Progress Report

Modeling the mechanism of topoisomerase

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June 23, 2022

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Outline

1. Goals

2. Literature Review

Goals

Overall goal

- Understand the interaction of *TOP2* and the topology of DNA.

This week goal

- Continue to experiment on the minimum force required to reduce the linking number.

Literature Review

- Let say there is an exist of the energy-state mapping $E : \mathcal{S} \to \Omega$ for state domain $\mathcal{S}$.
- with our assumption last time, we can estimate the energy required to transform a state $s_1 \in \mathcal{S}$ to $s_2 \in \mathcal{S}$. Essentially it is $\Delta E = E(s_1) - E(s_2)$.
- Ziraldo *et al.* (2019) suggests that there is a dynamic that can identify the path given the state $(K, \Delta Lk)$ for knot type K.
    - The energy landscape is defined as $E(K, \Delta Lk) = -k_B T \ln\big(P(K, \Delta Lk)\big)$
    - That is, in **static** system, we can estimate the work required for *TOP2*

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Podtelezhnikov *et al.* (1999) come up with the approximation for $P(\Delta Lk|K)$

$$P(\Delta Lk|K) \overset{\text{approx}}{\sim} \mathcal{N}\left(c_K, \sigma_K^2\right)$$

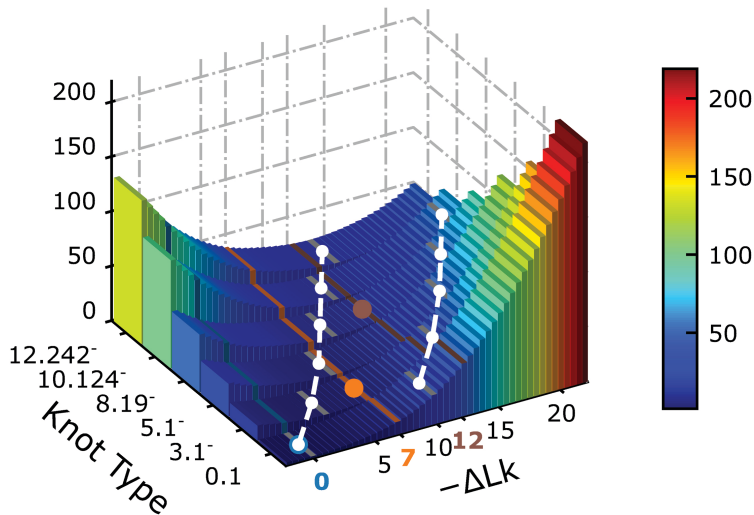where $c_K = \mathbb{E}_K(Wr)$

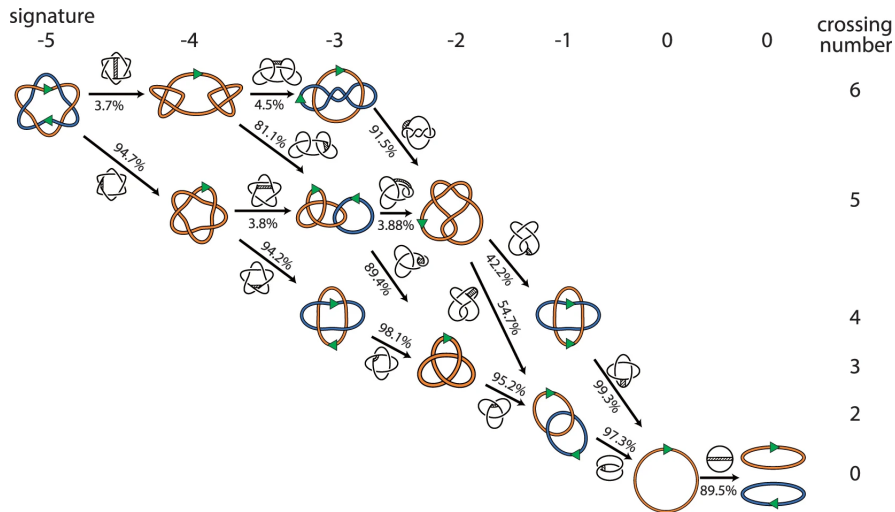Figure 1: Energy minimization pathway

Figure 2: Topological simplification pathway

📄 Podtelezhnikov, A. A., Cozzarelli, N. R., and Vologodskii, A. V.
Equilibrium distributions of topological states in circular dna: Interplay of supercoiling and knotting.
Proceedings of the National Academy of Sciences 96, 23 (1999), 12974–12979.

📄 Stolz, R., Yoshida, M., Brasher, R., Flanner, M., Ishihara, K., Sherratt, D. J., Shimokawa, K., and Vazquez, M.
Pathways of dna unlinking: A story of stepwise simplification.
Scientific Reports 7, 1 (Sep 2017), 12420.

📄 ZIRALDO, R., HANKE, A., AND LEVENE, S. D.
Kinetic pathways of topology simplification by Type-II topoisomerases in knotted supercoiled DNA.
Nucleic Acids Research 47, 1 (11 2018), 69–84.