Progress Report

Modeling the mechanism of topoisomerase

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Outline

1. Goals
2. Literature Review
3. Initial Ideas

Goals

Goals

Overall goal

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

This week goal

- Understand the dynamics and fluid-coupled system of DNA.
- (Hopefully) Start to model.

Literature Review

Topology of DNA

Linking number

$$Lk\left(\mathcal{C}_1, \mathcal{C}_2\right) = \frac{1}{4\pi} \oint_{\mathcal{C}_1} \oint_{\mathcal{C}_2} \frac{\mathbf{x}_1'(s_1) \times \mathbf{x}_2'(s_2) \cdot \left[\mathbf{x}_1(s_1) - \mathbf{x}_2(s_2)\right]}{\left|\mathbf{x}_1(s_1) - \mathbf{x}_2(s_2)\right|^3} \, ds_2 \, ds_1$$

Writhe

$$Wr\left(\mathcal{C}\right) = \frac{1}{4\pi} \oint_{\mathcal{C}} \oint_{\mathcal{C}} \frac{\mathbf{x}'(s_1) \times \mathbf{x}'(s_2) \cdot \left[\mathbf{x}(s_1) - \mathbf{x}(s_2)\right]}{\left|\mathbf{x}(s_1) - \mathbf{x}(s_2)\right|^3} \, ds_2 \, ds_1$$

Twist

$$Tw\left(\mathcal{C}_2, \mathcal{C}_1\right) = Lk(\mathcal{C}_1, \mathcal{C}_2) - Wr(\mathcal{C}_1)$$

Simplified Model (Swigon, 2009)

Elastic Energy

$$\Psi = \frac{1}{2}\int_0^L \overbrace{A\left|\mathbf{t}'\right|^2}^{\text{bending}} + C\underbrace{\left(\left[\mathbf{t}_1 \times \mathbf{d}\right]\cdot \mathbf{d}'(s) - \bar{\Omega}\right)^2}_{\text{squared difference of twist density}} ds \implies A\left(\mathbf{t}\times\mathbf{t}''\right) + C\Delta\Omega\mathbf{t}' = \mathbf{F}\times\mathbf{t}$$

Under standard condition: $A \approx 50\mathrm{kT}\cdot\mathrm{nm},\ C \in [25, 100]\mathrm{kT}\cdot\mathrm{nm}$

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Electrostatic Energy

For M charged sites,

$$\Phi = \frac{4\delta^2}{4\pi\epsilon}\sum_{m=1}^{M-1}\sum_{n=m+1}^{M}\frac{\exp\left(-\kappa\left|\mathbf{x}_m - \mathbf{x}_n\right|\right)}{\left|\mathbf{x}_m - \mathbf{x}_n\right|}$$

Simplified Model (con't) (Swigon, 2009)

Generalized Kirchhoff's Rod Dynamics

$$\partial_t \mathsf{P} = \mathsf{F}' + \mathsf{f} \qquad \text{(linear momentum)}$$

$$\partial_t \mathsf{R} = \mathsf{M}' + \mathsf{x}' \times \mathsf{F} + \mathsf{m} \qquad \text{(angular momentum)}$$

Initial Ideas

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Naive Ideas (con't)

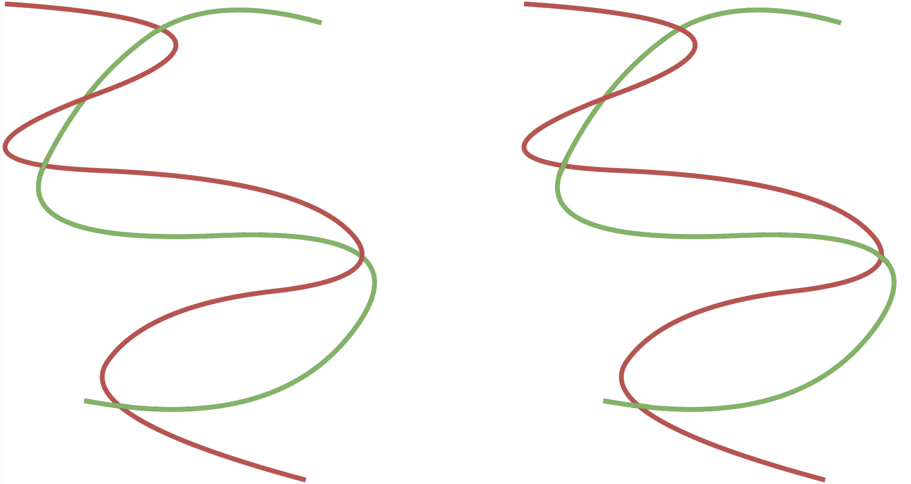

Figure 1: Visualize the process. Left side is original and right side is randomly transformed

Question

- How can *TOP2* knows the cleavage site?