Dynamics of torsionally stressed DNA replication intermediates

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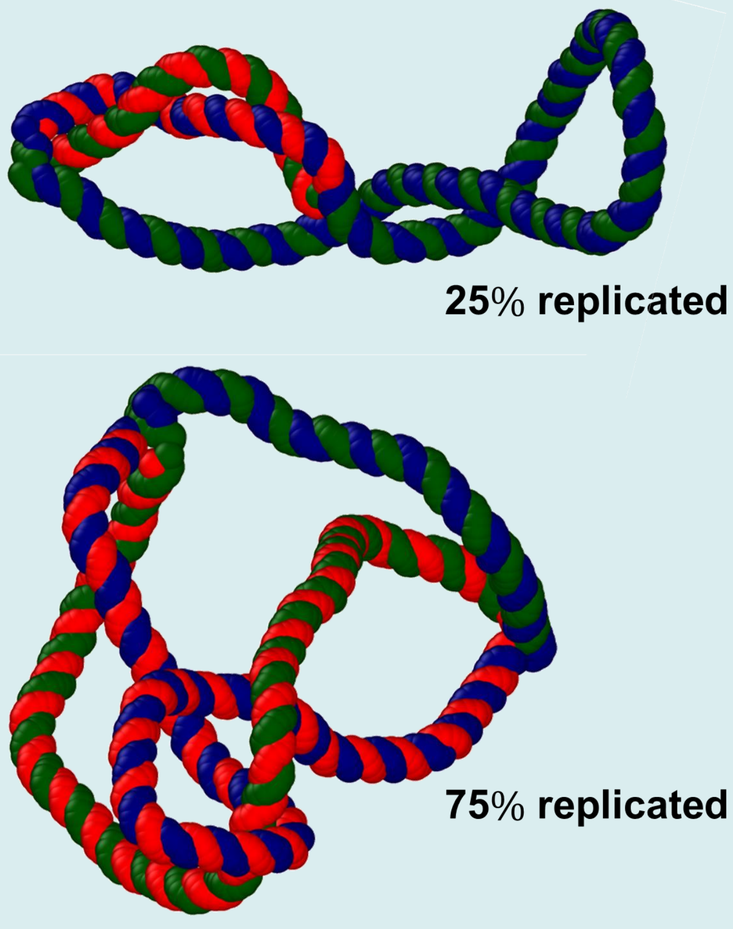


Snapshots of simulated molecules. The parental strands are depicted in blue and green. Newly synthesized strands are depicted in red.

We used molecular dynamics simulations to study the conformational properties of partially replicated circular DNA molecules

Our results

We used oxDNA model and molecular dynamics simulation to study the kinetic and topological changes of partially replicated molecules that initially harbored all the torsional stress in the unreplicated region. We found that fork swiveling redistributed the torsional stress between both regions, causing the formation of pre-catenanes in the replicated one.

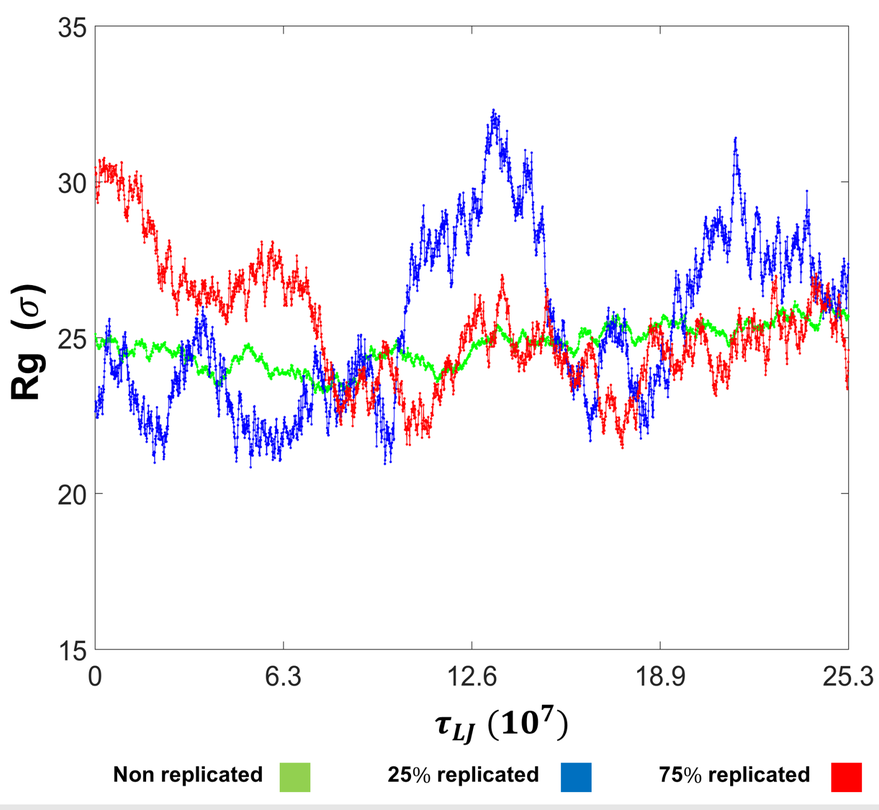
We observed a dynamic interplay between supercoiling and pre-catenation that is related to the advance of replication forks

Introduction

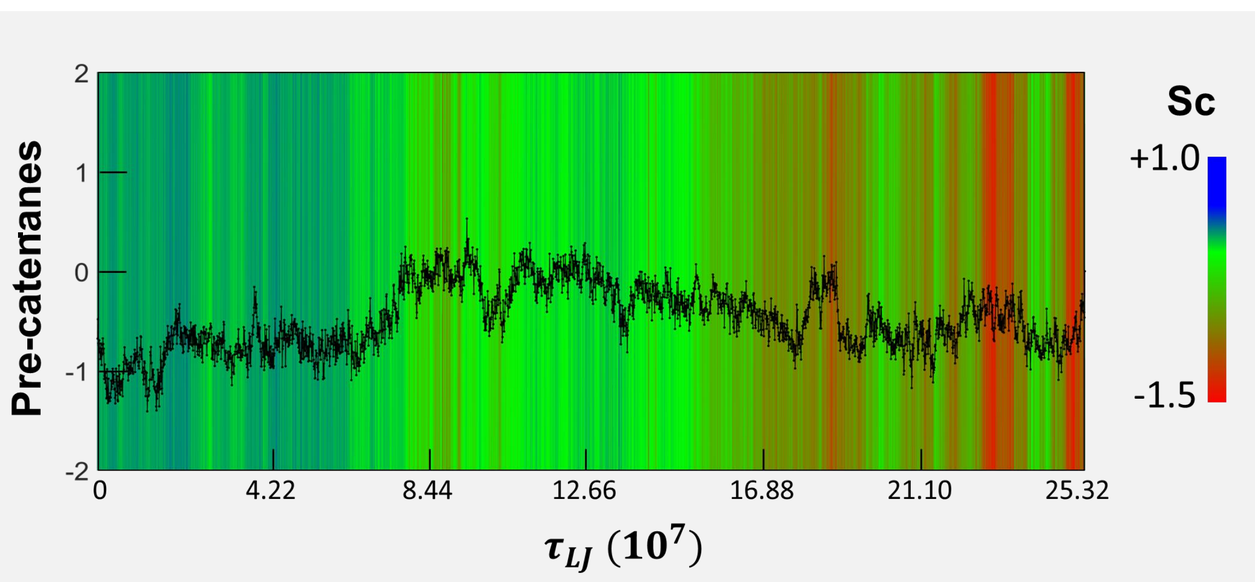
We use the coarse-grained oxDNA model and molecular dynamics simulations with the LAMMPS package to analyze the dynamic evolution of the conformational properties of DNA circles with stalled replication forks for early and late stages of DNA replication. The non replicated form consisted of 420bp-long DNA rings and the early and late replicating forms corresponded to 25% and 75% replicated molecules, respectively. The ΔLk value was -3 for all the simulated molecules.

First, initial conformations with supercoiling in the unreplicated region and devoid of pre-catenanes in the replicated one, were set to an equilibration simulation. Finally, we used Langevin dynamics simulation to analyze the stability of the conformations.

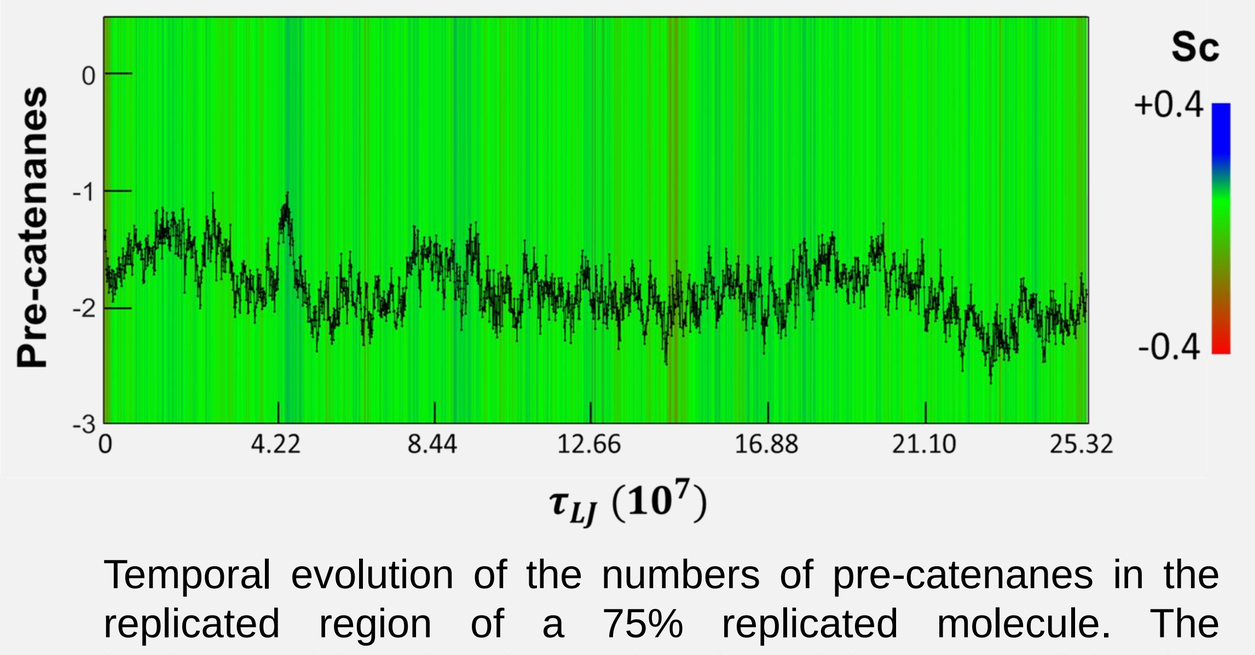
Since the time unit is given by $\tau_{LJ} = \sigma\sqrt{m/\epsilon}$ the time scales were standardized considering the different sizes of the three types of molecules simulated.



Temporal evolution of the radius of gyration (Rg) of a non replicating molecule and 25% and 75% replicated molecules.



Temporal evolution of the number of pre-catenanes in the replicated region of a 25% replicated molecule. The background is colored according to the supercoil level in the unreplicated region.



Temporal evolution of the numbers of pre-catenanes in the replicated region of a 75% replicated molecule. The background is colored as a function of the supercoil level in the unreplicated region.

As an extension of this study we project the simulation of DNA molecules with a size similar to that of DNA circles that are capable to self-replicate. We also want to expand the study to other mechanical and thermodynamic properties of replication intermediates..

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