Molecular Dynamics Simulation of The Force-Extension Relation in Simple Models of Semiflexible Biopolymers

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Outline

- Background and Scientific Motivation
- Theory
  - Entropic elasticity
- Description of Methodology
  - Molecular Dynamics Simulation
- Progress
  - Flexible polymer chain
  - Semiflexible polymer chain
- Summary and Outlook

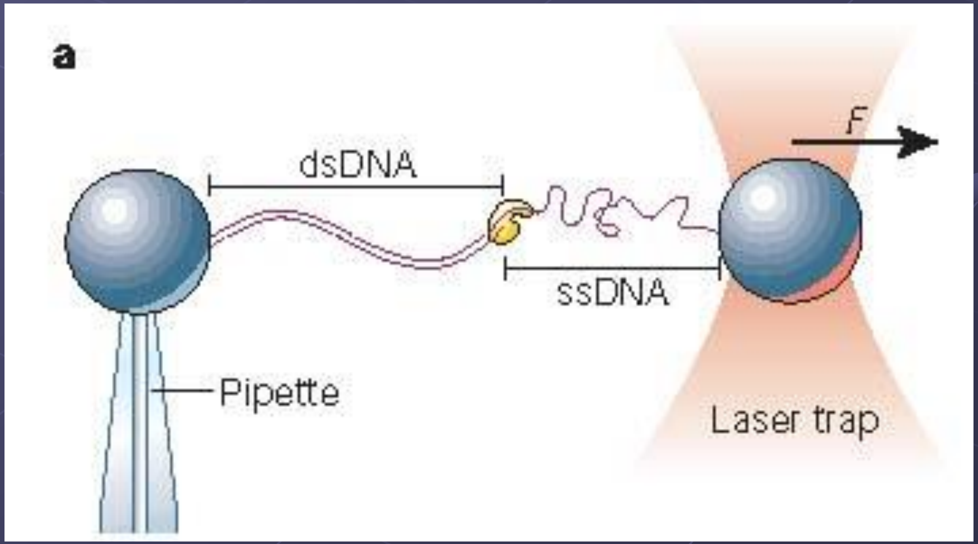
Background

- Bio-polymer Physics
  - Elasticity
    - Experimental
    - Theoretical
    - Computational

•Flexible chain
•Semi-flexible chain
•Cross-linked

- Magnets
- Fluid flow
- Optical traps

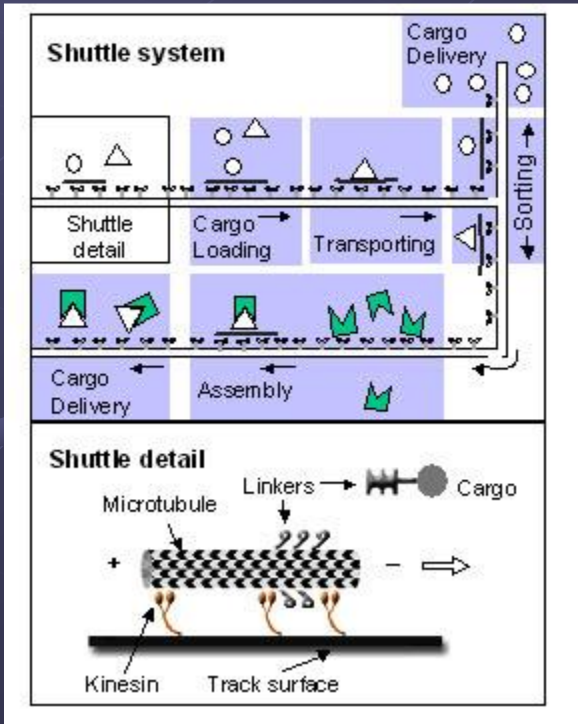
Bustamante, Bryant, and Smith. Nature, 2003



Scientific Motivation

- Possible Application:
  - Biological
    - Understand cell wall rigidity
    - Understand DNA and protein interactions
  - Medical
    - DNA & Actin mechanical properties
  - Bioengineering
  - Nanotechnology
    - Nanoscale biological machines

Tucker, Vogel, and Hess.
The 1st Adv. Nanotech. Conf. 2004
Molecular Shuttle System



Theory
Origin of Polymer Elasticity: Entropy

$$S = k_B \ln \Omega \longrightarrow F = \cancel{U} + TS \longrightarrow \frac{\partial F}{\partial R} = f(R)$$

- Force-extension (F-R) relation for the flexible case (FJC):

$$f(R) = \frac{3k_B T}{Nb^2} R \qquad k_{entropy} \propto T \propto \frac{1}{N}$$

- F-R relation for the semiflexible case (WLC):

$$f(R/L) = \frac{k_B T}{l_p}\left(\frac{R}{L} + \frac{1}{4(1-R/L)^2} - \frac{1}{4}\right)$$

Marko & Siggia
1995
interpolation formula

Methodology: MD Simulation

- Model polymer with potentials:
  - Lennard-Jones (LJ) → hard sphere

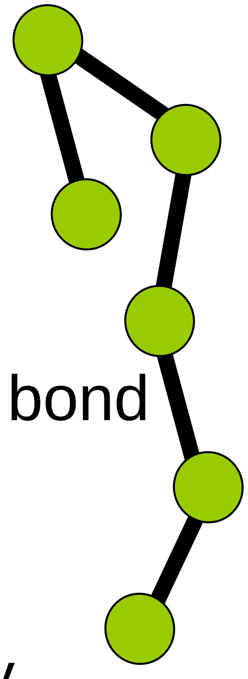
$$U^{LJ}(R) = 4\varepsilon\left[(\sigma / R)^{12} - (\sigma / R)^{6}\right]$$

  - Finitely-extensible Non-linear Elastic (FENE) → bond

$$U^{FENE}(R) = -\frac{1}{2} k R_0^{\ 2} \ln\left[1 - (R / R_0)^2\right]$$

  - Angle potential (semi-flexible) → bending rigidity

$$U^{A}(\theta) = K_A\left[1 + \cos(\theta)\right]$$



Bead-Spring Model

Moves and bends

Theory
Classical MD Simulation

- Numerical Integrator : Verlet Algorithm

$$p_i(t+\frac{1}{2}\delta t) = p_i(t) + \frac{1}{2}\delta t f_i(t),$$

$$r_i(t+\delta t) = r_i(t) + \delta t p_i(t+\frac{1}{2}\delta t)/m_i,$$

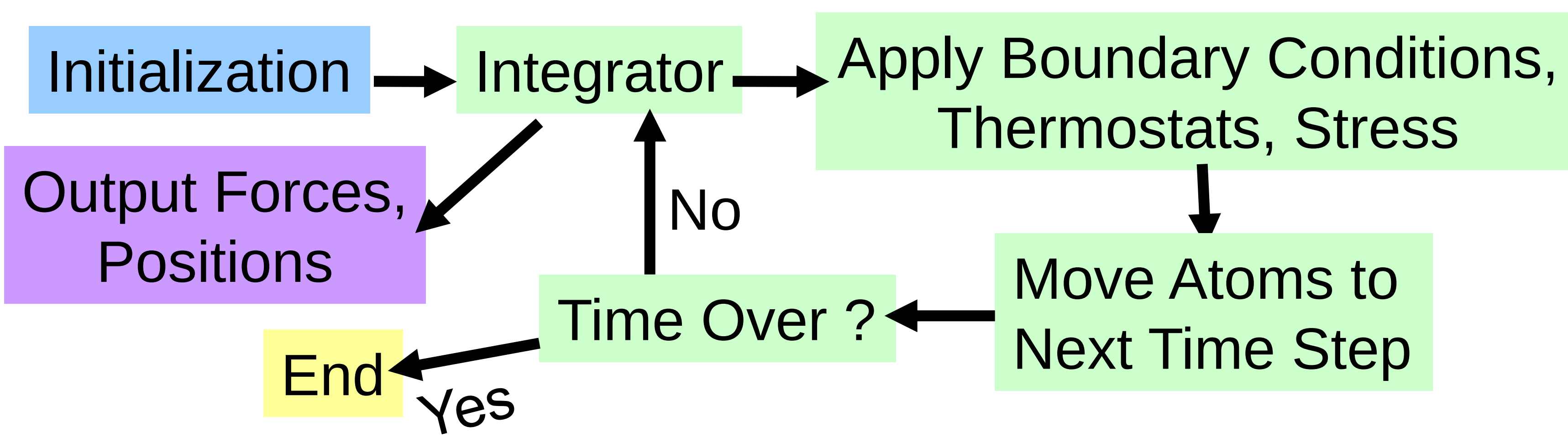
$$p_i(t+\delta t) = p_i(t+\frac{1}{2}\delta t) + \frac{1}{2}\delta t f_i(t+\frac{1}{2}\delta t).$$

- Temperature: Langevin

$$\vec{f_i} - \gamma_i \vec{v_i} + \vec{R}_i(t) = m_i \vec{a_i}$$

$$\left\langle \vec{R}_i(t) \right\rangle = 0$$

$$\left\langle \vec{R}_i(t) \cdot \vec{R}_i(t') \right\rangle = 6k_B T \gamma_i \delta(t-t')$$

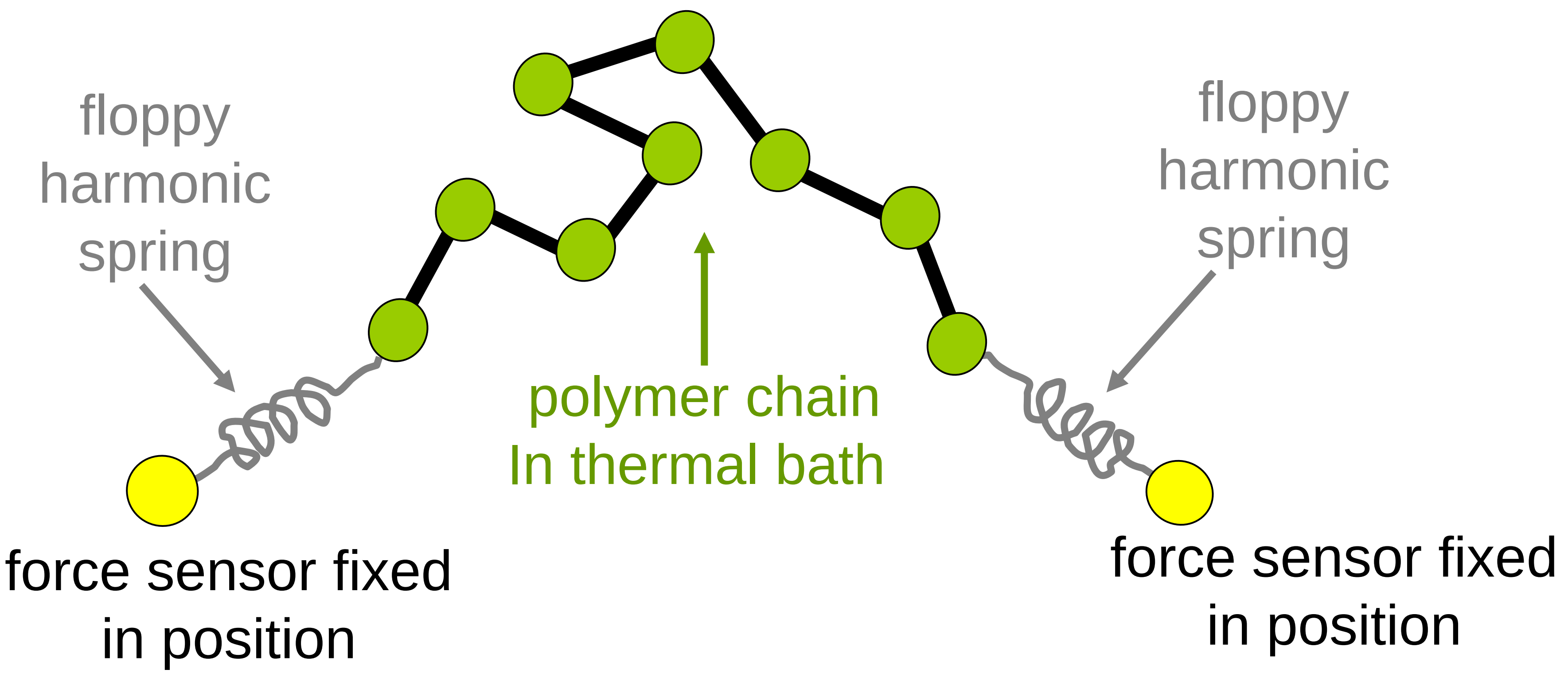


Outline of Progress

- Implemented model using MD simulation
- Tested theoretical results for the flexible chain:
  - force-extension relationship
  - k_entr $\propto$ T $\propto$ 1/N?
- Testing behavior of semiflexible chain:
  - Normalization (Rescaling)
  - Different Values of K_A $$U^A(\theta) = K_A\left[1+\cos(\theta)\right]$$
  - Stability of force-extension relation

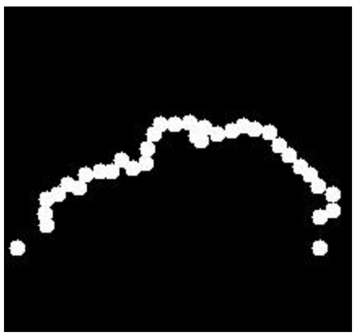
Measuring Stretching Force

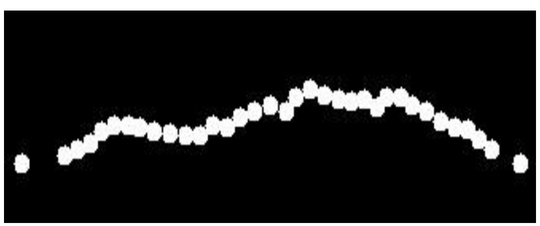
- Spring sensors on polymer ends:
  - Average measured forces



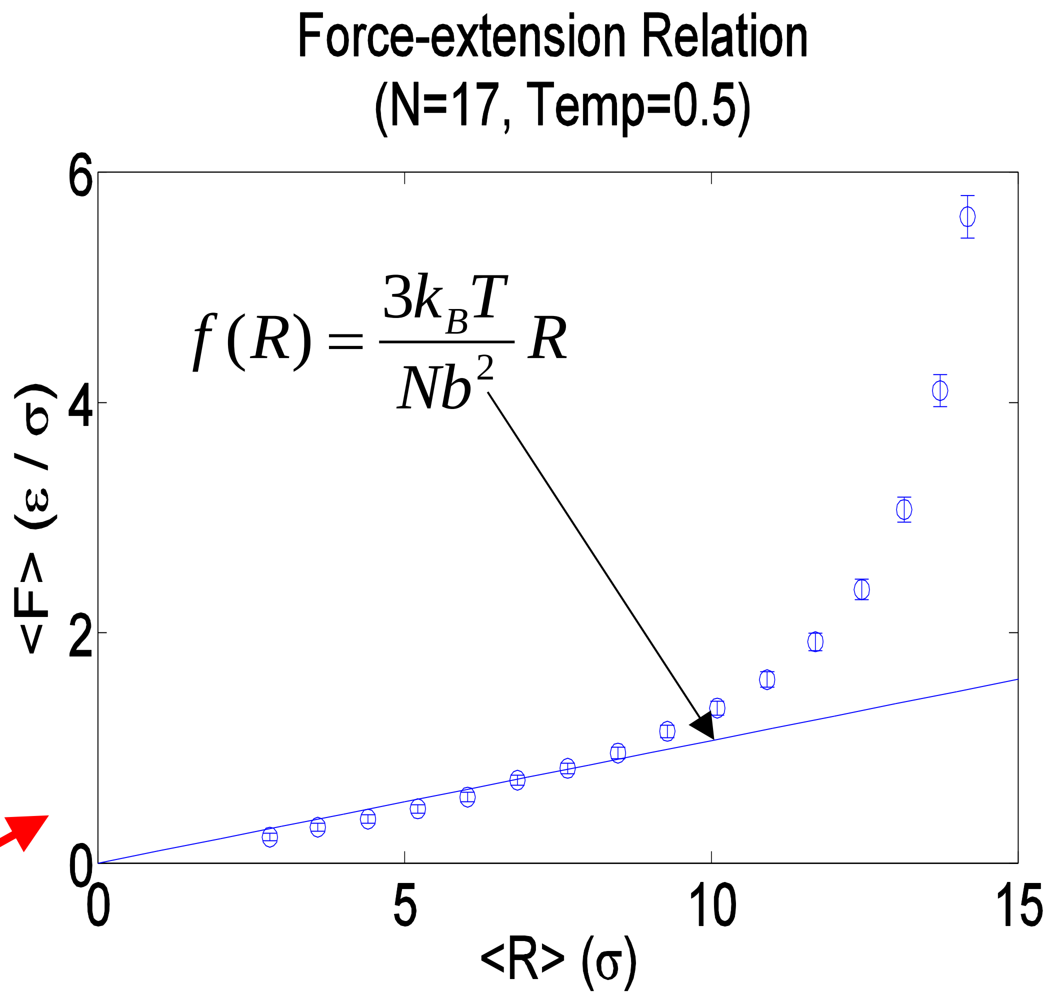
Force-extension Relation
Flexible Case

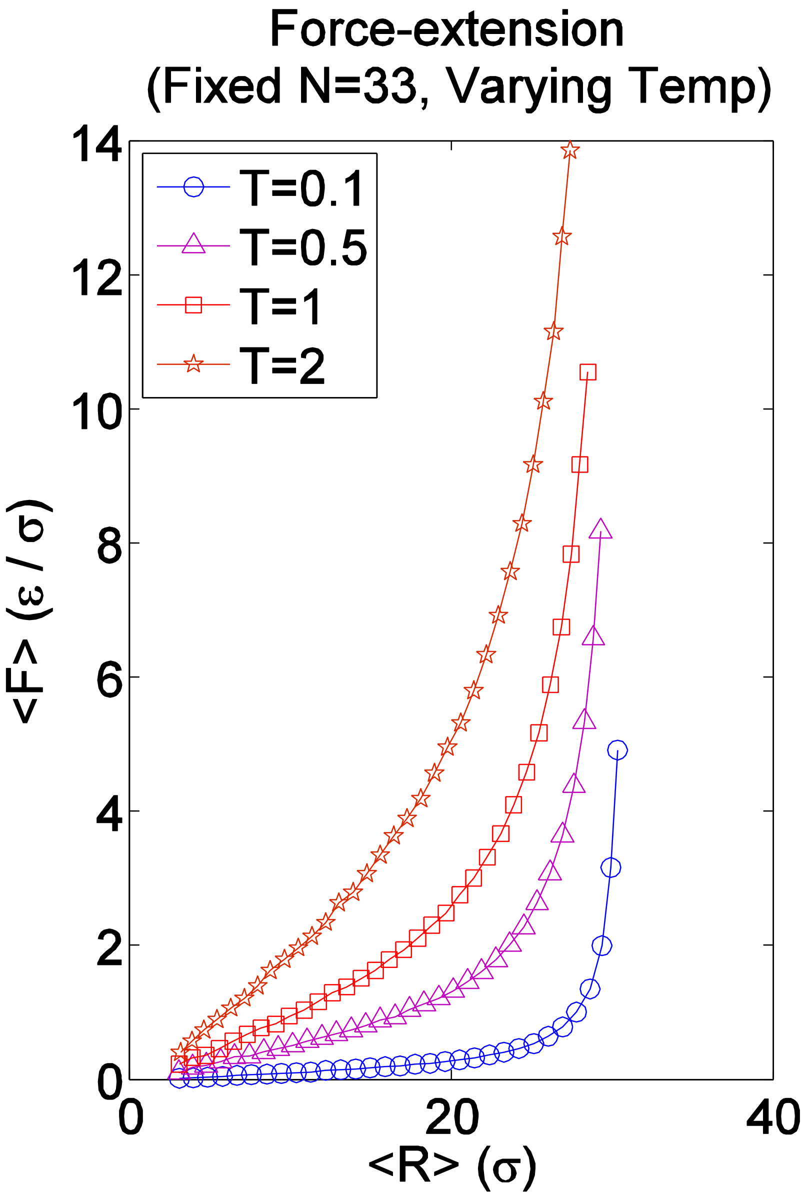
- Vary initial R → obtain different <R> and <F>

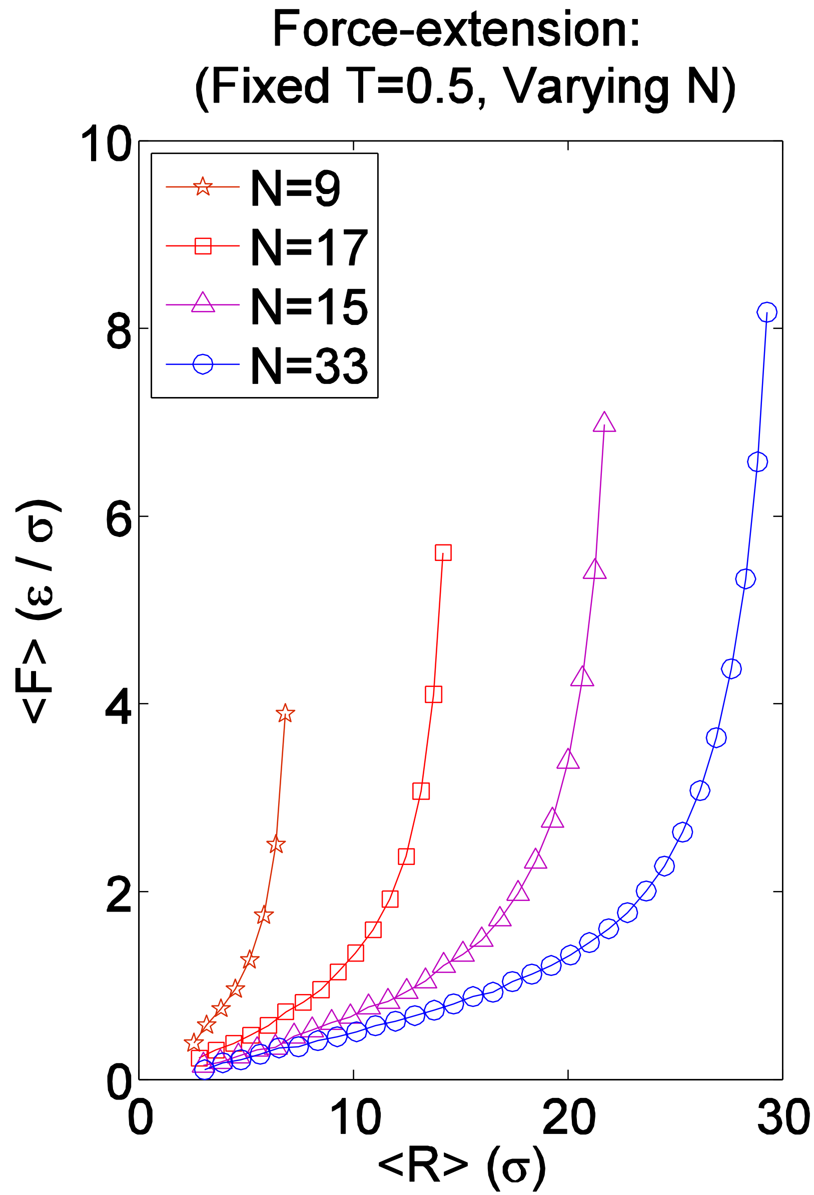




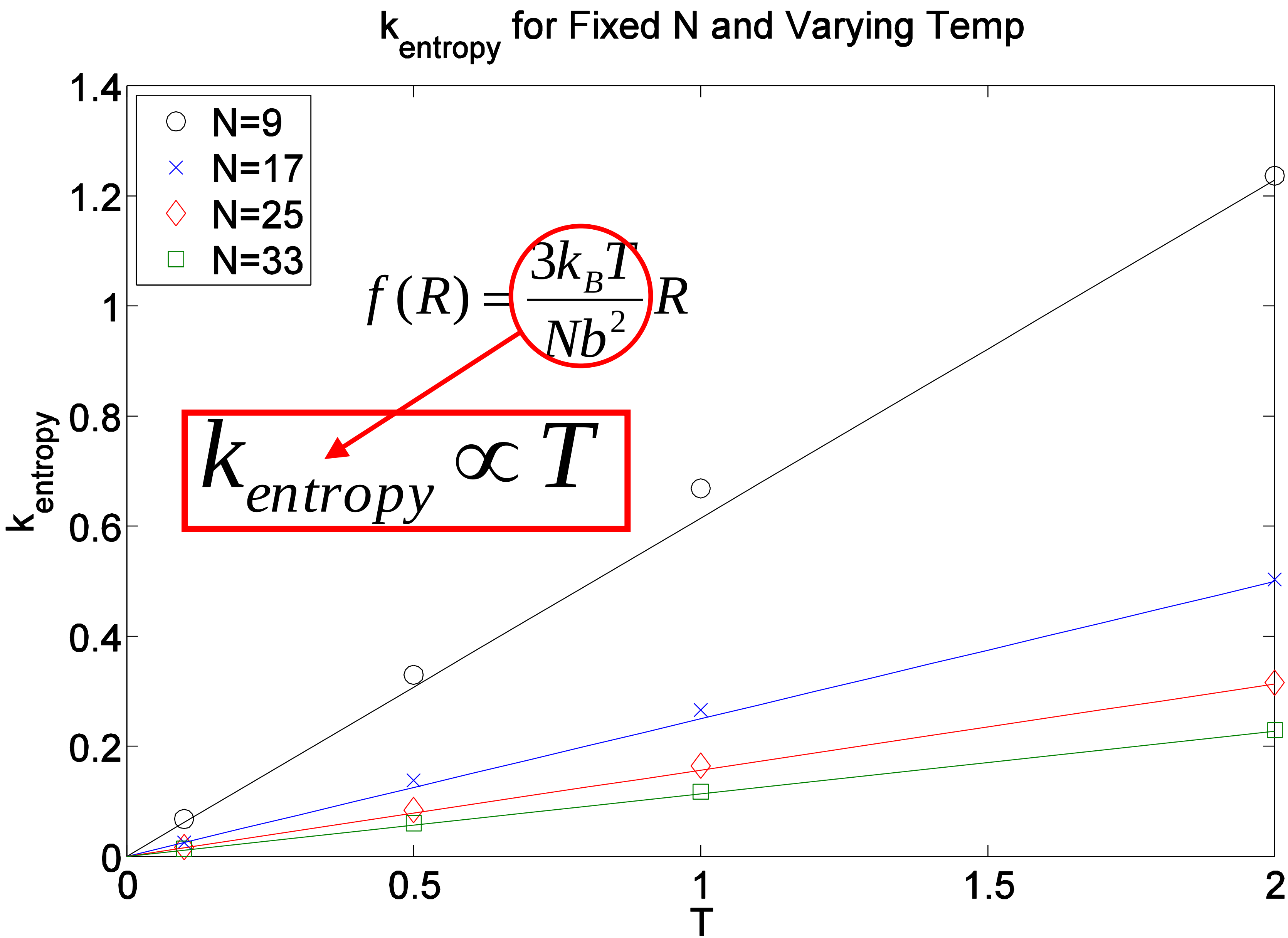
Sample
force-extension plot

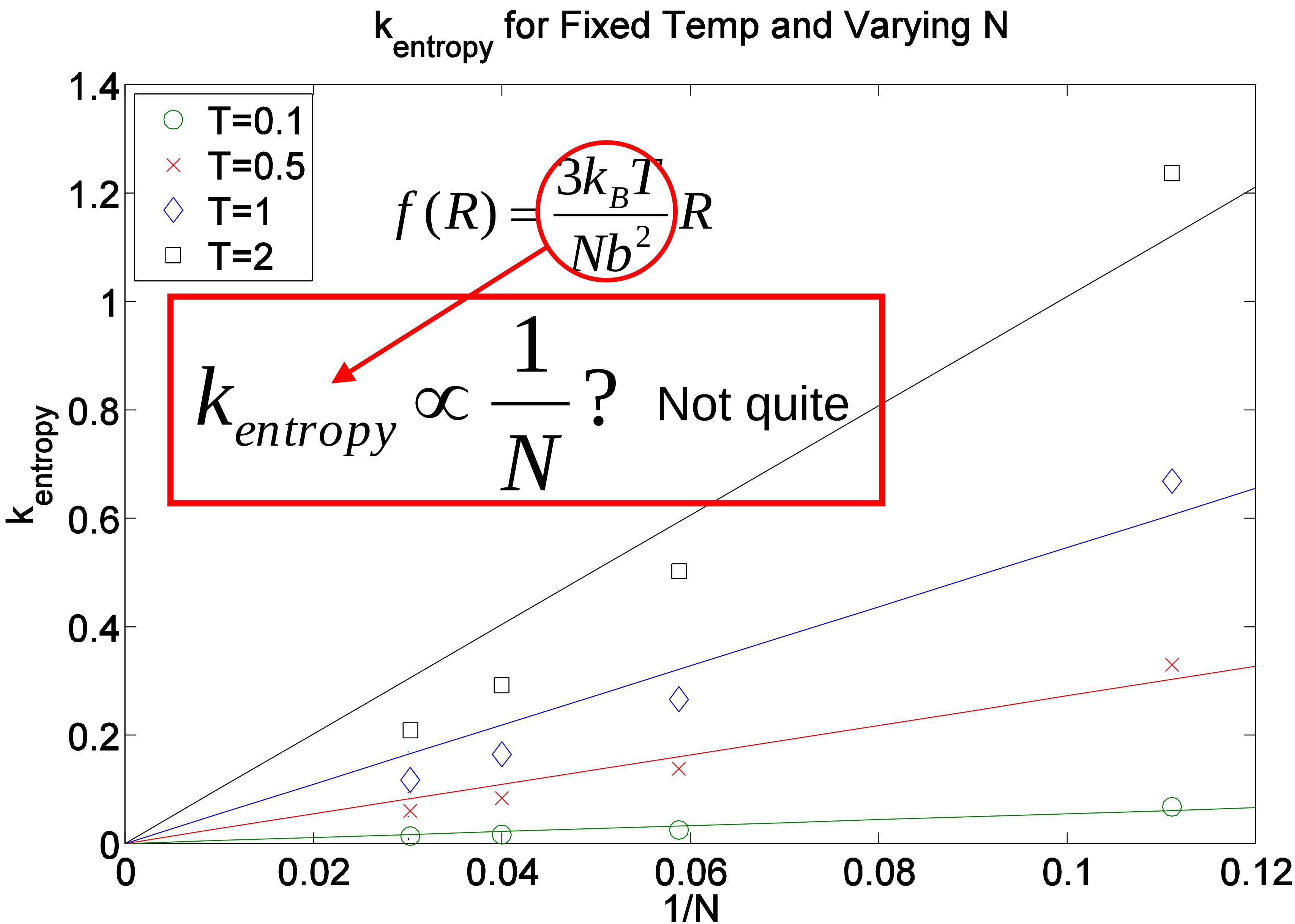






$$f(R) = \frac{3k_BT}{Nb^2}R \quad k_{entropy} \propto T \propto \frac{1}{N}\,?$$

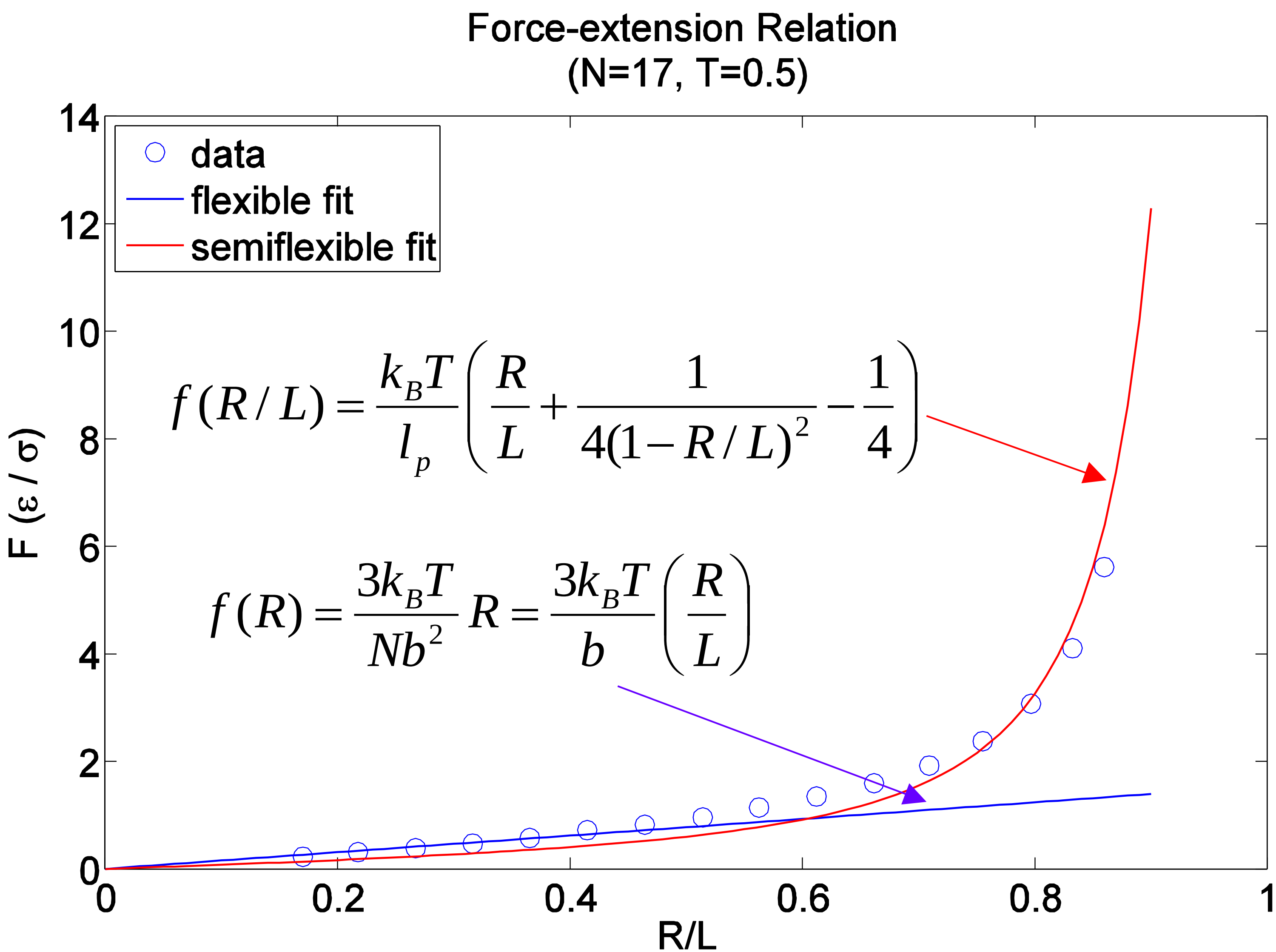

$k_{entropy}$ for Fixed N and Varying Temp
N=9
N=17
N=25
N=33
$f(R) = \frac{3k_B T}{Nb^2} R$
$k_{entropy} \propto T$
$k_{entropy}$
T
0
0.2
0.4
0.6
0.8
1
1.2
1.4
0.5
1.5
2



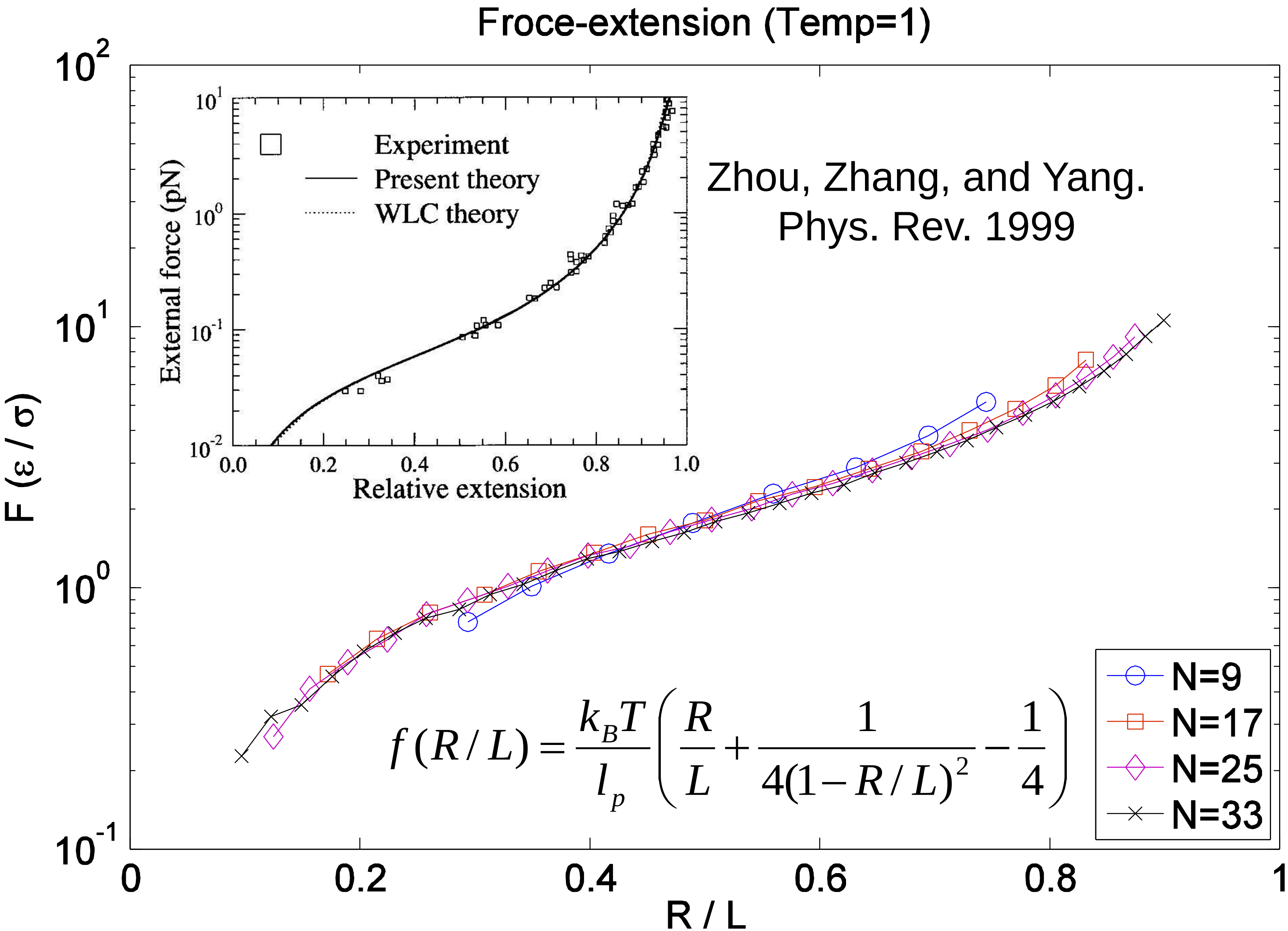
$k_{entropy}$ for Fixed Temp and Varying N
T=0.1
T=0.5
T=1
T=2
$f(R) = \frac{3k_B T}{Nb^2} R$
$k_{entropy} \propto \frac{1}{N}$?
Not quite
$k_{entropy}$
1/N
0
0.2
0.4
0.6
0.8
1
1.2
1.4
0.02
0.04
0.06
0.08
0.1
0.12

Why Is That?

Turning to Semiflexible Chain



Normalized Force-extension Relation for K_A=0

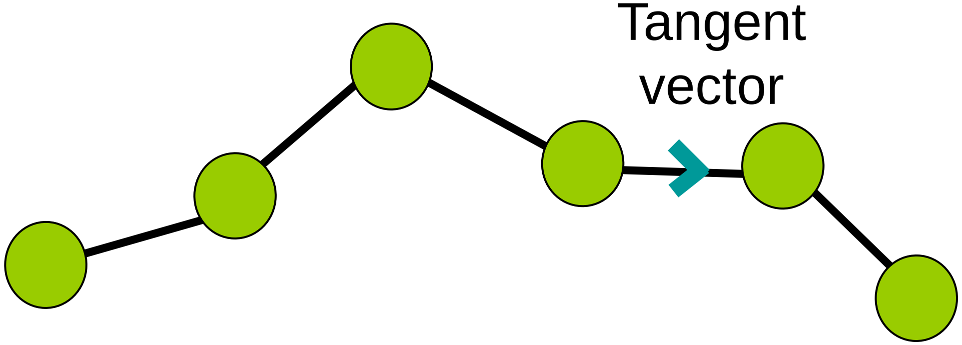


Persistence Length

$$f(R/L) = \frac{k_B T}{l_p}\left(\frac{R}{L} + \frac{1}{4(1-R/L)^2} - \frac{1}{4}\right)$$

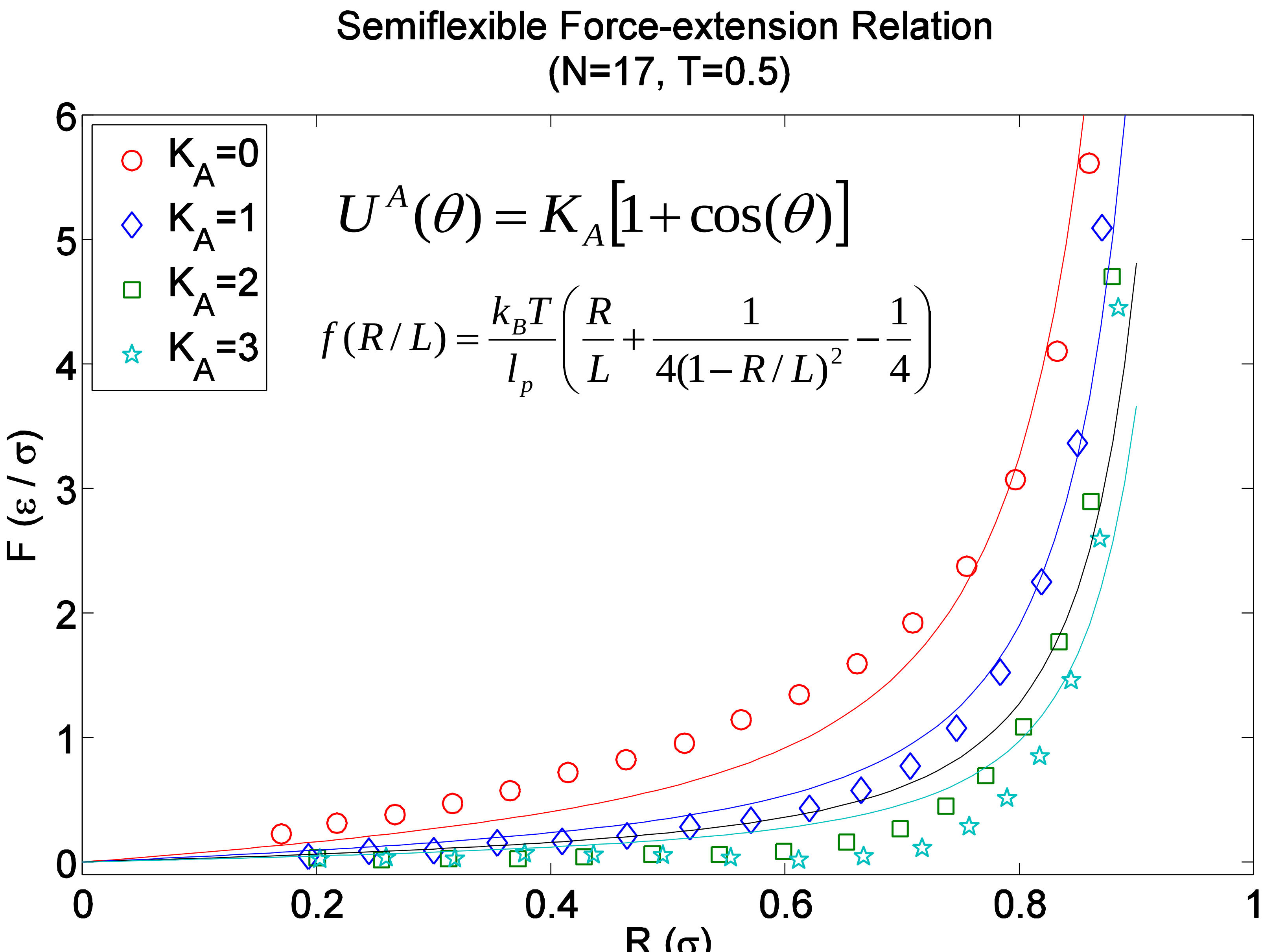
$$U^A(\theta) = K_A\left[1+\cos(\theta)\right]$$

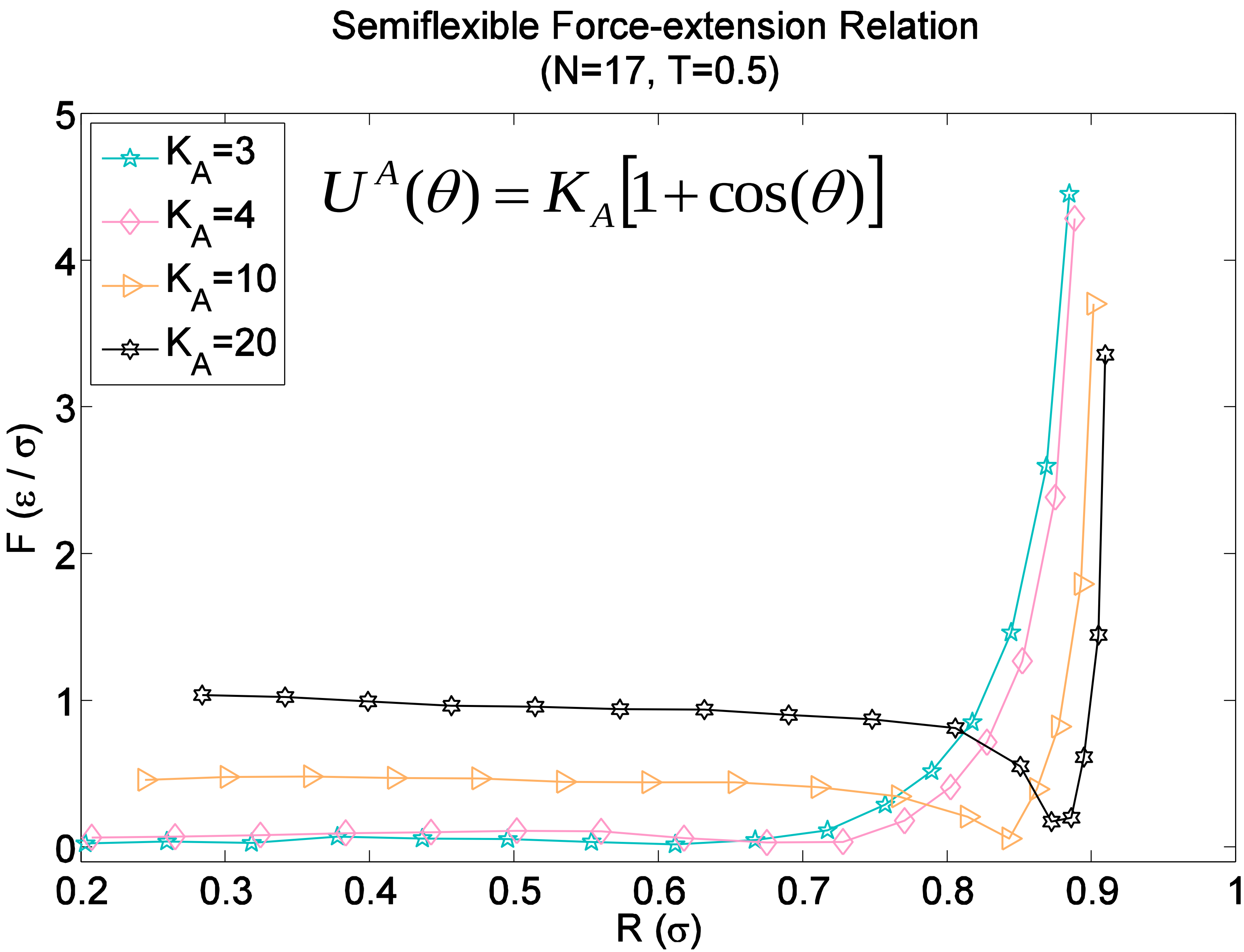
- Characteristic distance over which the tangent correlation die off
- A measure of bending rigidity



Temp	K_A	l_p
1	0	0.9759
1	3	2.584
0.5	0	1.044
0.5	1	1.789
0.5	2	2.666
0.5	3	3.498

Different Values of K_A

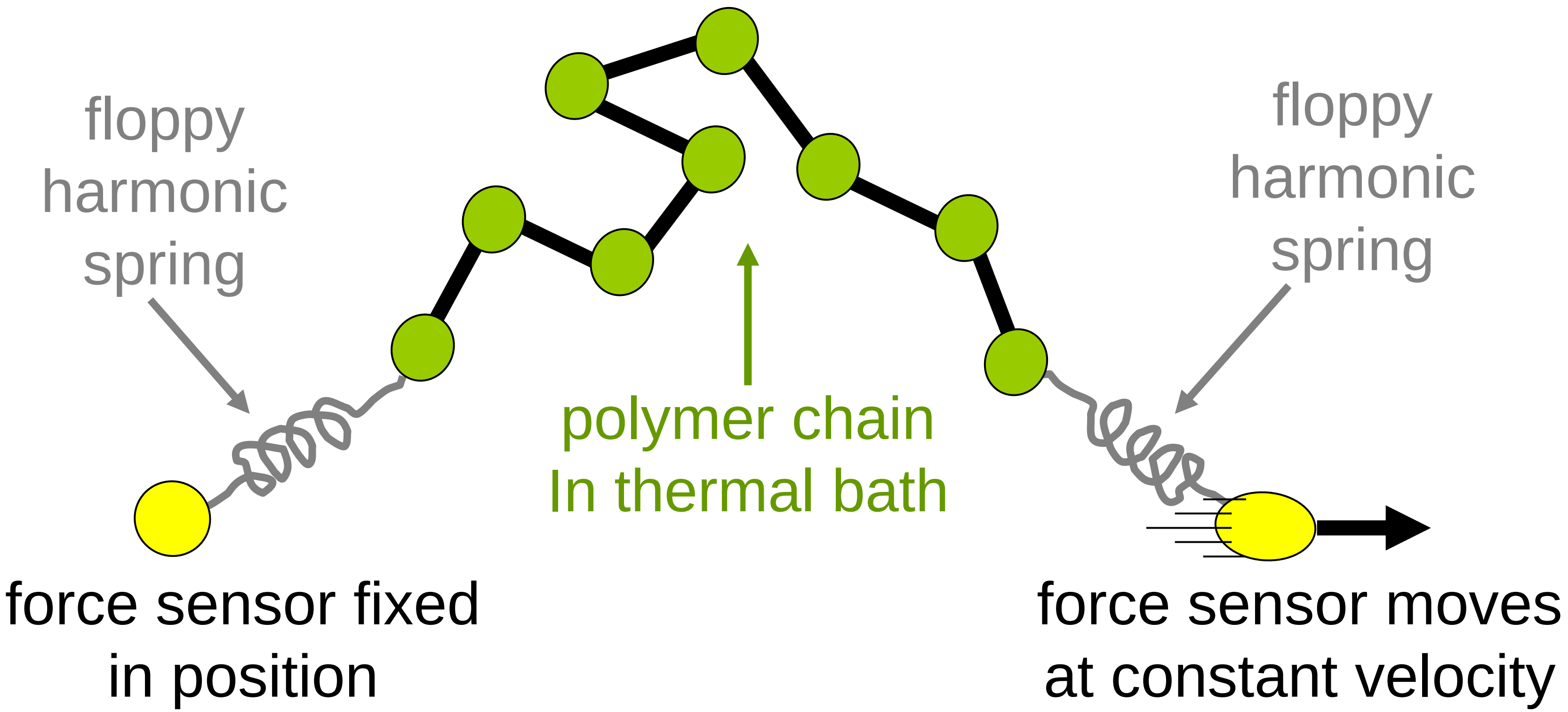


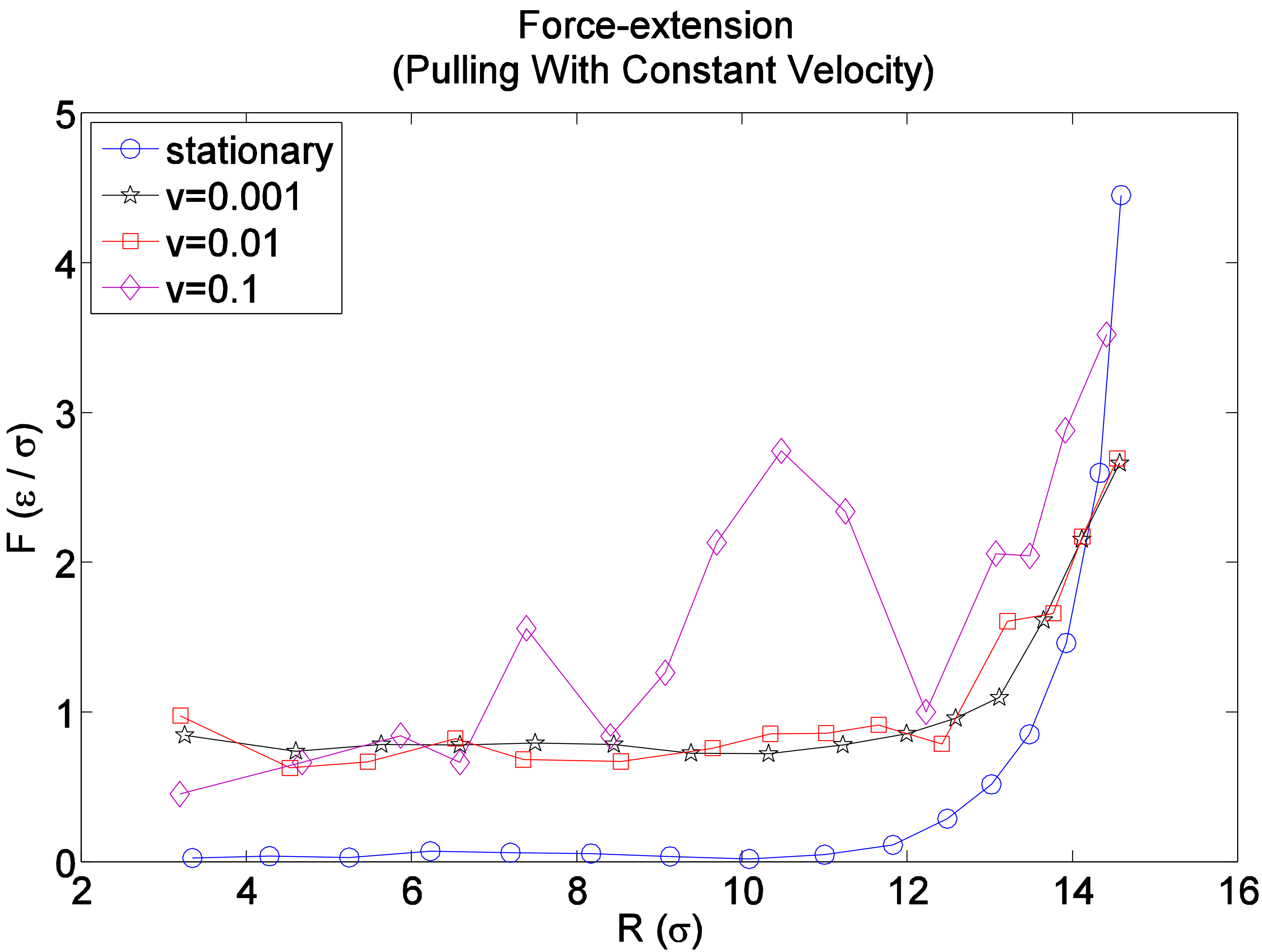


Semiflexible Force-extension Relation
(N=17, T=0.5)
K_A=3
K_A=4
K_A=10
K_A=20
$U^A(\theta) = K_A[1+\cos(\theta)]$
F (ε / σ)
R (σ)
0
1
2
3
4
5
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1

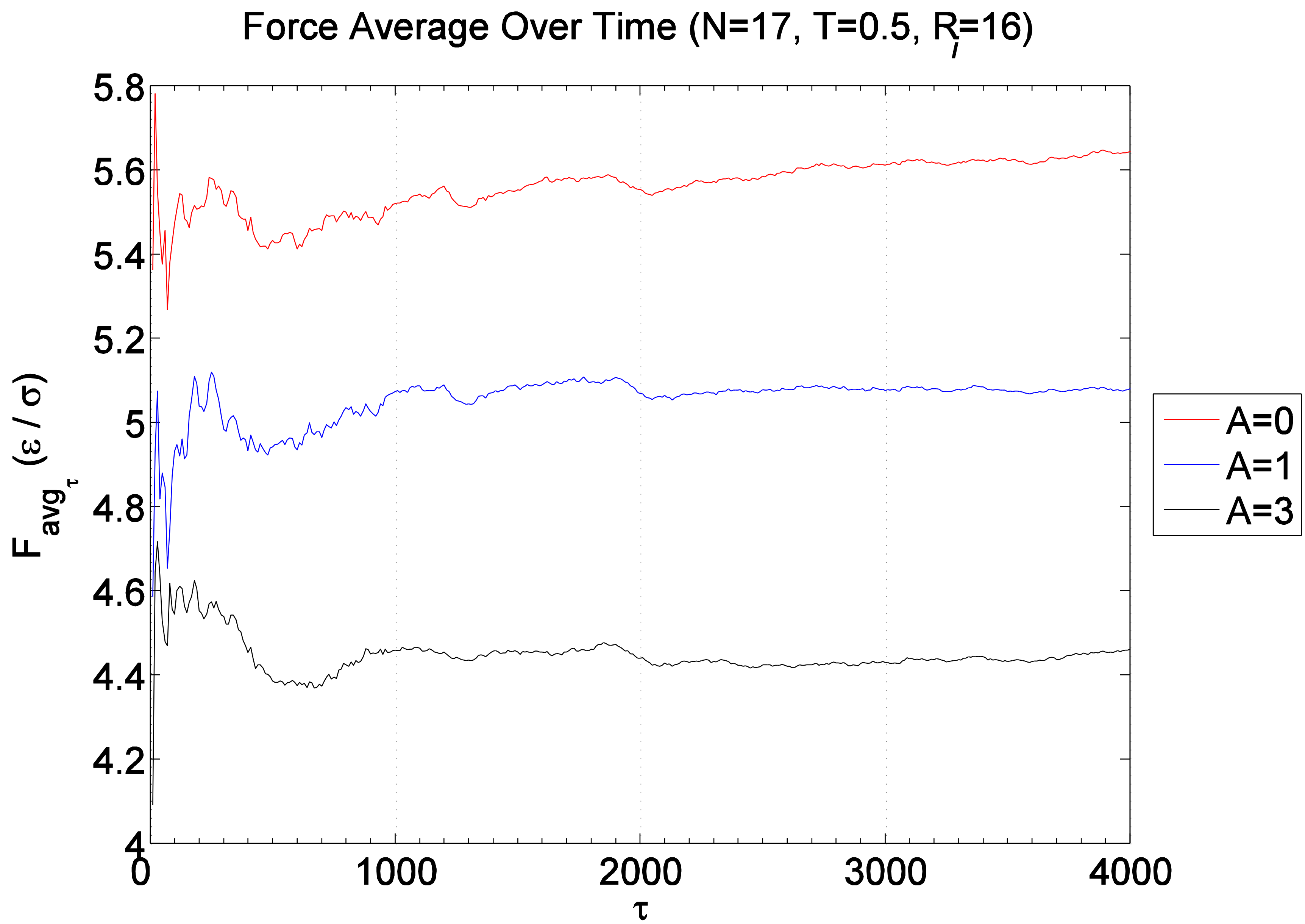
How fast Can I Pull?

- Testing stability of the force-extension relation
  - Time-scale of force convergence
  - Statistical mechanics: reaching all configurations





Force-extension
(Pulling With Constant Velocity)
stationary
v=0.001
v=0.01
v=0.1
F (ε / σ)
R (σ)
0
1
2
3
4
5
2
4
6
8
10
12
14
16

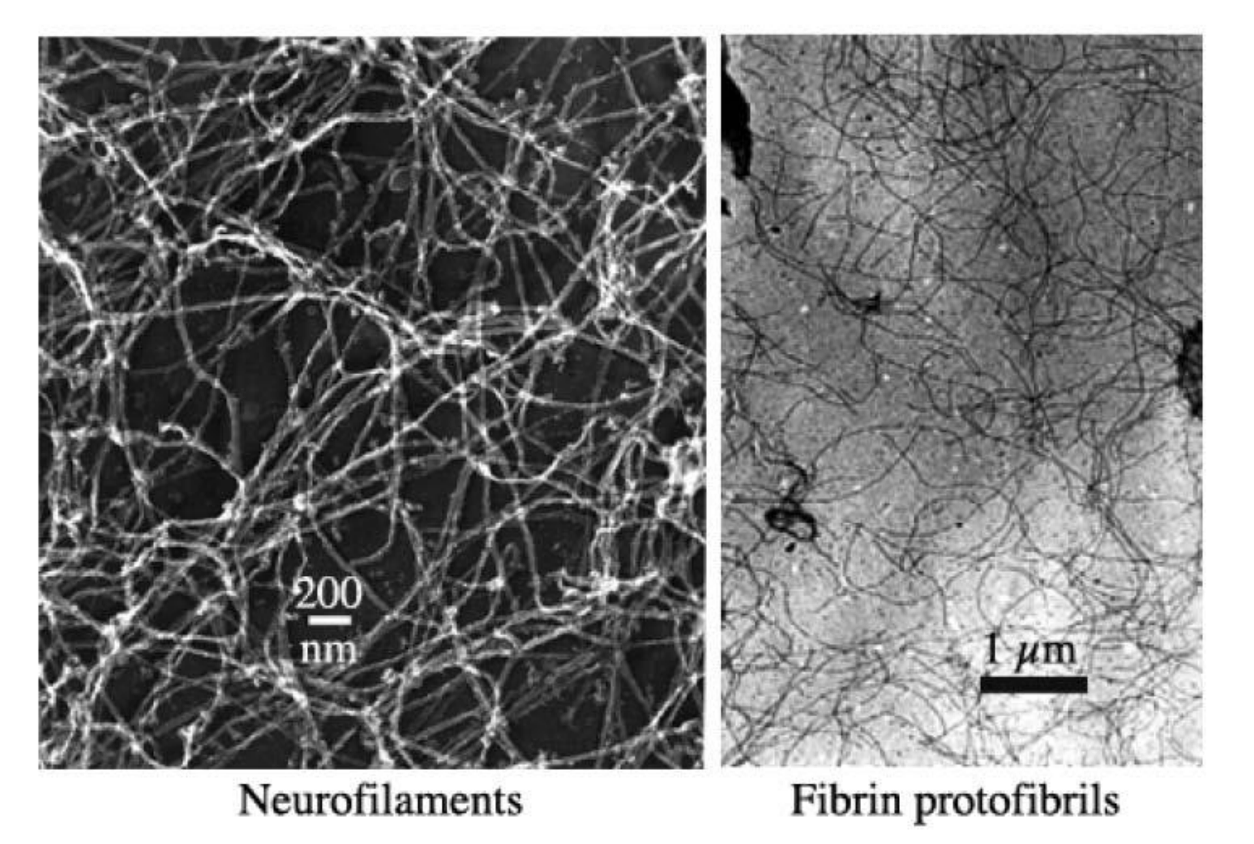

Force Average Over Time (N=17, T=0.5, R_i=16)
F_{avg_τ} (ϵ / σ)
5.8
5.6
5.4
5.2
5
4.8
4.6
4.4
4.2
4
0
1000
2000
3000
4000
τ
A=0
A=1
A=3

Summary

- Verified theoretical results for flexible chain:
  - F-R relation at low F
  - trend of T and N dependence of k_entr
- Semiflexible:
  - Force-extension relation for different K_A
  - Time-scale of stabilized force-extension relation
- Validity of using MD simulation to mimic experimental data and theoretical result

Outlook

- Mechanical properties of cross-linked network of semiflexible biopolymer chains



Storm et al.
Nature, 2005

History of Polymer Physics

Discovery of chain structure of polymer molecule

H.Staudinger, 1920-1930

First papers in polymer physics:

molecular explanation of rubber high elasticity

W.Kuhn, E.Guth, H.Mark, 1930-1935

Physico-Chemical" Period (1935-1965)

P.Flory, V.A.Kargin

Discovery of DNA double helix

Watson and Crick, 1953

Penetration of physical methods to polymer science (from 1965)

I.M.Lifshitz (Russia),

P.de Gennes (France),

S.Edwards (England)