ANALYZING NUCLEOSOME PLASTICITY VIA ATOMISTIC MD SIMULATIONS

Author Block: Anastasiia Kniazeva, Grigorii Armeev, Iunona Pospelova, **Alexey K. Shaytan**. Department of Biology, Lomonosov Moscow State University, Moscow, Russian Federation.

Nucleosomes are fundamental units of chromatin compaction, which organize ~200 DNA base pairs using an octamer of histone proteins. Their ubiquitous presence in the cell nucleus since the first eukaryotes compelled the chromatin machinery to coevolve and learn how to exploit delicate modes of nucleosome dynamics. Through recent experimental advances a picture is emerging where internal deformations of histones and DNA inside nucleosomes are important for nucleosome assembly, repositioning and remodeling. The connection between nucleosome dynamics and its functional motions, however, remains elusive. We report multi microsecond all-atom molecular dynamics (MD) simulations of various nucleosome core particles (NCP) in explicit solvent and perform detailed analysis of their conformational motions. Particularly nucleosome dynamics is characterized by aligning the complex in the nucleosomal super helical reference frame and quantifying the fluctuations and orientation of the individual histone alpha-helices. We observe spontaneous DNA unwrapping/rewrapping in simulations of NCPs without histone tails and analyze the molecular mechanisms of this process as well as the response of the histone octamer to the DNA unwrapping. The implication of the introduction of disulfide cross-links into the histone octamer is also analyzed. Using the simulations of NCPs with full histone tails we quantify the interaction patterns of histone tails with the nucleosomal DNA and their effects on DNA dynamics. This work was supported by the Russian Science Foundation grant 18-74-10006 and the shared research facilities of HPC computing resources at Lomonosov Moscow State University.