Possible role of DNA supercoiling in formation of topological domains

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Abstract

Understanding how interphase chromosomes are organized is essential for elucidation of regulatory mechanisms of gene expression. During recent years, the development of high-throughput DNA sequencing expanded the power of chromosome conformation capture (3C) methods that provide information about spatial proximity of chromosomal loci. Since 2012, it is known that interphase chromosomes are organized into regions with strongly increased frequency of internal contacts. These regions, with the average size of 1 Mb, were named topological domains. The mechanisms responsible for increased frequency of contacts within individual topological domains are unknown yet. Several recent studies demonstrated though that transcription induces DNA supercoiling in interphase chromosomes. Using Brownian dynamics simulations, we show that by including supercoiling into models of chromosomes composed of topological domains one can reproduce and thus provide possible explanations of several experimentally observed characteristics of interphase chromosomes, such as their complex contact maps. We also show that supercoiling stimulates interactions between enhancers and promoters located in the same topological domain and represses interdomain interactions.

References:
Models that include supercoiling of topological domains reproduce several known features of interphase chromosomes.
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