Two-Phase Dynamics of DNA Supercoiling Based on Model of DNA Polymer Physics

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Introduction
DNA supercoils are generated in genome regulation processes, such as transcription and replication and provide mechanical feedback to such processes. Under tension, DNA supercoiling can present a coexistence state of stretched and plectonemic phases. Experiments have revealed the dynamic behaviors of plectoneme, e.g., diffusion, nucleation andショップ(Geanoui,M.T. et al (2012) Science,338, 84-87). We demonstrate fast dynamics of DNA on torque transport and reaching equilibrium within the two phases. Correspondingly, we could average out the fast dynamics and drive the dynamics via slow degrees of freedom identified as phase-boundaries, thus provides a numerical description of supercoiling dynamics at trivial computational cost. Our two-phase model can be made consistent with generally used discrete worm-like chain method and it well reproduces the diffusion and hopping of plectoneme measured experimentally.

Supercoiling's role in genome regulation processes
DNA Supercoils generation and feedback to transcription
Formation of twin domain model of DNA supercoiling during transcription elongation

Supercoiling Dynamics
Coexistence state of plectonemic and stretched phases
The thermodynamics of the coexistence state of DNA supercoiling can be seen in models(Delpeux et al (2012) Physical Review E,85,041905), where DNA is regarded as a polymer, specifically, a worm-like chain.

Measuring torque transport within two phases
The discrete worm-like chain method(dWLC)
Double-helical DNA is coarse-grained as the discrete segments represented by cylinders. The cylinders are described by vertices (L_z,L_y,L_x) and vectors (x,y,z) to mimic the conformation of DNA and its torsional properties.

Two-phase dynamics of supercoiling
Compared to the fast dynamics of DNA: from 0.2-10μm/second for 10^7 psec.
Phase boundaries can be identified as slow variables to describe the dynamics.

Summary
Based on the polymer physics of DNA, we have constructed a two-phase dynamics of DNA supercoiling, and then successfully reproduced the supercoiling dynamics, including plectoneme nucleation, diffusion and hopping at trivial computational cost. The studies can be further implemented to construct multi-scale physics model of supercoiling in gene regulations.

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References


Diffusion of plectoneme allows a conformational rearrangement of DNA at about tens of milliseconds for a displacement of thousands of bp.

Compared with diffusion of plectoneme, hopping is fast and long range, e.g., tens of milliseconds for a displacement of thousands of bp.

The left boundary or the right boundary of the α-th plectoneme follows

The discontinuities on torque and extension curves indicate the buckling transition followed by phase-coexistence

The continuous plectoneme nucleation and vanishing are all captured (21kbp).

The coexistence of multiple plectonemes, the plectoneme nucleating and vanishing are all captured (21kbp).

Reproducing experimentally measured plectoneme dynamics
Kymograph of plectonemes
The coexistence of multiple plectonemes, the plectoneme nucleating and vanishing are all captured (21kbp).

Reproducing plectoneme diffusion

Torque transport on the stretched phase
Torque transport on the plectoneme phase

Two-phase dynamics of supercoiling
Compared to the fast dynamics of DNA: from 0.2-10μm/second for 10^7 psec.
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The build up supercoils slow down transcription

The left boundary or the right boundary of the α-th plectoneme follows

where v_r is the friction felt by the plectoneme, ΔΦ is the free energy associated with ΔΦ accompanied with ν beating events, and Φ is the Gaussian noise.

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