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ORAL ABSTRACT PRESENTATIONS

SESSION TITLE: COMPLEX AND EMERGING TECHNIQUES IN STRUCTURAL BIOLOGY

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Abstract OR-19: Integrative Approach on Nucleosome Complexes Modeling

Grigoriy A. Armeev¹, Anna Panchenko², Alexey K. Shaytan¹

¹*Lomonosov Moscow State University, Faculty of Biology, Moscow, Russia*

²*National Institutes of Health, National Center for Biotechnology Information, Moscow, Russia*

Background: Nucleosomes are the key structural elements of chromatin in all higher organisms. While X-ray crystallography studies of nucleosomes have consistently yielded similar atomistic structures, many biophysical and biochemical techniques suggest that nucleosomes and nucleosome complexes exhibit substantial conformational polymorphism, which is functionally important. The interpretation of such experimental data with such sufficient details is often a tedious task, thus a set of molecular modeling tools is required.

Methods: We performed full-atom molecular dynamics of nucleosomes and DNA fluorescent labels to sample the conformations used for single particle Förster Resonance Energy Transfer (spFRET) measurements. We developed an approach for donor and acceptor quantum yield estimation, during spFRET measurements in a single laser excitation setup. We also implemented a set of methods for the integrative modeling of nucleosome structures based on spFRET constraints.

Results: Using these approaches, we have constructed atomistic models of nucleosomes structural reorganization induced by histone chaperones or histone H1. Besides the distances derived from corrected spFRET efficiencies, histone - DNA contacts are crucial for nucleosome formation and function. We used hydroxyl DNA footprinting data, in conjunction with atomistic structures of nucleosomes enhanced by molecular dynamics simulations, to develop a computational method for the precise determination of DNA positioning in nucleosomes with single base pair resolution.

Conclusion: We have developed a set of techniques for chromatin modeling on the nucleosomal level. Such approaches tightly integrate various experimental data (mainly corrected spFRET efficiencies and hydroxyl DNA footprints) into molecular modeling pipelines.

Key Words: nucleosome • chromatin • integrative modeling

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