Topological polymorphism of nucleosome fibers and folding of chromatin

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Solenoid and zigzag model



Paradigm shift





Liquid phase separation



Model updates from experimental data







Topological polymorphism of chromatin fibers

SV40 minichromosome

1 negative superhelical turn per nucleosome

'DNA linking number paradox"

1.6–1.7 negative turns expected

Lk - linking number

Tw - DNA twisting

Wr - writhing

dLk = dTw + Wr

T1 and T2 types



Nucleosome spacing and the level of transcription

T1 $\Delta Lk \approx -1.5$ $\Delta Lk \approx -1$

weak supercoiling

predominantly downstream

highly transcribed genes

{10n+5}

T2

stabilized in the upstream regions

regions with a low level of transcription

{10n}

yeast genes from the top and bottom 25% of the expression level scale

NRL ~ 161 bp	NRL ~ 167 bp
<l> = 14 bp</l>	<l> = 20 bp</l>



{10n}

low superhelical density

higher superhelical density

greater plasticity

higher stability of the chromatin fiber

facilitation of gene loops formation

and enhancer-promoter loops

prevalent for inactive genes

Conformational dynamics of chromatin fibers and nucleosome spacing



T2: NRL = 187 bp

T1: NRL = 182 bp

Radioprobing DNA folding in situ and topological state of chromatin



Conclusion

in vitro

The {10n+5} but not {10n} nucleosome arrays have a strong propensity for macroscopic self-association in vitro , which can be explained by more pronounced flexibility of the T1 topoisomer

Genome-wide DNA cleavage induced by ionizing radiation, RICC-seq, was shown to reflect the spatial proximity of nucleosomes in chromatin fibers. The DNA cleavage pattern depends on the fiber configuration (i.e., T1 or T2); at the same time, it can be linked to the epigenetic maps of the active and repressed states of chromatin.

in vivo

Micro-C and Hi-CO experiments revealed various structural motifs characterized by distinct nucleosome folding in vivo, from yeast to humans

in silico Authors, Monte Carlo (MC)