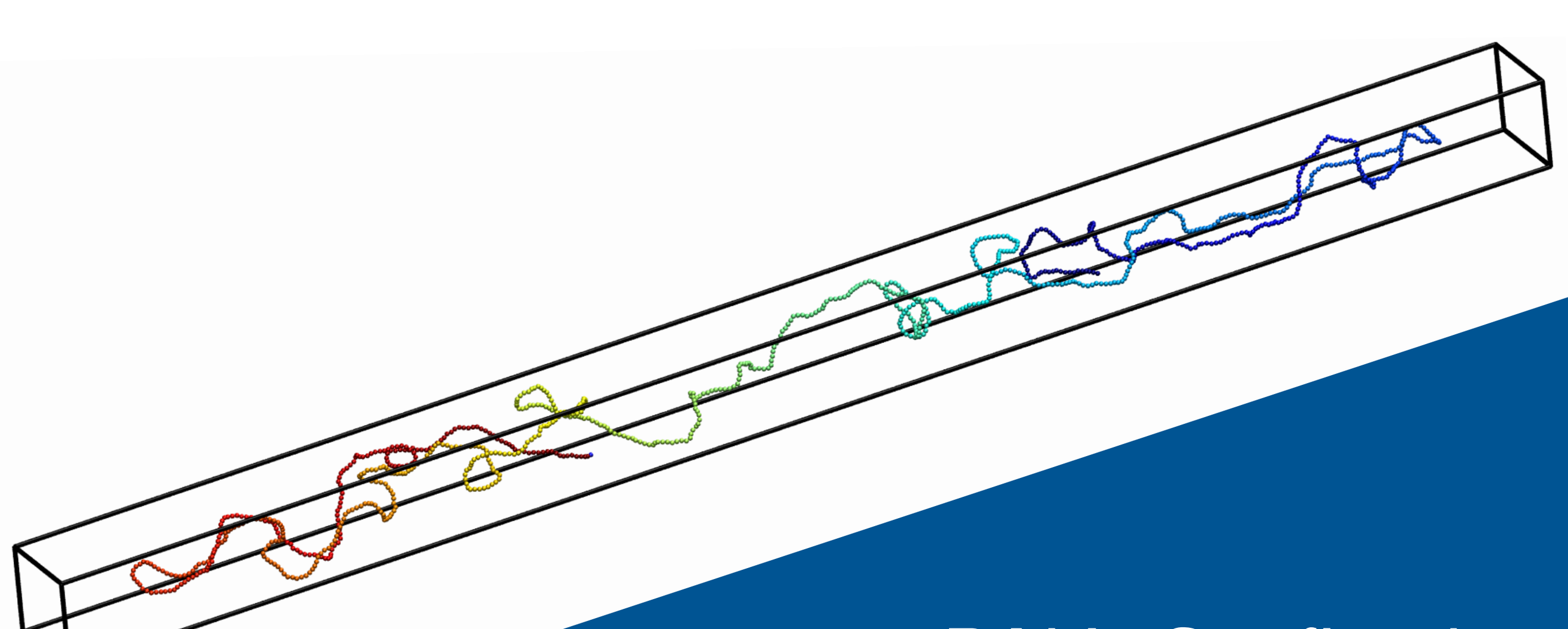


DNA Confined in Nanochannels and Nanoslits

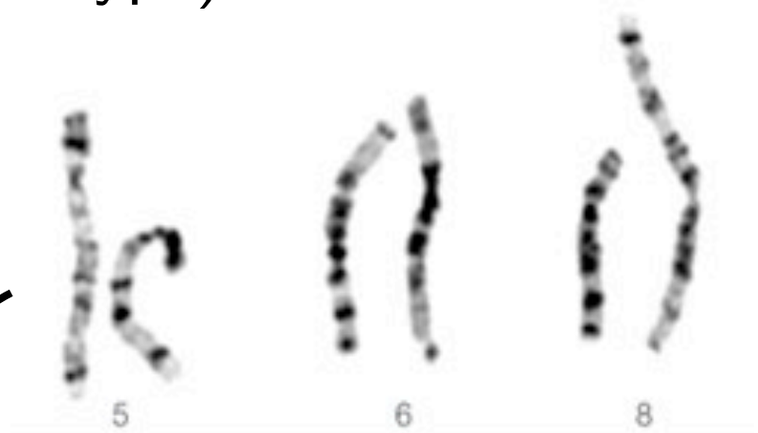
Douglas Tree

Dissertation Defense
University of Minnesota
Thursday May 1, 2014

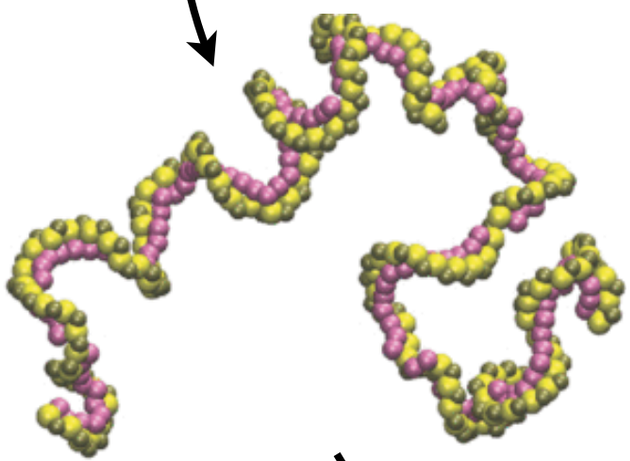
Connecting genotype to phenotype

Central Dogma in Molecular Biology

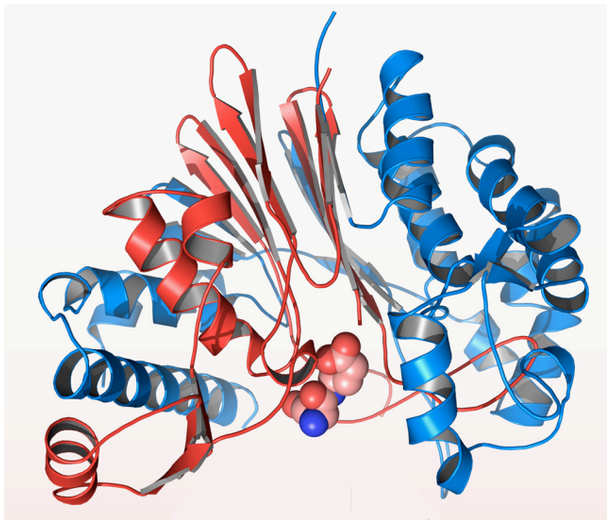
DNA (Genotype)



RNA



Protein



Applications (Phenotype)

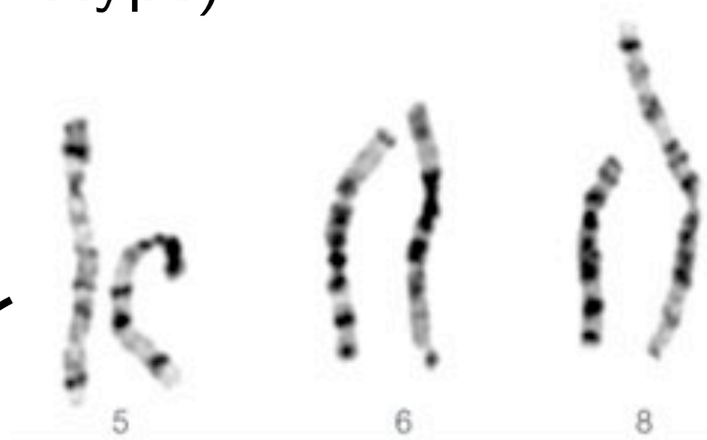
- Human Pathology
- Agriculture
- Environment

Speicher and Carter. *Nat. Rev. Genetics.* 6, 782 (2005)
Hinckley et al. *J. Chem. Phys.* 139, 144903 (2013)
http://en.wikipedia.org/wiki/Bacillus_anthracis

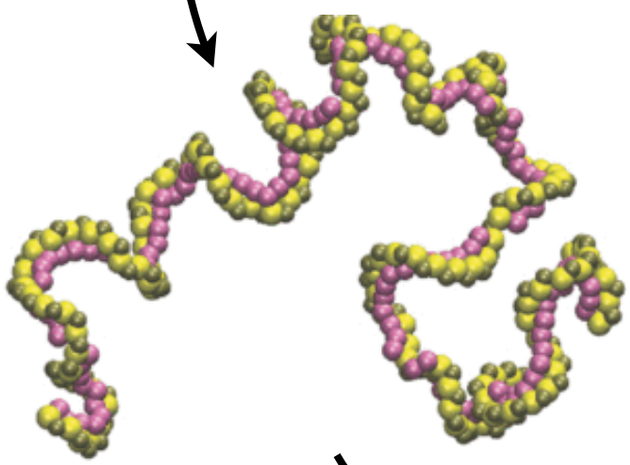
Connecting genotype to phenotype

Central Dogma in Molecular Biology

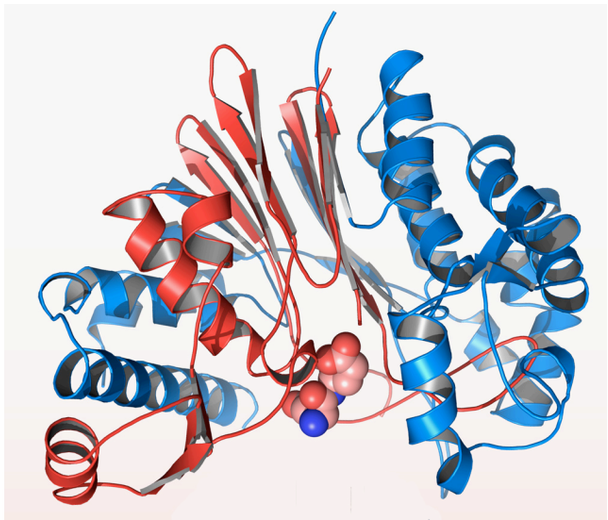
DNA (Genotype)



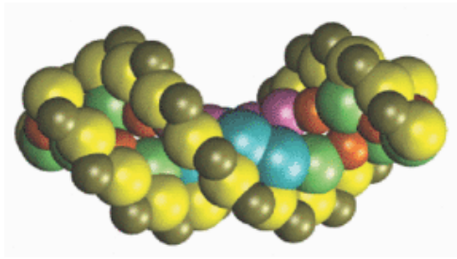
RNA



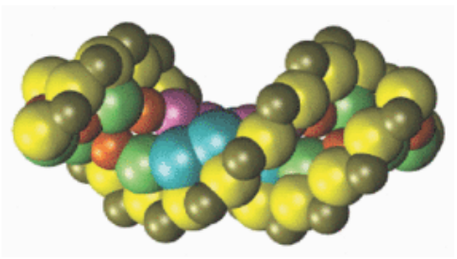
Protein



Genomic Variability



...ACTGACGA...



...ACCAGTGA...

Applications (Phenotype)

Human Pathology

Agriculture

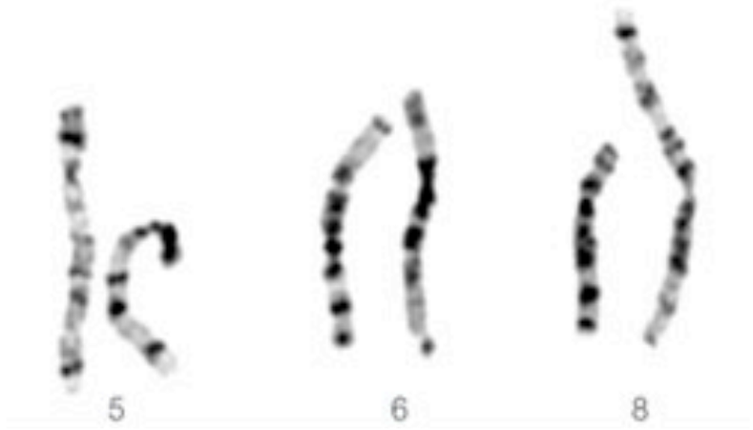
Environment

Speicher and Carter. *Nat. Rev. Genetics.* 6, 782 (2005)
Hinckley et al. *J. Chem. Phys.* 139, 144903 (2013)
http://en.wikipedia.org/wiki/Bacillus_anthracis

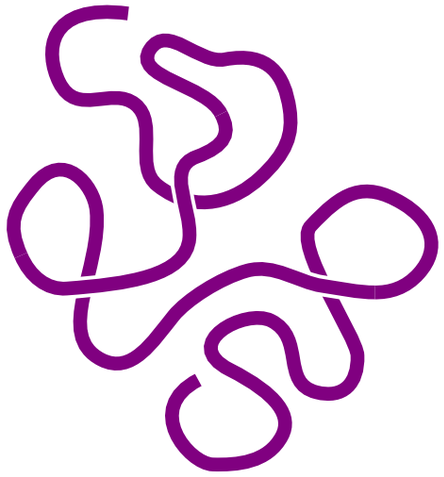
Genomic variability

Variability is a multi-scale phenomena

Chromosome

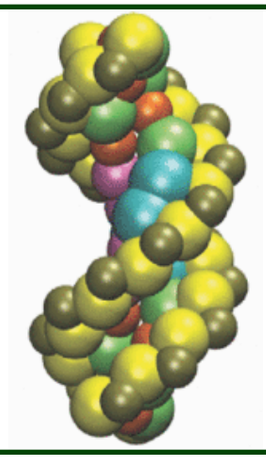


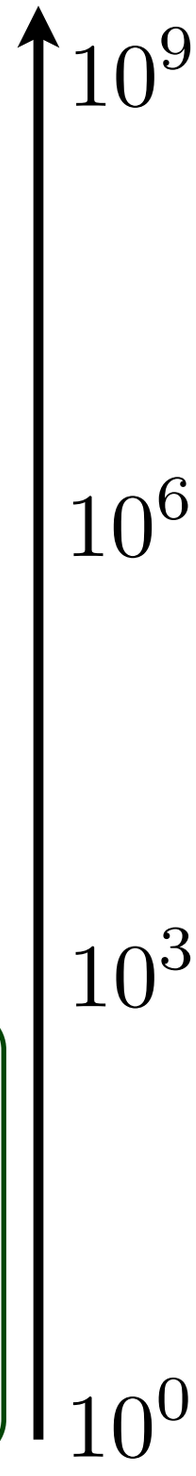
Gene



Sequencing

Nucleotide





Speicher and Carter. *Nat. Rev. Genetics.* 6, 782 (2005)
Hinckley et al. *J. Chem. Phys.* 139, 144903 (2013)
Levy-Sakin and Ebenstein. *Curr. Opin. Biotech.* 24, 690 (2013)

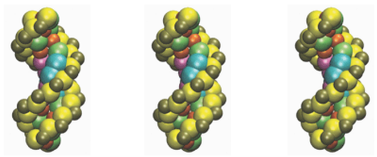
Genomic sequencing

Modern Sequencing

Chromosomal DNA

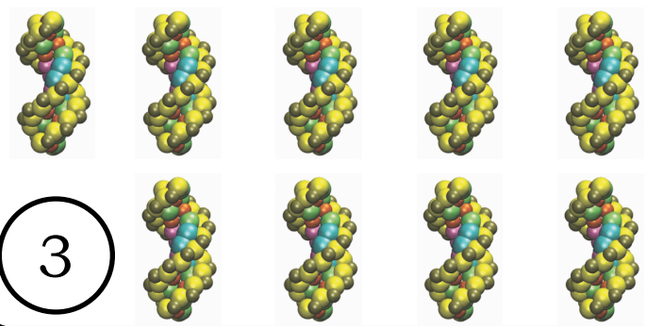
1

Shear into Fragments

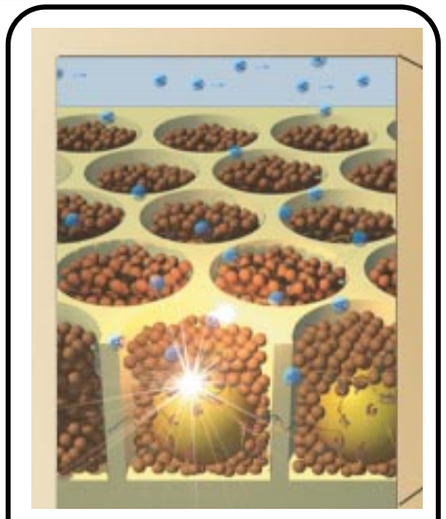


2

PCR Amplification



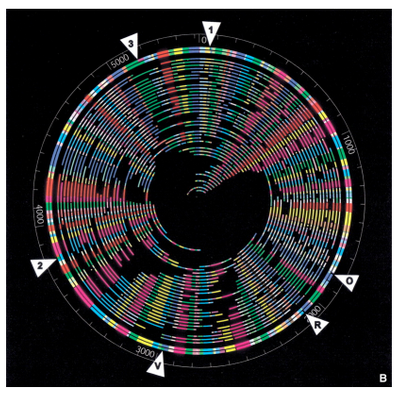
3



Fragment Sequencing

4

Sequence Assembly



5

Margulies et al. *Nature.* 437, 376 (2005)
Speicher and Carter. *Nat. Rev. Genetics.* 6, 782 (2005)
Hinckley et al. *J. Chem. Phys.* 139, 144903 (2013)
Zhou et al. *Appl. Environ. Microbiol.* 68, 6321 (2002)

Genomic sequencing

Modern Sequencing

Chromosomal DNA

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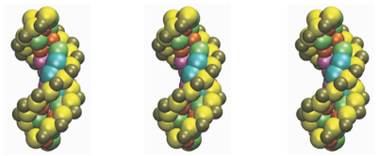
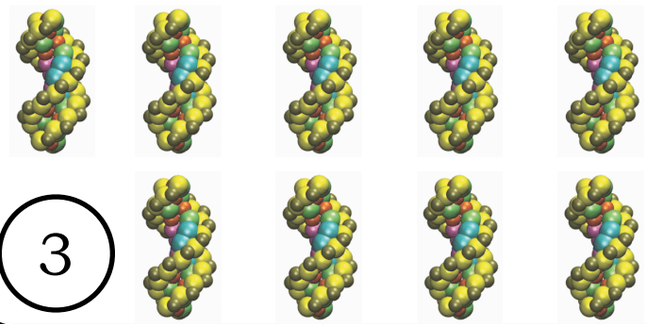
Shear into Fragments

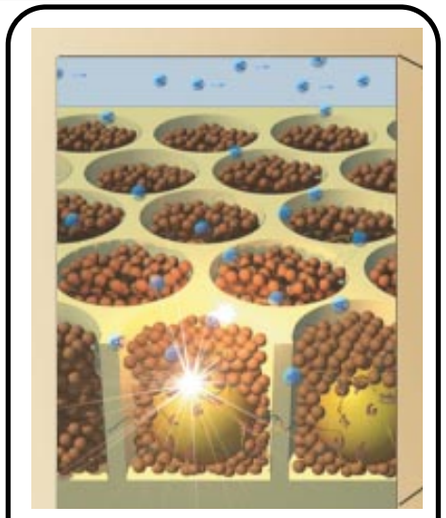
2



PCR Amplification



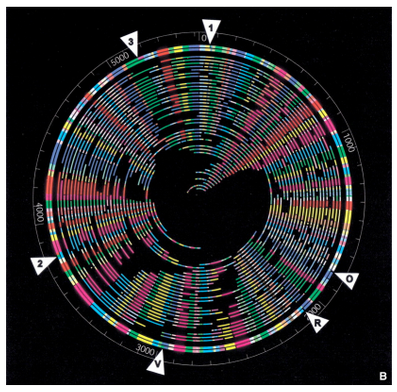
3



Fragment Sequencing

4

Sequence Assembly



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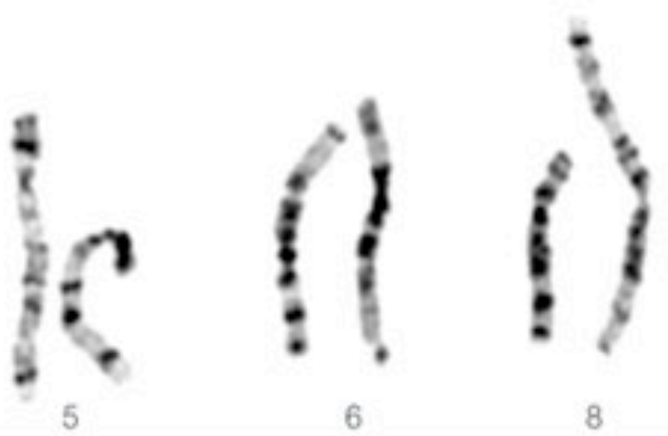
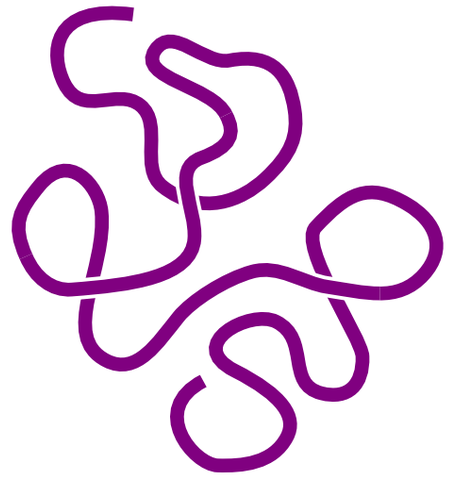
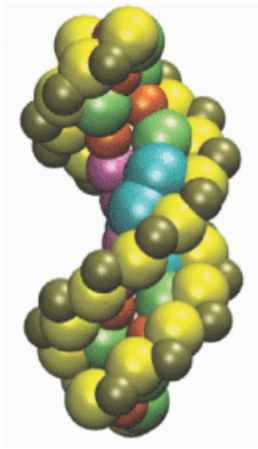
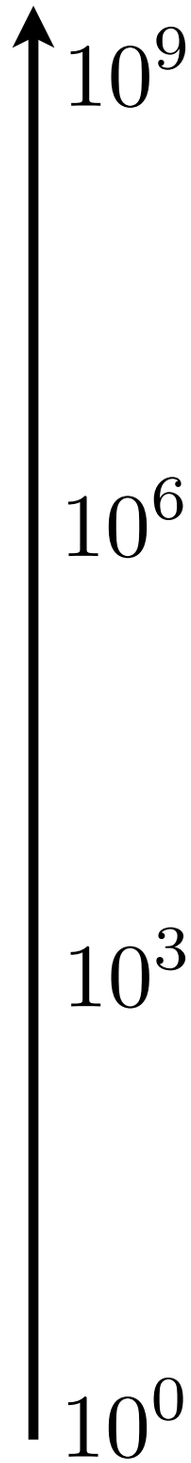




Sequencing Read Lengths





Margulies et al. *Nature.* 437, 376 (2005)
Speicher and Carter. *Nat. Rev. Genetics.* 6, 782 (2005)
Hinckley et al. *J. Chem. Phys.* 139, 144903 (2013)
Zhou et al. *Appl. Environ. Microbiol.* 68, 6321 (2002)

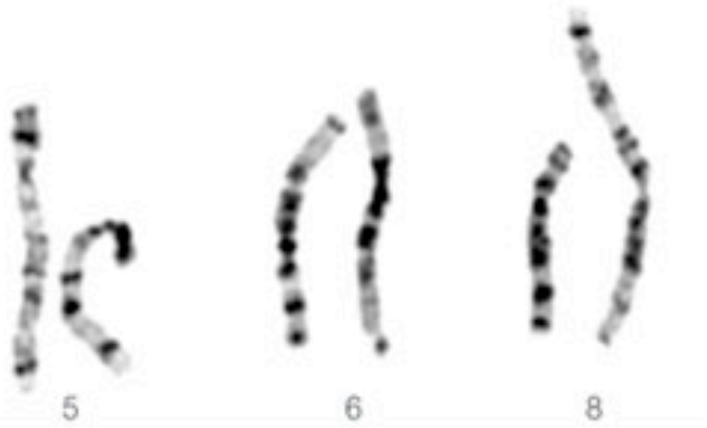
The genome puzzle

http://www.turbosquid.com/FullPreview/Index.cfm/ID/438424
http://www.gotchocolate.com/2011/02/1000-piece-chocolate-jigsaw-puzzle/

Genomic variability

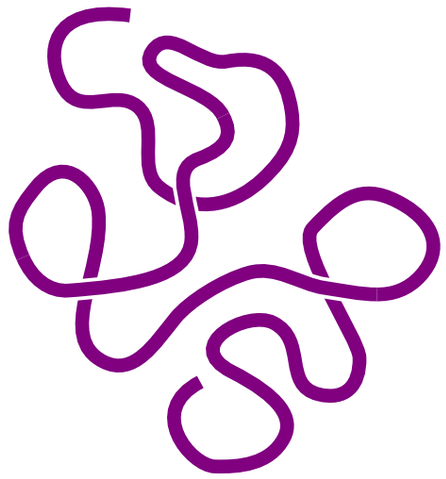
Variability is a multi-scale phenomena

Chromosome



Mapping

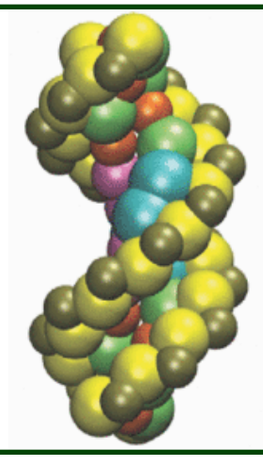
Gene



Sequencing Read Lengths

Sequencing

Nucleotide



10^9

10^6

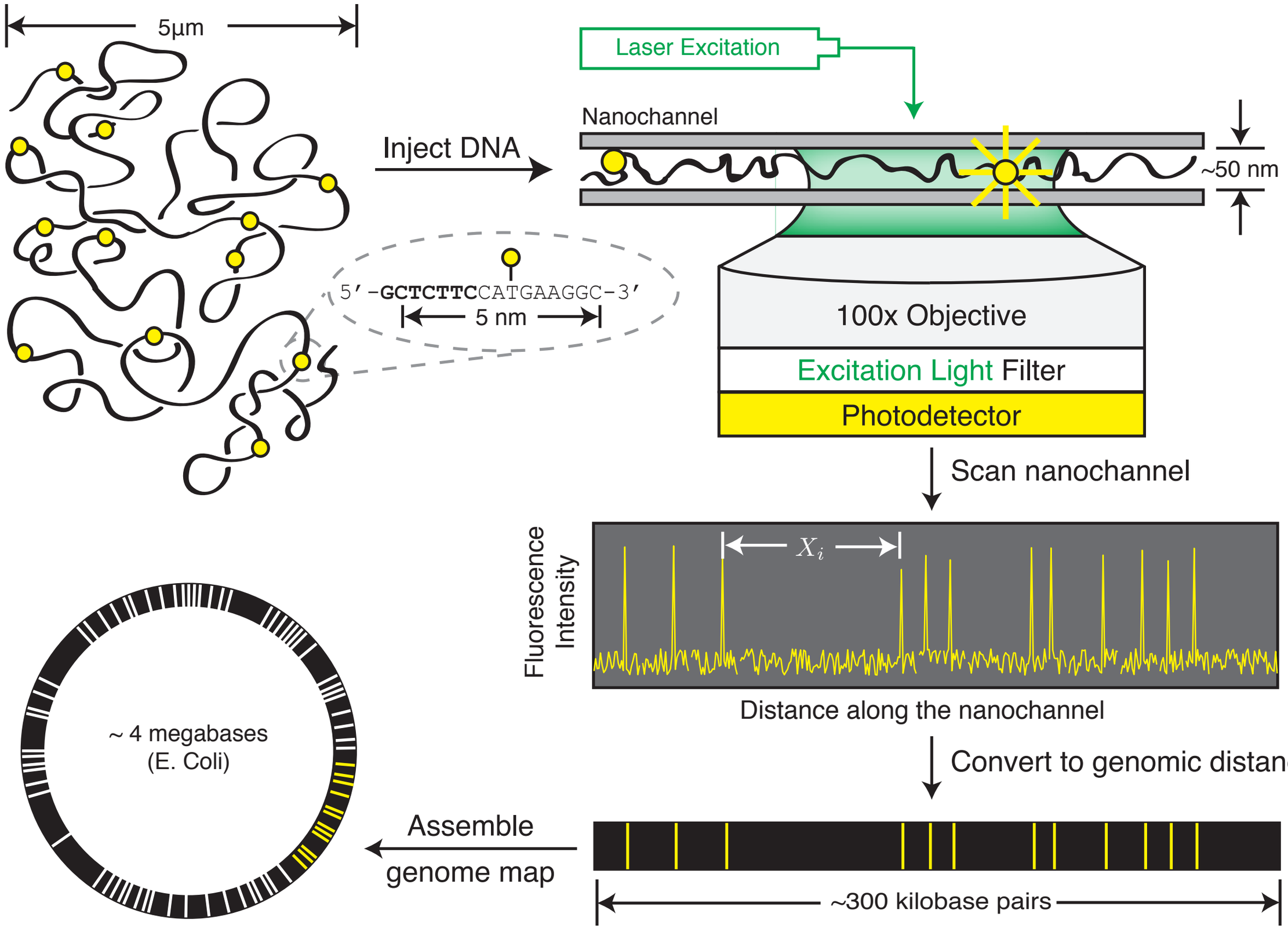
10^3

10^0

Base Pairs

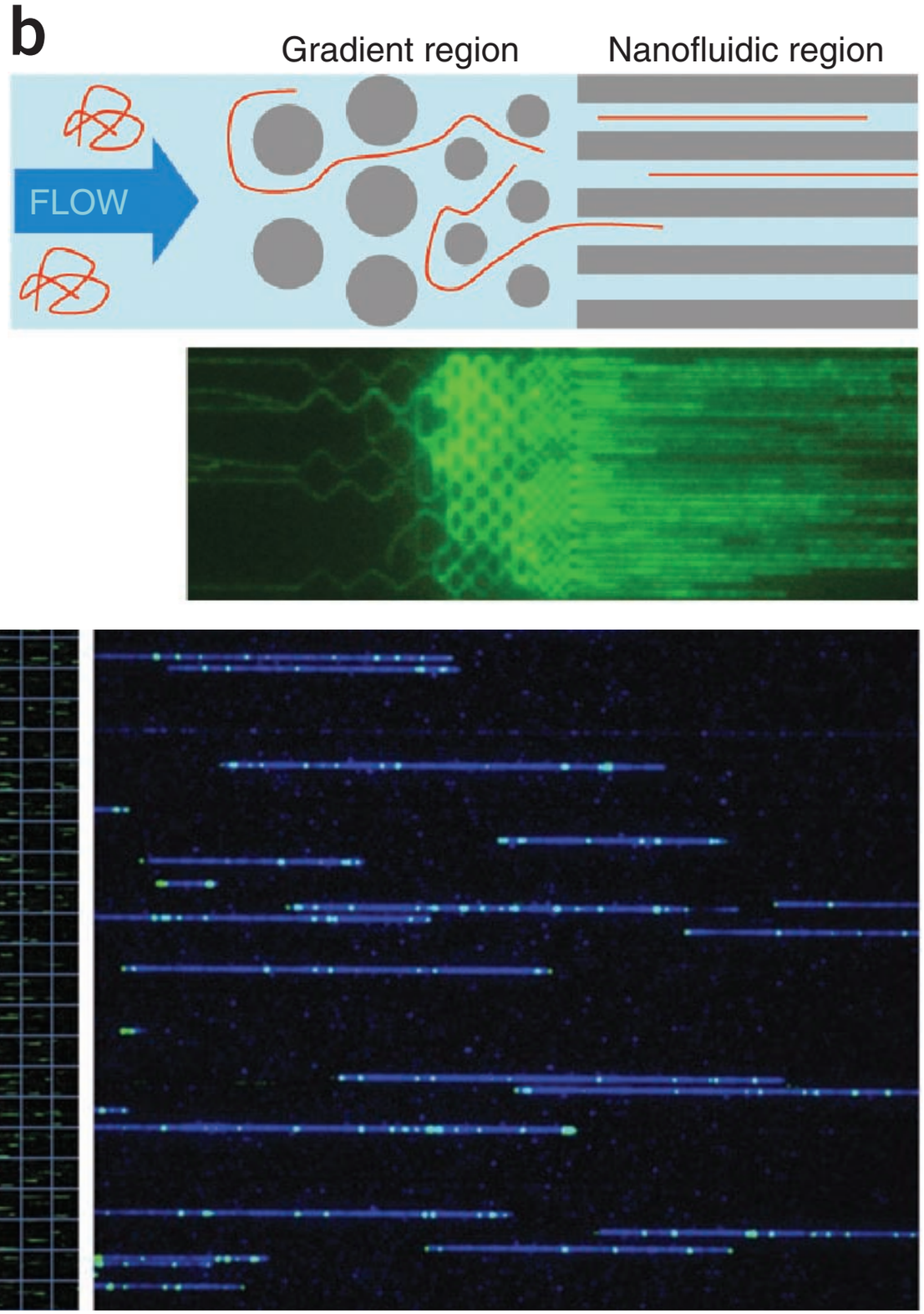
Speicher and Carter. *Nat. Rev. Genetics.* 6, 782 (2005)
Hinckley et al. *J. Chem. Phys.* 139, 144903 (2013)
Levy-Sakin and Ebenstein. *Curr. Opin. Biotech.* 24, 690 (2013)

Genomic mapping



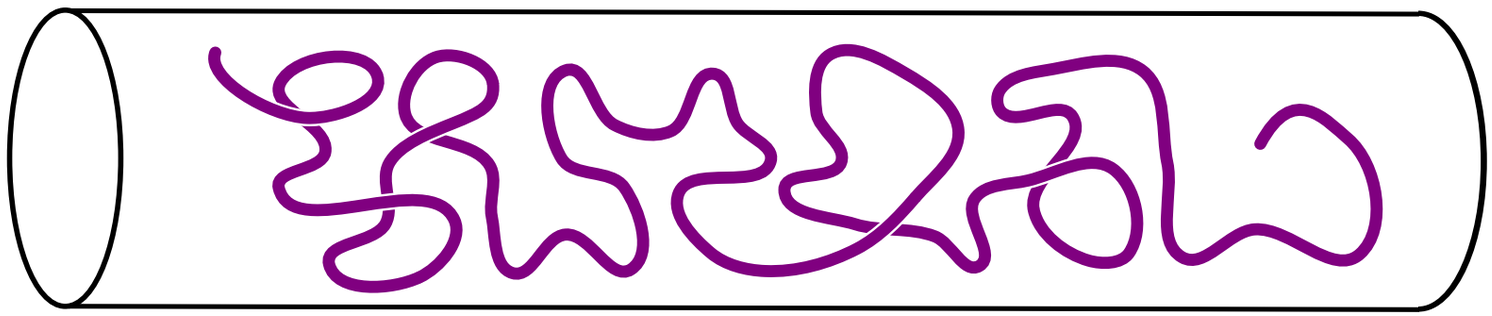
DNA linearization by confinement

BIONANO GENOMICS



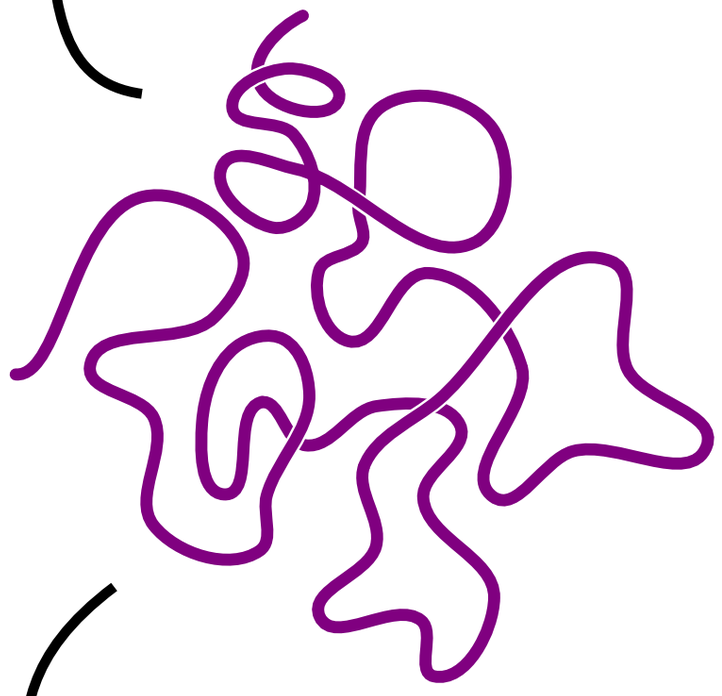
Lam et al., *Nat. Biotech.* 30, 771 (2012)

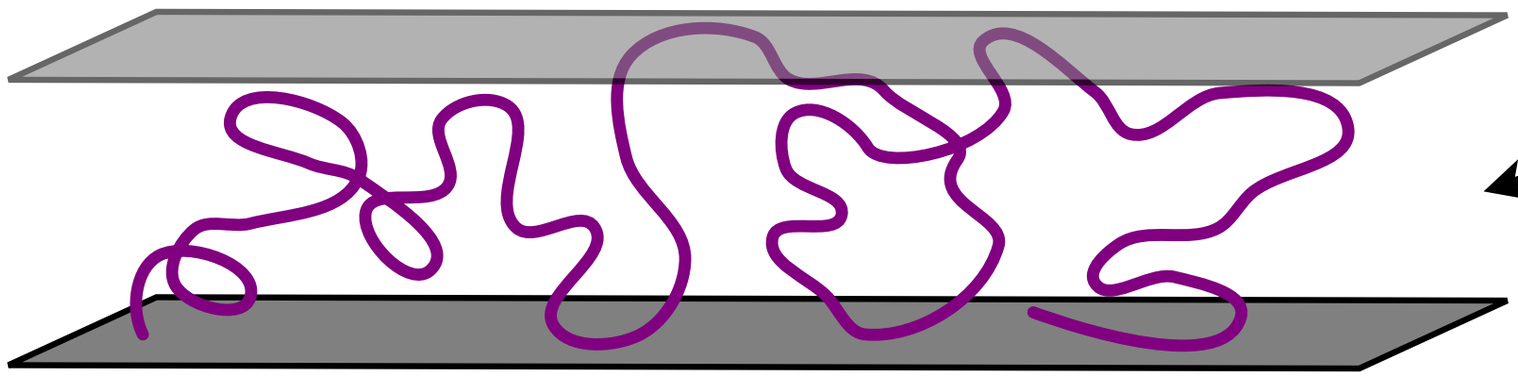
DNA confinement is complicated



Nanochannel

- Polymer Physics
- Hydrodynamics
- Electrostatics
- Geometry
- Surface Chemistry





Nanoslit

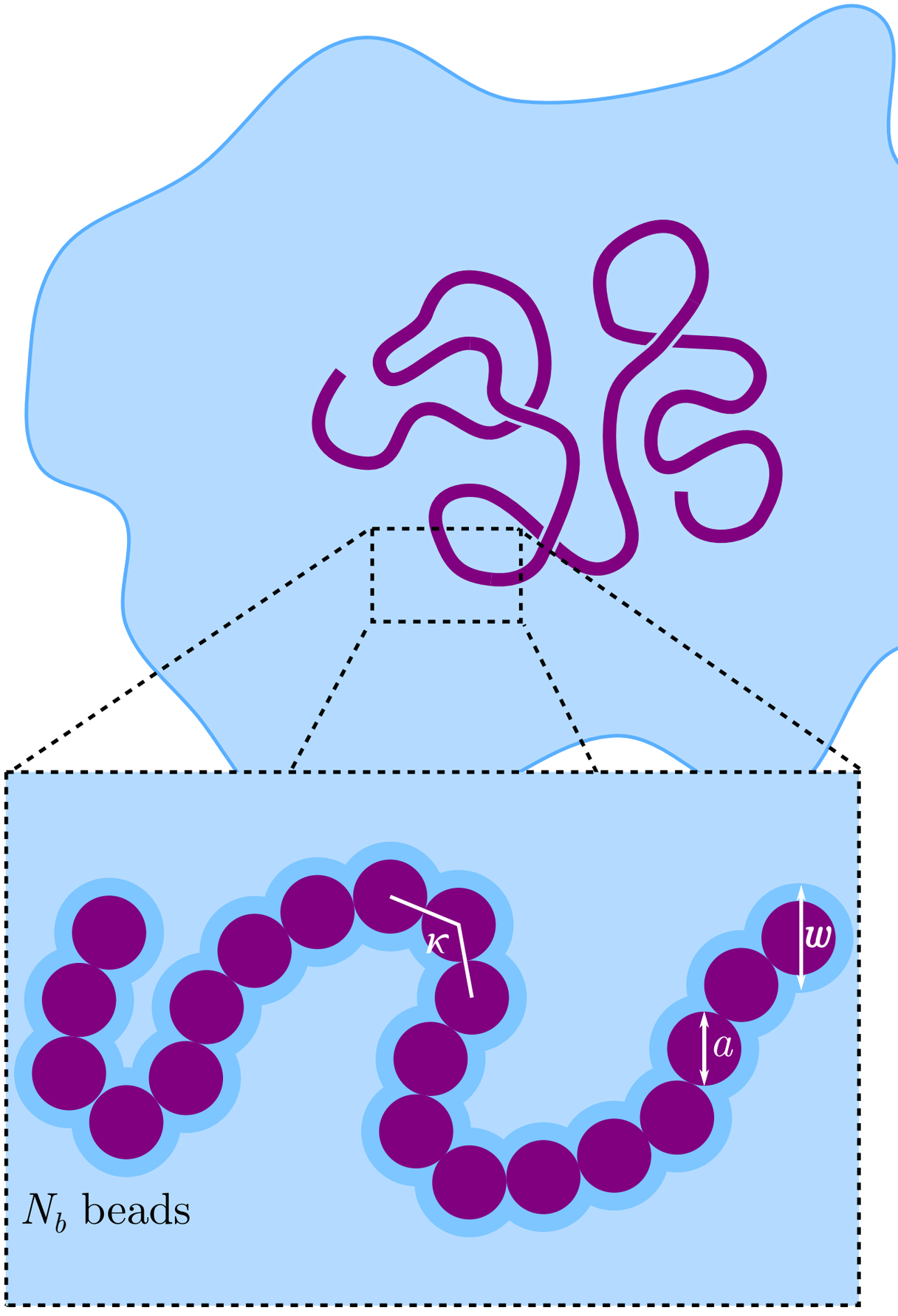
A Numerical Model

DNA as a wormlike chain:

- sequence independent
- locally stiff
- short-range excluded volume interactions
- neutral polymer

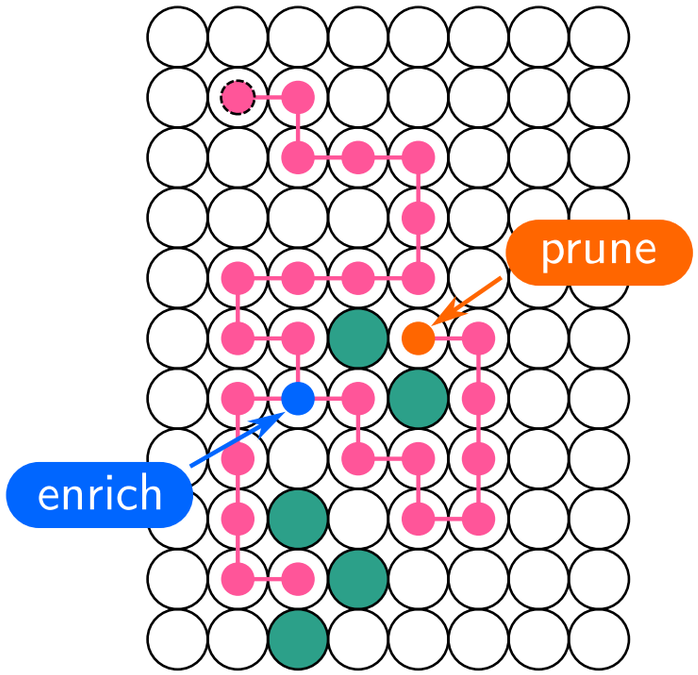
Appropriate length scale:

- Small enough to model confinement
- Large enough to reach experimental molecular weights

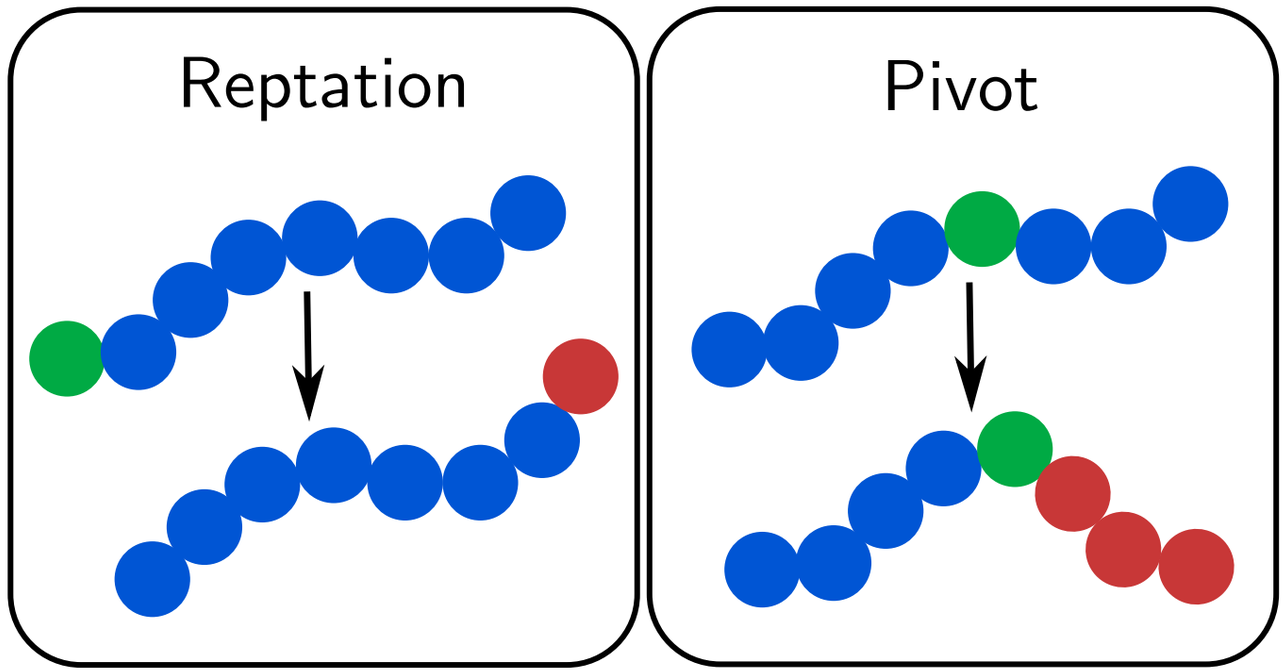


Advanced Monte Carlo Simulations

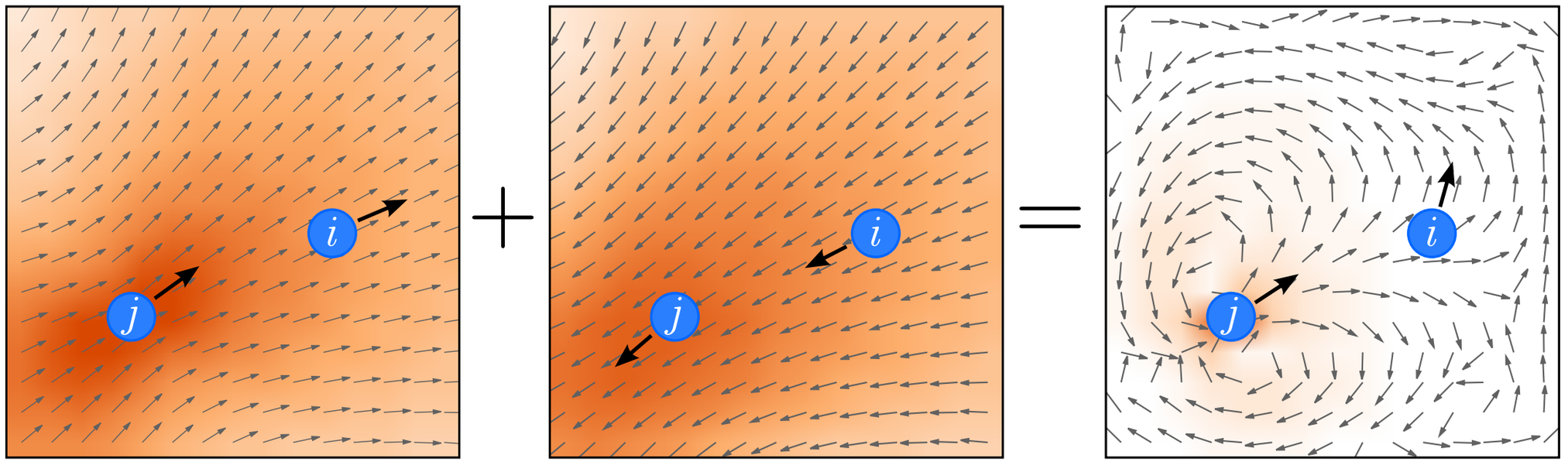
(a) PERM



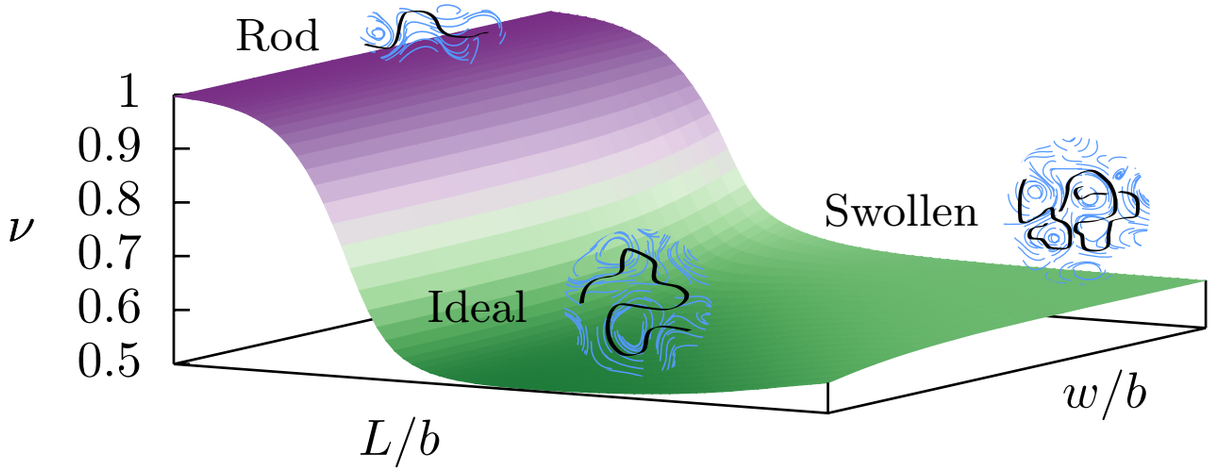
(b) Metropolis



CFD for Stokes Hydrodynamics

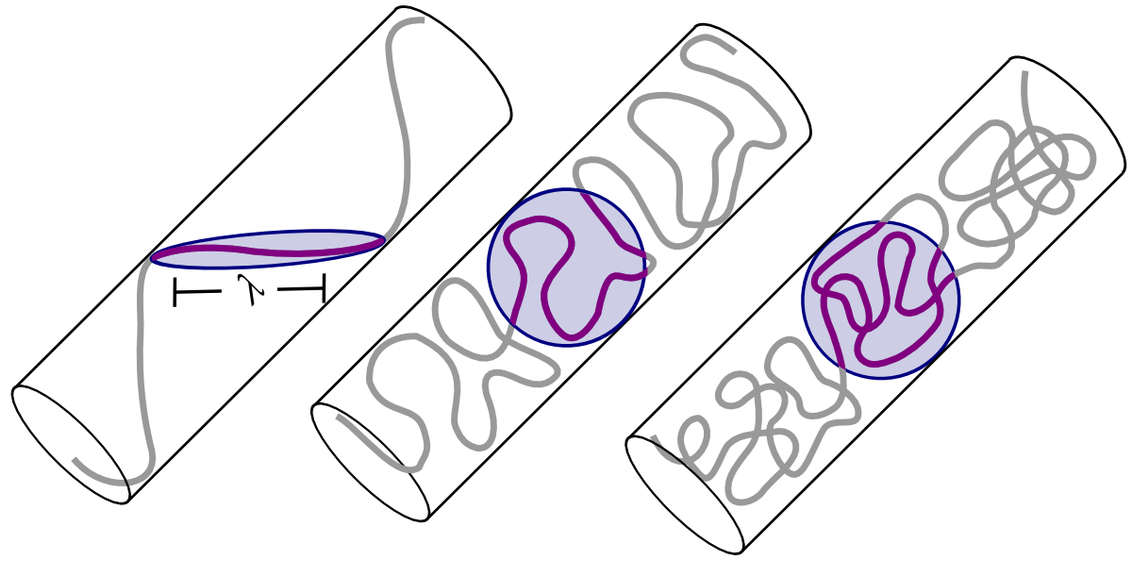


DNA in Free Solution



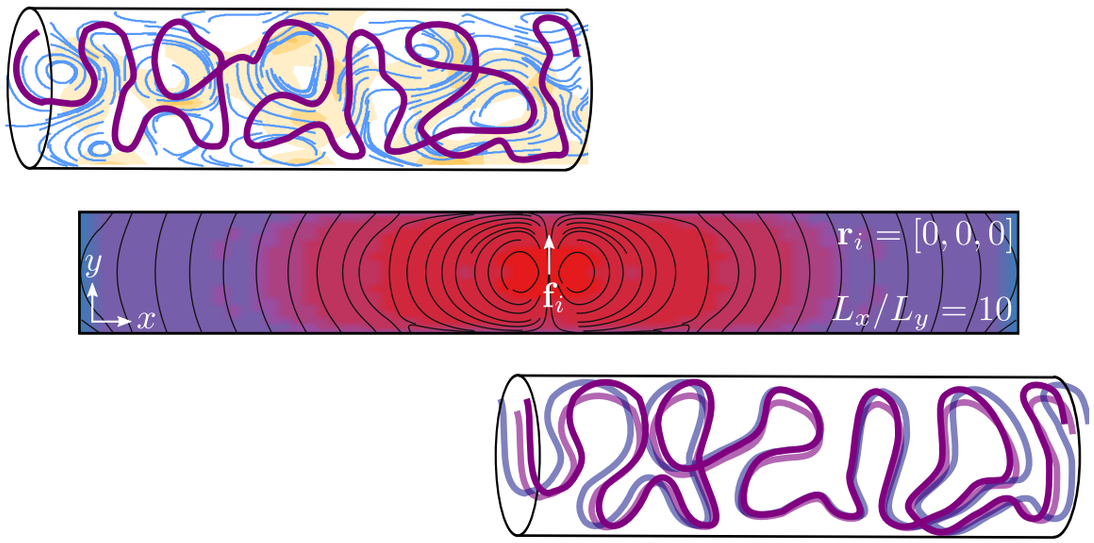
Tree et al. *Macromolecules* 46, 8369 (2013)

Regimes of Confined DNA



Tree et al. *Phys. Rev. Lett.* 110, 208103 (2013)

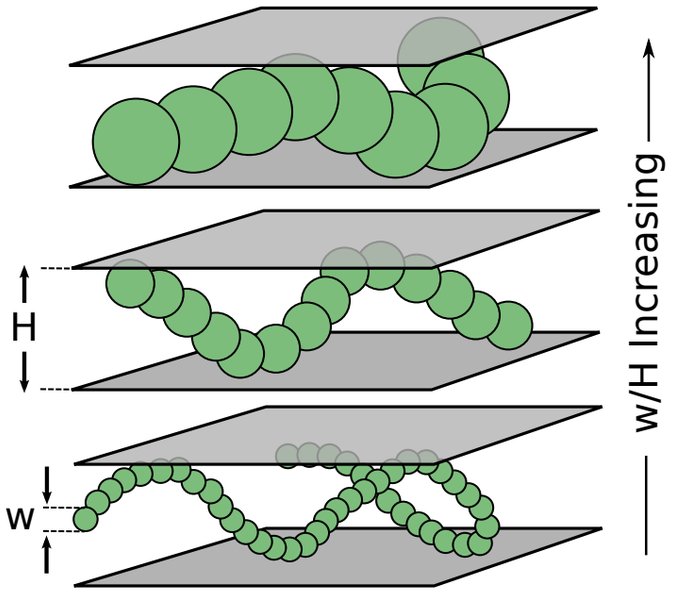
Dynamics of Confined DNA



Tree et al. *Phys. Rev. Lett.* 108, 228105 (2012)

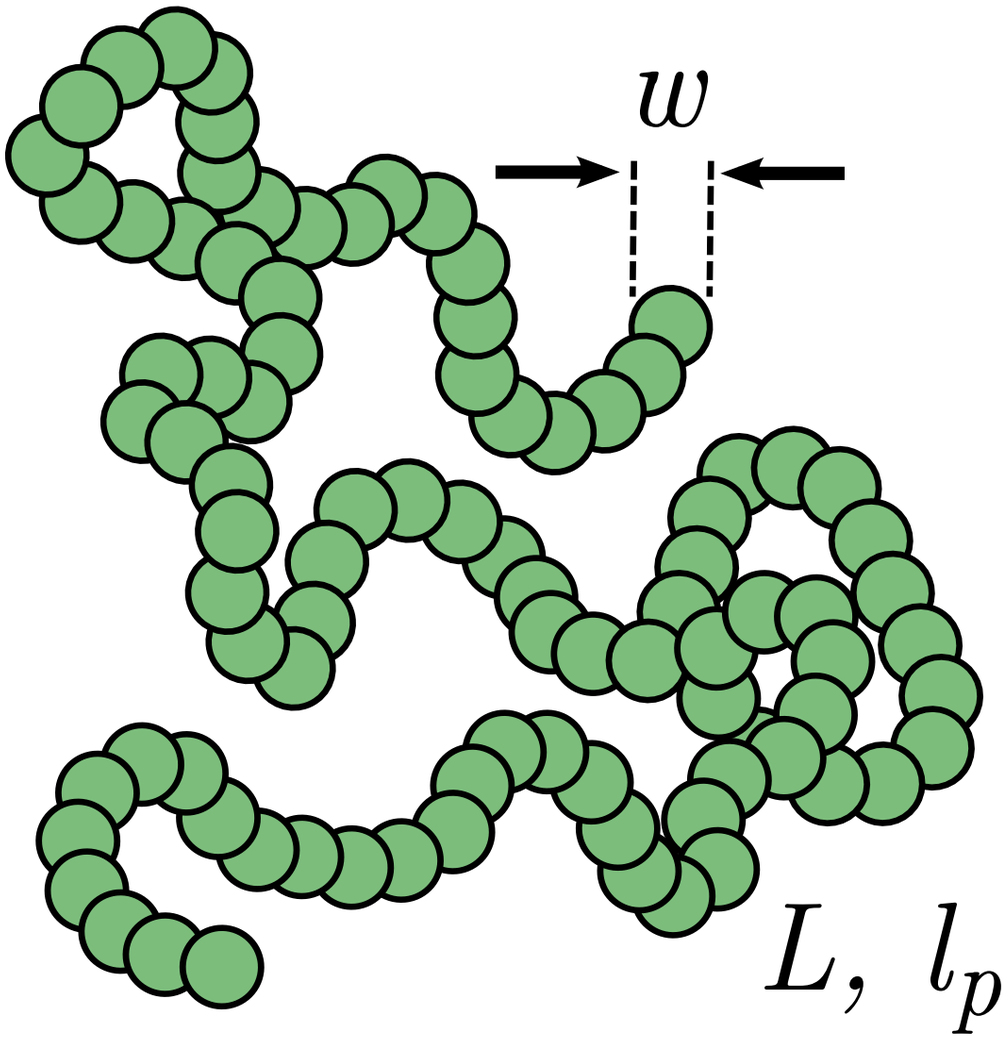
Tree et al. *Biomicrofluidics* 7, 054118 (2013)

DNA in Slits

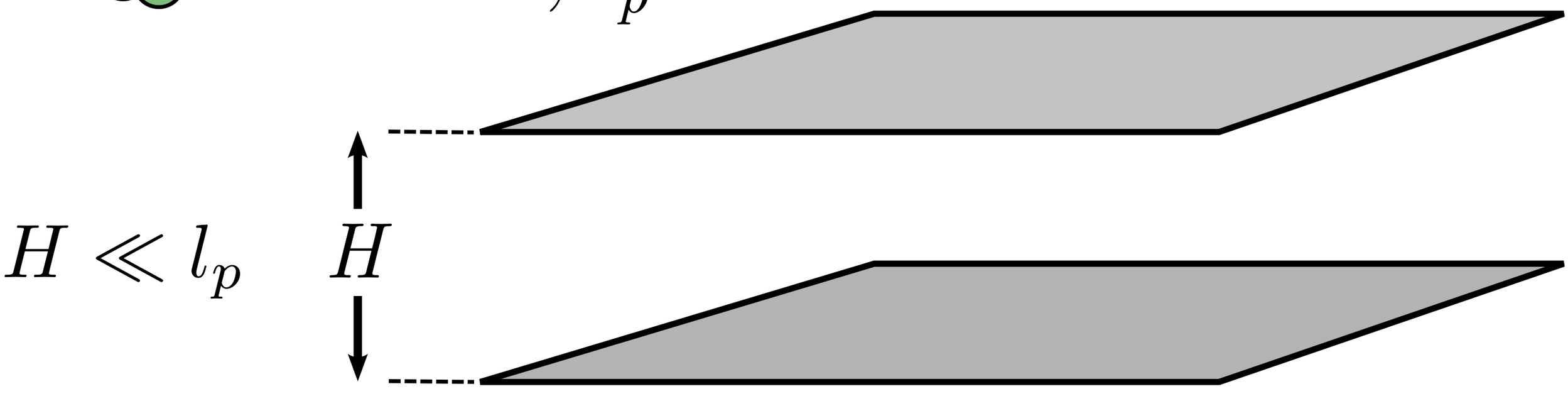


Tree et al. *In Review*

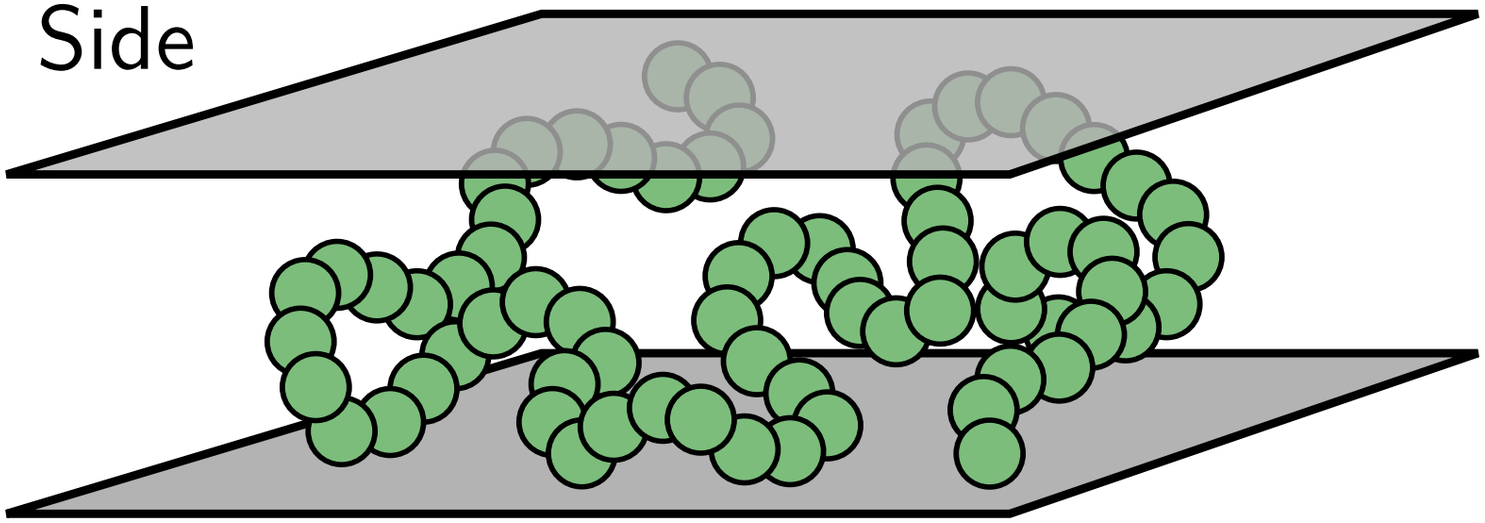
DNA strongly confined in a slit



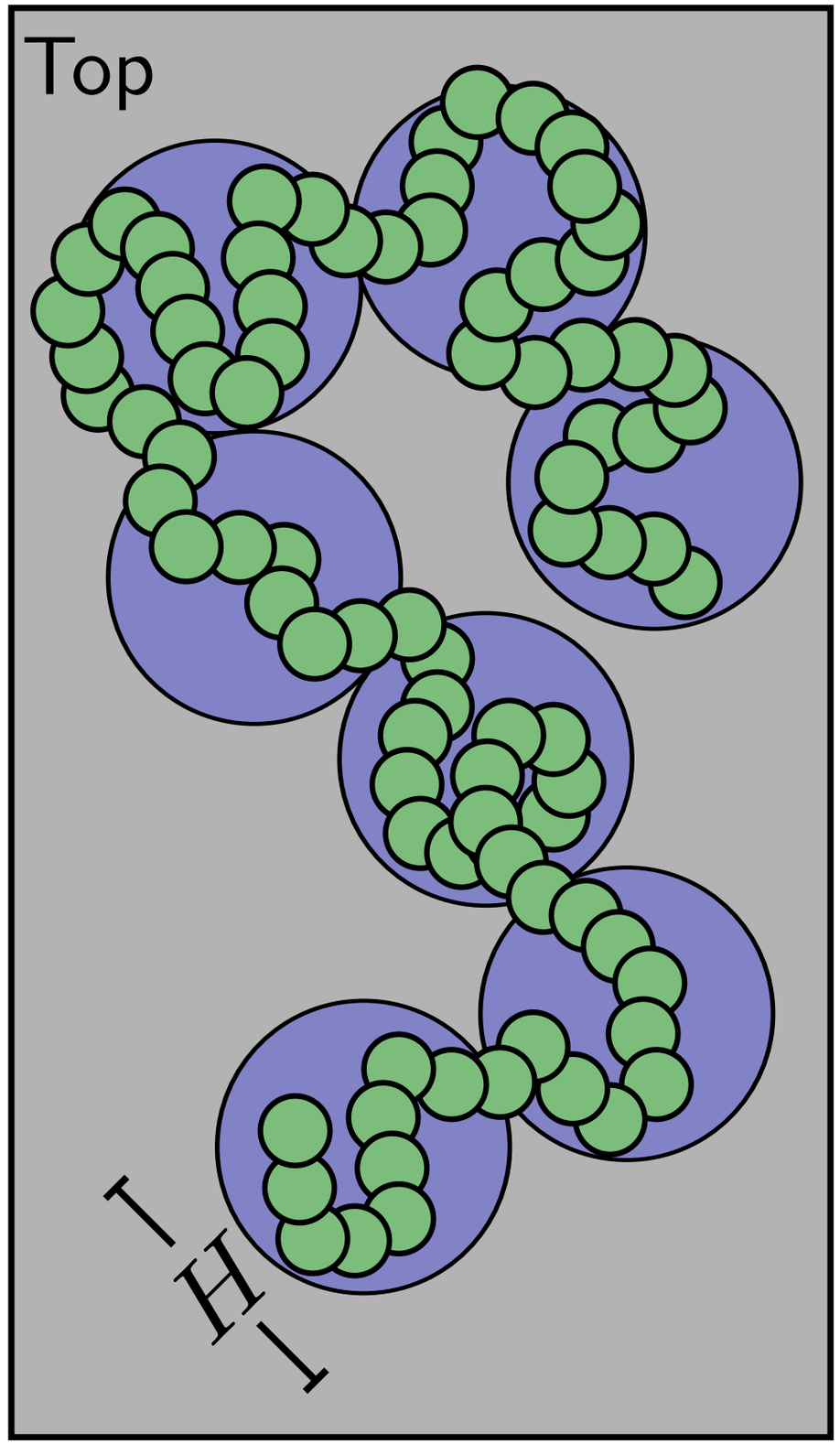
What are the equilibrium properties of a wormlike chain confined in a slit much smaller than its persistence length?



Weakly confined chains



$$H \gg l_p$$



Blob Theory (de Gennes)

$$R \approx L^{\frac{3}{4}} l_p{}^{\frac{1}{4}} \left(\frac{w}{H}\right)^{\frac{1}{4}}$$

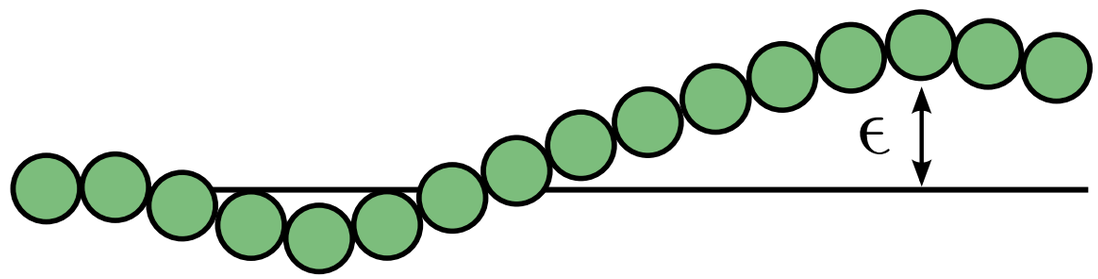
$$F \approx k_B T L l_p H^{-\frac{5}{3}} w^{-\frac{1}{3}}$$

Daoud, M. and de Gennes, P.-G. *J. Phys. France* 38, 85 (1977)

Deflection Segments (Odijk)

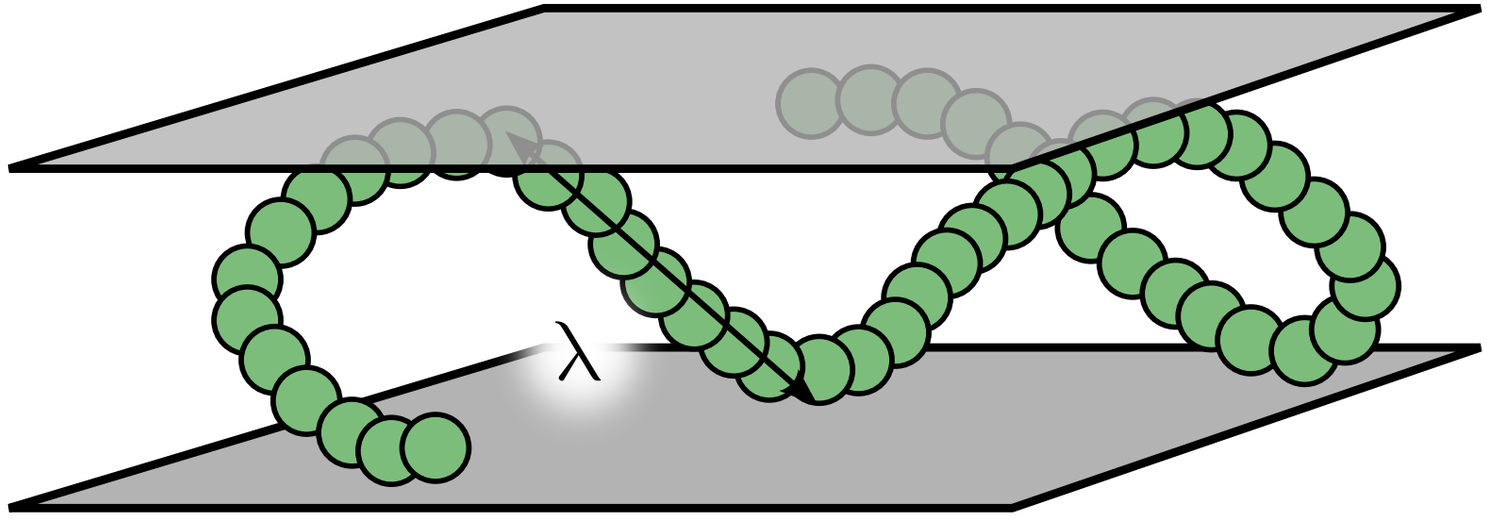
Mean square deviation
of a free solution WLC

$$\langle \epsilon^2 \rangle \approx \frac{\lambda^3}{l_p}$$



Confinement
Length Scale

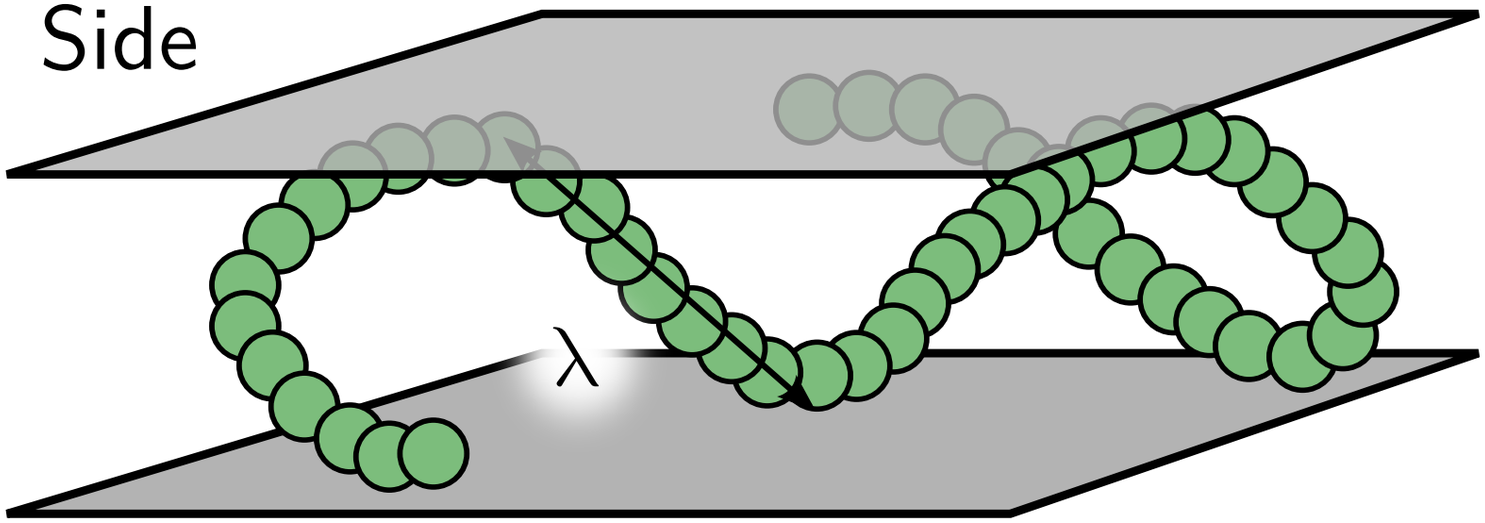
$$\langle \epsilon^2 \rangle \approx H^2$$

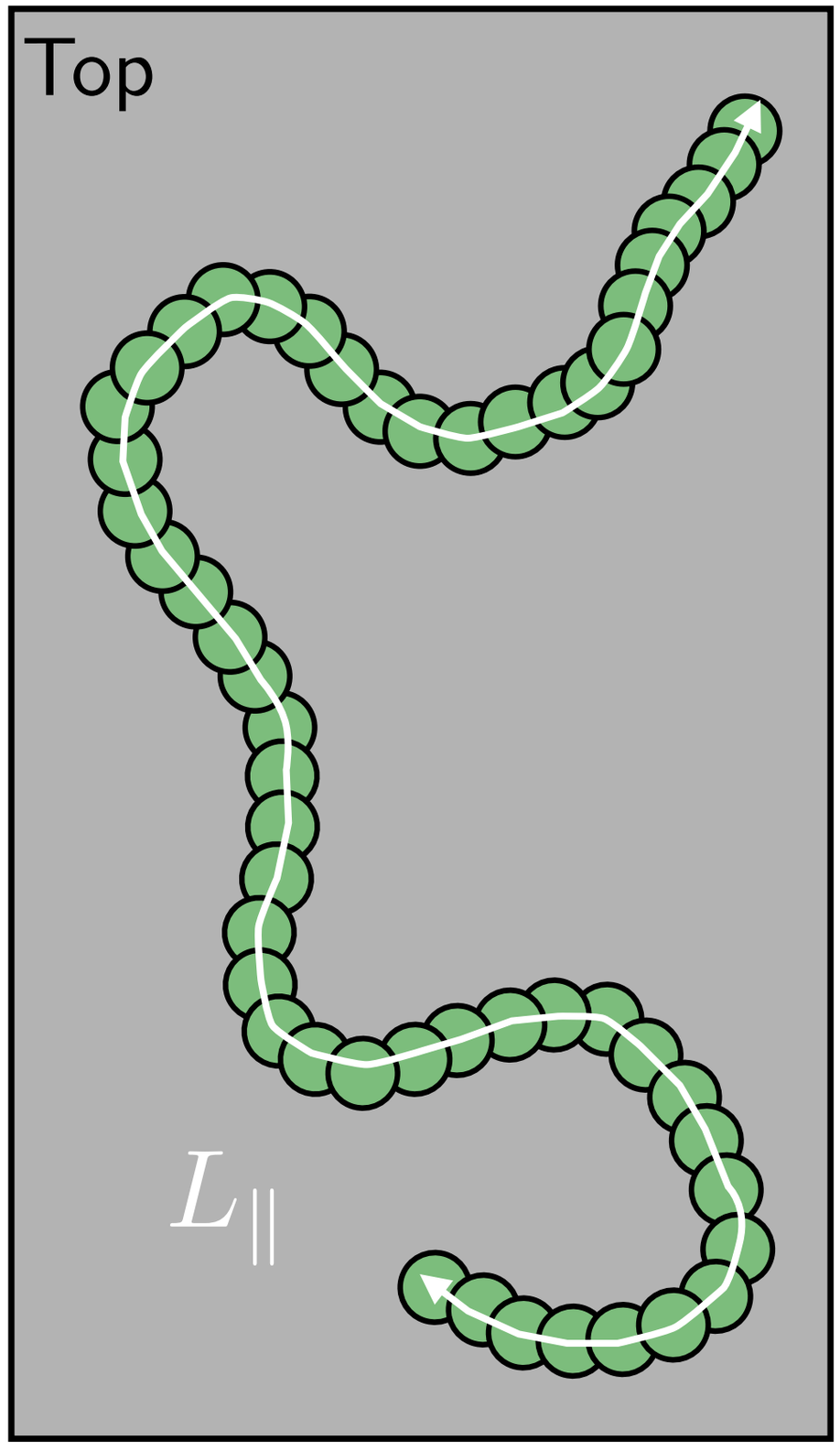


Deflection Length $\lambda \approx l_p{}^{\frac{1}{3}} H^{\frac{2}{3}}$

Odijk. *Macromolecules* 16, 1340 (1983)

Ideal Chains





$$\frac{L_\parallel}{L} = 1 - 0.09137\frac{\lambda}{l_p}$$

$$\frac{F}{k_B T} = 1.1036\frac{L}{\lambda}$$

Yang et al. *Phys. Rev. E* 76, 011804 (2007)

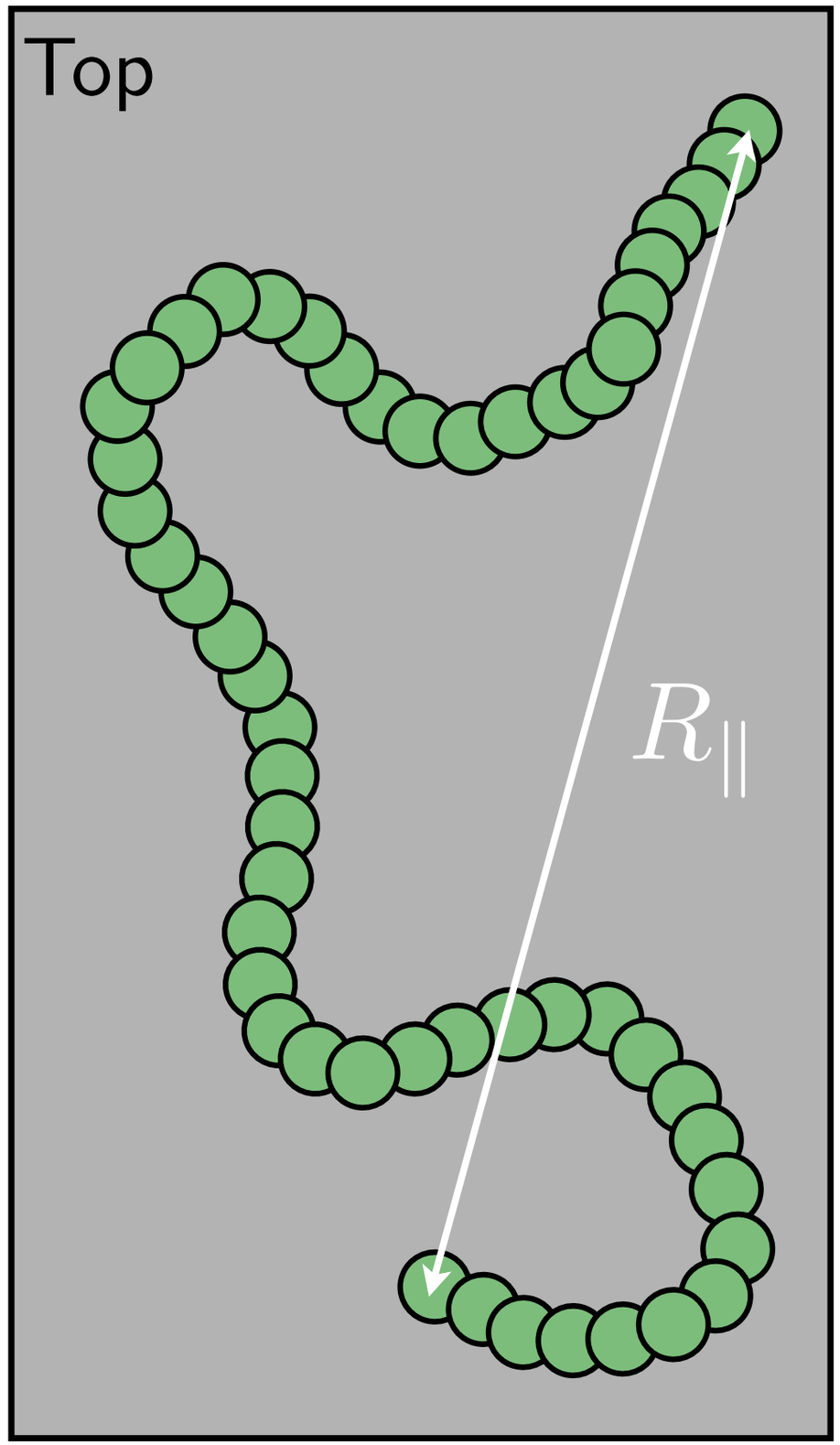
Real Chains

- Incorporate excluded volume
- Hypothesis of Dai *et al.*: DNA is a 2D self-avoiding walk of a virtual projected chain.

$$a_{\text{excluded}} = l_{p,\parallel}^2$$

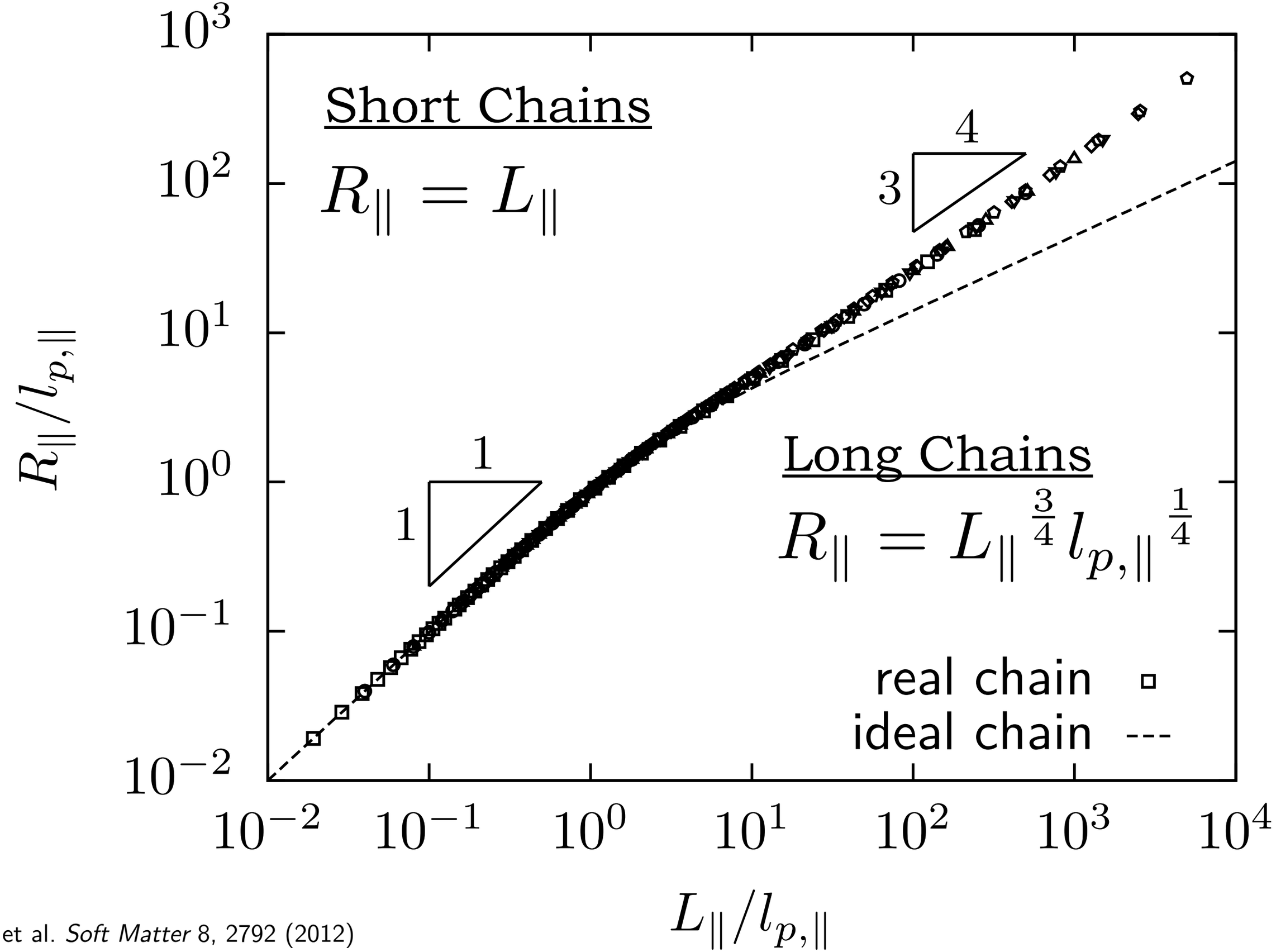
- Parameters for virtual chain are obtained by mapping back to 3D chain

$$l_{p,\parallel} = 2l_p$$



Dai et al. *Soft Matter* 8, 2792 (2012)

2D Wormlike Chains



Hsu et al. *Soft Matter* 8, 2792 (2012)

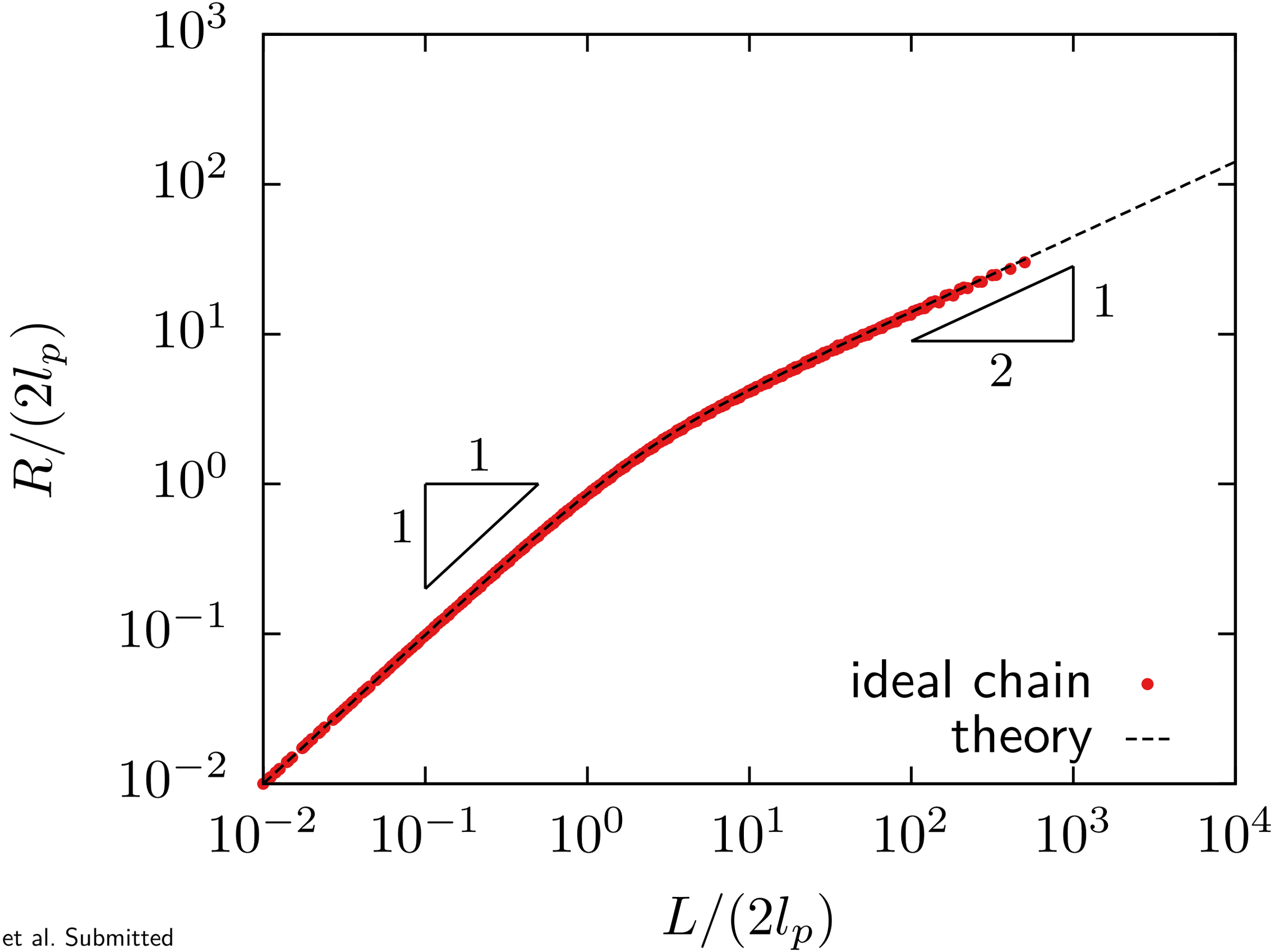
Pruned Enriched Rosenbluth Method

- Chain-growth Monte Carlo technique
- Efficient for O(10^4-10^5) beads

- Applicable to confined and unconfined systems
- Off-lattice
- Can estimate free energies

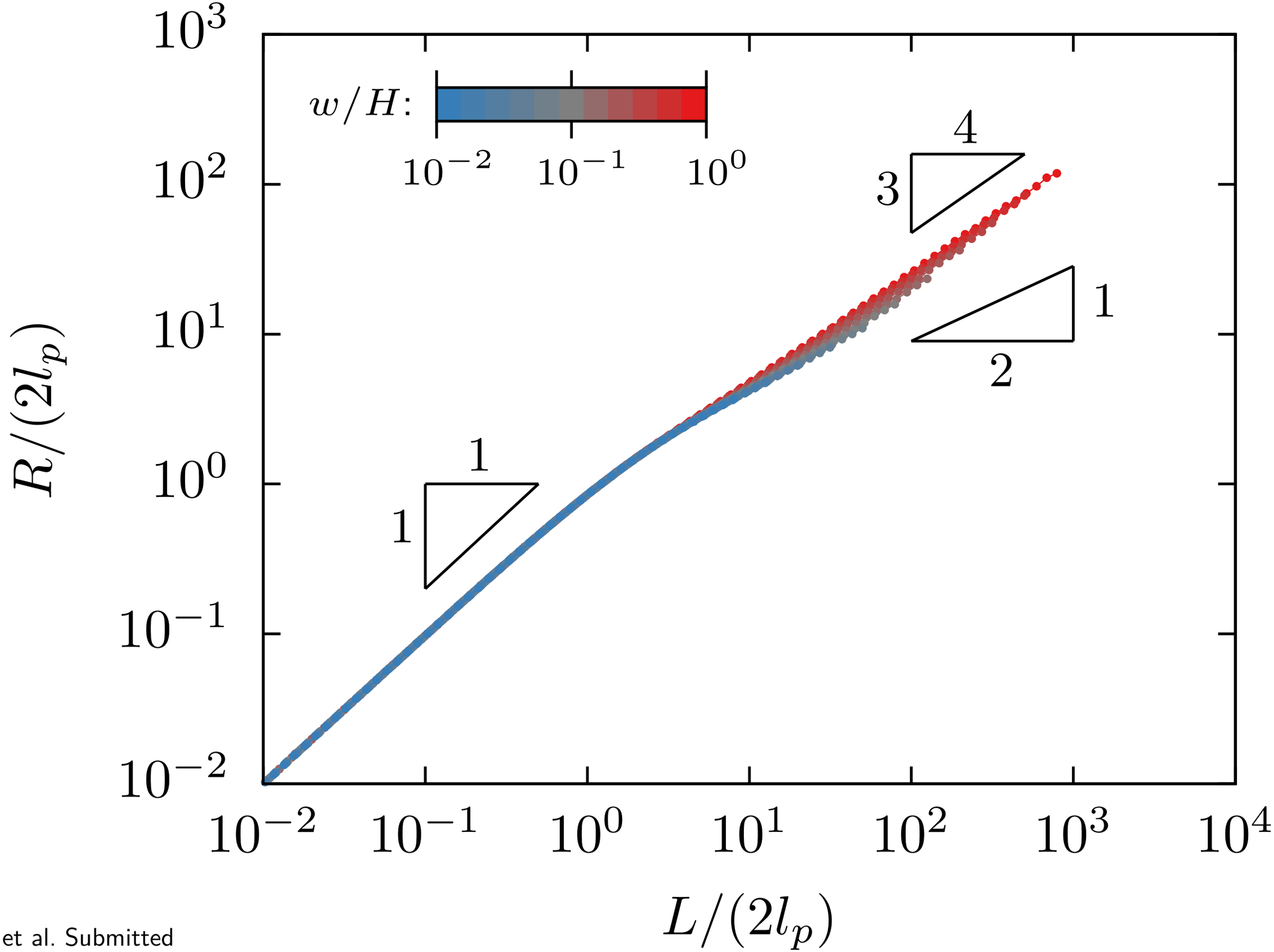
Tree et al. *Macromolecules*. 46, 8369 (2013)
Grassberger. *Phys. Rev. E.* 56, 3682 (1997).
Prellberg and Krawczyk. *Phys. Rev. Lett.* 92, 120602 (2004).

PERM Results - Ideal Chains



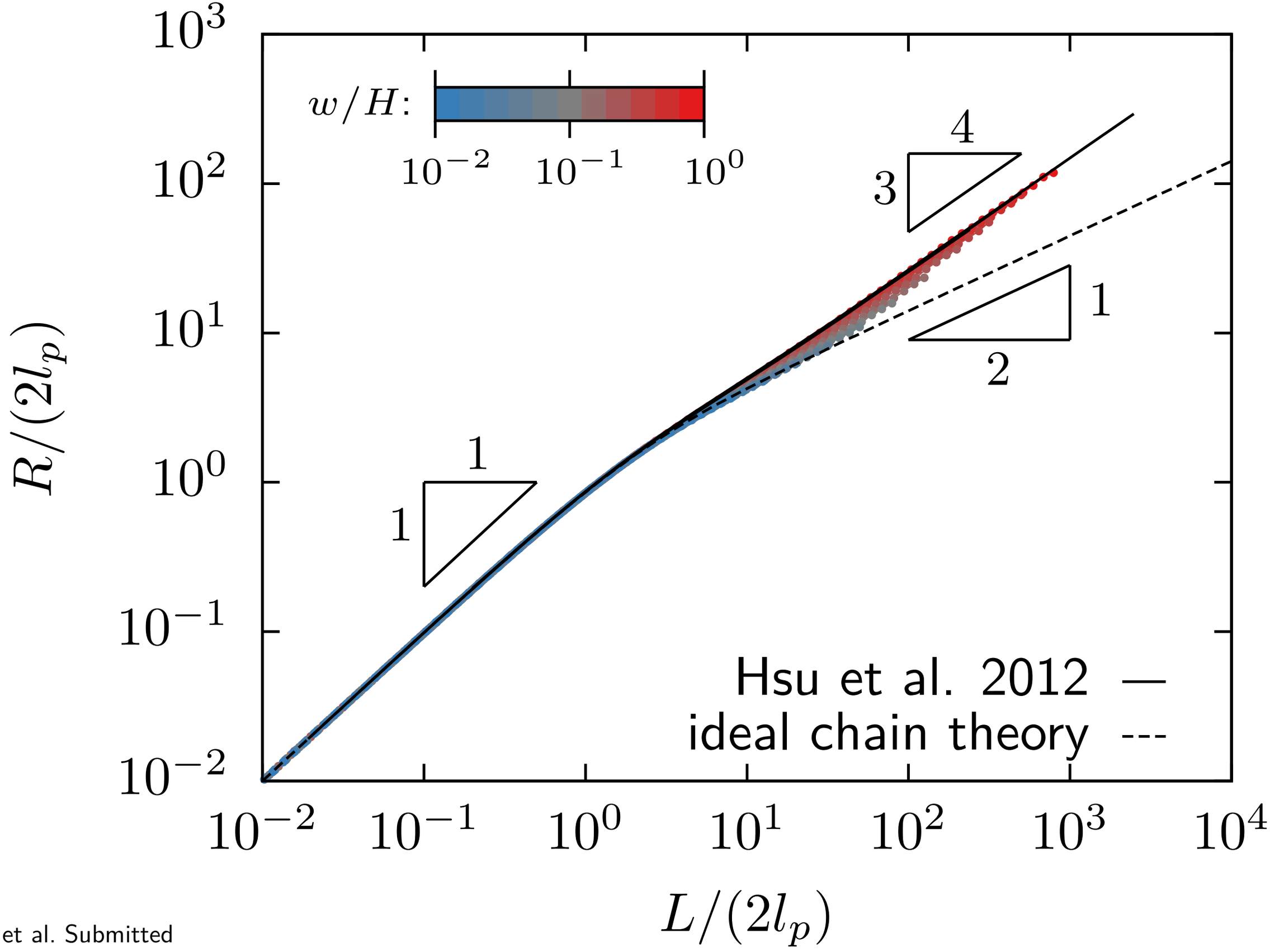
Tree et al. Submitted

PERM Results - Real Chains



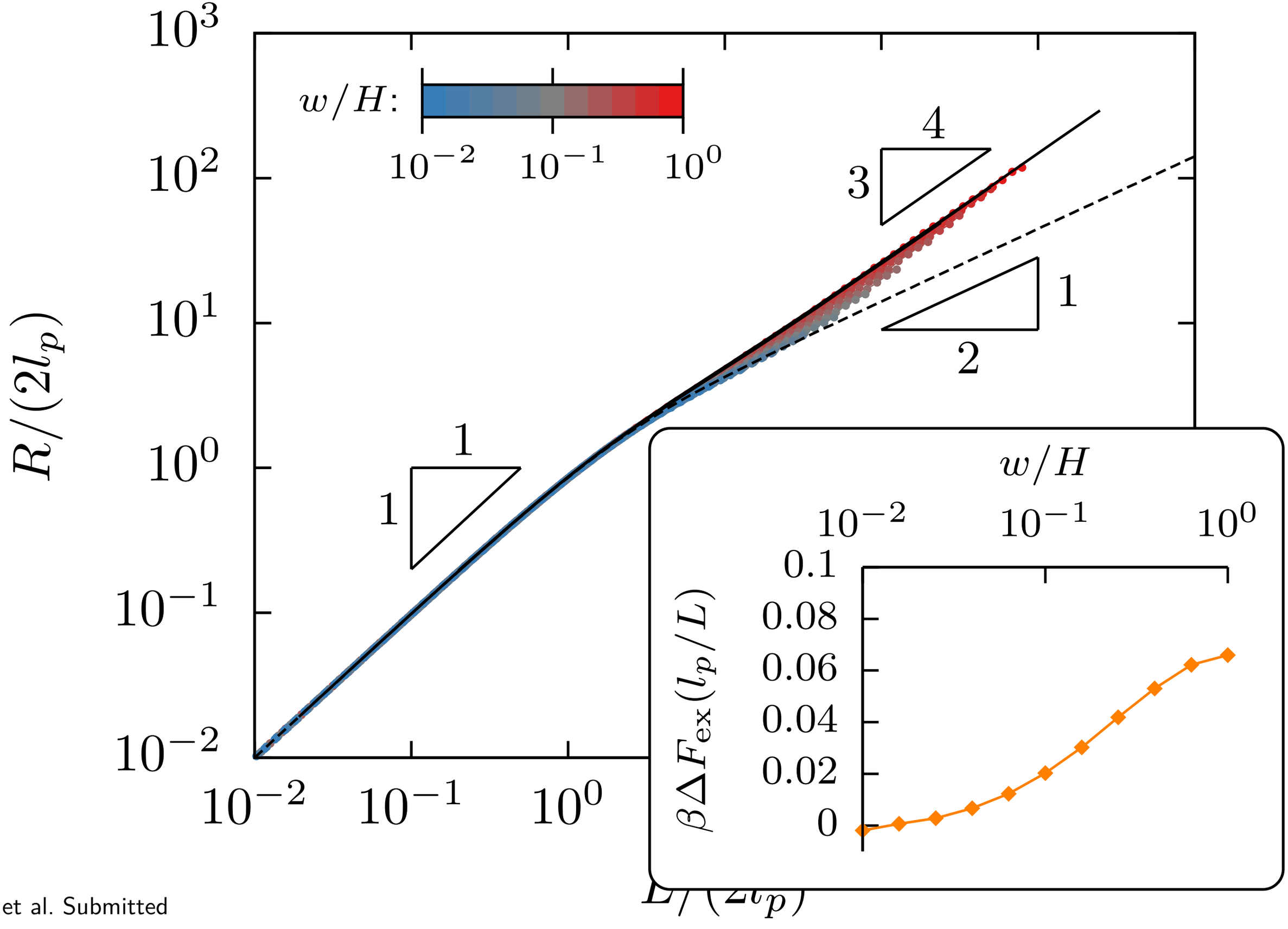
Tree et al. Submitted

PERM Results - Real Chains



Tree et al. Submitted

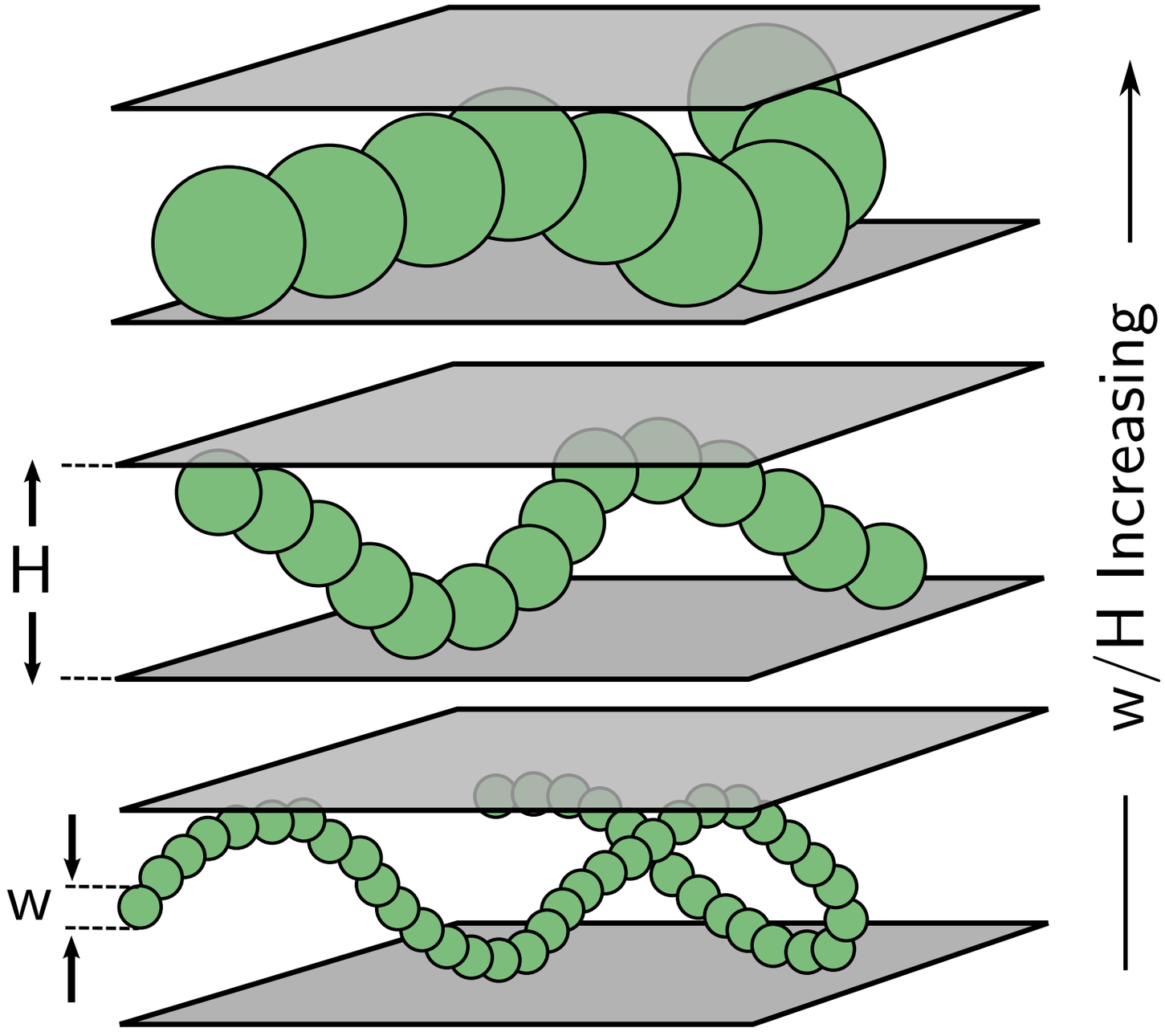
PERM Results - Real Chains



Tree et al. Submitted

What is wrong?

- Projected chain theory doesn't treat excluded volume correctly!



- But, it has the right idea about a nearly 2D chain.

Tree et al. Submitted

Following De Gennes - Renormalize

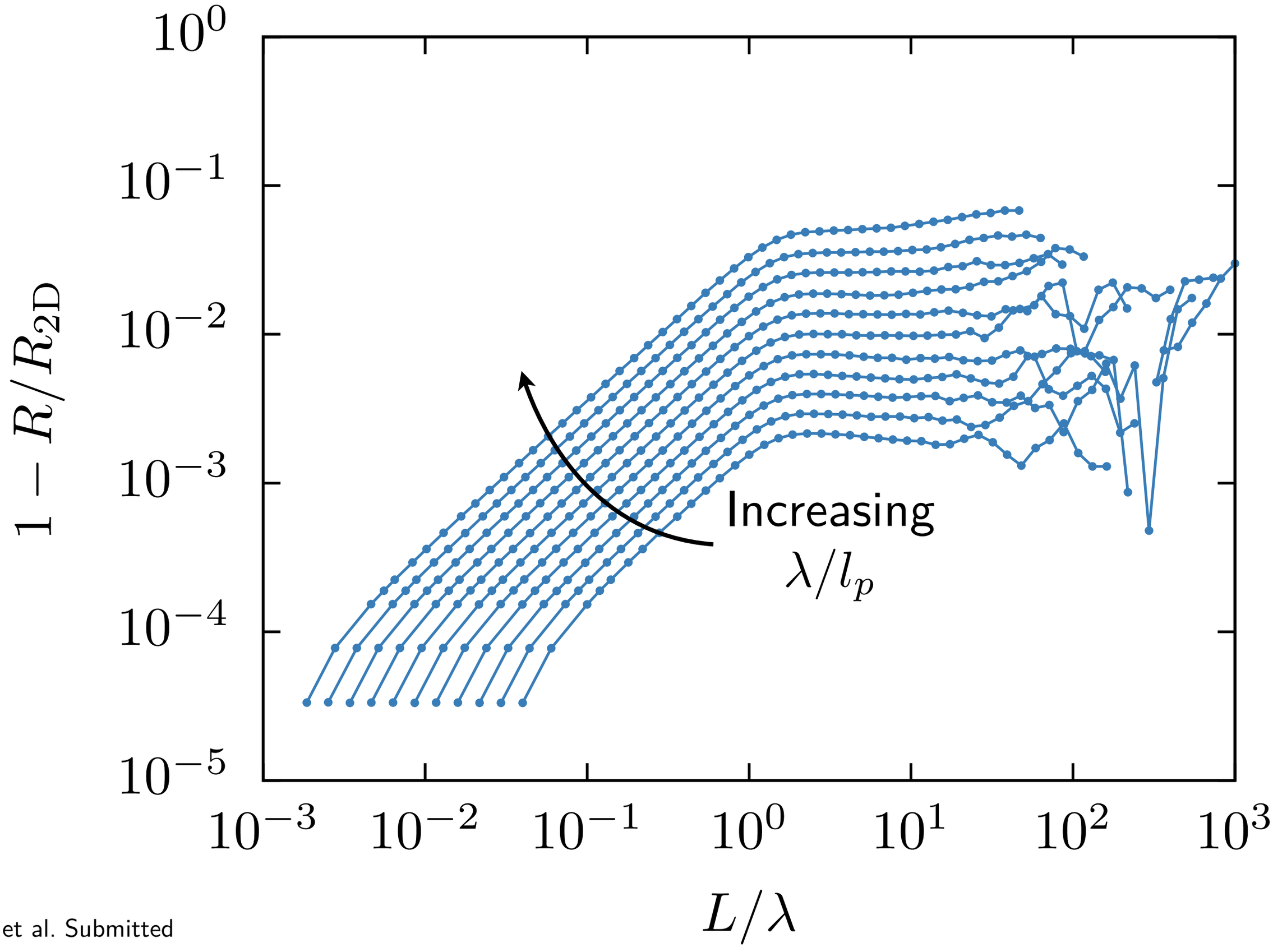
- Chain is a two-dimensional walk of deflection segments
- As such we need to incorporate the correct excluded volume...

$$v_{\mathrm{excluded}} = {l_p}^2 w$$

... and the dependence on the deflection segment length

$$R = R_{2\mathrm{D}} h \left(\frac{\lambda}{l_p} \right)$$

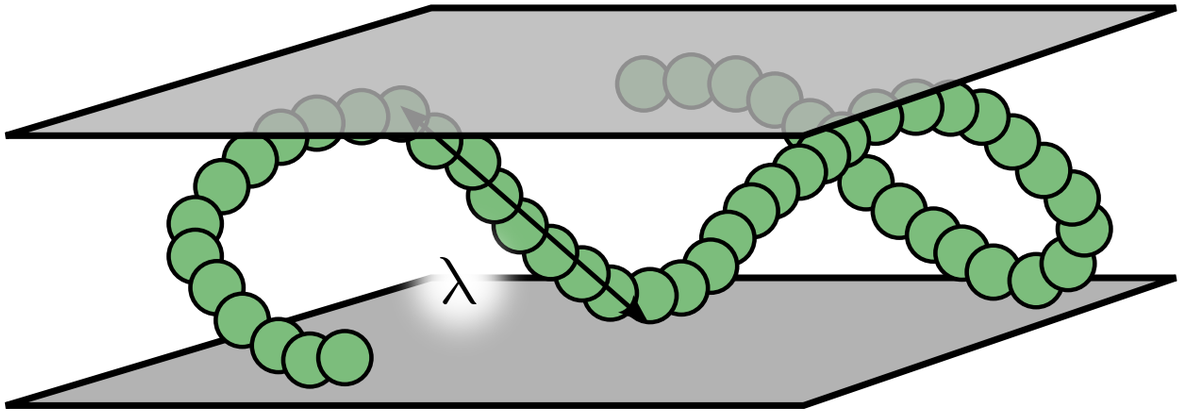
Odijk, T. *Phys. Rev. E* 77, 060901(R) (2008)
Tree et al. Submitted

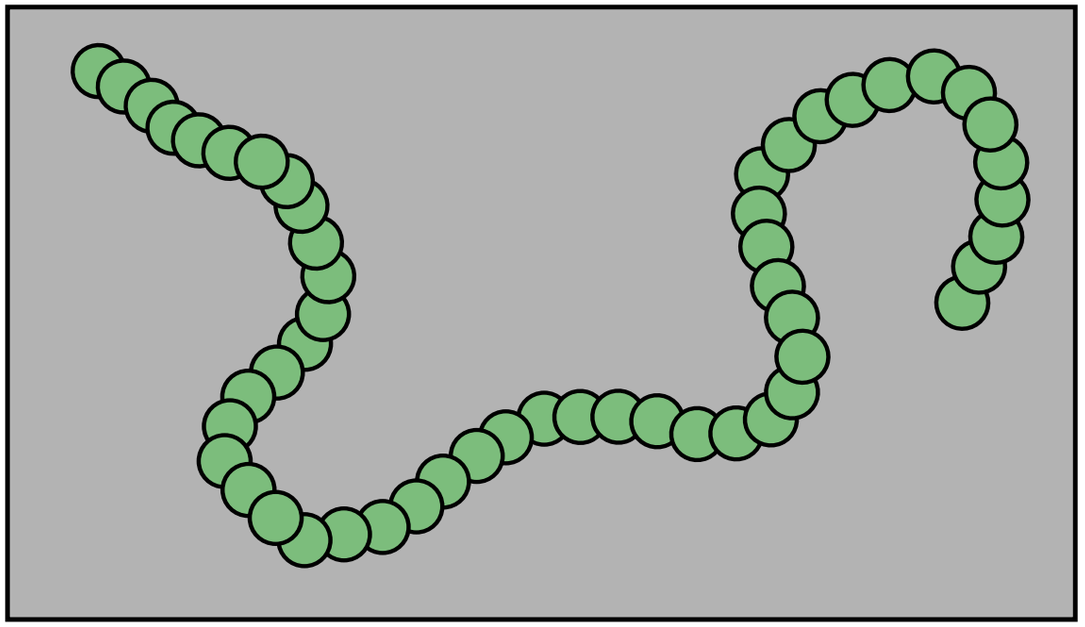


Tree et al. Submitted

Conclusion

Odijk regime in slits is best described as a nearly two-dimensional walk of deflection segments.



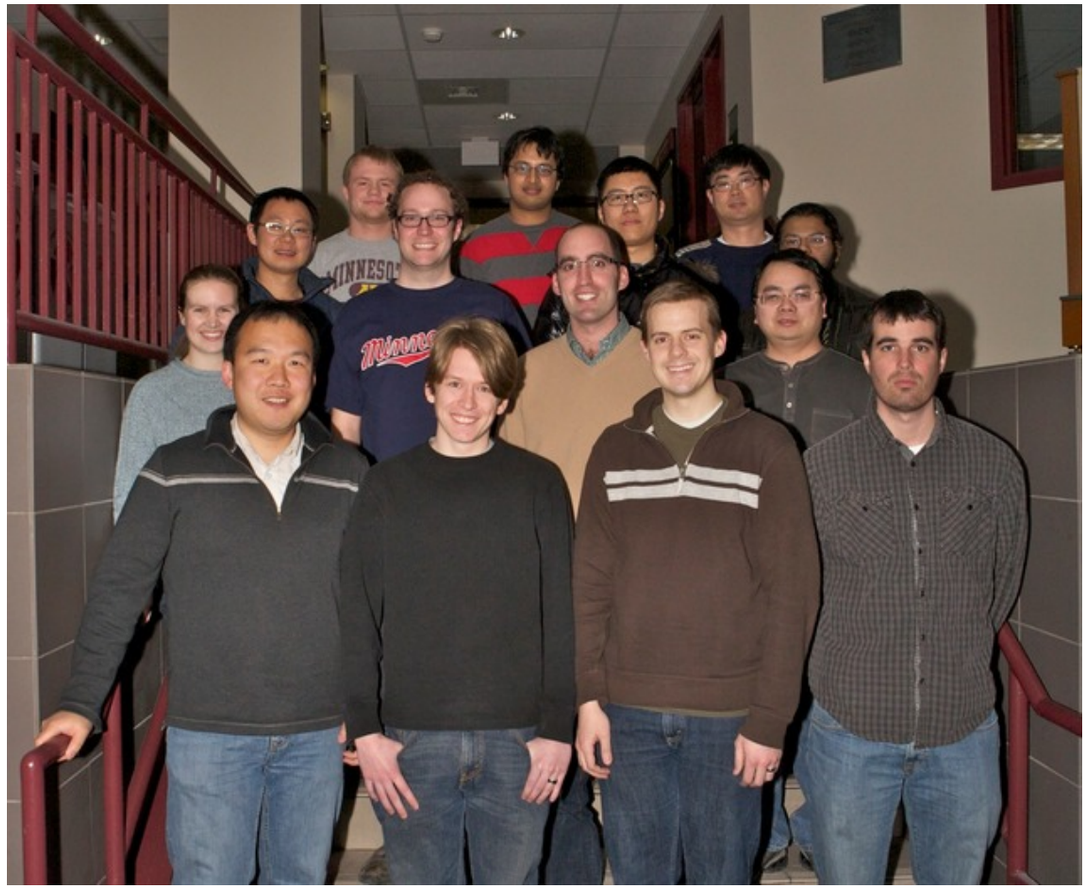


This accounting gives three sub-regimes in strong confinement:

- Rod-like chains when contour length is small
- Nearly ideal chains when chain width is small
- Self-avoiding chains otherwise

Tree et al. Submitted

Acknowledgments



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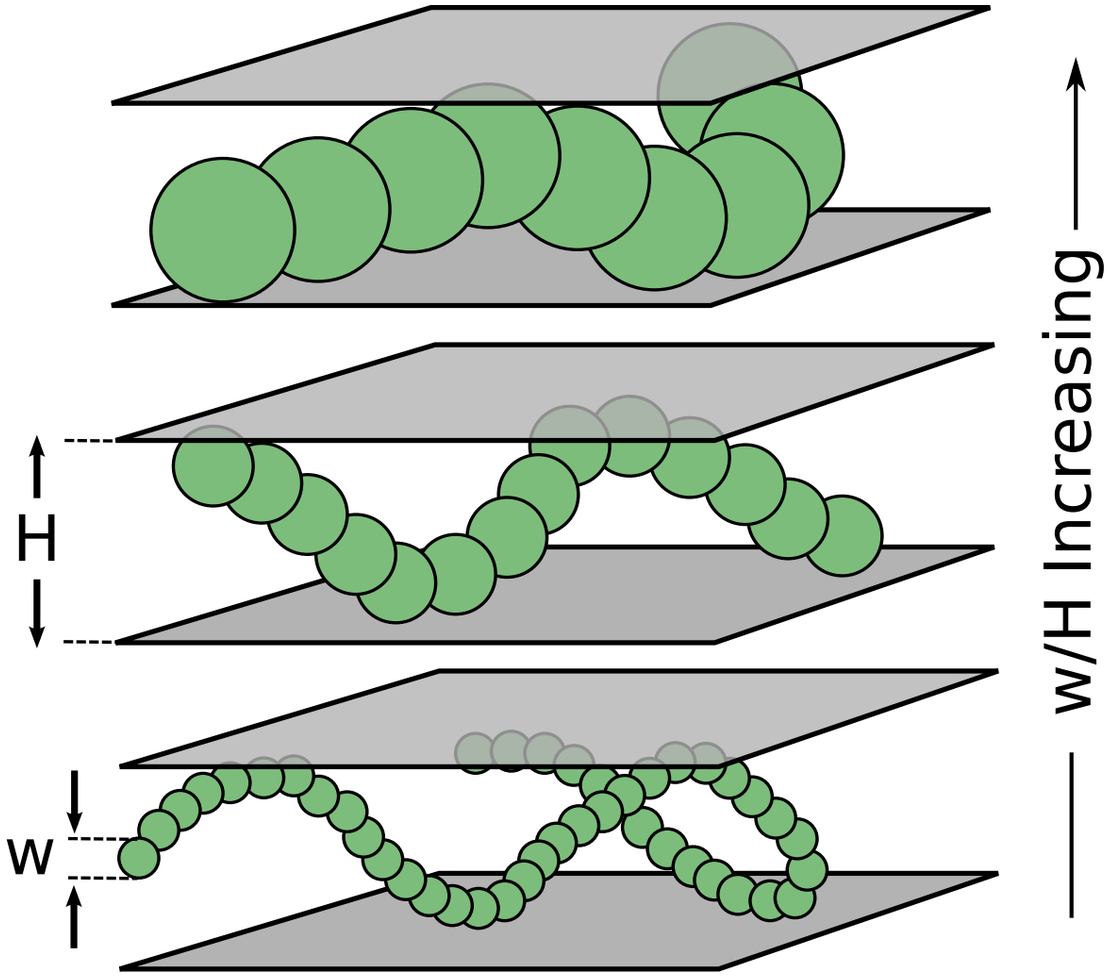
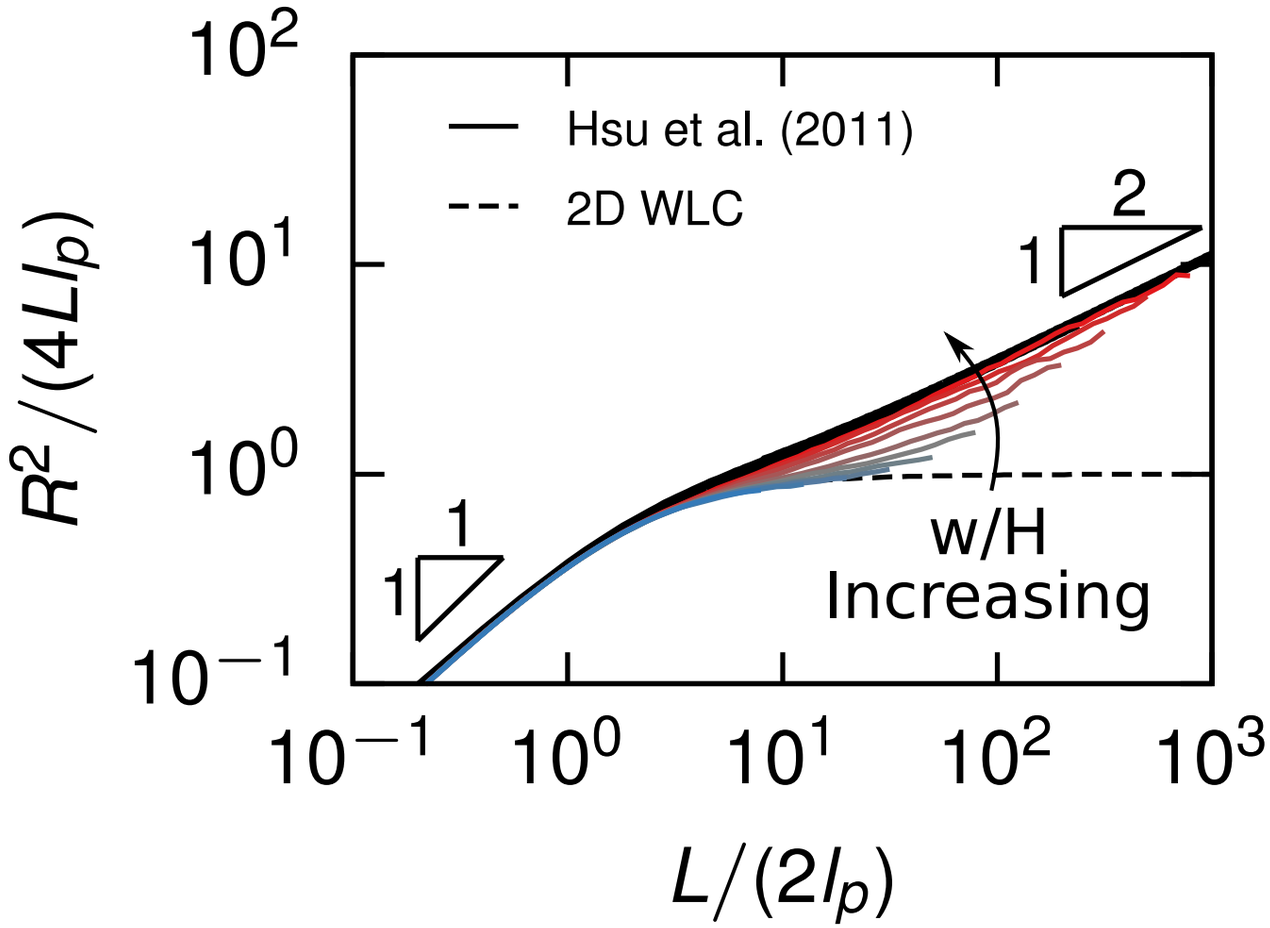
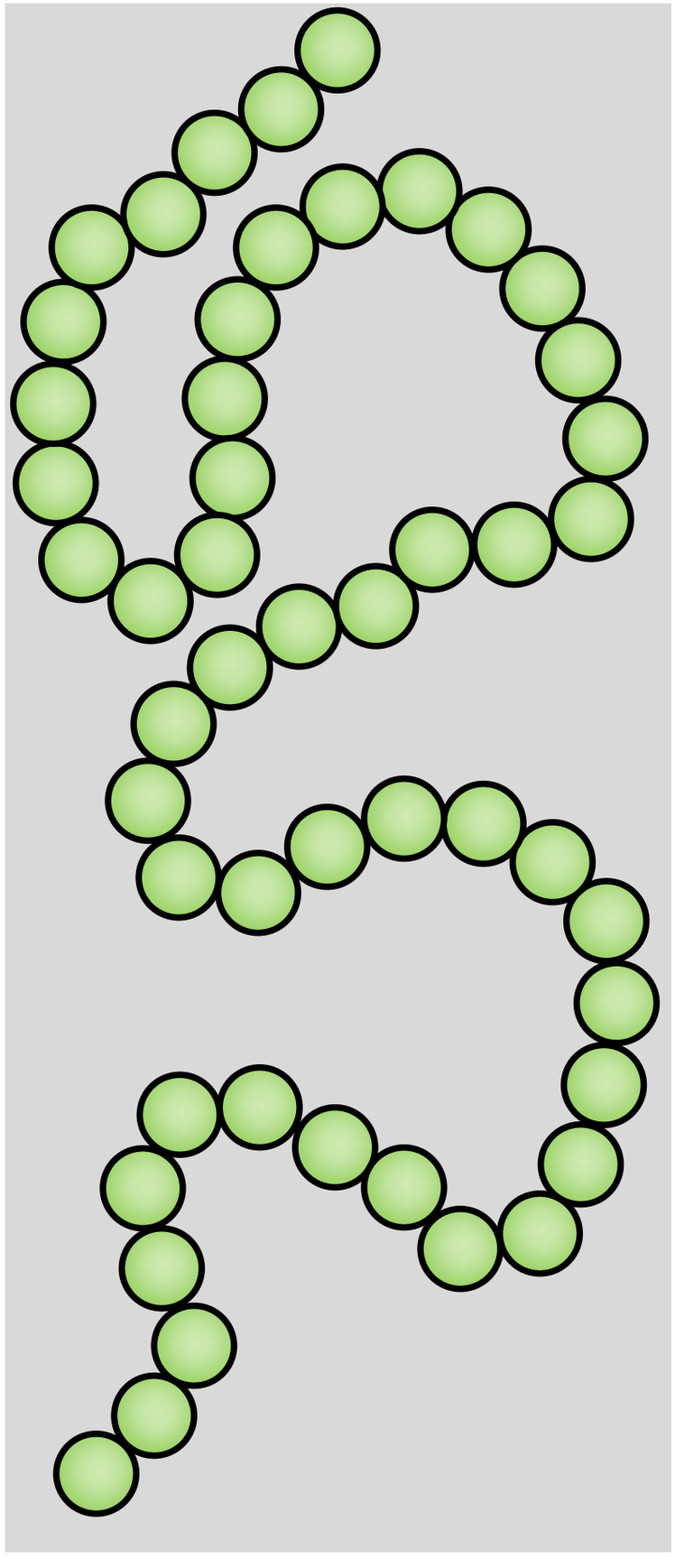
Odijk Regime in Slits

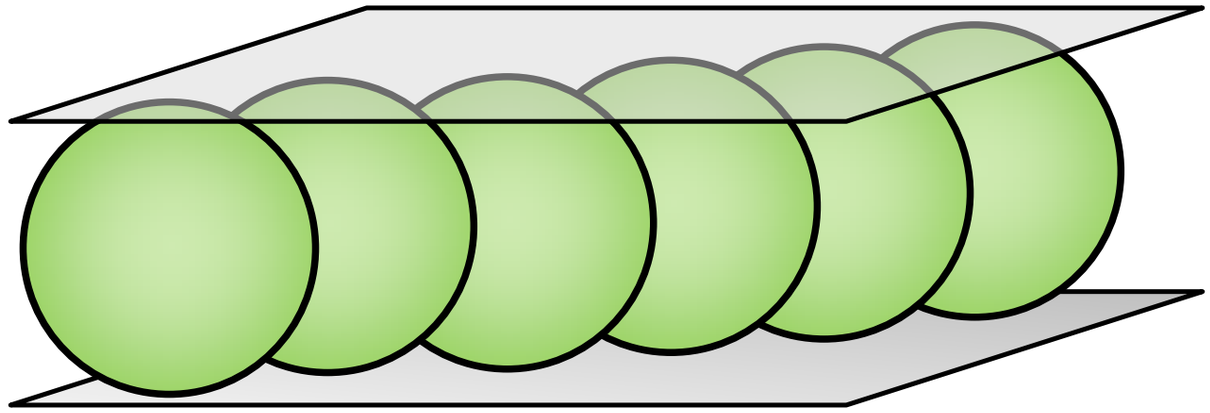




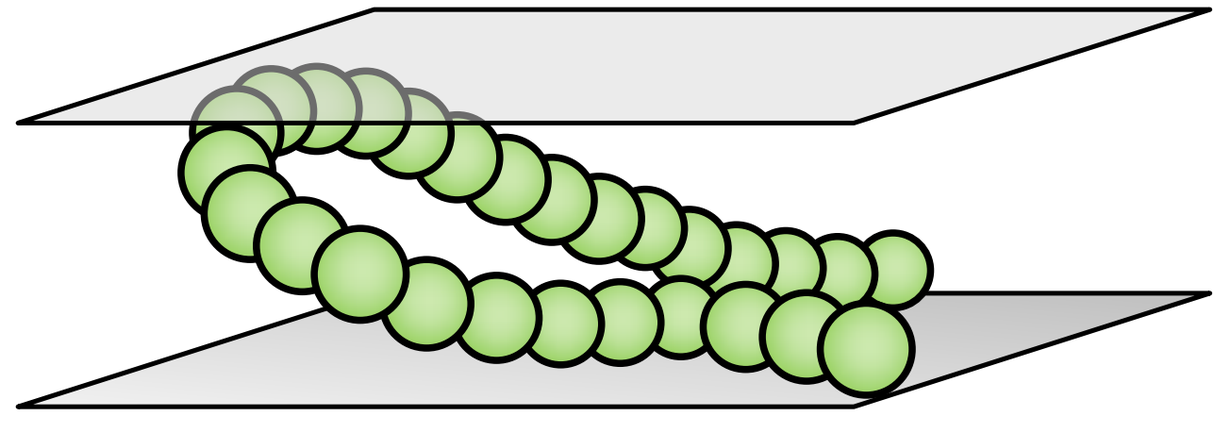
Top View



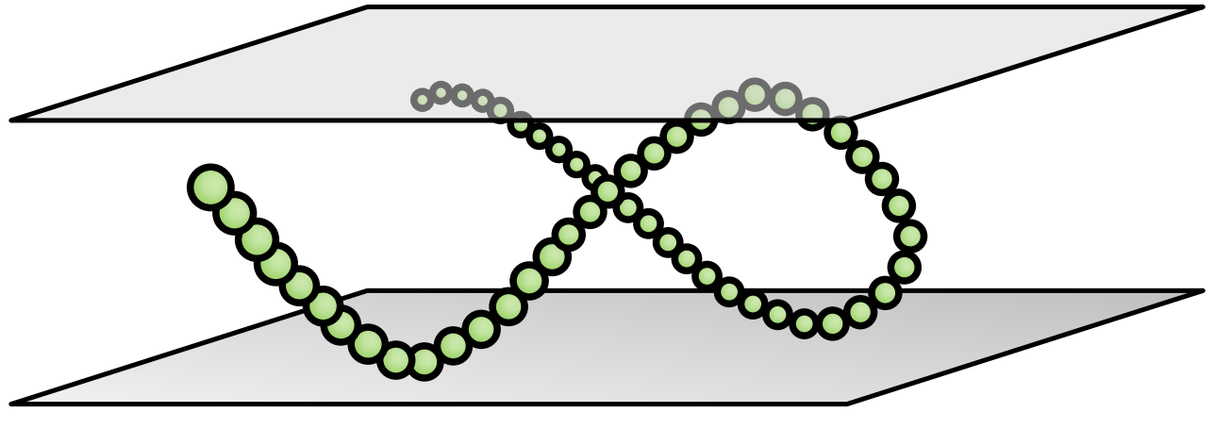
Side View



$H = w$



$H > w$



$H \gg w$

(a)

10^0

10^{-1}

10^{-2}

10^{-3}

10^{-4}

$1 - L_{\parallel}/L$

set 1

set 2

Eq. 5

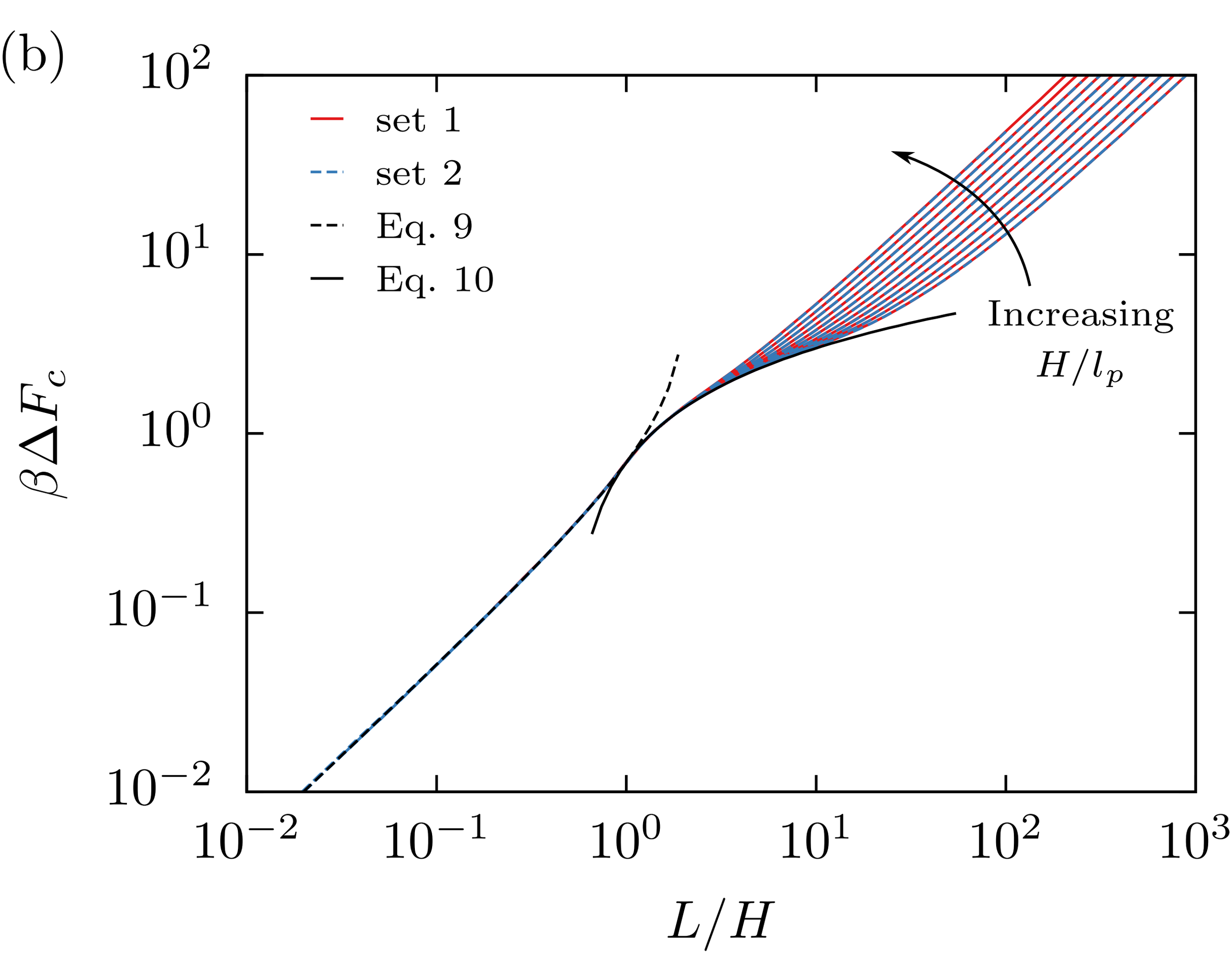
Eq. 7

Increasing H/l_p

10^{-2} 10^{-1} 10^0 10^1 10^2 10^3

L/H

(b)


set 1
set 2
Eq. 9
Eq. 10
Increasing
H/l_p
$\beta\Delta F_c$
L/H
10^{2}
10^{1}
10^{0}
10^{-1}
10^{-2}
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}

(a)

$(\lambda/l_p)\left(1 - L_{\|}/L\right)$

10^2

10^0

10^{-2}

10^{-2} 10^0 10^2 10^4

L/λ

Increasing
H/l_p

set 1
set 2
Eq. 7
Eq. 8

(b)

set 1

set 2

Eq. 8

2

3

10^{-1}

10^{-2}

10^{-3}

10^{-4}

10^{-3}

10^{-2}

10^{-1}

$1 - L_{\parallel}/L$

H/l_p

(a)

set 1
set 2
Eq. 12

$\beta\Delta F_c(\lambda/L)$

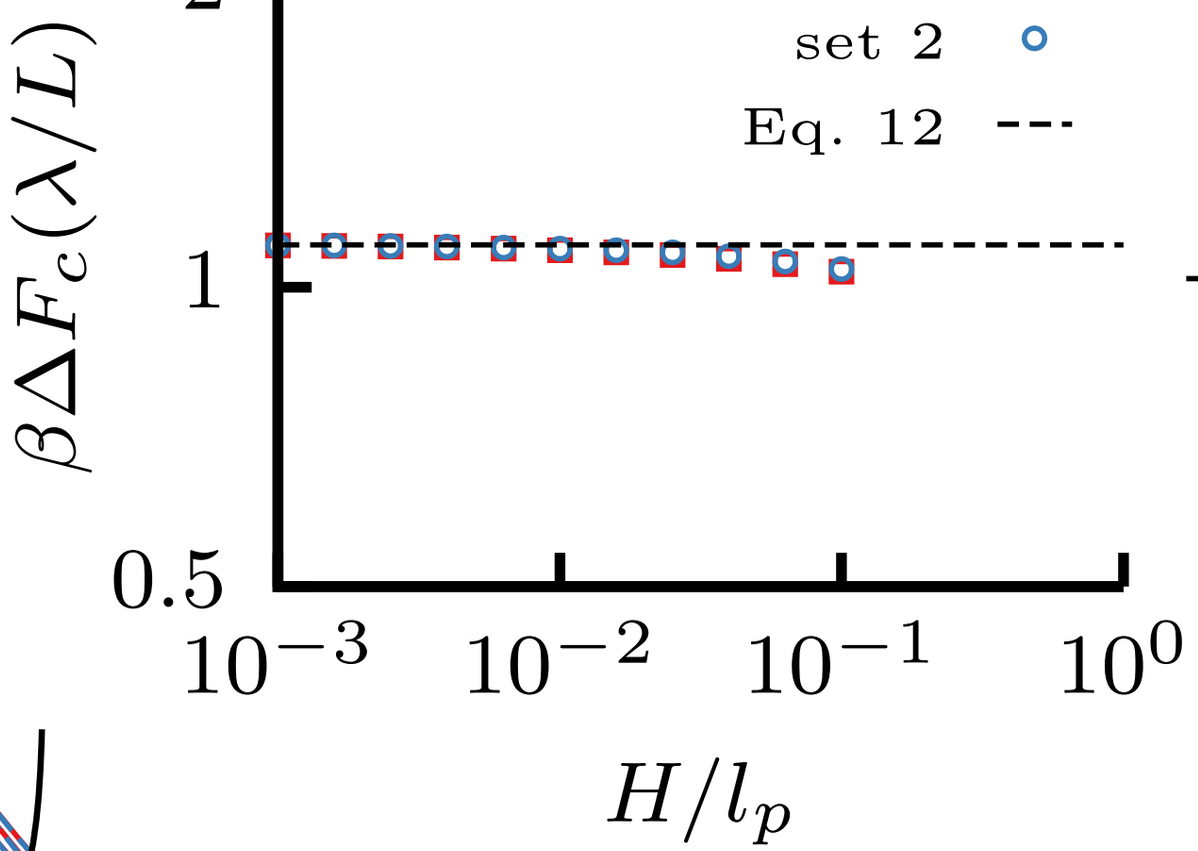
10^1

10^0

Increasing
H/l_p

10^{-2} 10^{-1} 10^0 10^1 10^2 10^3 10^4

L/λ



(b)

$\beta \Delta F_c(l_p/L)$

H/l_p

set 1
set 2
set 4
Eq. 12
Eq. 13

3
2
2
1

10^0

10^{-2}

10^{-4}

10^{-6}

10^{-8}

$1 - R_\parallel^2 / R^2$

1

2

set 1

set 2

10^{-2} 10^0 10^2 10^4

R/H

10^0

10^{-1}

10^{-2}

10^{-3}

$C(s)l_p/\lambda$

set 1

set 2

2

1

1

1

0 2 4 6 8 10 12 14

s/λ

(a)

set 1
set 2
Eq. 18
Eq. 23
Eq. 24

$R^2/(4Ll_p)$

10^0
10^{-1}
10^{-2}
10^{-3}

10^{-2} 10^{-1} 10^0 10^1 10^2 10^3

$L/(2l_p)$

$1-h$

10^0
10^{-2}
10^{-4}

Increasing
H/l_p

10^{-2} 10^0 10^2 10^4

L/λ

(b)

$(l_p/\lambda)(1-h)$

10^{2}
10^{1}
10^{0}
10^{-1}
10^{-2}
10^{-3}
10^{-4}
10^{-5}

1
1

set 1
set 2
Eq. 21

10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4}

L/λ

(a)

w/H:

10^{-2} 10^{-1} 10^{0}

$R^2/(4Ll_p)$

10^{2} 10^{1} 10^{0} 10^{-1} 10^{-2}

2

1

1

1

Increasing w/H

Hsu et al. (2011)

set 6

2D WLC

10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4}

$L/(2l_p)$

(b)

set 6

Hsu et al. (2011)

Increasing w/H

$R^2/(4Ll_p)$

z

10^{2}
10^{1}
10^{0}
10^{-1}
10^{-2}
10^{-3}

10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2}

$$\left|1-\frac{R^2}{R_0^2}\right|\left(\frac{\lambda}{l_p}-\frac{\lambda_0}{l_{p,0}}\right)^{-1}$$

10^{2}
10^{1}
10^{0}
10^{-1}
10^{-2}
10^{-3}

10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3}

L/λ

Increasing
H/l_p

10^{-1}
10^{-2}
10^{-3}
10^{-4}

$\left|1-R^2/R_0^2\right|$

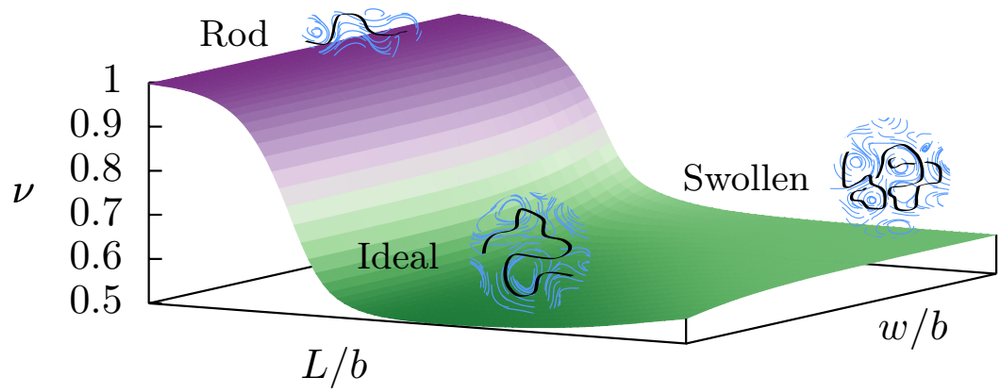
10^{-2} 10^{0} 10^{2} 10^{4}

L/λ

set 5
$2\alpha_R$ ---

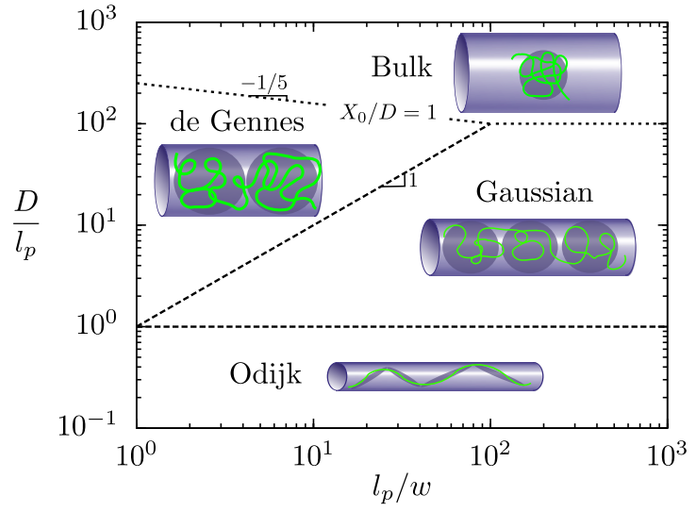
10^4
10^0
10^{-4}
10^{-8}
10^{-12}
$\beta\Delta F$
10^{-2}
10^{-1}
10^0
10^1
10^2
10^3
L/l_p
ΔF_c
$\Delta F_c'$
ΔF_{ex}
w/H
10^{-2}
10^{-1}
10^0
0.1
0.08
0.06
0.04
0.02
0
$\beta\Delta F_{\mathrm{ex}}(l_p/L)$

Polymer Physics of DNA in Solution



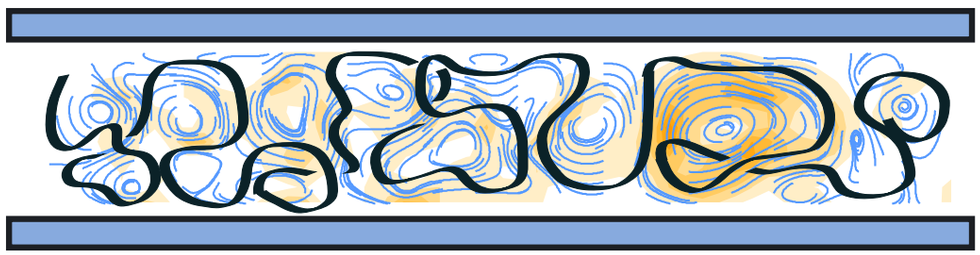
DR Tree, A Muralidhar, PS Doyle and KD Dorfman, Macromolecules (2013).

Regimes of Confined DNA



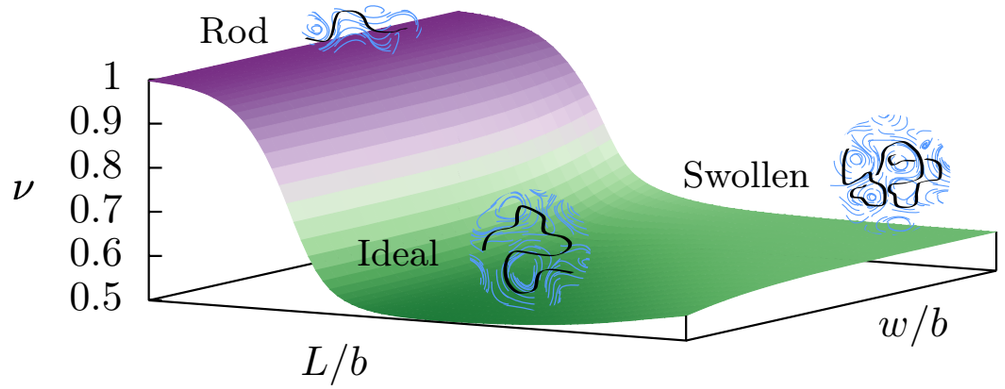
DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 110, 208103 (2013).

Hydrodynamics of Confined DNA



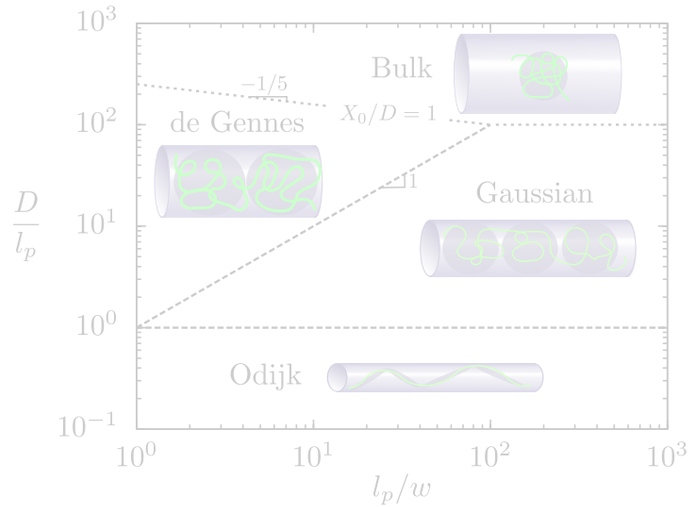
DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 108, 228015 (2012).

Polymer Physics of DNA in Solution



DR Tree, A Muralidhar, PS Doyle and KD Dorfman, Macromolecules (2013).

Regimes of Confined DNA



DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 110, 208103 (2013).

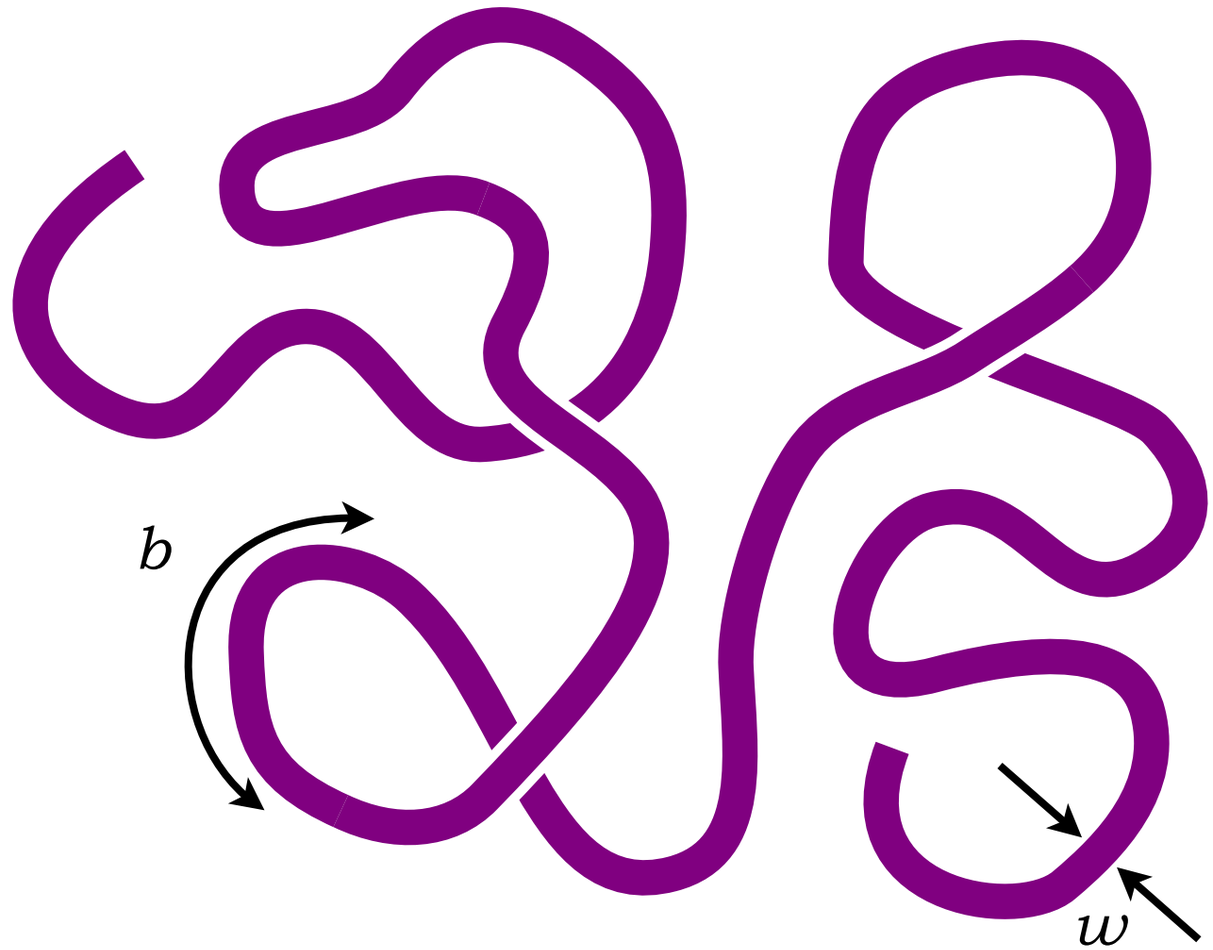
Hydrodynamics of Confined DNA

DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 108, 228015 (2012).

DNA is a Wormlike Chain (WLC)

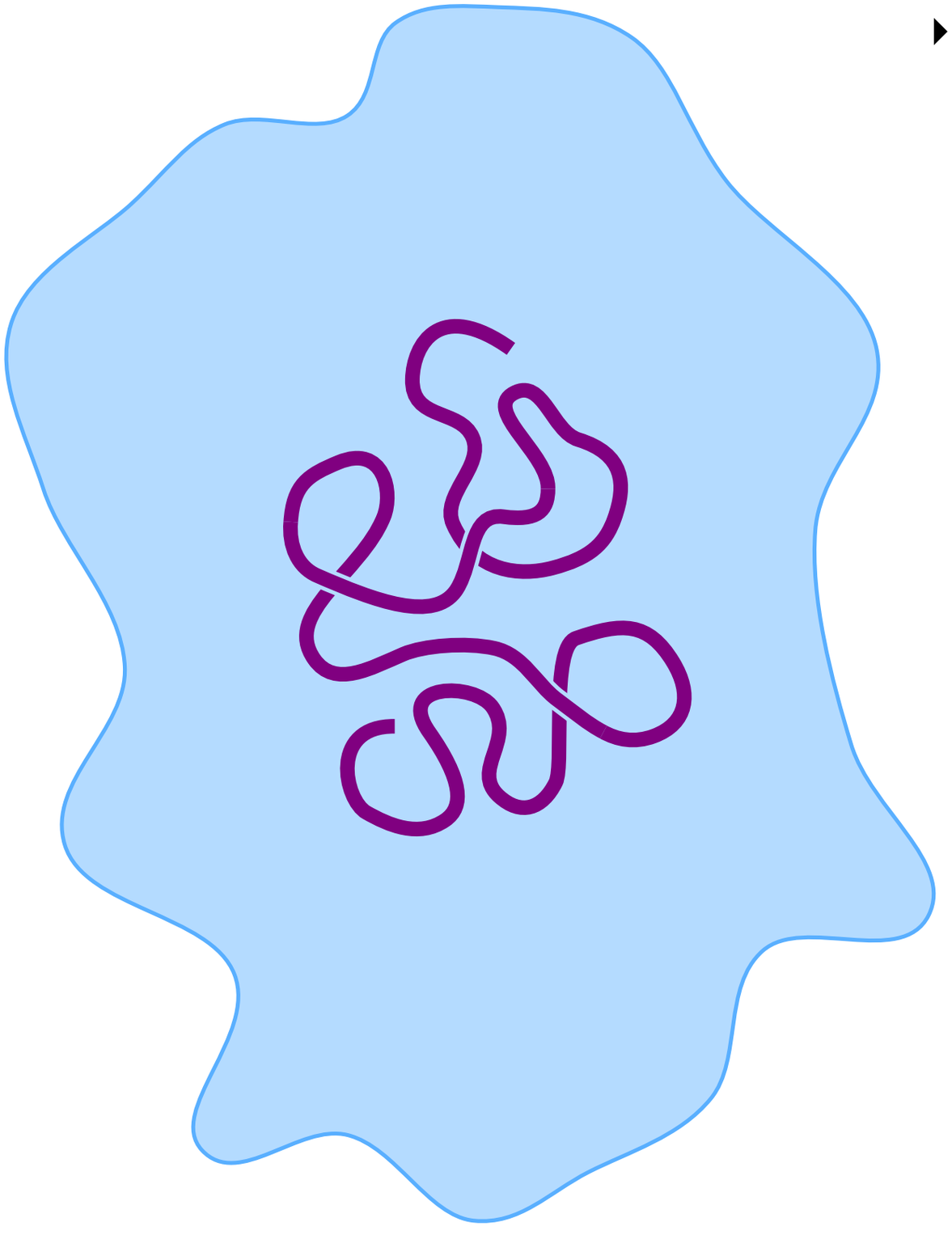
The WLC model assumes DNA to be:

- sequence independent
- locally stiff
- space-filling with short-range interactions



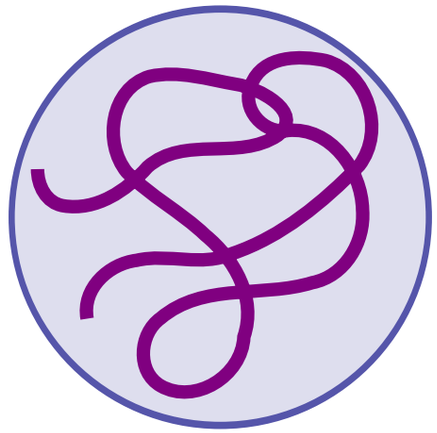
Physical Quantity	Symbol	Value for λ-DNA
chain length	L	21 μm
Kuhn length (stiffness)	b or $2l_p$	106 nm
effective width	w	4.6 nm
hydrodynamic radius	a	2.9 nm

Bulk, Infinitely Dilute Solution



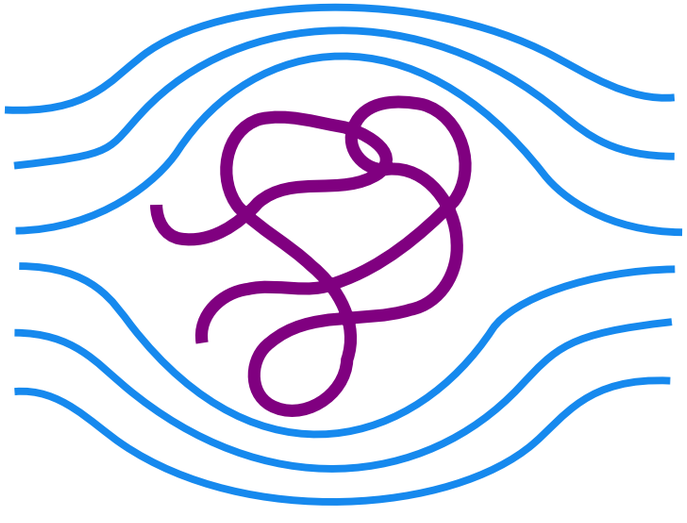
- What is the equilibrium coil size?

$$R_g = f(L, b, w)$$



- What is the coil diffusion coefficient?

$$D = f(L, b, w, a)$$

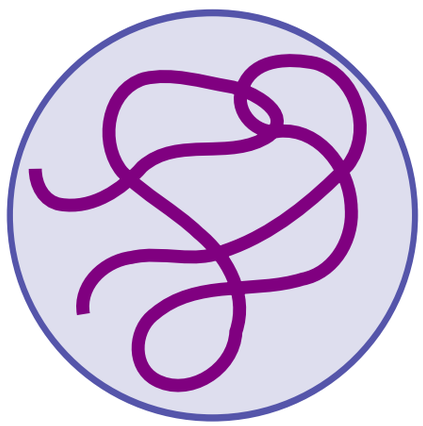


The Thermodynamic Limit

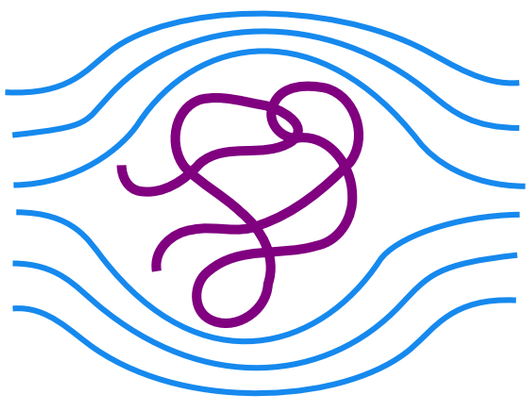
Real (self-avoiding), dilute polymers are expected to show universal behavior in the thermodynamic limit,

$$L \to \infty$$

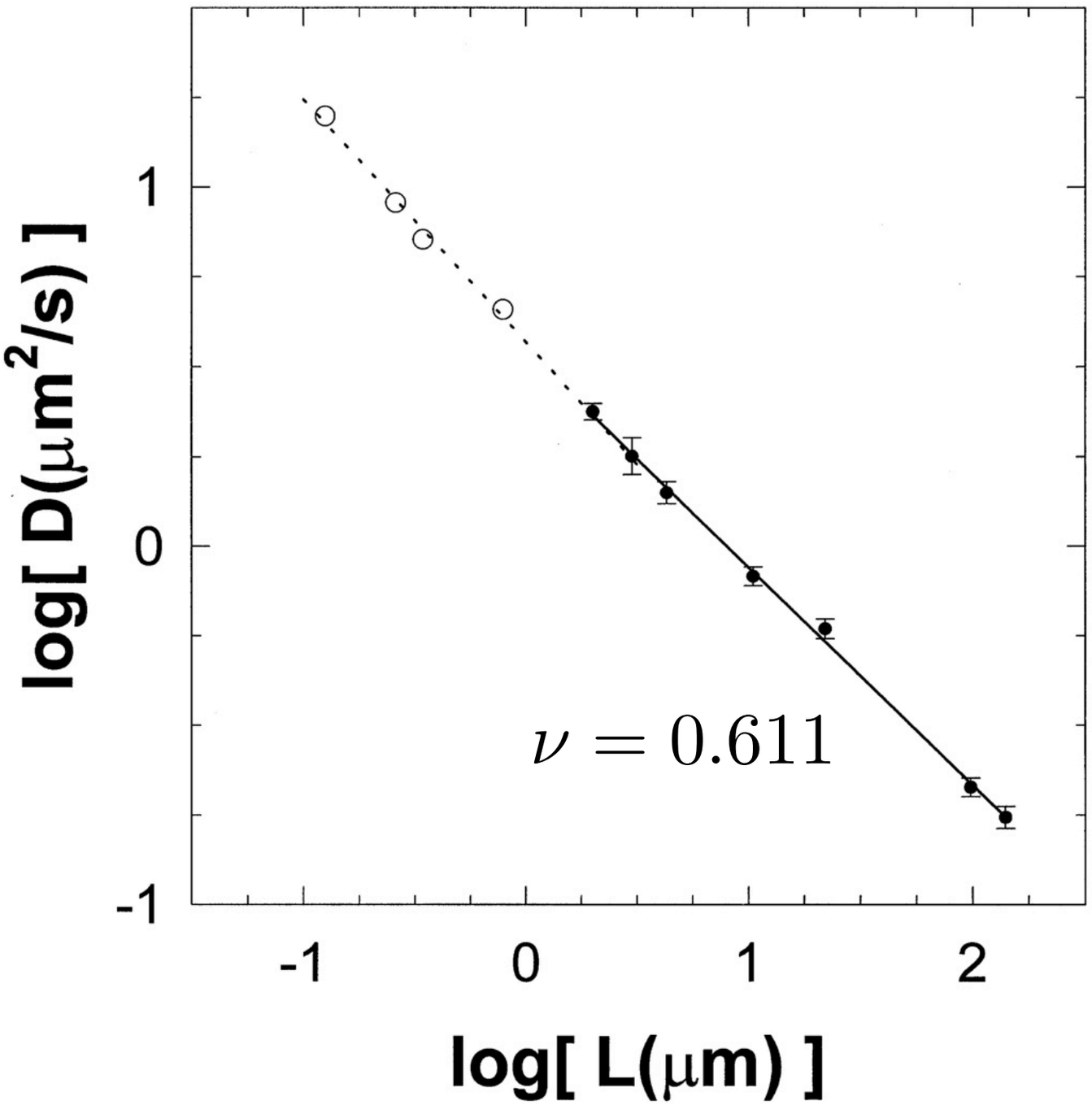
$$R_g \sim L^{\nu}$$



$$D \sim L^{-\nu}$$



$$\nu = 0.588$$



Smith et al. Macromolecules. (1996)

Swollen Coil

Gaussian Coil

$\nu = 0.588$

2

1

$\nu = 0.5$

Rod

$\nu = 1$

$\frac{L}{b}$

b/w

10^{4}

10^{3}

10^{2}

10^{1}

10^{0}

10^{-1}

10^{0}

10^{1}

10^{2}

10^{3}

Swollen Coil

L^*

Gaussian Coil

2

1

$\nu = 0.588$

$\nu = 0.5$

Rod

$\nu = 1$

$\frac{L}{b}$

10^4

10^3

10^2

10^1

10^0

10^{-1}

10^0

10^1

10^2

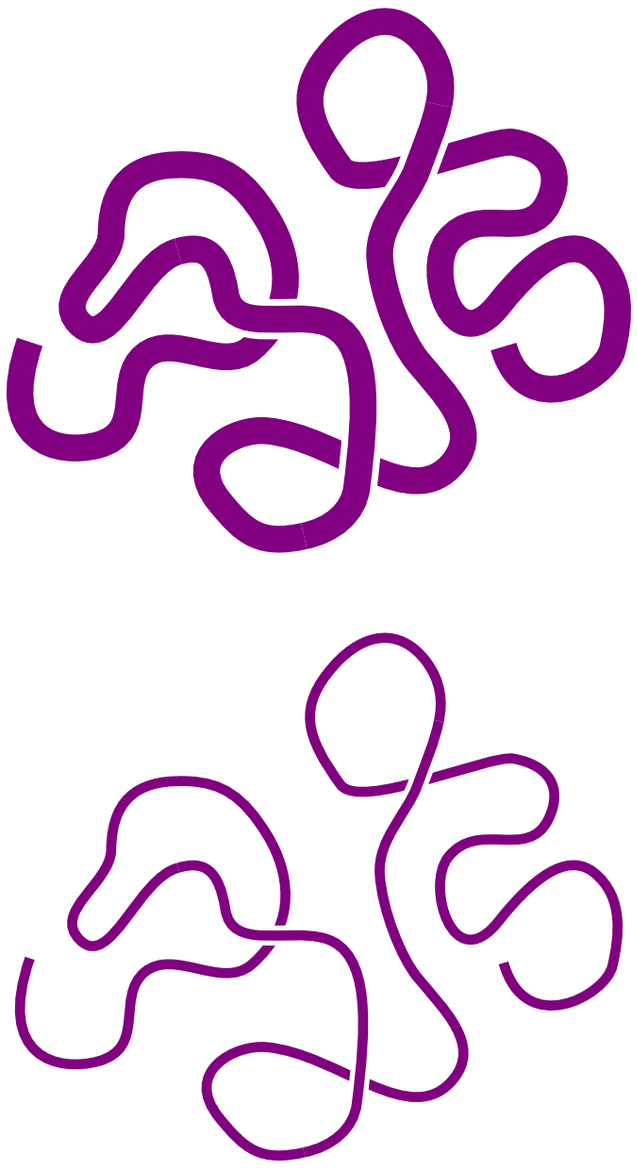
10^3

b/w

Monomer Anisotropy

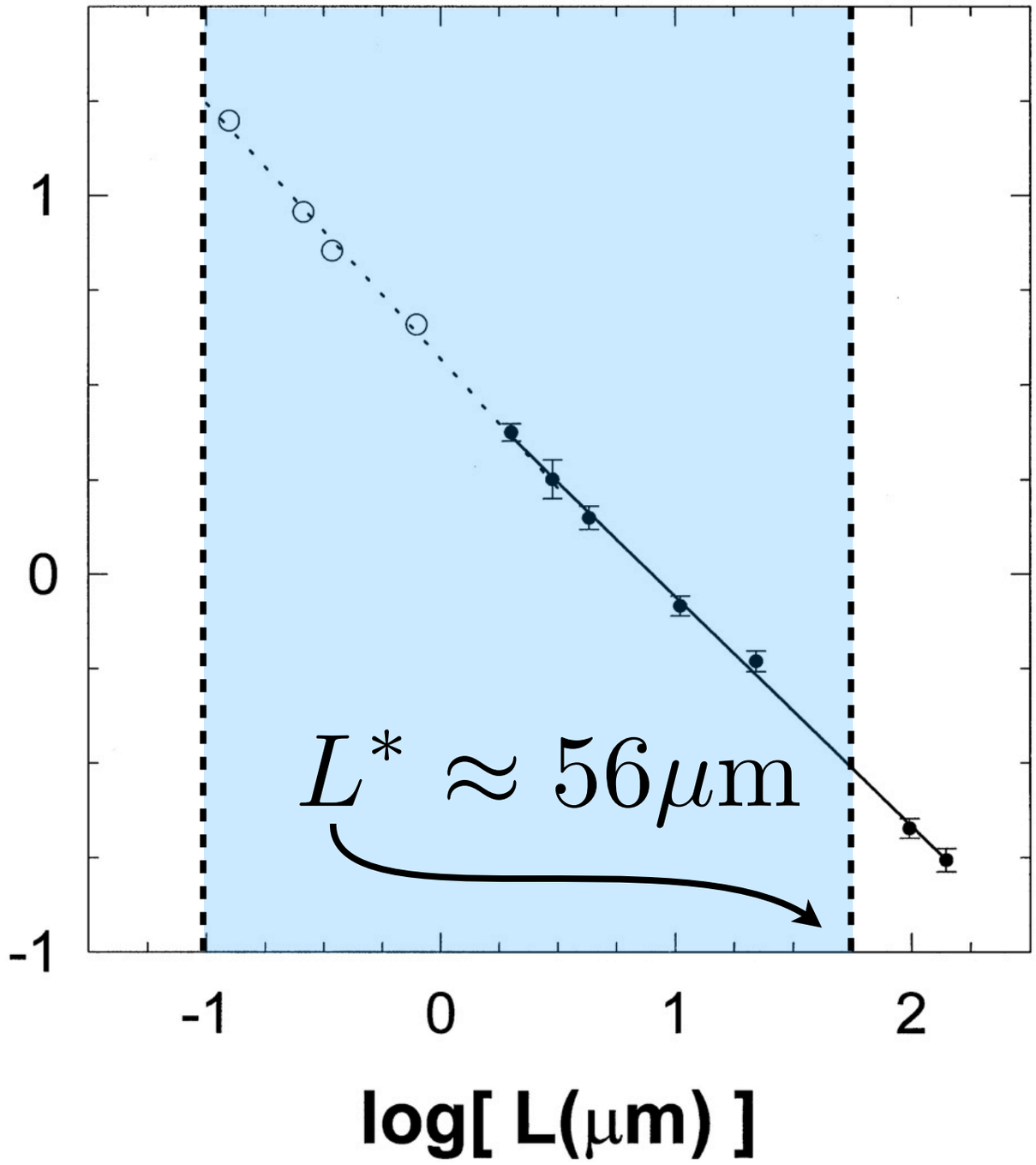
The monomer anisotropy is a dimensionless ratio of the strength of the excluded volume to the stiffness.

$$\frac{L^*}{b} \sim \left(\frac{w}{b}\right)^{-2}$$



$$\frac{w}{b} \sim 1$$

$$\frac{w}{b} \ll 1$$



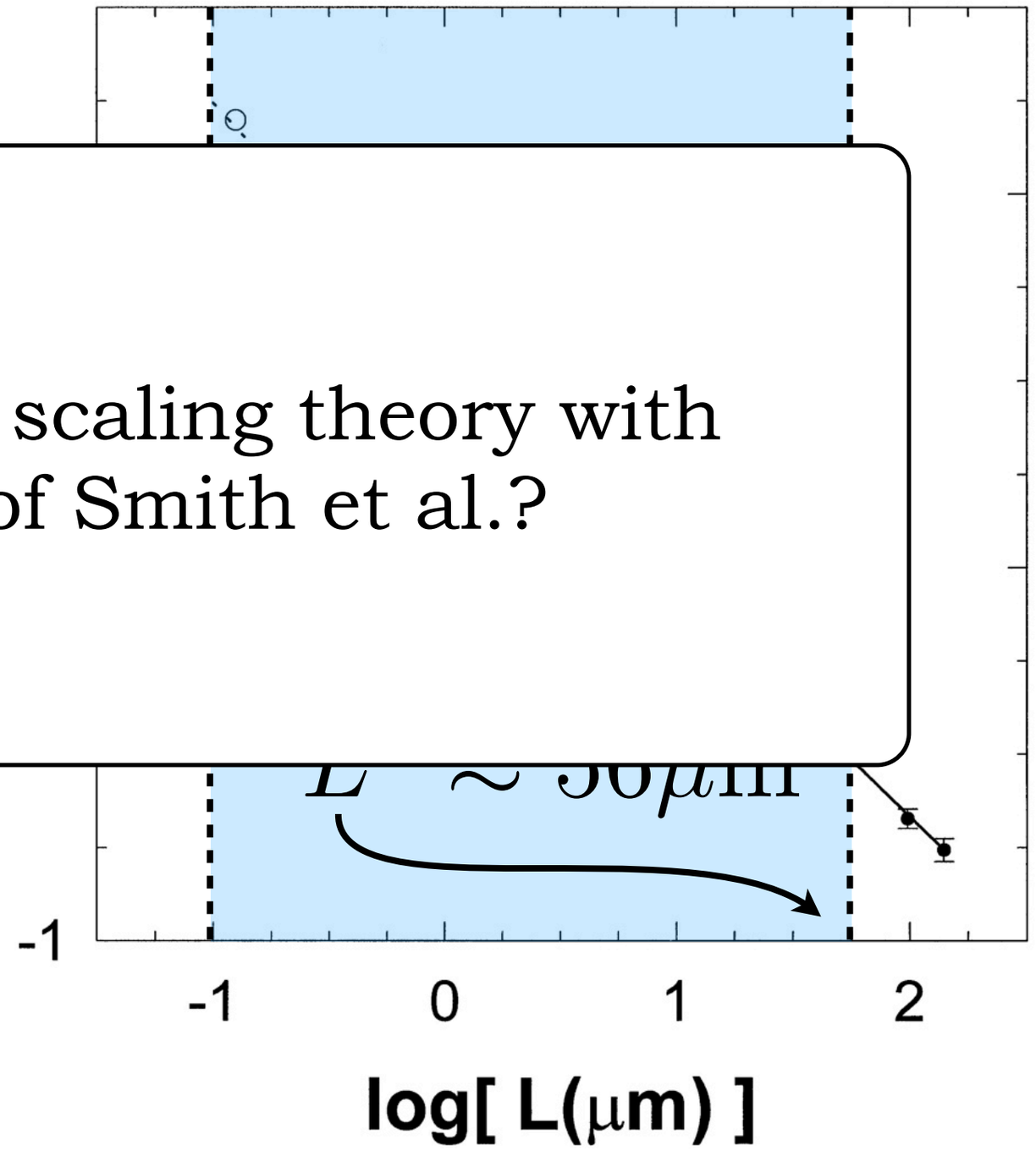
Monomer Anisotropy

The monomer anisotropy is a dimensionless ratio of the strength of the excluded volume to the stiffness.

$$\frac{L^*}{b} \sim \left(\frac{w}{b}\right)^{-2}$$

Can we reconcile scaling theory with the experiments of Smith et al.?

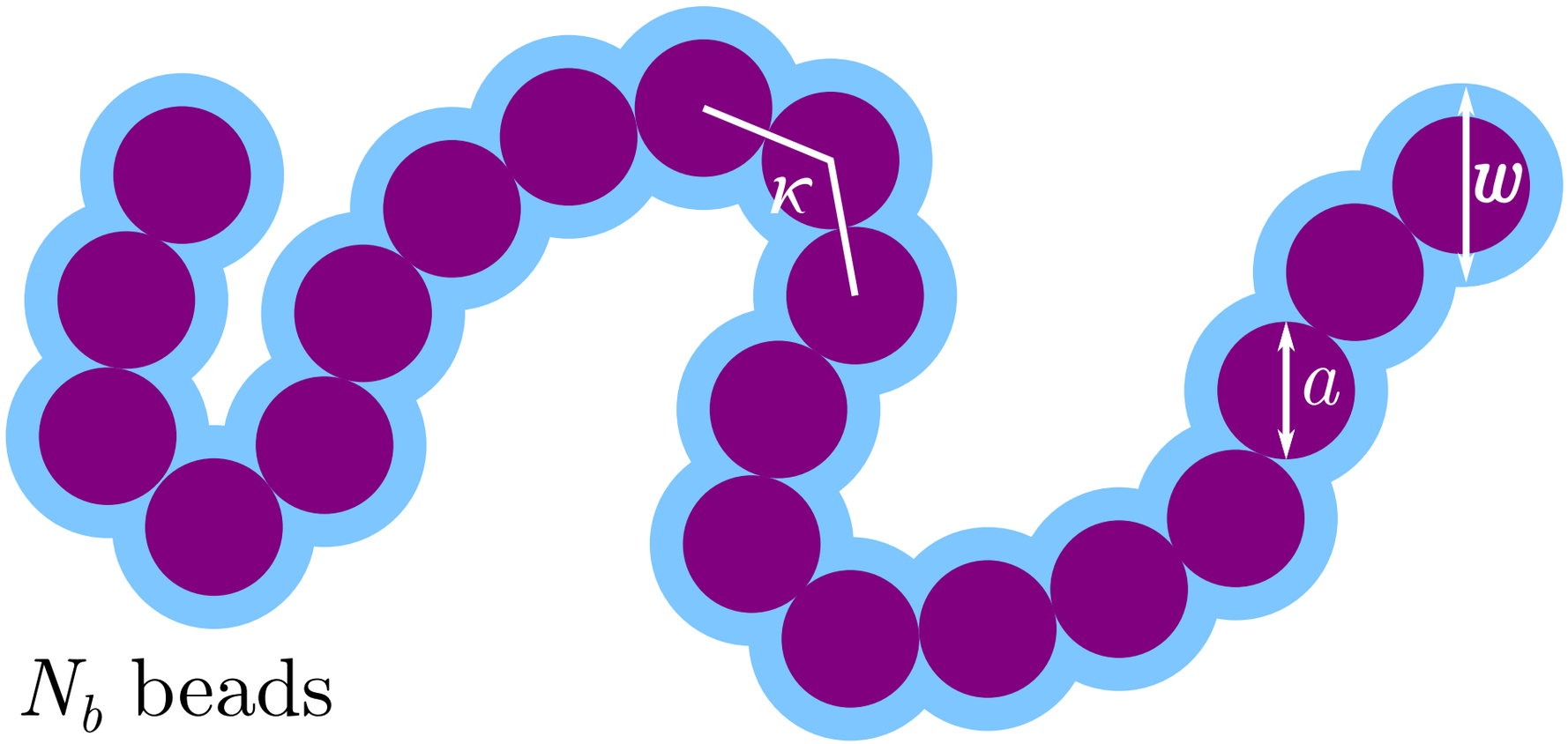
$$\frac{w}{b} \ll 1$$



A Numerical Approach

Discrete wormlike chain (DWLC)

- N_b touching hydrodynamic beads of size, a
- Hard-core beads of size, w
- Bending constant, $\kappa \approx l_p/a$

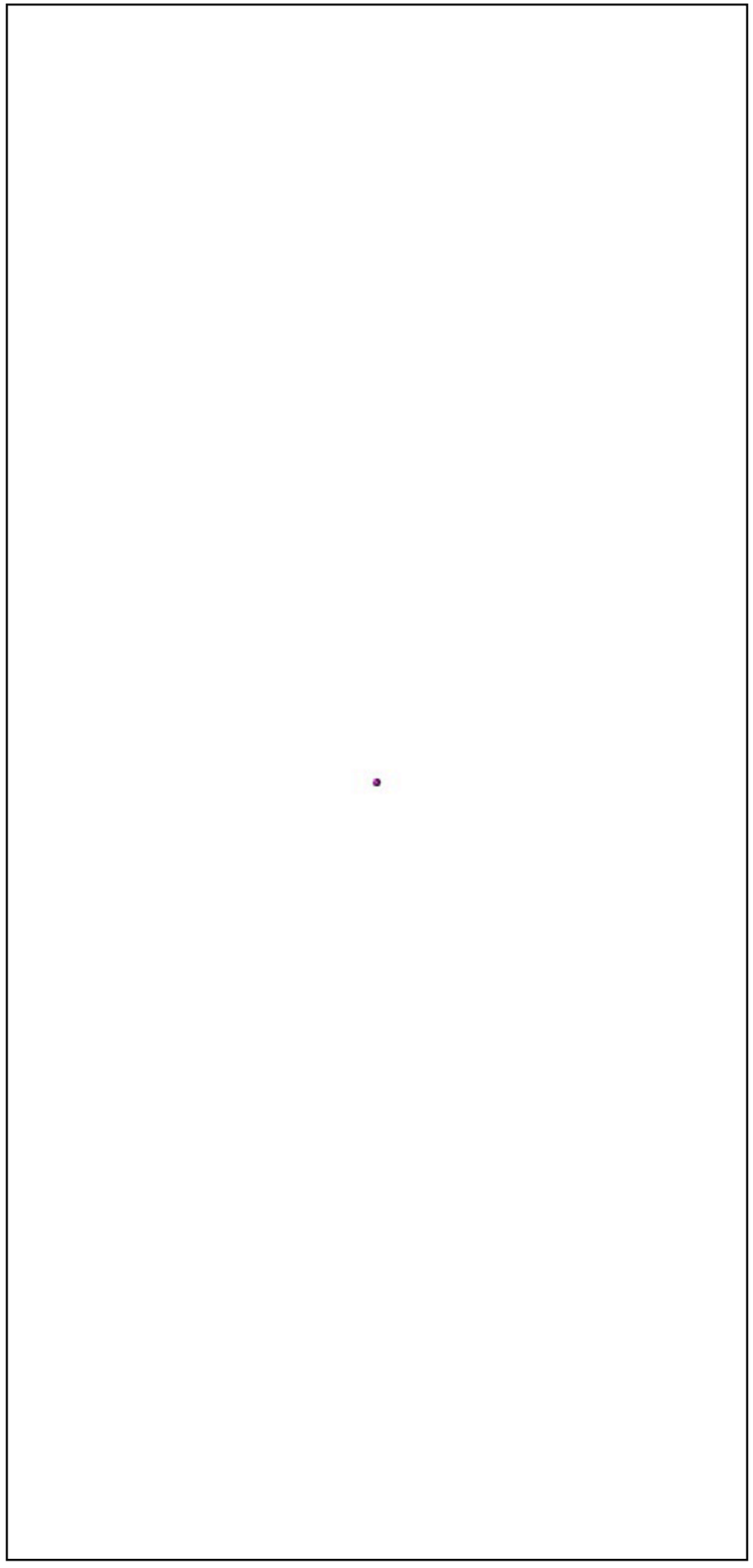


A Numerical Approach

- Long chains are needed for experimentally relevant length scales (λ-DNA requires about 5500 beads).
- Metropolis algorithm: chain relaxation time scales like L^2

Pruned-enriched Rosenbluth Method (PERM)

- MC chain-growth method
- Off-lattice
- Chain lengths up to 10^5 beads

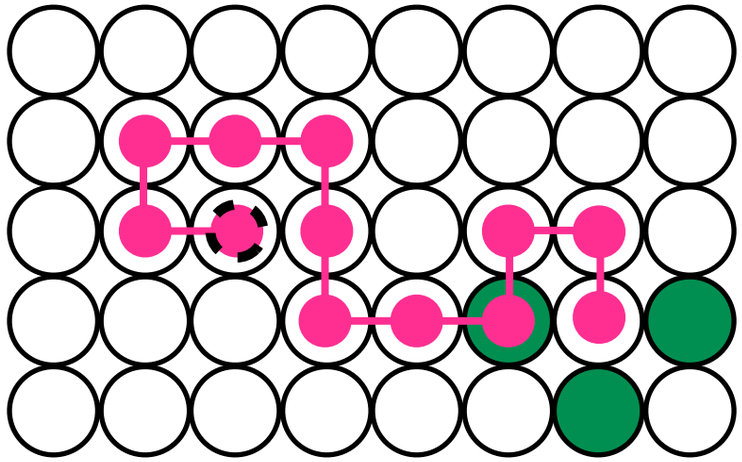


Grassberger. Phys. Rev. E. (1997).
Prellberg and Krawczyk. Phys. Rev. Lett. (2004).

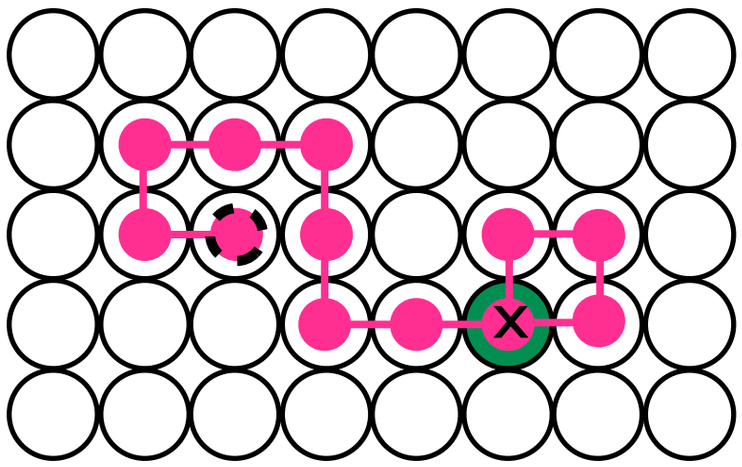
Basics of PERM

- Rosenbluth Method suffers from exponential attrition rate

Growth



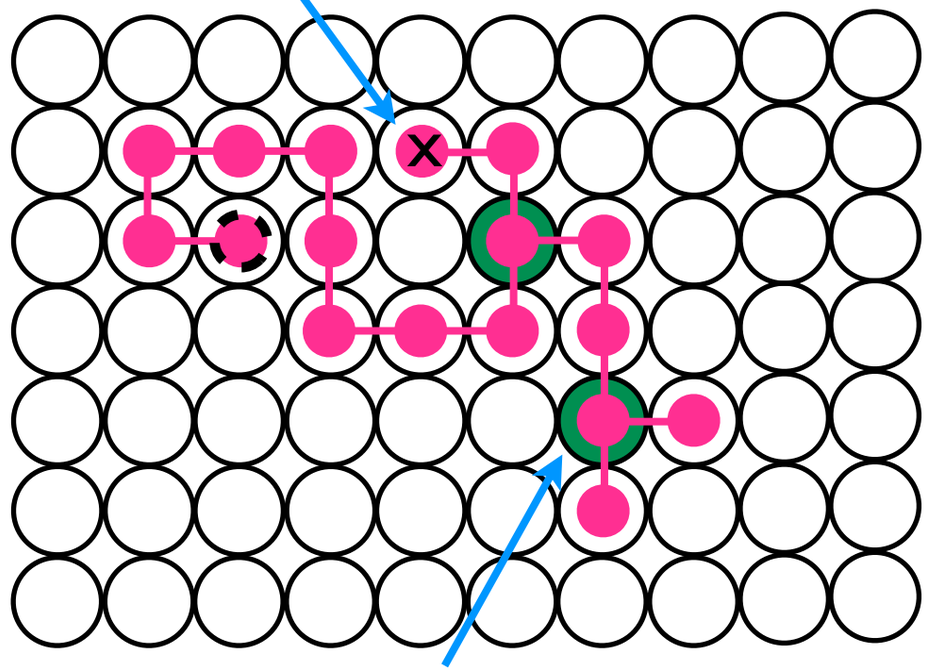
Attrition



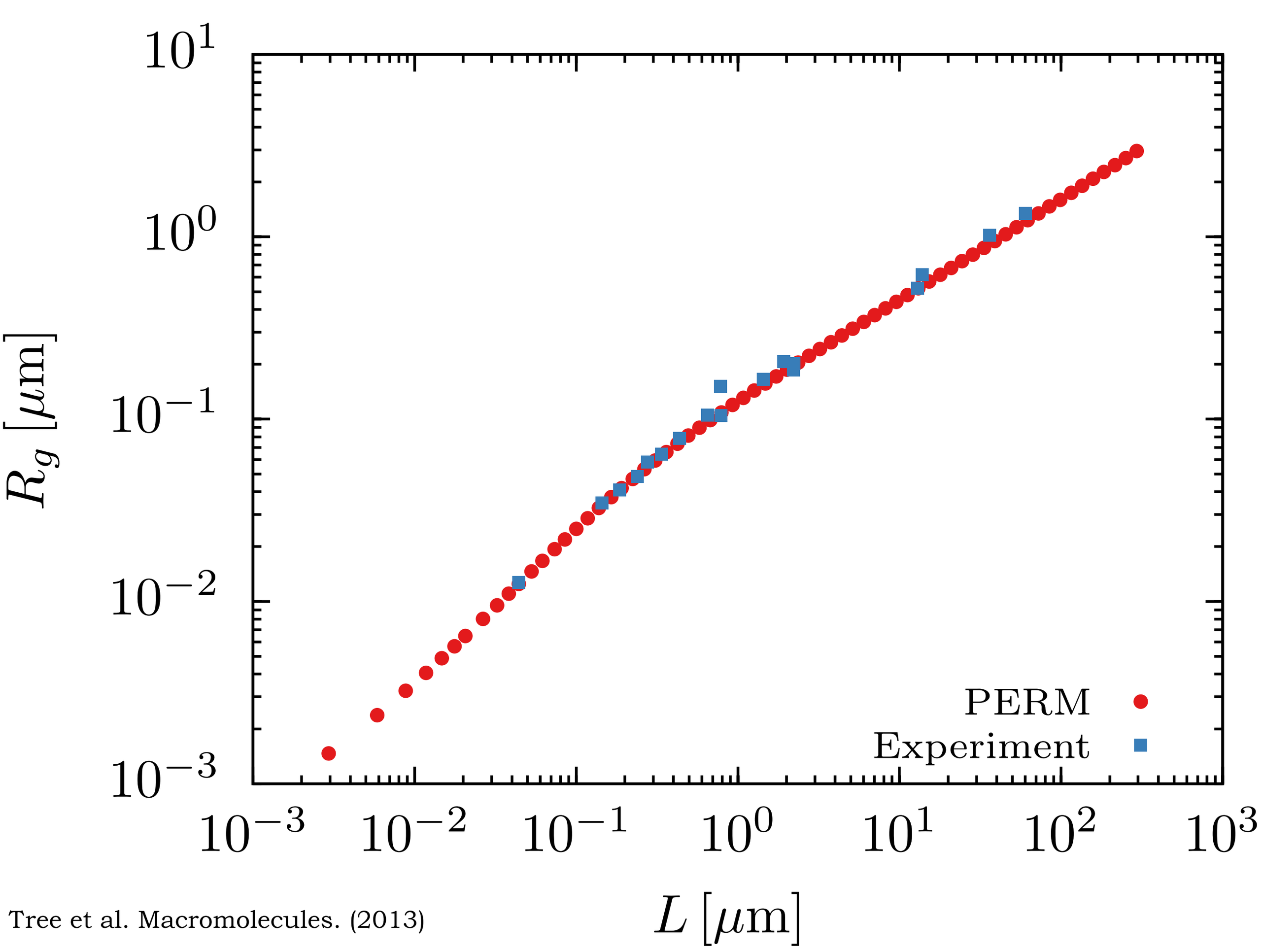
- PERM grows *tours* of chains and handles attrition statistically by *pruning* and *enrichment*.

Tour

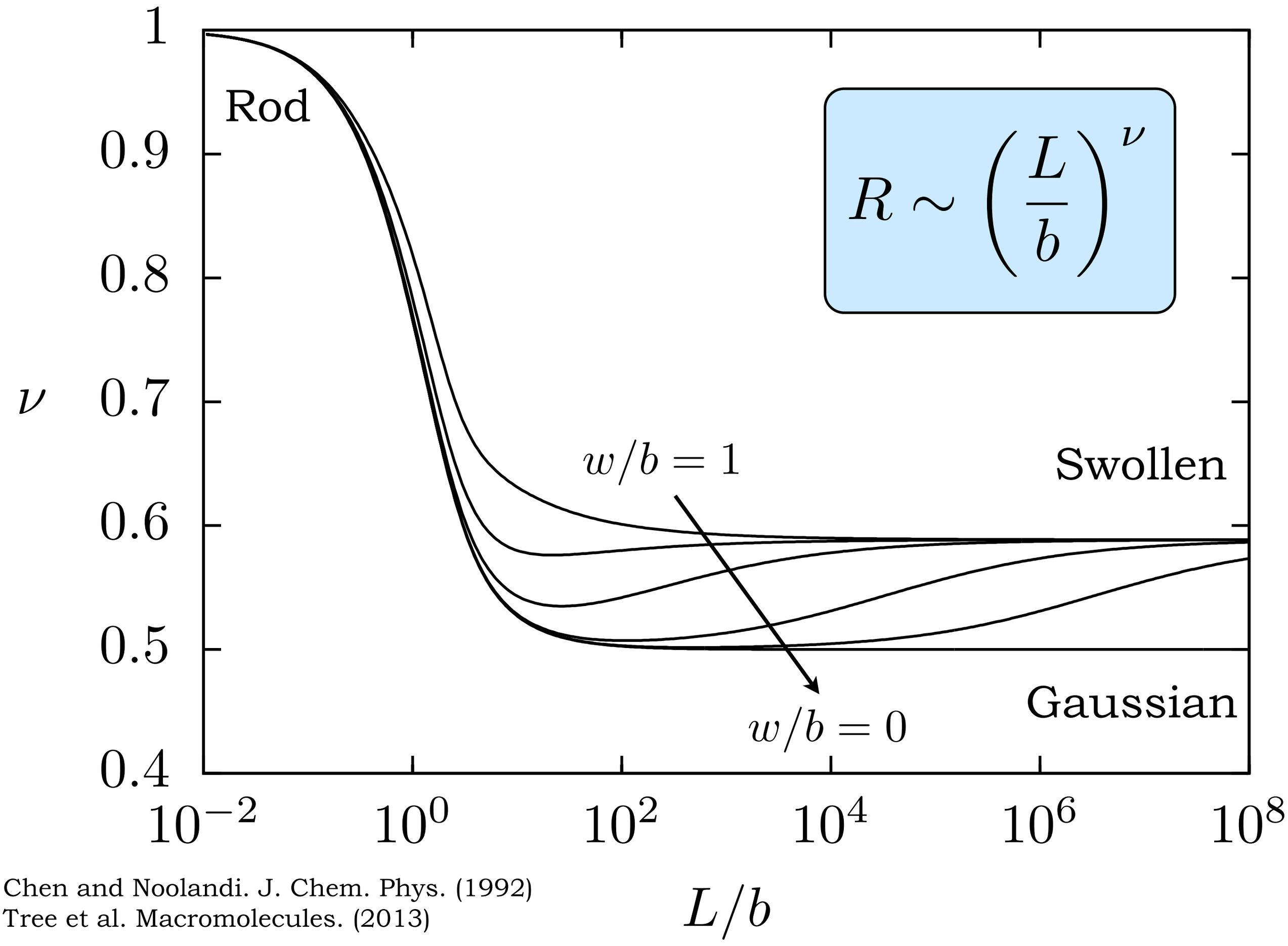
prune



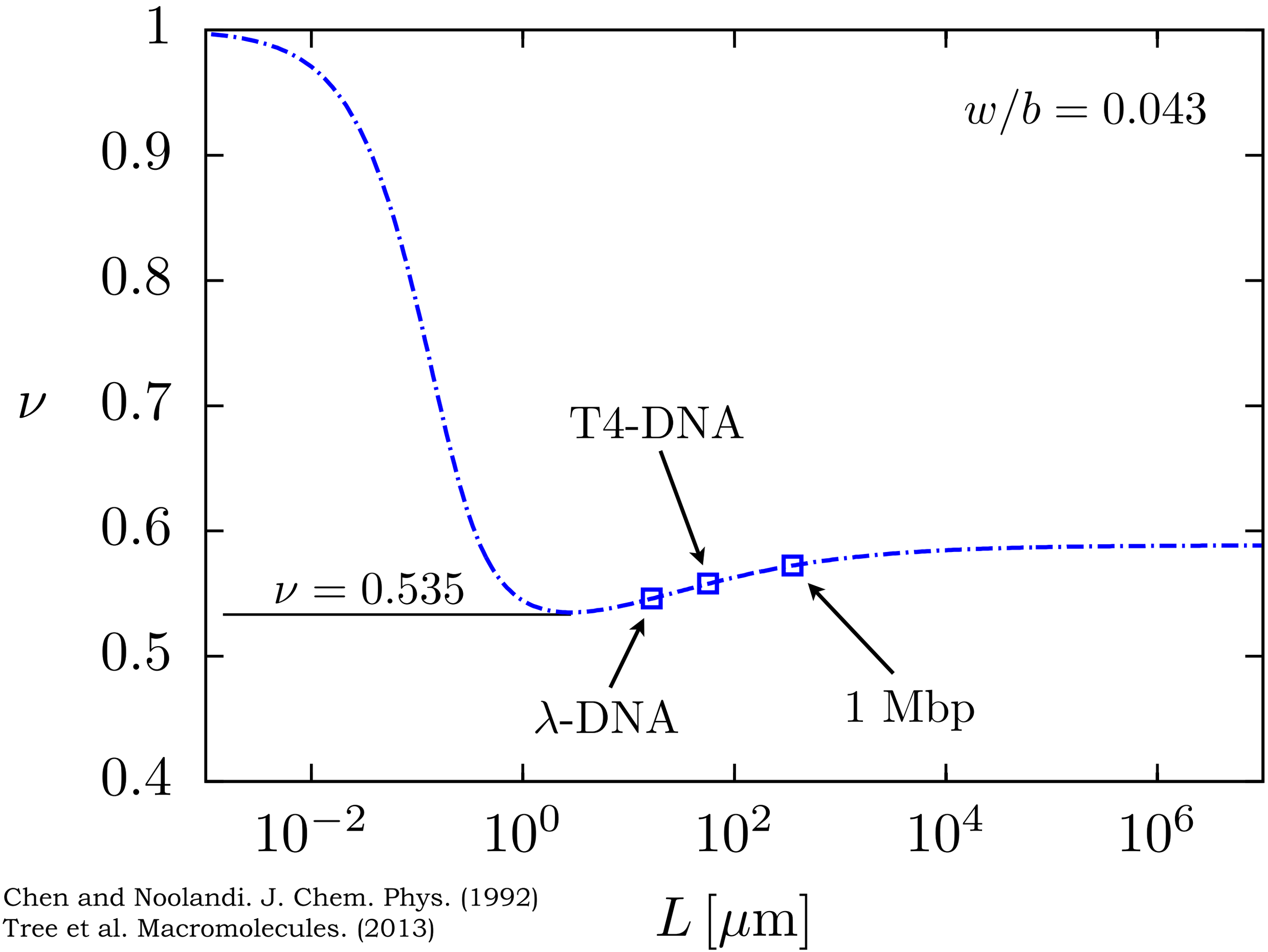
enrich



Tree et al. Macromolecules. (2013)



Chen and Noolandi. J. Chem. Phys. (1992)
Tree et al. Macromolecules. (2013)



Chen and Noolandi. J. Chem. Phys. (1992)
Tree et al. Macromolecules. (2013)

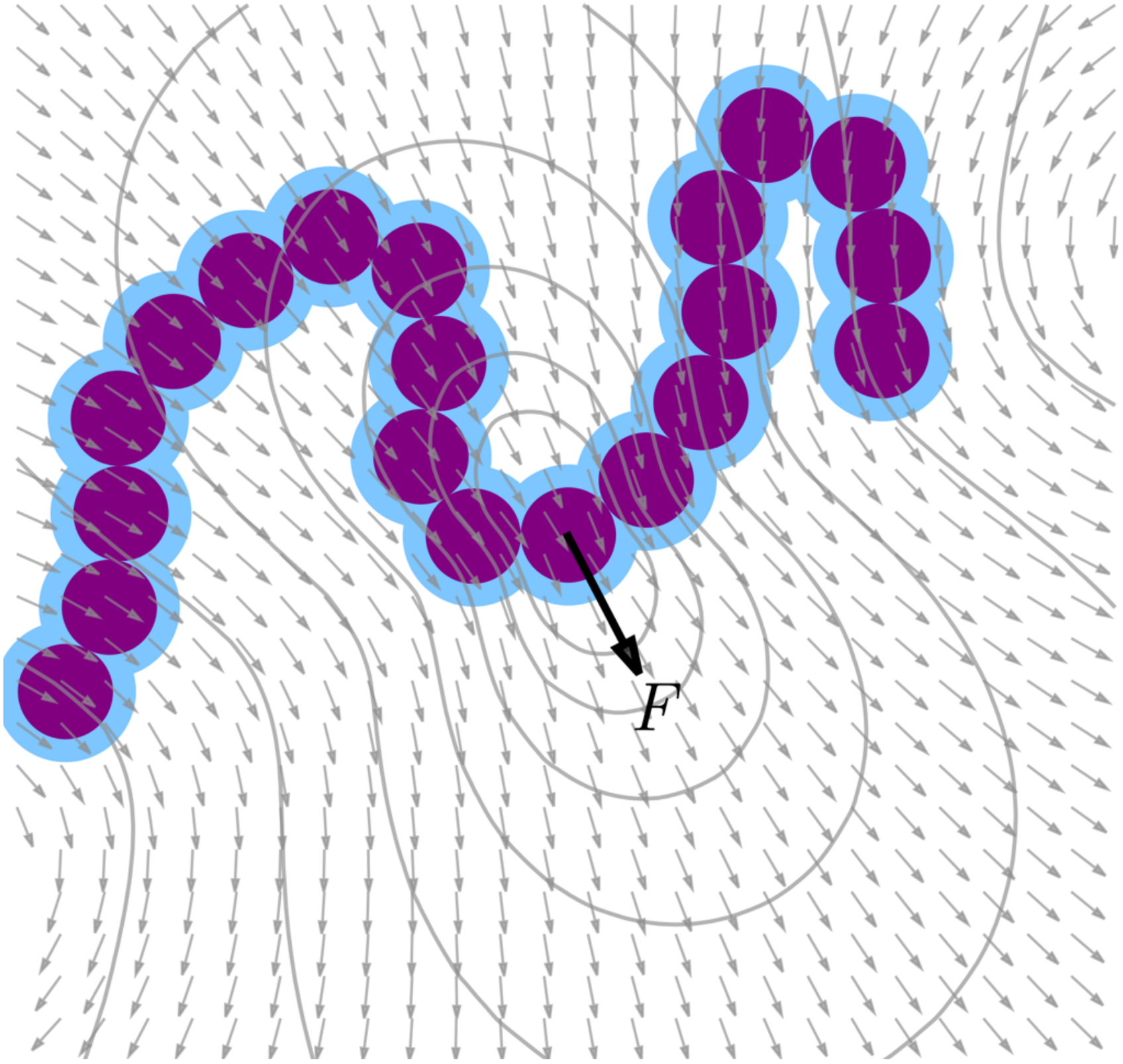
Results

Radius of gyration calculations:

- Confirm basic results of scaling theory (3 regimes, dependence on anisotropy)
- Scaling transitions are broad and continuous.
- Crossover length is *longer* than anticipated (1 Mbp) -- opposite of what we expected from experiments.

What do dynamics tell us?

Hydrodynamic interactions

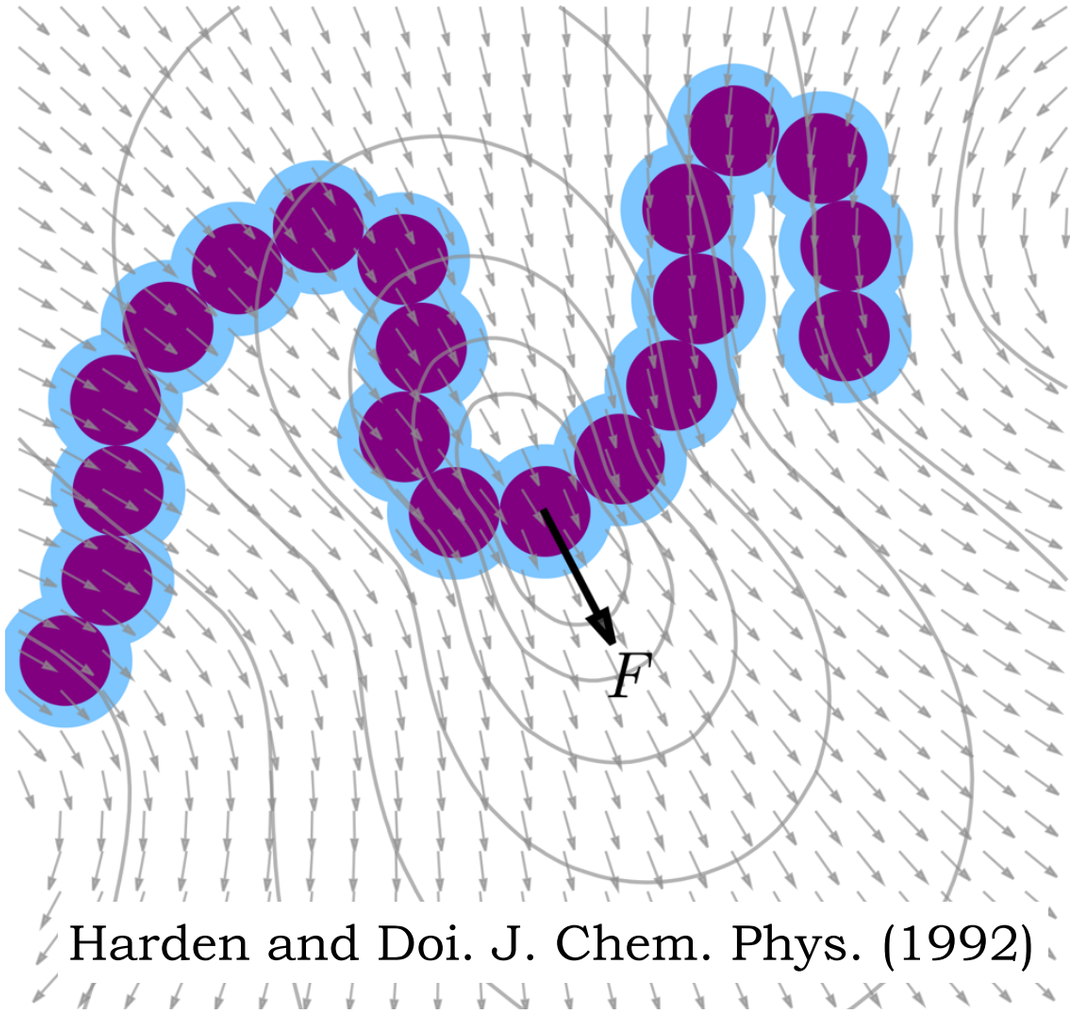


Rigid-Body Approximation to HI

Diffusivity is approximated as the thermal averaged hydrodynamic mobility.

$$D = \frac{k_B T}{3} \langle \mathrm{Tr}(\mathbf{\Omega}) \rangle$$

- Assumes near-equilibrium configurations which are perturbed by infinitesimal forces.
- Neglects correlations due to Brownian motion (mean field approximation).



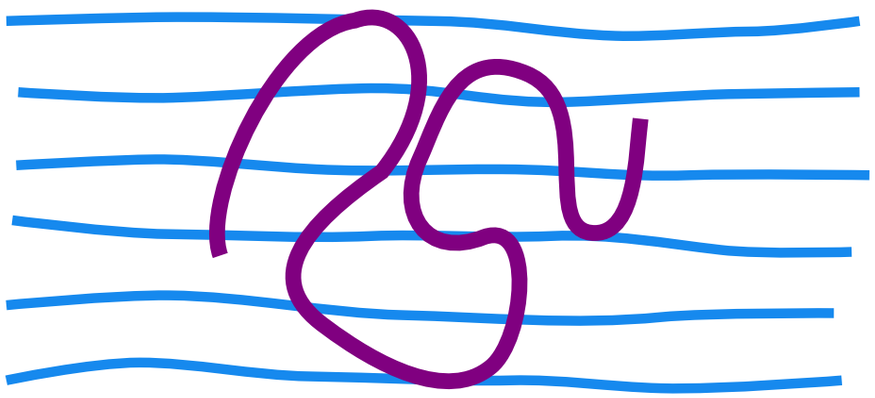
Harden and Doi. J. Chem. Phys. (1992)

$$\mathbf{\Omega} = \frac{1}{N^2} \sum_{i,j} \left[\left(\frac{\delta_{ij}}{3\pi\eta a} + \frac{1-\delta_{ij}}{8\pi\eta r_{ij}} \right) \mathbf{I} + \frac{\mathbf{r}_{ij}\mathbf{r}_{ij}}{r_{ij}^2} \right]$$

Hydrodynamics of WLCs

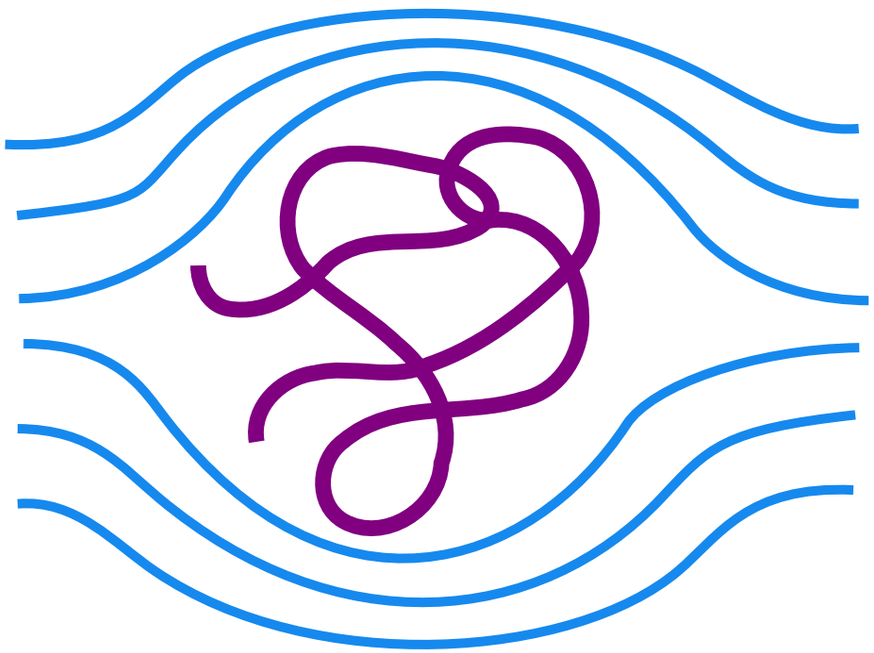
Rod

$$D \sim \frac{k_B T}{\eta L} \ln\left(\frac{L}{2a}\right)$$



Draining Coil
(weak HI)

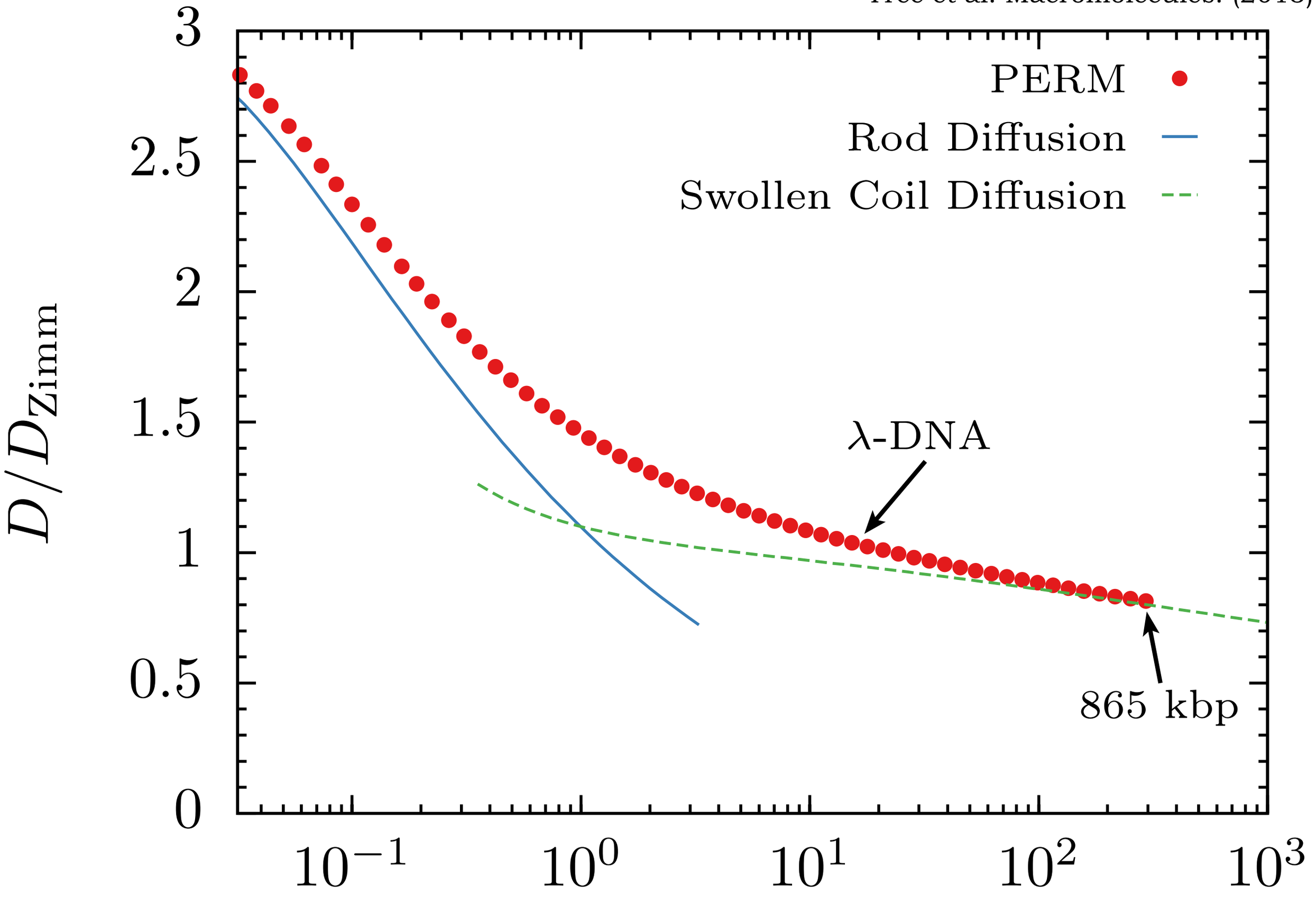
$$D \sim \frac{k_B T}{\eta L}$$



Non-Draining Coil
(strong HI)

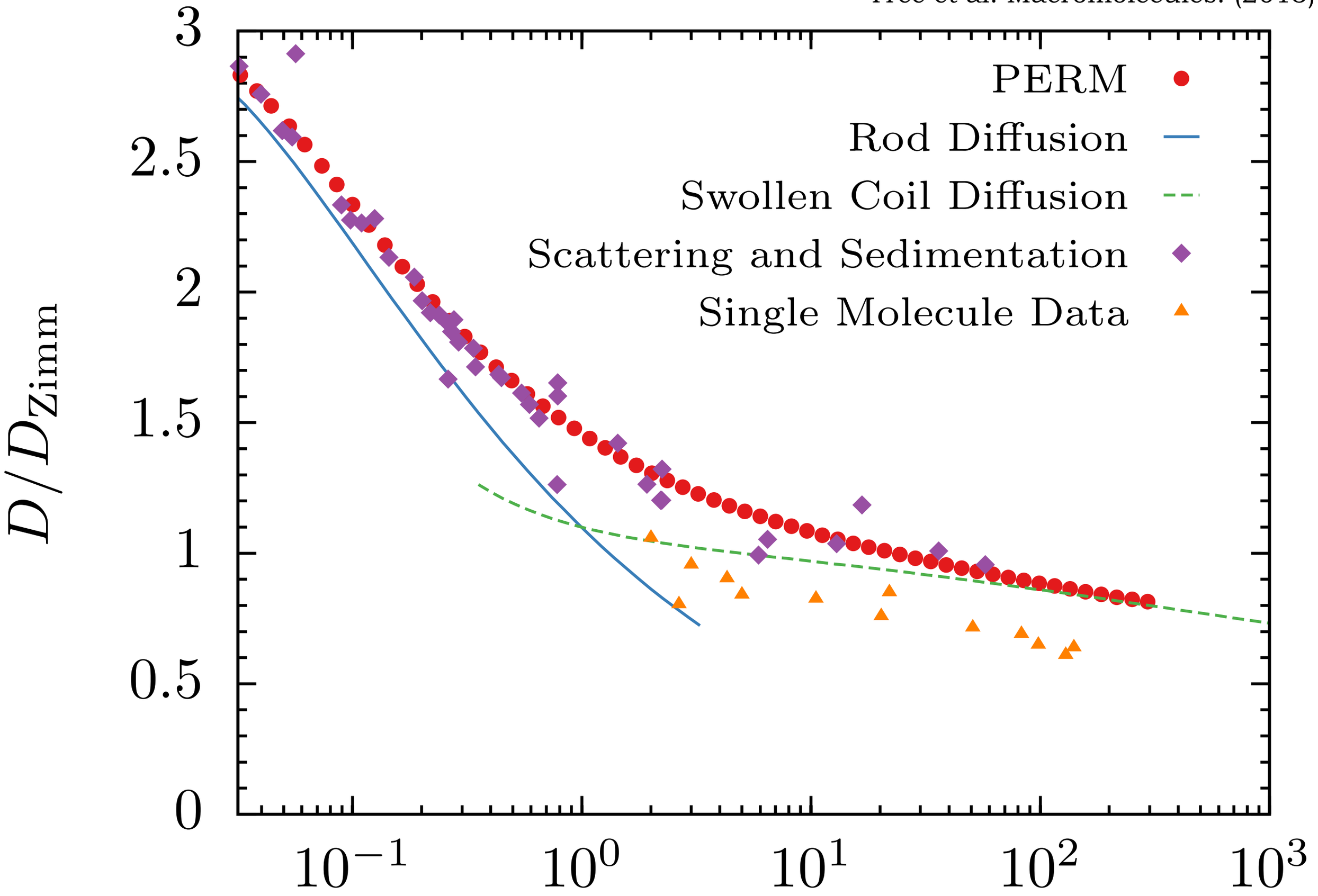
$$D \sim \frac{k_B T}{\eta R_g}$$

Tree et al. Macromolecules. (2013)

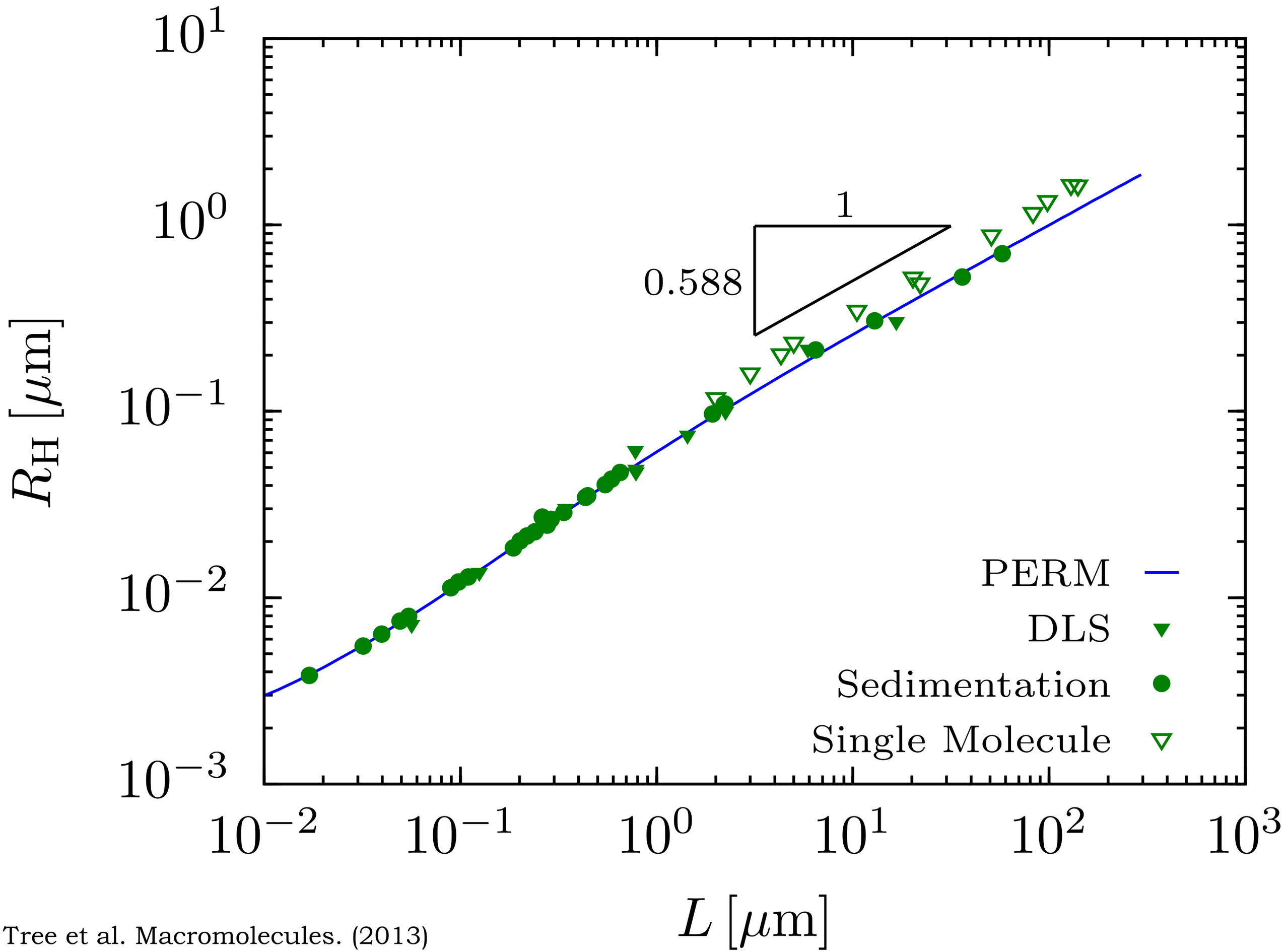


$$D_{\mathrm{Zimm}} = \frac{8}{3\sqrt{6\pi^3}} \frac{k_B T}{\eta \sqrt{L b}}$$

Tree et al. Macromolecules. (2013)



$$D_{\mathrm{Zimm}} = \frac{8}{3\sqrt{6\pi^3}} \frac{k_B T}{\eta \sqrt{Lb}}$$



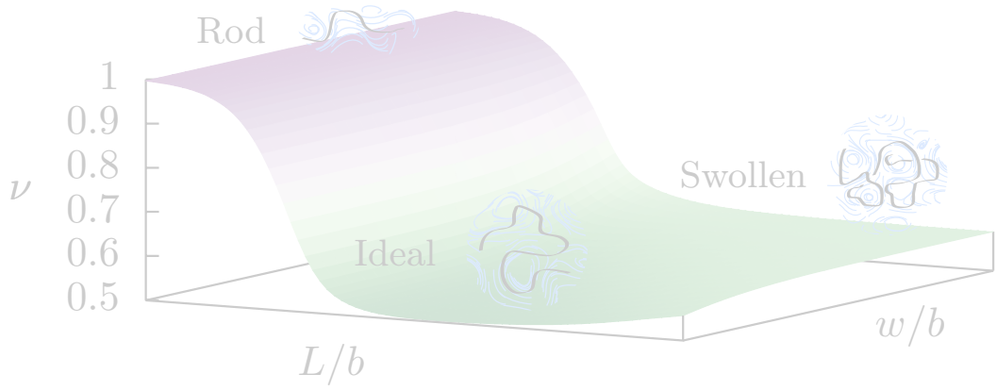
Tree et al. Macromolecules. (2013)

Conclusions

- Can model DNA as a wormlike chain.
- Basic scaling theory results are confirmed using Monte Carlo simulation.
- Crossover to universal behavior happens at very long contour lengths -- greater than 1 Mbp.
- The measured scaling exponent is not sensitive enough to indicate subtle changes in polymer draining behavior.

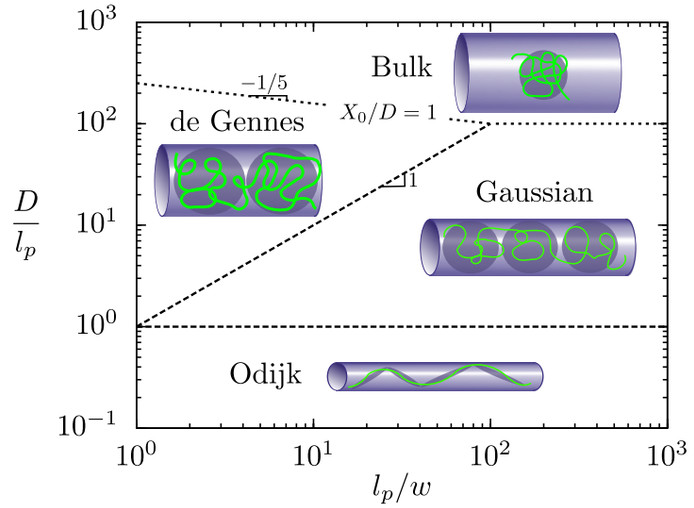
DR Tree, A Muralidhar, PS Doyle and KD Dorfman,
Macromolecules. 46 (20) 8369-8382 (2013).

Polymer Physics of DNA in Solution



DR Tree, A Muralidhar, PS Doyle and KD Dorfman, Macromolecules (2013).

Regimes of Confined DNA



DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 110, 208103 (2013).

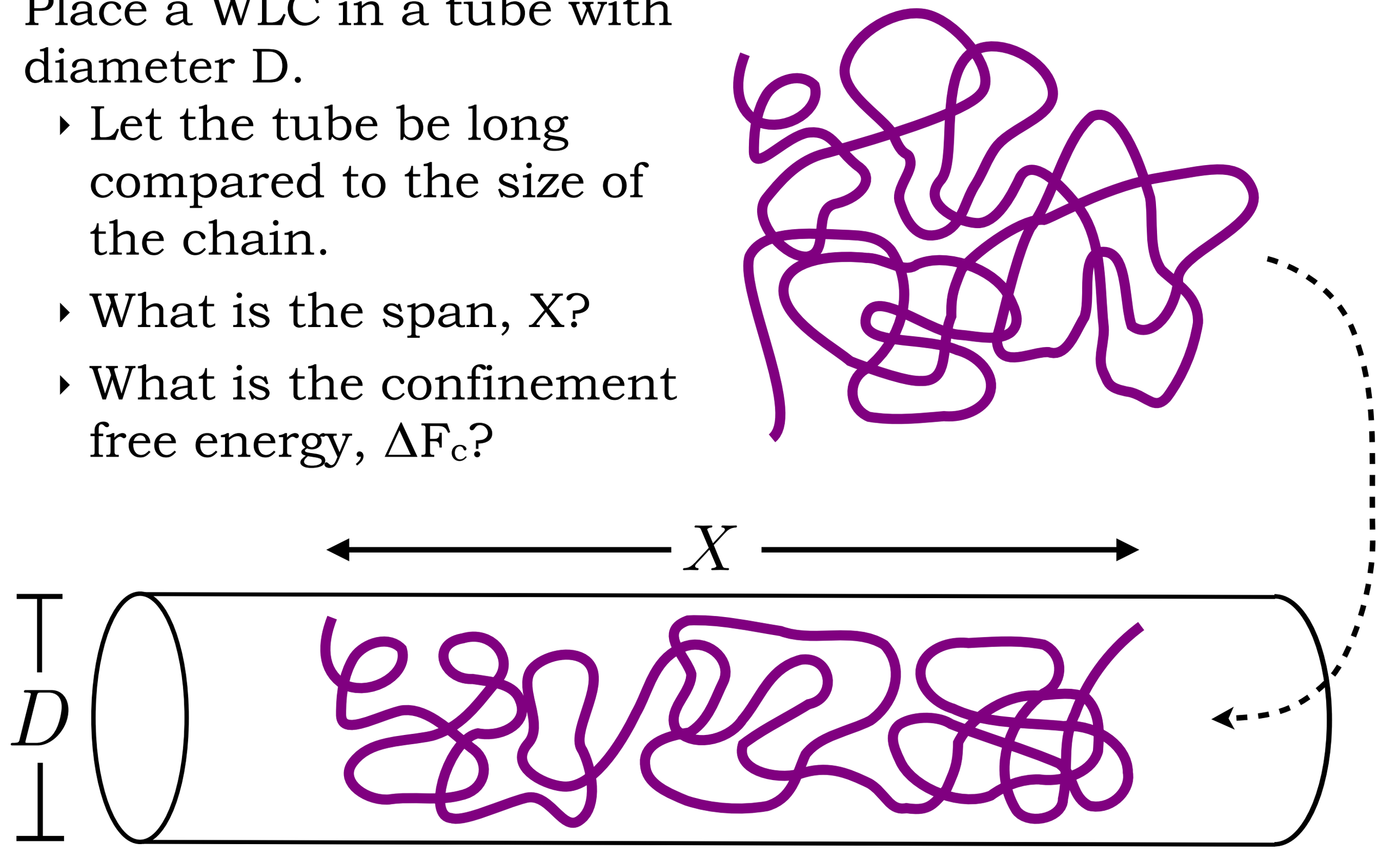
Hydrodynamics of Confined DNA

DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 108, 228015 (2012).

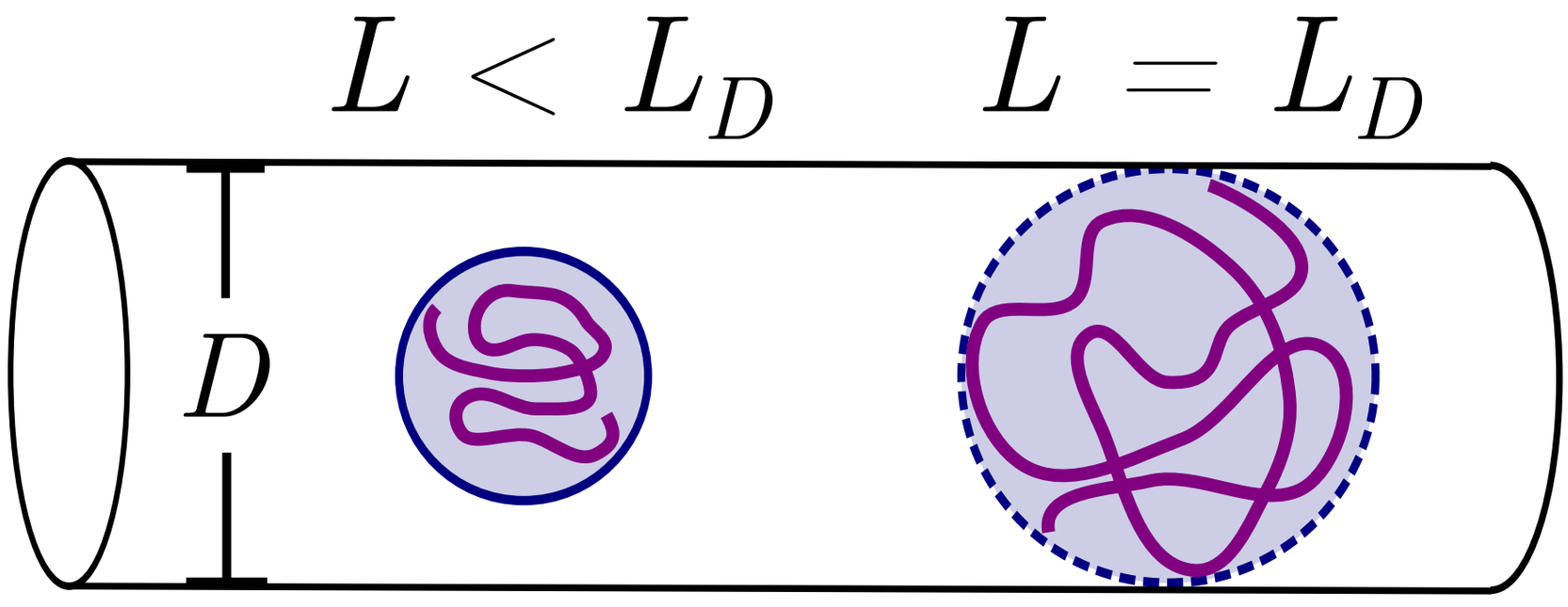
Confined Semiflexible Polymer

Place a WLC in a tube with diameter D.

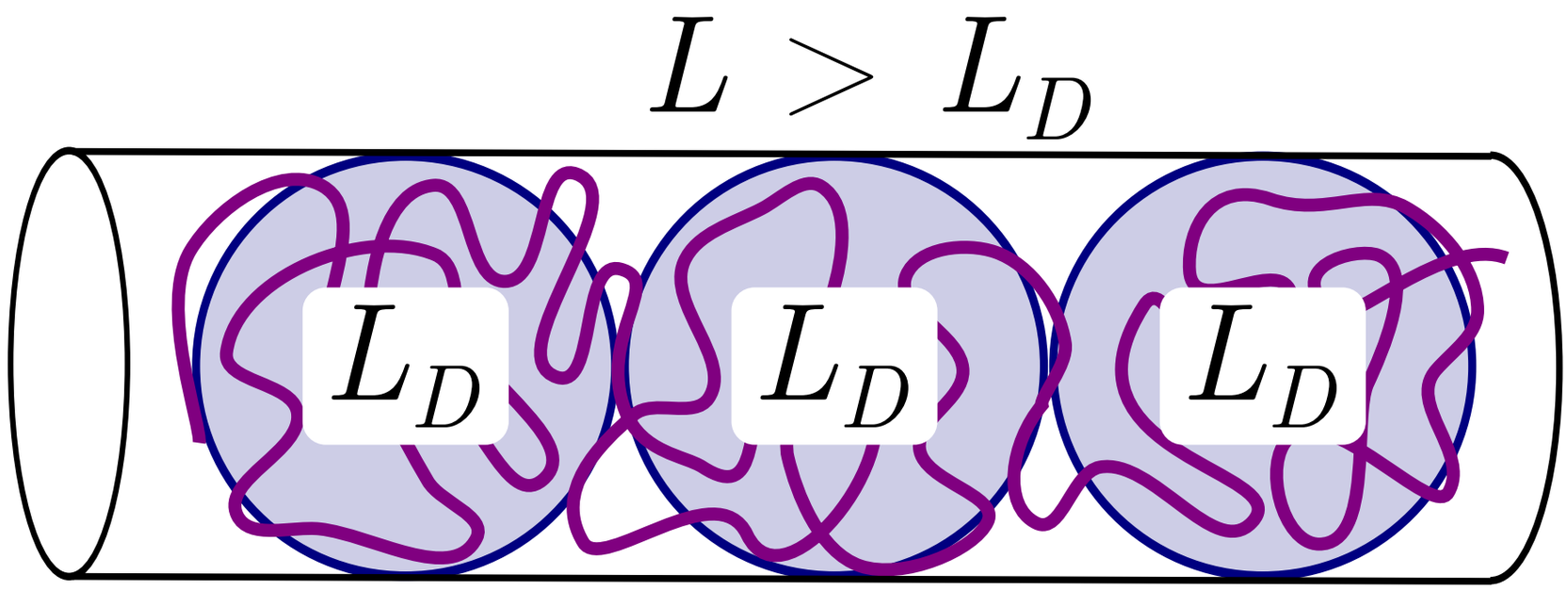
- Let the tube be long compared to the size of the chain.
- What is the span, X?
- What is the confinement free energy, ΔF_c?



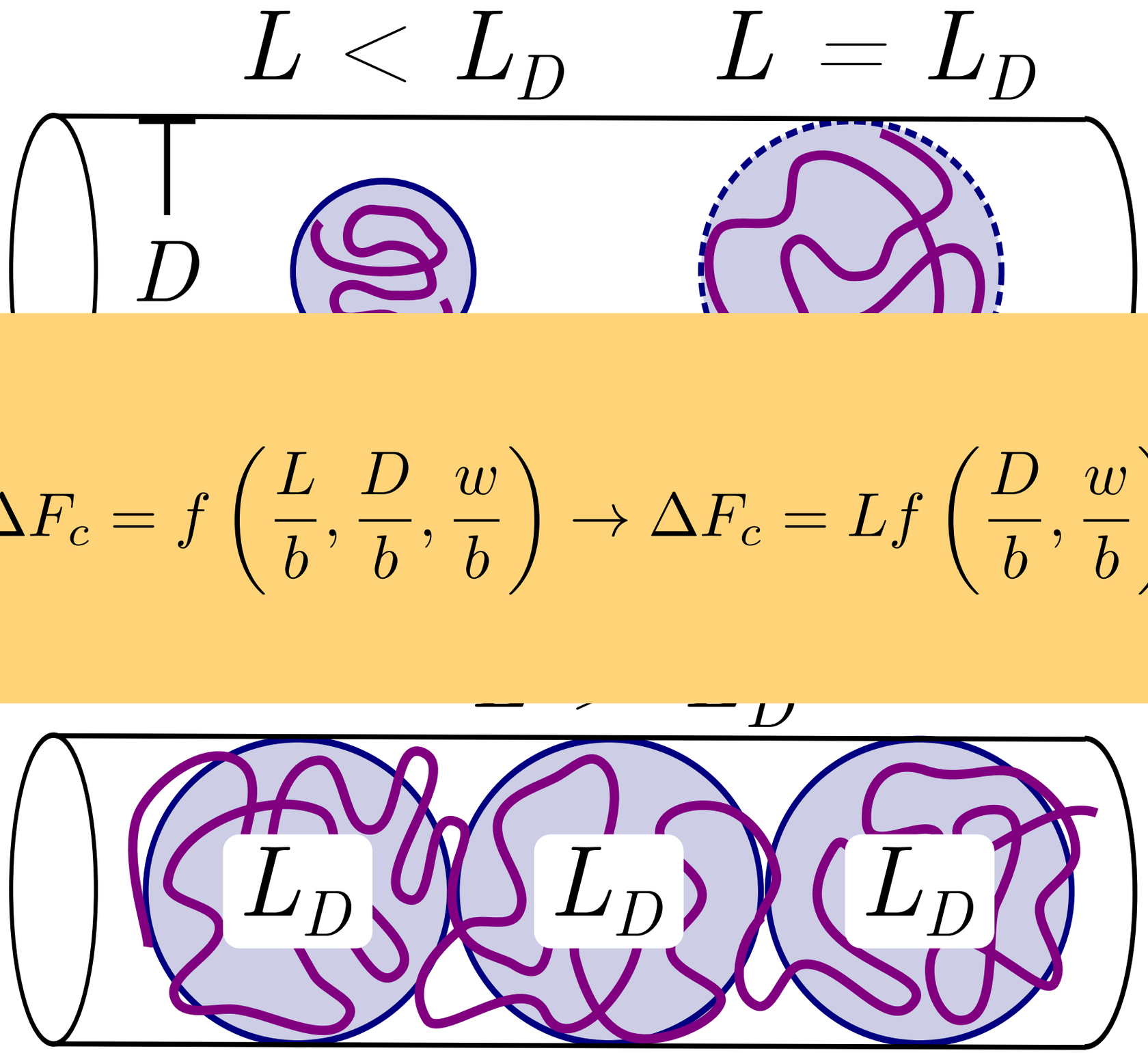
Confining a Chain



- Properties for long chains are extensive in subunits made of length L_D.



Confining a Chain



$$\Delta F_c = f\left(\frac{L}{b}, \frac{D}{b}, \frac{w}{b}\right) \rightarrow \Delta F_c = Lf\left(\frac{D}{b}, \frac{w}{b}\right)$$

- Prop made of ler

Swollen Coil

Gaussian Coil

$\nu = 0.588$

2

1

$\nu = 0.5$

Rod

$\nu = 1$

$\frac{L}{b}$

b/w

10^{4}

10^{3}

10^{2}

10^{1}

10^{0}

10^{-1}

10^{0}

10^{1}

10^{2}

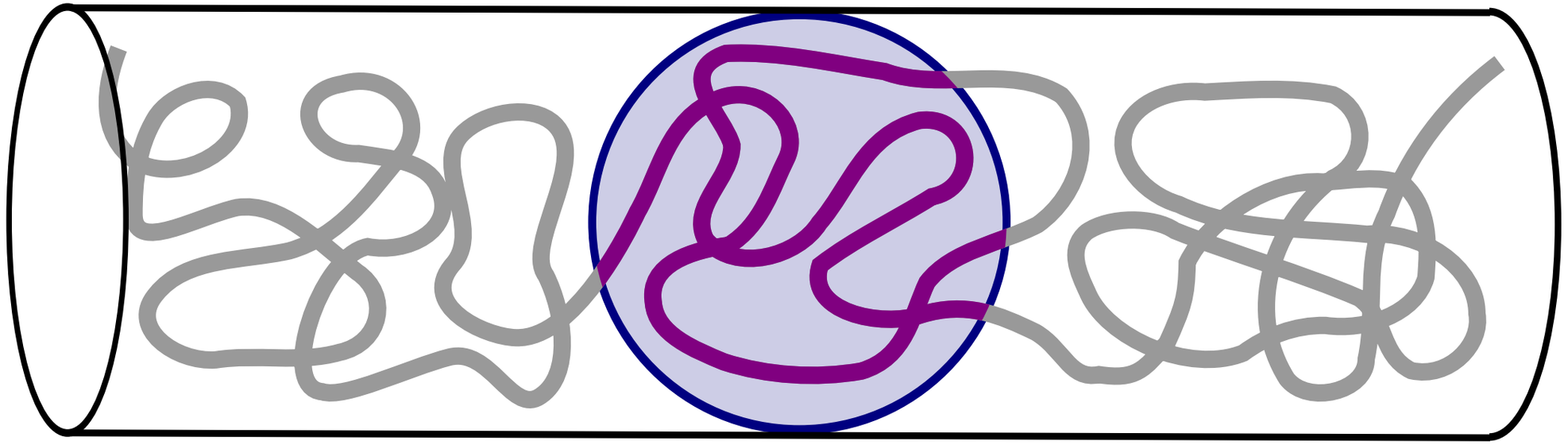
10^{3}

Confined Chain -- de Gennes

- The chain is composed of a linear string of blobs.

$$l_p \ll D \ll R_g$$

$$D \sim L_{\text{blob}}^{3/5} \qquad F \sim k_B T \frac{L}{L_{\text{blob}}}$$

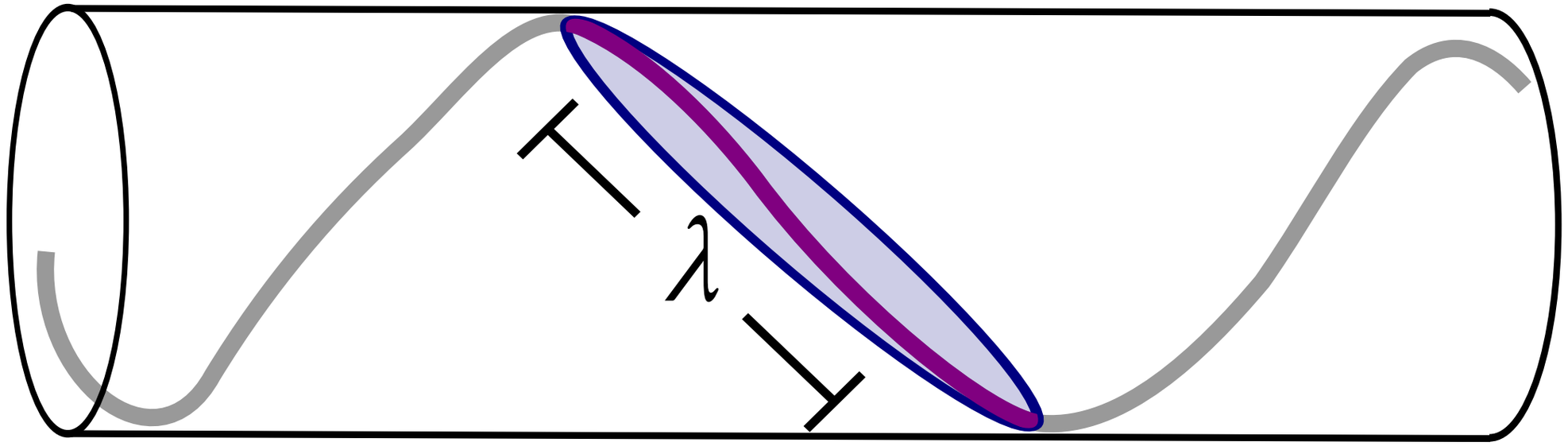


$$F \sim k_B T L D^{-5/3}$$

Confined Chain -- Odijk

$$D \ll l_p$$

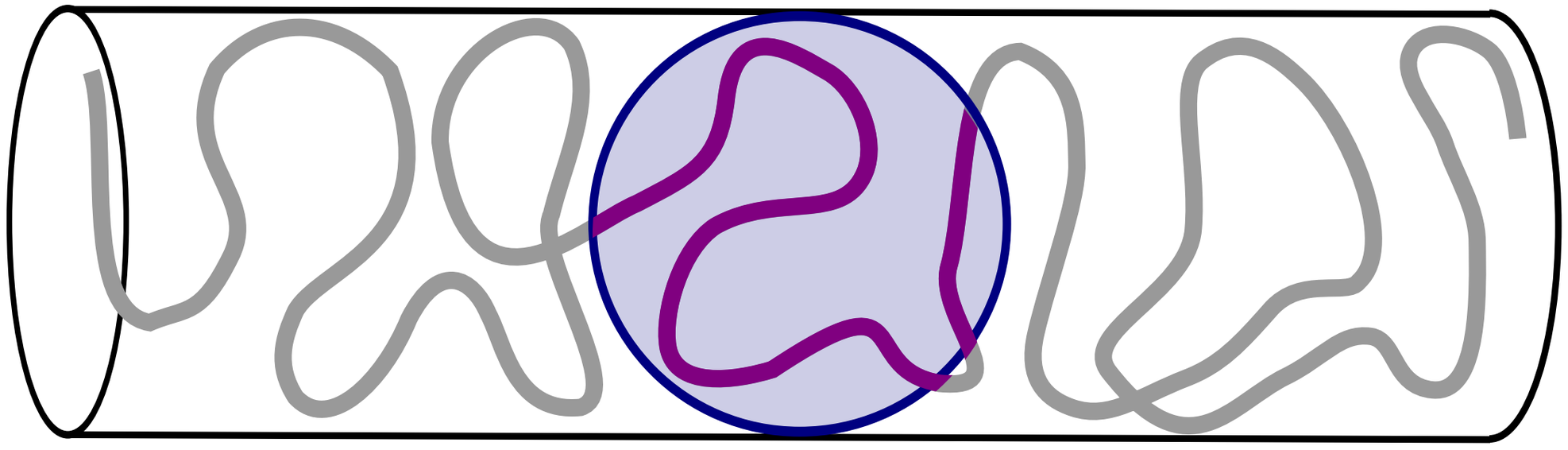
$$\lambda \sim D^{2/3} l_p^{1/3} \qquad F \sim k_B T \frac{L}{\lambda}$$



$$F \sim k_B T L D^{-2/3}$$

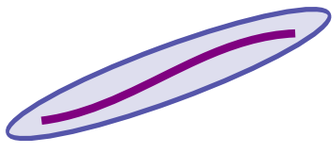
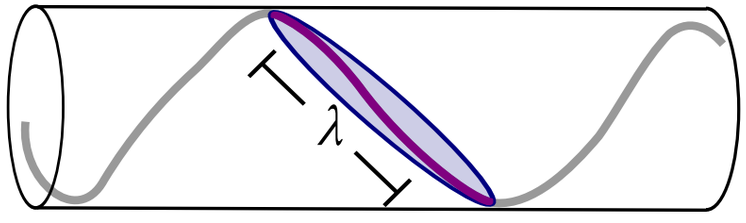
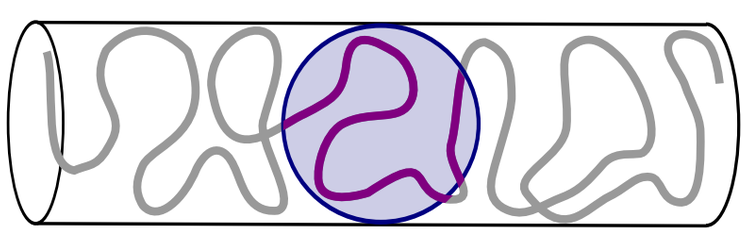
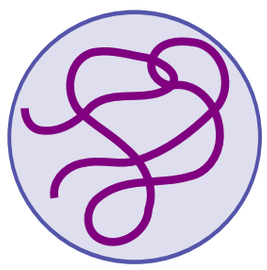
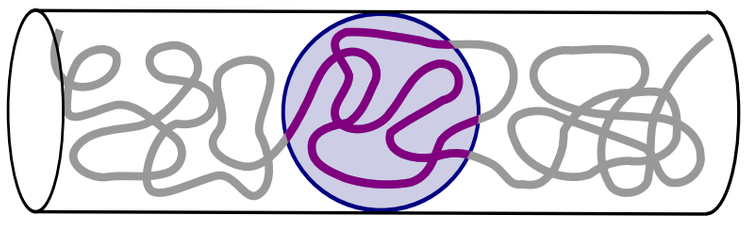
What about a Gaussian-like regime?

$$D \sim L_{\text{blob}}^{1/2}$$



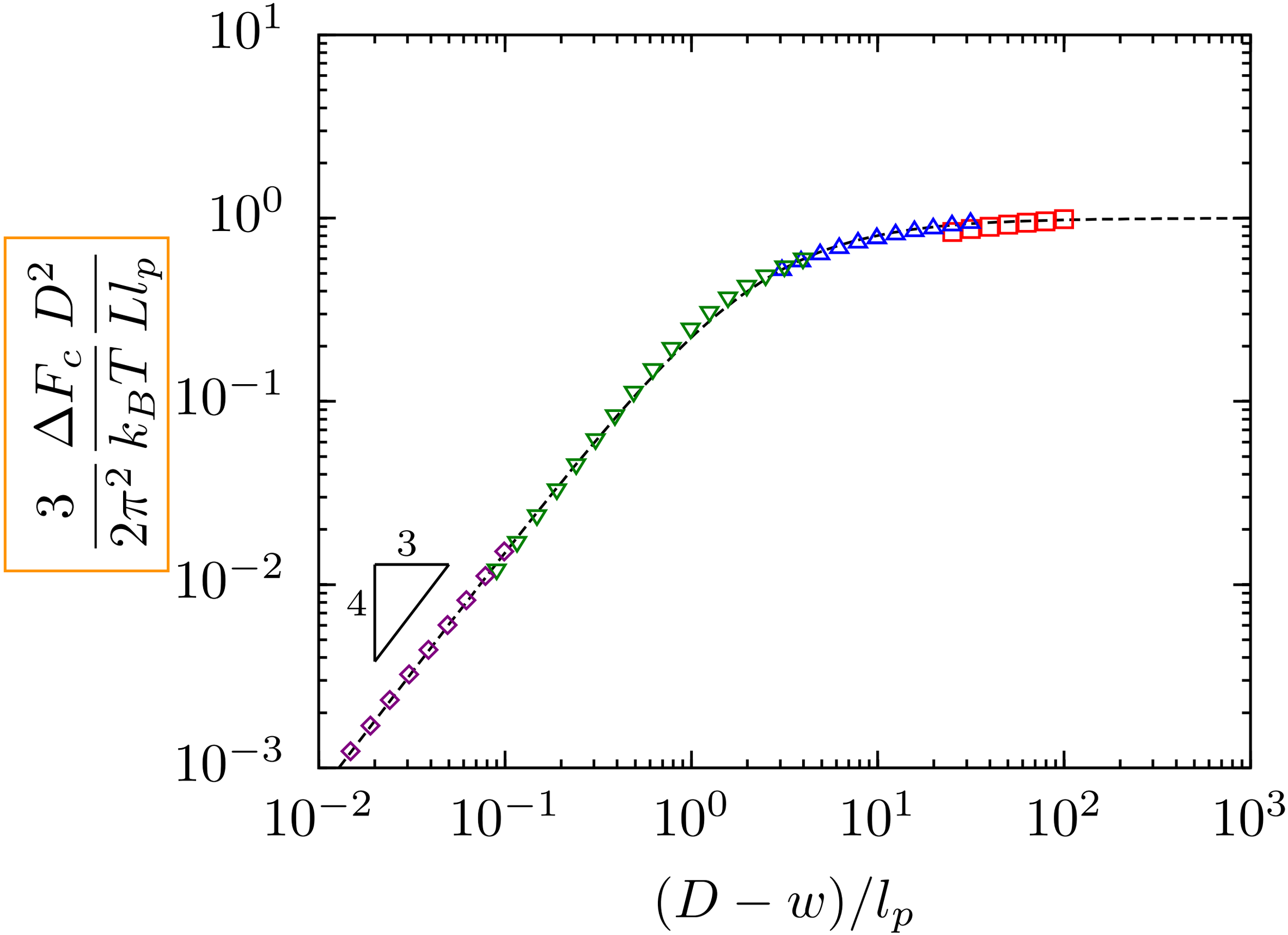
$$F \sim k_B T L D^{-2}$$

Summary of Confined Chain Theory

Unconfined	Confined	
		$F \sim D^{-2/3}$
		$F \sim D^{-2}$
		$F \sim D^{-5/3}$

DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 110, 208103 (2013).

Confined Chain without Excluded Volume



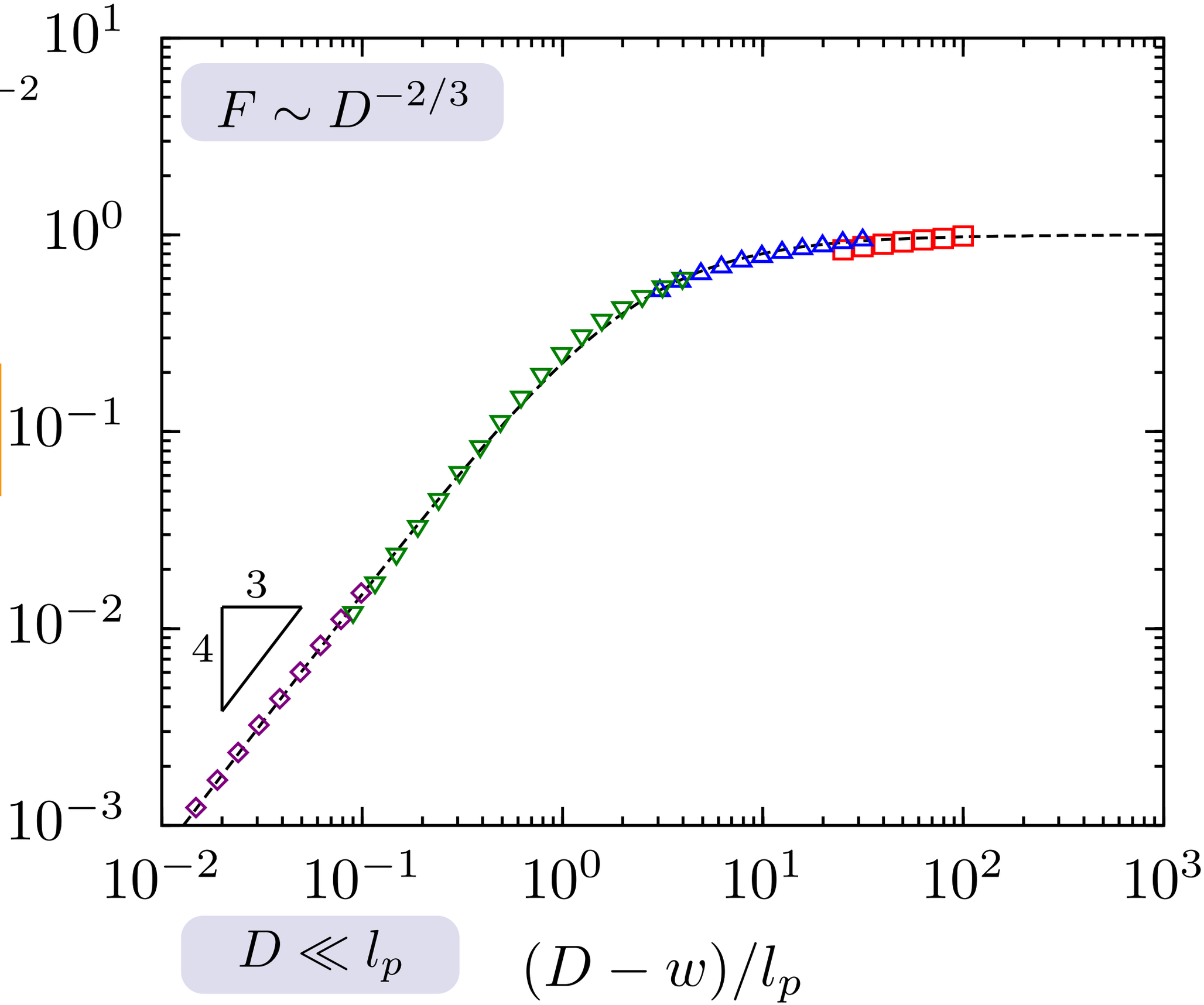
Confined Chain without Excluded Volume

$F_0 \sim D^{-2}$

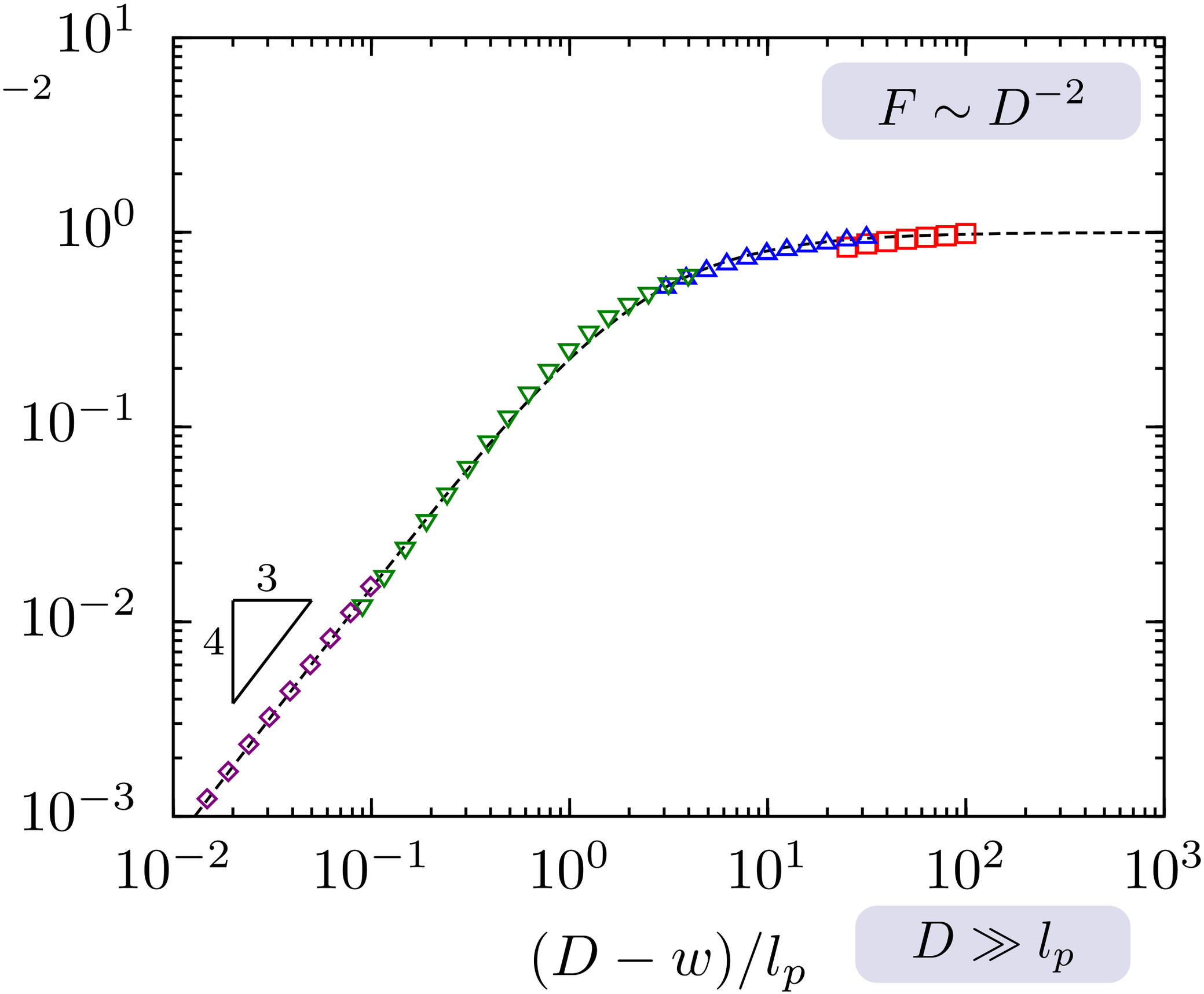
$F \sim D^{-2/3}$

$\frac{F}{F_0}$

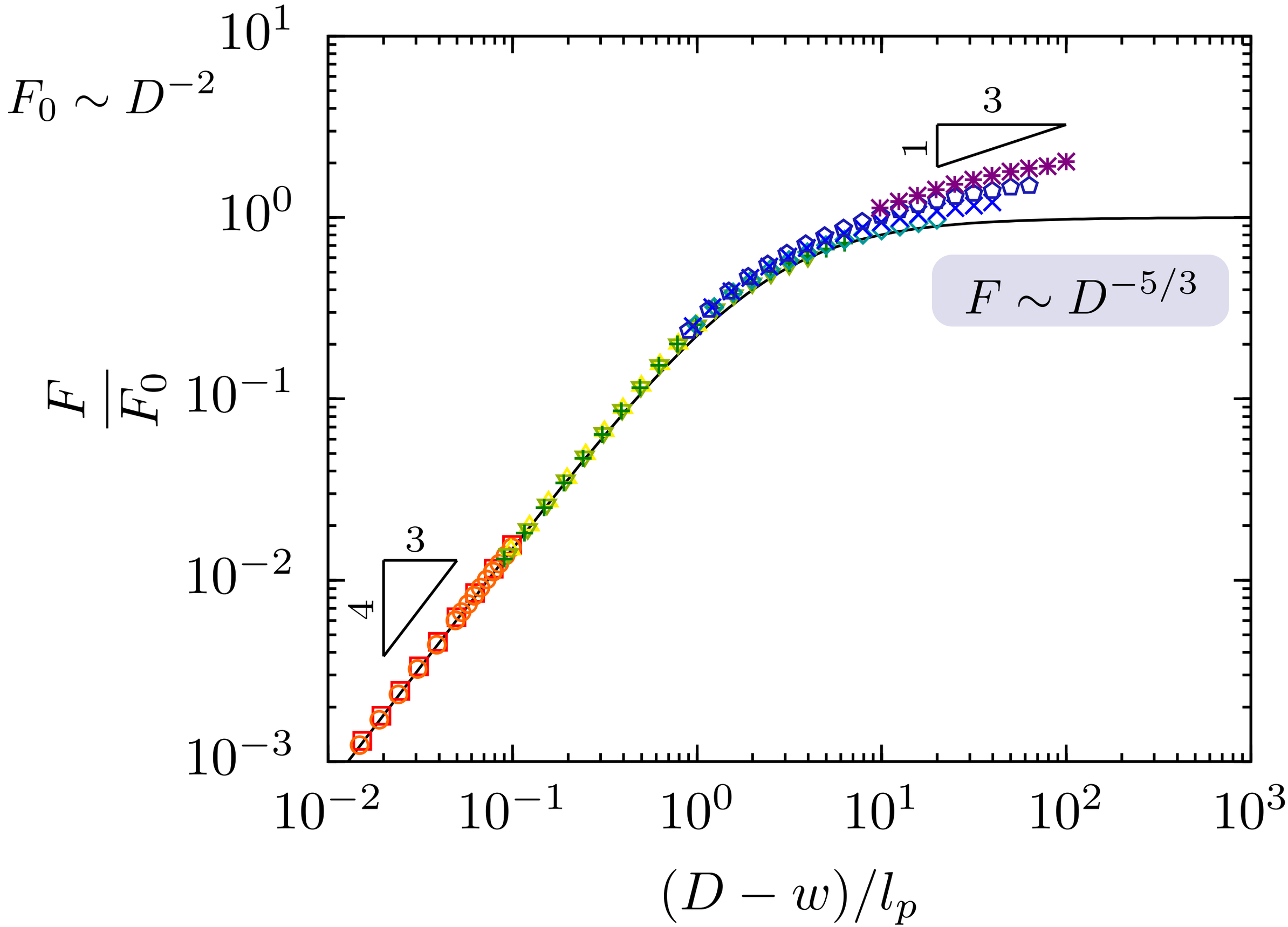
$D \ll l_p$



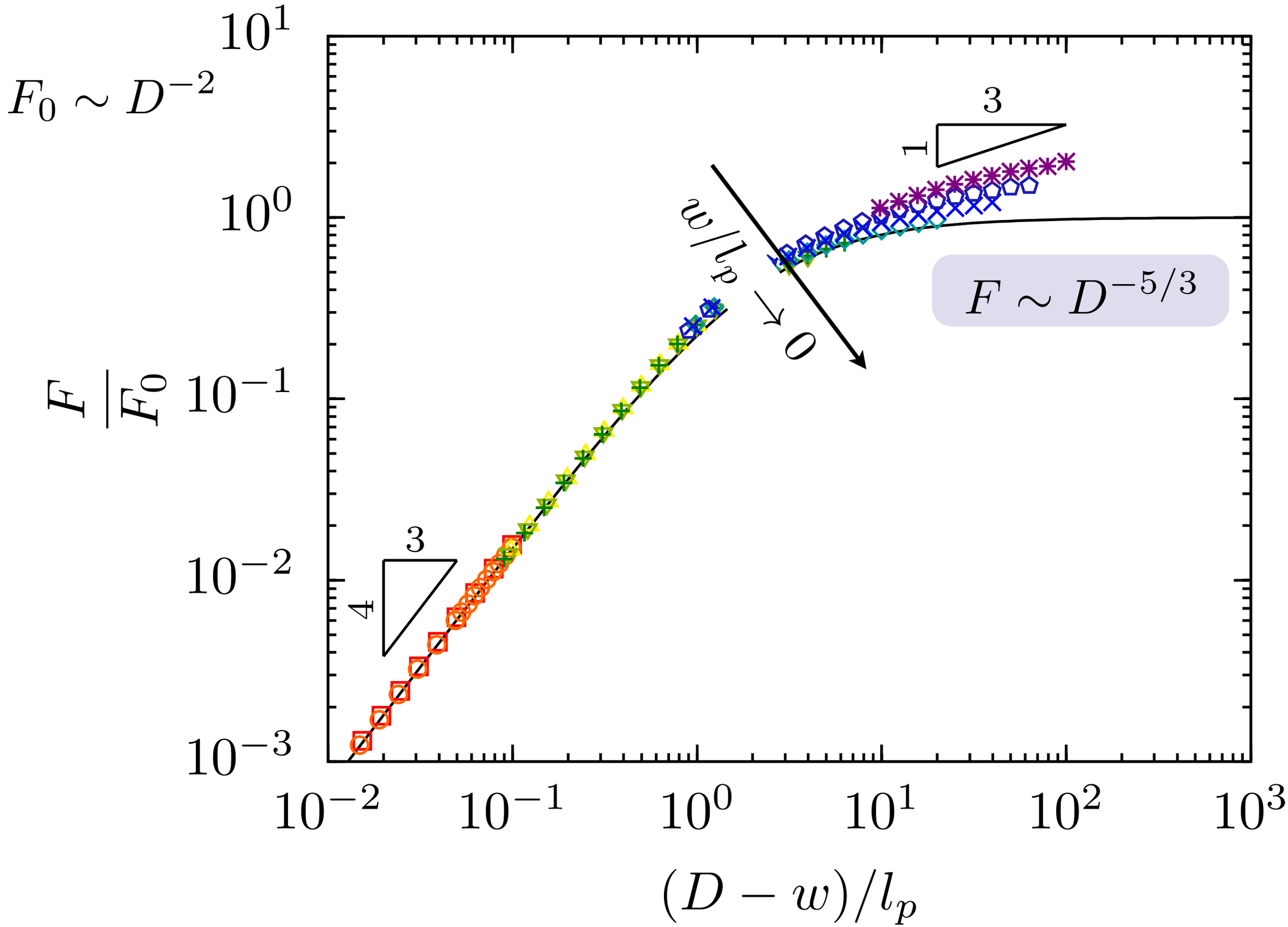
Confined Chain without Excluded Volume



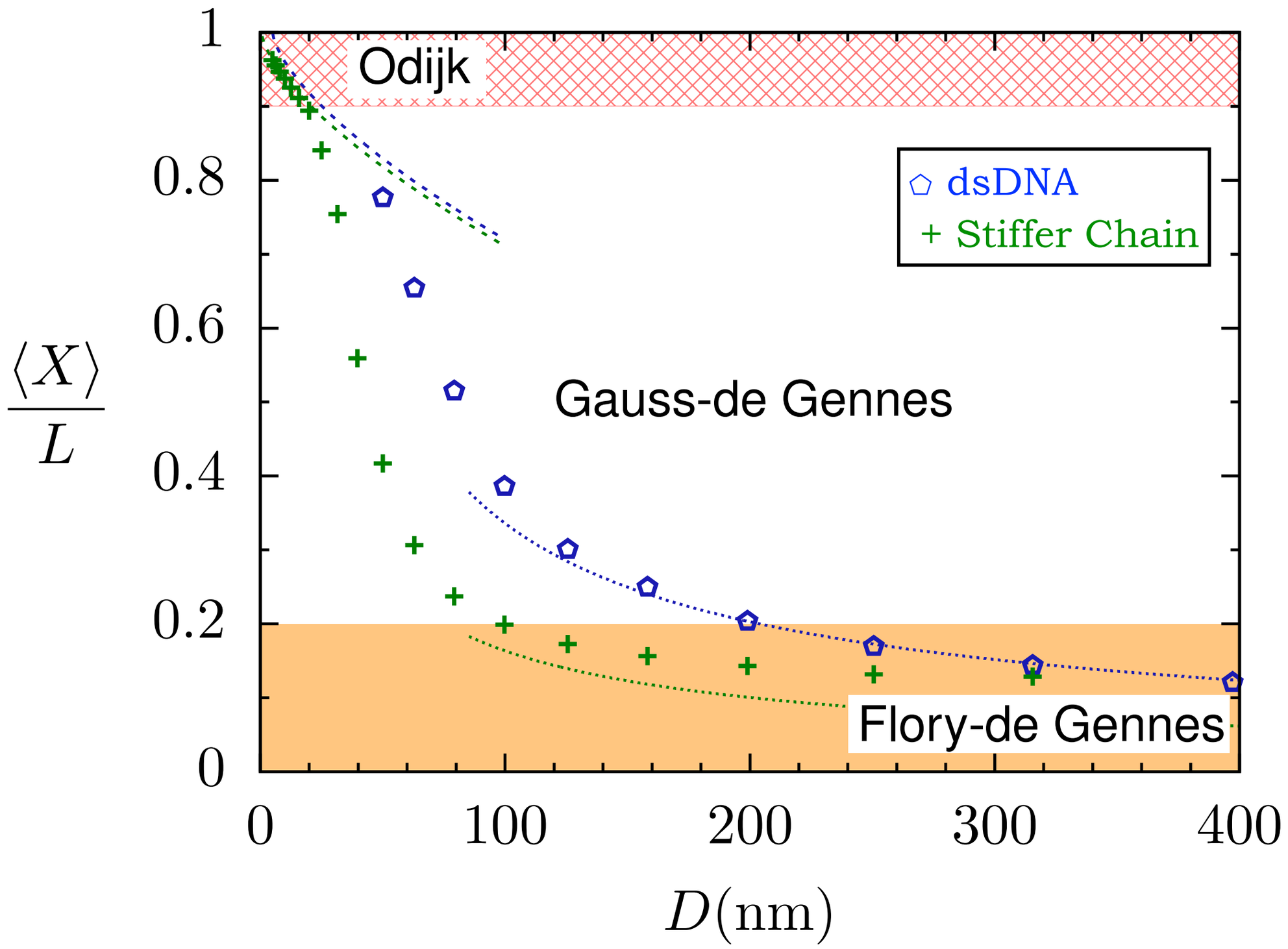
Confined Chain with Excluded Volume



Confined Chain with Excluded Volume



Where are the regimes?



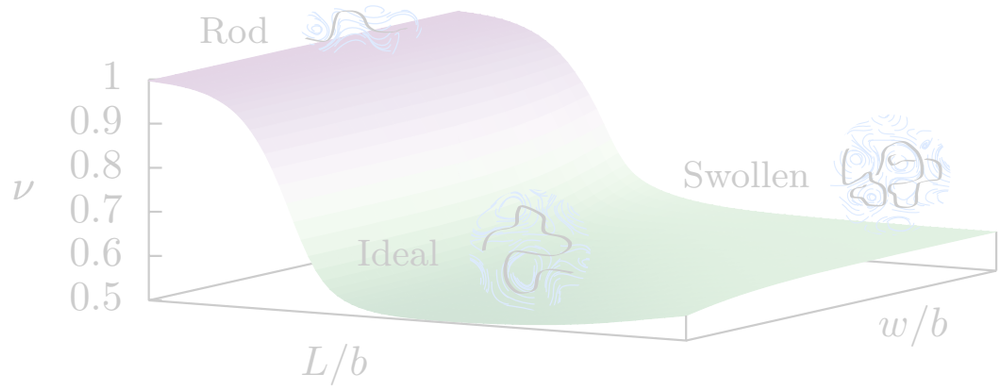
DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 110, 208103 (2013).

Conclusion

- There is an analogy between the behavior of confined chains and free solution chains
- There is a Gaussian-like regime for large monomer anisotropies.
- This regime is the most practically relevant regime for confined DNA.

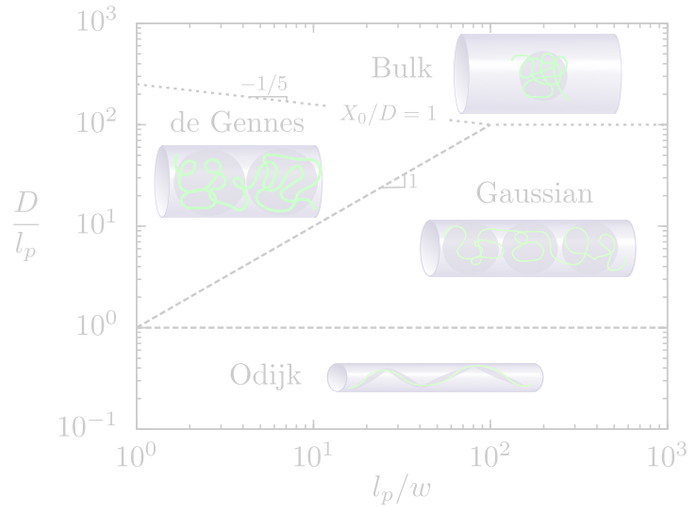
DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 110, 208103 (2013).

Polymer Physics of DNA in Solution



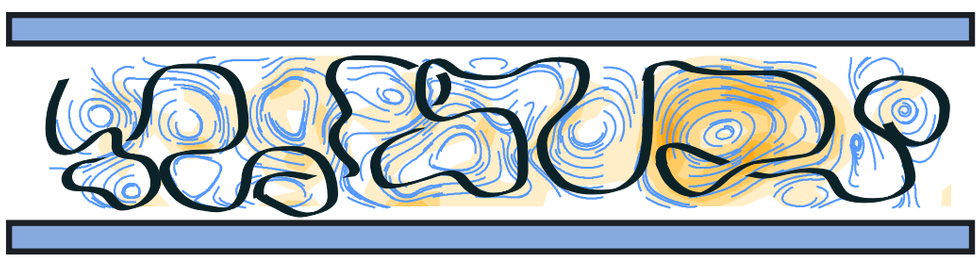
DR Tree, A Muralidhar, PS Doyle and KD Dorfman, Macromolecules (2013).

Regimes of Confined DNA



DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 110, 208103 (2013).

Hydrodynamics of Confined DNA



DR Tree, Y Wang and KD Dorfman, Phys. Rev. Lett. 108, 228015 (2012).

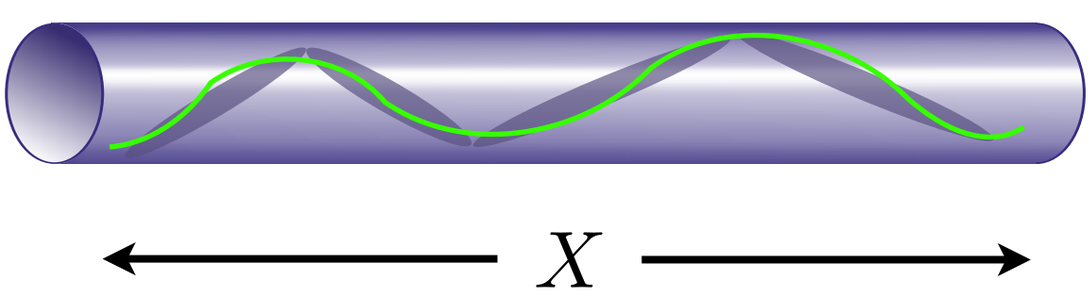
Classic Analytical Results

Definition of the mobility in the Kirkwood approximation

$$\mu \equiv \langle \Omega_{xx} \rangle = N^{-1} \int g(\mathbf{r}) \Omega_{xx}(\mathbf{r}) d^3\mathbf{r}$$

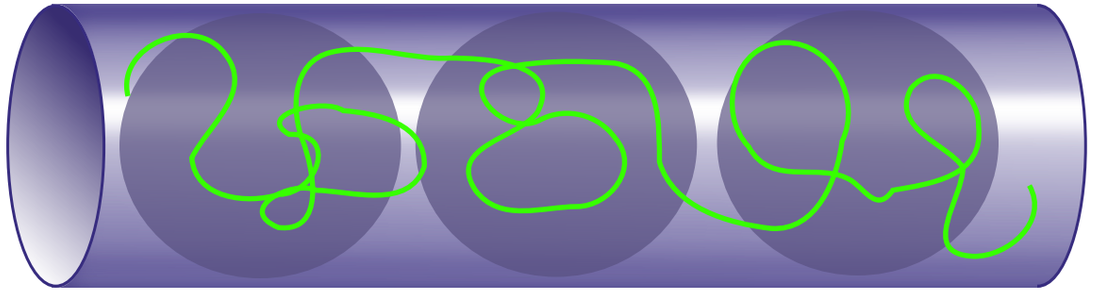
$$\mu = \frac{\mathcal{D}}{k_B T}$$

Odijk (rods): D << l_p



$$\mu \sim \frac{1}{\eta L} \ln\left(\frac{D}{2a}\right)$$

de Gennes (coils): D >> l_p



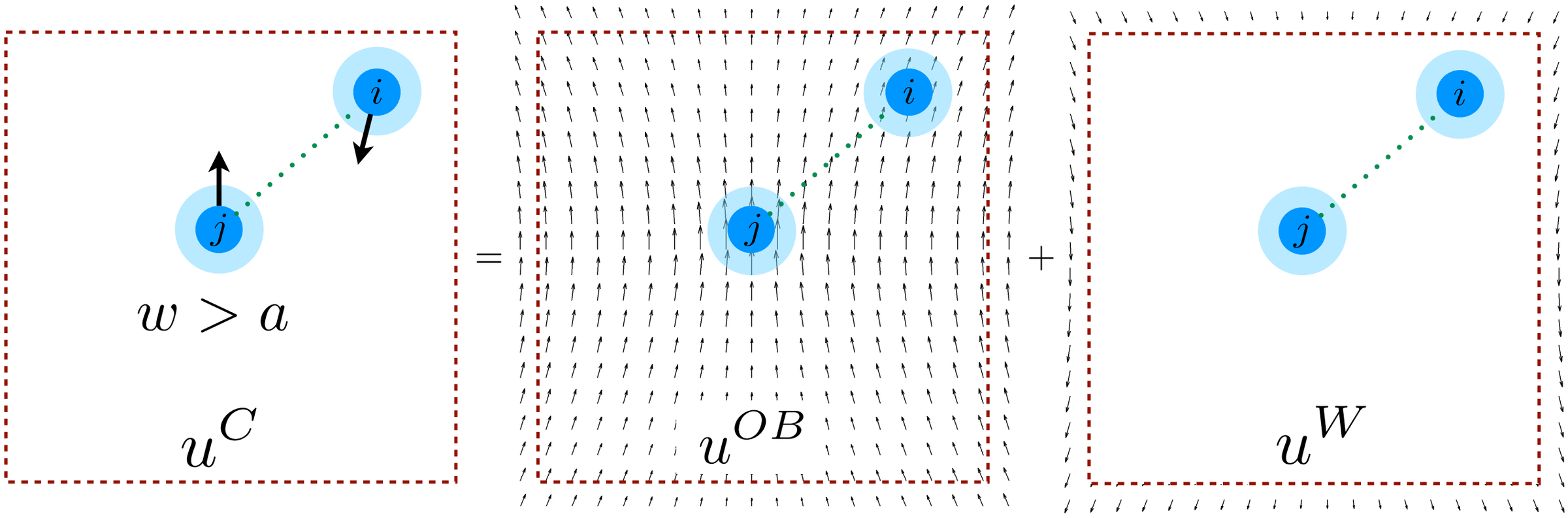
$$\mu \sim \frac{1}{\eta \langle X \rangle} \sim \left(\frac{1}{\eta L}\right) \frac{1}{\langle X/L \rangle}$$

Confined Chain Hydrodynamics

Mobility of the confined chain

Free solution hydrodynamics

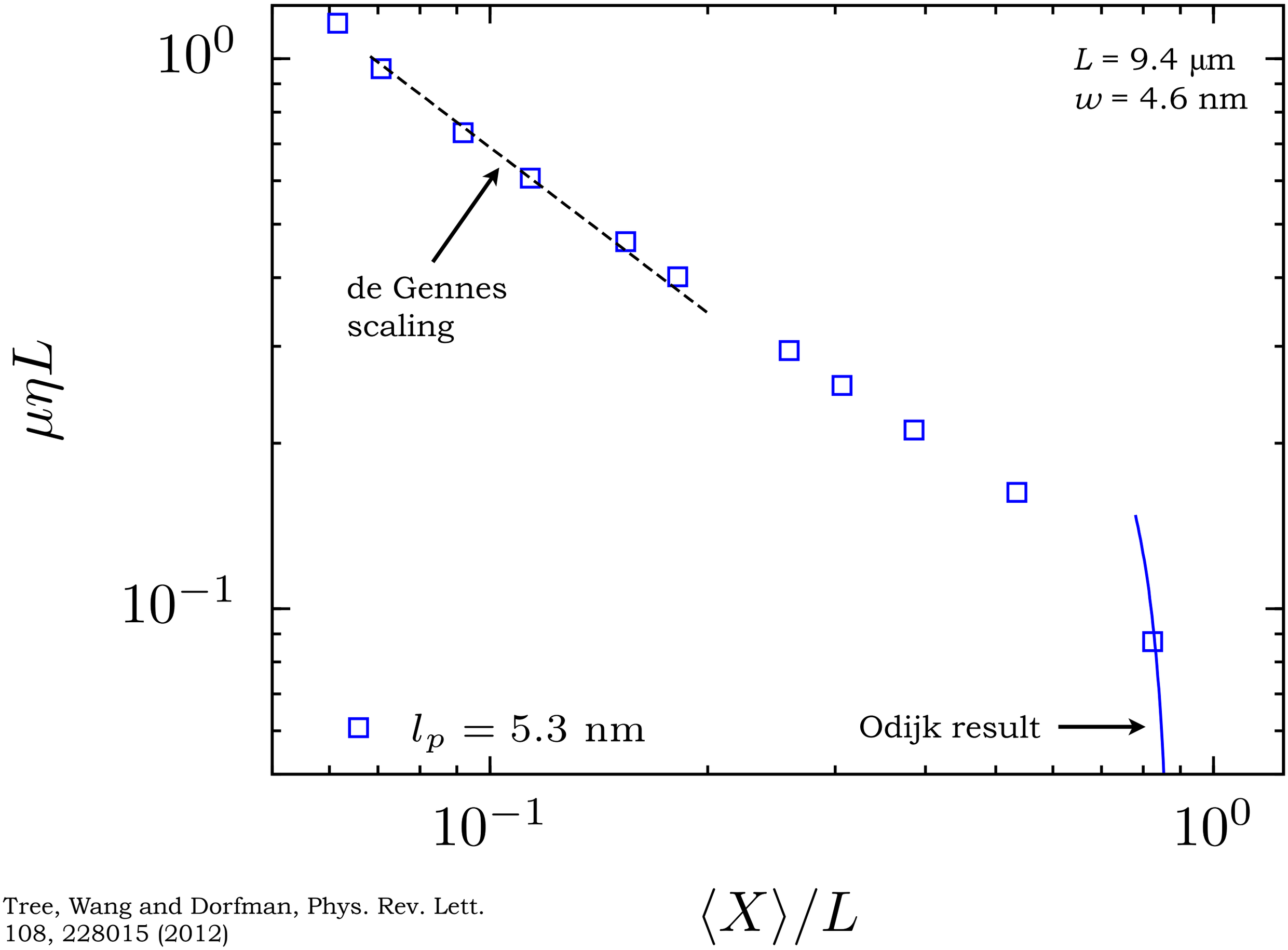
Wall hydrodynamics



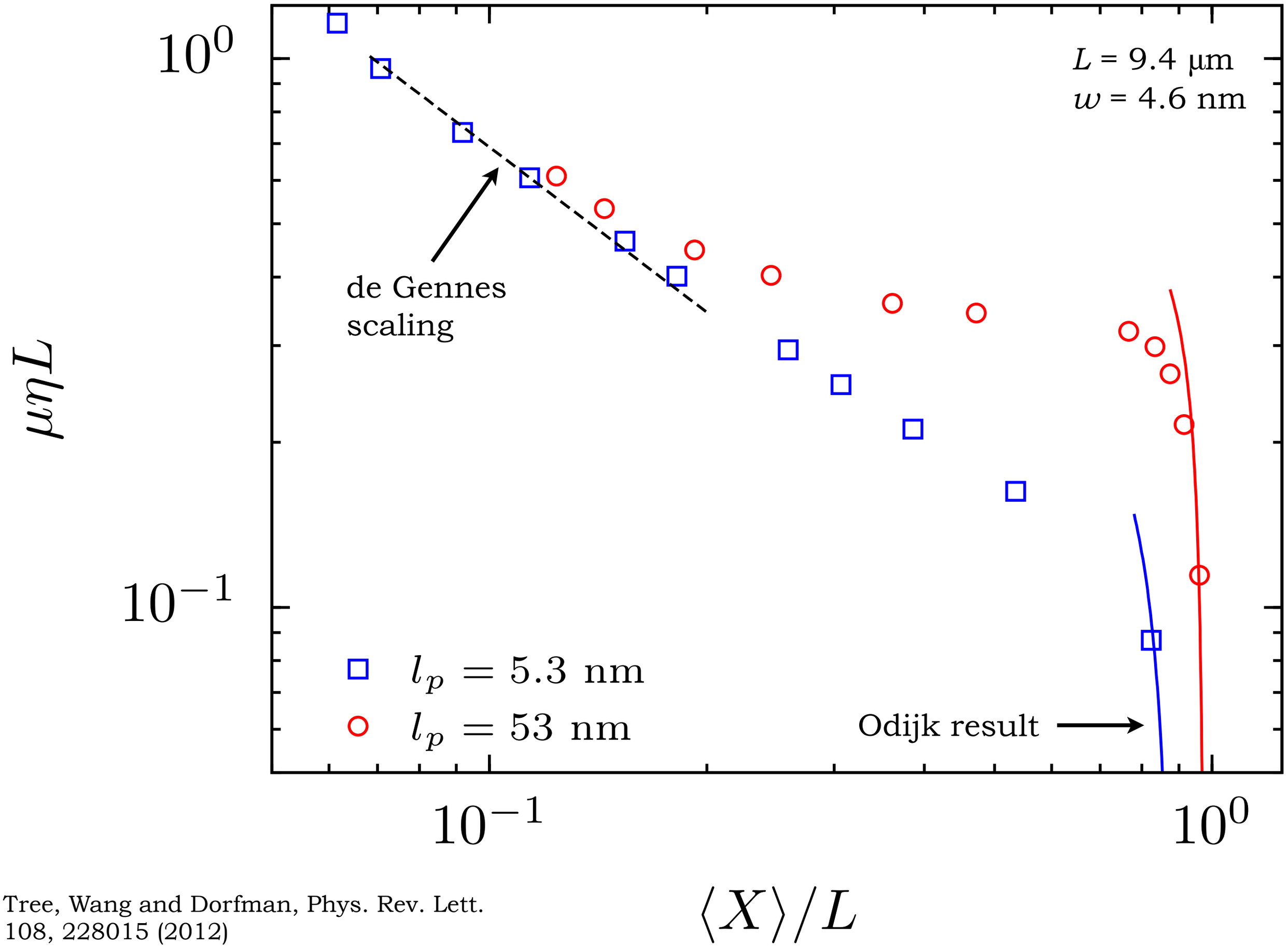
The three dimensional mobility tensor of the confined chain is the sum of effects

$$\mathbf{\Omega} = \frac{1}{{N_b}^2} \sum_{i,j}^{N_b} \left[\frac{\delta_{ij}}{6\pi\eta a}\mathbf{I} + (1-\delta_{ij})\mathbf{\Omega}^{\mathrm{OB}}(\mathbf{r}_{ij}) + \mathbf{\Omega}^{\mathrm{W}}(\mathbf{r}_i, \mathbf{r}_j) \right]$$

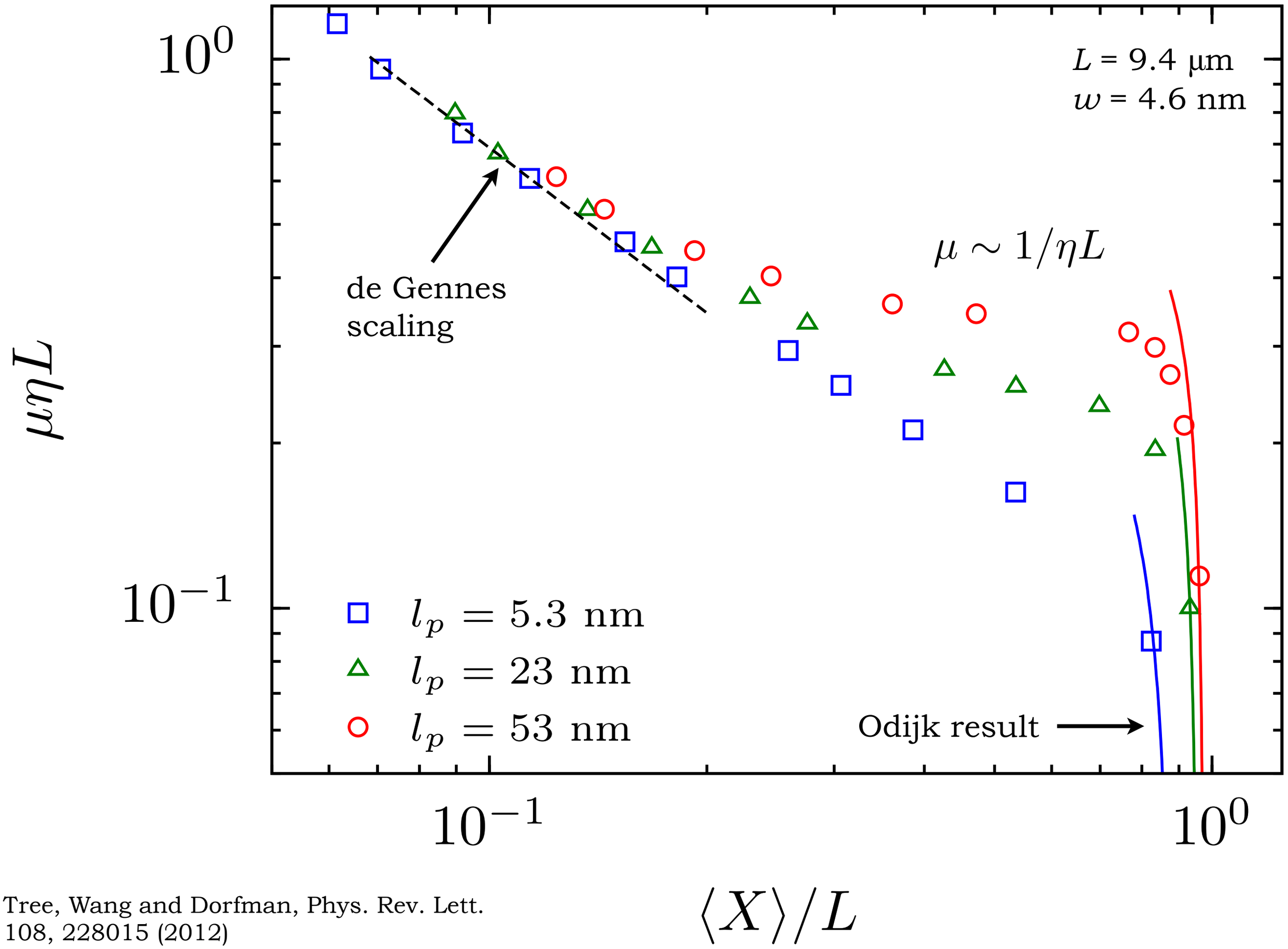
Jendrejack, Schwartz, de Pablo and Graham, J. Chem. Phys. 116, 7752-7759 (2002)



Tree, Wang and Dorfman, Phys. Rev. Lett. 108, 228015 (2012)

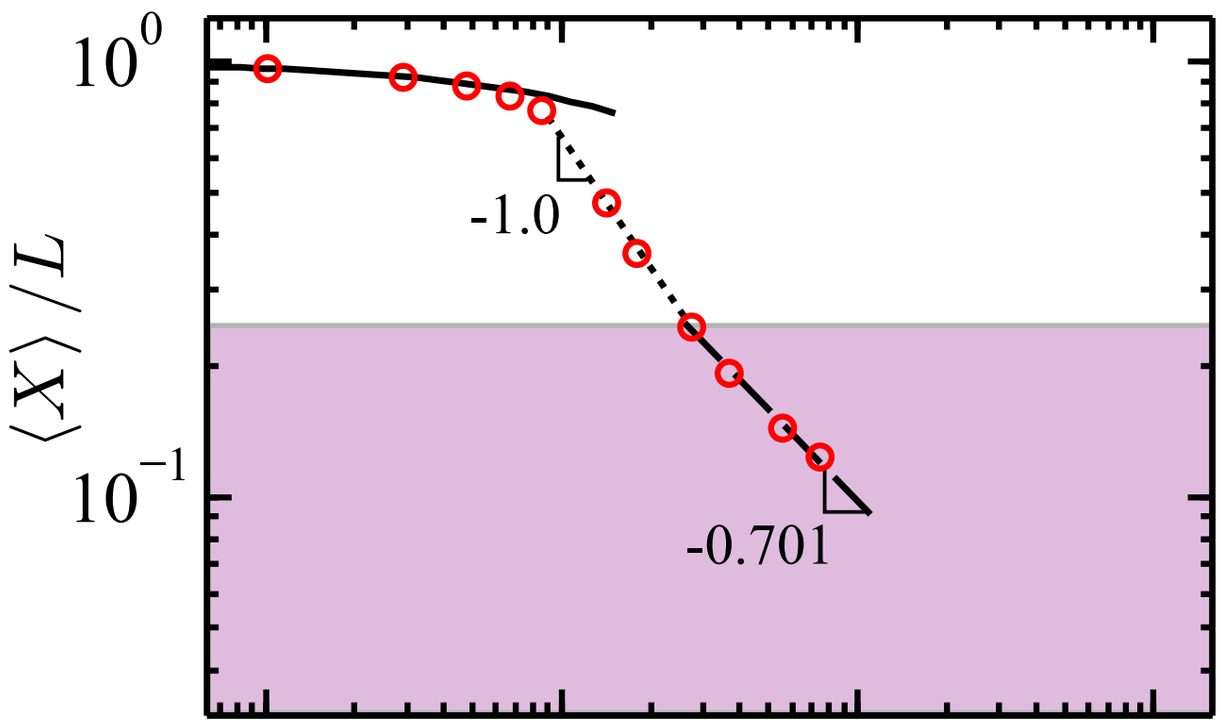


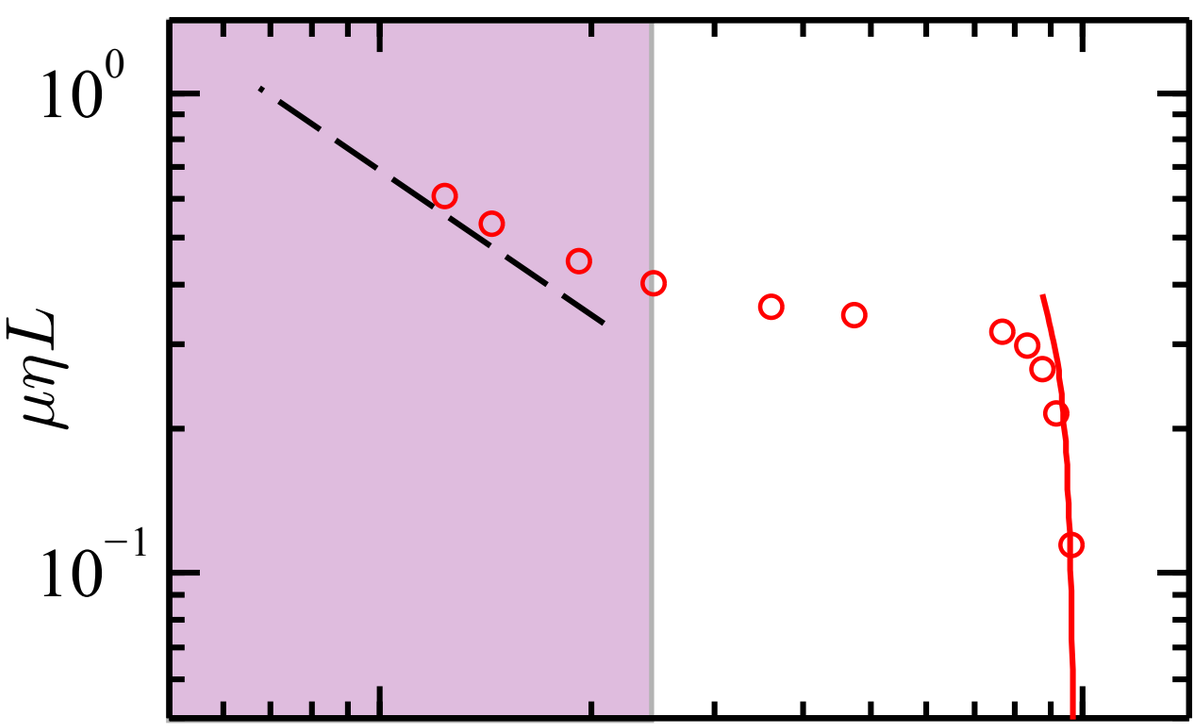
Tree, Wang and Dorfman, Phys. Rev. Lett. 108, 228015 (2012)



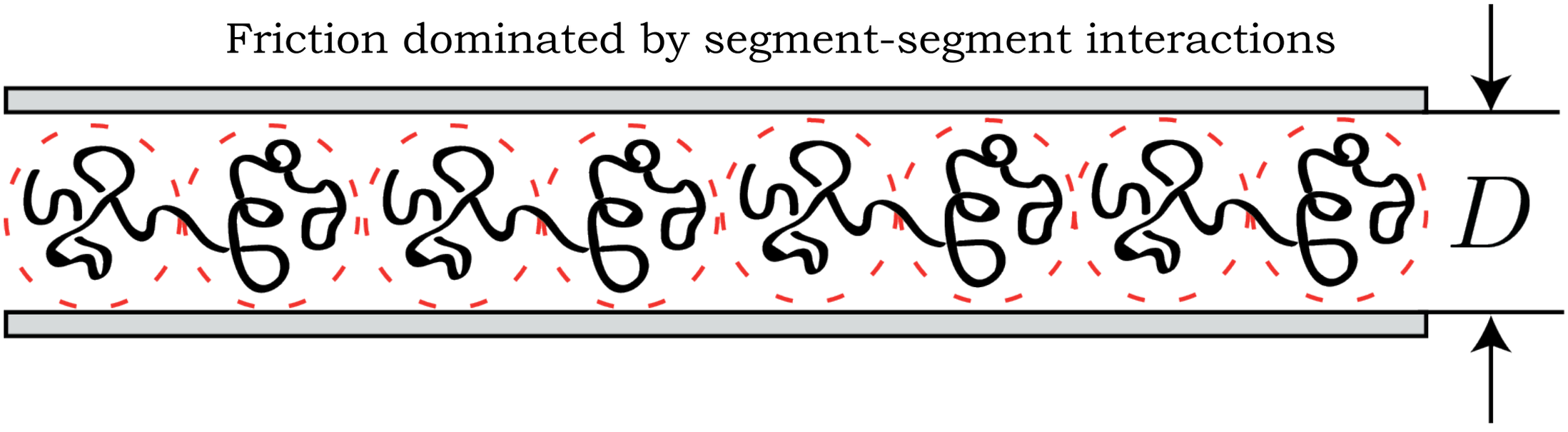
Tree, Wang and Dorfman, Phys. Rev. Lett. 108, 228015 (2012)

Connecting Mobility to Conformation

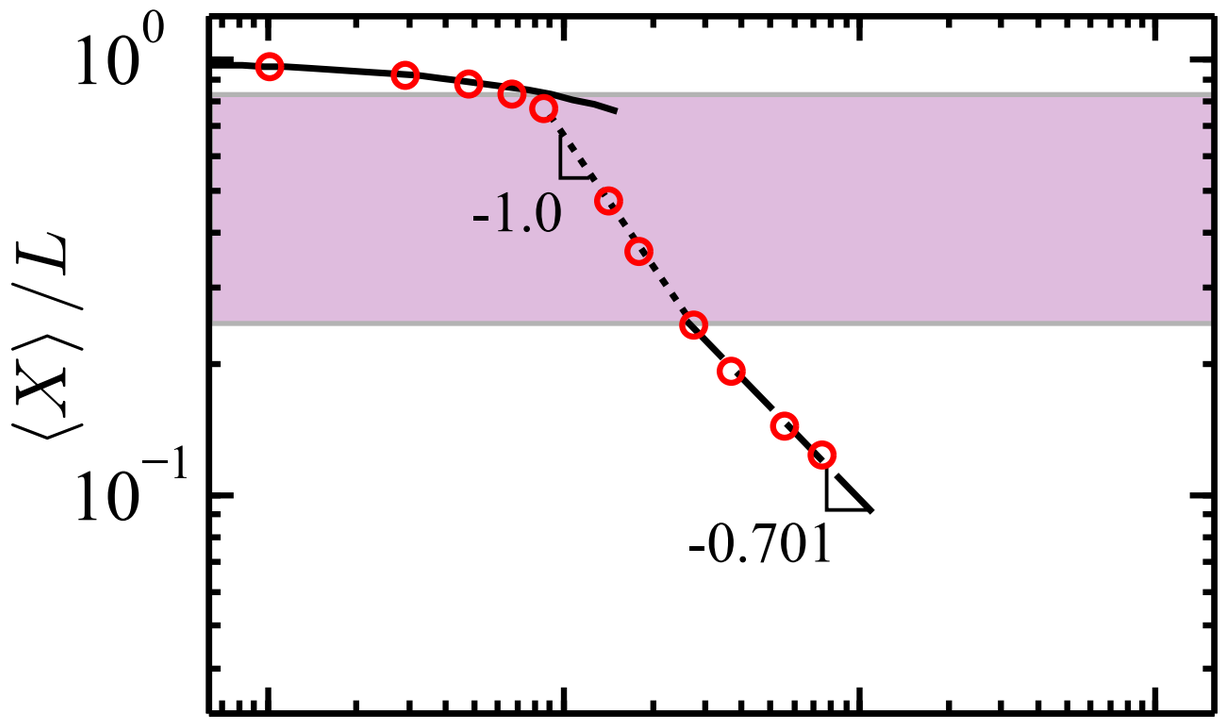


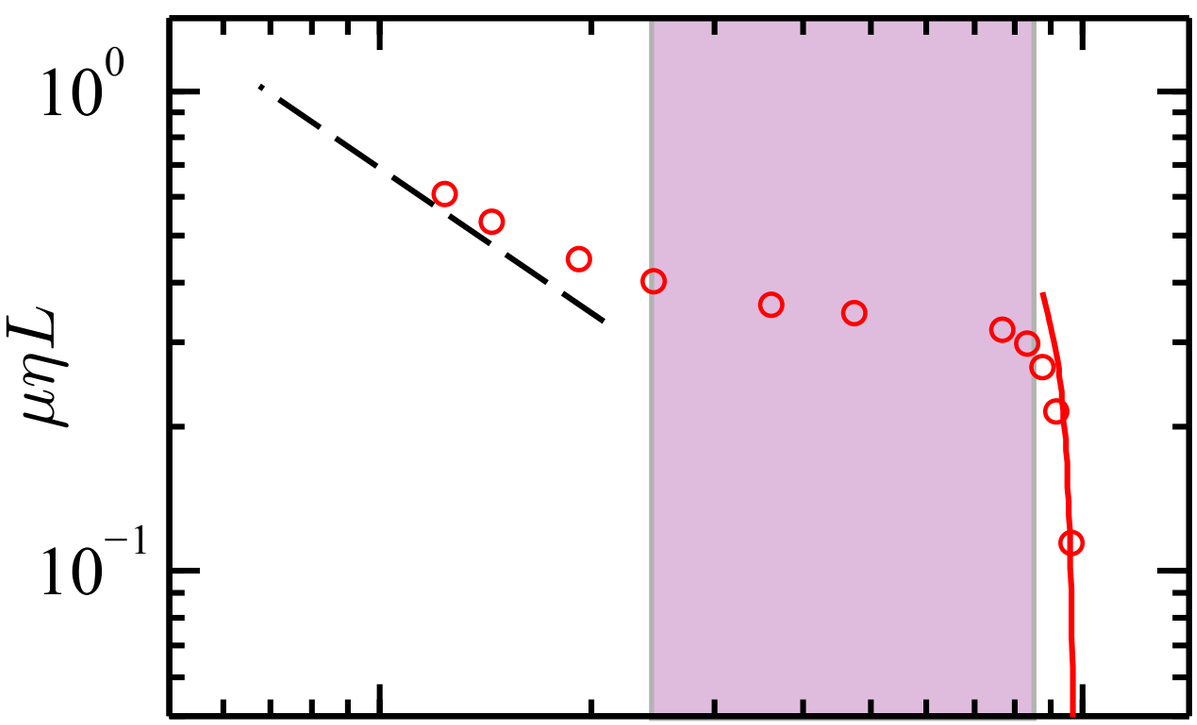


Friction dominated by segment-segment interactions

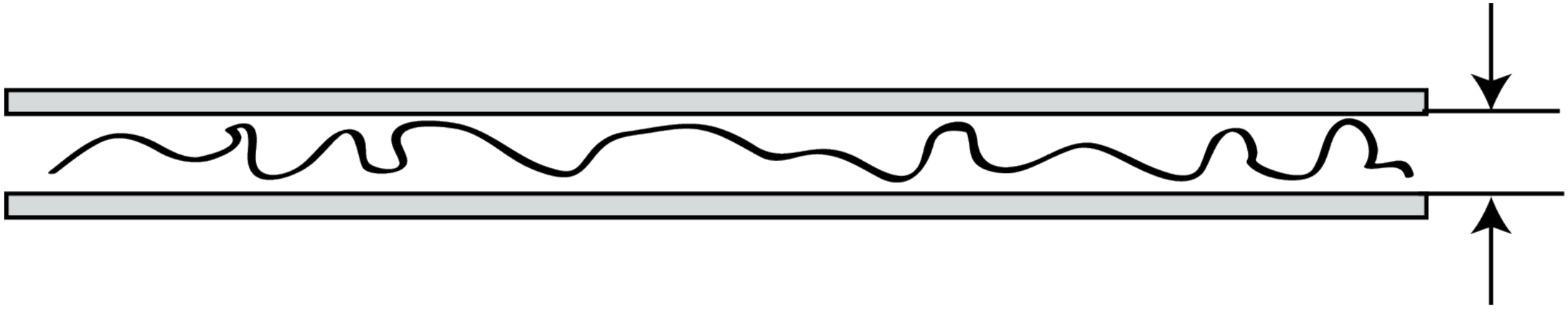


Connecting Mobility to Conformation

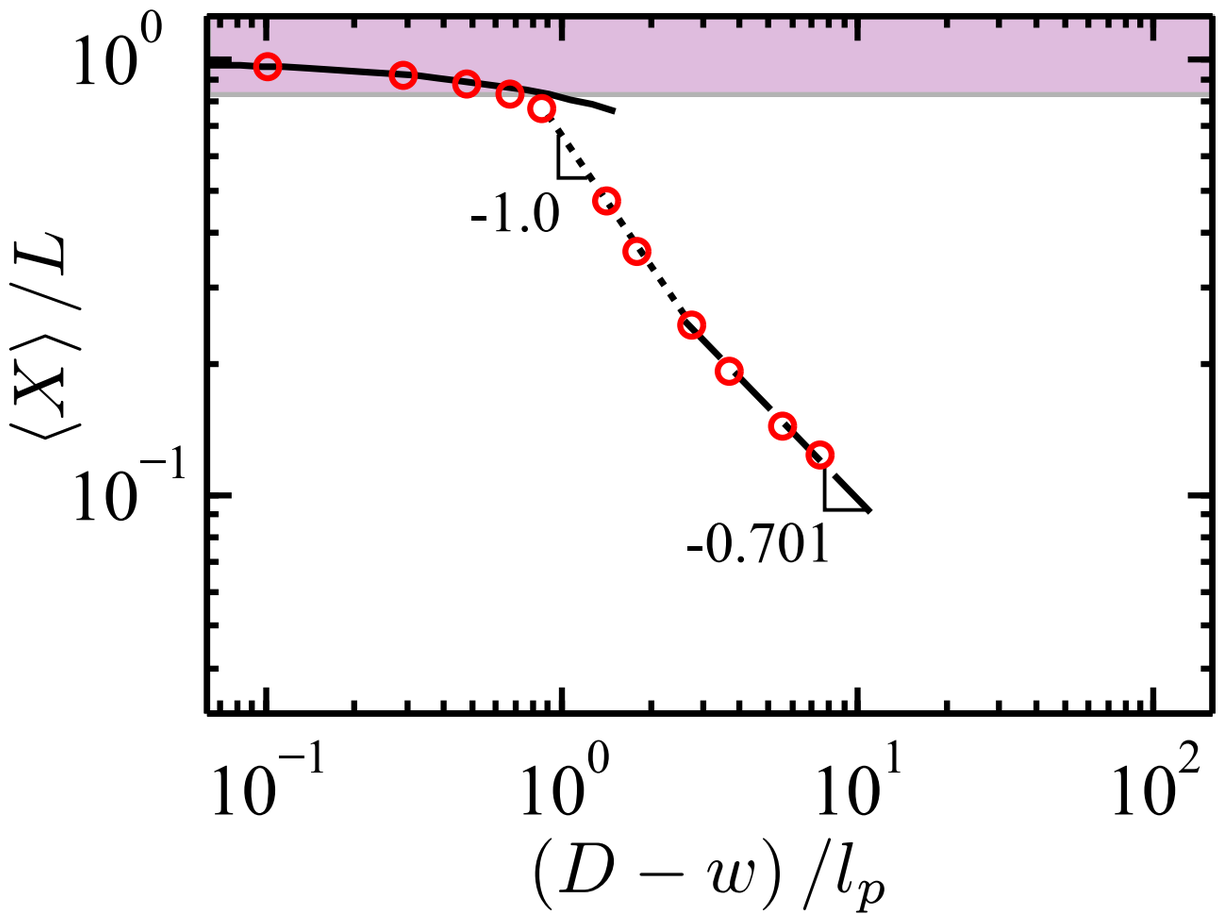


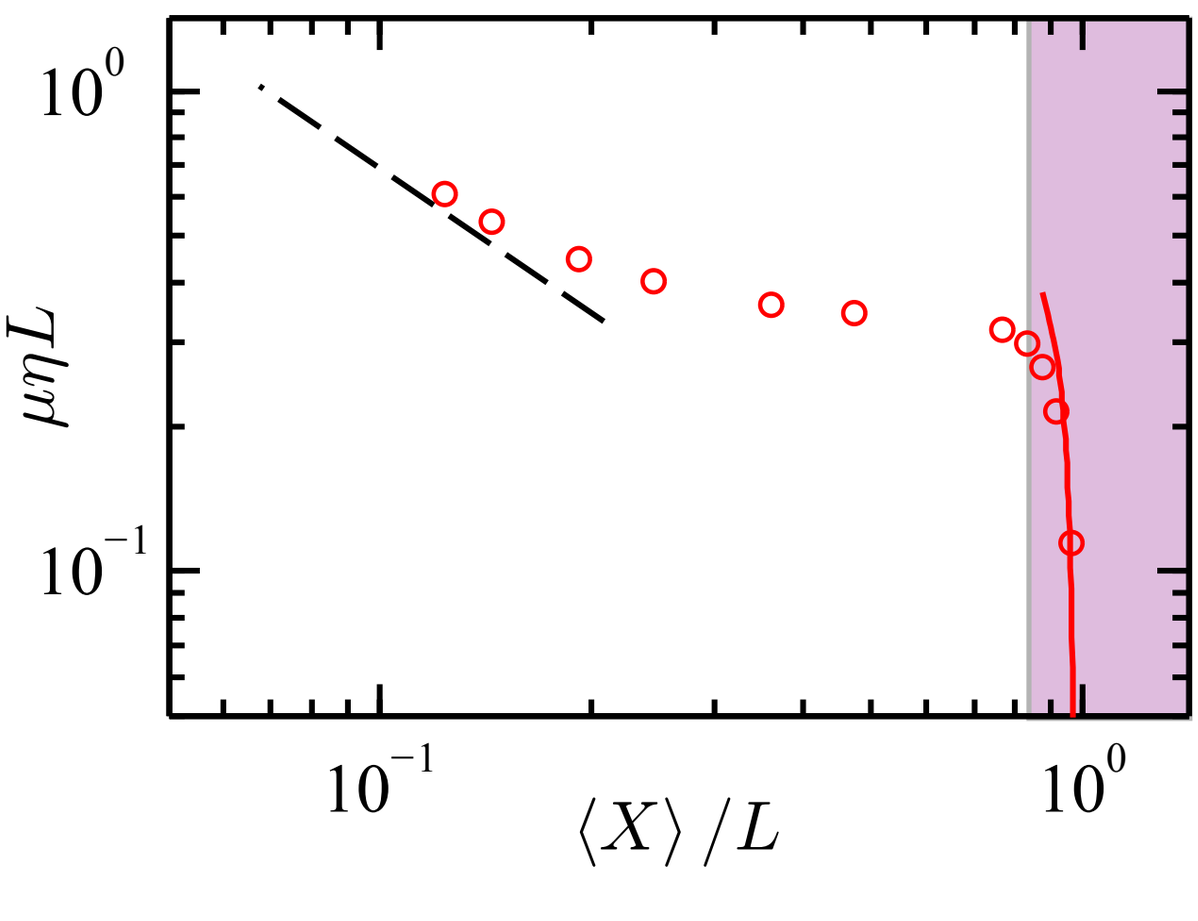


Friction dominated by segment-fluid interactions

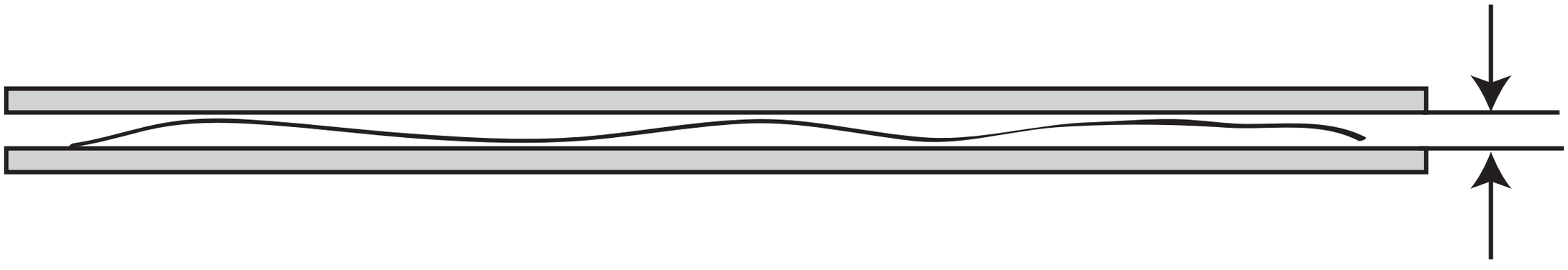


Connecting Mobility to Conformation





Friction dominated by segment-wall interactions



Conclusions

- Monomer anisotropy also affect the hydrodynamic interactions and the chain mobility
- Predict that the hydrodynamic mobility will be proportional to chain length for DNA in nanochannels.

Tree, Wang and Dorfman, Phys. Rev. Lett. 108, 228015 (2012)