Project 09

Free energy calculation: enveloping distribution sampling

Keywords: Free energy calculation, free energy perturbation, thermodynamic integration
Deadline: Please, hand in your report by **Tuesday, 29 July 2014**

1 Introduction

The Gibbs free energy difference between two states A and B is given as

$$\Delta G_{AB} = G_A - G_B = -\frac{1}{k_B T} \ln \frac{Q_A}{Q_B} \tag{1}$$

where G is the Gibbs free energy, k_B is the Boltzmann constant, T is the absolute temperature, and Q_A and Q_B are the partition functions of state A and B, respectively. This free energy difference can be estimated from molecular dynamics simulations using the free-energy perturbation formula

$$\Delta G_{AB} = \quad = \quad -k_B T \ln \left\langle \exp\left(\frac{H_A(\mathbf{p},\mathbf{q}) - H_B(\mathbf{p},\mathbf{q})}{k_B T} \right) \right\rangle_A . \tag{2}$$

where $H_A(\mathbf{p},\mathbf{q})$ and $H_B(\mathbf{p},\mathbf{q})$ are the Hamilton functions of state A and state B, respectively, and $\langle ... \rangle_A$ denotes the ensemble average over the Boltzmann distribution in state A. This method requires a simulation of state A, but not necessarily of state B. An obvious extension of the free-energy perturbation method, is to construct an artificial reference state R, which replaces state A in the above equations, and use this state to calculate the free energy differences to a series of states B_1, B_2, B_3, ... Ref. 1 introduces as systematic way to construct an optimal reference state R from the Hamilton functions of a series of target states.

2 Outline of the project

1. Read and understand Ref. 1.
2. How is the reference state constructed? Why is this a suitable way to construct a reference state?
3. Implement and test the enveloping distribution sampling using a series of one-dimensional potential energy functions. To sample these potential energy functions, you can use the MCMC sampler which you implemented in exercise 7.
4. Document your results and compare them to normal free energy perturbation between the target states.

3 Literature

3.1 Primary literature

1. C. D. Christ, W. F. van Gunsteren, "Enveloping distribution sampling: A method to calculate free energy differences from a single simulation", *J. Chem. Phys.*, **126**, p. 184110 (2007)

3.2 Supporting literature

- Lecture notes and exercises.
- Chapters 7 and 10 in: D. Frenkel, B. Smit, "Understanding Molecular Simulation - From Algorithms to Applications", Academic Press, Elsevier (USA) 2002.
- D. Wu, D. A. Kofke, "Phase-space overlap measures. II. Design and implementation of staging methods for free-energy calculations", *J. Chem. Phys.* **123**, p. 084109 (2005).
- C. D. Christ, A. E. Mark, W. F. van Gunsteren, "Basic ingredients of free energy calculations: a review", *J. Comp. Chem.*, **31**, p. 1569-1582 (2009).

Project requirements

- Describe the results of the your project in a report of 5 to 12 pages (font size 11 pt).
- The report should also contain a short description of the theory and the methods. If you implement an algorithm, briefly describe the algorithm.
- Hand in your program along with the report.
- You will present the results of your project in a 20-minute presentation, after which we will have about 10 minutes time for discussion.
- Besides questions which are directly related to the results of the project, the discussion will also cover the theory of the project and the course content which is relevant to the project.
- If you run into problems during the project or have questions, please contact us
  - Bettina Keller, bettina.keller@fu-berlin.de
  - Francesca Vitalini, francesca.vitalini11@gmail.com
- During the lecture hours (Thu, 2.15 - 3.45 pm) one of us will be in the library to answer questions.