Distribution of torsional stress between the un-replicated and replicated regions in partially replicated molecules

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Abstract

DNA topology changes continuously as replication proceeds. Unwinding of the DNA duplex by helicases is favored by negative supercoiling but it causes the progressive accumulation of positive supercoiling ahead of the fork. This torsional stress must be removed for the fork to keep advancing. Elimination of this positive torsional stress may be accomplished by topoisomerases acting solely ahead of the fork or simultaneously in the un-replicated and replicated regions after diffusion of some positive torsional strain from the un-replicated to the replicated regions by swivelling of the replication forks. In any case, once replication is completed fully replicated molecules are known to be heavily catenated and this catenation derives from pre-catenanes formed during replication. Although there is still controversy as to whether fork swiveling redistributes this positive torsional stress continuously or only as termination approaches, the forces that cause fork rotation and the generation of pre-catenanes are still poorly characterized. Here we used a numerical simulation, based on the worm-like chain model and the Metropolis Monte Carlo method, to study the interchange of supercoiling and pre-catenation in a naked circular DNA molecule of 4,440 bp partially replicated in vivo and in vitro. We propose that a dynamic gradient of torsional stress between the un-replicated and replicated regions drives fork swiveling allowing the interchange of supercoiling and pre-catenation.