Nucleosome-Level Coarse-Grained Modeling and Simulations of Chromatin Structures

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2015/05/22

Abstract:

Chromatin structures are considered to be, at least partially, regulated by chemical modification such as methylation and acetylation; atomic details of the molecules modulate the structural and dynamical properties, which in turn affect the physiological functions. To study their structural dynamics computationally, molecular dynamics simulations are widely adopted. However, all-atom simulations are computationally too expensive, limiting their application only up to ～10 nucleosomes and ～μs even with supercomputers. Hence, it is crucial to construct coarse-grained and simplified models, including only some important chemical details. In this seminar, I will introduce recent advances in modeling techniques with nucleosome-level coarse-graining (i.e., each nucleosome as one to several elements) and their applications, to discuss possible directions of modeling at relatively microscopic scales that can reflect some flavor of chemistry.

References:

1. A. P. Lyubartsev *et al.*, Multiscale modelling of nucleosome core particle aggregation, J. Phys. Cond. Matt. 27, 064111 (2015).

A nucleosome model was constructed by "coarse-graining of a coarse-grained model" introduced in the following paper, which successfully reproduced clustering behavior.

1a. Y. Fan *et al.*, An advanced coarse-grained nucleosome core particle model for computer simulations of nucleosome-nucleosome interactions under varying ionic conditions, PLoS ONE 8, e54228 (2013).

A residue-level coarse-grained model of nucleosomes, considering counterions.

1b. A. Mirzoev & A. P. Lyubartsev, MagiC: software package for multiscale modeling, J. Chem. Theory Comput. 9, 1512 (2013).

A toolkit for coarse-graining using the Inverse Monte Carlo method, used in ref. [1].

2. O. Müller *et al.*, Changing Chromatin Fiber Conformation by Nucleosome Repositioning, Biophys. J. 107, 2141 (2014).

Strong effects of nucleosome repositioning, represented by changes in the linker lengths, on the chromatin fiber conformation were elucidated, using the model in the following papers.

2a. R. Stehr *et al.*, The effect of internucleosomal interaction on folding of the chromatin fiber, Biophys. J. 95, 3677 (2008).

2b. R. Stehr *et al.*, Exploring the conformational space of chromatin fibers and their stability by numerical dynamic phase diagrams, Biophys. J. 98, 1028 (2010).