

Topology driven mixing of Knots in DNA

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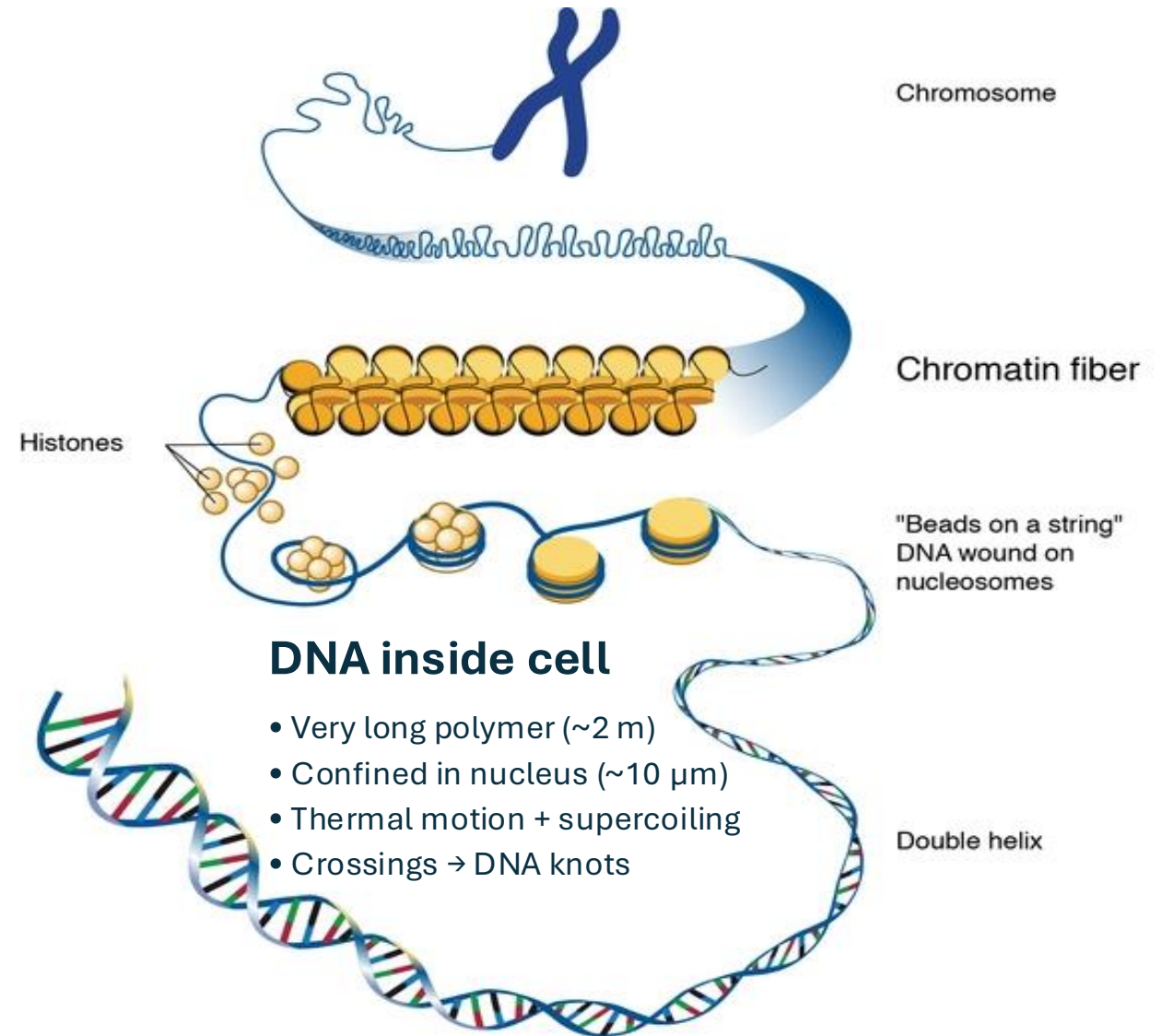


Souradeep Sengupta,
Ashoka University, India.

<https://arxiv.org/html/2609.10188v1>

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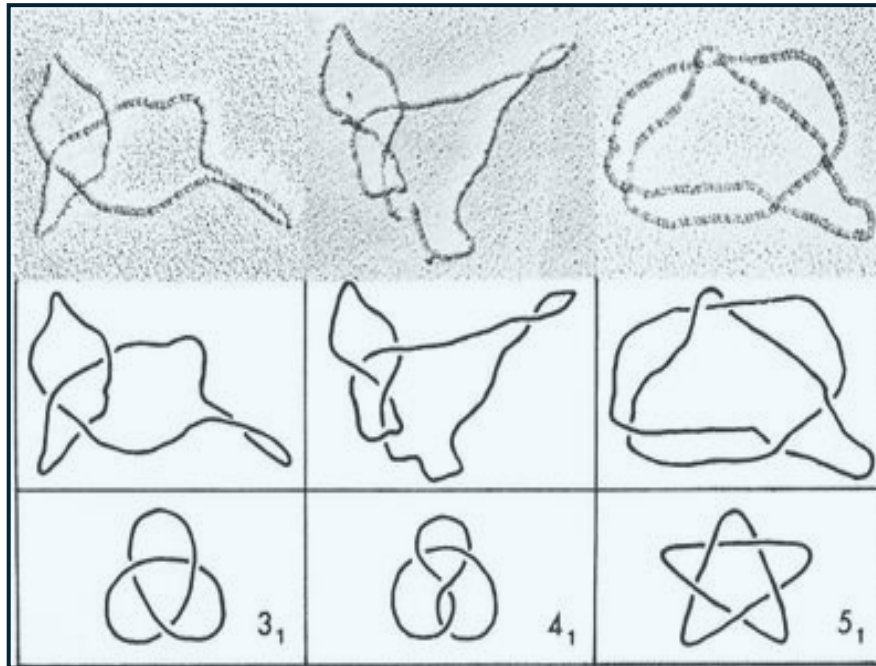
From Everyday Knots to DNA Knots



Long polymers under confinement naturally form knots.

How Do We Classify Knots?

Knots are labeled by their minimal crossing number



Trefoil 3_1 Figure-eight 4_1 Cinquefoil 5_1

Dean *et.al.*, J Biol Chem., 260. 4975 (1985)

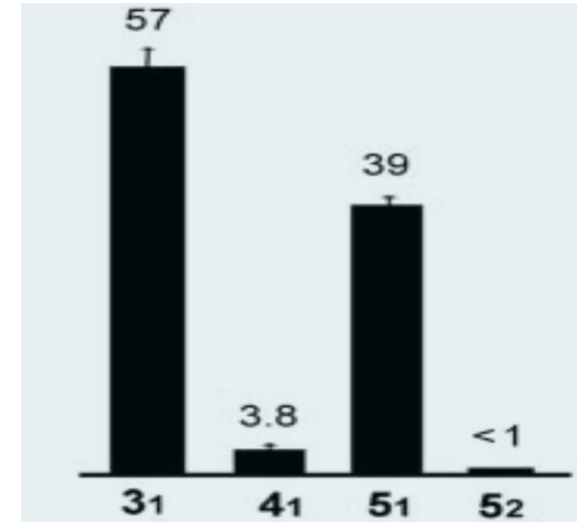
Topological invariant: Alexander polynomial

$$\Delta_{3_1}(t) = 1 - t + t^2$$

DNA topology matters, and cells regulate it.

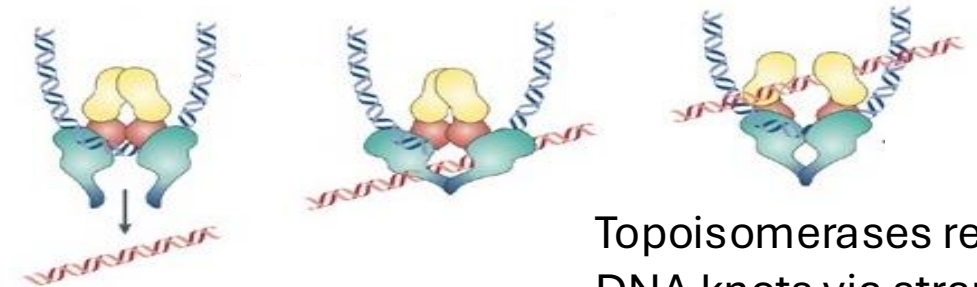
Knots observed in DNA

Experimental DNA knot probabilities



Does DNA topology influence biological processes?

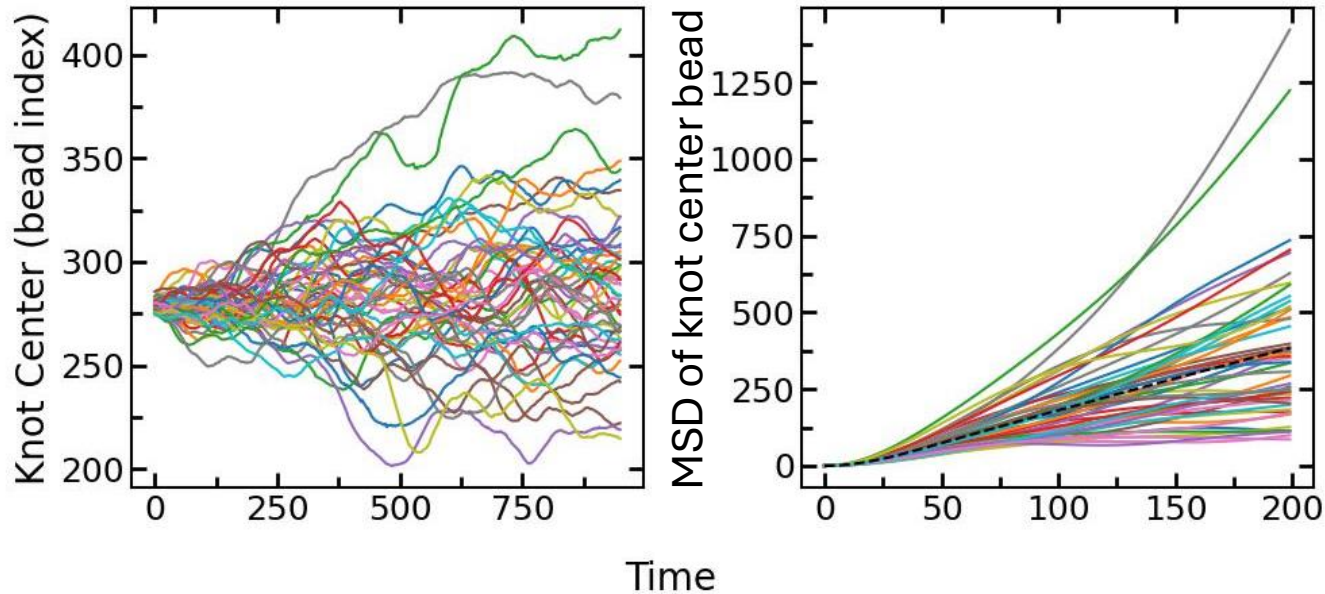
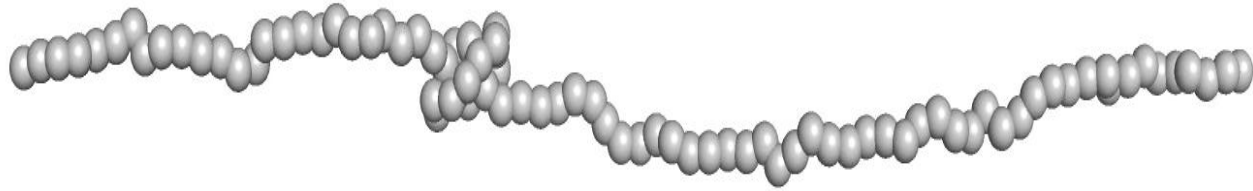
Arsuaga, *et.al.*, PNAS, **102** 9165(2005)



Topoisomerases resolve DNA knots via strand passage

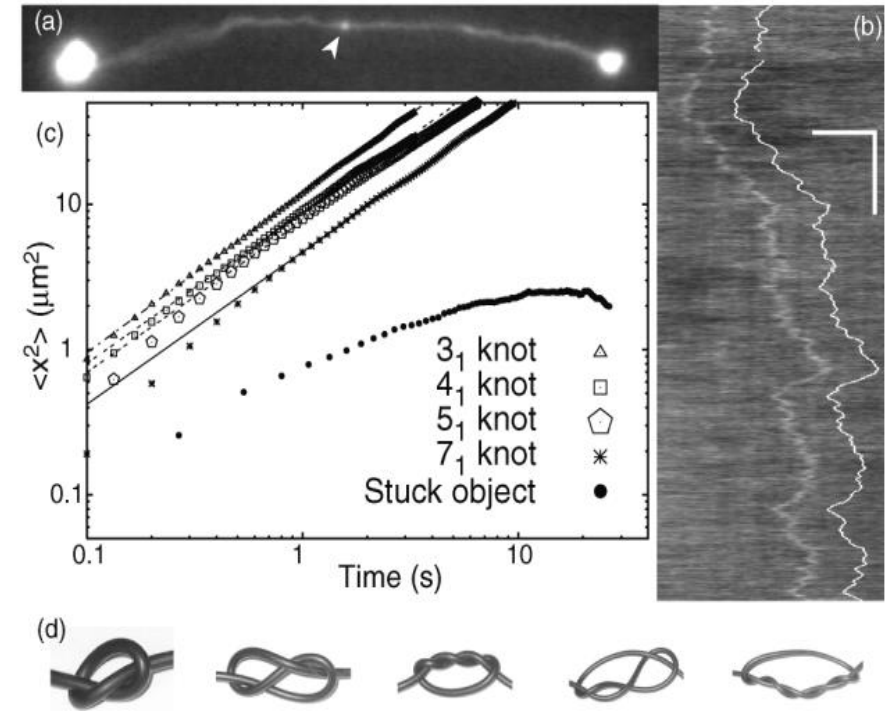
Nat. Rev. Cancer, 327 (2009)

Dynamics of a Single Knot on DNA



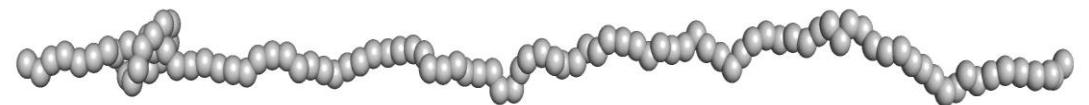
$$\langle nt^2(t) \rangle \sim t$$

Knots are not static-they move along DNA.



Quake et.al. PRL 91, 265506 (2003)

Klotz et.al. PRL, 120, 188003(2018)



Modelling Knot Diffusion Under Wall Confinement

Model potential for flexible polymer $E_{\text{tot}} = E_{\text{bond}} + E_{\text{excl}} + E_{\text{wall}}$



(i) Bond Stretching Potential

$$E_{\text{bond}} = \sum_{i=1}^{N-1} k(r_{i,i+1} - d_0)^2$$

(ii) Excluded Volume Interaction

$$E_{\text{excl}} = \sum_{i=1}^{N-2} \sum_{j=i+2}^N 4\epsilon_1 \left[\left(\frac{\sigma}{r_{i,j}} \right)^{12} - \left(\frac{\sigma}{r_{i,j}} \right)^6 + \frac{1}{4} \right] \quad r_{i,j} \leq 2^{1/6}\sigma$$

(iii) Wall Interaction

$$E_{\text{wall}} = \begin{cases} \sum_{i=2}^{N-1} 4\epsilon_2 \left[\left(\frac{\sigma}{d_i} \right)^{12} - \left(\frac{\sigma}{d_i} \right)^6 + \frac{1}{4} \right], & d_i \leq 2^{1/6}\sigma \\ 0, & d_i > 2^{1/6}\sigma \end{cases}$$

Brownian Dynamics Equation

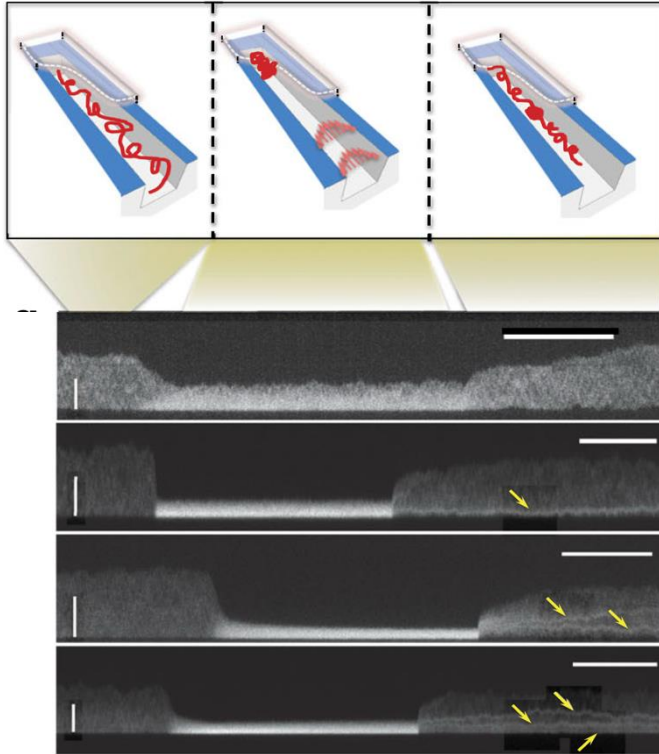
$$\frac{\zeta}{m} \frac{d\vec{r}_i}{dt} = \vec{F}_{i,c} + \vec{\Gamma}$$

$\vec{F}_{i,c}$: deterministic force from interactions

$\vec{\Gamma}$: thermal noise $\langle \Gamma_i(t) \Gamma_j(t') \rangle = 2\zeta k_B T \delta_{ij}(t - t')$

Interaction of Multiple Knots on a Single DNA Molecule

Nanofluidic compression experiment

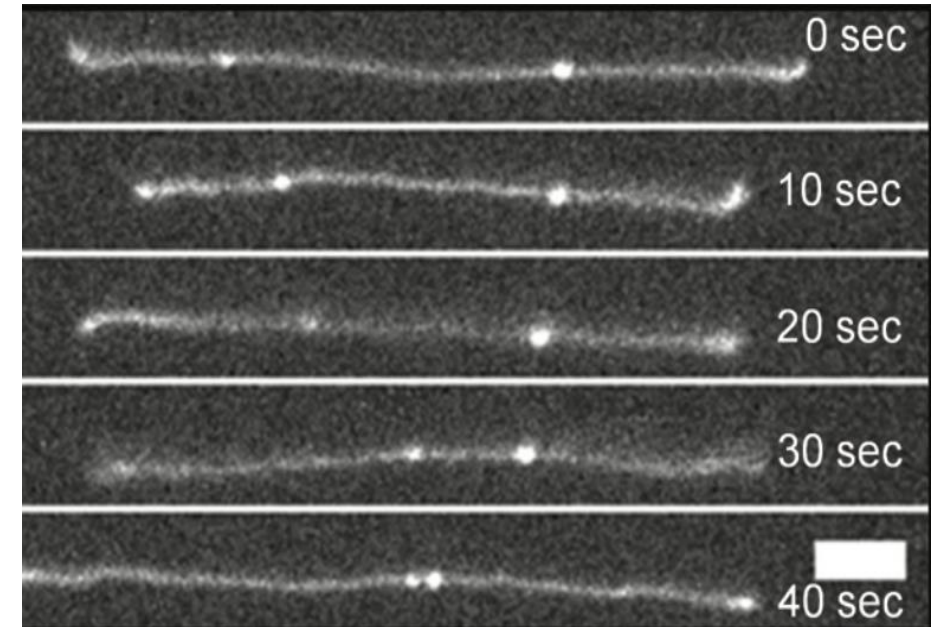


Knots are mobile topological structures that diffuse along the polymer contour due to thermal fluctuations

- Long polymers frequently form multiple knots
- Probability of multi-knot states increases with chain length.

Amin et.al. Nat. Comm **9**, 1506 (2018)

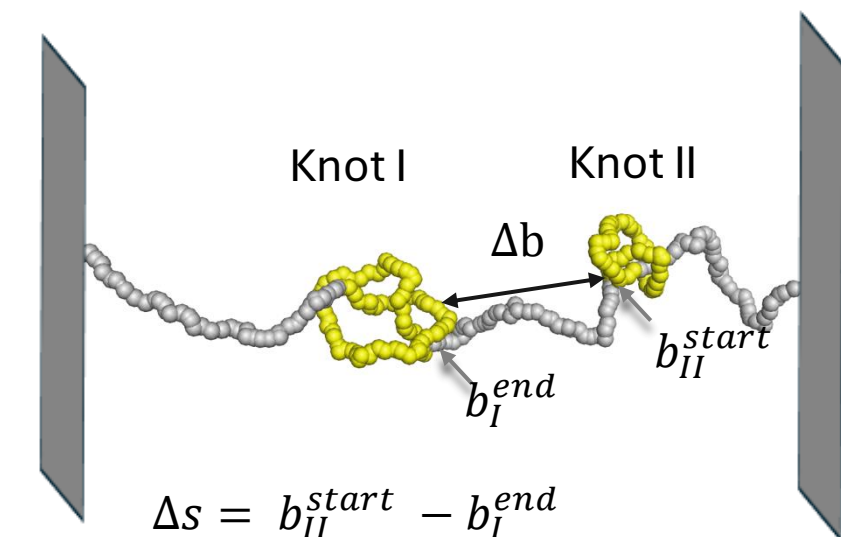
Experimental Evidence of Knot–Knot Attraction



- Two knots exhibit effective entropic attraction
- Knots tend to cluster along the polymer
- Clustering releases free contour length, increasing configurational entropy

Klotz et.al. EPL, 129, 68001 (2020)

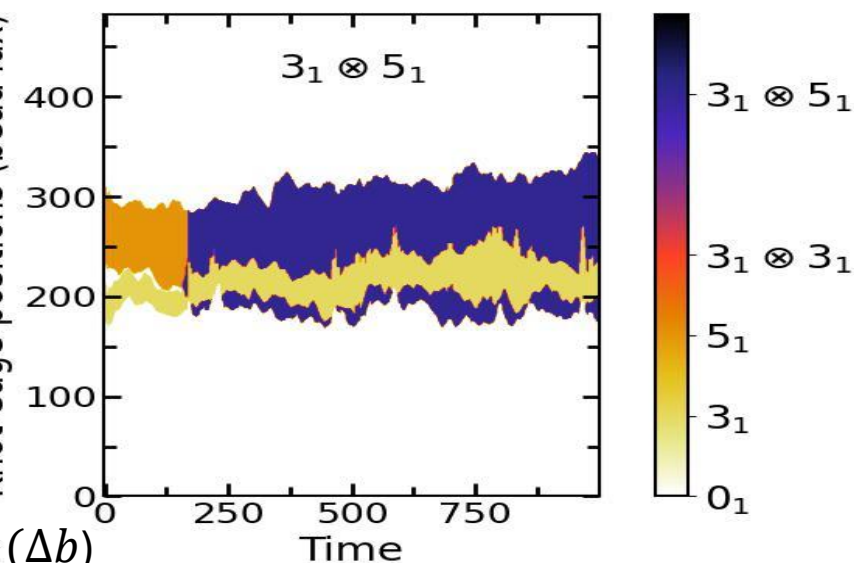
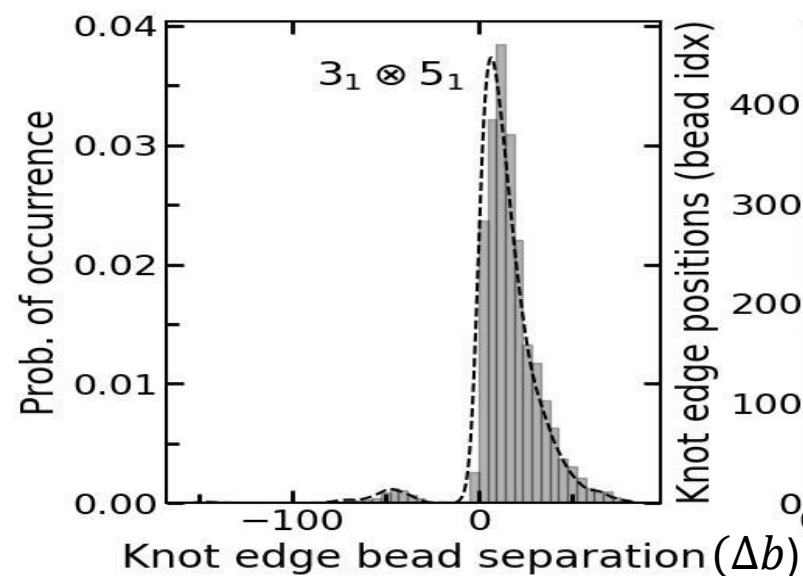
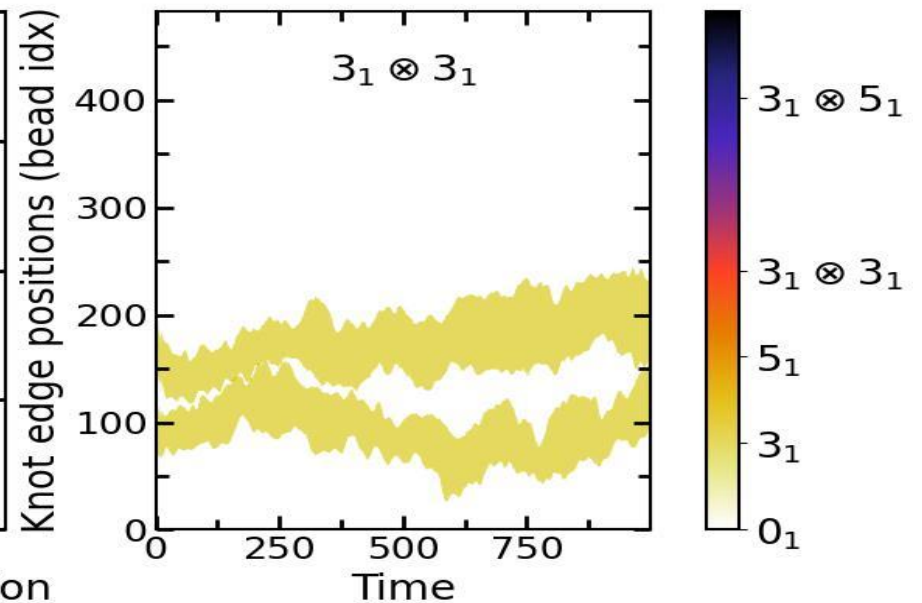
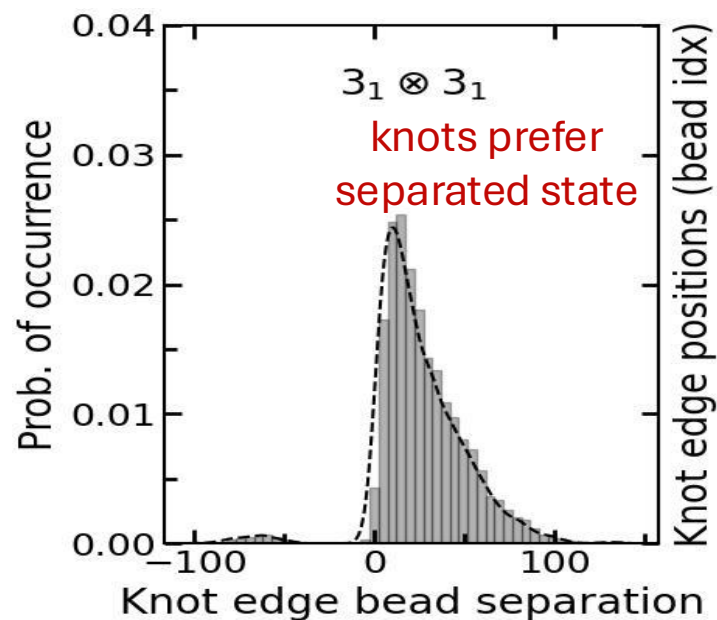
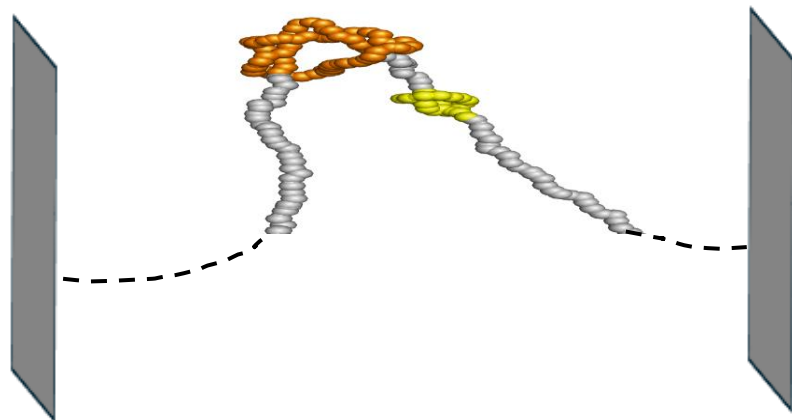
Mixing Probability of Two knots



$$\Delta s = b_{II}^{start} - b_I^{end}$$

$\Delta b \leq 0$ mixing

$\Delta b > 0$ no mixing

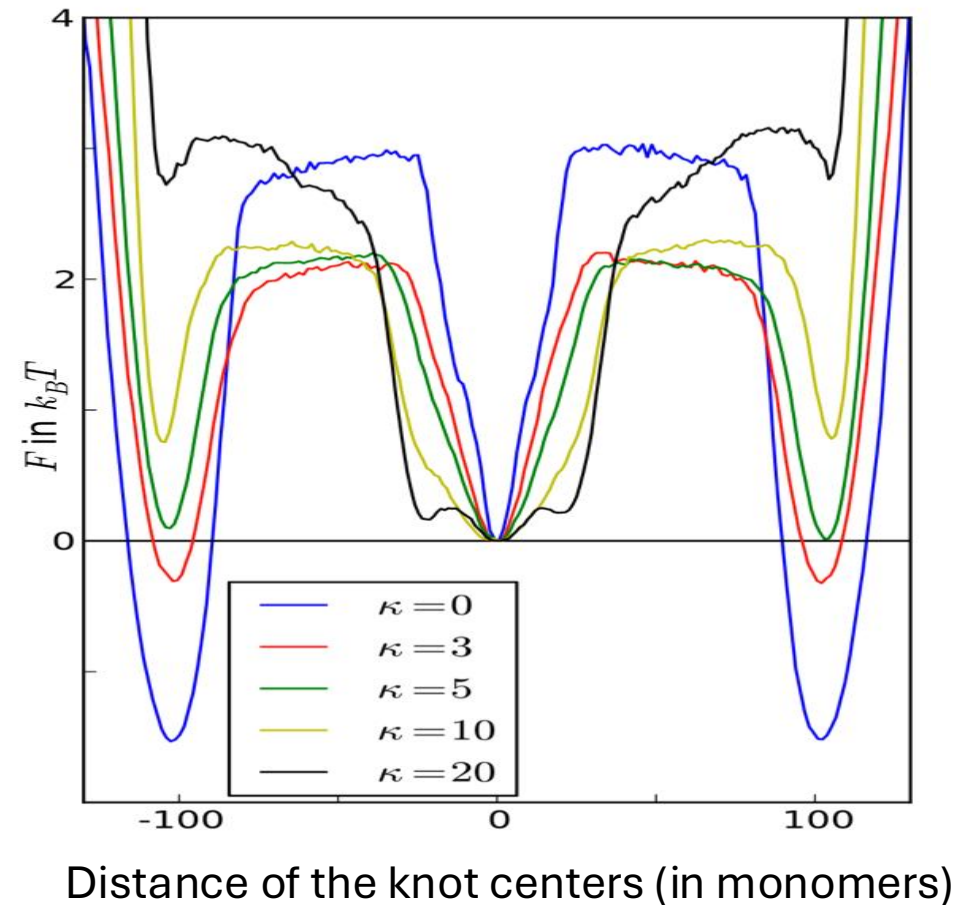


Mixing depends strongly on knot topology

Free-energy barrier suppresses knot mixing

In absence of bending stiffness ($\kappa = 0$) mixing of knots is not favored

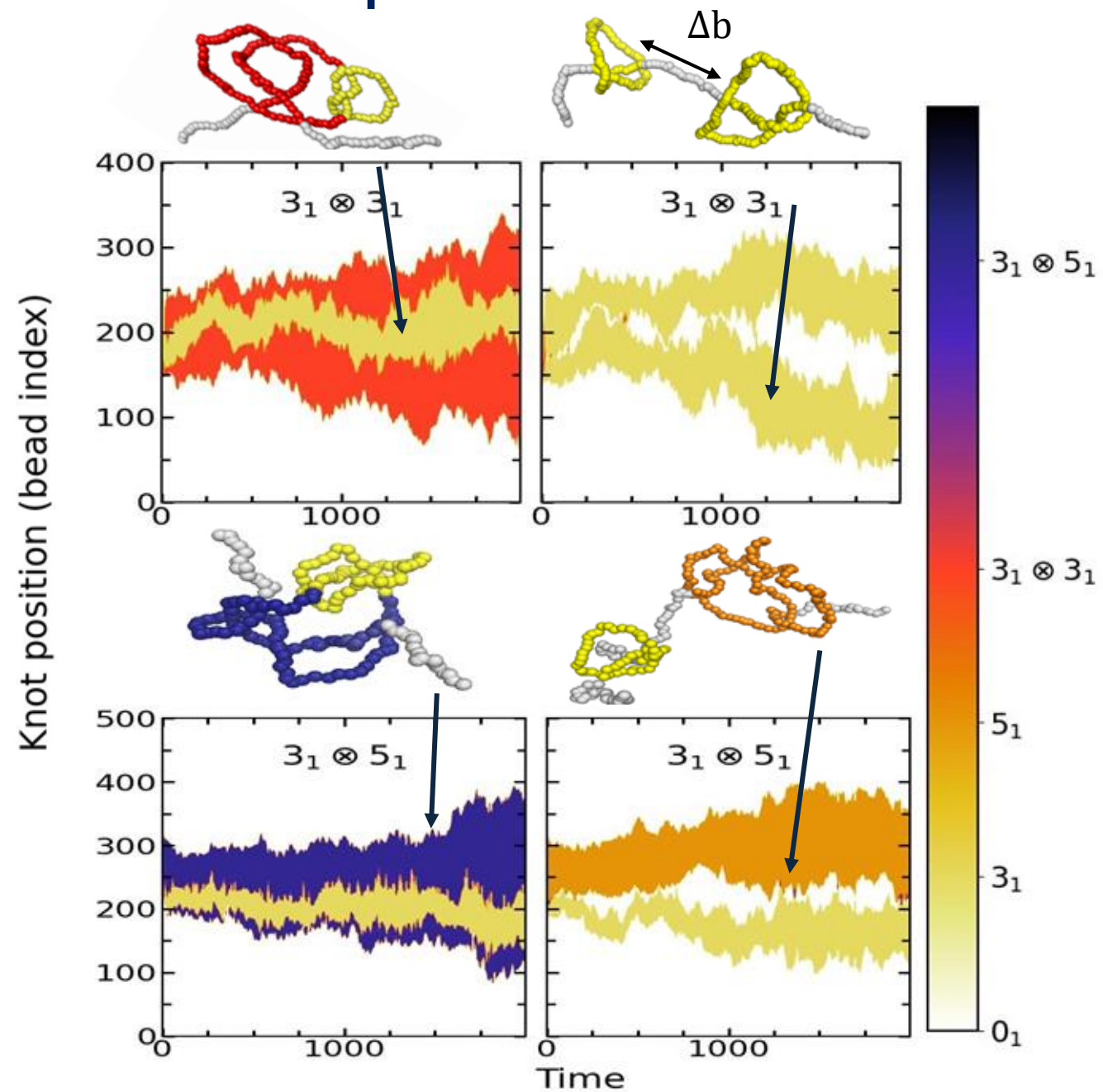
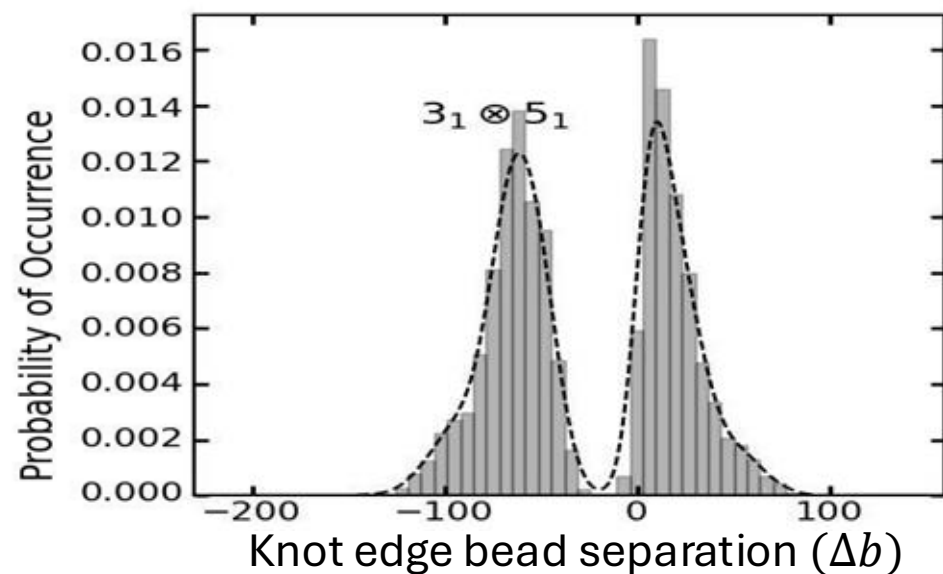
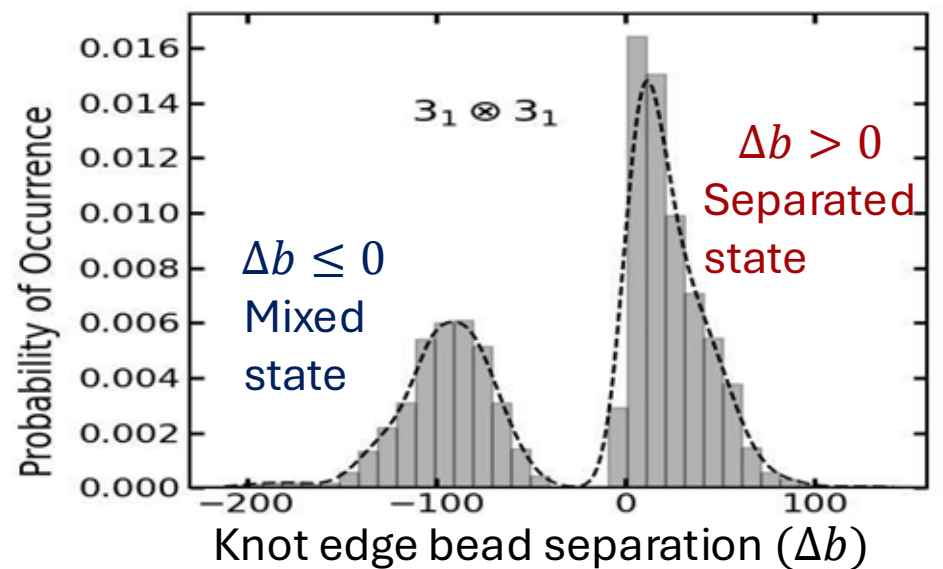
A large free-energy barrier separates the mixed and separated states, making mixing unlikely within typical simulation time scales.



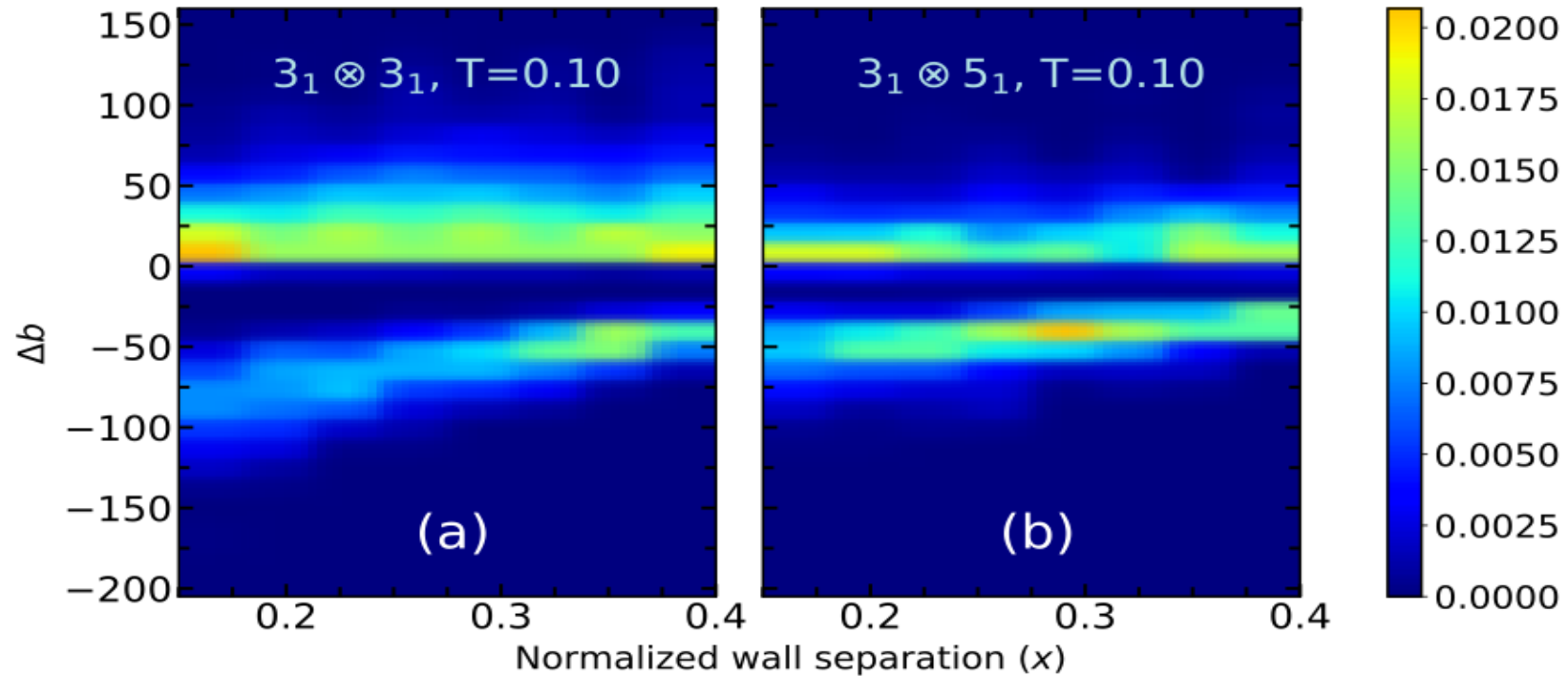
PNAS, **111**, 7948–7951 (2014)

Increasing bending stiffness suppresses knot formation!

Sampling of knots conformational space



Effect of wall separation on two-knot mixing



Positive Δb : demixed state

Negative Δb : mixed or nested state.

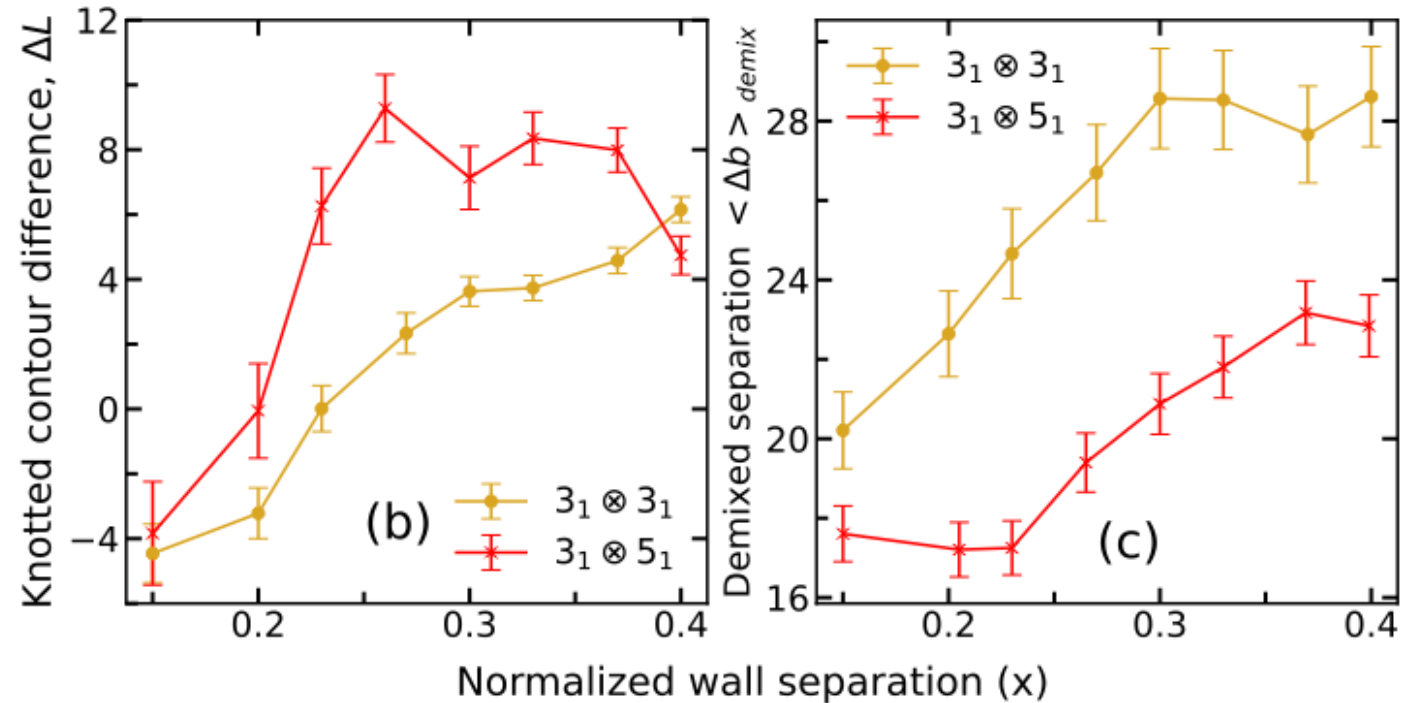
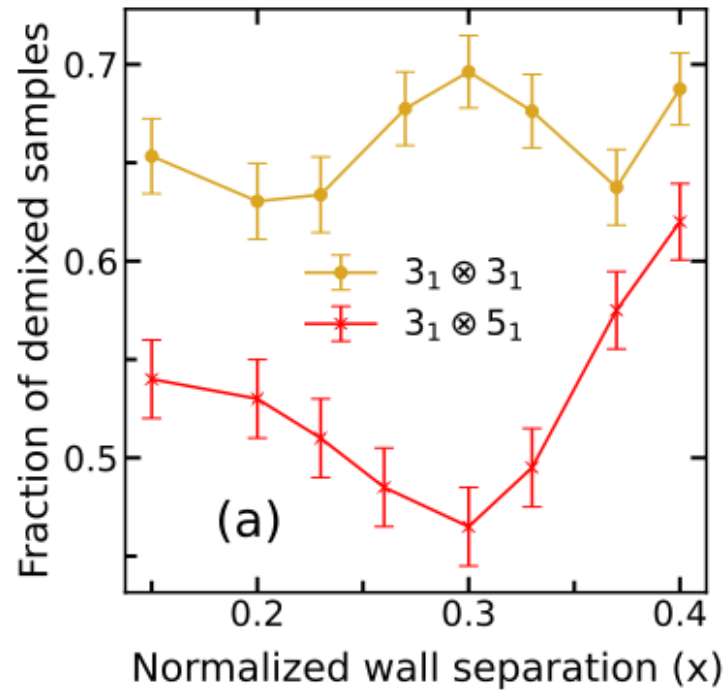
$3_1 \otimes 3_1$ mostly remains demixed

$3_1 \otimes 5_1$ mixes more at intermediate x

Increasing x , tightens the knots and shifts the mixed-state branch toward $\Delta b = 0$.

Topology-Dependent Mixing and Contour Organization

$$\Delta L = L_1 + L_2 - L_{comp}$$

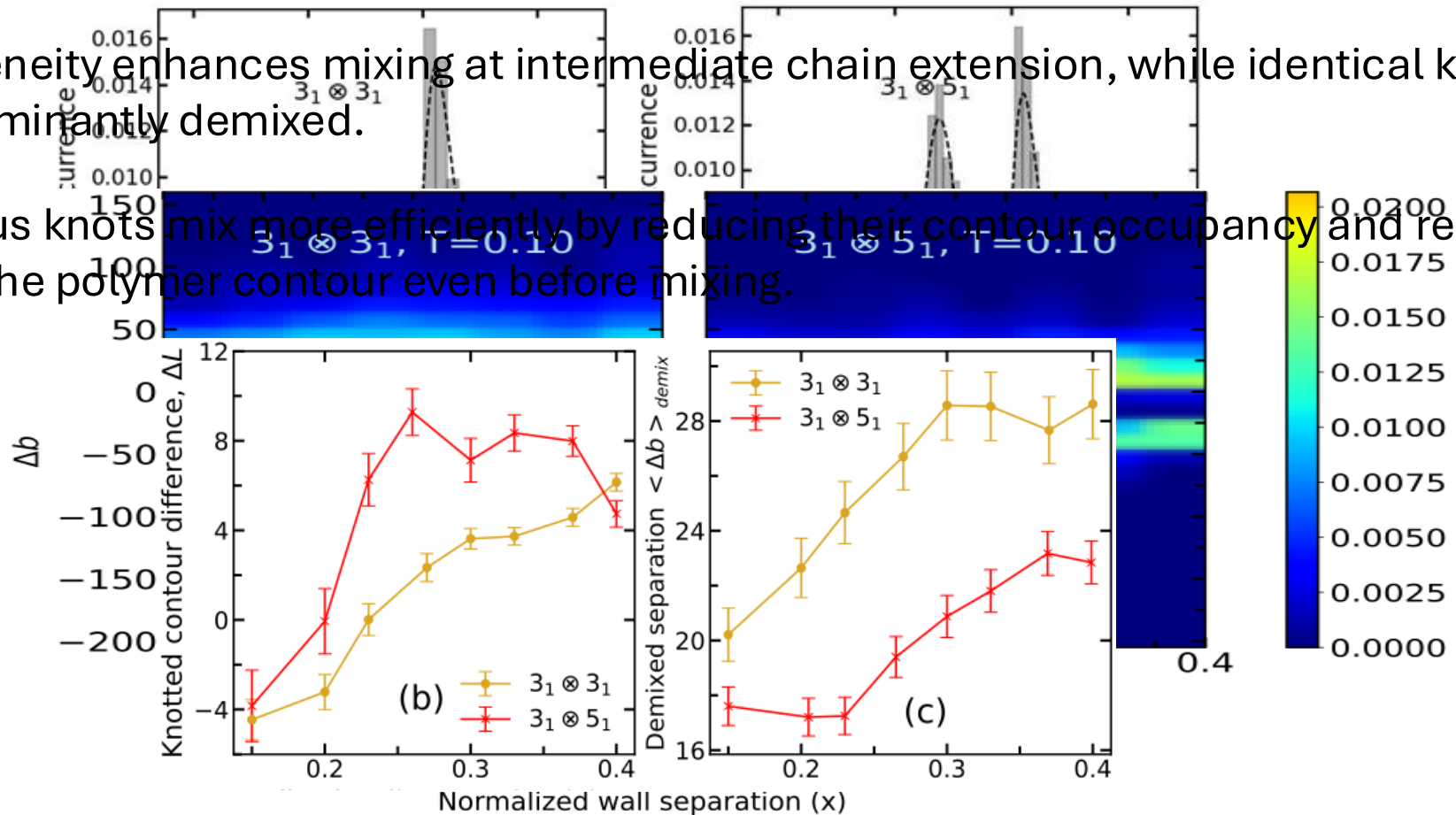


$\Delta b < 0$ Mixing produces a larger contour-occupancy reduction for $3_1 \otimes 5_1$.

$\Delta b > 0$ Heterogeneous knots remain closer along the contour, demonstrating topology-dependent organization before mixing.

Conclusions

- Heterogeneous knot pairs mix and aggregate more readily than homogeneous knot pairs.
- Knot heterogeneity enhances mixing at intermediate chain extension, while identical knots remain predominantly demixed.
- Heterogeneous knots mix more efficiently by reducing their contour occupancy and remain closer along the polymer contour even before mixing.



Thanks