An Electrostatic/Geometric Mechanism for Compact Chromatin Stabilization Revealed by Mesoscale Modeling

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Eukaryotic chromatin is the fundamental protein/nucleic acid unit that stores the genetic material. Understanding how chromatin fibers fold and unfold in physiological conditions (divalent ions, with linker histones) is important for interpreting fundamental biological processes like DNA replication and transcription regulation. Using a mesoscopic model of oligonucleosome chains and tailored sampling protocols, we elucidate the energetics of oligonucleosome folding/unfolding and the role of each histone tail, linker histones, and divalent ions in regulating chromatin structure. The geometric/electrostatic mechanism by which linker histones, histone tails, and divalent ions consort to form chromatin higher-order structure involves: a rigid DNA ``stem" formed by linker histones to reduce nucleosome triplet angles and change the internucleosomal arrangement from a loose to tight two-start zigzag with straight linker DNA dominated by interactions between alternate nucleosomes; bends by divalent ions in some linker DNAs to accommodate linker DNA crossings at the fiber axis; and mediation of internucleosomal interactions by the H3 and H4 histone tails to shield electrostatic repulsion at the fiber core. The overall compact topologies reconcile features of the zigzag model with straight linker DNAs with the solenoid model with bent linker DNAs for optimal fiber organization and reveal a dynamic synergism of internal and external factors in chromatin compaction.

Of possible interest:

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