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Prediction of octanol-water partition coefficients for the SAMPL6 molecules using molecular dynamics simulations with OPLS-AA, AMBER and CHARMM force fields SHUJIE FAN, OLIVER BECKSTEIN, Department of Physics, Arizona State University, BOGDAN IORGA, Institut de Chimie des Substances Naturelles — All-atom molecular dynamics simulations were used to predict the octanol-water partition coefficient logPow of a range of small molecules as part of the SAMPL6 blind prediction challenge. All molecules were parameterized using the MOL2FF algorithm and LigParGen with the OPLS-AA force field, ACPYPE and GAFF with the AMBER99sb force field, and 8 of the molecules were parameterized using CGenFF with the CHARMM36 force field. logPow was calculated from the solvation free energy for the compounds in water and dry octanol, or water and "wet" octanol using windowed alchemical free energy perturbation calculations in explicit solvent. Within the data sets that contained all molecules, the GAFF set gave the best overall prediction of logPow with an overall RMSE in logPow of 1.8 log units and an overall ME of -1.7 compared to experimental data. Considering the eight molecules parameterized by CGenFF, the CGenFF set gave the best overall prediction with an overall RMSE of 1.3 and an overall ME of 0.2. Compared with dry octanol results, wet octanol improved the performance of MOL2FF and LigParGen data sets, but increased the RMSE and ME in logPow for GAFF and CGenFF. The signed errors of MOL2FF, LigPargen and GAFF suggest a systematic error which may be caused by insufficient sampling.

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