Emergence of Helicity in Double-stranded Semiflexible Chains with Interstrand Interactions

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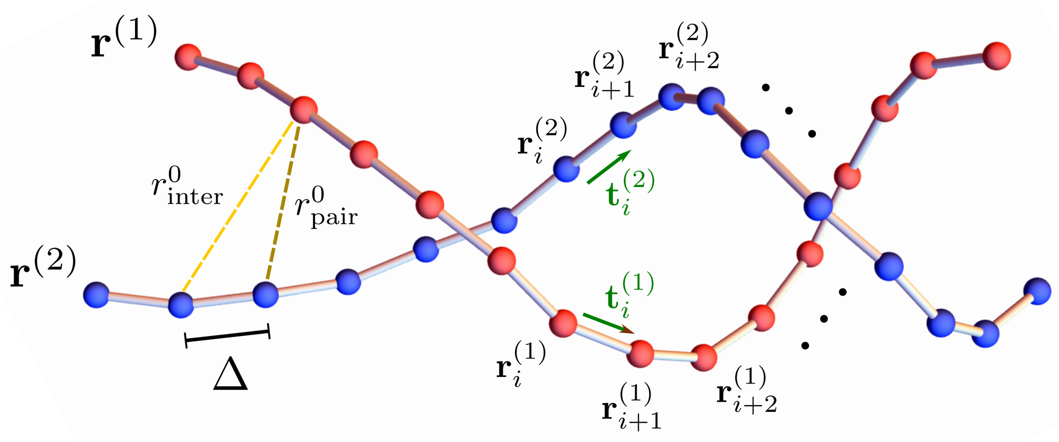
Abstract

In literatures, there are models with varying levels of complexity and coarse-graining schemes that accurately describe the mechanical and structural properties of dsDNA. However, the interplay between base-stacking interactions in dsDNA and its intrinsic handedness is rarely discussed despite their importance in preserving the double-helix structure of dsDNA. Here we investigate the delicate balance required for the strength of base-stacking interactions D and the twist stiffness P to preserve the double-helix structure in a model made up of two semiflexible chains. We found that our model supports several distinct morphological phases in the parameter space (P,D): flat, random coil, and the double-helix phase. Transitions between these phases are of different order, and there is also a morphological transition within the double-helix phase signified by the unwinding of the double-helix.

Methods

Model and Parameters



Bending energy:

$$E^{(k)}_{\rm bend} = \sum_{i=0}^{N-2} \frac{\ell_p^0}{\Delta}\left(1 - \mathbf{t}_i^{(k)} \cdot \mathbf{t}_{i-1}^{(k)}\right)$$

Base-pairing:

$$E_{\rm bond} = \sum_{i=0}^{N-1} \frac{k}{r_H^2}\left(r_{{\rm bond},i} - r^0_{\rm bond}\right)^2$$

where $r_{{\rm bond},i} = |\mathbf{r}_i^{(1)} - \mathbf{r}_i^{(2)}|$

Fixed parameters:

ℓ_p^0	= 2 nm (bare persistence length)
Δ	= 0.64 nm (distance between monomers)
$r^0_{\rm bond}$	= 2 nm (pair distance)
k	= 12 k_BT_0 (strength of base-pairing)
r_H	= 0.3 nm (hydrogen bond length)
$r^0_{\rm inter}$	= 1.8 nm (diagonal distance)
χ_0	= 0.2 π rad (twist angle)

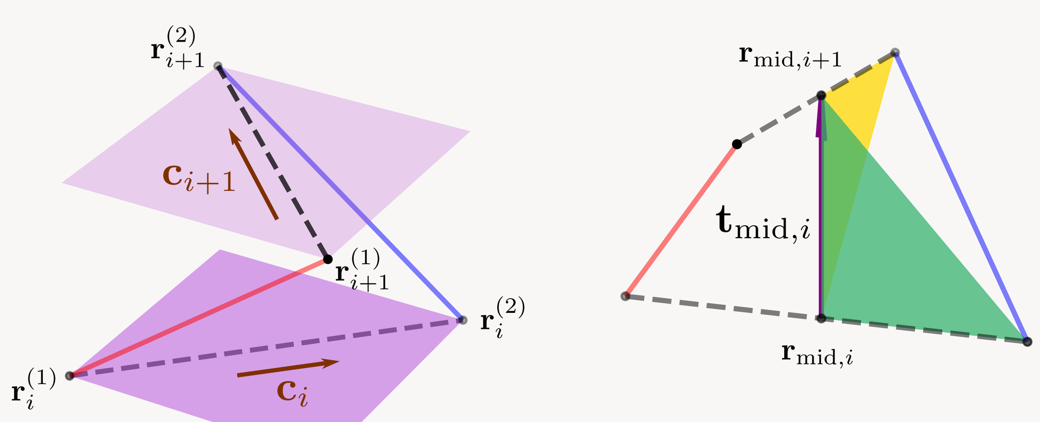
Base-stacking:

$$E_{\rm inter} = D\sum_{i=0}^{N-2}\left[(r_i^{1,2} - r^0_{\rm inter})^2 + (r_i^{2,1} - r^0_{\rm inter})^2\right]$$

where $r_i^{m,n} = |\mathbf{r}_i^{(m)} - \mathbf{r}_{i+1}^{(n)}|$

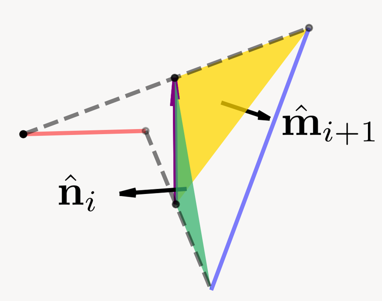
Twist energy:

$$E_{\rm twist} = P\sum_{i=0}^{N-2}(\chi_i - \chi_0)^2$$



where

$$\chi_i = \begin{cases} \operatorname{acos}(\hat{\mathbf{t}}_{{\rm mid},i}\cdot(\hat{\mathbf{n}}_i \times \hat{\mathbf{m}}_{i+1})) & \text{if } \operatorname{sign}(\hat{\mathbf{t}}_{{\rm mid},i}\cdot(\hat{\mathbf{n}}_i \times \hat{\mathbf{m}}_{i+1})) = 1 \\ 2\pi - \operatorname{acos}(\hat{\mathbf{t}}_{{\rm mid},i}\cdot(\hat{\mathbf{n}}_i \times \hat{\mathbf{m}}_{i+1})) & \text{if } \operatorname{sign}(\hat{\mathbf{t}}_{{\rm mid},i}\cdot(\hat{\mathbf{n}}_i \times \hat{\mathbf{m}}_{i+1})) = -1 \end{cases}$$



Simulation

Both chains are initially free. The total energy of the system,

$$E = E^{(1)}_{\rm bend} + E^{(2)}_{\rm bend} + E_{\rm bond} + E_{\rm inter} + E_{\rm twist}$$

is driven to minimum using Monte Carlo (MC) simulation with 4 × 10^6 sweeps whereby samplings for each sweep are taken in parallel using 64 CPU-cores. We devote the first half of the MC steps to equilibration, and the configuration of both chains are accepted or rejected via Metropolis algorithm.

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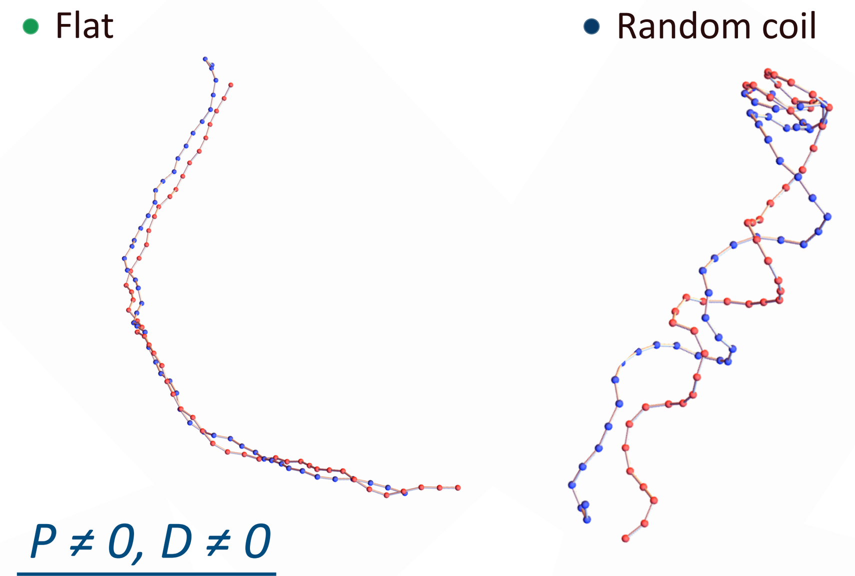
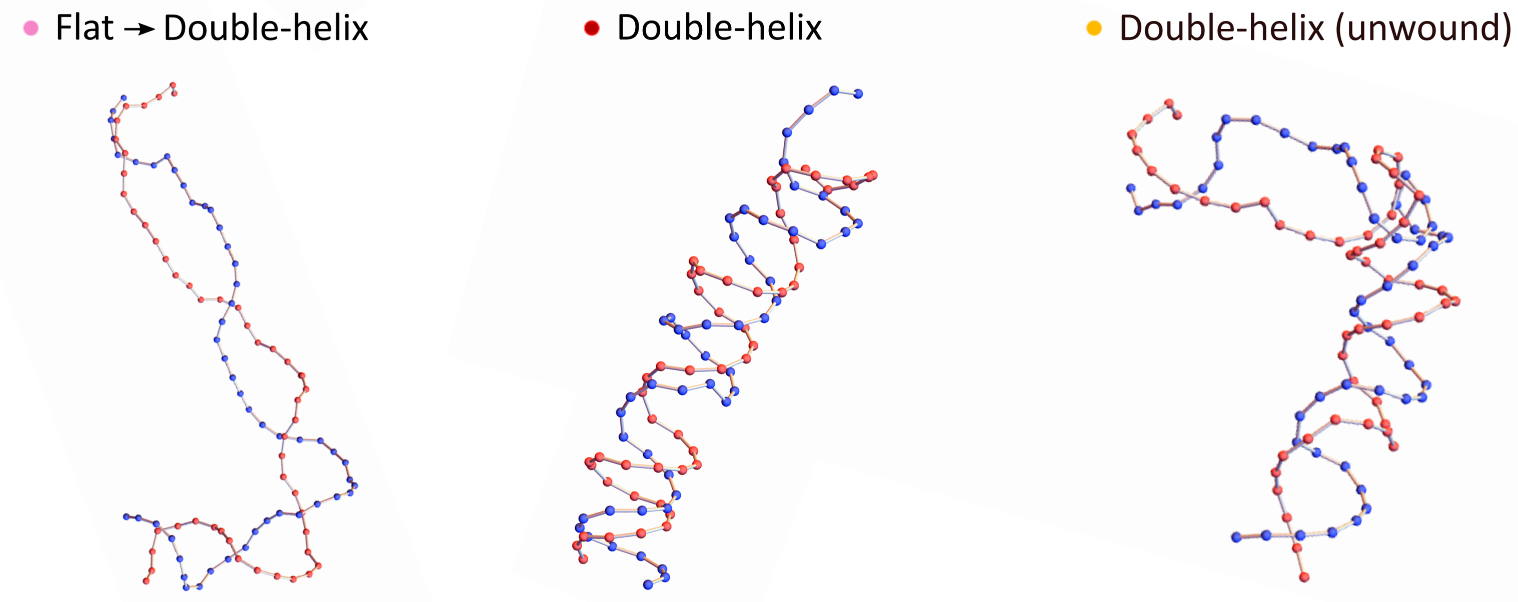
Results

P = 0 or P ≠ 0, D = 0 *P = 0, D ≠ 0*



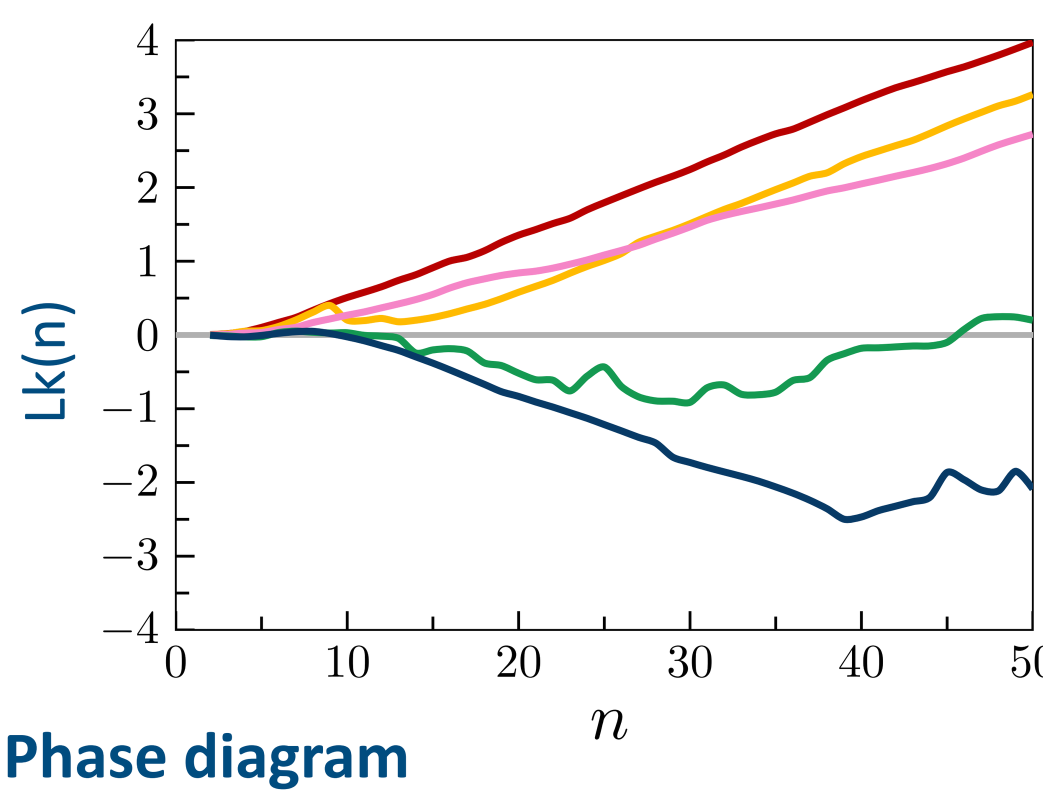
In the case D = 0, the chains rarely twist and bend. When D is not zero, the chains start to wind around each other. In the absence of P, the twist direction is not regulated. If P is not zero, only right-handed twist is allowed. For nonzero P and D, the chains gradually form right-handed double-helix as D increases with fixed P. Increasing D further would give rise to the instability in the structure which causes the unwinding of the double helix.

P ≠ 0, D ≠ 0



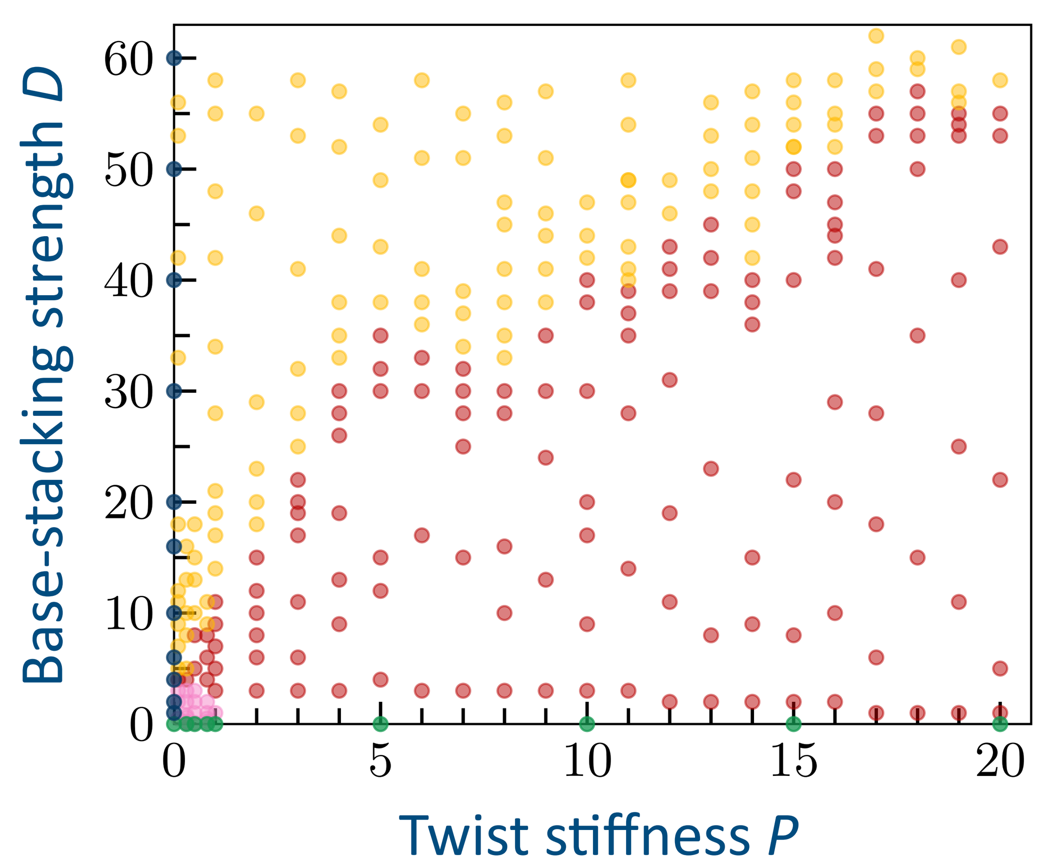
The variation of Gauss linking number

$$\mathrm{Lk}(n) = \frac{1}{4\pi}\sum_{i=1}^{n-1}\sum_{j=1}^{n-1}\frac{\mathbf{r}_i^{(1)} - \mathbf{r}_j^{(2)}}{|\mathbf{r}_i^{(1)} - \mathbf{r}_j^{(2)}|^3}\cdot\left[\left(\mathbf{r}_i^{(1)} - \mathbf{r}_{i-1}^{(1)}\right)\times\left(\mathbf{r}_j^{(2)} - \mathbf{r}_{j-1}^{(2)}\right)\right]$$



In the **double-helix** phase, the link increases linearly along the chains. Likewise for the **double-helix (unwound)** phase and **flat → double-helix**, though the total link will be smaller. The link is small in the **flat** phase since bending and twisting are rare. The link can go below zero in the **random coil** phase because there is no preferred twisting direction.

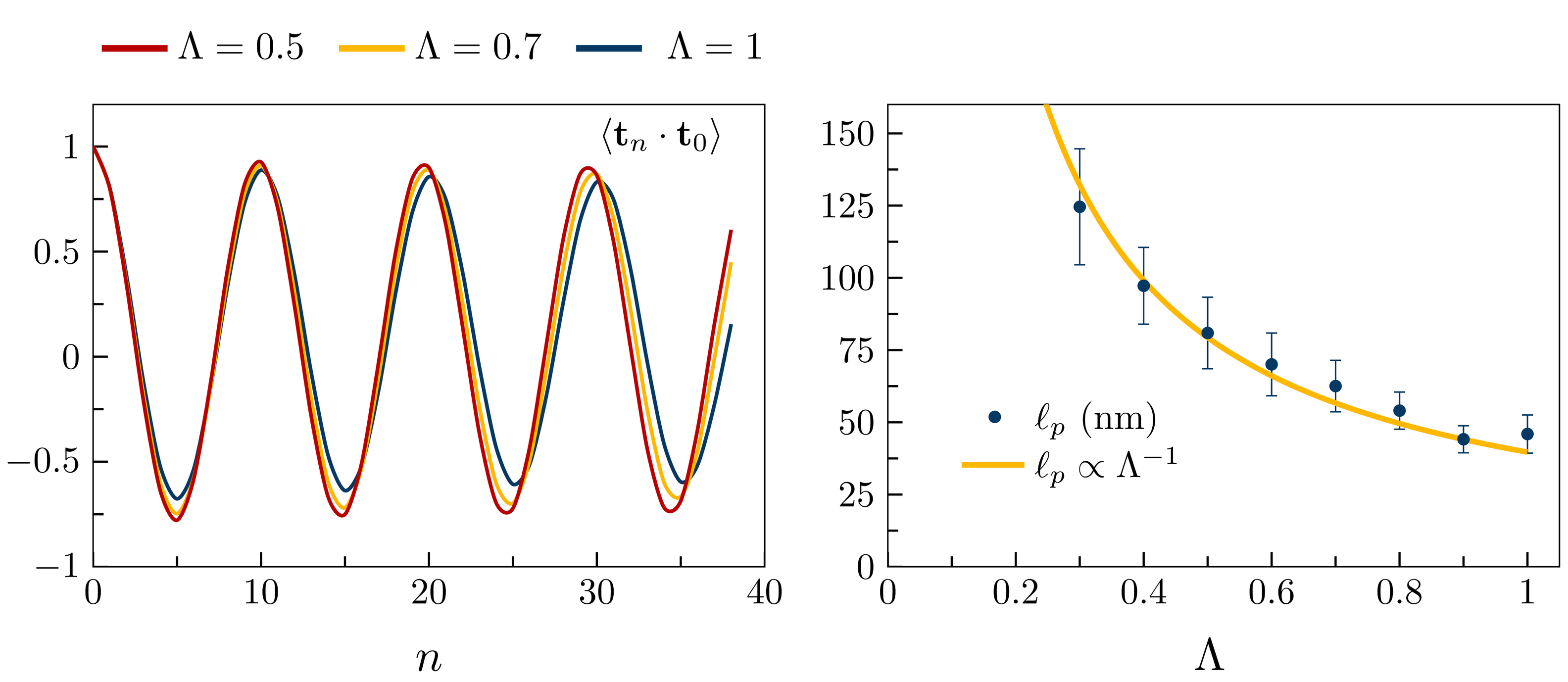
Phase diagram



Morphological phase diagram of our model subject to different base-stacking strength D and twist stiffness P at normalized temperature Λ = 1.

The phase transitions **flat** → **double-helix** and **double-helix** → **double-helix (unwound)** are continuous, while the phase transitions from **random coil** phase to the other phases are abrupt due to the handedness-symmetry breaking.

Correlation functions and persistence length



The correlation function $\langle \mathbf{t}_n \cdot \mathbf{t}_0 \rangle$ at temperature $\Lambda = T/T_0$ exhibits oscillatory behavior with amplitudes that decay exponentially: $\langle \mathbf{t}_n \cdot \mathbf{t}_0 \rangle = e^{-s/\ell_p}\cos(\lambda_p s)$, where $s = n\Delta$. The bending persistence length ℓ_p increases as the temperature Λ is lowered.