 | 90.4 | 25.4 | 908.1 | 284.4 | 70.4 | 72.4 | 59.9 | 23.8 | 36.6 | 28.0 |
| 8 | 92.3 | 89.4 | 23.8 | 1055.6 | 319.3 | 67.1 | 72.4 | 59.9 | 23.4 | 36.6 | 28.0 |
| 9 | 91.0 | 86.6 | 28.2 | 572.8 | 263.9 | 43.6 | 72.4 | 59.9 | 24.5 | 36.6 | 28.0 |
| 10 | 91.2 | 86.2 | 25.7 | 517.1 | 170.8 | 33.7 | 72.4 | 59.9 | 24.3 | 36.6 | 28.0 |
| 11 | 91.6 | 84.9 | 24.4 | 451.6 | 141.7 | 15.2 | 72.4 | 59.9 | 24.1 | 36.6 | 28.0 |
| 12 | 88.8 | 81.0 | 28.3 | 270.3 | 114.8 | 9.3 | 72.4 | 59.9 | 24.5 | 36.6 | 28.0 |
| 13 | 89.9 | 85.1 | 25.2 | 499.6 | 237.7 | 27.3 | 72.4 | 59.9 | 24.1 | 36.6 | 28.0 |
| 14 | 92.1 | 88.1 | 25.6 | 694.0 | 274.1 | 25.5 | 72.4 | 59.9 | 24.3 | 36.6 | 28.0 |
| 15 | 91.1 | 84.6 | 28.5 | 549.2 | 180.8 | 24.9 | 72.4 | 59.9 | 24.6 | 36.6 | 28.0 |
| 16 | 92.3 | 88.5 | 24.4 | 763.2 | 239.7 | 57.4 | 72.4 | 59.9 | 23.3 | 36.6 | 28.0 |

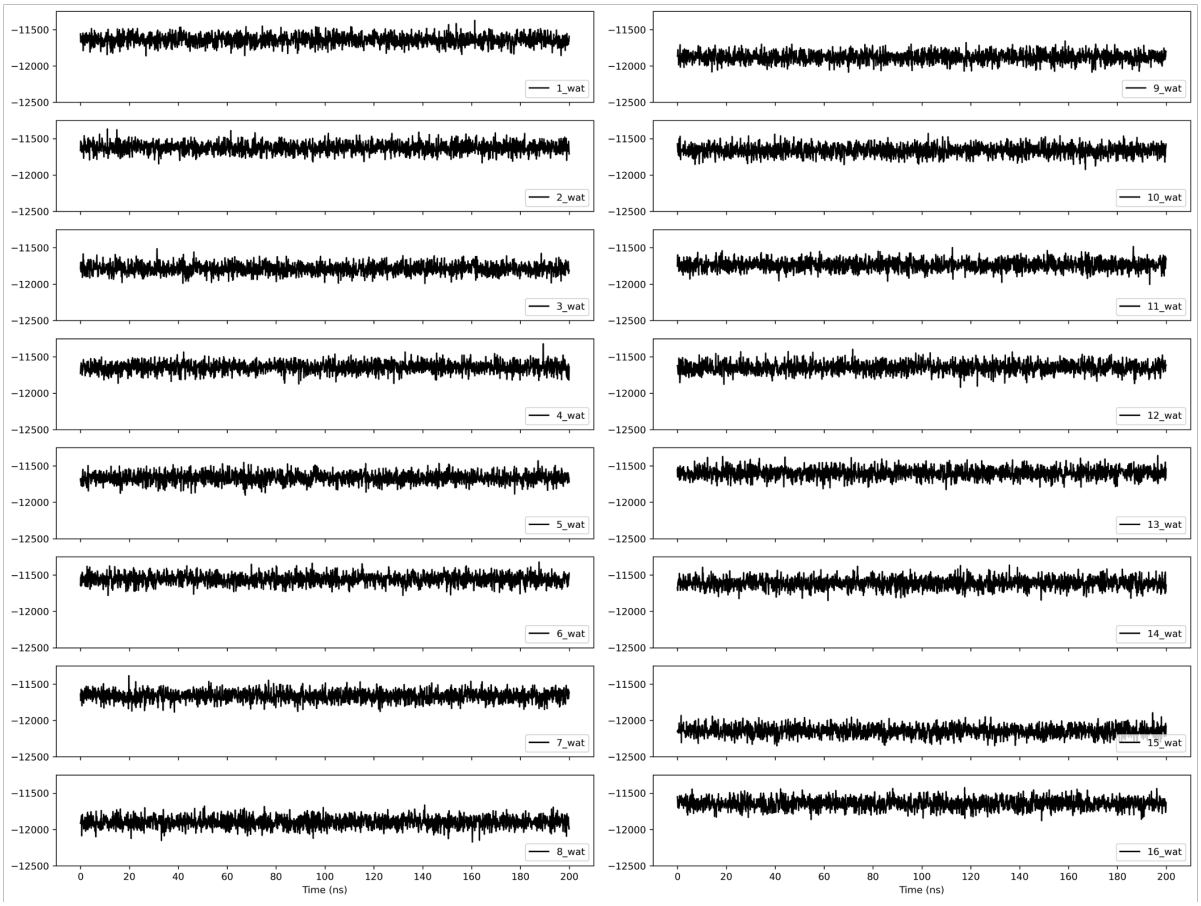


**Figure S1.** Energy versus simulation time for the 16 drug molecules in water.

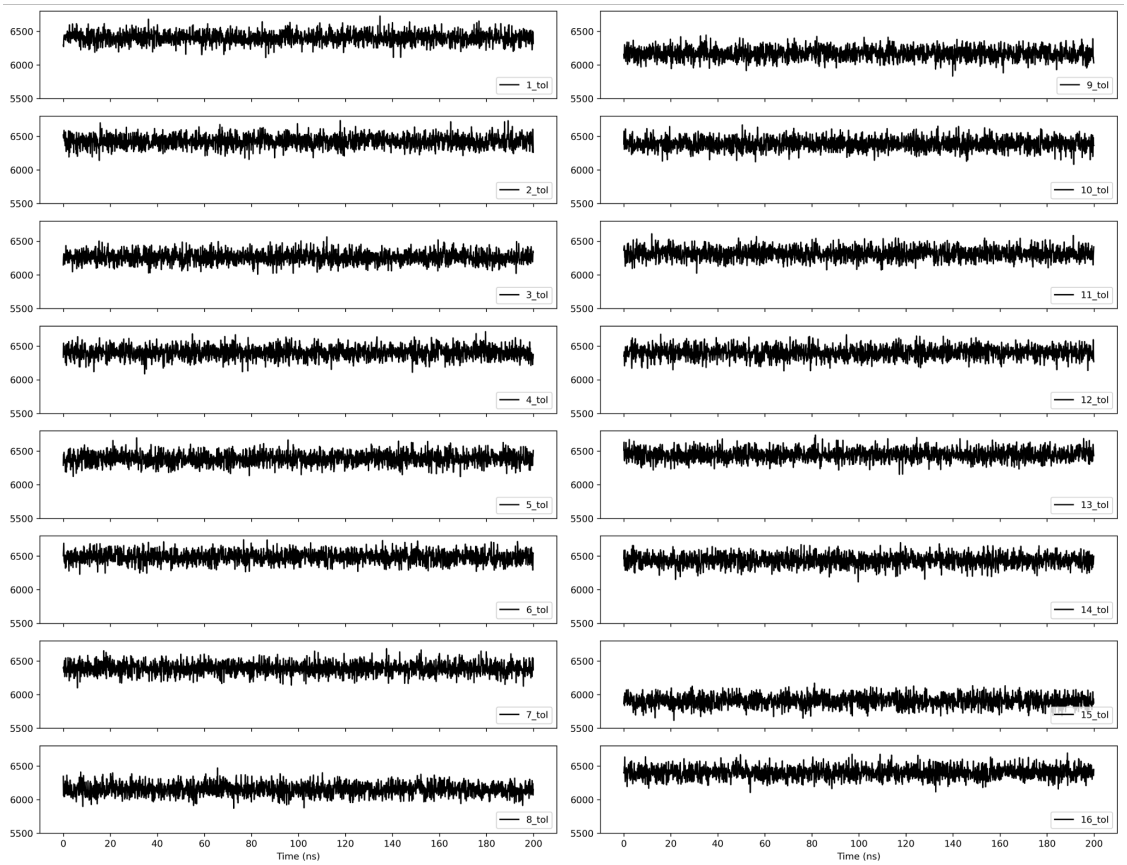


**Figure S2.** Energy versus simulation time for the 16 drug molecules in toluene.

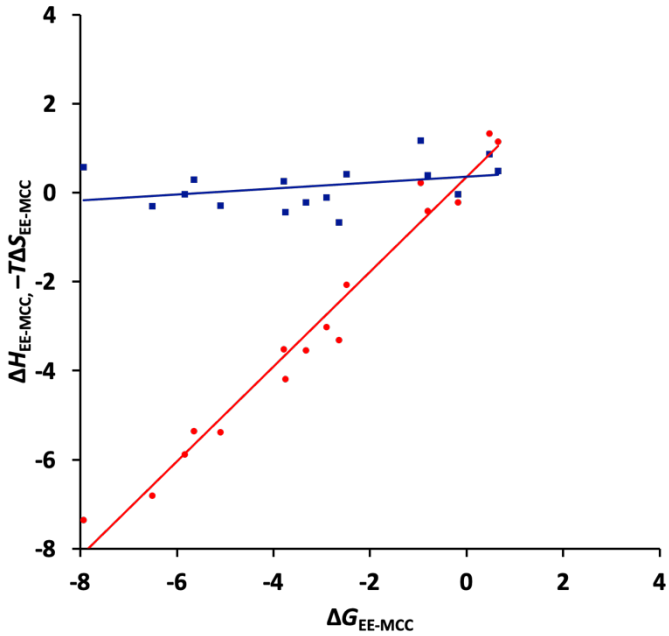


**Fig. S3.** $\Delta G_{\text{EE-MCC}}$ versus $\Delta H_{\text{EE-MCC}}$ (red) and $\Delta G_{\text{EE-MCC}}$ versus $-T\Delta S_{\text{EE-MCC}}$ (blue) for the transfer of the 16 drug molecules from water to toluene, including the corresponding lines of best fit.

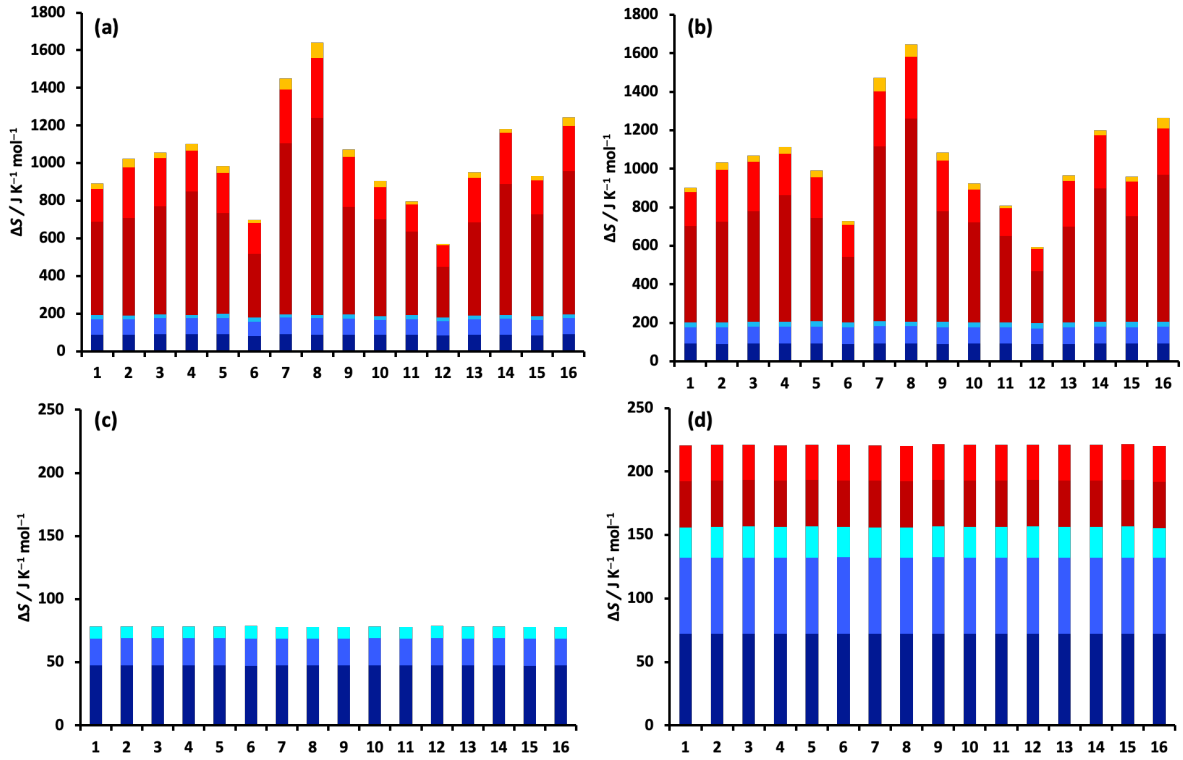


**Fig. S4.** MCC entropy components for the (a) drugs solvated in water, (b) drugs solvated in toluene, (c) pure water and (d) pure toluene. The colour scheme is as in **Fig. 3**.