Rheology of Suspensions of Fluctuating, Inextensible, Semiflexible Fibers in Stokes Flow

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Outline

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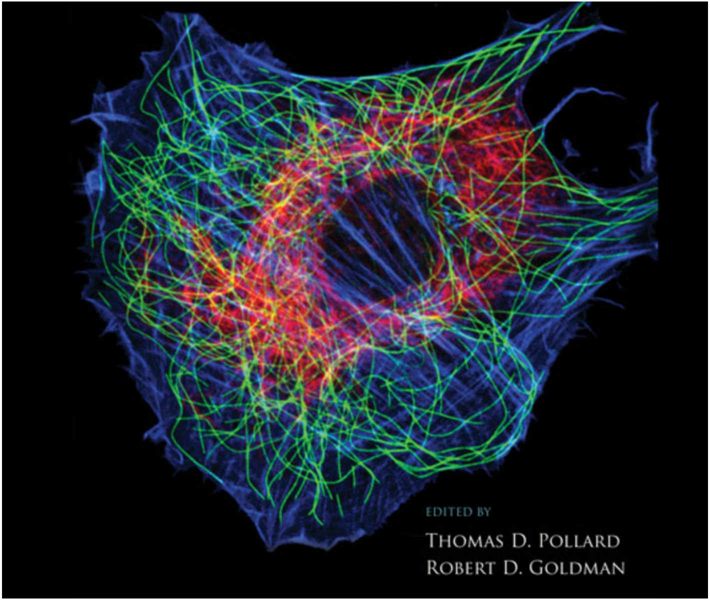
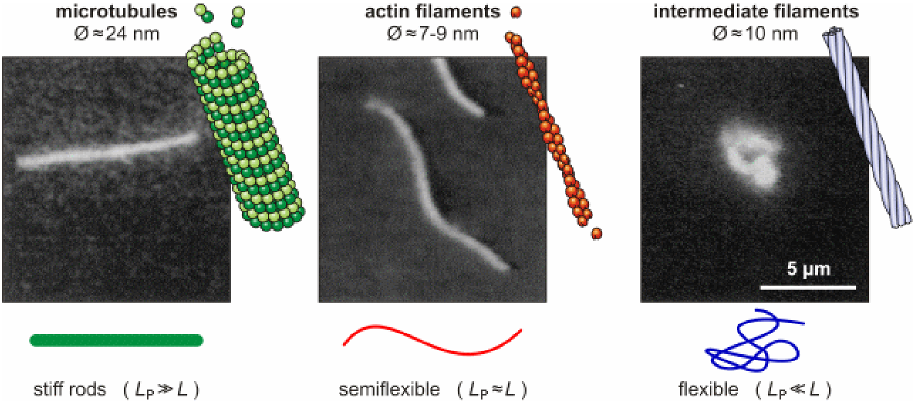
The cell cytoskeleton



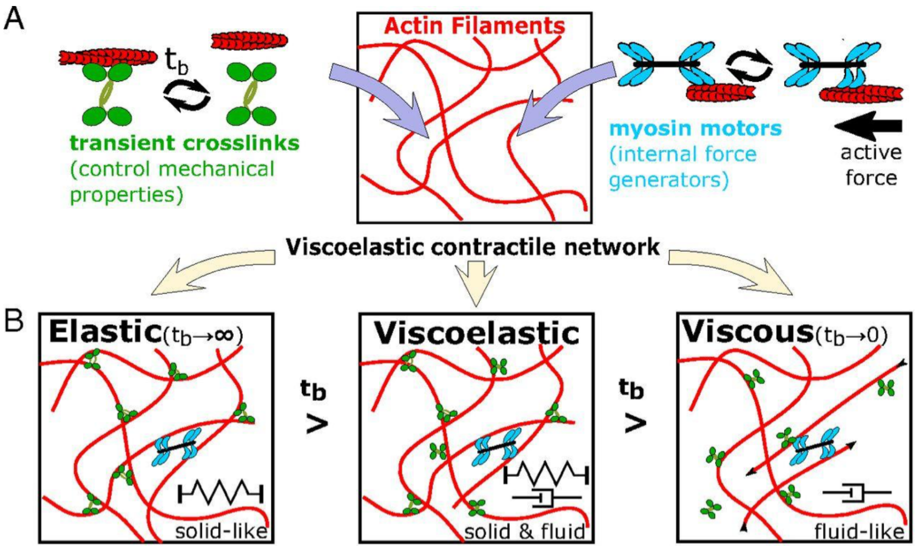
Fibers involved in cell mechanics



Pawlizak and Käs, University of Leipzig

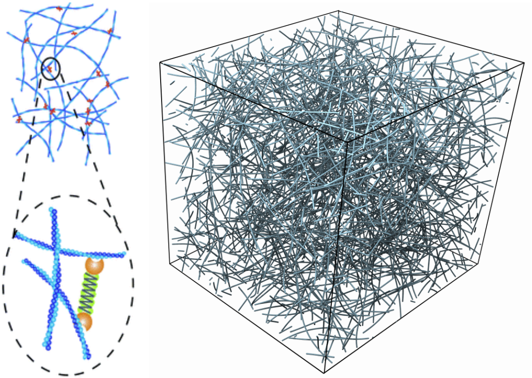
L_p =persistence length, L =fiber length, $a = \epsilon L$ =fiber radius, ϵ =slenderness ratio

Cytoskeleton rheology



Ahmed and Betz. *PNAS*. (2015)

Cross-linked actin gels



- Very **slender semi-flexible fibers** (aspect ratio $10^2 - 10^4$) suspended in a **viscous solvent**.
- For now **cross linkers** modeled as simple elastic springs.
- **Periodic cyclically sheared** unit cell: **viscoelastic moduli**.

Open scientific questions

- Role of **long-ranged (nonlocal) hydrodynamics** unclear for **rheology** of cross-linked actin gels.
- Importance/role of **Brownian bending fluctuations** of fibers on rheology also not fully clear.

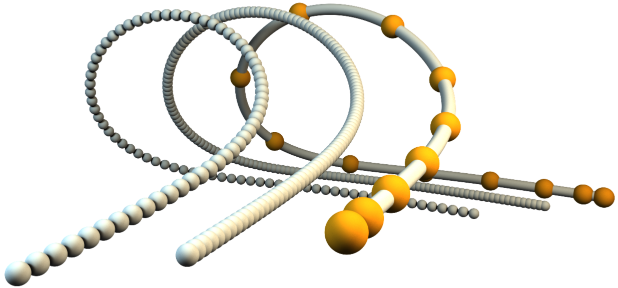
Dynamics of Flexible Fibers in Viscous Flows and Fluids, Ann. Rev. Fluid Mech. 51:539, du Roure, Lindner, Nazockdast, Shelley

Outline

1. Cytoskeleton
2. Inextensible non-Brownian fibers in Stokes flow
   - Elasticity
   - Hydrodynamics
   - Inextensibility
   - Actin gels
3. Adding Brownian motion

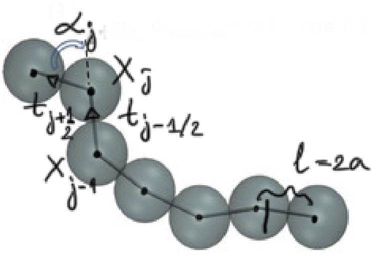
Fiber Representation

Simple approach is to represent a fiber as a **discrete chain** of beads/blobs: **multiblob model**



More efficient approach is to represent a fibers as **continuum curve**
O. Maxian et al. **ArXiv:2201.04187**
PRF 2021 [1]and now with twist in *PRF 2022* [2]

Inextensible multiblob chains



Worm-like polymer chain

- Inextensibility: $\|\mathbf{X}_{j+1} - \mathbf{X}_j\| = l \sim a$ (e.g., a or $2a$).
- **Tangent vectors**:
  $\boldsymbol{\tau}_{j+1/2} = \left(\mathbf{X}_{j+1} - \mathbf{X}_j\right)/l$
- Bending angles:
  $\cos\alpha_j = \boldsymbol{\tau}_{j+1/2} \cdot \boldsymbol{\tau}_{j-1/2}$
- Elastic energy (bending modulus κ_b)

$$E_b = \frac{2\kappa_b}{l} \sum_{j=1}^{N-1} \sin^2\left(\frac{\alpha_j}{2}\right)$$

Inextensible continuum fibers

- Persistence length due to thermal fluctuations $\xi = 2\kappa_b / (k_B T) \gg l$ gives us a **continuum limit**, $\alpha_j \ll 1$.
- Fiber centerline $\mathbf{X}(s)$ where the **arc length** $0 \le s \le L$.
- The tangent vector is $\boldsymbol{\tau} = \partial \mathbf{X} / \partial s = \mathbf{X}_s$, and the **fibers are inextensible**,

$$\boldsymbol{\tau}(s,t) \cdot \boldsymbol{\tau}(s,t) = 1 \quad \forall (s,t).$$

- Bending energy functional is integral of curvature squared:

$$E_b(\mathbf{X}) = \frac{2\kappa_b}{l} \sum_{j=1}^{N-1} \left(\frac{\alpha_j}{2} \right)^2 \quad \Rightarrow \quad E_b[\mathbf{X}(\cdot)] = \frac{\kappa_b}{2} \int ds \, \| \mathbf{X}_{ss}(s) \|^2$$

Bending elasticity

- Bending force in limit gives us **elastic force density**

$$\mathbf{F}_b \approx -l\kappa_b \mathbf{D}^4\mathbf{X} \quad \Rightarrow \quad \mathbf{f}_b = -\frac{\delta E_{\text{bend}}}{\delta X} = -\kappa_b \mathbf{X}_{ssss}$$

- Natural **boundary conditions** for free fibers:

$$\mathbf{X}_{ss}\left(0/L\right) = 0, \quad \mathbf{X}_{sss}\left(0/L\right) = 0.$$

- **Tensions** $T_{j+1/2} \to T(s)$ are **unknown** and resist stretching,

$$\boldsymbol{\Lambda}_i = T_{i+1/2}\boldsymbol{\tau}_{i+1/2} - T_{i-1/2}\boldsymbol{\tau}_{i-1/2} \quad \Rightarrow \quad \boldsymbol{\lambda} = \left(T\boldsymbol{\tau}\right)_s.$$

Fluid dynamics of an immersed fiber

- Immersed blob continuum hydrodynamic model (without Brownian fluctuations):

$$\nabla\pi\left(\mathbf{r},t\right)=\eta\nabla^{2}\mathbf{v}\left(\mathbf{r},t\right)+\int_{0}^{L}ds\;\mathbf{f}(s,t)\delta_{a}\left(\mathbf{X}(s,t)-\mathbf{r}\right)$$

$$\mathbf{U}\left(s,t\right)=\partial_{t}\mathbf{X}\left(s,t\right)=\int d\mathbf{r}\;\mathbf{v}\left(\mathbf{r},t\right)\delta_{a}\left(\mathbf{X}(s,t)-\mathbf{r}\right)$$

$$\mathbf{f}=-\kappa_{b}\mathbf{X}_{ssss}+\boldsymbol{\lambda}$$

- For the discrete case just replace integrals by sums over blobs.

Hydrodynamic mobility kernel

- We can (temporarily) eliminate the fluid velocity to write an equation for **fiber only**.
- Define the positive semi-definite **hydrodynamic kernel**

$$\mathcal{R}\left(\mathbf{r}_1, \mathbf{r}_2\right) = \int \delta_a\left(\mathbf{r}_1 - \mathbf{r}'\right) \mathbb{G}\left(\mathbf{r}', \mathbf{r}''\right) \delta_a\left(\mathbf{r}_2 - \mathbf{r}''\right) d\mathbf{r}' d\mathbf{r}'',$$

  where $\mathbb{G}$ is the Green's function for (periodic) Stokes flow.
- Choosing a surface delta function

$$\delta_a\left(\mathbf{r}\right) = \left(4\pi a^2\right)^{-1} \delta\left(r - a\right)$$

  gives the **Rotne-Prager-Yamakawa (RPY) kernel**.

Nonlocal PDE

- Define a positive semidefinite **mobility operator**

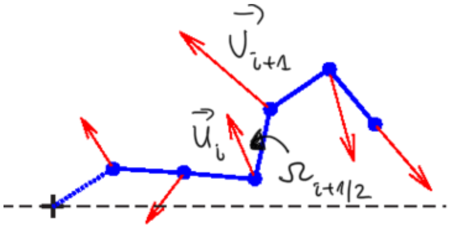
$$\left(\mathcal{M}\left[\mathbf{X}\left(\cdot\right)\right]\mathbf{f}\left(\cdot\right)\right)(s)=\int_0^L ds'\,\mathcal{R}\left(\mathbf{X}(s),\mathbf{X}(s')\right)\mathbf{f}(s')$$

- Continuum dynamics is a **non-local PDE**

$$\mathbf{U}=\mathbf{X}_t=\mathcal{M}\left[\mathbf{X}\right]\left(-\kappa_b\mathbf{X}_{ssss}+\boldsymbol{\lambda}\right)$$
$$\boldsymbol{\tau}(s,t)\cdot\boldsymbol{\tau}(s,t)=1\quad\forall(s,t).$$

- We have developed **spectral methods** for solving this for suspensions of fibers, *without fluctuations*.

Inextensible motions



$$\frac{\mathbf{U}_i - \mathbf{U}_{i-1}}{\Delta s} = \boldsymbol{\Omega}_{j+1/2} \times \boldsymbol{\tau}_{j+1/2} \quad \Rightarrow$$

$$\mathbf{U} = \mathbf{K}\boldsymbol{\Omega}^{\perp} = \left[\mathbf{U}_0, \cdots, \mathbf{U}_0 + \Delta s \sum_{j=0}^{i-1} \boldsymbol{\Omega}^{\perp}_{j+1/2} \times \boldsymbol{\tau}_{j+1/2}, \cdots \right] \rightarrow$$

$$\mathbf{U}(s) = \left(\mathcal{K}\left[\mathbf{X}(\cdot) \right] \boldsymbol{\Omega}^{\perp}(\cdot) \right)(s) := \mathbf{U}(0) + \int_0^s ds' \left(\boldsymbol{\Omega}^{\perp}(s') \times \boldsymbol{\tau}(s') \right).$$

Constrained energy descent formulation

- We can derive an update formula by minimizing the Lagrangian:

$$\mathcal{L}\left[\mathbf{X},\boldsymbol{\Omega},\boldsymbol{\lambda}\right]=\frac{\kappa}{2}\int_0^L\mathbf{X}_{ss}(s)\cdot\mathbf{X}_{ss}(s)\,ds\ \text{(energy)}$$

$$+\frac{1}{\Delta t}\int_0^L\left(\mathbf{X}(s)-\mathbf{X}^n(s)\right)\cdot\left(\mathbf{M}^n\right)^{-1}\left(\mathbf{X}(s)-\mathbf{X}^n(s)\right)\,ds\ \text{(dissipation)}$$

$$+\int_0^L\left(\mathbf{U}\left(0\right)+\int_0^s ds'\,\left(\boldsymbol{\Omega}\left(s'\right)\times\boldsymbol{\tau}\left(s'\right)\right)-\left(\mathbf{X}-\mathbf{X}^n\right)\right)\cdot\boldsymbol{\lambda}(s)\,ds,$$

- This leads to **backward Euler** time integration:

$$\left(\frac{\delta\mathcal{L}}{\delta\mathbf{X}}\right)^{n+1}=\mathbf{0}\quad\text{and}\quad\left(\frac{\delta\mathcal{L}}{\delta\boldsymbol{\lambda}}\right)^{n+1}=\mathbf{0}\quad\Rightarrow$$

$$\frac{\mathbf{X}^{n+1}-\mathbf{X}^n}{\Delta t}=\mathbf{M}^n\left(-\kappa\mathbf{X}_{ssss}^{n+1}+\boldsymbol{\lambda}^{n+1}\right)=$$

$$\mathcal{K}\left[\mathbf{X}^n\right]\boldsymbol{\Omega}^{n+1}=\mathbf{U}^n\left(0\right)+\int_0^s ds'\,\left(\boldsymbol{\Omega}^{n+1}\left(s'\right)\times\boldsymbol{\tau}\left(s'\right)\right)$$

Principle of virtual work

- Lastly, we get the **principle of virtual work**:

$$\left(\frac{\delta\mathcal{L}}{\delta\mathbf{\Omega}}\right)^{n+1} = \mathbf{0} \rightarrow \mathbf{0} = \begin{pmatrix} \int_0^L \boldsymbol{\lambda}^{n+1}(s)\, ds \\ \boldsymbol{\tau}^n(s) \times \int_s^L \boldsymbol{\lambda}^{n+1}(s')\, ds' \end{pmatrix} := \mathcal{K}^* \left[\mathbf{X}^n\right] \boldsymbol{\lambda}^{n+1}.$$

  where $\mathcal{K}$ and $\mathcal{K}^*$ are L^2 adjoint operators.
- Physics wording: constraint forces should do no work for any inextensible motion of the fiber.
- We can express this in terms of tension as $\boldsymbol{\lambda}^{n+1} = \left(T^{n+1}\boldsymbol{\tau}^n\right)_s$ but better to use an **integral constraint**.

Galerkin discretization

- In our **Galerkin** numerical method, we represent functions by **orthogonal (Chebyshev) polynomials**, e.g.,

$$\mathbf{X}(s) = \sum_{k=1}^{N} \widehat{X}_k \phi_k(s).$$

- Bending energy is quadratic and discretized as a matrix

$$\mathbf{L}_{ij} = \int_0^L \phi_i''(s)\phi_j''(s)\, ds$$

- Hydrodynamic mobility gets discretizes as an **SPD mobility matrix**

$$\mathbf{M}_{ij} = \int_0^L ds \int_0^L ds' \, \phi_i(s) \boldsymbol{\mathcal{M}}(s, s') \phi_j(s'),$$

  which we approximate using accurate near-singular **special quadrature schemes**.

- All products can be computed exactly for polynomials on an upsampled Chebyshev grid of $3N$ nodes.

Strict inextensibility

- Unfortunately, polynomial curves cannot be strictly inextensible.
- Instead, we impose inextensibility pointwise at Chebyshev nodes:

$$\mathcal{L}\left[\widehat{\mathbf{X}}, \Omega, \lambda\right] = \frac{1}{2}\widehat{\mathbf{X}}^T \mathbf{L}\widehat{\mathbf{X}} + \frac{1}{2\Delta t}\left(\widehat{\mathbf{X}} - \widehat{\mathbf{X}}^n\right)^T \mathbf{M}^{-1}\left(\widehat{\mathbf{X}} - \widehat{\mathbf{X}}^n\right) \tag{1}$$

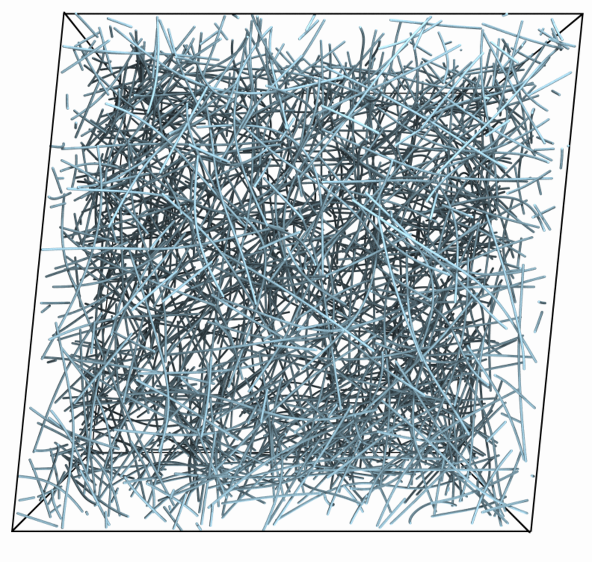
$$+\left[\int_0^L \left(\mathbf{U}(0) + \int_0^s ds' \left(\boldsymbol{\Omega}(s') \times \boldsymbol{\tau}(s')\right) - \left(\mathbf{X} - \mathbf{X}^n\right)\right) \cdot \boldsymbol{\lambda}(s)\, ds\right]_{3N}.$$

- To maintain **strict inextensibility** on the N-point grid, we **rotate tangent vectors**:

$$\boldsymbol{\tau}^{n+1} = \text{Rotate}\left(\boldsymbol{\tau}^n, \boldsymbol{\Omega}^{n+1}\Delta t\right) = \exp\left(\Delta t\left[\boldsymbol{\Omega}^{n+1}\right]_\times\right)\boldsymbol{\tau}^n \quad \text{(roughly)}$$

- **Open question**: How to represent inextensible curves or curves on the unit sphere in a basis set?

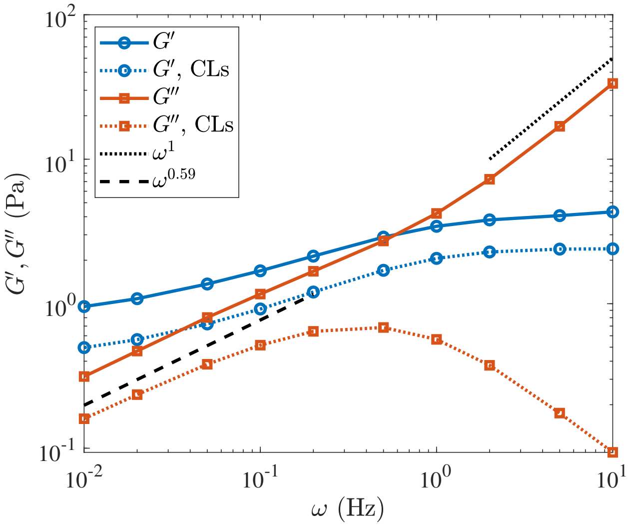
Actin network/gel



Cross-linked network

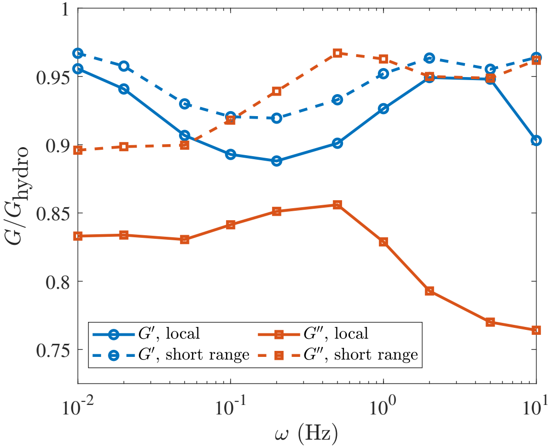
Randomly generated dense network of CLs (16 attachment sites per site) to give about 12 CLs per fiber (elastic network).

Viscoelastic moduli: Maxwell fluid



Elastic modulus G' and **viscous** modulus G'' for 700 fibers + 8400 CLs

Nonlocal hydrodynamics



Reduction in viscoelastic moduli with **only local drag** or **only inter-fiber nonlocal hydrodynamics**.

Outline

Thermal fluctuations (Brownian Motion)

- **Rigid fibers** are "easy" [3] and similar to a dumbbell (one-link chain) since **fully discreet** (dofs are only orientation and center for each fiber).
- The **equilibrium** (Gibbs-Boltzmann) distribution of a continuum worm-like chain:
  The tangent vector $\boldsymbol{\tau}(s)$ performs Brownian motion on the unit sphere with diffusion coefficient $\sim l_p$.
- *There is no continuum limit of a freely-jointed chain* which is already a problem (**no base measure**).

Fluctuating (hydro)dynamics

- Naive "SPDE" (fluctuating hydrodynamics)

$$\mathcal{K}[\mathbf{X}]\,\boldsymbol{\Omega}^{\perp} = \mathcal{M}[\mathbf{X}]\left(-\kappa_b \mathbf{X}_{ssss} + \sqrt{2k_B T}\,\mathcal{M}^{-\frac{1}{2}}[\mathbf{X}]\,\mathcal{W} + \boldsymbol{\lambda}\right)$$

$$\mathcal{K}^{\star}[\mathbf{X}]\,\boldsymbol{\lambda} = \mathbf{0}$$

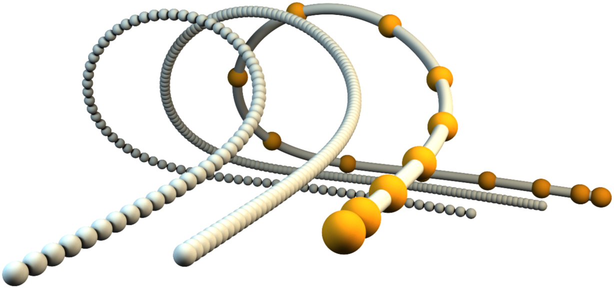
$$\partial_t \boldsymbol{\tau} = \boldsymbol{\Omega}^{\perp} \times \boldsymbol{\tau}$$

$$\mathbf{X}(s,t) = \mathbf{X}(0,t) + \int_0^s ds'\,\boldsymbol{\tau}\left(ds',\ t\right)$$

- Does it make sense to talk about (hydro)**dynamics** a Brownian (continuum) **curve**?
- Does the **Brownian stress** of a fiber converge in the continuum limit? (bending energy does not)
- How many modes do we need to track for a given ratio l_p/L?

Brownian multiblob chains

For **Brownian blob-link chains** there are no mathematical issues so start there!



Fast constrained BD-HI for blob-link chains based on rotating unit link vectors including Brownian stress (Brennan Sprinkle)

"Continuum" midpoint scheme

1. Generate a **random rotation** of the tangent vectors

$$\widetilde{\boldsymbol{\Omega}} = \tau^n \times \partial_s \left(\sqrt{\frac{2k_B T}{\Delta t}} (\mathcal{M}^n)^{1/2} \mathcal{W}^n \right)$$

where $\mathcal{W}^n(s)$ is white noise in space only.

2. Rotate the tangent vectors to the **midpoint in time**,

$$\boldsymbol{\tau}^{n+1/2,*} = \exp\left(\frac{\Delta t}{2} \left[\widetilde{\boldsymbol{\Omega}} \right]_\times \right) \boldsymbol{\tau}^n.$$

3. [compute **"divergence of mobility"** $\widetilde{\boldsymbol{\Psi}}$; subtle and omitted]

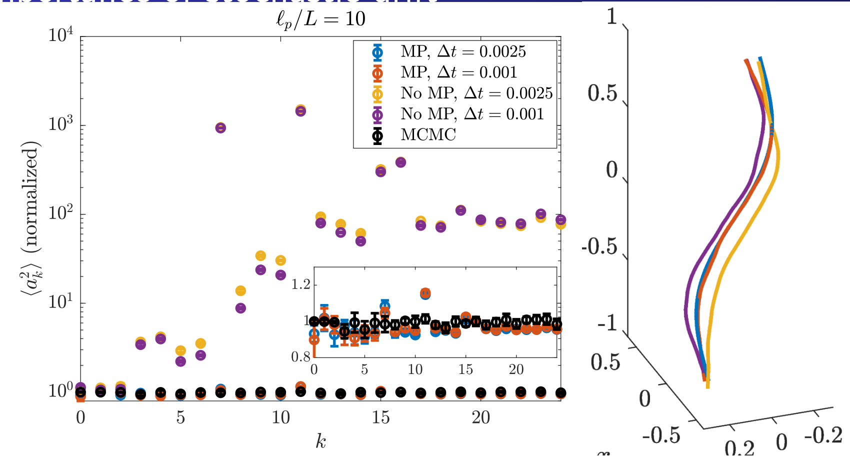
4. Solve the saddle-point system

$$\begin{bmatrix} \mathcal{M} & -\mathcal{K} \\ -\mathcal{K}^\star & \mathbf{0} \end{bmatrix}^{n+1/2,*} \begin{bmatrix} \boldsymbol{\lambda} \\ \boldsymbol{\Omega} \end{bmatrix} = \begin{bmatrix} \kappa_b \mathcal{M}^{n+1/2,*} \mathbf{X}_{ssss}^{n+1,\star} - \sqrt{\frac{2k_B T}{\Delta t}} (\mathcal{M}^n)^{1/2} \mathcal{W}^n - (k_B T)\, \widetilde{\boldsymbol{\Psi}} \\ \mathbf{0} \end{bmatrix}.$$

5. **Rotate** the tangent vectors:

$$\boldsymbol{\tau}^{n+1} = \exp\left(\frac{\Delta t}{2} \left[\boldsymbol{\Omega} \right]_\times \right) \boldsymbol{\tau}^n.$$

Importance of stochastic drift

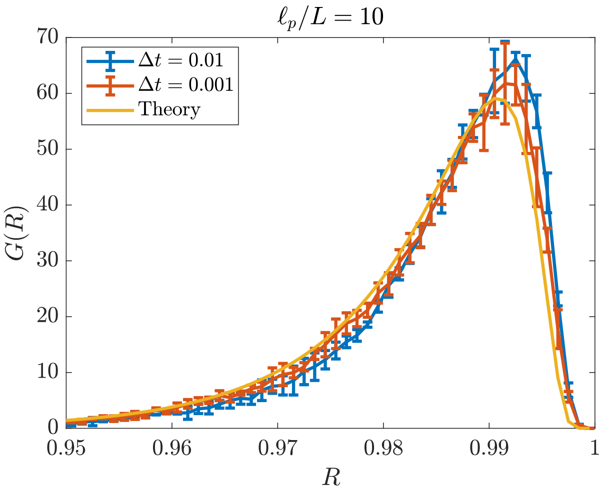


Normalized amplitudes of linear modes at *equilibrium* for

$$E = \frac{\kappa_b}{2} \int ds \, \| \mathbf{X}_{ss}(s) \|^2 + \frac{K}{2} \int ds \, \| \mathbf{X}(s) - X_0(s) \|^2$$

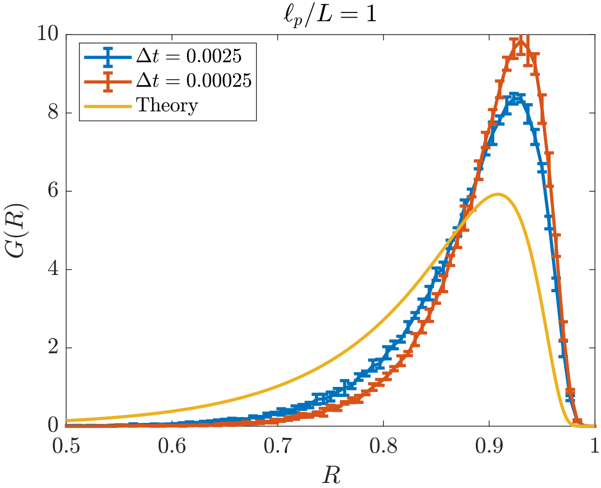
with (correct) and without (wrong!) **midpoint (MP) update**

WIP: end to end distance



Probability distribution of **end-to-end distance**: long persistence length

WIP: end to end distance



Probability distribution of **end-to-end distance**: short persistence length

References

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