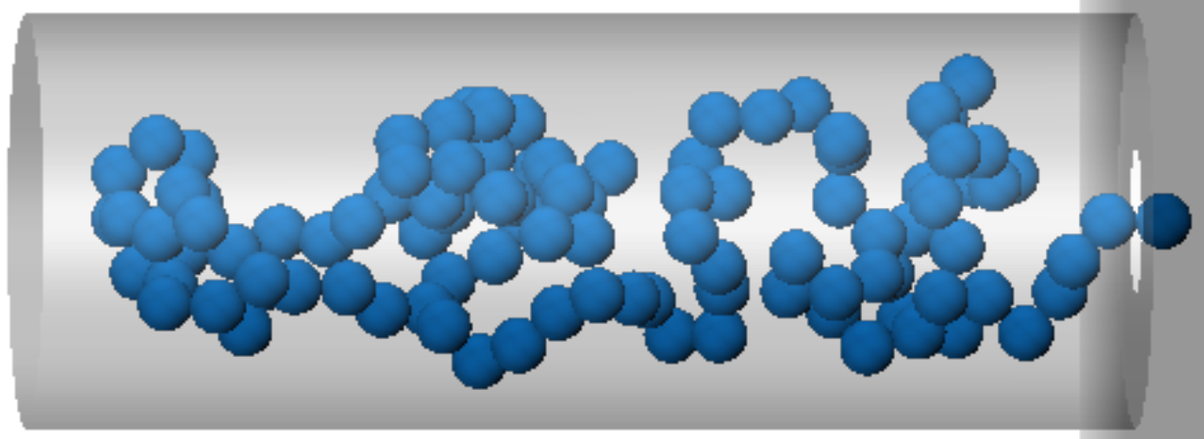
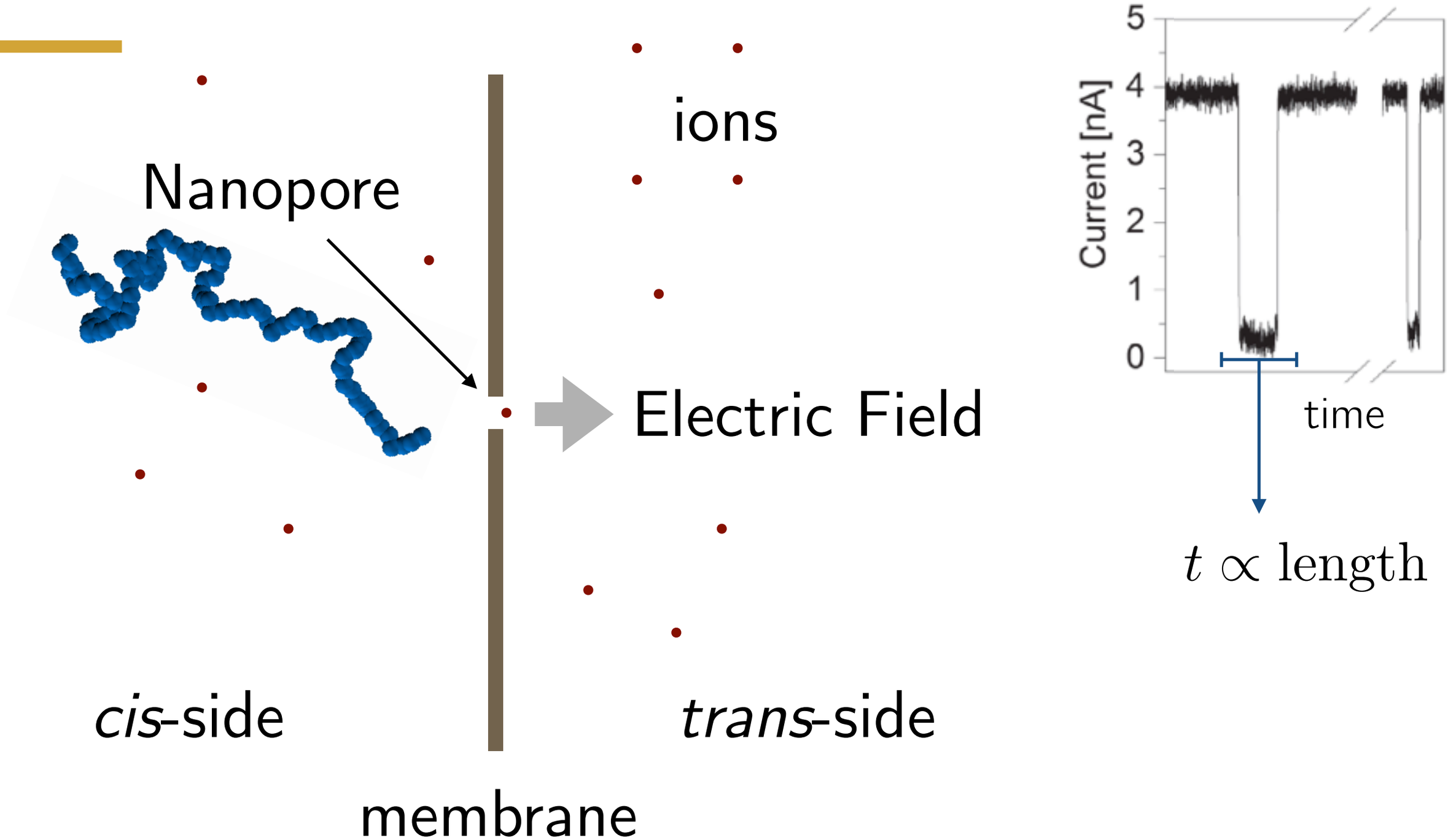
Coarse-grained simulations of highly driven DNA translocation from a confining nanotube



David Sean, Gary W. Slater

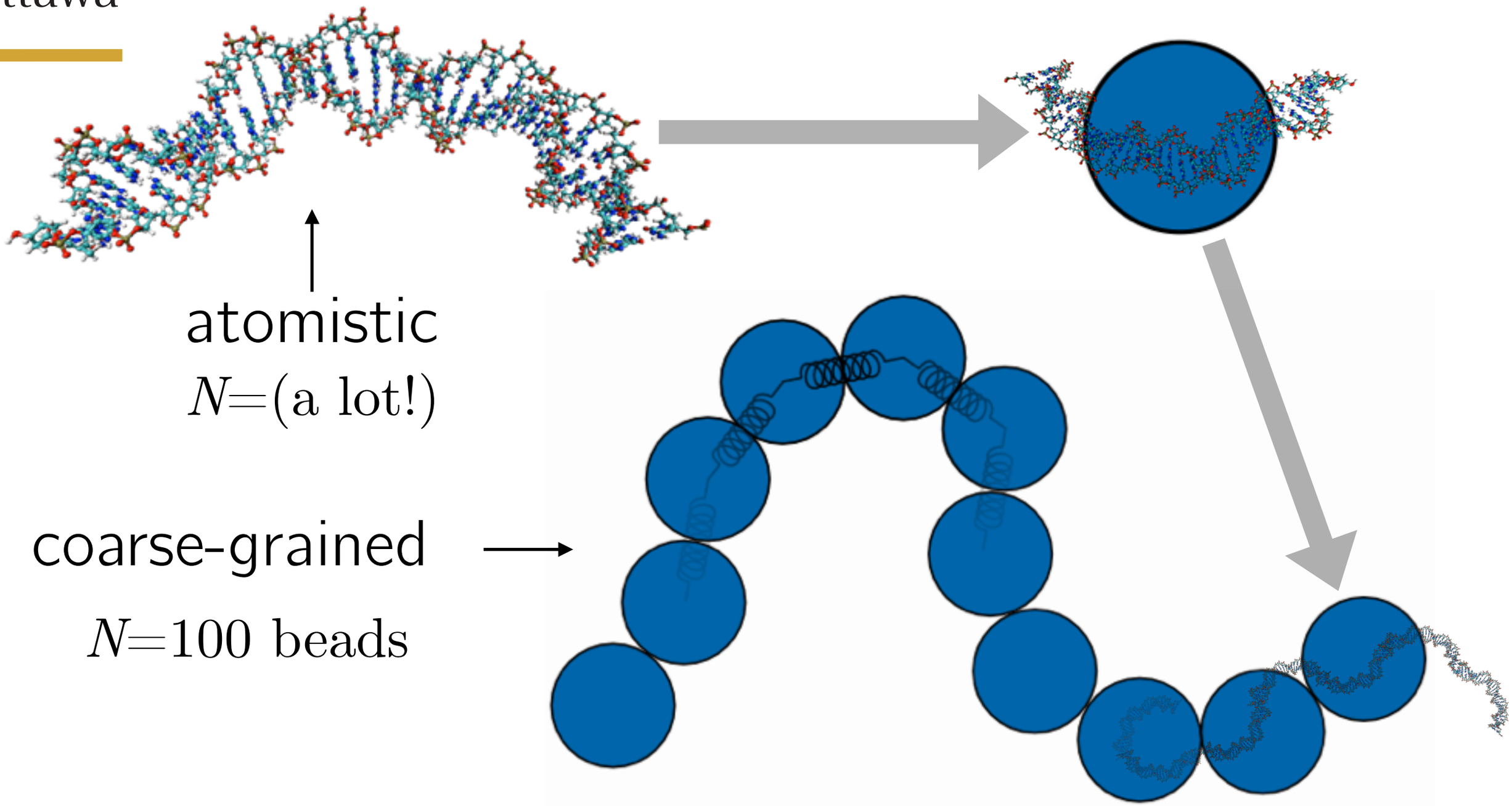
University of Ottawa, Canada

DNA Translocation



M. Waugh, A. Carlsen, **D. Sean**, G.W. Slater, K. Briggs, H. Kwok and V. Tabard-Cossa, *Electrophoresis*, (2015)

Coarse-graining



G. W. Slater, C. Holm, M. V. Chubynsky, H. W. de Haan, A. Dube, K. Grass, O. A Hickey, C. Kingsburry, **D. Sean**, T. N. Shendruk, L. Zhan Electrophoresis (2009)

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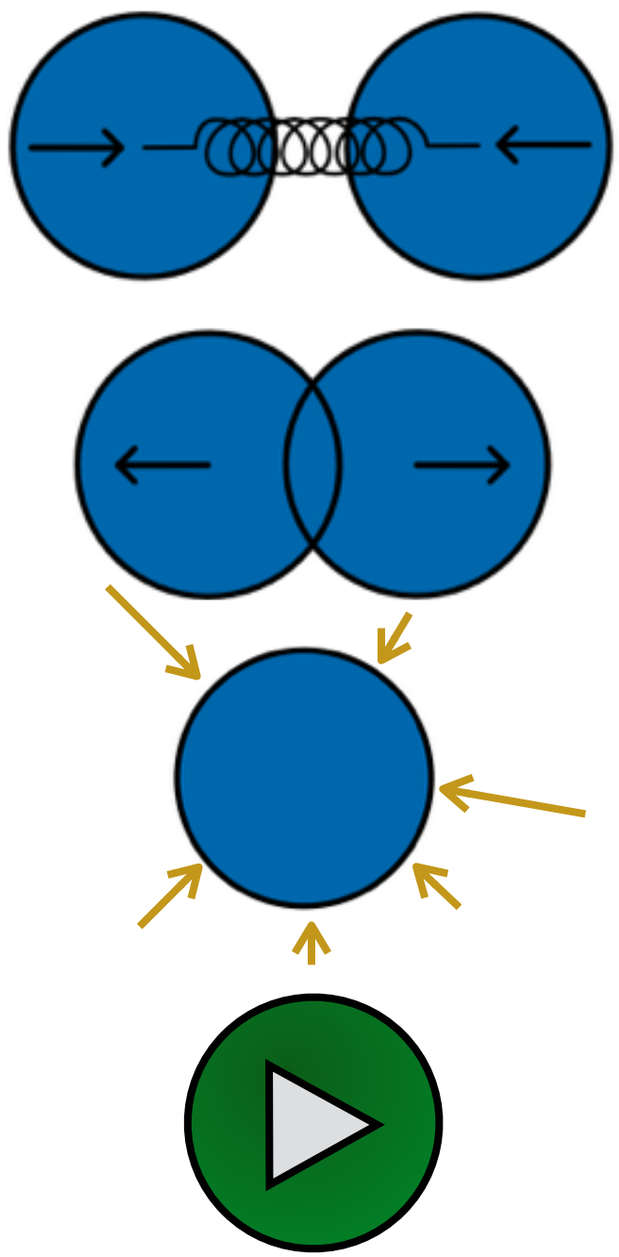
Coarse-graining



Finitely Extensible Nonlinear Elastic

$$U_{\mathrm{FENE}}(r) = -\frac{1}{2}\, k_{\mathrm{FENE}}\, {r_0}^2 \ln\left[1 - \frac{r^2}{{r_0}^2}\right]$$

truncated Lennard-Jones

$$U_{\mathrm{LJ}}(r) = \begin{cases} 4\epsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right] + \epsilon & \text{for } r < r_{\mathrm{c}} \\ 0 & \text{for } r \geq r_{\mathrm{c}} \end{cases}$$

$$\langle F_{\mathrm{B}}^2 \rangle = \frac{2\zeta k_{\mathrm{B}} T}{\Delta t}$$

random Brownian force

$$m\ddot{\mathbf{r}} = \mathbf{F}^{\mathrm{C}} - \zeta\dot{\mathbf{r}} + \mathbf{F}^{\mathrm{B}}$$

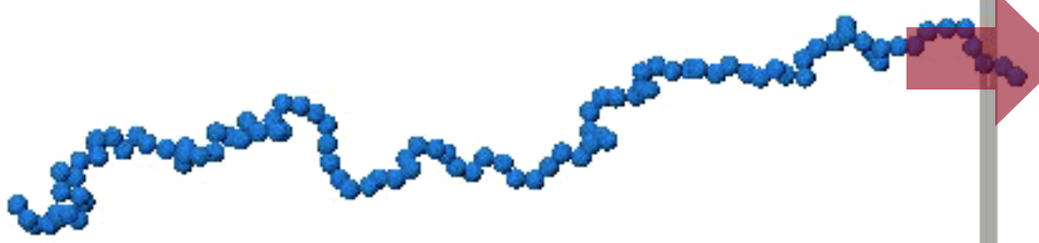
ESPResSo

G. W. Slater, C. Holm, M. V. Chubynsky, H. W. de Haan, A. Dube, K. Grass, O. A Hickey, C. Kingsburry, **D. Sean**, T. N. Shendruk, L. Zhan *Electrophoresis* (2009)

Putting it all Together

short-ranged repulsive membrane:

$$U_{\mathrm{LJ}}(r) = \begin{cases} 4\epsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right] + \epsilon & \text{for } r < r_{\mathrm{c}} \\ 0 & \text{for } r \geq r_{\mathrm{c}} \end{cases}$$



N=100 beads

field in the pore:

$$F_{\mathrm{drive}} = 50\left[\frac{k_{\mathrm{B}}T}{\sigma}\right]$$

Highly-Driven limit!

H.W. de Haan, **D. Sean** and G.W. Slater, *Phys Rev E* (2015)

Problems with Driven Translocation

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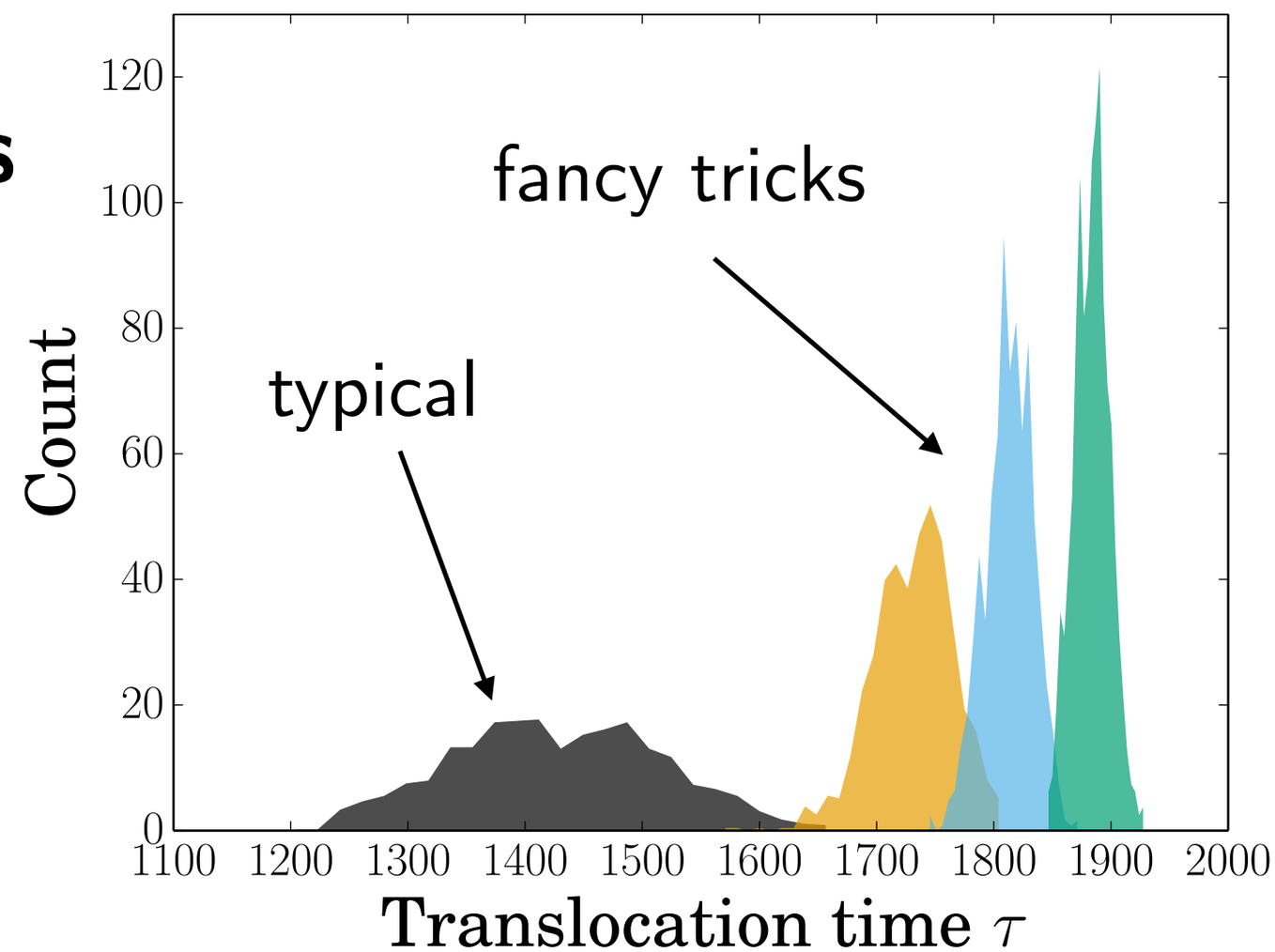
High variance amongst events.

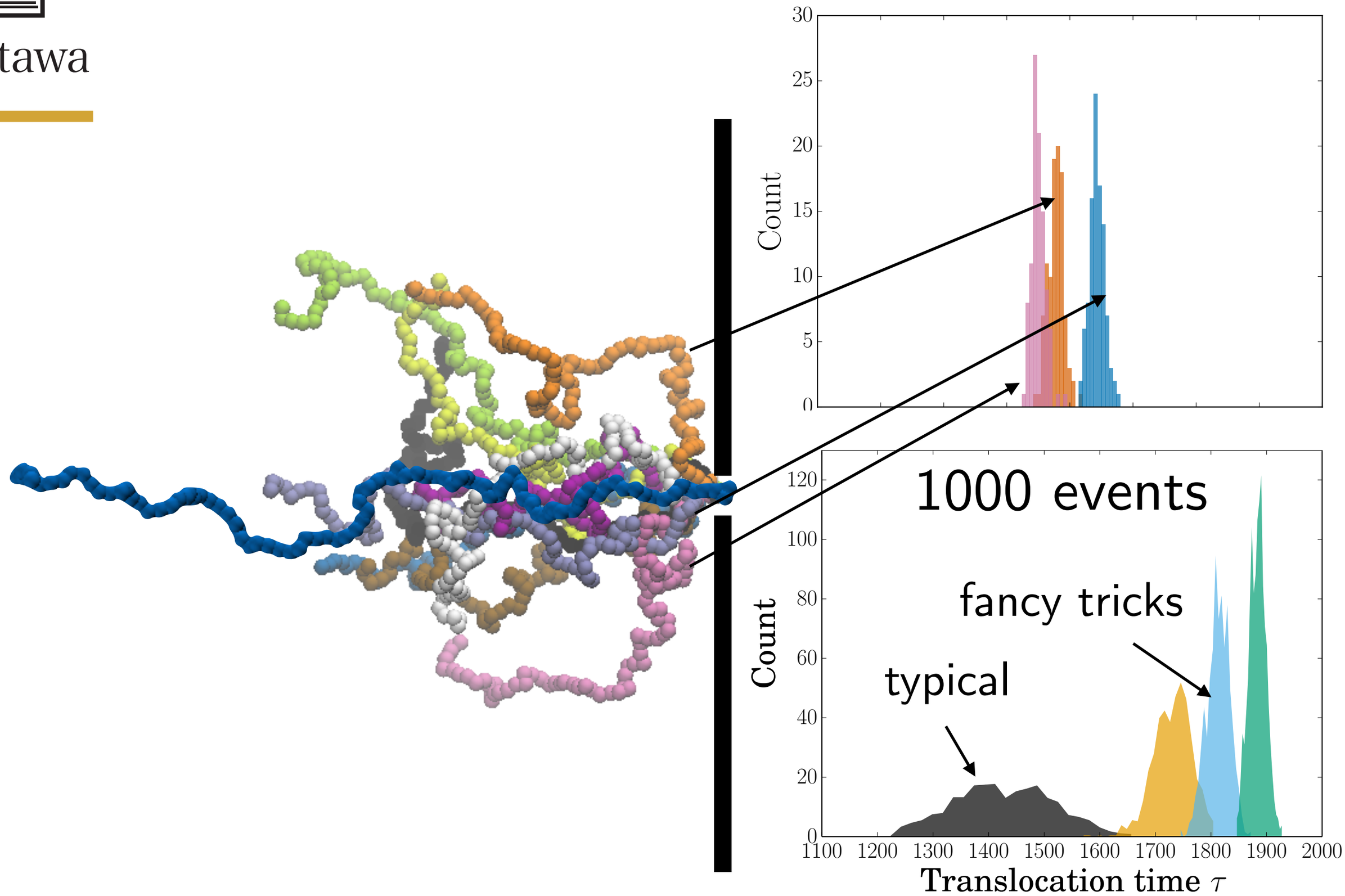
Two main sources for this variation:

i) thermal noise

ii) **initial conformations**



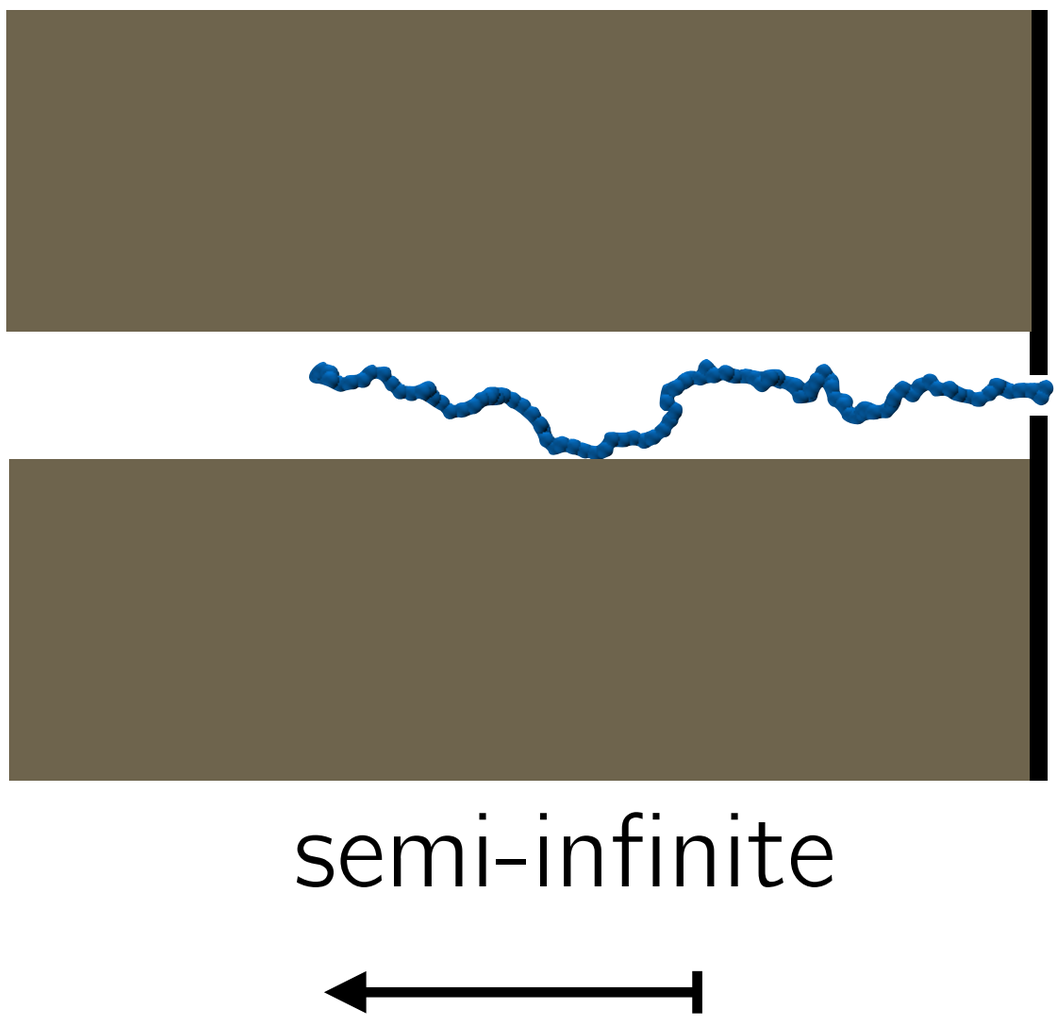
Initial conformations matter!



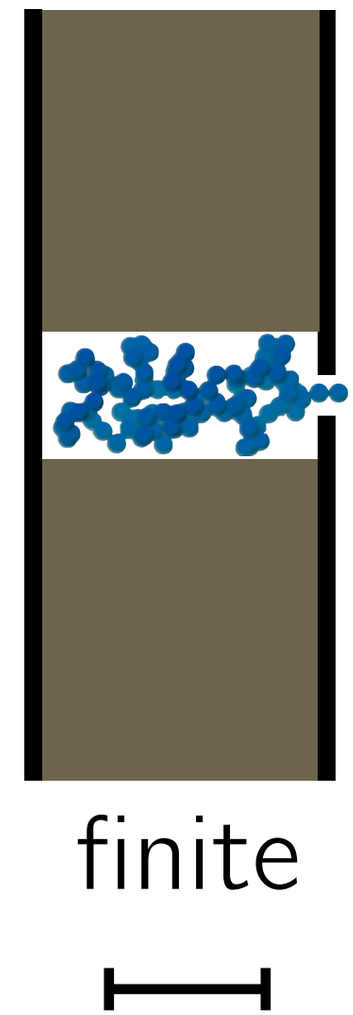
Geometric Restrictions

Use a confining tube to reduce the variance

Case 1



Case 2



D. Sean, G.W. Slater, (submitted to *J.Chem. Phys*)

D. Sean, H.W. de Haan, G.W. Slater, *Electrophoresis* (2015)

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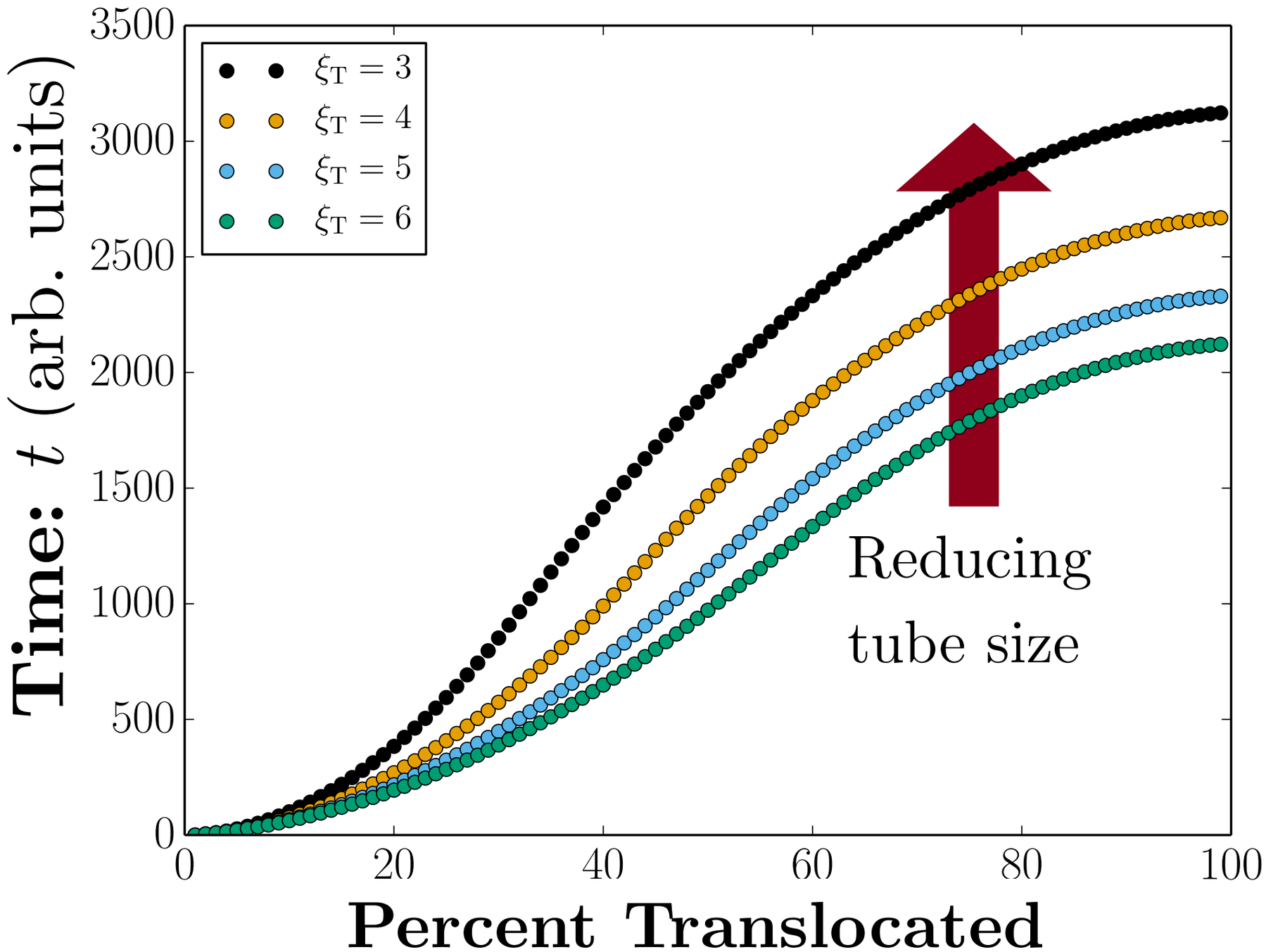
Translocation Dynamics

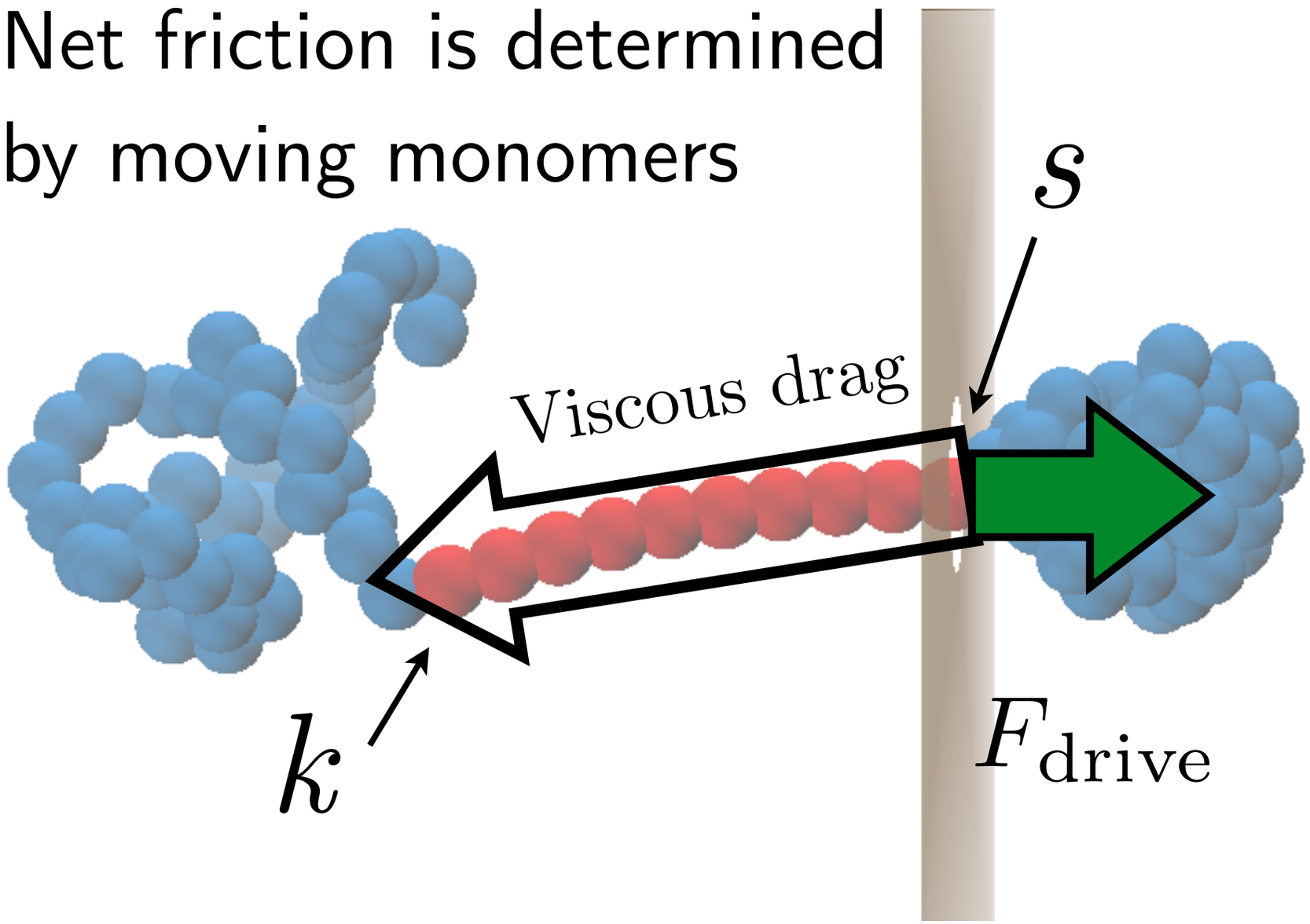
semi-infinite tube



D. Sean, H.W. de Haan, G.W. Slater, *Electrophoresis* (2015)

Tension Propagation

Net friction is determined by moving monomers

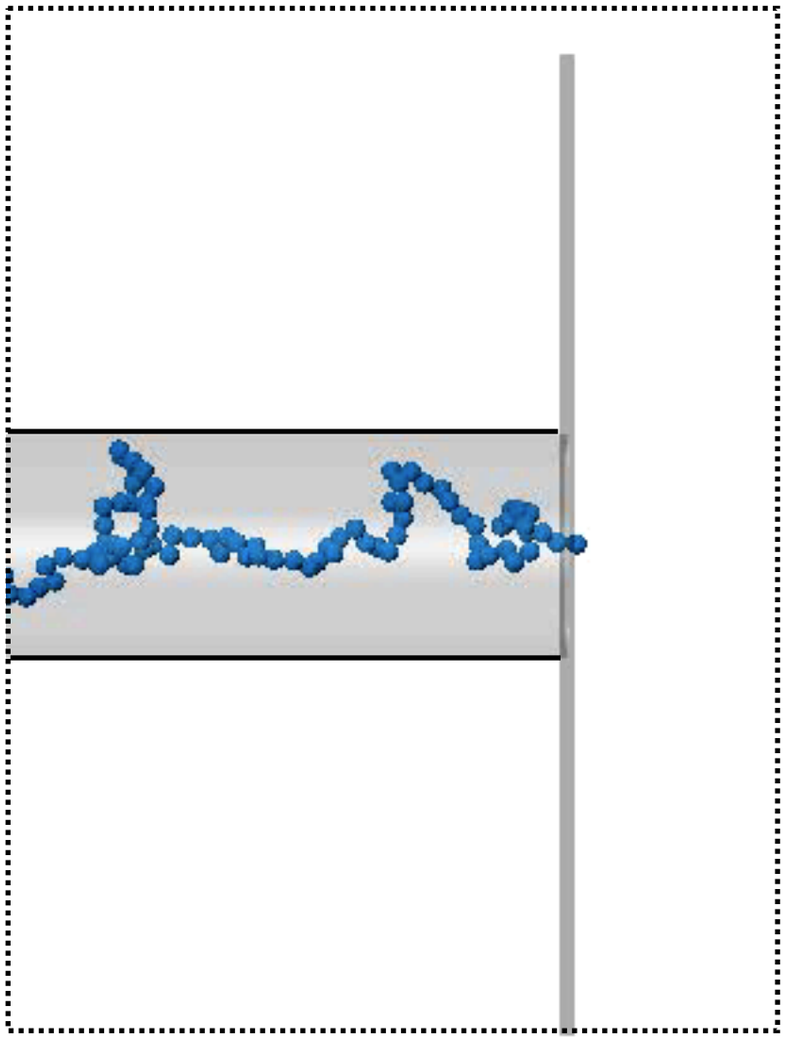


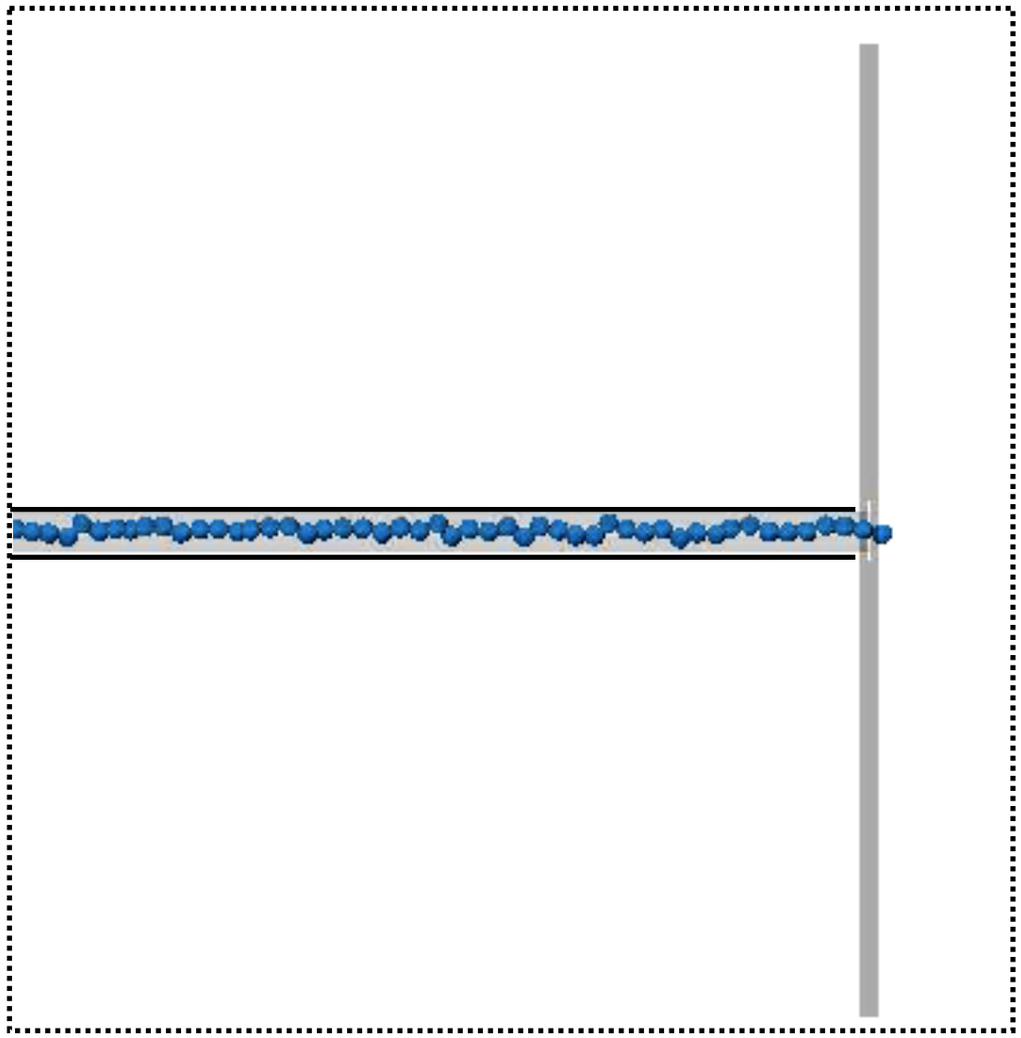
$$F_{\mathrm{drive}} = (k - s)\,\zeta v$$

T. Sakaue, *Phys Rev E* (2007)

Tension Propagation

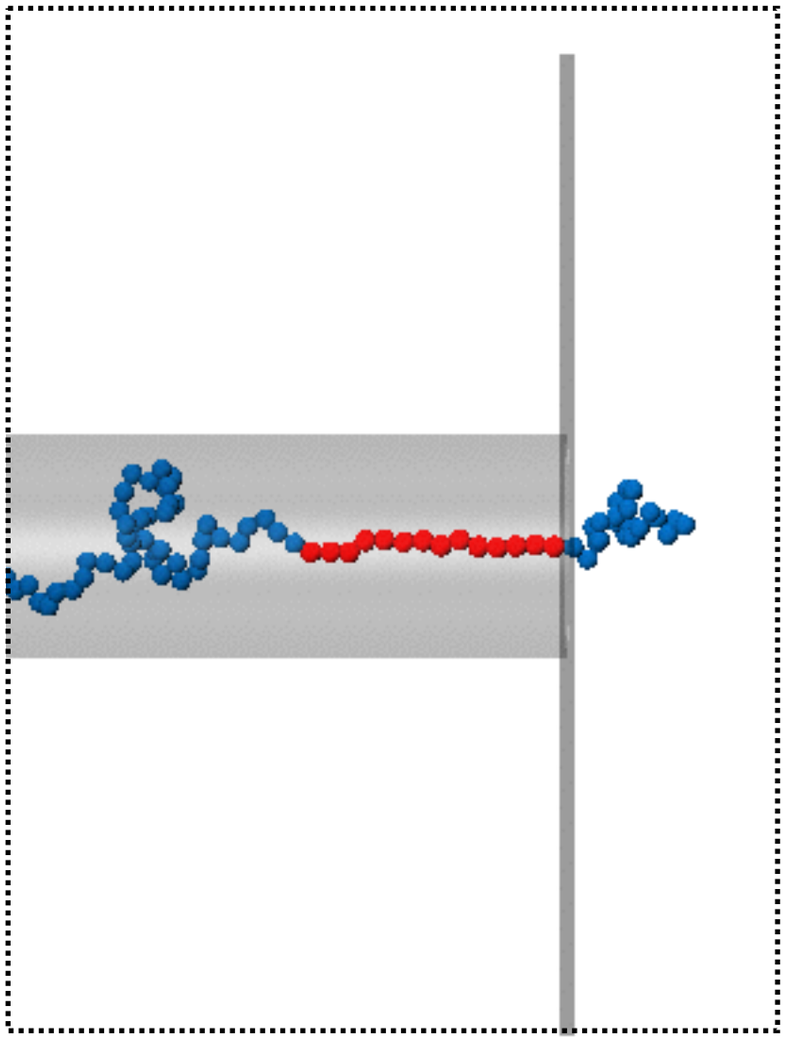
first few simulation frames

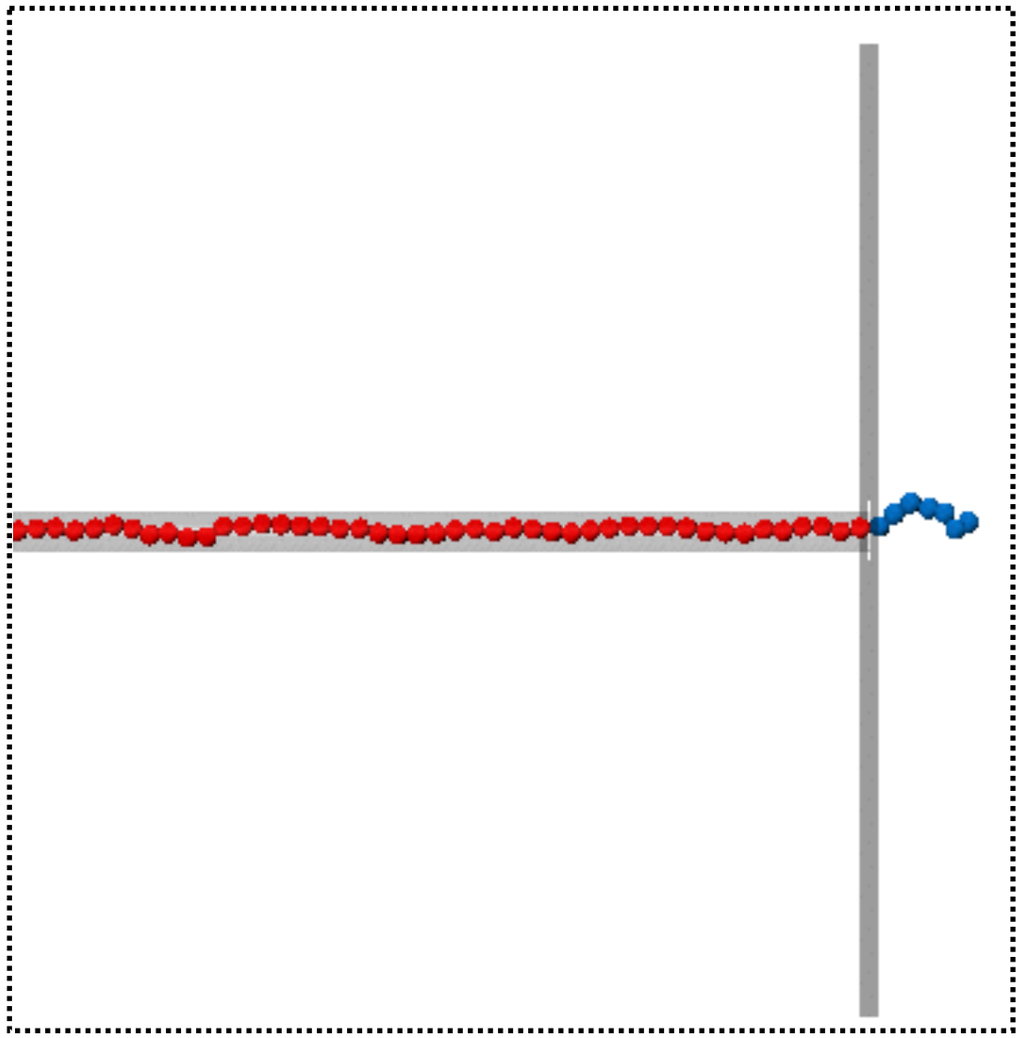




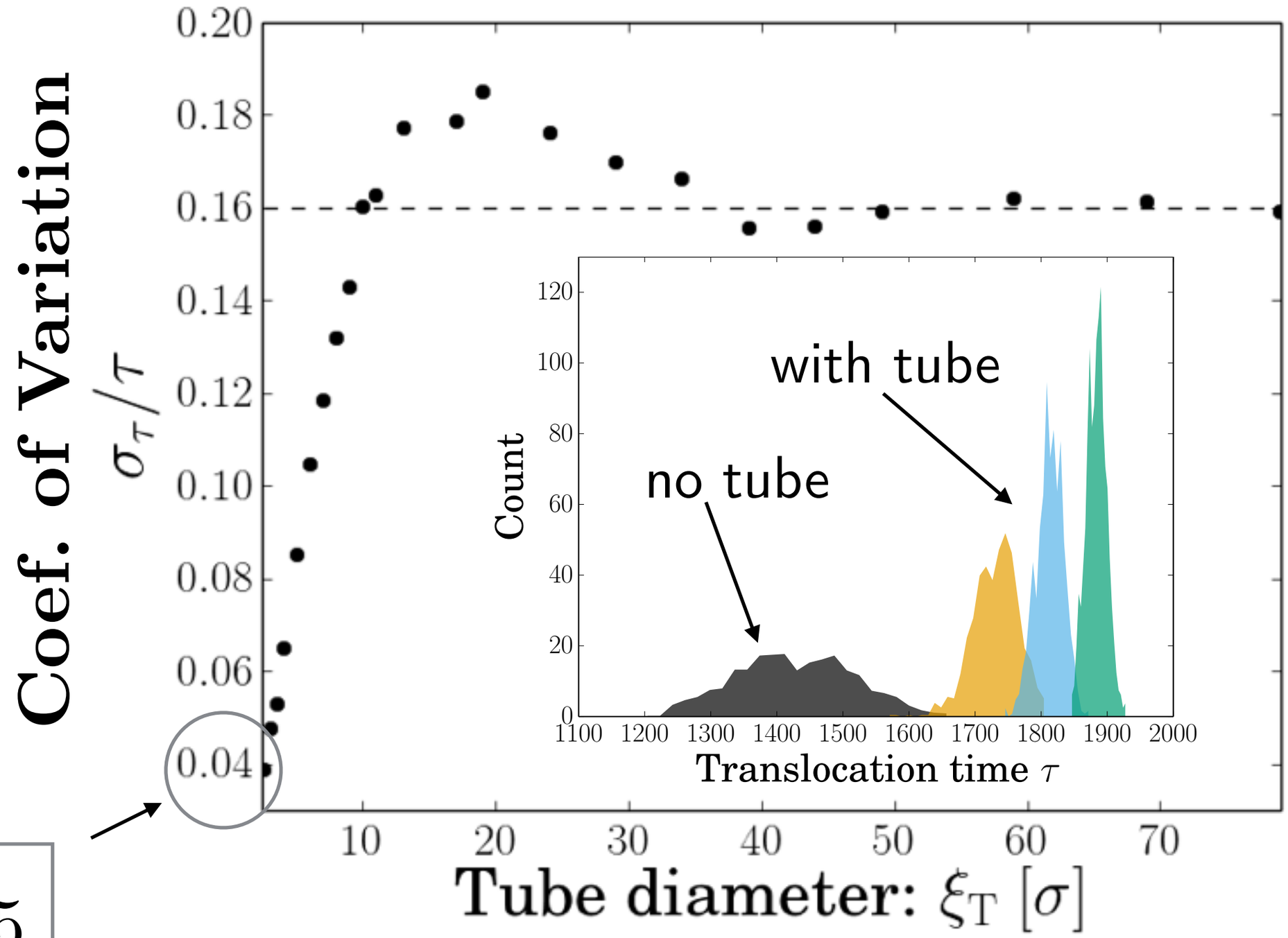
Tension Propagation

First few simulation frames





Decreasing the Variance



$$\xi_T = 2.5$$

D. Sean, H.W. de Haan, G.W. Slater, *Electrophoresis* (2015)

Recap: semi-infinite case

Use a confining tube to reduce the variance

Case 1

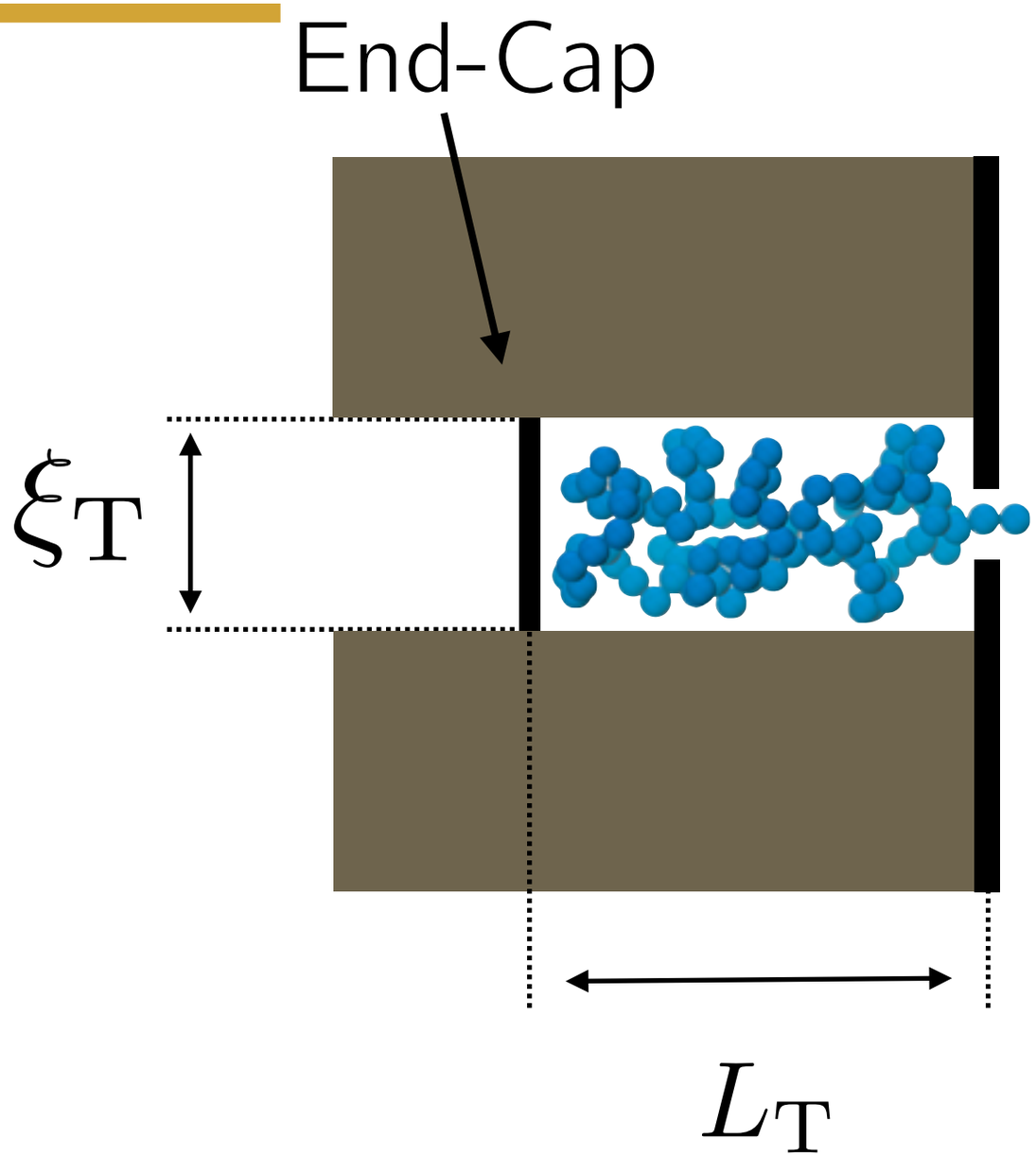
semi-infinite

Results

- ✓ Reduces variance: σ_τ
- ✓ Increases time: τ
- ✓ Reduces coef. var: σ_τ/τ

- ✗ Require high confinement (free energy cost)

Confinement in a Finite-tube



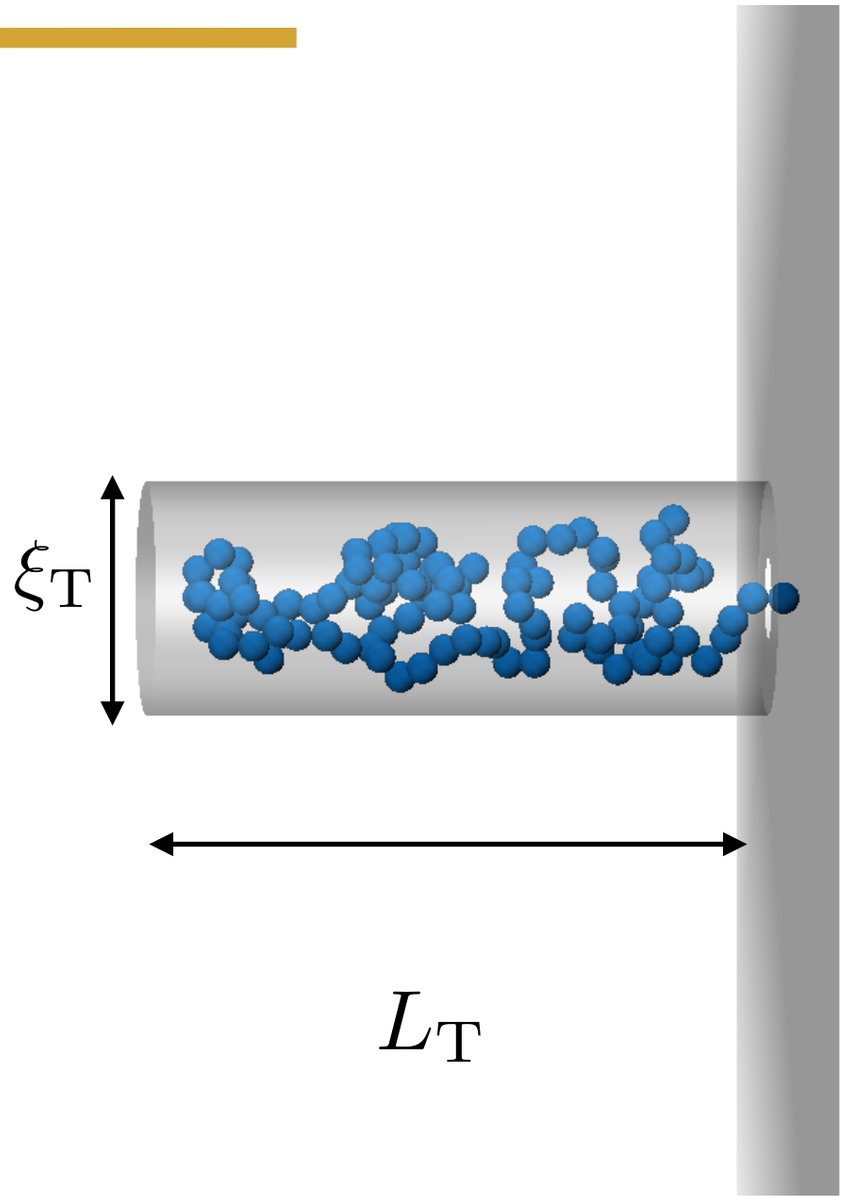
Here, we have additional parameters.

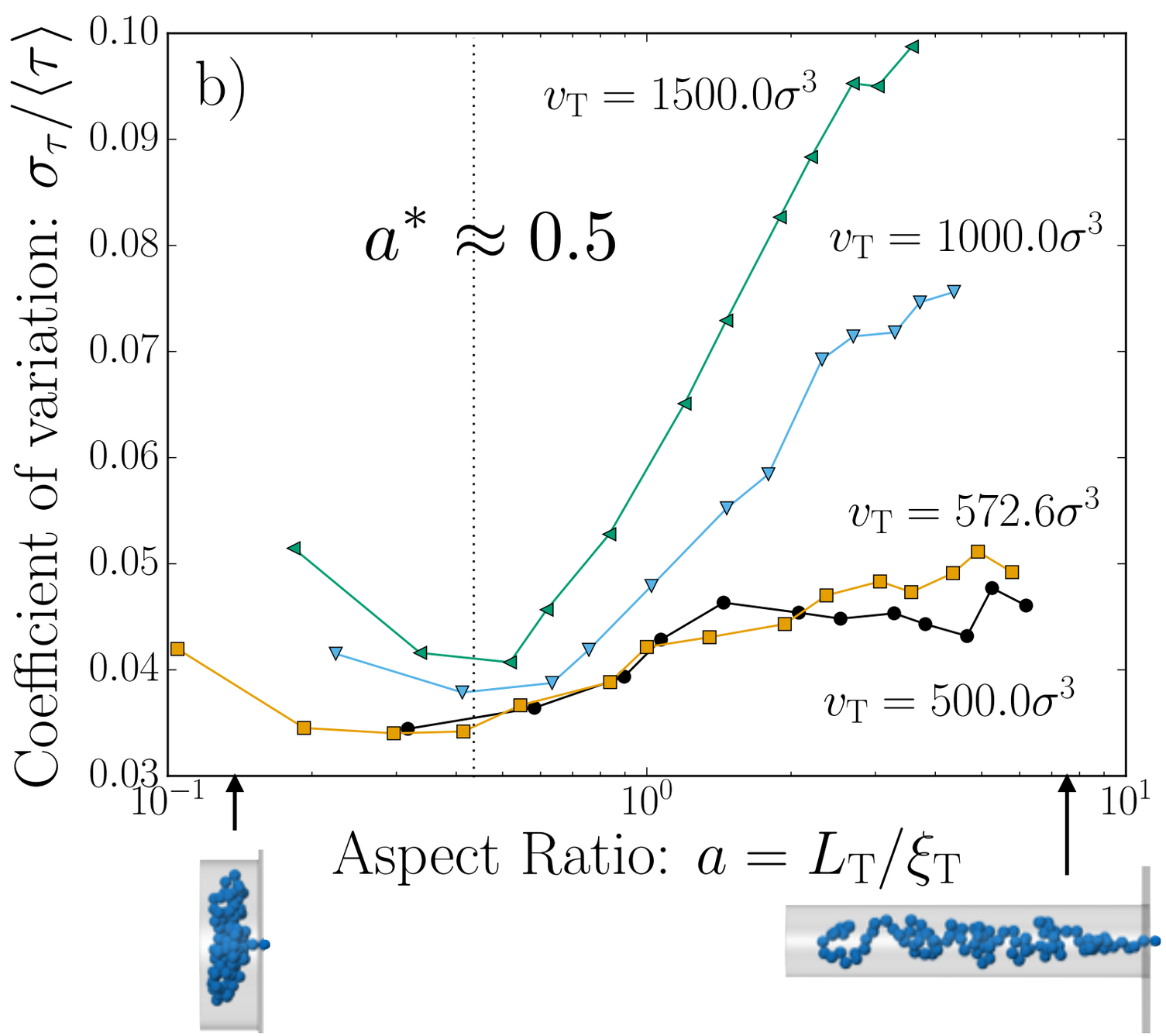
Can we do better than before?

Cast into volume and aspect-ratio

ξ_{T}, L_{T} ⇒ V_{T}, $a = L_{\mathrm{T}}/\xi_{\mathrm{T}}$

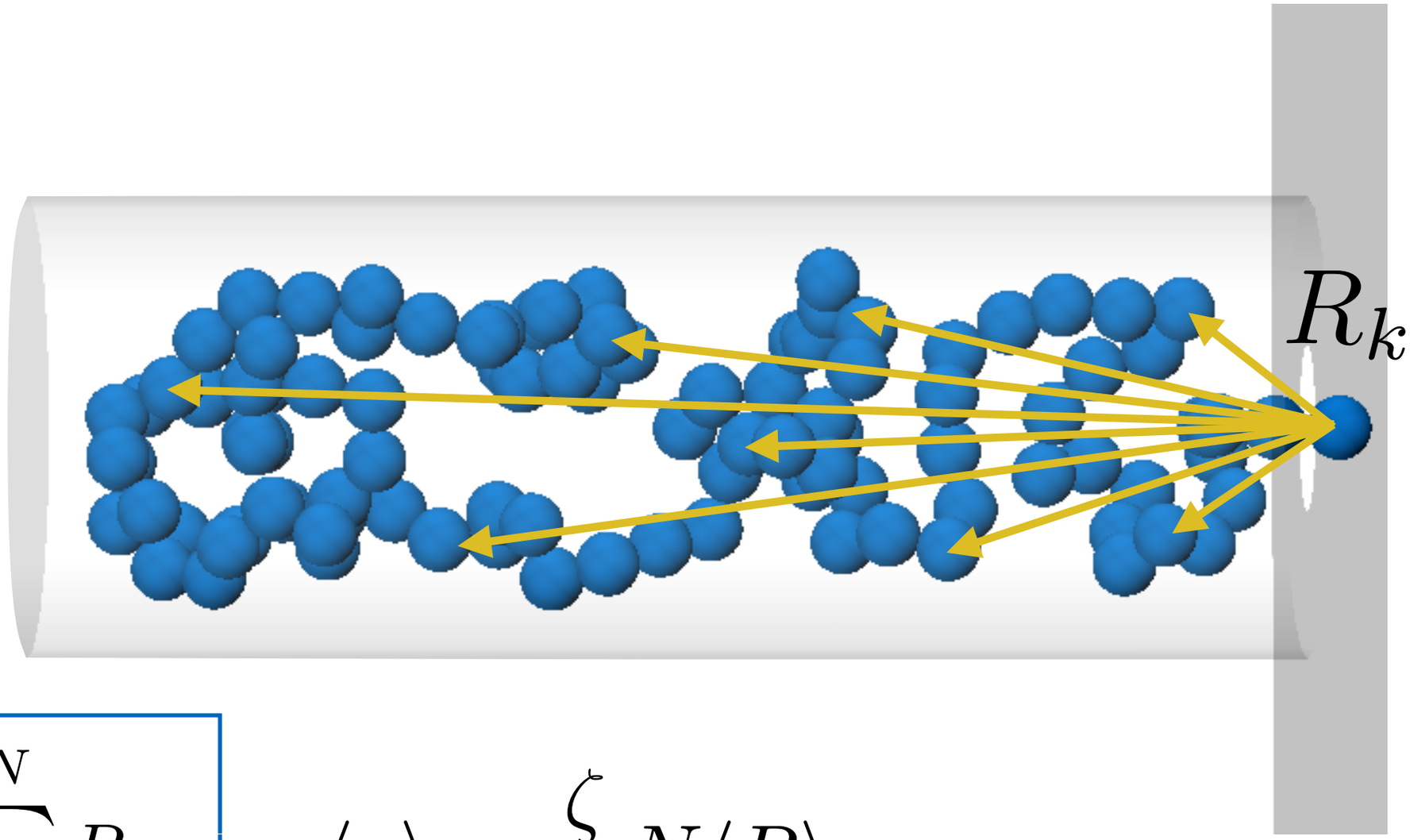
Iso-volume, vary $a = L_{\mathrm{T}}/\xi_{\mathrm{T}}$





D. Sean, G.W. Slater, (submitted to *J.Chem. Phys*)

Tension Propagation



$$\tau = \frac{\zeta}{F}\sum_{k=1}^{N} R_k$$

$$\langle \tau \rangle = \frac{\zeta}{F} N \langle R \rangle$$

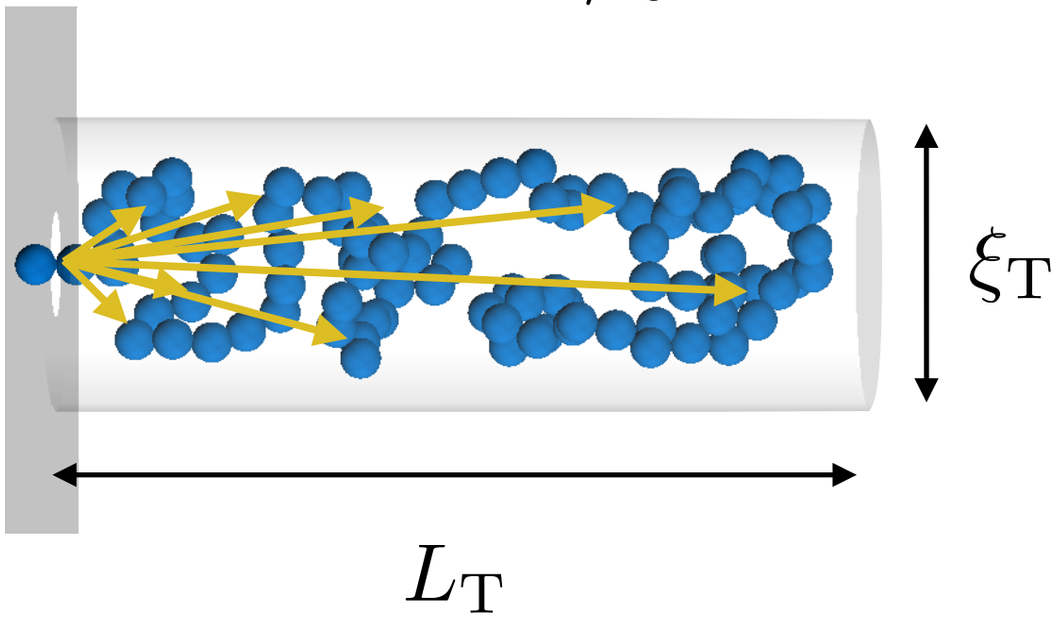
reducing σ_R should reduce σ_τ

T. Sakaue, *Phys Rev E* **76**, (2007)

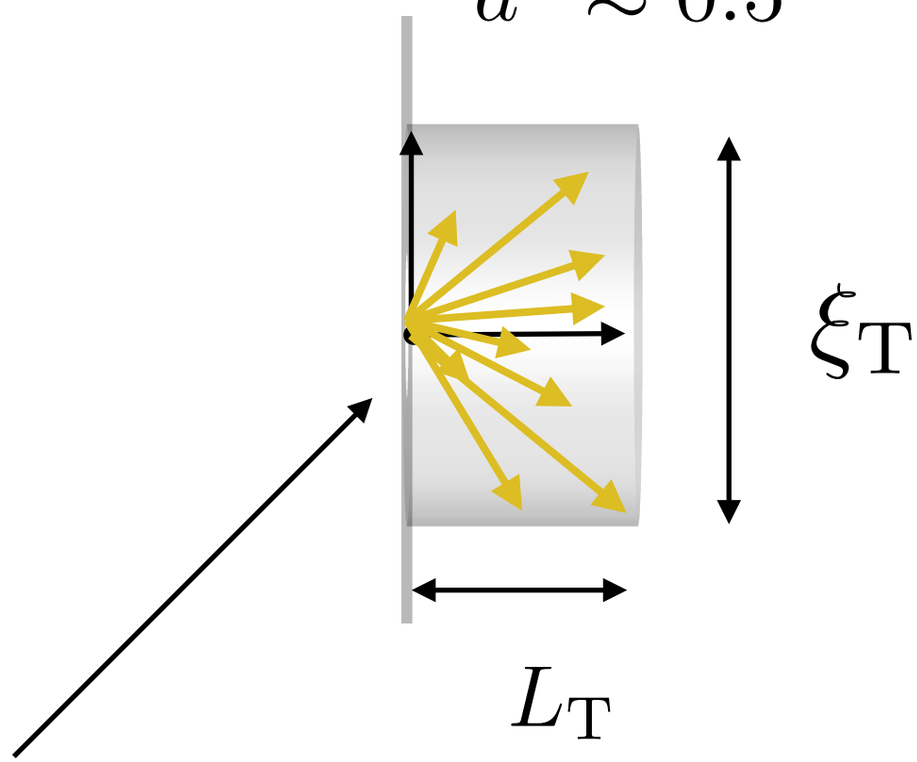
Why $a^* \approx 0.5$?

Since the pore (monomer sink) is centred, a≈0.5 corresponds to an isotropic span

$a = L_{\mathrm{T}}/\xi_{\mathrm{T}}$



$a^* \approx 0.5$



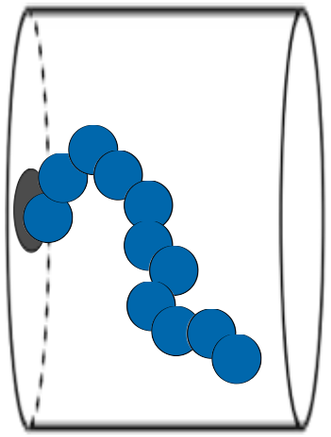
lower variance in these R vectors

Hemisphere is the Optimal Shape

variation in distances: $\sigma_R/\langle R\rangle$

cylinder

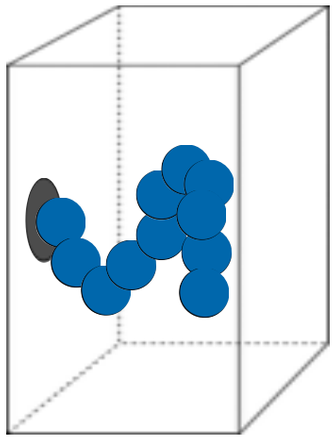
$a^* = 0.414$



$\sigma_R/\langle R\rangle = 0.277$

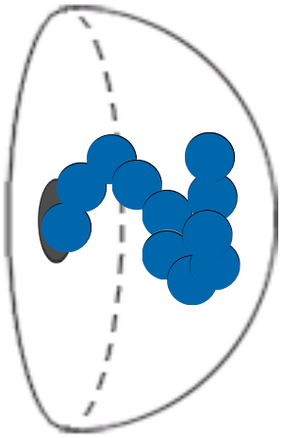
prism

$a^* = 1/2$



$\sigma_R/\langle R\rangle = 0.289$

hemisphere



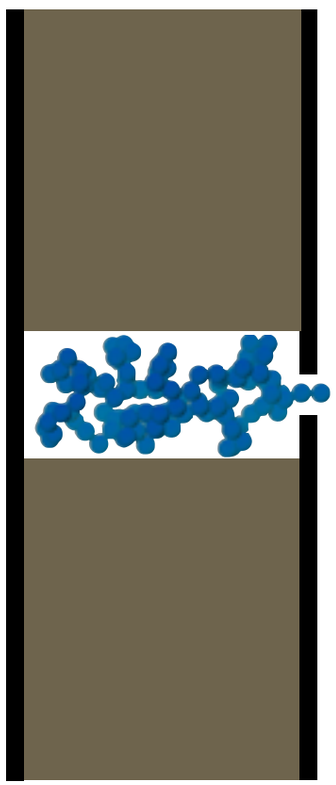
$\sigma_R/\langle R\rangle = 0.258$

D. Sean, G.W. Slater, (submitted to *J.Chem. Phys*)

Recap: finite case

Use a confining tube to reduce the variance

Case 2



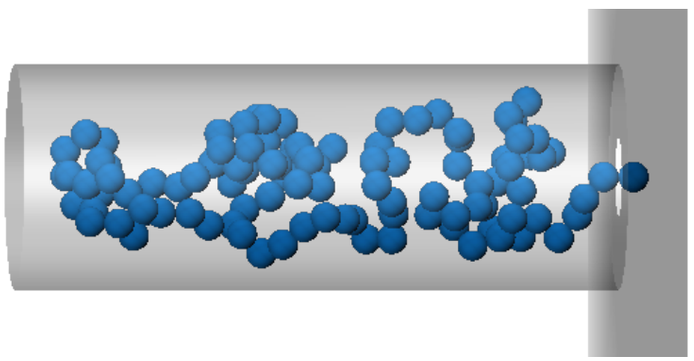
finite

Results

- ✓ Reduces variance: σ_τ
- ✗ Reduces time: τ
- ✓ Reduces coef. var: σ_τ/τ

- ✓ Less confining

Conclusion



- We used a geometric constraint (tube) to **limit** initial conformations prior to translocation
- Reduces the **variance**, and the **coefficient of variation**

- Semi-infinite: small radius increases the mean **time**
- Finite tube: ideal **aspect ratio** a≈0.5 (hemisphere)

uOttawa

Thanks!

compute • calcul CANADA

Gary W. Slater (U.Ottawa)

Maxime Ignacio

Mykyta Chubynsky

Hanyang Wang

CRSNG NSERC

SHARCNET™

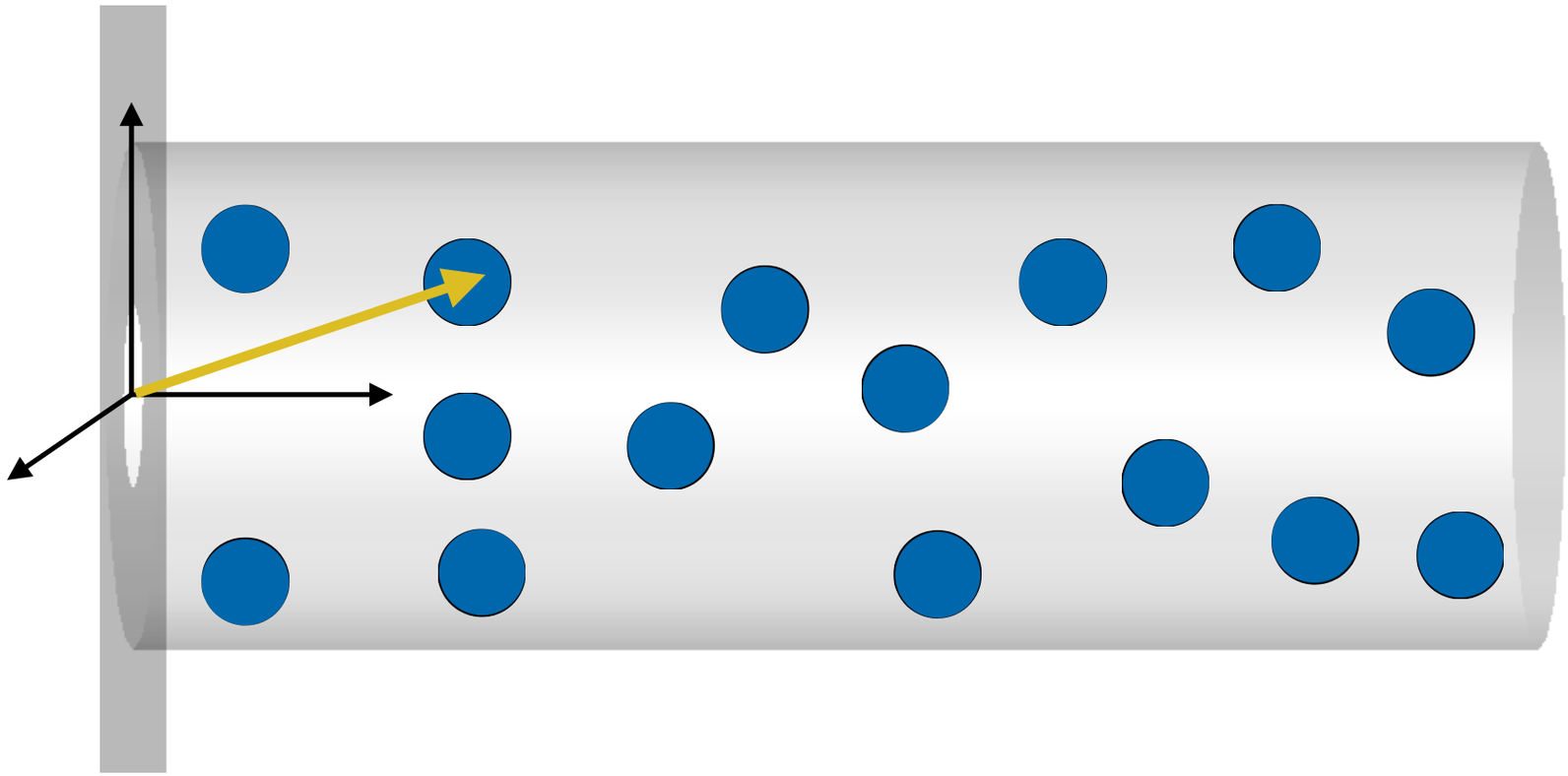
ESPResSo

Hendrick W. de Haan (U.O.I.T)

VMD Visual Molecular Dynamics

Average Distance in a Cavity

(if the polymer homogeneously fills the cavity)



$$\langle R \rangle = \frac{1}{v_{\mathrm{T}}} \int_{\phi=0}^{2\pi} \int_{\rho=0}^{\xi_{\mathrm{T}}/2} \int_{z=0}^{L_{\mathrm{T}}} R \rho d\phi d\rho dz$$

$$\sigma_R^2 = \langle R^2 \rangle - \langle R \rangle^2$$

Average Distance in a Cavity

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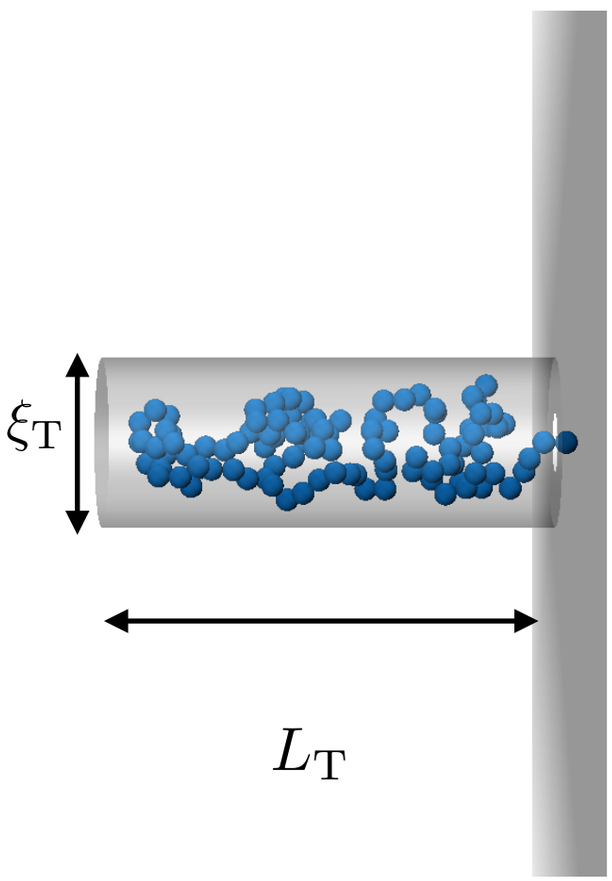
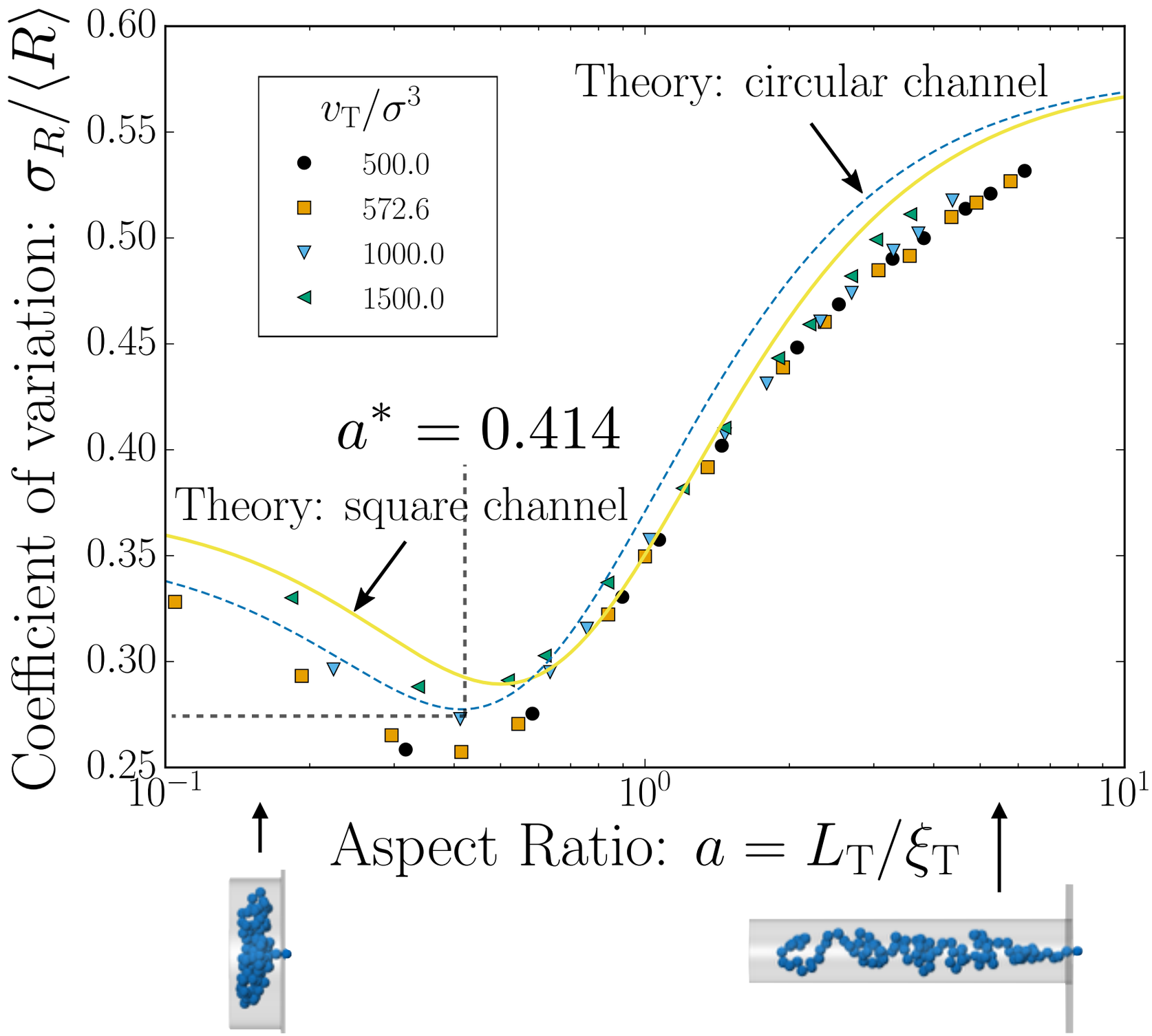
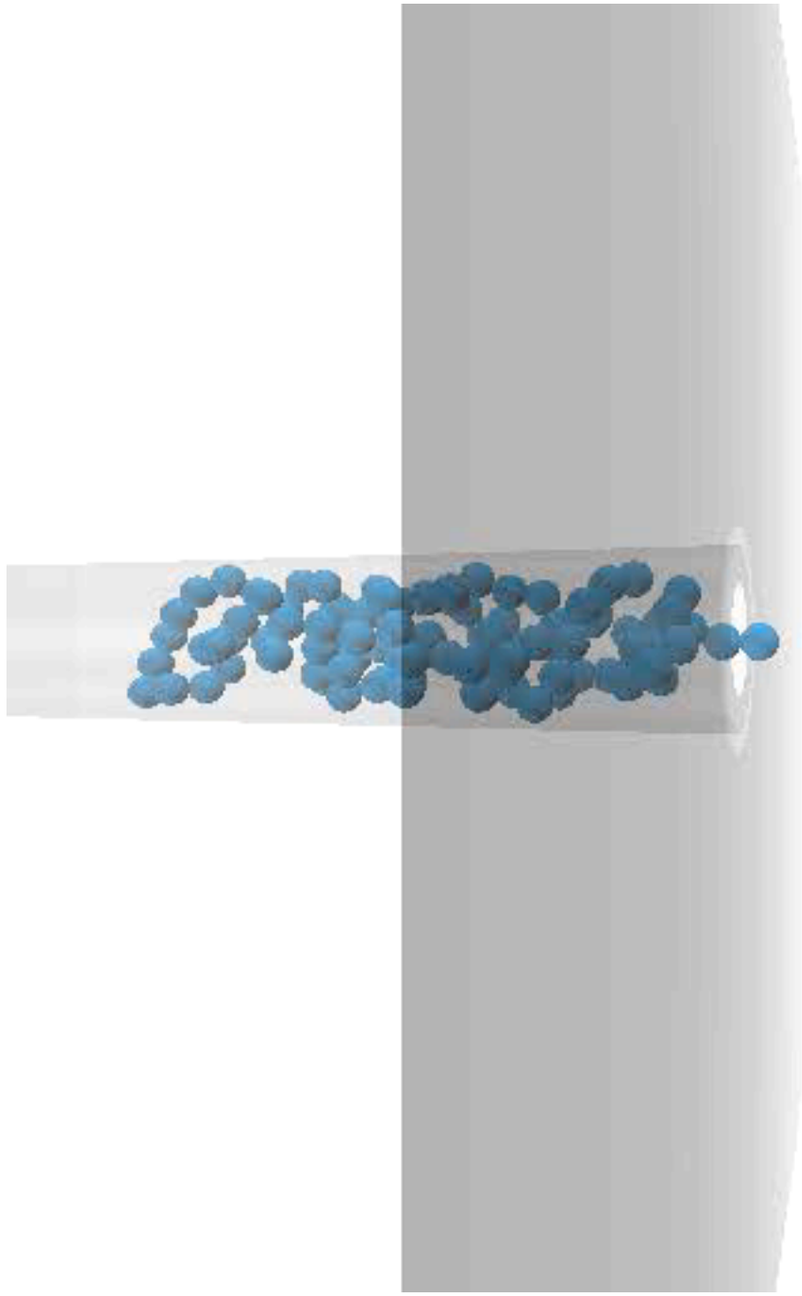
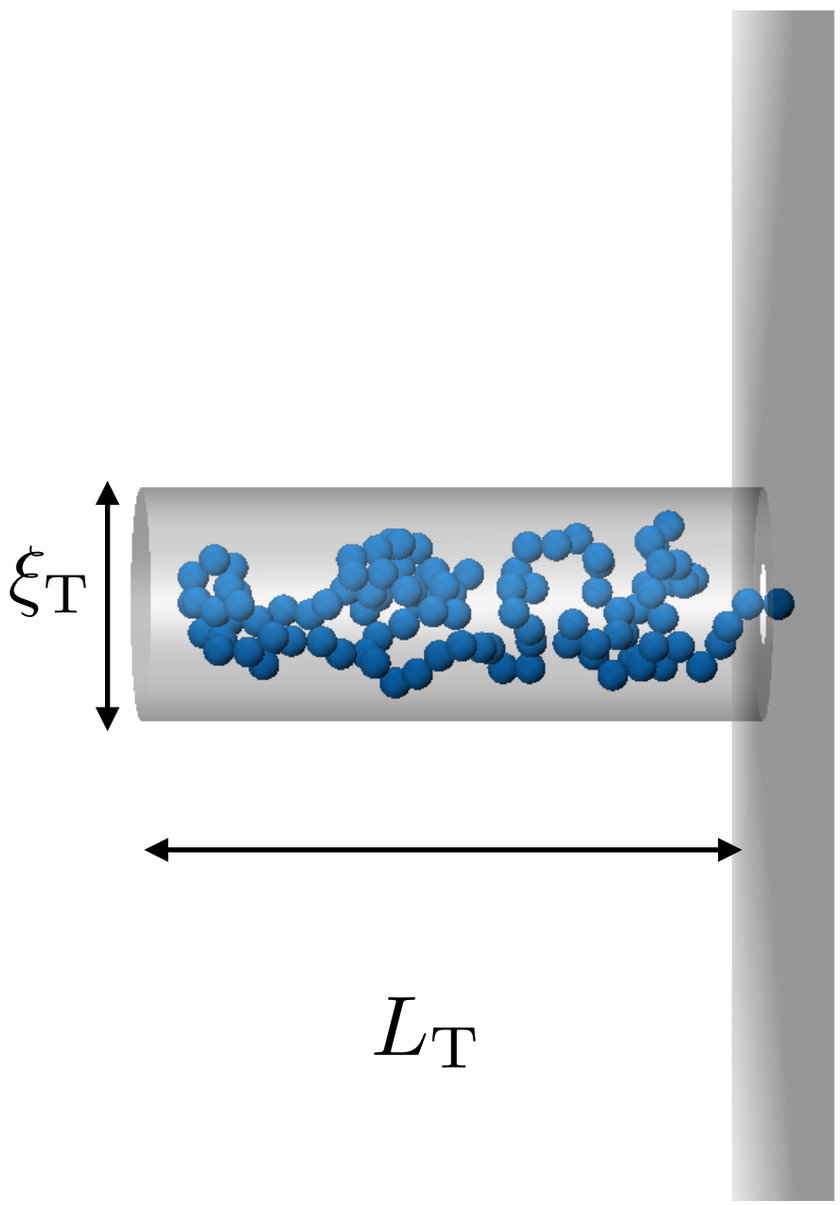


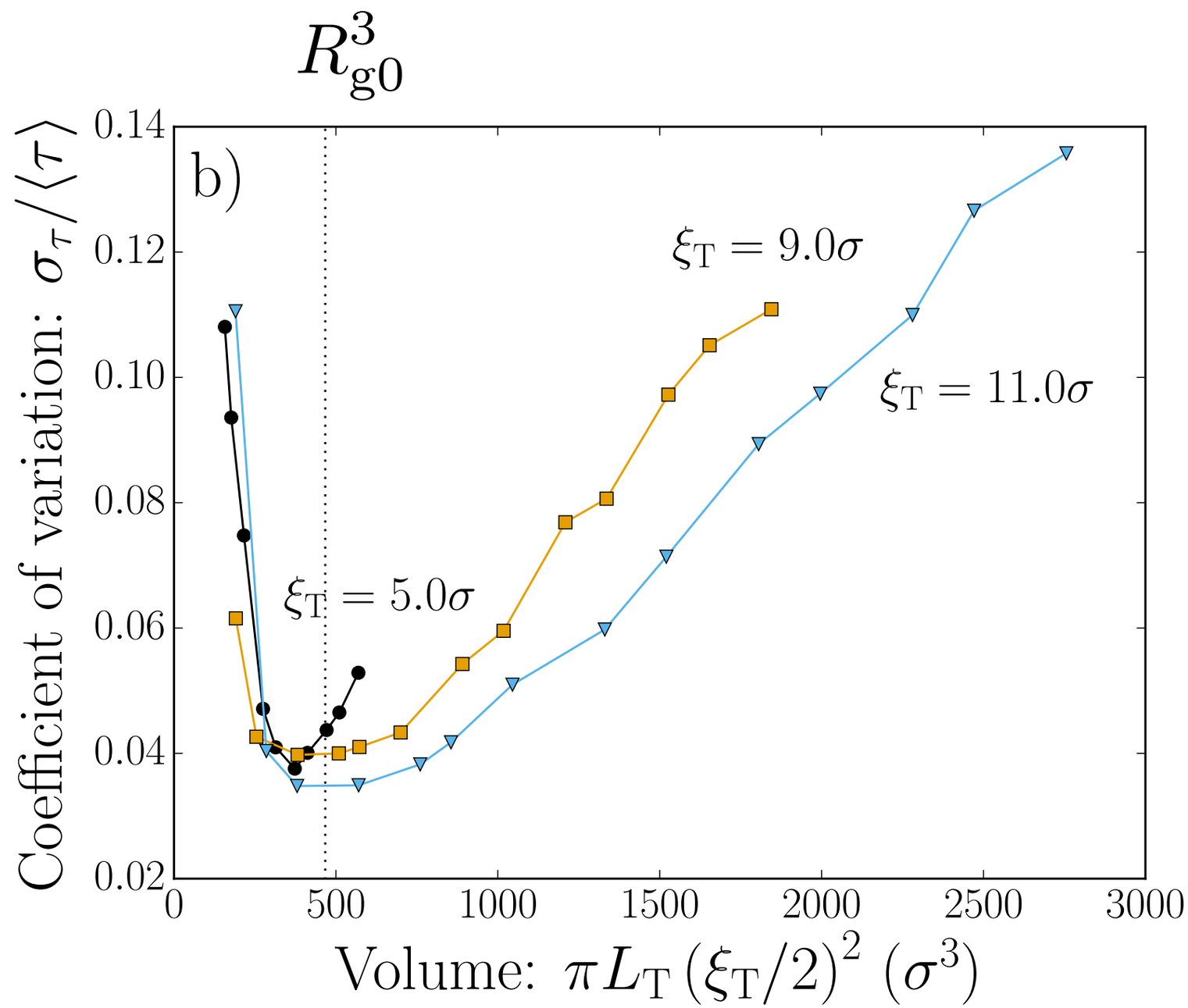


Moderate Tube size



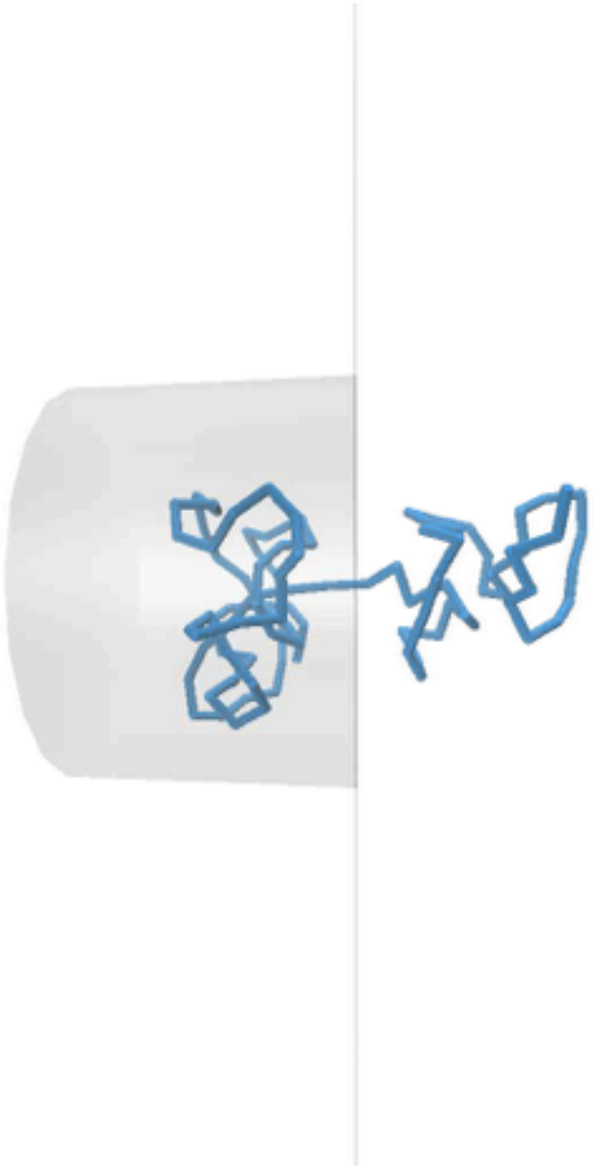
Reducing Volume



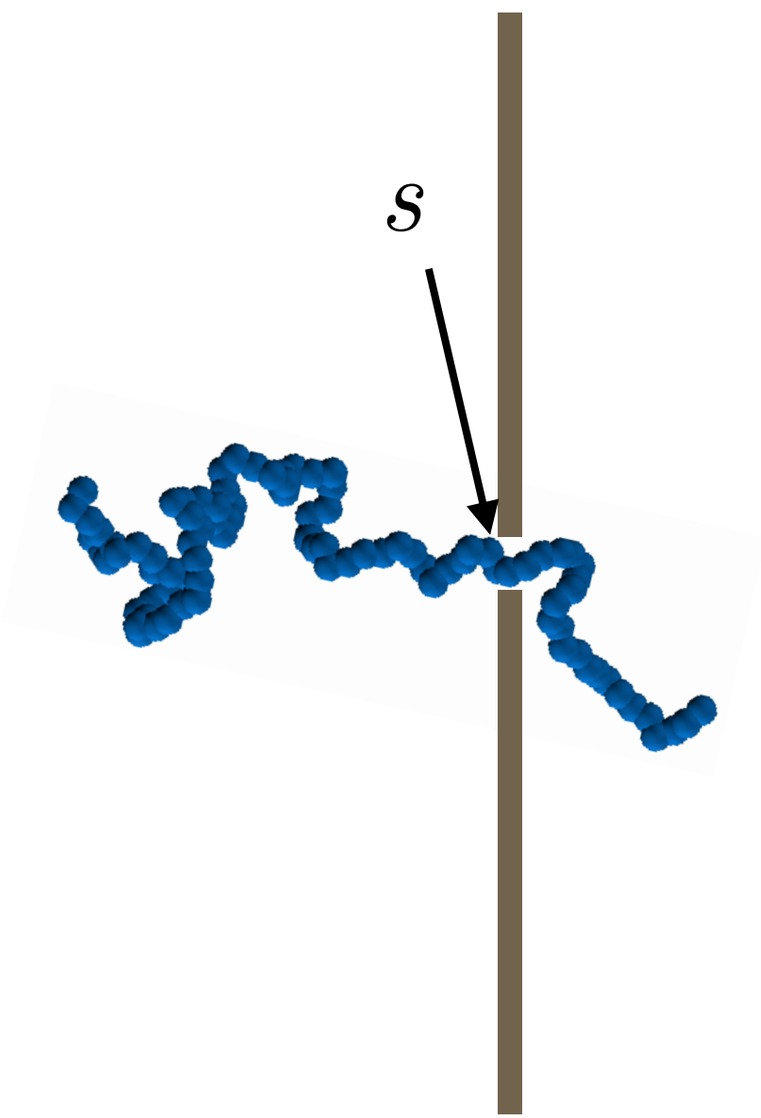


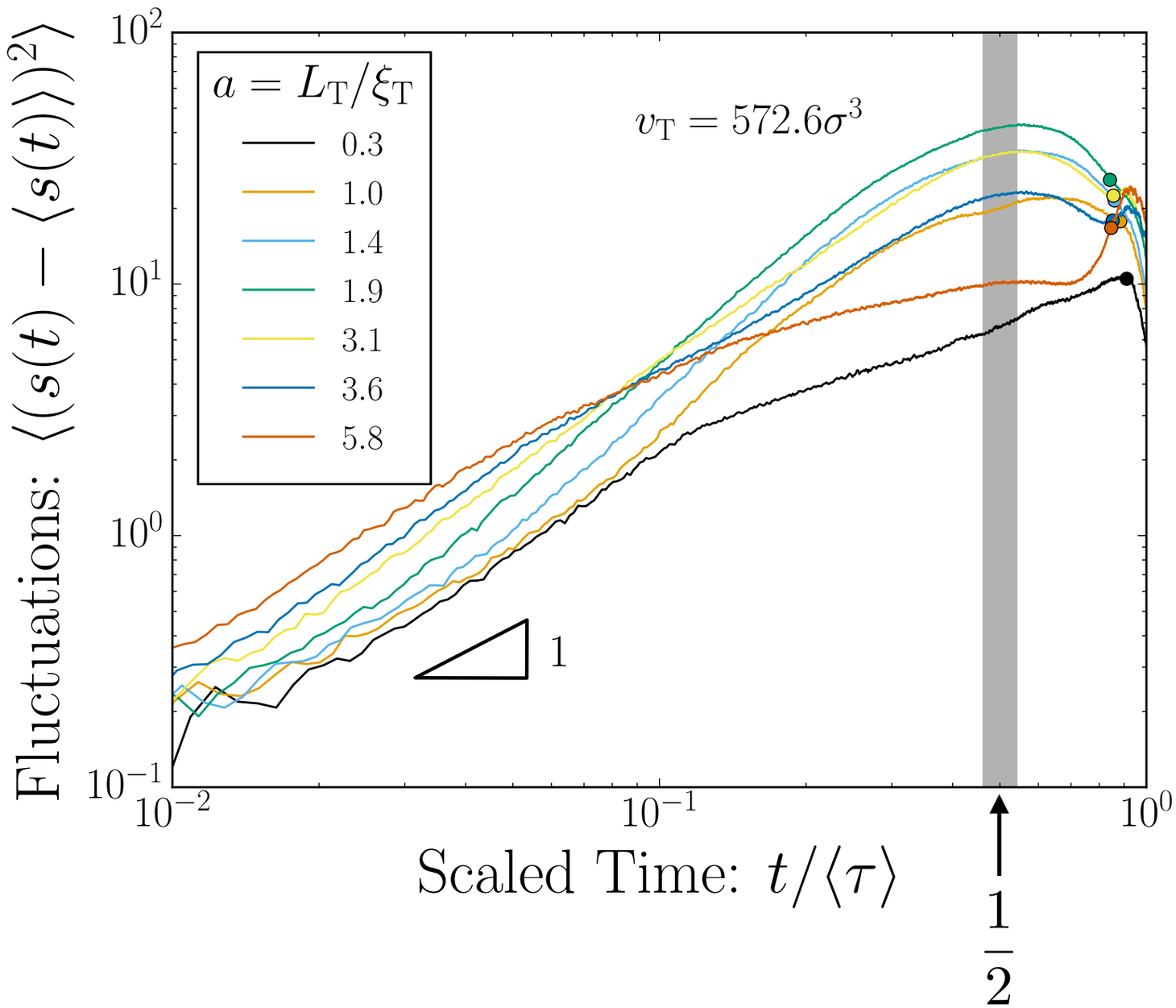
D. Sean, G.W. Slater, *J.Chem. Phys* (submitted)

Knots



Non-monotonic Fluctuations

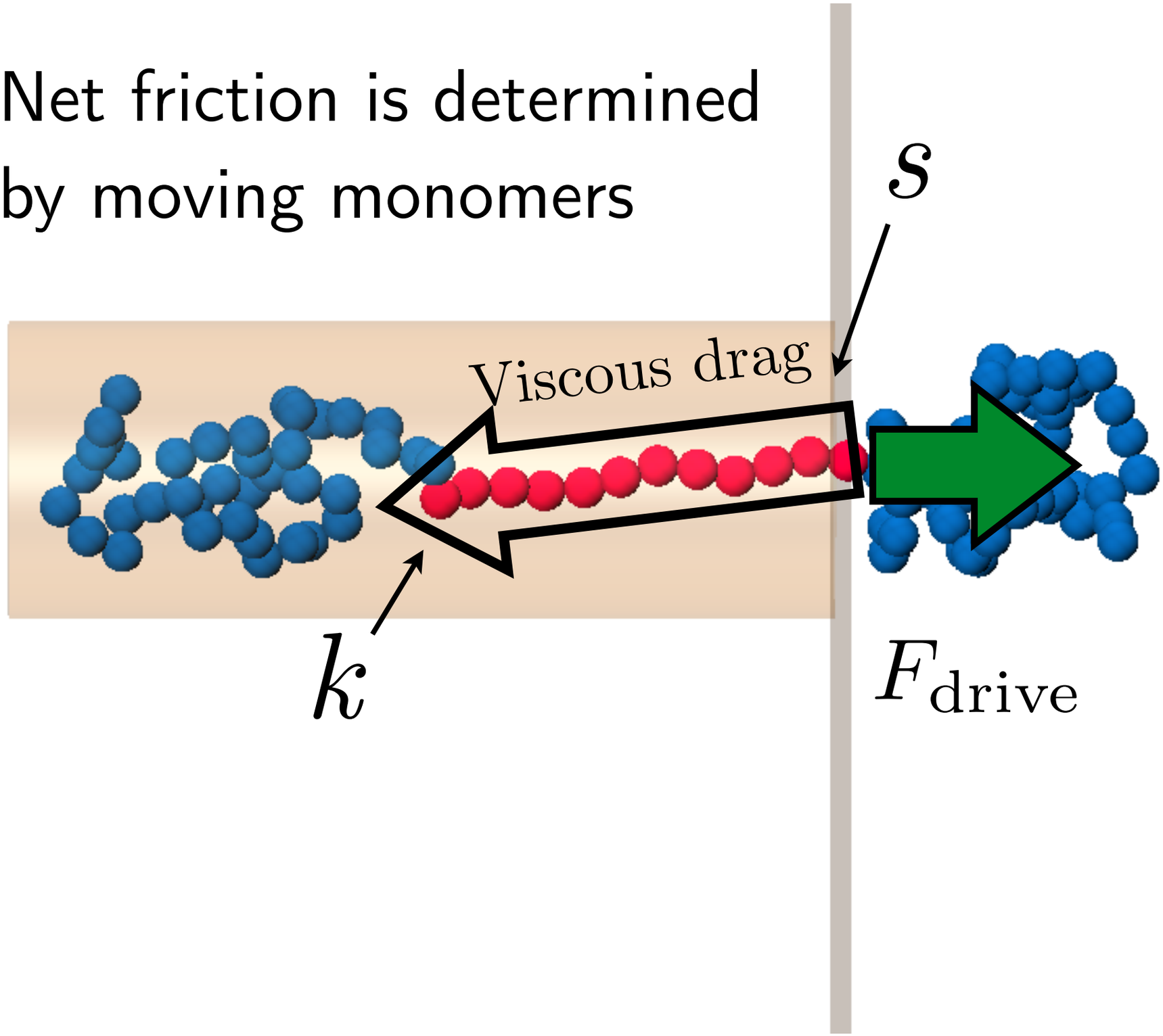




D. Sean, G.W. Slater, *J.Chem. Phys* (submitted)

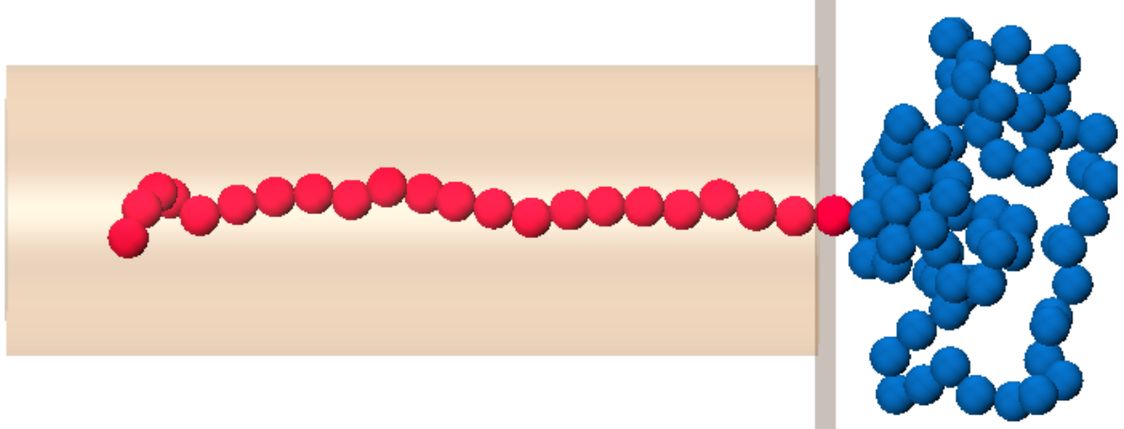
Tension Propagation Mechanics

Net friction is determined by moving monomers



Slowest state?

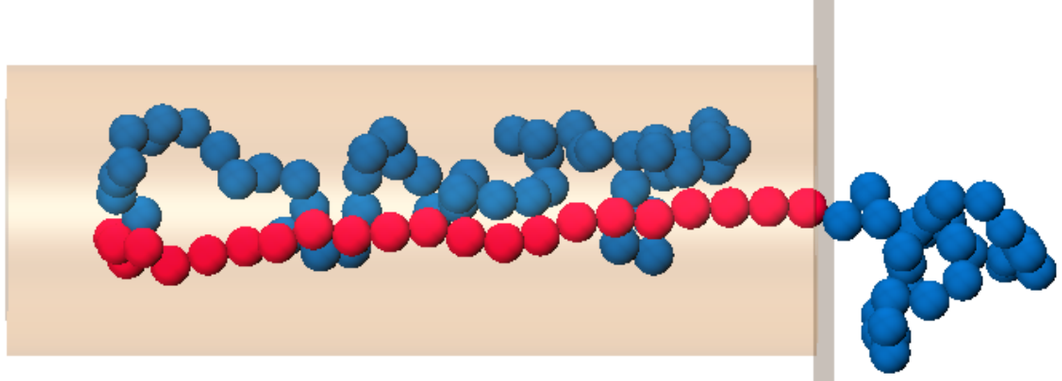
Blob-like



occurs later

(near the end)

Hairpin



occurs earlier

(about halfway)

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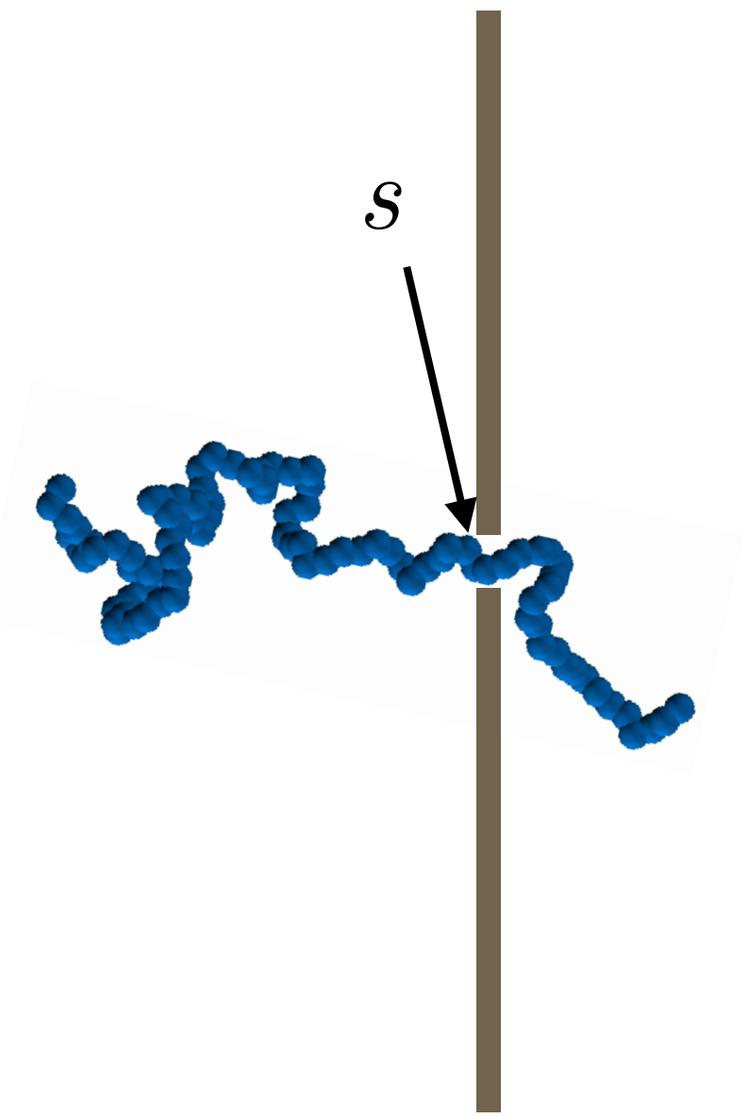
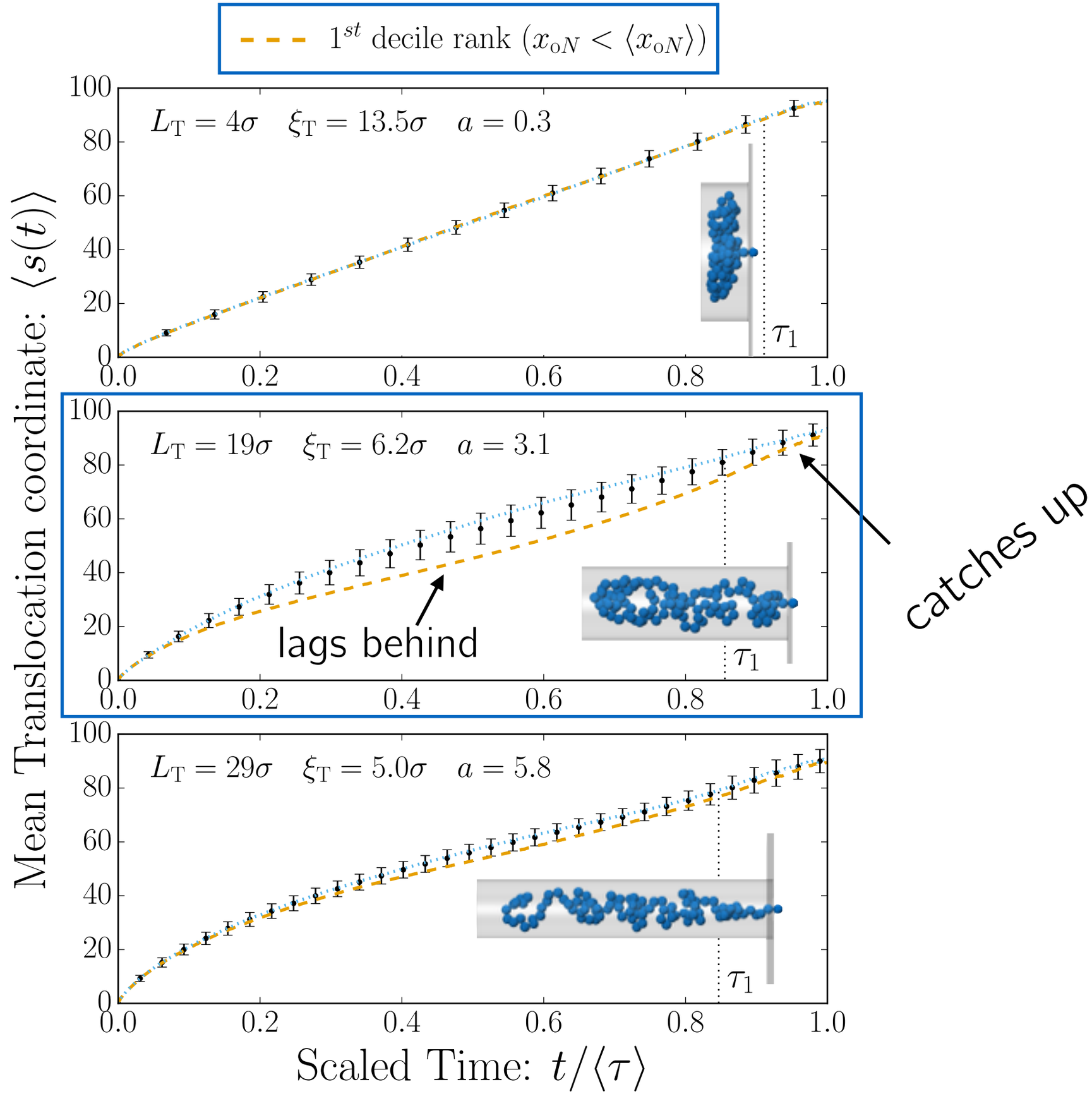

s


1st decile rank ($x_{oN} < \langle x_{oN} \rangle$)
$L_T = 4\sigma$ $\xi_T = 13.5\sigma$ $a = 0.3$
$L_T = 19\sigma$ $\xi_T = 6.2\sigma$ $a = 3.1$
$L_T = 29\sigma$ $\xi_T = 5.0\sigma$ $a = 5.8$
τ_1
lags behind
catches up
Mean Translocation coordinate: $\langle s(t) \rangle$
Scaled Time: $t/\langle \tau \rangle$