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Statistical physics of nucleosome positioning and chromatin structure[1]

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Genomic DNA is packaged into chromatin in eukaryotic cells. The fundamental building block of chromatin is the nucleosome, a 147 bp-long DNA molecule wrapped around the surface of a histone octamer. Arrays of nucleosomes are positioned along DNA according to their sequence preferences and folded into higher-order chromatin fibers whose structure is poorly understood. We have developed a framework for predicting sequence-specific histone-DNA interactions and the effective two-body potential responsible for ordering nucleosomes into regular higher-order structures. Our approach is based on the analogy between nucleosomal arrays and a one-dimensional fluid of finite-size particles with nearest-neighbor interactions. We derive simple rules which allow us to predict nucleosome occupancy solely from the dinucleotide content of the underlying DNA sequences.Dinucleotide content determines the degree of stiffness of the DNA polymer and thus defines its ability to bend into the nucleosomal superhelix. As expected, the nucleosome positioning rules are universal for chromatin assembled in vitro on genomic DNA from baker's yeast and from the nematode worm C.elegans, where nucleosome placement follows intrinsic sequence preferences and steric exclusion. However, the positioning rules inferred from in vivo C.elegans chromatin are affected by global nucleosome depletion from chromosome arms relative to central domains, likely caused by the attachment of the chromosome arms to the nuclear membrane. Furthermore, intrinsic nucleosome positioning rules are overwritten in transcribed regions, indicating that chromatin organization is actively managed by the transcriptional and splicing machinery.

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