

# Macromolecular Docking

Peter Mühlbacher - a1253030

March 18, 2015

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## **Abstract**

Weekly reports on advances, encountered difficulties and implementations for the seminar on artificial intelligence will be gathered in this document.

# Chapter 1

## Week 1

Originally I wanted to approach the problem of protein folding by investigating the asymptotic ( $t \rightarrow \infty$ ) behaviour of the probability density function of a given protein. As the changes over time of a given protein<sup>1</sup> can be modelled by a Langevin equation  $\dot{x} = -\nabla U(x) + \beta\dot{w}$ , the corresponding probability density function  $p(t, x)$  is described by the forward Fokker-Planck equation  $\frac{\partial p}{\partial t} = \beta\Delta p + \text{div}(p\nabla U)$  whose asymptotic behaviour has been investigated in Nadler et al. (2008).

However, there are (at least) two reasons why this does not work:

- In order to get a meaningful low dimensional representation of the system, a considerable margin between two adjacent eigenvalues  $\lambda_{k+1} \gg \lambda_k$  of the Fokker-Planck operator is needed and it can be shown that this roughly corresponds to having a potential function  $U$  with  $k$  local minima<sup>2</sup>. Taking these properties into consideration it seems futile to employ this method of dimensionality reduction as the potential function in the area of protein folding has thousands of local minima.
- Even if solutions could be found explicitly in a reasonable amount of time the problem of finding an exact potential function  $U$  still remains unsolved<sup>3</sup>. As we are working with approximations it does not seem to make any sense trying to study its asymptotic long-term behaviour.

As a result of above considerations my topic of this seminar was restricted to docking. In the special case of rigid docking both molecules are assumed

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<sup>1</sup>understood as a single point in high dimensional space

<sup>2</sup>c.f. Nadler et al. (2008), p.9

<sup>3</sup>c.f. Neumaier (2006), p.14ff

to be in a metastable state which drastically cuts the complexity of the state space.

# Bibliography

- Nadler, Boaz, Ronald R. Coifman, Ioannis G. Kevrekidis, Stéphane Lafon, and Mauro Maggioni (2008), “Diffusion maps, reduction coordinates, and low dimensional representation of stochastic systems.” *Society for Industrial and Applied Mathematics*, 842864, URL [http://www.wisdom.weizmann.ac.il/~nadler/Publications/diffusion\\_map\\_MMS.pdf](http://www.wisdom.weizmann.ac.il/~nadler/Publications/diffusion_map_MMS.pdf). Multiscale Model. Simul.
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