

Progress Report

Modeling the mechanism of topoisomerase

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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.
- Investigate energy minimization pathway

Literature Review

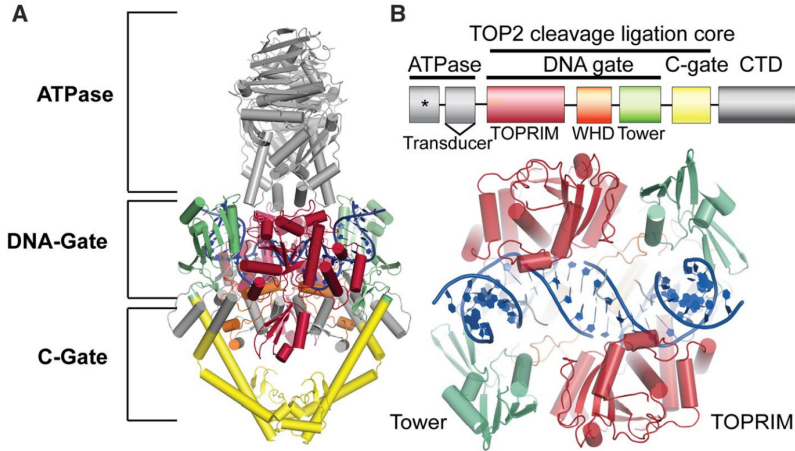


Figure 1: *TOP2* Schematic on *S. cerevisiae* (Riccio *et al.*, 2020)

Mechanism of TOP2

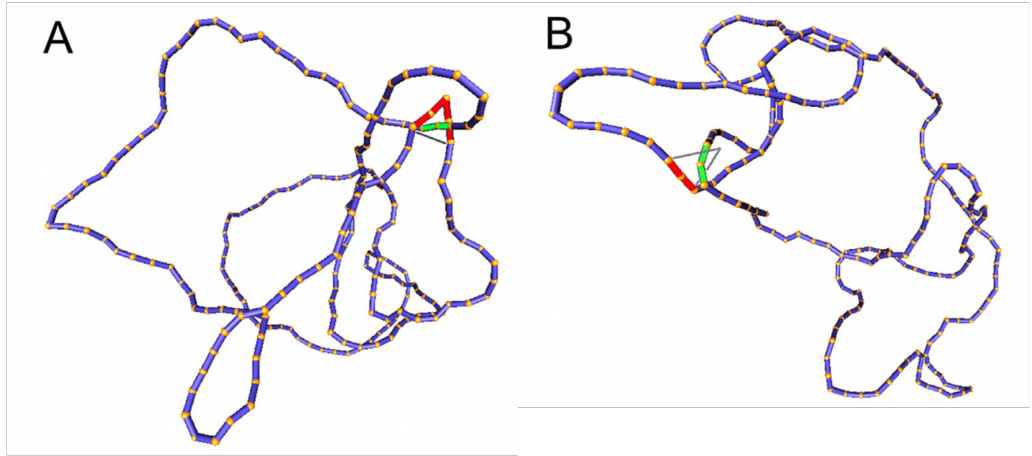




Figure 2: G segment (red) and T segment (green) of DNA, A representing hairpin G and B representing straight G (Ziraldo *et al.*, 2019)

Mechanism of *TOP2*

- Let say we track the topology of the DNA along its strand.
- If we can define the hairpin G segment and straight G segment, we can ideally model the (somewhat) realistic mechanism of *TOP2*.
- If G and T segment are closed enough (i.e. juxtapose). We can, with a probability model, works our way on the process.
- Vologodskii (1998) suggests that *TOP2* works like Maxwell demon altering DNA out of equilibrium. To do that, it requires energy (ATP).
- Parameter that needed to be considered: Concentration of *TOP2*, concentration of ATP, thermal energy, etc.

-  RICCIO, A. A., SCHELLENBERG, M. J., AND WILLIAMS, R. S.
Molecular mechanisms of topoisomerase 2 dna–protein crosslink resolution.
Cellular and Molecular Life Sciences 77, 1 (Jan 2020), 81–91.
-  VOLOGODSKII, A.
Maxwell demon and topology simplification by type ii topoisomerases.
In *Proceedings of the Second Annual International Conference on Computational Molecular Biology* (New York, NY, USA, 1998), RECOMB '98, Association for Computing Machinery, p. 266–269.

-  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.