ChE210D - Spring2010

Final Project

The free energy and conformations of a peptide between charged walls

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Abstract

A set of molecular dynamics simulations of a charged/neutral peptide between charged walls are performed. The distributions of end-to-end distances and radius of gyration show the differences in conformations between a charged peptide and a neutral peptide. The free energy coming from the charged walls is computed as a function of the distance between two walls using WHAM.

Background

Charged peptides can mediate interactions between biological membranes or cells by binding to oppositely charged surface receptors. Understanding the interplay of interactions (VdW, electrostatic, hydrophobic, etc.) regarding charged peptides and charged surfaces are important in controlling interface interactions and developing potential applications in nanotechnology.

Simulation Methods

A peptide is modeled as a string of beads; one bead is one amino acid, with a diameter of 10nm. This model peptide is hydrophilic, thus, the interaction energy between the beads is relatively low; the depth of the LJ potential well, ε is set to 0.4 kcal/mol. The interactions used in this project are listed below. The density of the system is very low, and just one peptide is included in a simulation box with periodic boundary conditions in x and y directions. A charged peptide has a positive charge (blue) on one end, and a negative charge (orange) on the other end (Fig. 6).

The Berendsen thermostat is used to maintain constant temperature. All simulations are performed for 3ns. After all the simulations finished, WHAM is performed to compute free energies coming from the charged walls as a functions of the distance between two charged walls, D. Those distances are 2.1, 2.2, 2.3, 2.4, 2.5, 2.7, 3.0, 3.2, 3.5, 4.0, 5.0, 6.0, 8.0 nm, and they are spaced close enough to ensure overlaps between probability distributions.

List of Interactions

Bond stretching interaction: $U_{bs}(r_{ij}) = \frac{k}{2}(r_{ij} - r_0)^2$

Lennard-Jones potential: $U_{LJ}(r_{ij}) = 4\varepsilon\left[\left(\frac{r_{ij}}{\sigma}\right)^{-12} - \left(\frac{r_{ij}}{\sigma}\right)^{-6}\right]$

Lennard-Jones potential with solid surfaces: $U_{LJs}(z) = \frac{4\pi\varepsilon\rho_s\sigma^3}{3} \times \frac{1}{15}\left(\frac{z}{\sigma}\right)^{-9}$

Electrostatic interaction between charged particles (screened Coulomb potential): $U_{EI}(r_{ij}) = \frac{q_i q_j e^{-r_{ij}/\lambda_D}}{4\pi\varepsilon_0\varepsilon_r r_{ij}}$

Electrostatic interaction with solid surfaces: $U_{EIs}(z) = \frac{\sigma_s q}{\varepsilon_0\varepsilon_r} z$

WHAM equation (Souaille and Roux, *Comput. Phys. Commun.* 2001**)**

$$e^{-\beta f_k} = \sum_{i=1}^{N}\sum_{l=1}^{n} \frac{e^{-\beta W_k(\boldsymbol{R}_{il})}}{\sum_{j=1}^{N} n \cdot e^{-\beta[W_j(\boldsymbol{R}_{il}) - f_j]}}$$

$W_k(z_{il}) = umbrella\ potential = PE_{plate}(D_k; z_{il}) = \frac{1}{5}\left(\left(\frac{D_k}{2} - z_{il}\right)^{-9} + \left(\frac{D_k}{2} + z_{il}\right)^{-9}\right)$

$f_k = the\ free\ energy\ coming\ form\ the\ adding\ of\ the\ biasing\ potential\ W_k$

$n = the\ length\ of\ the\ simulation$

$N = the\ number\ of\ umbrellas\ (windows)$

$D = the\ distance\ between\ two\ charged\ walls$

Results and Interpretation

Fig. 1 and Fig. 2 are the distributions of radius of gyrations of a charged and a neutral peptide. Due to the interaction between charged peptide's ends and charged walls, the radius of gyrations of the charged peptide is larger and the distribution is broader than that of a neutral peptide. For D smaller than 3.0nm, both peptides lose their spherical shape and get stretched. Fig. 3 and Fig. 4 are the distributions of end-to-end distances of a charged and a neutral peptide. Again, due to the interaction between charged peptide's ends and charged walls, the end-to-end distances of a charged peptide is larger for all D values.

Fig. 5 is the free energy graph of the charged peptide system. Here, the free energy is $f_k$in the above WHAM equation. It is the free energy coming from the LJ9 repulsive interaction, thus it increases as D decreases. There is a small bump near D =3.0nm, and it might be the indication of peptide's conformation changes. Potential of mean forces or other properties can be further computed using the configuration weights from WHAM.

Figures

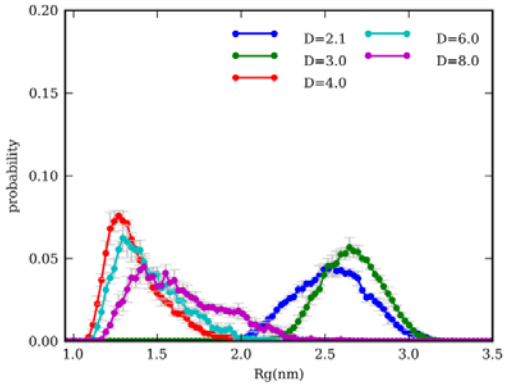

Fig. 1 Radius of gyration distribution of a charged peptide

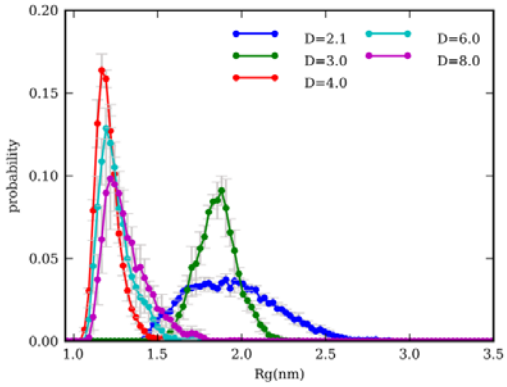

Fig. 2 Radius of gyration distribution of a neutral peptide

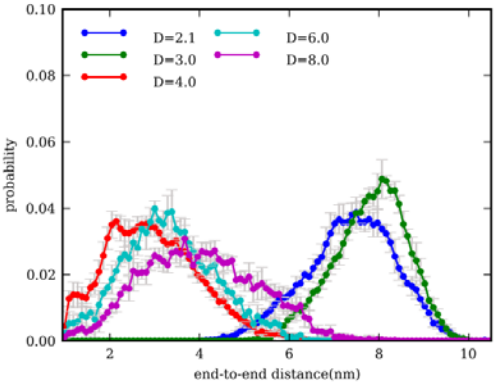

Fig. 3 End-to-end distance distribution of a charged peptide

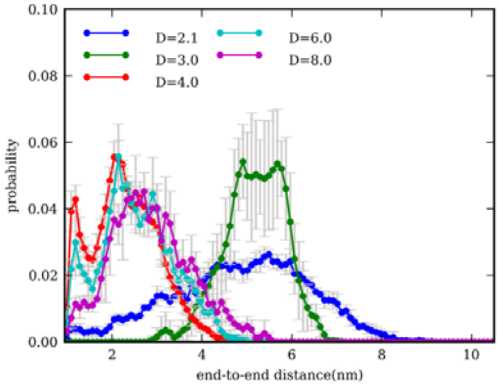

Fig. 4 End-to-end distance distribution of a neutral peptide

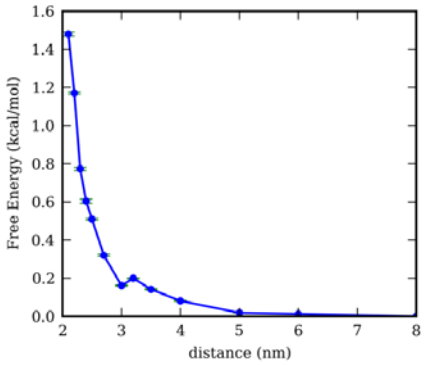

Fig. 5 Free energy as a function of the distance between two walls

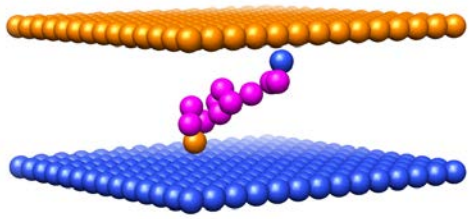

Fig. 6 A snapshot of a charged peptide between walls from the simulation with D=6.0

Movie

The movie shows a peptide between two charged walls. This peptide has charged ends, one is positively charged (blue), and the other is negatively charged (orange). Neutral atoms are colored with pink.