[P21] Confinement Solvation Free-energy (CSF): A new method computing conformational free energies in explicit solvent

Marco Cecchini

Laboratoire d'Ingenierie des Fonctions Moleculaires
ISIS, UMR 7006 CNRS, Universite de Strasbourg, F-67083 Strasbourg Cedex, France

The calculation of the free energy of conformation is key to understand the function of biomolecules and has attracted significant interest in recent years. Despite substantial progress has been made, current approaches are mostly limited to an implicit treatment of the solvent. Here, we present a variant of the confinement method designed to be used in the context of explicit solvent MD simulations. This variant involves an additional step in which the solvation free energy of the harmonically restrained conformers is accurately determined by multistage free energy perturbation simulations. The confinement/solvation free energy (CSF) approach was used to compute differences in free energy between conformers of the alanine dipeptide in explicit water as a test case. The results are in excellent agreement with benchmark calculations based on both converged molecular dynamics and umbrella sampling. The new development shows that differences in conformational free energy with a statistical uncertainty of 0.1 kcal/mol can be obtained at a moderate computational cost even with a full representation of the solvent.