Exploring the Effects of Post-Translational Modifications in Histone Tails on Nucleosome Core Particle Structure using Molecular Dynamics Simulations

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Abstract

The nucleosome core particle (NCP) is the basic unit of chromatin consisting of 147 bp of DNA wrapped around the histone octamer. Each histone protein has intrinsically disordered tails that protrude from the histone core. On the histone tails, multiple epigenetic changes occur through Post-Translational Modifications (PTMs), such as histone acetylation. Epigenetic changes are ubiquitous in disease development, such as cancer. Here, we demonstrate with all-atomistic MD simulations of the NCP that acetylation of the histone tails changes their conformational space and interaction with the neighboring DNA. We perform simulations of the H2B tails, a critical regulator in gene regulation, in both the lysine-acetylated (ACK) and unacetylated (WT) states. We use physiological NaCl concentration (150 mM) and perform over 0.5 μs timescale simulations. The ACK H2B tails shift their secondary structure by altering the helical propensity of tails. The number of contacts of the H2B tail with DNA decreases. The acetylation makes the tail more flexible and dynamic, characterized by principal component analysis (PCA). Mainly, H2B acetylation may make chromatin less compact, which aids in gene regulation and NCP stability.

References

1. Kornberg, R. D. Chromatin Structure: A Repeating Unit of Histones and DNA. *Science* **1974**, *184* (4139), 868–871. https://doi.org/10.1126/science.184.4139.868.

2. Chakraborty, K.; Kang, M.; Loverde, S. M. Molecular Mechanism for the Role of the H2A and H2B Histone Tails in Nucleosome Repositioning. *J. Phys. Chem. B* **2018**, *122* (50), 11827–11840. https://doi.org/10.1021/acs.jpcb.8b07881.

3. Chakraborty, K.; Loverde, S. M. Asymmetric Breathing Motions of Nucleosomal DNA and the Role of Histone Tails. *J. Chem. Phys.* **2017**, *147* (6), 065101. https://doi.org/10.1063/1.4997573.