
Modeling effects of nucleosome positioning in short and long chromatin fibers

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Abstract

In eukaryotes DNA is associated with proteins in a complex structure termed chromatin. The basic packaging unit of chromatin is the nucleosome in which DNA is wrapped around a histone octamer. The mechanisms of the folding of DNA into chromatin are still under debate. Experiments indicate that chromatin has different packaging conditions connected to distinct activation states. Experimental evidence showed that packaging and activation states are closely linked to positions of nucleosomes on the DNA which are actively regulated. To improve the understanding of the interplay between nucleosome positions and chromatin structure we applied computer simulations of a coarse-grained chromatin model including fundamental physical properties such as elasticity, electrostatics and nucleosome interactions. We calculated the effect of nucleosome positioning on the structure of polynucleosomes of different length scales, up to the size of a gene locus. We studied the effects of nucleosome repositioning in a system with regular spaced nucleosomes. Fiber curvature and flexibility of the chromatin fiber were largely increased and long range contacts between distant nucleosomes on the chain were promoted. The 3D structure imposed an energy barrier towards repositioning of a nucleosome depending of the chromatin structure in the order of several kBT. For different loci we simulated chromatin models based on experimentally derived nucleosome positions from cells at different stages of cell differentiation and after stimulation with a cytokine. Simulation results revealed a significant influence of nucleosome positions on the three dimensional structure of chromatin.

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