

Binding Free Energies of Host-Guest Complexes Using 3D RISM

Patrick McMillin

February 13, 2018

1. Abstract

- (a) Abstract goes here! I have a draft for this, but I moved it so it will be the base of the introduction.

2. Introduction

- (a) Binding information is very important to drug design because drugs must bind to structures in the cell to be effective. Simulation of protein bindings yields valuable information to drug designers, since it helps map the areas where drugs can stick well. However, explicitly simulating every atom is massively expensive because of the size of typical proteins and the number of water molecules in the system. To overcome this computational cost, we used the 3D reference interaction site model (RISM), rather than explicitly simulating each water molecule. We simulated the small host molecule cucurbit[7]uril CB7 with 16 guest molecules in order to calculate their binding energies.

3. Theory

- (a) Binding Energies
 - i. The statistical mechanics and thermodynamics of the binding process.
- (b) 3D-RISM
 - i. The implicit solvent model used which models water as a continuum.
 - ii. The Universal Correction
 - A. This is used to correct for the partial molar volume of the molecules which 3D-RISM can't handle.
 - iii. Enclosures
 - A. These are part of the RISM parameters, and I still need to do some reading.
- (c) Effective Potential

- i. 3D-RISM gives us some potentials that we use to find the effective potential needed in binding calculations (I will make the equation soon to put here in the outline).
- (d) Exponential Averaging
 - i. Essential part of the analysis. Uses partition functions to find the average energy (I have to make this equation as well).
- 4. Methods
 - (a) Molecule Parameterization
 - i. Used TLEAP to parameterize molecules for simulation, define parameters used and the minimization/equilibration process.
 - (b) Simulation Preparation
 - i. How we used the cluster to run batch jobs.
 - ii. How we pulled data out and we will use.
- 5. Results
 - (a) Here will be the figures of the data. Still working on the analysis, so I do not have a placeholder yet.
- 6. Discussion
 - (a) Discussion of important figures/tables. Will look at the comparison between our results and experiment.
- 7. Conclusions
 - (a) Here we make claims about the effectiveness of the water model.