Characteristics of pinned polymer loop in external field

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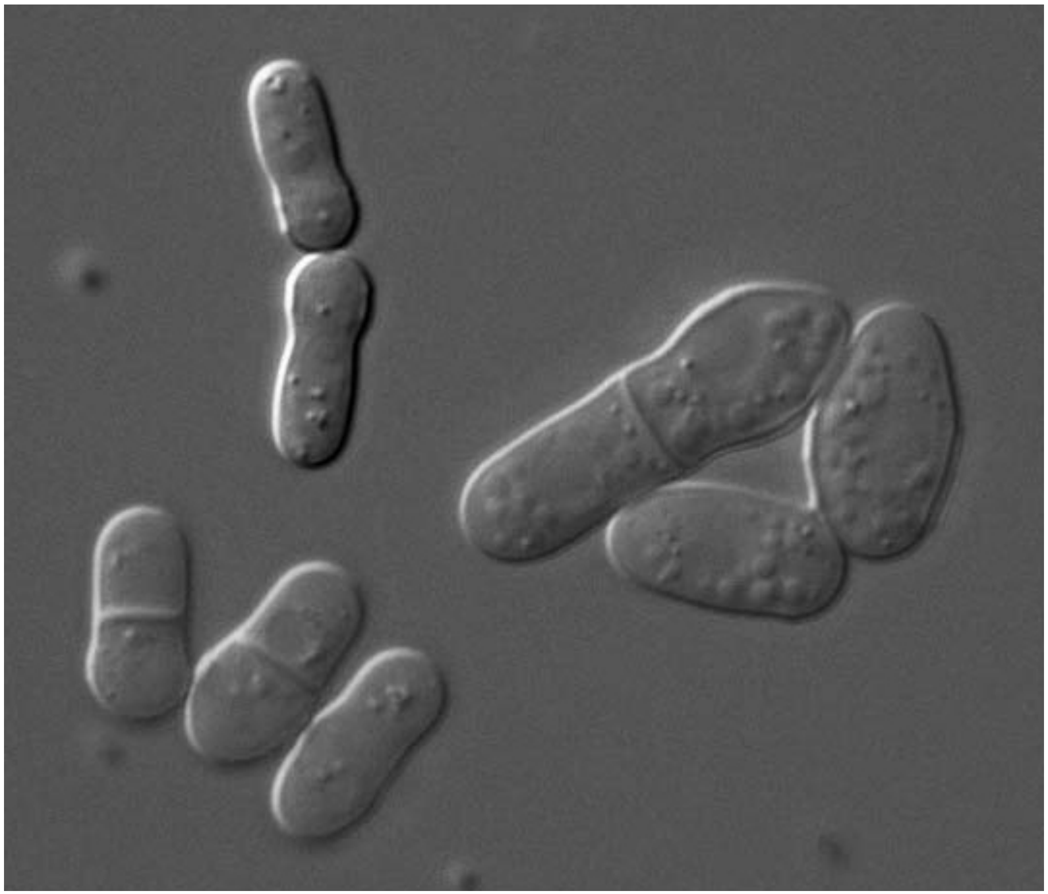
For PhD seminar

Outline

- Background Reminder
- Results
- TODO

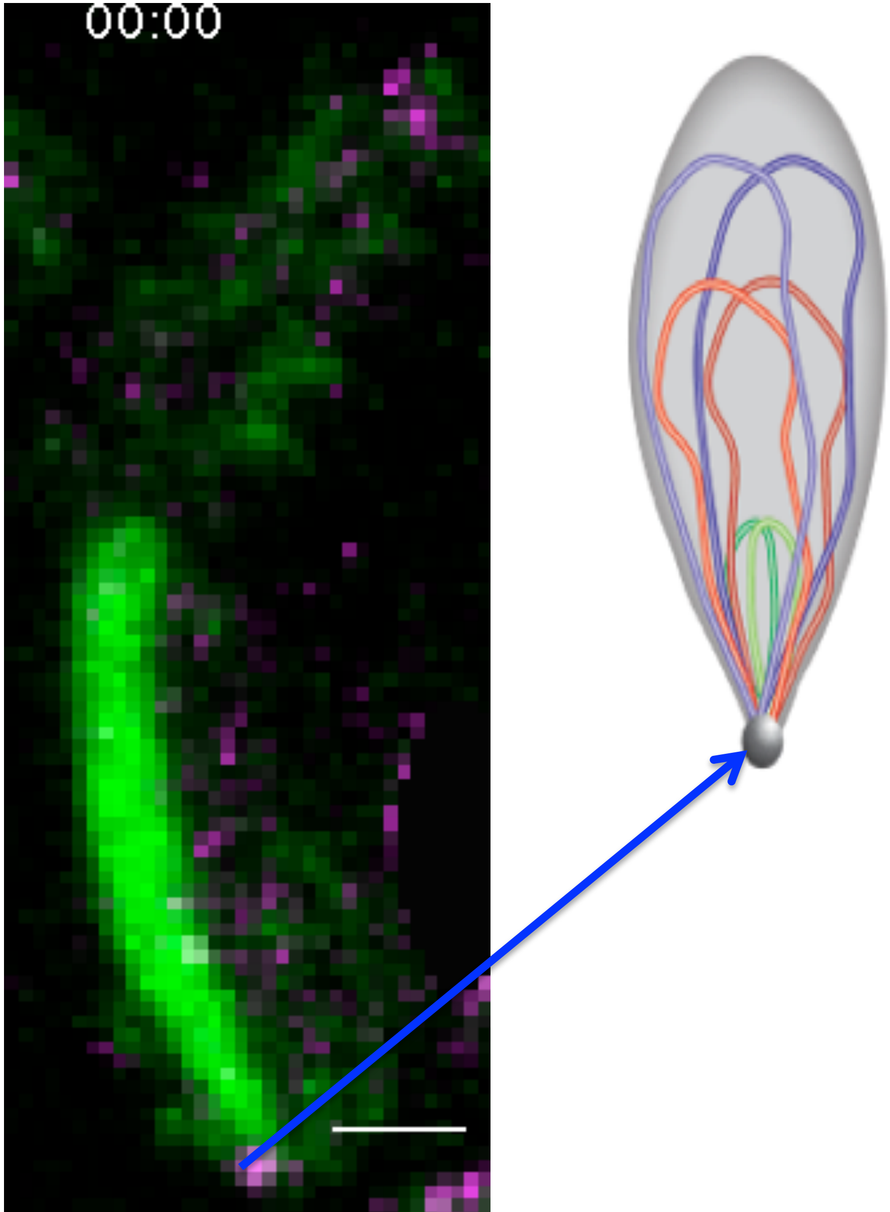
Fission Yeast(*S. pombe)*



Rhind N et al. Science. April 21, 2011

Sketch of fission yeast during cell division

Chromosome Movement (S. *pombe)*



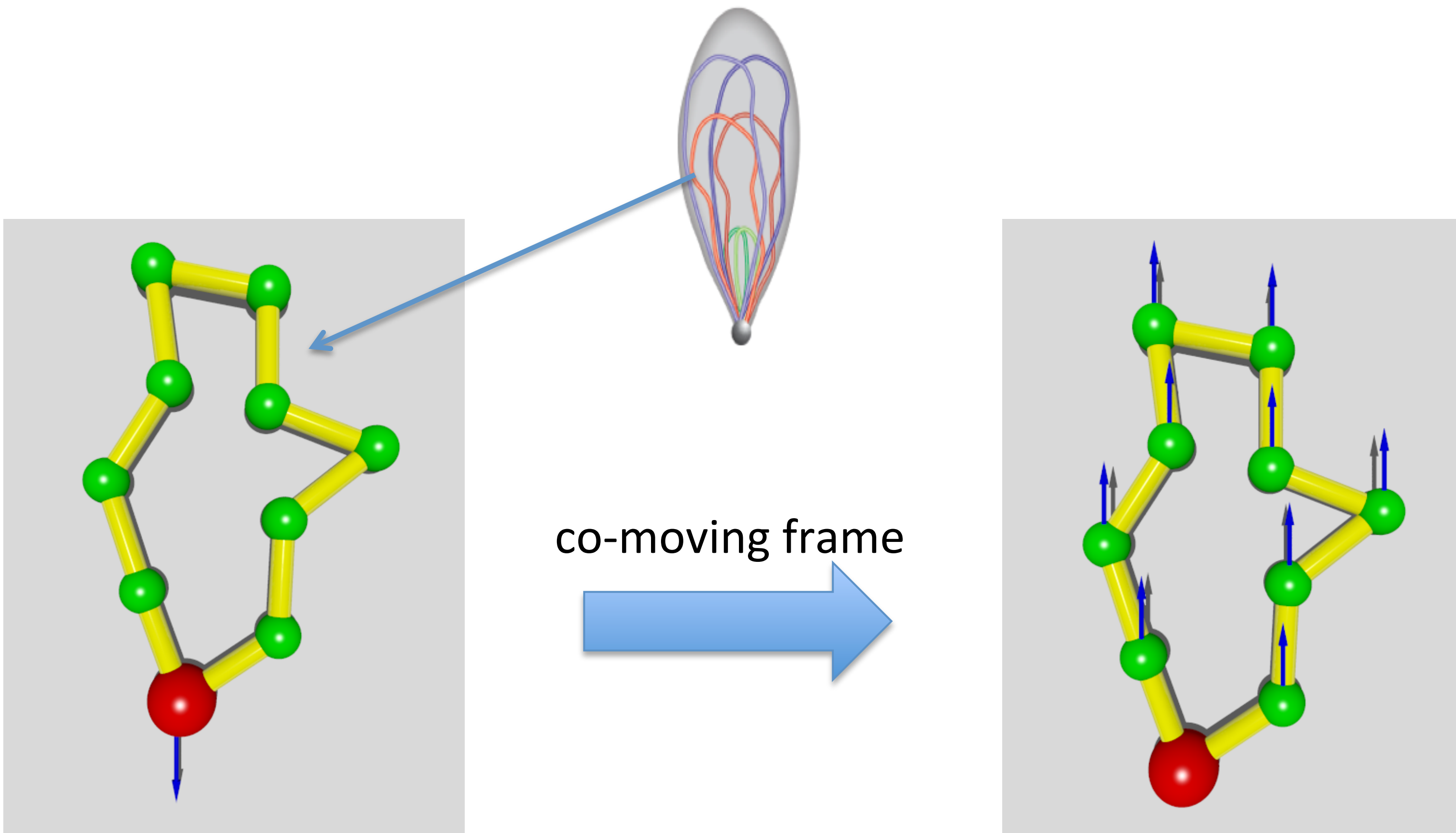
- 3 pairs of chromosomes
- Telomere bond to SPB
- Oscillation is driven by SPB

In the mean time:
Homologous chromosomes paring and recombination

Chikashige et al., Science 1994
Yamamoto et al, JCB 1999
Ding et al., DevCell 2004

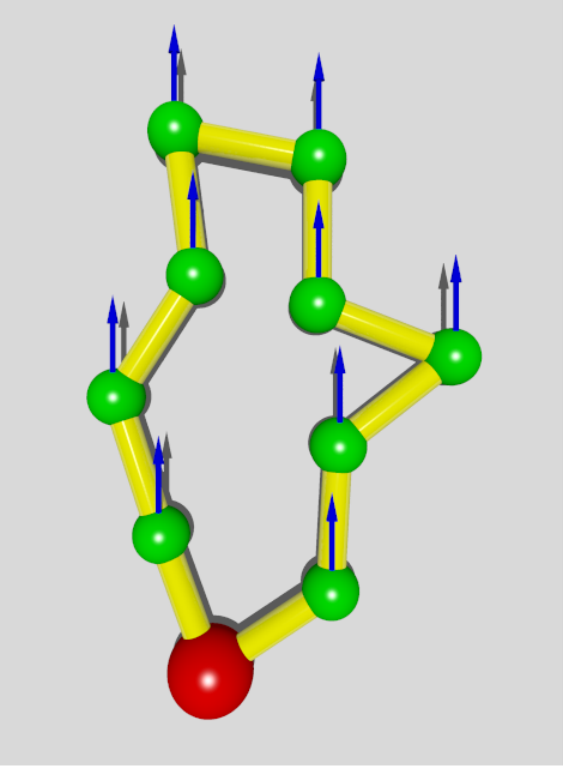
Polymer Ring

- One Chromosome is represented by a polymer ring with the driven bead be the **SPB**(spindle pole body).



Freely Joined Bead-Rod Ring

- Bead:
  position ---- $\mathbf{r}_i$
- Rod:
  length --- a

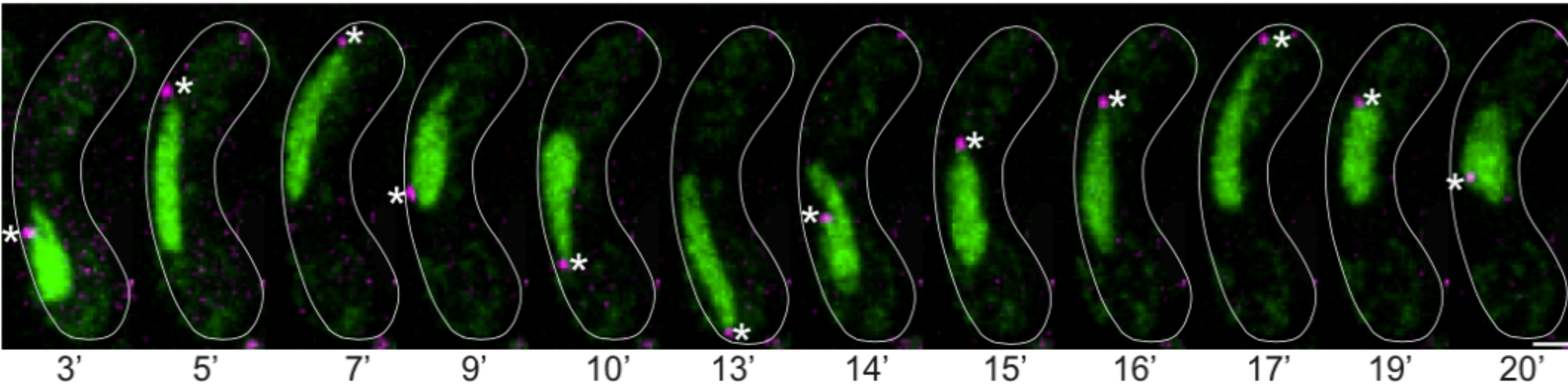


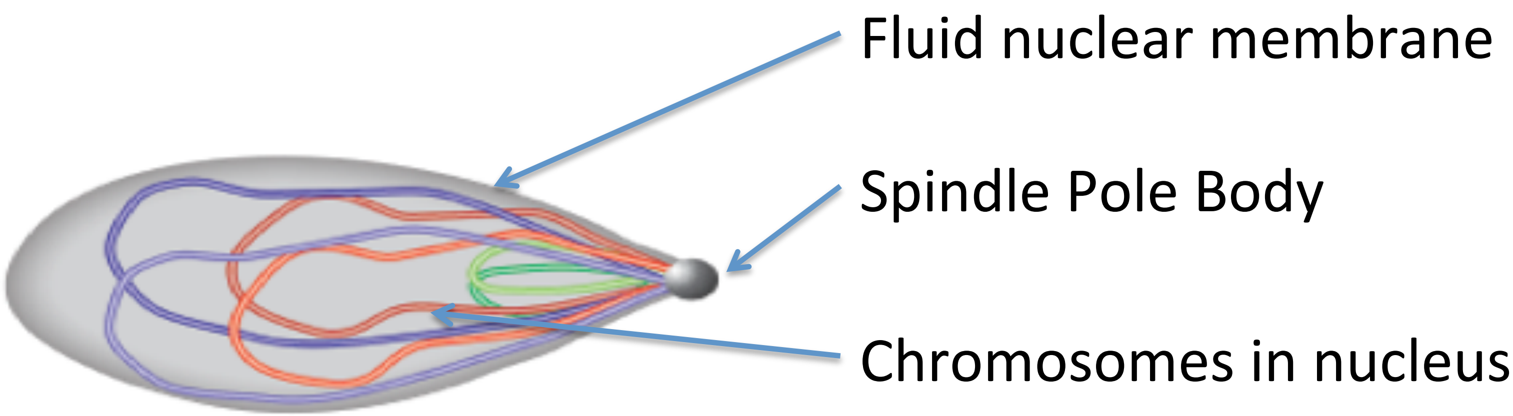
Results we already have:

Mean position: $<\mathbf{r}_i>$

Position Variance: $Var[\mathbf{r}_i]$

Shape of nucleus





Assume the shape of nucleus is determined by chromosomes in it

Characteristic quantities

- Gyration radius: $$R_g^2 = \left\langle \frac{1}{N} \sum_{i=1}^{N} (\mathbf{r}_i - \mathbf{r}_{CM})^2 \right\rangle$$
- Gyration tensor: $$Q_{xy} = \frac{1}{N} \sum_{i=1}^{N} \mathbf{r}_x^i \mathbf{r}_y^i$$

$$Q = \begin{bmatrix} Q_{xx} & Q_{xy} & Q_{xz} \\ Q_{yx} & Q_{yy} & Q_{yz} \\ Q_{zx} & Q_{zy} & Q_{zz} \end{bmatrix} = \begin{bmatrix} \lambda_x^2 & 0 & 0 \\ 0 & \lambda_y^2 & 0 \\ 0 & 0 & \lambda_z^2 \end{bmatrix}$$

$$\lambda_x^2 \leq \lambda_y^2 \leq \lambda_z^2$$

Asphericity

$$b = \lambda_z^2 - \frac{1}{2}(\lambda_x^2 + \lambda_y^2)$$

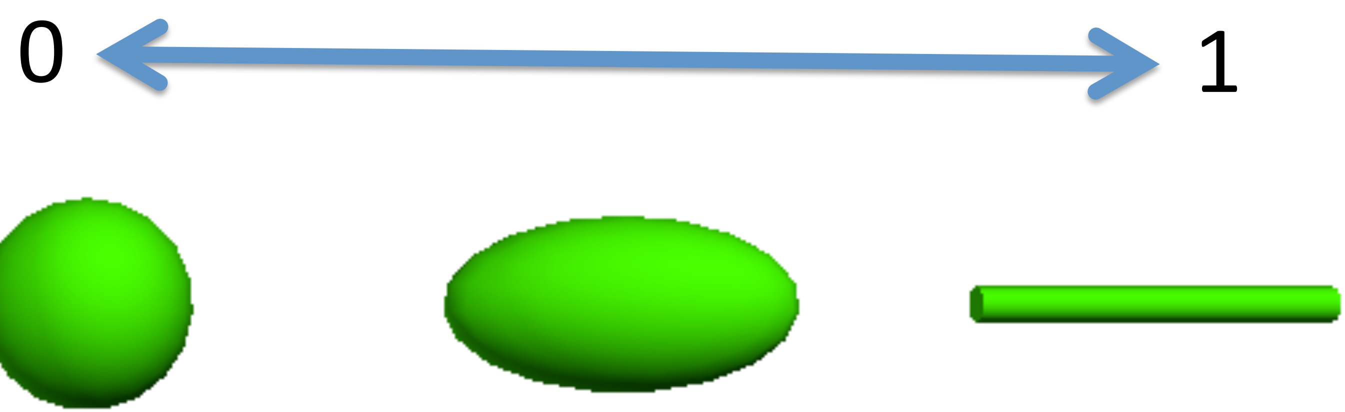
Acylindricity

$$c = \lambda_y^2 - \lambda_x^2$$

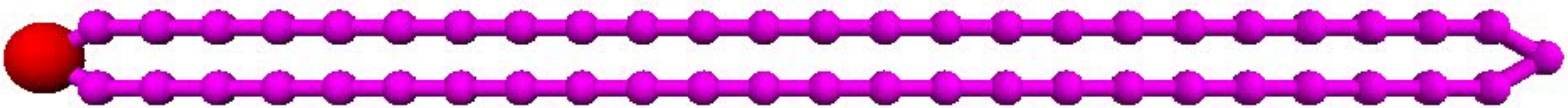
Relative shape anisotropy

$$\kappa^2 = \frac{3}{2}\frac{\lambda_x^4 + \lambda_y^4 + \lambda_z^4}{(\lambda_x^2 + \lambda_y^2 + \lambda_z^2)^2} - \frac{1}{2}$$

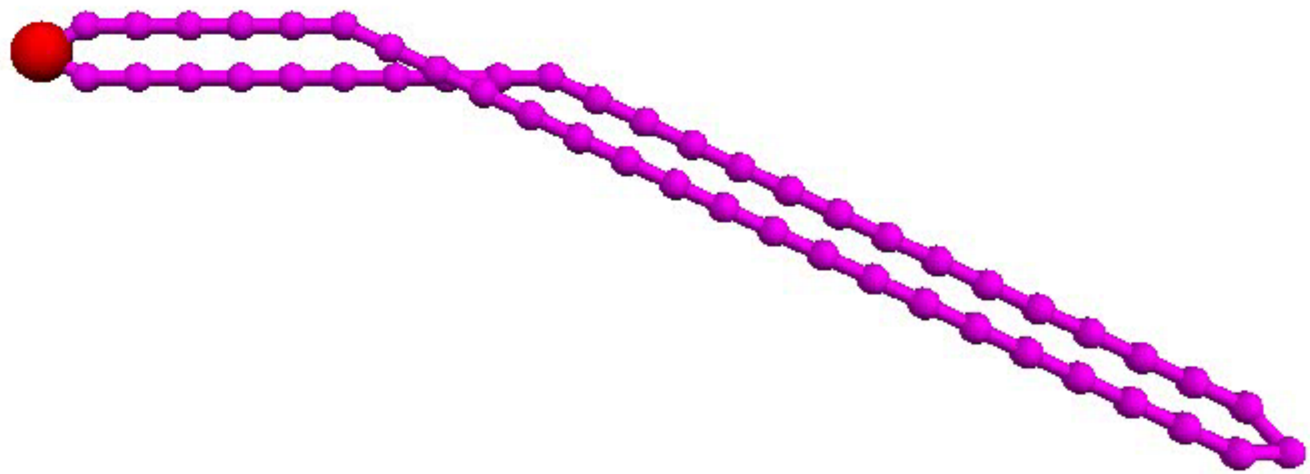
$$0 \leq \kappa \leq 1$$



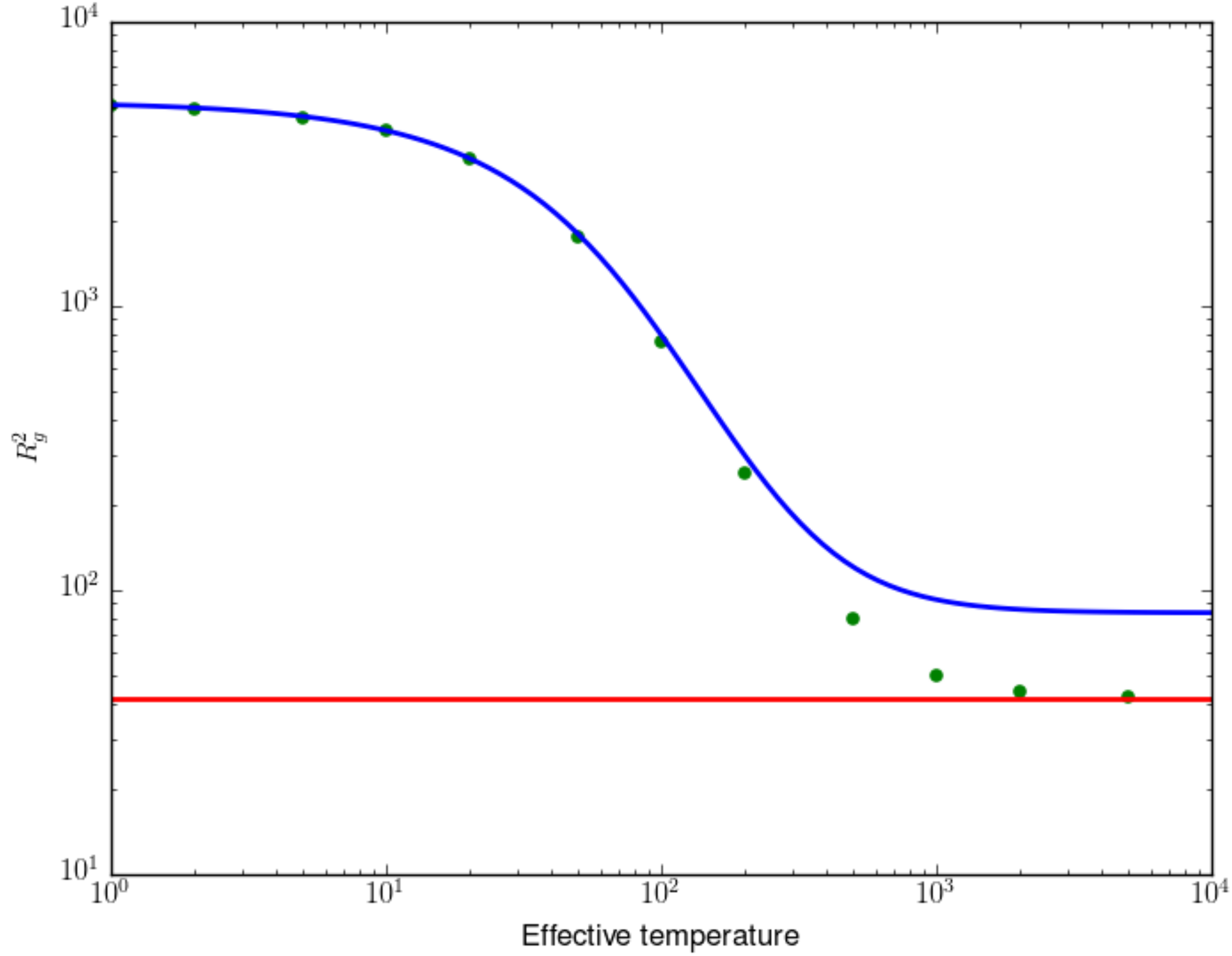
Results (T = 1, N =50)



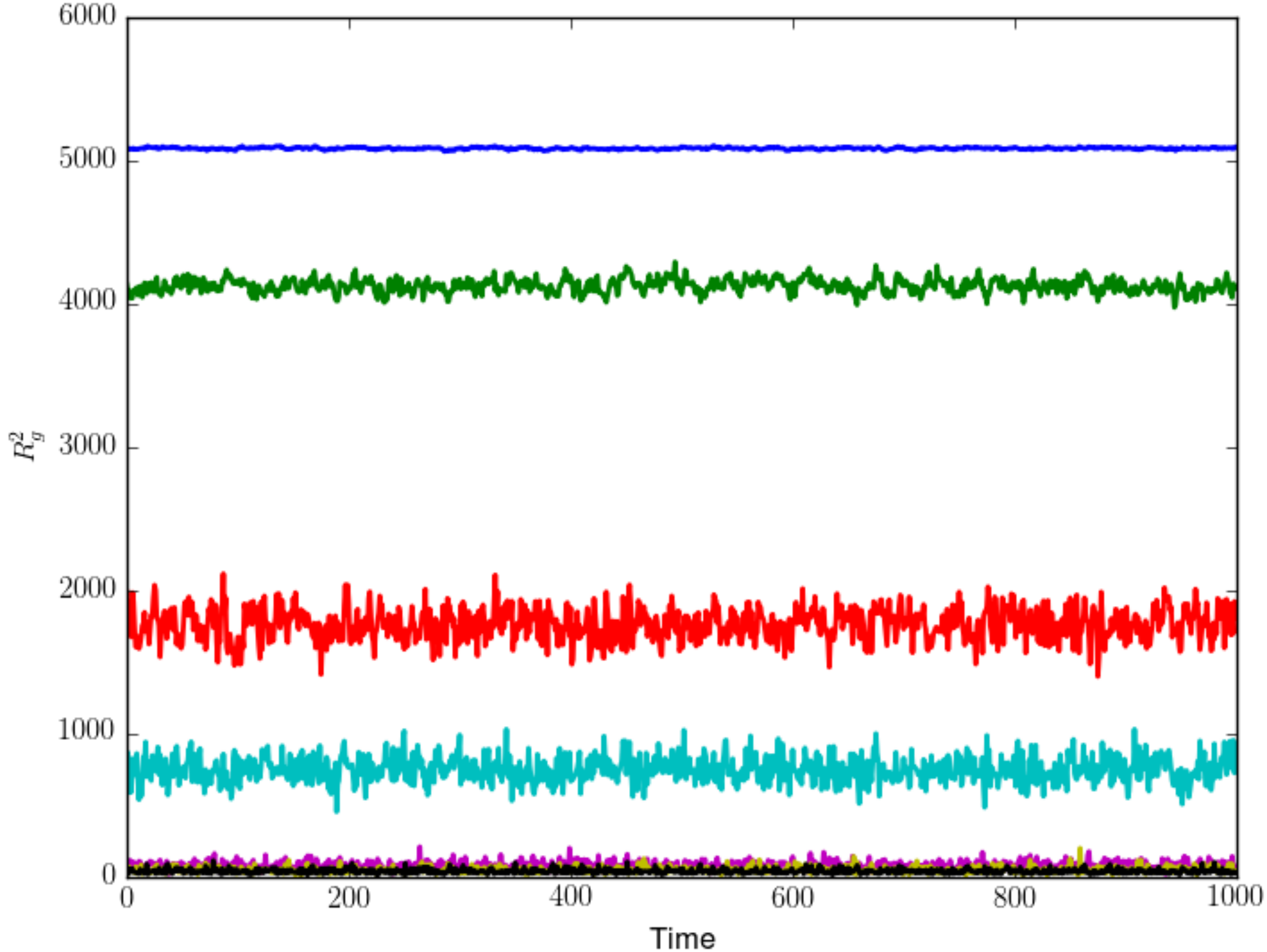
Results (T=10000, N =50)



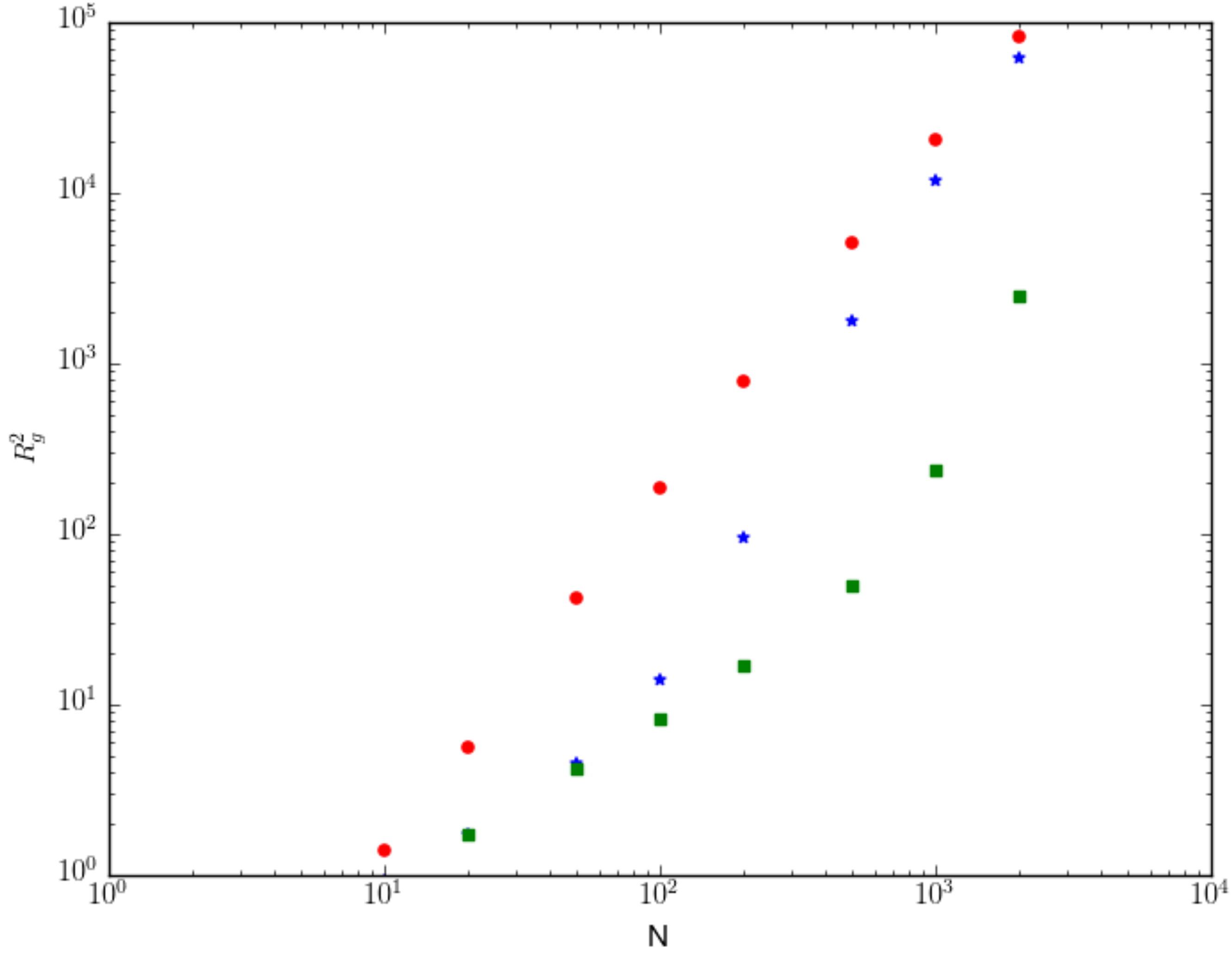
Results (N=500)



Results (N=500)



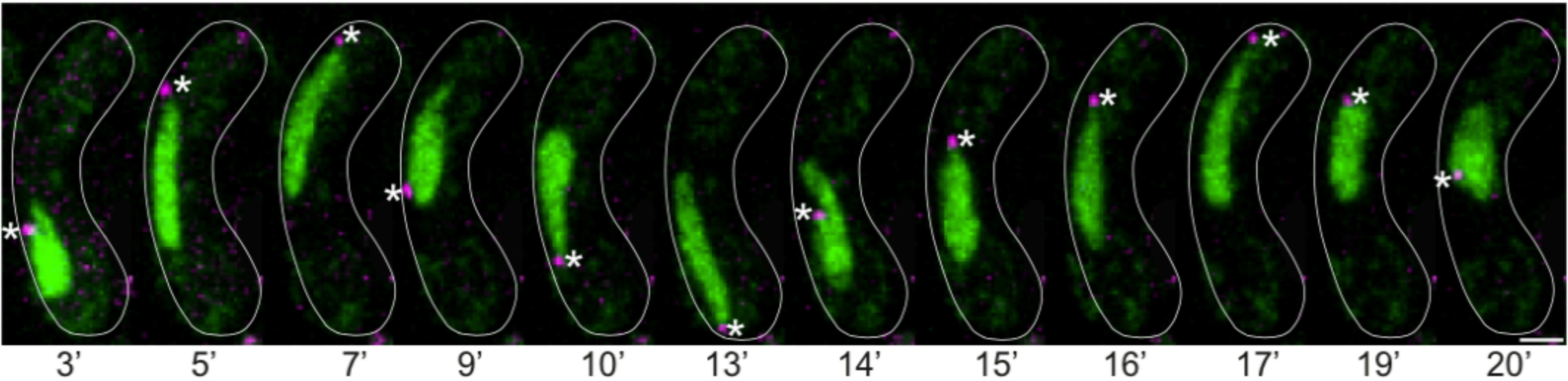
Results (r: T=1, b: T=50, g: T=1000)



TODO

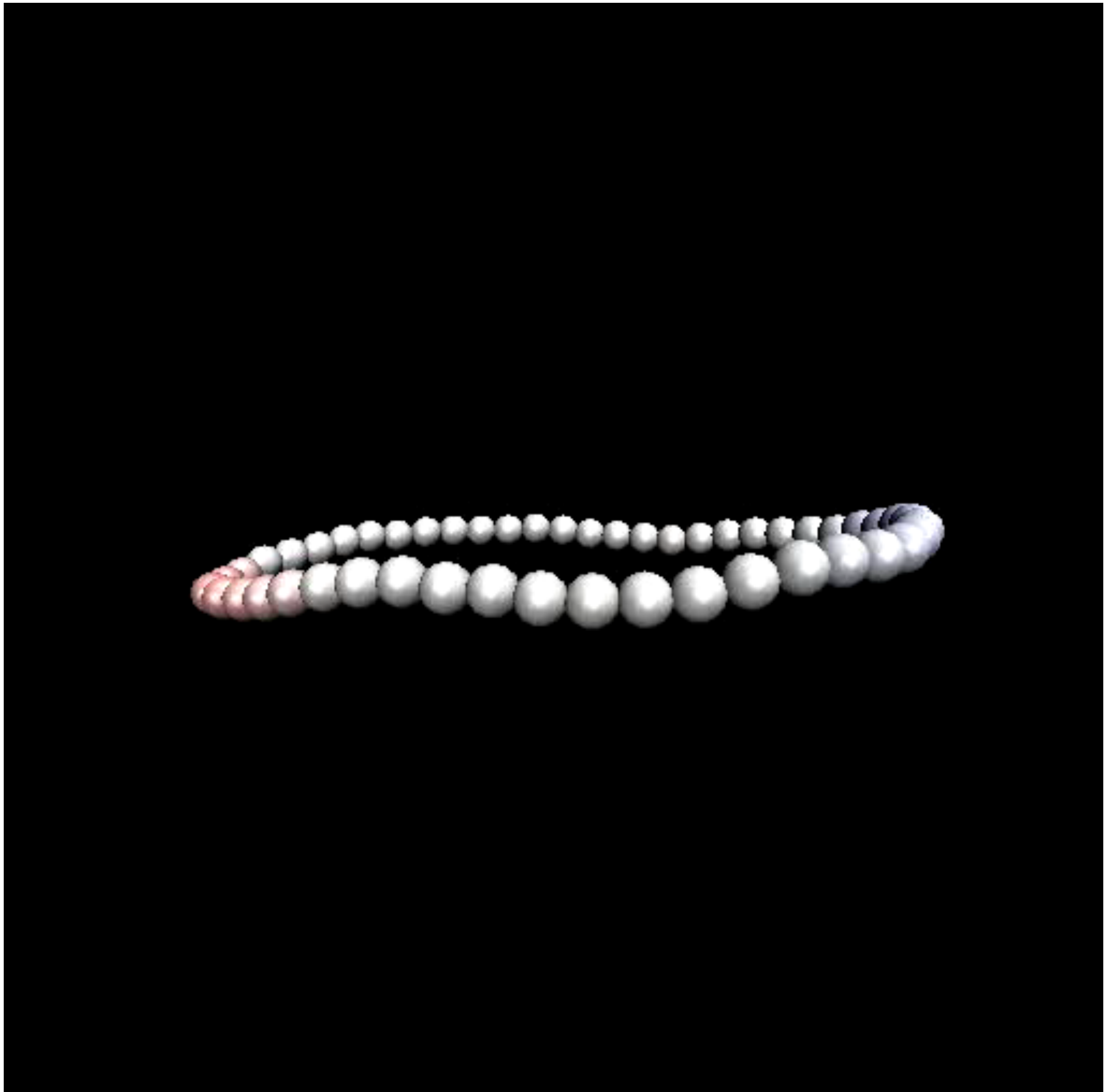
- Gyration tensor: both numerically and analytically
- Multiple polymer rings ---- Lennard-Jones interaction?
- Shape at turning point → Tumbling dynamics

?



Tumbling dynamics

Philipp S. Lang etal. Phys. Rev. E 89, 022606 (2014)



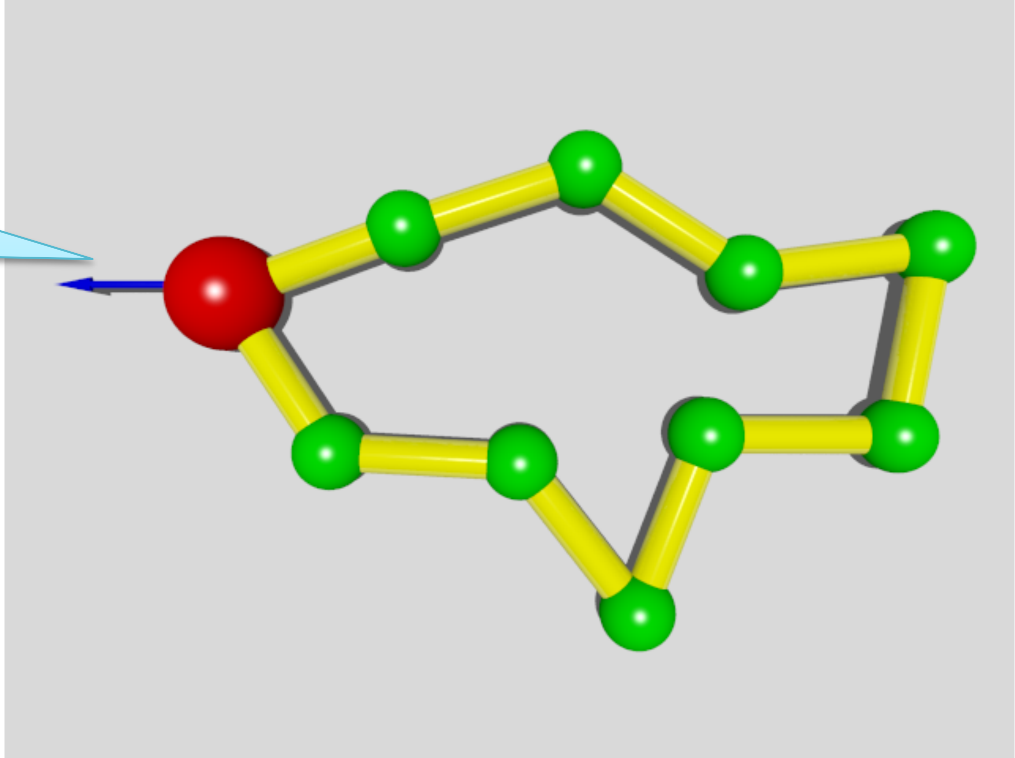
All suggestions and comments are greatly appreciated!

Thank you!

Bead-Rod Ring Model

A Chromosome is represented by a bead-rod ring with the driven bead be the **SPB**(spindle pole body).

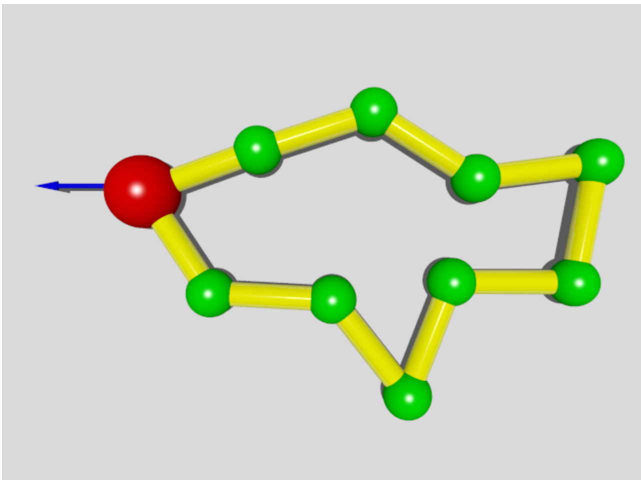
Ring driven by a Constant force

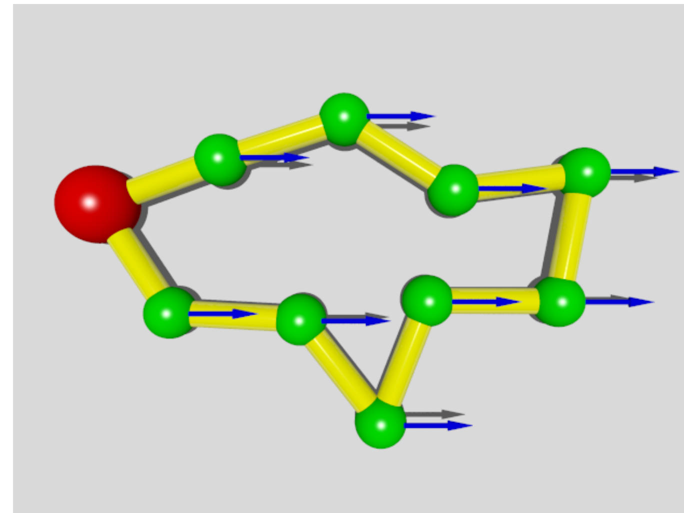


- Bead:
  position ---- $\mathbf{r}_i$
- Rod:
  length --- a

Theory for 1D model

Transfer to co-moving frame:





Constant driven force on SPB

Constant force field and pinned SPB

For 1D system: $\Delta x_j \in \{-1,+1\} \xrightarrow{n_j=(\Delta x_j+1)/2} n_j \in \{0,1\}$

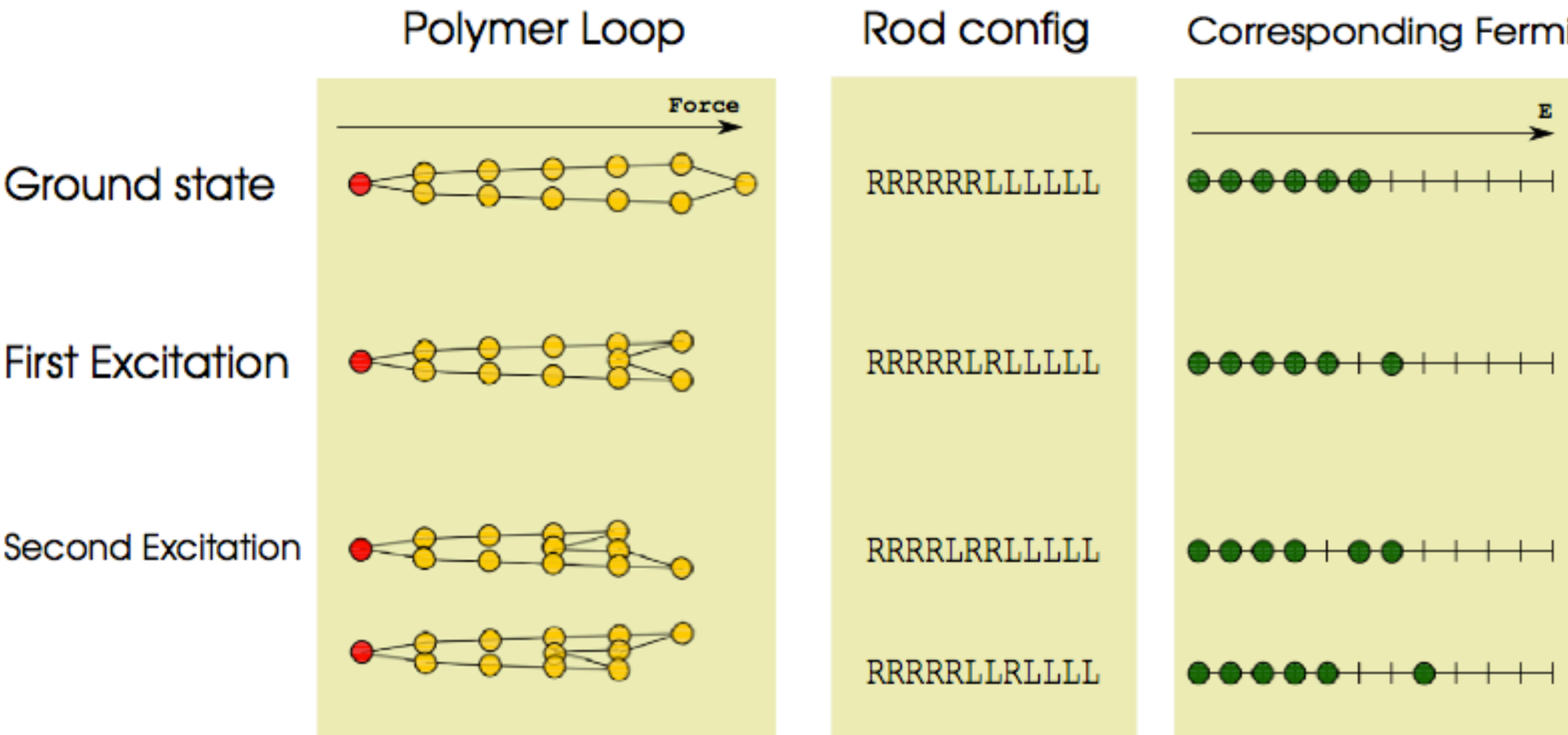
$$H = E_0 - V_0 \sum_{j=1}^{N} j\Delta x_j \xrightarrow{z_j=(\Delta x_j+1)/2} H = E_0^{'} - 2V_0 \sum_{j=1}^{N} jn_j$$

Loop Constraint: $\sum_{j=1}^{N} \Delta x_j = 0 \rightarrow \sum_{j=1}^{N} n_j = \frac{N}{2}$

Theory for 1D model

Hamiltonian: $$H = E_0^{'} - 2V_0 \sum_{j=1}^{N} j n_j$$

$n_j \in \{0,1\}$ ⇨ Equivalent to N/2 Fermions in N energy levels



Theory for 1D model

- Partition function $$\mathrm{P} \propto \exp\left[-\frac{1}{T_{eff}}\sum_{j=1}^{N} j n_j\right]$$

By setting natural temperature unit $2V_0 / k_B \equiv 1$

- Fermi-Dirac distribution

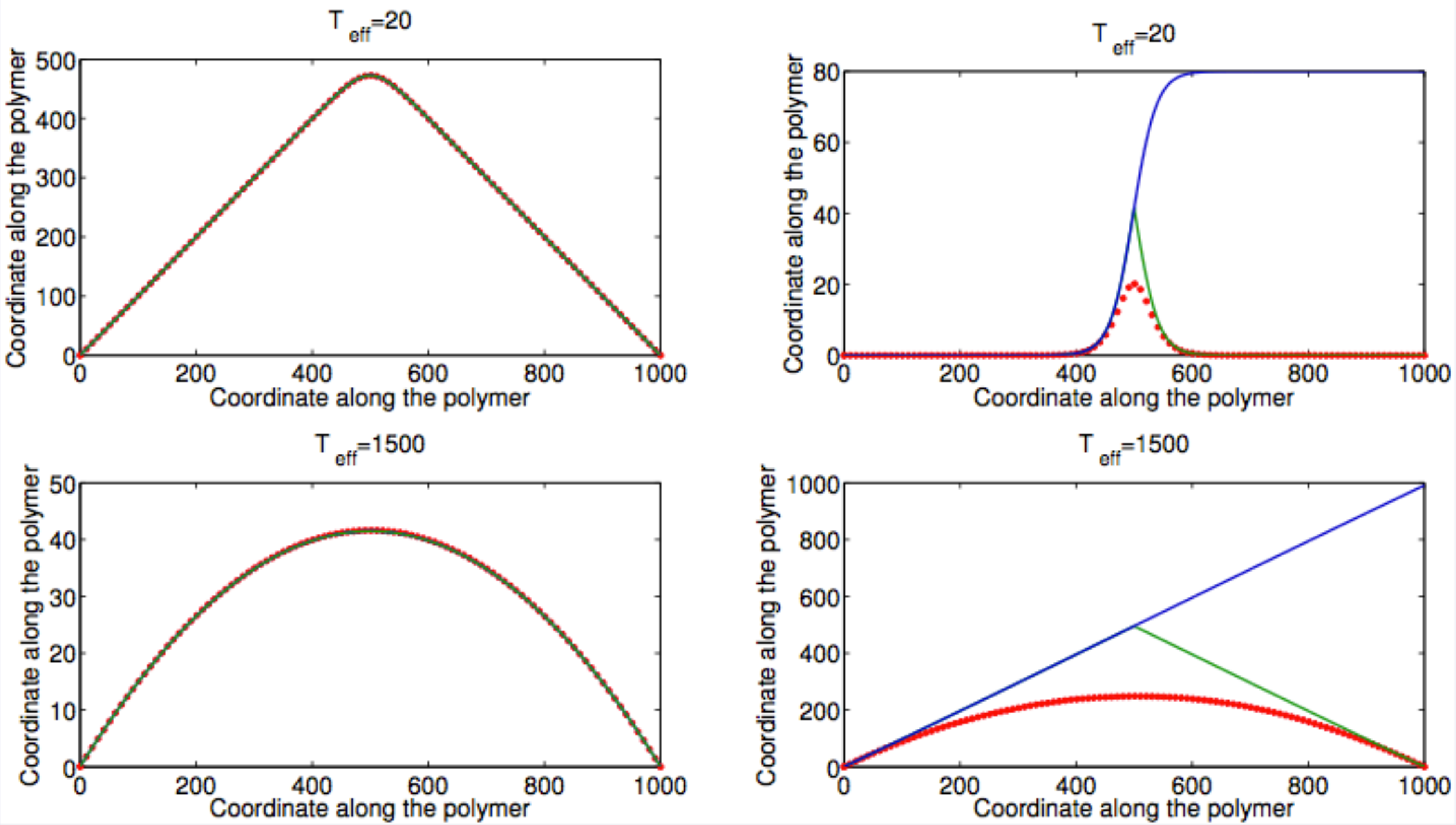
$$\mathrm{P}\{n_j = 1\} = \frac{1}{1 + e^{j - \frac{N}{2}}}$$

- Statistical Results

$$\left\langle x_i \right\rangle = \sum_{j=1}^{i} \left\langle \Delta x_j \right\rangle = 2\sum_{j=1}^{i} \left\langle n_j \right\rangle - i = 2T_{eff} \ln \frac{1 + e^{N/2T_{eff}}}{e^{i/2T_{eff}} + e^{(N-i)/2T_{eff}}}$$

$$\mathrm{var}[x_i] = 4\sum_{j=1}^{N} \mathrm{var}[n_j]$$

1D Theory



T_{eff}=20
Coordinate along the polymer
Coordinate along the polymer
T_{eff}=20
Coordinate along the polymer
Coordinate along the polymer
T_{eff}=1500
Coordinate along the polymer
Coordinate along the polymer
T_{eff}=1500
Coordinate along the polymer
Coordinate along the polymer

Brownian Bridge Approach

--- devise an effective stochastic process satisfies $Z_N = Z_0$

Step 1: construct effective process:

- $Z_0 = 0$;
- Z_l is almost surely continuous;
- Z_l has independent increments;
- $Z_n - Z_m = \mathrm{N}(\bar{z}_{m\to n}, \bar{\sigma}^2_{m\to n})$

Where the mean and the variance is determined by:

$$\mathbb{E}[z_p - z_q] = \sum_{j=p+1}^{q} \mathbb{P}\{r_i = 1\} - \cdot\mathbb{P}\{r_i = -1\}$$
$$= \sum_{j=p+1}^{q} \left[\frac{2}{1+e^{\frac{j-\mu}{k_B T}}} - 1\right],$$
$$\mathrm{var}[z_p - z_q] = 4\sum_{j=m+1}^{n} \mathrm{var}[r_i]$$
$$= 4\sum_{j=p+1}^{q} \frac{e^{\frac{j-\mu}{k_B T}}}{\left(1+e^{\frac{j-\mu}{k_B T}}\right)^2}.$$

$$\bar{z}_{m\to n} := k_B T \int_m^n \left[\frac{2}{1+e^{\zeta - \frac{N}{2k_B T}}} - 1\right] d\zeta$$

$$\bar{\sigma}^2_{m\to n;z} = 4k_B T \int_m^n \frac{e^{\zeta - \frac{N}{2k_B T}}}{\left(1+e^{\zeta - \frac{N}{2k_B T}}\right)^2} d\xi$$

Brownian Bridge Approach

--- devise an effective stochastic process satisfies $Z_N = Z_0$

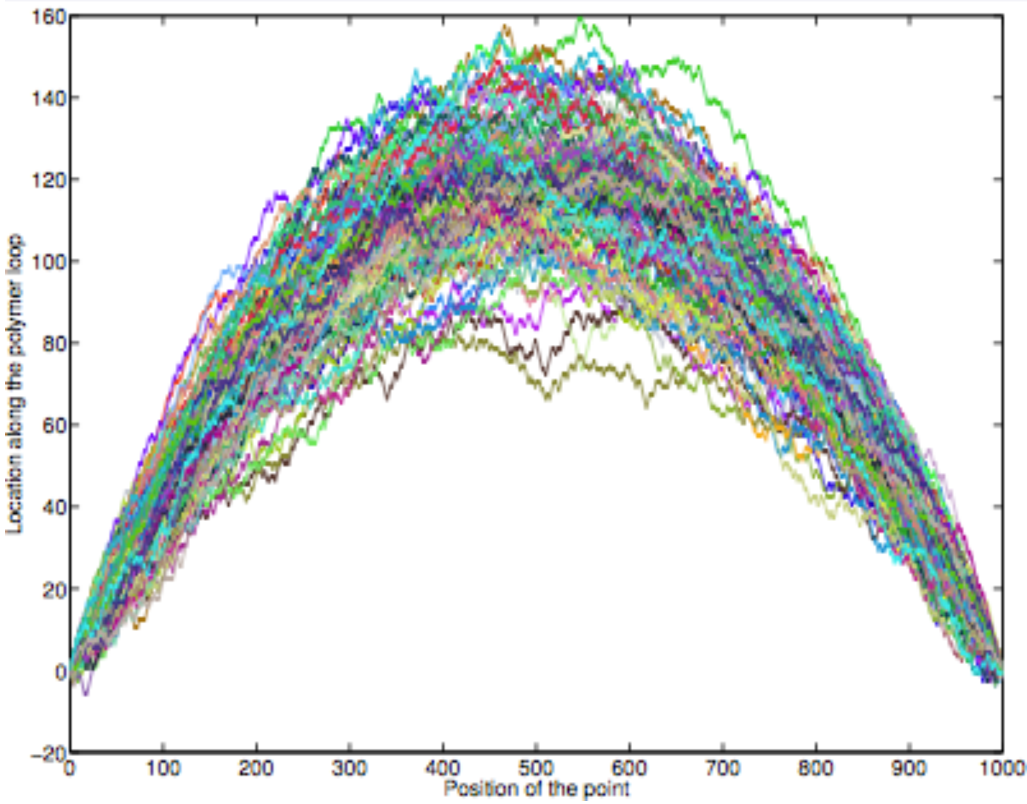
Step 2: introduce loop condition

Construct conditional process:

$$Z_l^0 = (Z_l \mid Z_l = 0), l \in (0, N)$$

where

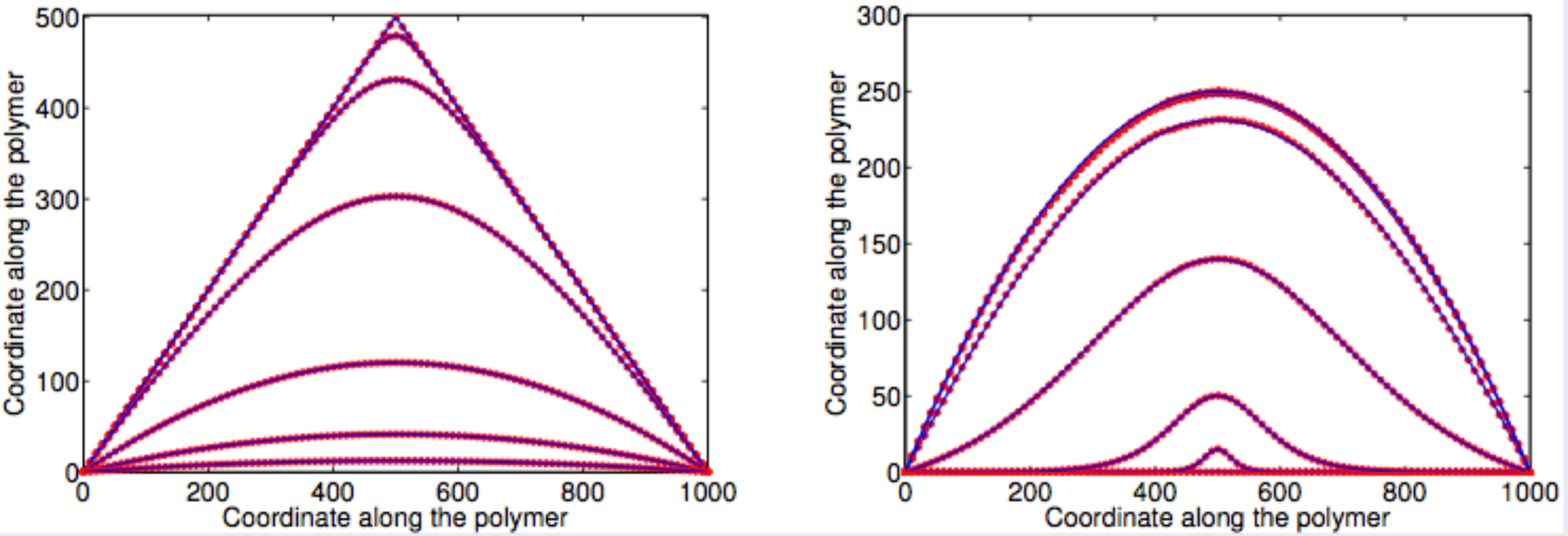
$$Z_l^0 = Z_l - \frac{\bar{\sigma}^2_{0\to l;z}}{\bar{\sigma}^2_{0\to N;z}} Z_N$$



Numerical Verification of 1D model

Our analysis yields the following conclusion:

$$\mathbb{E}\left[x_i\right] = 2T_{\text{eff}} \ln \frac{1 + e^{N/T_{\text{eff}}}}{e^{i/2T_{\text{eff}}} + e^{(N-i)/2T_{\text{eff}}}}, \quad \text{var}\left[x_i\right] = \frac{\sigma_{0i}^2 \sigma_{iN}^2}{\sigma_{0N}^2}$$



3D Continuous Model

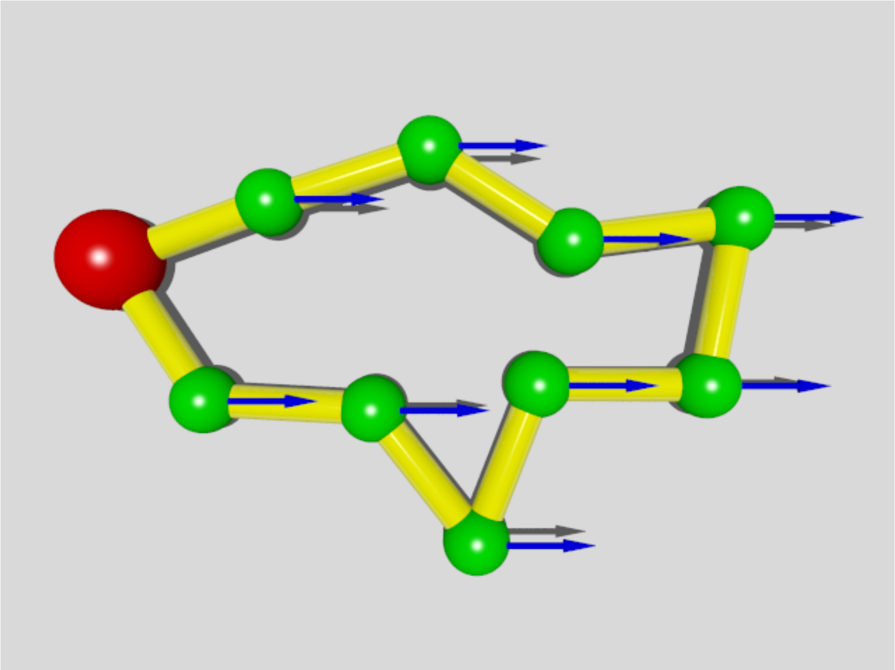
- Hamiltonian

$$H = E_0 - V_0 \sum_{i=1}^{N} \sum_{j=1}^{i} \cos\theta_j$$

Heisenberg model

- Partition function

$$\begin{aligned}\mathcal{P}_C &= \prod_{j=1}^{N} \mathcal{P}_j \\ &= \prod_{j=1}^{N} \int_0^{2\pi} d\phi_j \int_0^{\pi} \sin\theta_j \; d\theta_j e^{-\frac{-(j-\mu)\cos\theta_j}{k_B T}} \\ &= \frac{4\pi k_B T \sinh\frac{\mu-j}{k_B T}}{\mu - j}\end{aligned}$$



$$\boxed{\begin{aligned}\mathbb{E}\left[\cos\theta_j\right] &= k_B T \partial_\mu \mathcal{P}_j \\ &= \coth\frac{\mu-j}{k_B T} - \frac{k_B T}{\mu - j}, \\ \mathrm{var}\left[\cos\theta_j\right] &= \left(k_B T \partial_\mu\right)^2 \mathcal{P}_j \\ &= \left(\frac{k_B T}{\mu-j}\right)^2 - \mathrm{csch}^2\frac{\mu-j}{k_B T}.\end{aligned}}$$

Adopt Brownian Bridge Approach

Define Effective 3D stochastic process:

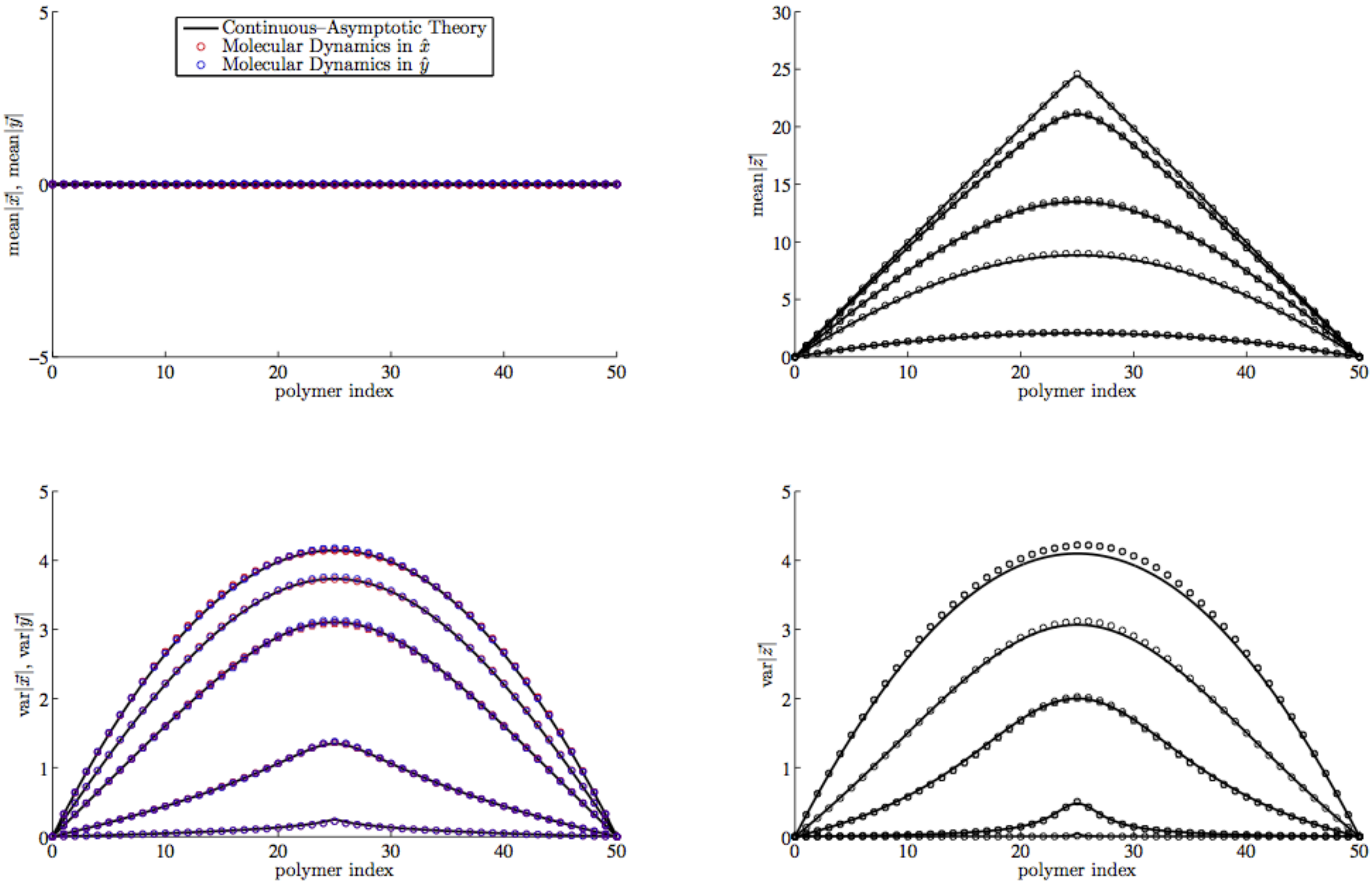
- $W_0 = 0,$
- W_l is almost surely continuous,
- W_l has independent increments,
- $W_n - W_m \sim \mathcal{N}\left(\bar{w}_{m\to n}, \bar{\sigma}^2_{m\to n;w}\right), 0 < n \leq m < N,$

$$\bar{x}_{m\to n} = 0,$$
$$\bar{y}_{m\to n} = 0,$$
$$\bar{x}_{m\to n} = k_B T \left[\log \frac{l - \frac{N}{2}}{k_B T \sinh\left(\frac{l - \frac{N}{2}}{k_B T}\right)}\right]_{l=m}^{n}$$

$$\bar{\sigma}^2_{m\to n;x} = k_B T \int_m^n \mathrm{var}\left[\vec{s}_{k_B T \zeta}\right] \cdot \hat{x}\, d\zeta,$$
$$\bar{\sigma}^2_{m\to n;y} = k_B T \int_m^n \mathrm{var}\left[\vec{s}_{k_B T \zeta}\right] \cdot \hat{y}\, d\zeta,$$
$$\bar{\sigma}^2_{m\to n;z} = k_B T \left[\coth \frac{l - \frac{N}{2}}{k_B T} - \frac{1}{l - \frac{N}{2}}\right]_{l=m}^{n}$$

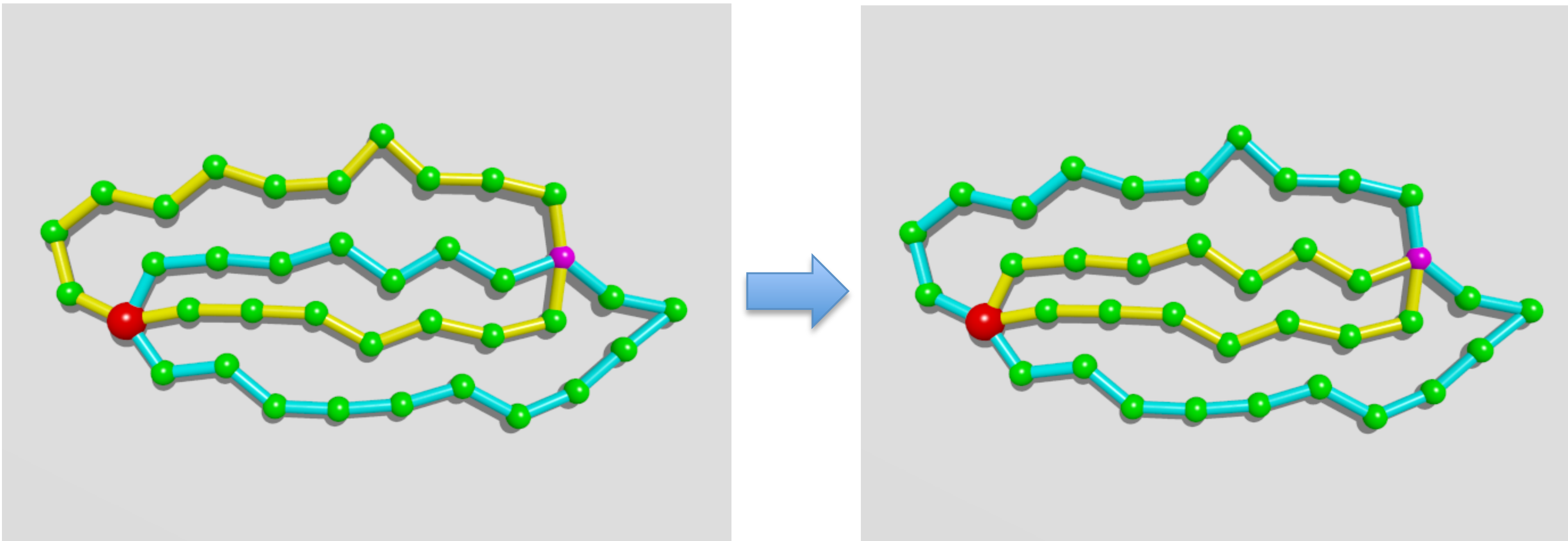
Conditional effective process: $W_l^0 = (W_l \mid W_l = 0), l \in (0, N)$

Numerical Verification of 3D model



A Pair of Rings with Centromere

- Re-label the loops



- Brownian Bridge

$$\bar{w}_{m\to n,\mathcal{C}_1} := \bar{w}_{0\to n,\mathcal{C}_1} - \bar{w}_{0\to m,\mathcal{C}_1}$$

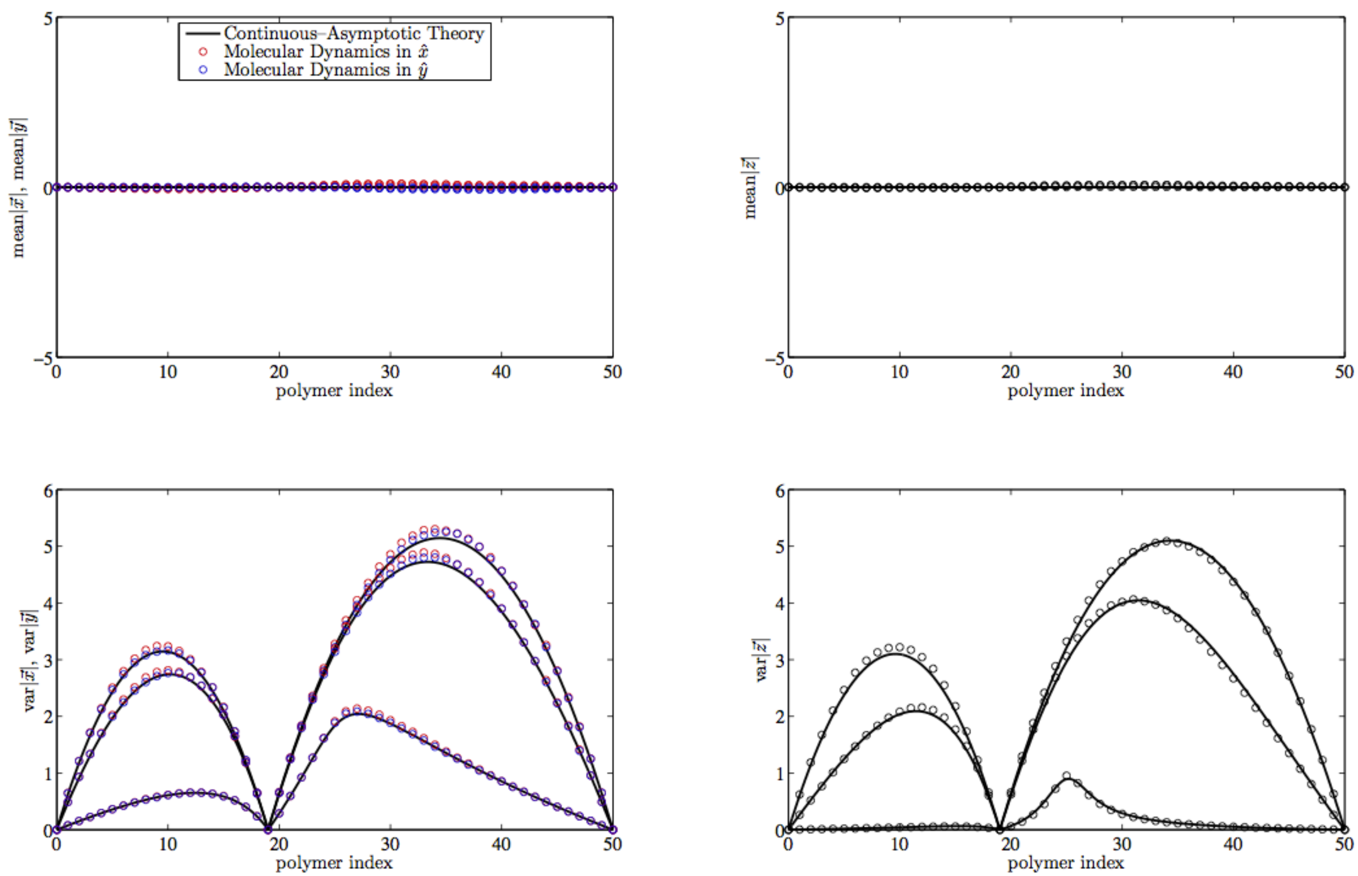
- $W_{0;\mathcal{C}_1} = 0,$

Bridge Condition: $$W^0_{l;\mathcal{C}_1} \equiv W_{l;\mathcal{C}_1} - \frac{\bar{\sigma}^2_{0\to l;w,\mathcal{C}_1}}{\bar{\sigma}^2_{0\to N;w,\mathcal{C}_1}} W_{N;\mathcal{C}_1}$$

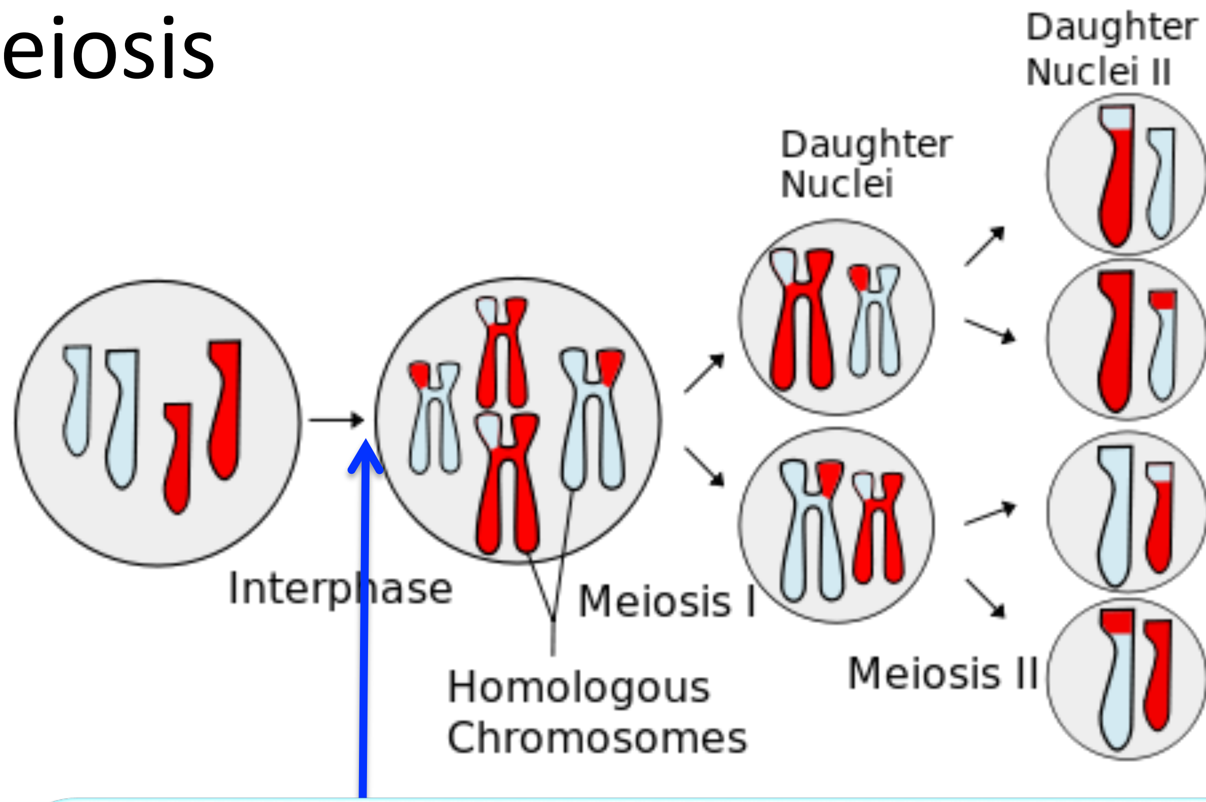
Numerical Verification

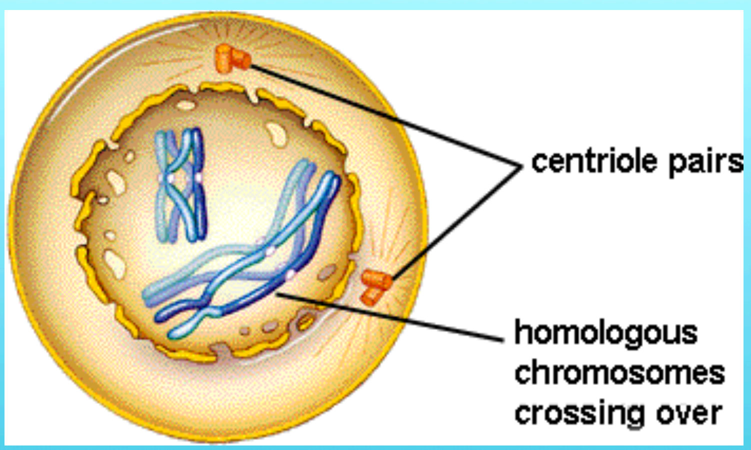
- Theoretical Result

$$\operatorname{var}\left[W^0_{\mu;\mathcal{C}_1} - W^0_{\mu';\mathcal{C}_1}\right] = \mathbb{E}\left[\left(W^0_{\mu;\mathcal{C}_1} - W^0_{\mu';\mathcal{C}_1}\right)^2\right] = \frac{2\bar{\sigma}^2_{0\to\mu;w}\bar{\sigma}^2_{\mu\to\lambda;w}}{\bar{\sigma}^2_{0\to\lambda;w}}$$



Meiosis





Prophase I

- Chromosome movements
- Pairing
- Recombination

Brownian Dynamics:

Inertia-less assumption $\mathbf{F}_i = \mathbf{0}$

$$\mathbf{F}_i = \mathbf{F}_i^h + \mathbf{F}_i^\phi + \mathbf{F}_i^c + \mathbf{F}_i^b + \mathbf{F}_i^e$$

i is the index of bead

$\mathbf{F}_i^h$ is hydrodynamic force

$\mathbf{F}_i^\phi$ represents force generate from potential

$\mathbf{F}_i^c$ is constraint force to keep the rod length

$\mathbf{F}_i^b$ is brownian force

$\mathbf{F}_i^e$ is external force

Brownian Dynamics:

$$\mathbf{F}_i = \mathbf{F}_i^h + \mathbf{F}_i^\phi + \mathbf{F}_i^c + \mathbf{F}_i^b + \mathbf{F}_i^e = \mathbf{0}$$

$$\mathbf{F}_i^h = -\zeta \dot{\mathbf{r}}_i$$

$$\mathbf{F}_i^\phi = -\nabla U(\mathbf{r})$$

$$\mathbf{F}_i^c = T_i \mathbf{u}_i - T_{i-1}\mathbf{u}_{i-1}; \mathbf{u}_i = (\mathbf{r}_{i+1} - \mathbf{r}_i)/a$$

$$\left\langle \mathbf{F}_i^b(t) \right\rangle = \mathbf{0}; \left\langle \mathbf{F}_i^b(t)\mathbf{F}_j^b(t+\Delta t) \right\rangle = 2k_B T \zeta \delta_{ij} \delta(\Delta t)$$

$$\mathbf{F}_i^e = f(\mathbf{r}_i, t)$$

- Dynamical differential equation:

$$\boxed{\frac{d\mathbf{r}_i}{dt} = \zeta^{-1}(\mathbf{F}_i^\phi + \mathbf{F}_i^c + \mathbf{F}_i^b + \mathbf{F}_i^e)}$$

Numerical Scheme

- Predictor-corrector algorithm:

Step 1: predict using known forces

$$\mathbf{r}_i^*(t+\Delta t) = \mathbf{r}_i(t) + \zeta^{-1}(\mathbf{F}_i^\phi + \mathbf{F}_i^b + \mathbf{F}_i^e)\Delta t$$

Step 2: correct using constraint force

$$\mathbf{r}_i(t+\Delta t) = \mathbf{r}_i^*(t+\Delta t) + \zeta^{-1}\mathbf{F}_i^c \Delta t \qquad (*)$$

Step 3: substitute eq. (*) to constraint equations

$$(\mathbf{r}_{i+1} - \mathbf{r}_i)^2 - a^2 = 0$$

Solve a set of nonlinear algebraic equations ⇨ $\mathbf{F}_i^c$

Step 4: re-substitute $\mathbf{F}_i^c$ to (*) obtain the final $\mathbf{r}_i(t+\Delta t)$

Parameter Estimation

- Length of Chromosomes in base pairs:

  There are 3 pairs of chromosomes in prophase fission yeast

  Chromosome I: 5.579.133 bp ~ 5,6Mbp

  Chromosome II: 4.539.804 bp ~ 4,5Mbp

  Chromosome III: 2.452.833 bp ~ 2,5Mbp

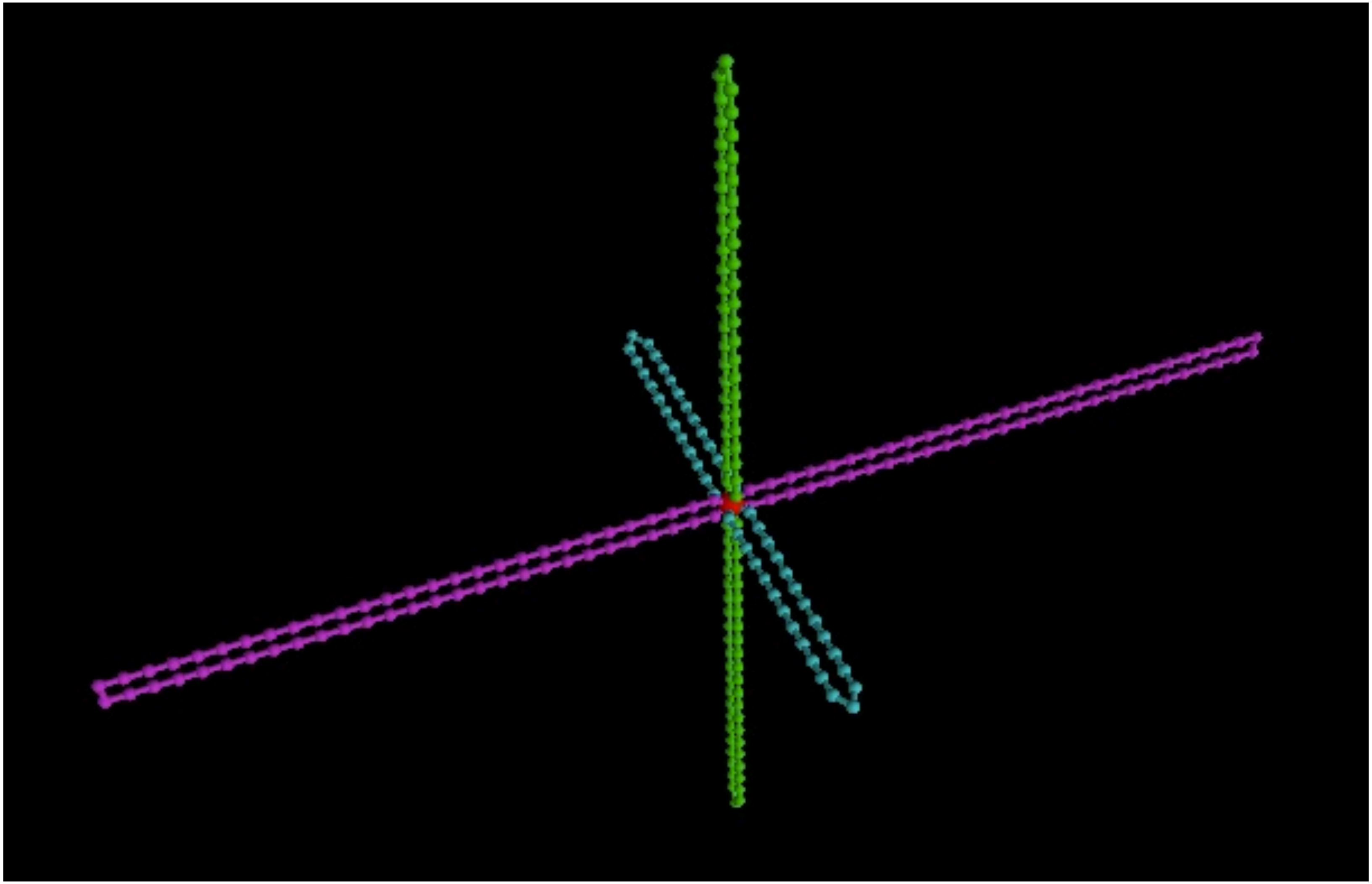
- Compaction ratio of chromosomes: ~ 100bp/nm

- Kuhn length(rod length): ~ 100nm

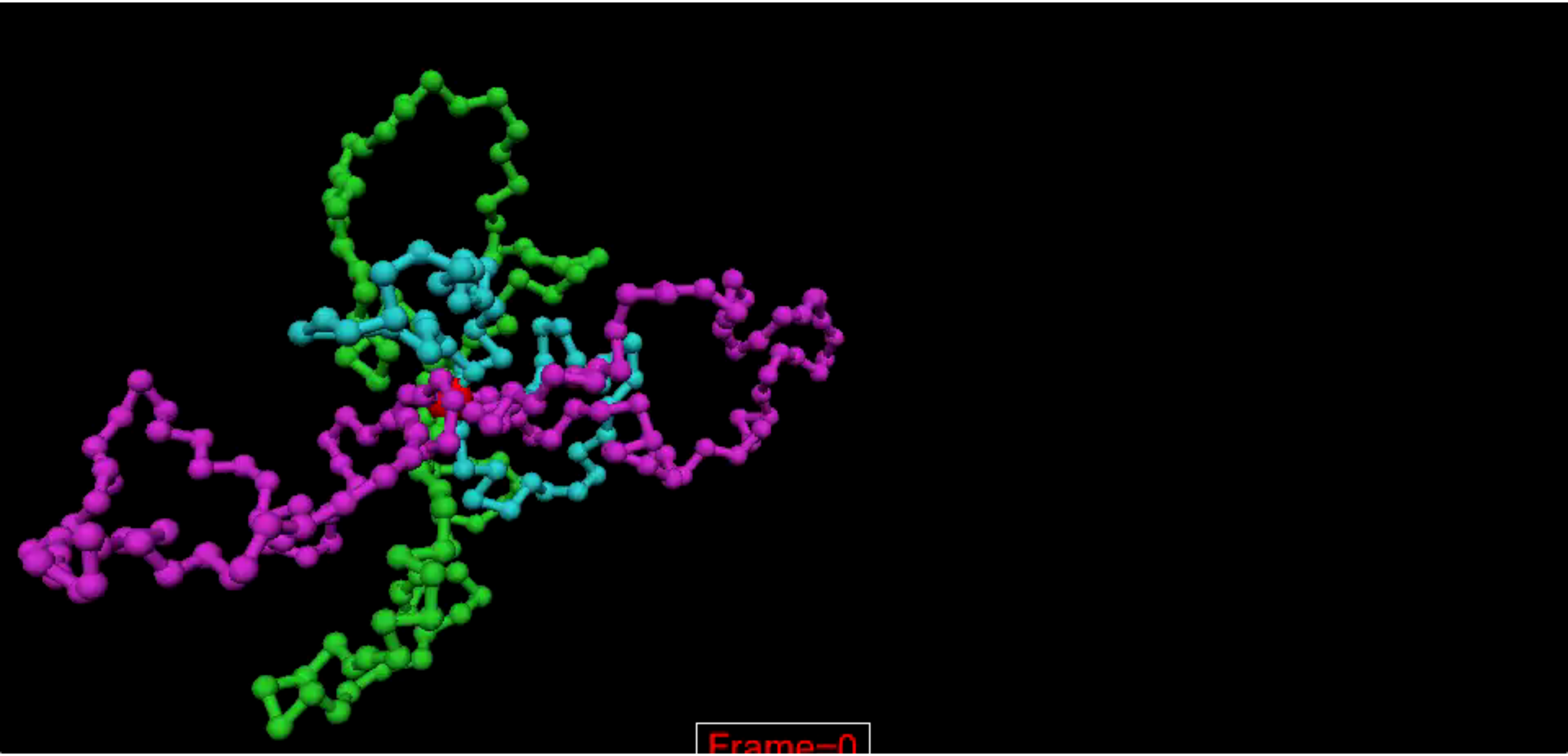
- System size for 3 pairs of chromosomes: ~ 2000-3000

  monomers in one ring : 200 ~ 600

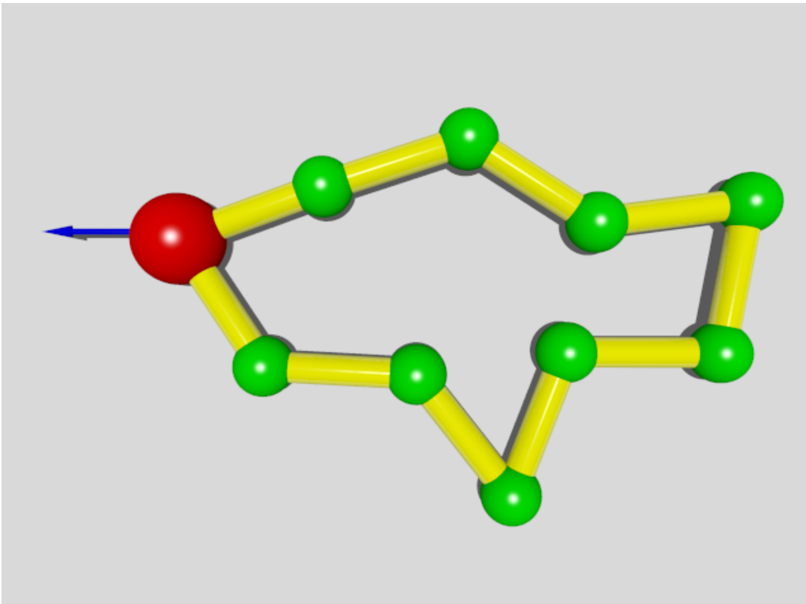
Initial configuration

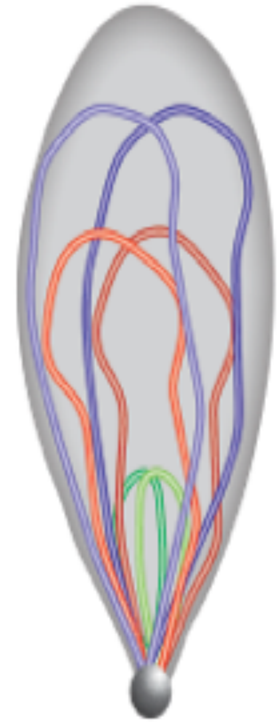


Animation Movie



Problem





Toy model with
100 beads

Real System

Solution: Parallel computation

Ways to go

- Use some kinds of sophisticated MD packages

  Advantage:

  easier to go, parallelize automatically

  Disadvantage:

  cannot control some details, e.g. random force

  not so flexible

- Write a parallel program

  Totally under control but need more time on technique details

My Strategy

Try MD packages $\xrightarrow{\text{Doesn't work}}$ Write a parallel program

List of MD packages

http://en.wikipedia.org/wiki/List_of_software_for_molecular_mechanics_modeling

Rules of selection

- No commercial, should be free
- Need GPU acceleration
- Widely used

Selected packages:

- Gromacs
- LAMMPS
- ESPResSo