Progress Report

Modeling the mechanism of topoisomerase

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Outline

1. Goals
2. Literature Review
3. Idea

Goals

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Overall goal

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

This week goal

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

Literature Review

Immersed Boundary (IB) method

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- Then, the conservation of force and momentum

$$\mathbf{f} = -\partial_s \mathbf{F}, \ \mathbf{m} + \partial_s \mathbf{M} = \mathbf{F} \times \partial_s \mathbf{X}$$

$\mathbf{F}$ and $\mathbf{X}$ can be represented in terms of the reference frame and can be transformed between Eulerian and Lagrangian coordinate system.

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$$(f * g)(t) := \int_{-\infty}^{\infty} f(\tau) \underbrace{g(t-\tau)}_{\text{kernel}} d\tau$$

Immersed Boundary (IB) method (Con't)

Algorithm

1. Calculate $\mathbf{f}$ and $\mathbf{m}$ from conservation of force and momentum.
2. Calculate $\mathbf{f}_b$ and use that as a forcing term
3. Solve Navier-Stokes equation and update the velocity
4. Use new information to update $\mathbf{f}$ and $\mathbf{m}$

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- Now, we just need to solve the linear system and span it for the solutions along the interested points.
- The kernel for this method would be slightly different compared to the IB method where the smoothed Dirac delta function is used.

Idea

Ideas

- Last time we discussed about random process that reflecting *TOP2* **after interacting with DNA**.
- We have defined the linking number of two closed curves as

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

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- **Problem**: For our probabilistic process $\mathcal{P}(C_1, C_2, t)$ case, how can we know (or guarantee) that for the continuous sub-region of curve $\mathcal{K}_i \subseteq \mathcal{C}_i$ such that $Lk\,(\mathcal{K}_1, \mathcal{K}_2) > c$ for $c \in \mathbb{Z}^+$, $Lk(\mathcal{P}(\mathcal{K}_1, \mathcal{K}_2, t)) - Lk(\mathcal{P}(\mathcal{K}_1, \mathcal{K}_2, t+1)) < 0$ for all $t \in \Gamma$?

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- Our goal is to find the force needed to move the DNA to the state that we expected.
- Large $|Lk|$ implies that DNA has high energy.
- **Goal**: Find the minimum force required to move a point out of the local minima which would be the **lower bound** for the force needed by *TOP2*.

Similar Problem

- Let say we want to optimize a function $f(x)$. We can use gradient descent method to find the minima of the function.

Theorem

If f is α-strongly convex and ∇f is β-Lipschitz, then the iteration needed for reaching the global minimum is $t \in O\left(\log\left(\frac{1}{\varepsilon}\right)\right)$ for $f(x_{T=t}) - f(x^*) \leq \varepsilon$.

- The theorem implies that there is another exponentially related parameter that governed the rate of transition to another state given that the energy state function is convex.
- What if the function is not necessary convex? How can we reach the global minimum? What determine the rate?

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