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Mechanisms of chromatin unknotting.

Chromosomes undergo repeated structural transitions between highly compact form during cell divisions and a decondensed form during interphase i.e. between cell divisions. During interphase genes are expressed and DNA is replicated. Studies of the scaling behaviour of chromatin fibres concluded that interphase chromosomes are not at topological equilibrium and thus are unknotted (1). This contrasts with the natural expectation that long and crowded chromatin fibres should reach highly knotted state in the presence of DNA topoisomerases permitting DNA-DNA passages. One of possible explanations for the paucity of chromatin knots is that regular chromatin fibres may not permit topoisomerase-mediated passages (2). It is also possible that chromatin knots do form (3), but are actively removed by specialized biological mechanisms. Our Brownian dynamics simulations show that chromatin loop extrusion, known to be involved in organizing interphase chromosomes (4), provides very efficient mean of chromatin unknotting. 1. E. Lieberman-Aiden et al., Science 326, 289-293 (2009). 2. J. Dorier, A. Stasiak, Nucleic acids research 37, 6316-6322 (2009). 3. J. T. Siebert et al., Polymers 9, 317 (2017). 4. A. L. Sanborn et al., Proc Natl Acad Sci U S A 112, E6456-6465 (2015). (Received February 16, 2018)