Project 12

Markov state models: discretization error

Keywords: Markov state model
Deadline: Please, hand in your report by **Tuesday, 29 July 2014**

1 Introduction

Molecular conformational dynamics is a process which is continuous in time and conformational space. Markov state models approximate this process by a stochastic jump process between discrete states in the conformational space, i.e. the conformational dynamics is approximated by process which discrete both in time and space. How well this approximation represents the true dynamics depends sensitively on the chosen boundaries of the conformational (micro-) states. In this project, you will explore the approximation quality of Markov state models for different discretizations. We will provide you with two trajectories

- a trajectory which samples a one-dimensional potential energy function $V(x)$.
- the ϕ- and ψ- torsion angle trajectories of a a capped alanine molecule (Ac-A-NHMe).

2 Outline of the project

2.1 One-dimensional potential energy function

1. Use a fine discretization of the coordinate x and convert the trajectory into a microstate trajectory. Write a program which estimates a transition matrix from the microstate trajectory. This is the reference model.
2. Plot the eigenvalue spectrum. How many slow processes are there.
3. Plot the implied time scales of the slowest processes as a function of the lag time. What is a suitable lag time for this system and this discretization?
4. Plot the dominant left and right eigenvectors. Does the Markov state model yield the correct Boltzmann distribution?
5. How does the approximation quality of a Markov state model depend on the lag time and the chosen discretization?
6. Illustrate the effects of poor and good discretizations by constructing Markov state models with different discretizations. Calculate the discretization error to the reference model (Ref 2 and 3).

2.2 ϕ- and ψ-torsion angle trajectories

1. Discretize the ϕ-ψ-space into a regular grid with equally sized state 36 $\times$ 36 microstates (each microstate has a length of 10°). Construct a Markov state model on this grid.
2. What are the slow processes of this molecule and what are the associated time scales.
3. Choose a good and a poor coarse discretization (3 to 6 microstates). Compare the resulting Markov state models.

3 Literature

1. Lecture notes and exercises.
2. Chapter 2 and 3 in : G. R. Bowman, V. S. Pande, F. Noé, "An Introduction to Markov State Models and Their Application to Long Timescale Molecular Simulation", Springer, Dordrecht (2014) MSM buch
3. M. Senne et. al. "EMMA: A Software Package for Markov Model Building and Analysis", *J. Chem. Theory Comput.*, **8**, p. 2223-2238 (2012)
4. J.-H. Prinz et. al. , "Markov models of molecular kinetics: generation and validation", *J. Chem. Phys.*, **134**, p. 174105 (2011).
5. N. Buchete, G. Hummer, "Coarse master equations for peptide folding dynamics.", *J. Phys. Chem. B*, **112**, p. 6057-6069 (2008).

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.