Nucleosome Core and Chromatin Fiber Structure

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The fundamental building block of chromatin is the nucleosome comprising 157 to 240 bp of DNA, two each of the four core histones, and a single linker histone H1/H5. The nucleosome core is the greater part of the nucleosome and contains 147 bp of DNA wrapped in 1.67 left-handed superhelical turns around the histone octamer.

The crystal structure of the nucleosome core particle has been refined to 1.9 Å resolution and reveals for the first time the details of DNA conformation as well as all the direct and water-mediated histone-DNA contacts. The acute DNA bending induced by the histone-fold domains of the octamer yields a superhelix with a radius of curvature only twice that of the double helix, and results in DNA form changes occurring every five base pairs. Sequence-dependent DNA conformations are also apparent. The structural attributes observed have important implications for both DNA sequence-dependent nucleosome positioning and recognition by DNA-binding proteins.

Two nucleosome core particle structures containing different 146 bp DNA sequences contain distinct regions in which the DNA is relatively over-twisted and stretched. These regions represent trapped-intermediates relevant to the "twist-defect diffusion" mechanism for nucleosome sliding. DNA stretching may be a means of buffering DNA linker length variation in the chromatin fiber. Comparison with DNA twist values measured for native chromatin suggests that DNA stretching is a regular feature of chromatin.

Sedimentation analyses of defined arrays of nucleosomes containing wild–type and mutant histones show that array compaction depends on the root of the histone-H4 N-terminal tail, as suggested by the nucleosome core particle crystals. Analysis of material with specific inter-nucleosomal crosslinks that form on compaction between the H4 tail and the surface of H2A reveal that the secondary structure of the chromatin fiber is a two-start rather than a one-start arrangement.

Crystal structures for two defined nucleosome arrays containing different DNA linker lengths have been determined at 8 Å resolution. They both display a two-start secondary structure for the nucleosome higher-order structure. Importantly, the two structures suggest that the arrangement of nucleosomes in the chromatin fiber can differ substantially depending on DNA linker length.