Steered Molecular Dynamics Simulations of Nucleosomes

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Abstract:

Conformational dynamics of nucleosomes is (one of) the microscopic basis of chromatin structure. Molecular dynamics (MD) is a useful tool to show the structural changes in detail, difficult to follow experimentally. However, even a single nucleosome is so big that we can typically run all-atom MD simulations only for sub-micro- to microseconds. To accelerate conformational changes, a number of methods have been developed, and SMD is one of them; we apply designated forces to atoms, analogous to optical traps or atomic force microscopy.

In this seminar, I will briefly review steered molecular dynamics (SMD) simulations [1], and introduce (rather straight-forward) examples of SMD applied to nucleosomes [2], to discuss the applicability to our chromatin live dynamics studies. Some coarse-grained SMD studies [3,4] will be also introduced.

References:

1. S. Izrailev et al., "Molecular Dynamics Study of Unbinding of the Avidin-Biotin Complex", *Biophys. J.* **72**, 1568 (1997).

The first paper referred as steered molecular dynamics (by K. Schulten's group), mimicking the unbinding process induced by AFM.

2. R. Ettig et al., "Dissecting DNA-Histone Interactions in the Nucleosome by Molecular Dynamics Simulations of DNA Unwrapping", *Biophys. J.* **101**, 1999 (2011).

The nucleosome structure was shown to be stable at 100 ns scale; spontaneous unwrapping was limited to 1 to 2 basepairs. By using SMD with forces to the linker DNA, the DNA unwrapping process was simulated. Intermediate structures, and two main energetic barriers were shown.

3. I. V. Dobrovolskaia & G. Arya, "Dynamics of Forced Nucleosome Unraveling and Role of Nonuniform Histone-DNA Interactions", *Biophys. J.* **103**, 989 (2012).

Similar to [2], but using a coarse-grained model to show unraveling at sub-milliseconds. The role of nonuniform histone/DNA interactions in the prevention of DNA dissociation was suggested.

4. G. Lanzani & H. Schiessel, "Nucleosome Response to Tension and Torque", *Europhys. Lett.* **100**, 48001 (2012).

A more coarse-grained and simplified model (not usual MD but simplified worm-like chain), to elucidate effects of tension and torque on unwrapping.

5. M. Biswas et al., "Atomistic Simulations of Nucleosomes", *WIREs Comput. Mol. Sci.* **3**, 378 (2013). *(A recent review paper for reference.)*