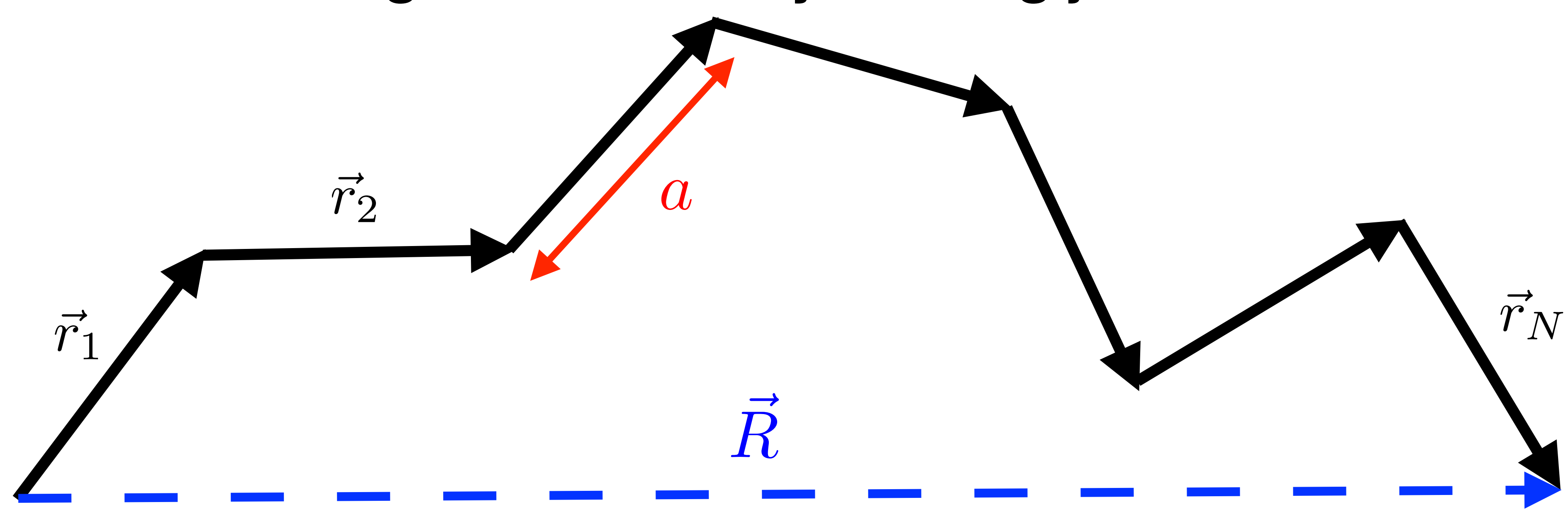
MAE 545: Lecture 4 (9/29)

Statistical mechanics of proteins

Ideal freely jointed chain

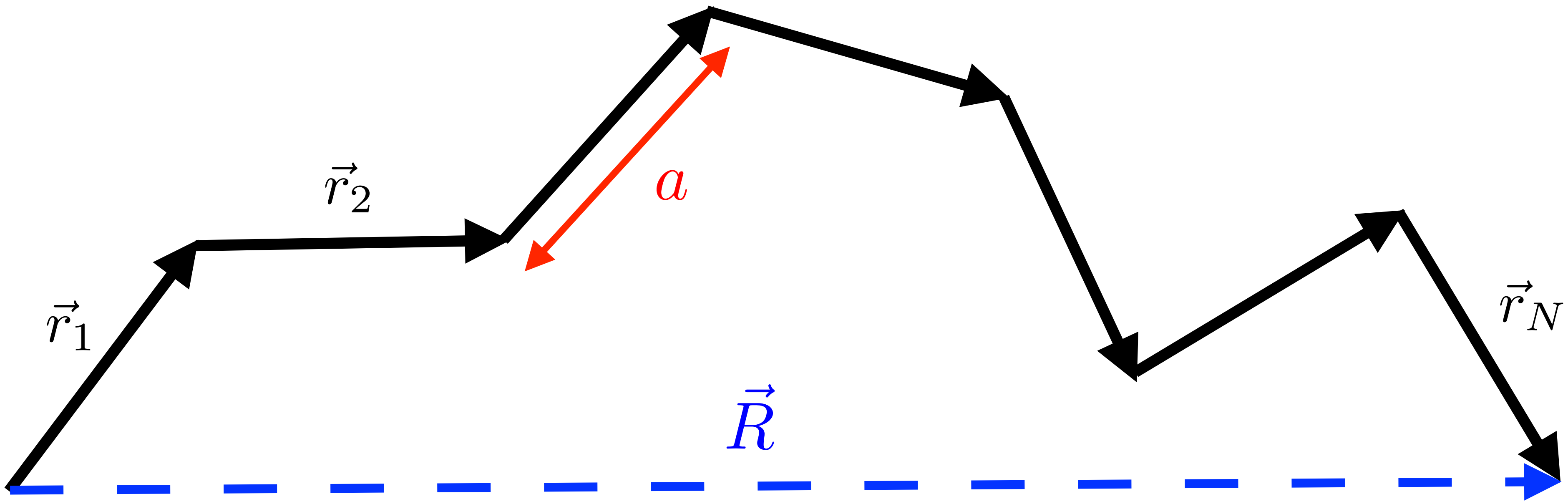
N **identical unstretchable links (Kuhn segments) of length *a* with freely rotating joints**



In first part of the lecture we will ignore interactions between different segments: e.g. steric interactions, van der Waals interactions, etc.

Ideal freely jointed chain

N **identical unstretchable links (Kuhn segments) of length *a* with freely rotating joints**



What are statistical properties of the end to end vector $\vec{R}$?

Statistical mechanics

partition function (sum over all possible chain configurations)

$$Z = \sum_c e^{-E_c/k_B T}$$

expected value of observables

$$\langle \mathcal{O} \rangle = \sum_c \mathcal{O}_c \frac{e^{-E_c/k_B T}}{Z}$$

E_c **energy of a given configuration**

T **temperature**

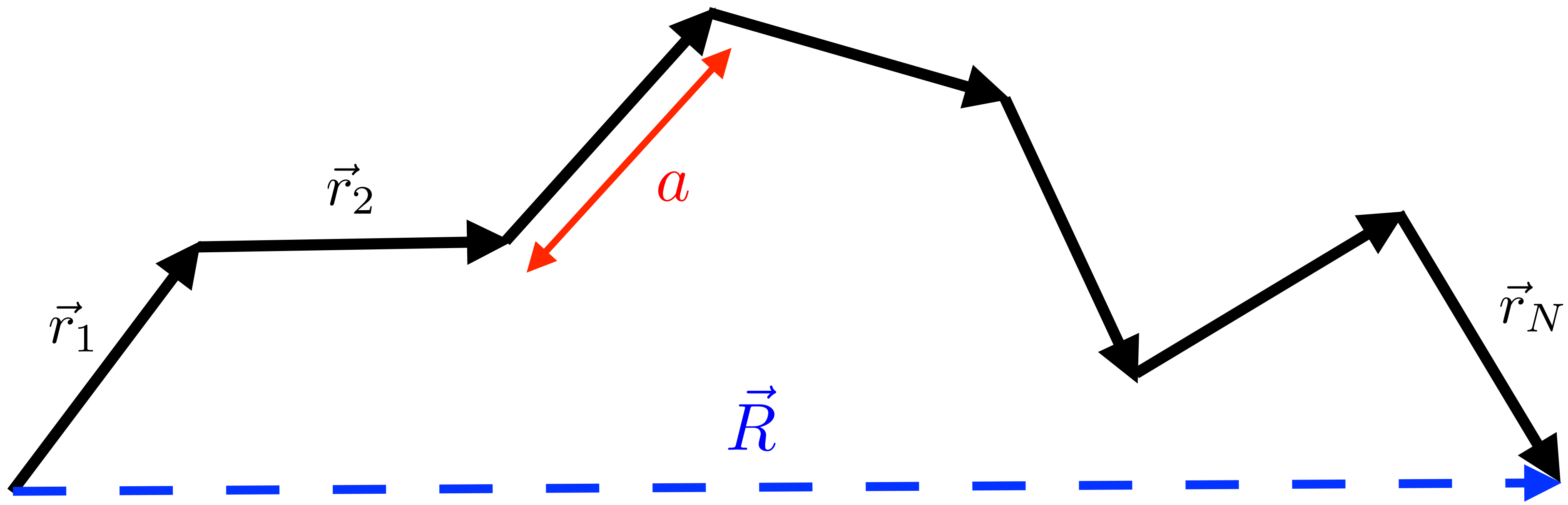
k_B **Boltzmann constant**

$$k_B = 1.38 \times 10^{-23} \mathrm{JK}^{-1}$$

For ideal chain all configurations have zero energy cost and contribute equally!

Ideal freely jointed chain

***N* identical unstretchable links of length *a* with freely rotating joints**



Each ideal chain configuration is a realization of random walk.

individual links $\langle \vec{r}_i \rangle = 0 \qquad \langle \vec{r}_i^{\,2} \rangle = a^2$

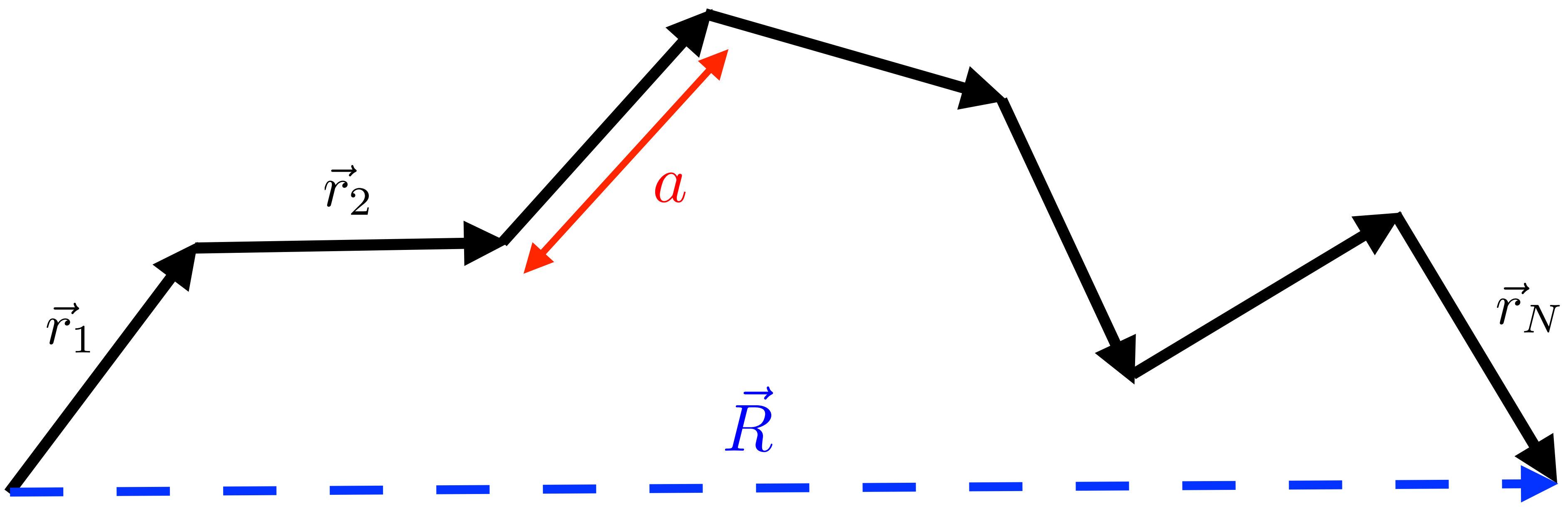
end to end distance $\vec{R} = \sum_{i=1}^{N} \vec{r}_i \qquad \left\langle \vec{R} \right\rangle = 0 \qquad \left\langle \vec{R}^2 \right\rangle = Na^2$

For large *N* the probability distribution for $\vec{R}$ approaches

$$p\left(\vec{R}\right) \approx \frac{1}{(2\pi Na^2/3)^{3/2}} \times e^{-\vec{R}^2/(2Na^2/3)}$$

Note: not accurate in tails of distribution where $|\vec{R}| \sim Na$

Ideal freely jointed chain



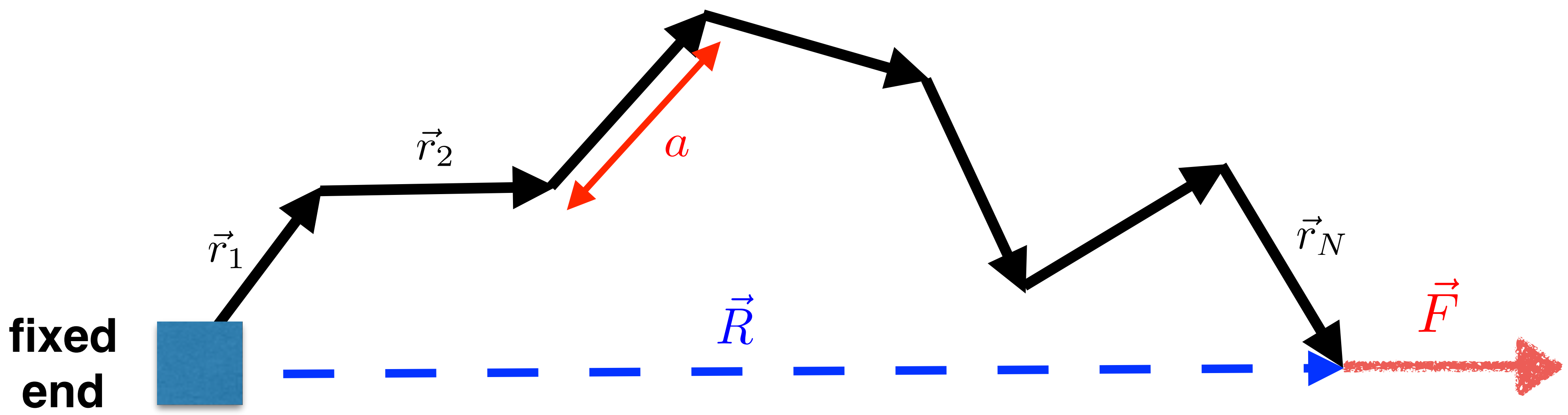
Statistical mechanics

$$\left\langle \vec{R}^m \right\rangle = \sum_c \vec{R}_c^m \frac{e^{-E_c/k_B T}}{Z}$$

$$\left\langle \vec{R}^m \right\rangle = \int d^3\vec{R}\ \vec{R}^m \times \underbrace{\frac{1}{\left(2\pi N a^2/3\right)^{3/2}} \times e^{-\vec{R}^2/(2Na^2/3)}}$$

proportional to the number of random walks with end to end distance $\vec{R}$.

Stretching of ideal freely jointed chain



Each chain configuration is a realization of biased random walk.

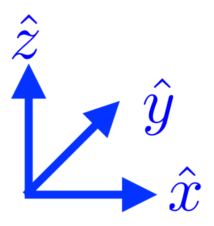
Work due to external force $$W = \vec{F} \cdot \vec{R}$$

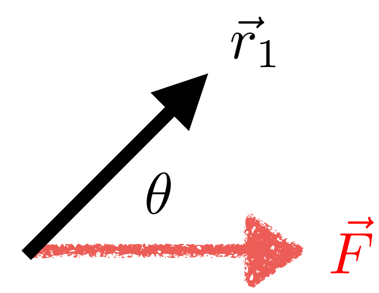
Statistical mechanics

partition function $$Z = \sum_c e^{-(E_c - W_c)/k_B T} = \sum_c e^{-(E_c - \vec{F}\cdot\vec{R}_c)/k_B T}$$

average end to end distance $$\left\langle \vec{R} \right\rangle = \sum_c \vec{R}_c \frac{e^{-(E_c - \vec{F}\cdot\vec{R}_c)/k_B T}}{Z} = +k_B T \frac{\partial \ln Z}{\partial \vec{F}}$$

Bias for a single chain link





partition function

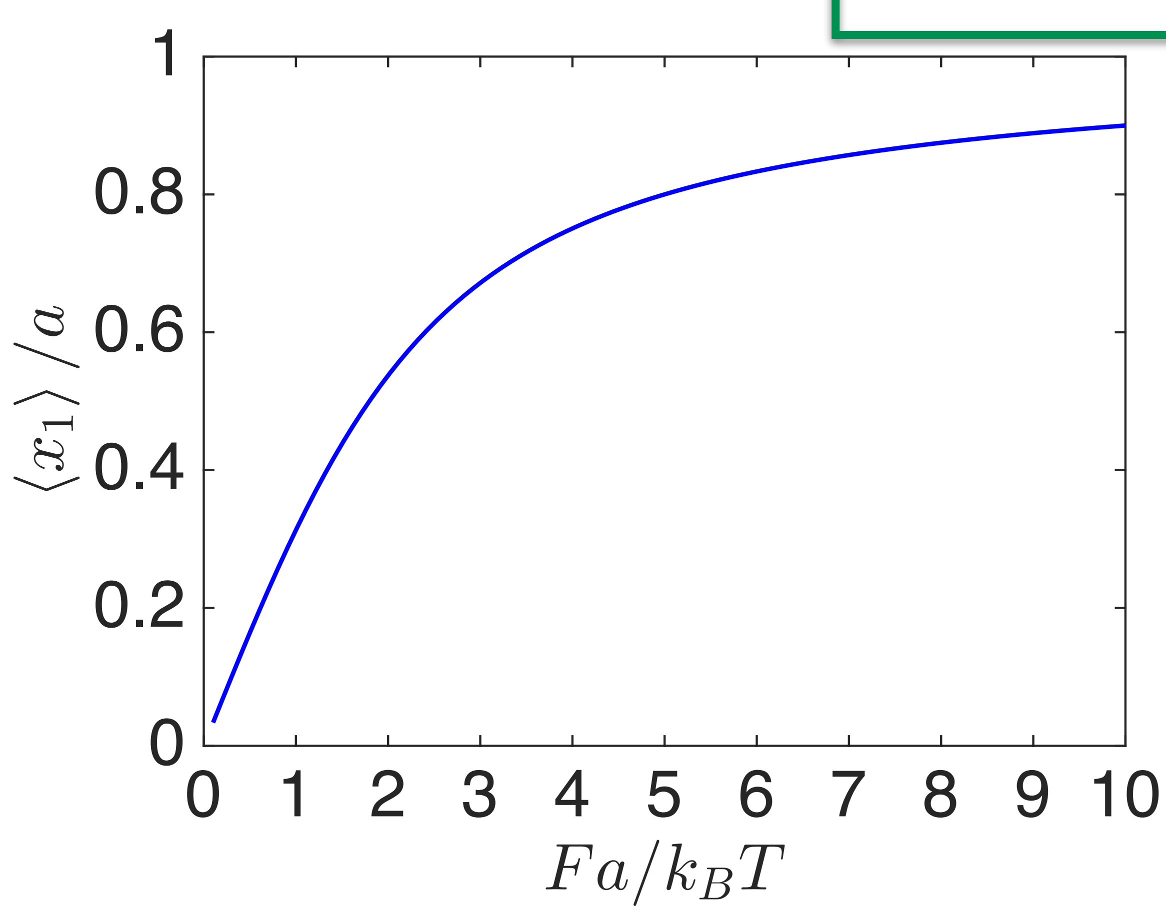
$$Z_1 = \int_{-1}^{1} \frac{d(\cos\theta)}{2} e^{-Fa\cos\theta/k_BT} = \frac{\sinh\left(Fa/k_BT\right)}{Fa/k_BT}$$

bias in direction of force

$$\langle x_1 \rangle = \int_{-1}^{1} \frac{d(\cos\theta)}{2} \times a\cos\theta \times \frac{e^{+Fa\cos\theta/k_BT}}{Z_1}$$

$$\langle x_1 \rangle = a\left(\coth\left[\frac{Fa}{k_BT}\right] - \frac{k_BT}{Fa}\right)$$

Langevin function



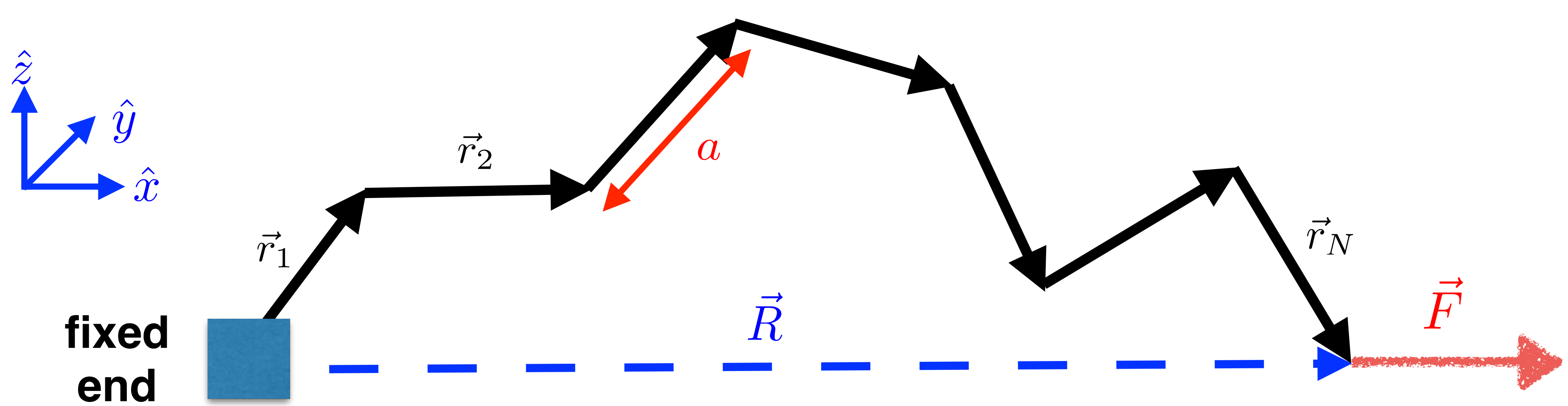
small force $Fa \ll k_BT$

$$\langle x_1 \rangle \approx \frac{Fa^2}{3k_BT}$$

large force $Fa \gg k_BT$

$$\langle x_1 \rangle \approx a - \frac{k_BT}{F}$$

Stretching of ideal freely jointed chain



Exact result for stretching of ideal chain

$$\langle x \rangle = N \langle x_1 \rangle = Na \left(\coth\left[\frac{Fa}{k_B T}\right] - \frac{k_B T}{Fa} \right)$$

small force $\langle x \rangle \approx \frac{NFa^2}{3k_B T} \equiv \frac{F}{k}$ → **entropic spring constant** $k = \frac{3k_B T}{Na^2}$

Gaussian approximation

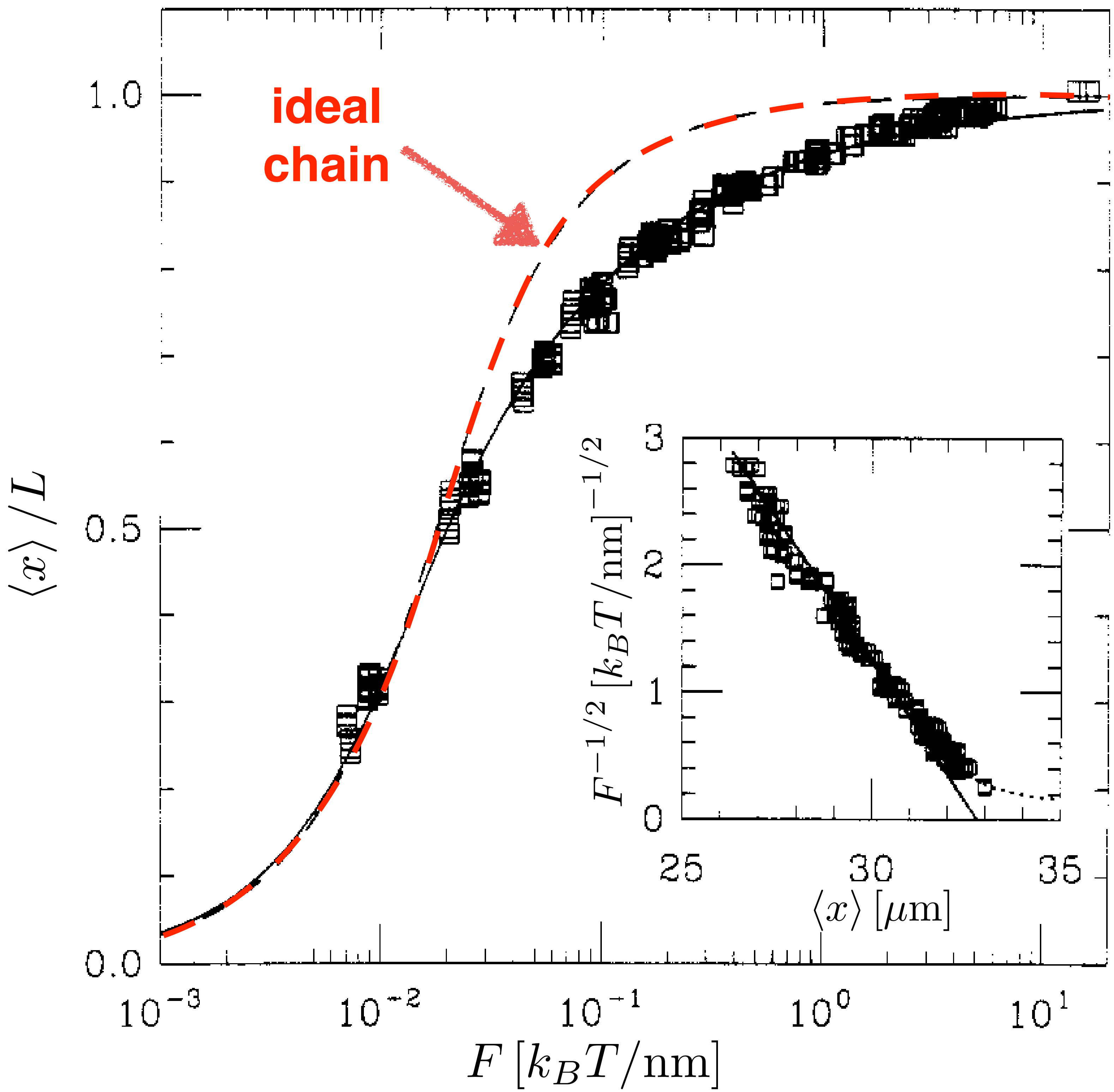
$$Z = \int d^3\vec{R}\, \frac{1}{[2\pi N a^2/3]^{3/2}} e^{-\vec{R}^2/(2Na^2/3)} \times e^{\vec{F}\cdot\vec{R}/k_B T} = e^{NF^2a^2/6k_B^2T^2}$$

$$\langle x \rangle = k_B T \frac{\partial \ln Z}{\partial F} = \frac{NFa^2}{3k_B T}$$

Gaussian approximation is only valid for small forces!

Experimental results for stretching of DNA

$L = 32.8\mu\text{m}$



$1 k_BT/\text{nm} \approx 4\text{pN}$

Ideal chain fails to explain experimental data at large forces!

Ideal chain predicts

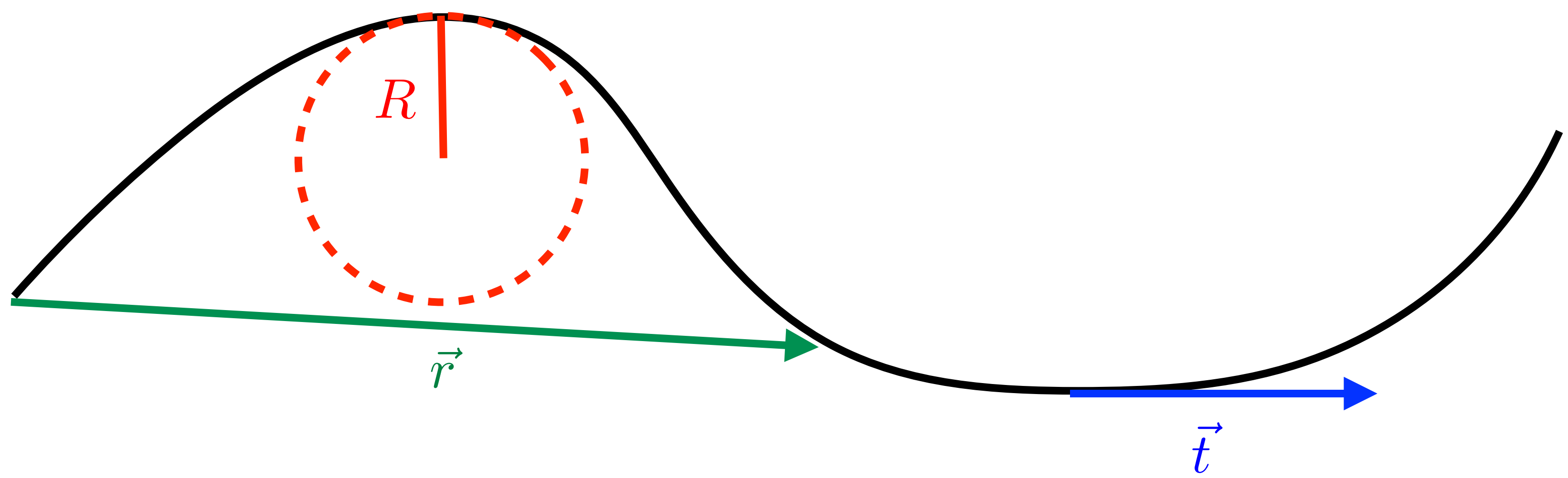
$$\frac{\langle x \rangle}{L} \approx 1 - \frac{k_BT}{Fa}$$

Experiments suggest

$$\frac{\langle x \rangle}{L} \approx 1 - \frac{C}{\sqrt{F}}$$

J.F. Marko and E.D. Siggia, Macromolecules 28, 8759-8770 (1995)

Worm-like chain



Coordinate along the chain

$$s \in [0, L]$$

Position vector

$$\vec{r}(s)$$

Unit tanget vector

$$\vec{t}(s) = \frac{d\vec{r}(s)}{ds}$$

Radius of curvature

$$R(s) = \left|\frac{d\vec{t}(s)}{ds}\right| = \left|\frac{d^2\vec{r}(s)}{ds^2}\right|$$

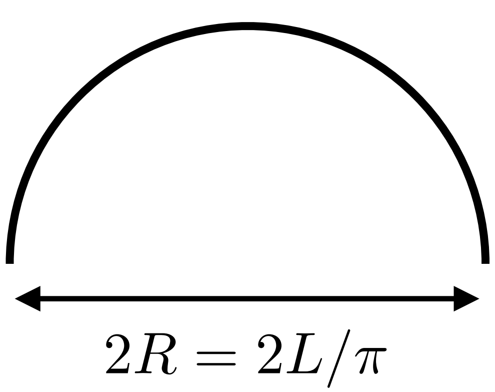
Unstretchable chain of length *L*, but energy cost of bending is included.

$$E_{\text{bend}} = \frac{\kappa}{2}\int_0^L ds \frac{1}{R(s)^2} = \frac{\kappa}{2}\int_0^L ds \left|\frac{d\vec{t}(s)}{ds}\right|^2$$

bending modulus

$$\kappa$$

Example: energy cost for bending of chain to semicircle



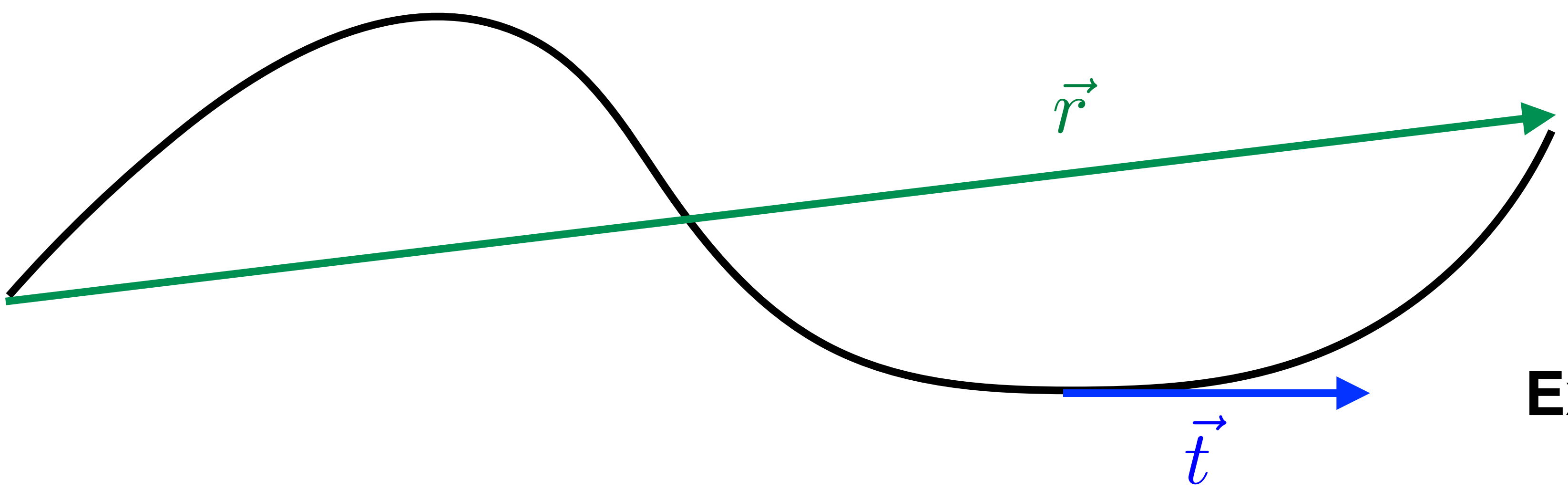
$$E_{\text{bend}} = \frac{\kappa}{2} \times \frac{L}{R^2} = \frac{\pi^2}{2}\frac{\kappa}{L}$$

Thermal fluctuations can easily bend chains that are longer than

$$L \gg \ell_p = \frac{\kappa}{k_B T}$$

$$E_{\text{bend}} \ll k_B T$$

Worm-like chain



Persistence length

$$\langle \vec{t}(s) \cdot \vec{t}(s+\ell) \rangle = e^{-|\ell|/\ell_p}$$

$$\ell_p \equiv \frac{\kappa}{k_B T}$$

Example: DNA at room temperature

$$\ell_p \approx 50\mathrm{nm}$$

Distribution of end to end distances

$$\vec{r}(L) = \int_0^L ds\ \vec{t}(s) \qquad \langle \vec{r}(L) \rangle = 0$$

$$\langle \vec{r}(L)^2 \rangle = \left\langle \int_0^L ds_1\, \vec{t}(s_1) \cdot \int_0^L ds_2\, \vec{t}(s_2) \right\rangle = \int_0^L ds_1 \int_0^L ds_2\ \langle \vec{t}(s_1) \cdot \vec{t}(s_2) \rangle = \int_0^L ds_1 \int_0^L ds_2\, e^{-|s_1 - s_2|/\ell_p}$$

$$\langle \vec{r}(L)^2 \rangle = 2\ell_p L \left[1 - \frac{\ell_p}{L} \left(1 - e^{-L/\ell_p} \right) \right] \xrightarrow{L \gg \ell_p} \langle \vec{r}(L)^2 \rangle = 2\ell_p L = \frac{2L\kappa}{k_B T}$$

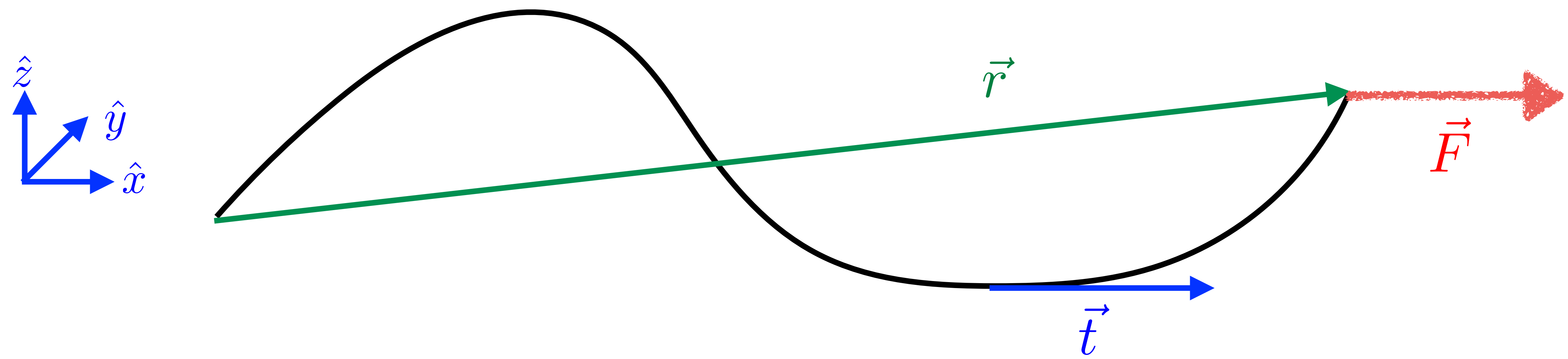
This is equivalent to ideal chain for

$L = Na$ $\quad a = 2\ell_p$ **length of Kuhn segment**

$\langle \vec{r}(L)^2 \rangle = Na^2$ $\quad N = L/(2\ell_p)$ **number of Kuhn segments**

Polymers shrink, when temperature is increases!

Stretching of worm-like chains



In order to calculate the response of worm-like chains to external force, we need to evaluate partition function

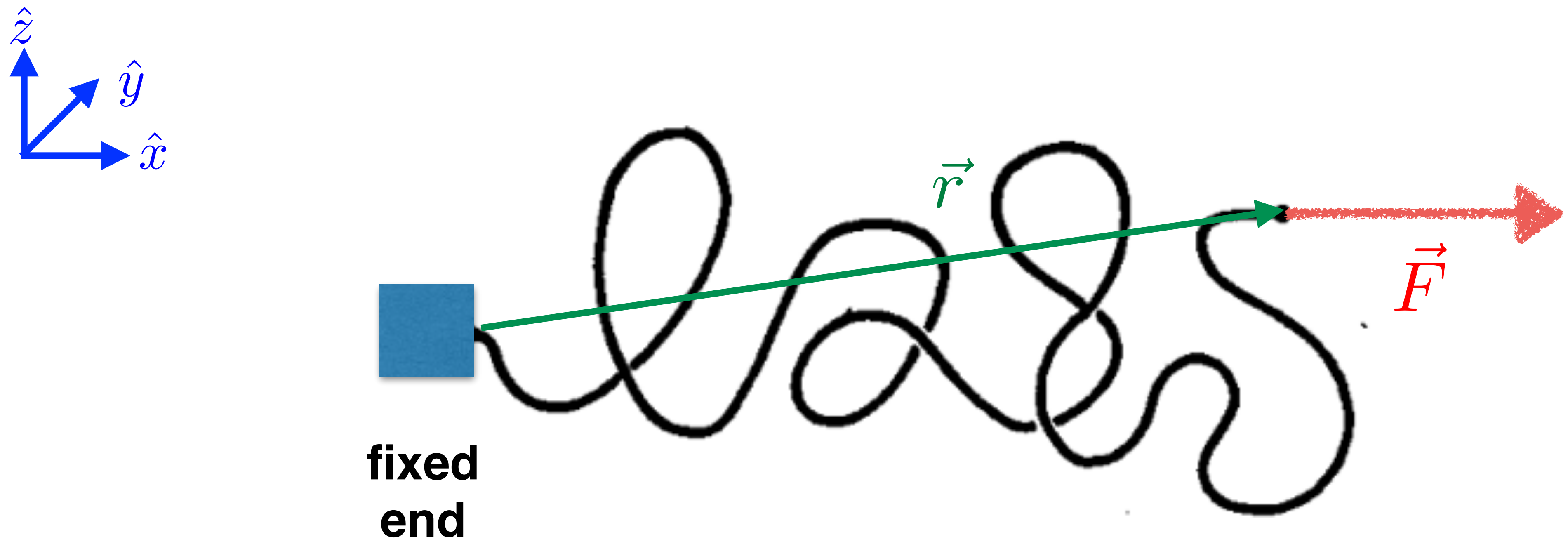
$$Z = \sum_c e^{-E_{\text{bend}}(c)/k_B T}$$

$$\langle x \rangle = k_B T \frac{\partial \ln Z}{\partial F}$$

This is very hard to do analytically for the whole range of forces, but we can treat asymptotic cases of small and large forces.

Stretching of worm-like chains at small forces

$F\ell_p \ll k_B T$



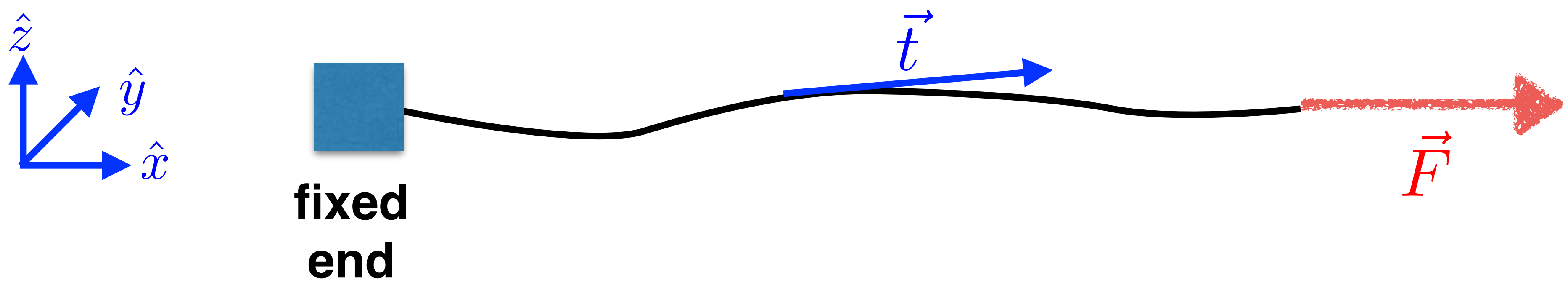
At small forces Gaussian approximation works well

$$\langle x \rangle \approx \frac{NFa^2}{3k_BT} = \frac{2FL\ell_p}{3k_BT} = \frac{2FL\kappa}{3k_B^2T^2} \equiv \frac{F}{k}$$

entropic spring constant

$$k = \frac{3k_BT}{2L\ell_p} = \frac{3k_B^2T^2}{2L\kappa}$$

Stretching of worm-like chains at large forces



At large forces chains are nearly straight and oriented along *x* direction.

$$\vec{t}(s) = \sqrt{1 - A_y(s)^2 - A_z(s)^2}\,\hat{\mathbf{x}} + A_y(s)\hat{\mathbf{y}} + A_z(s)\hat{\mathbf{z}}$$

$$A_y(s), A_z(s) \ll 1$$

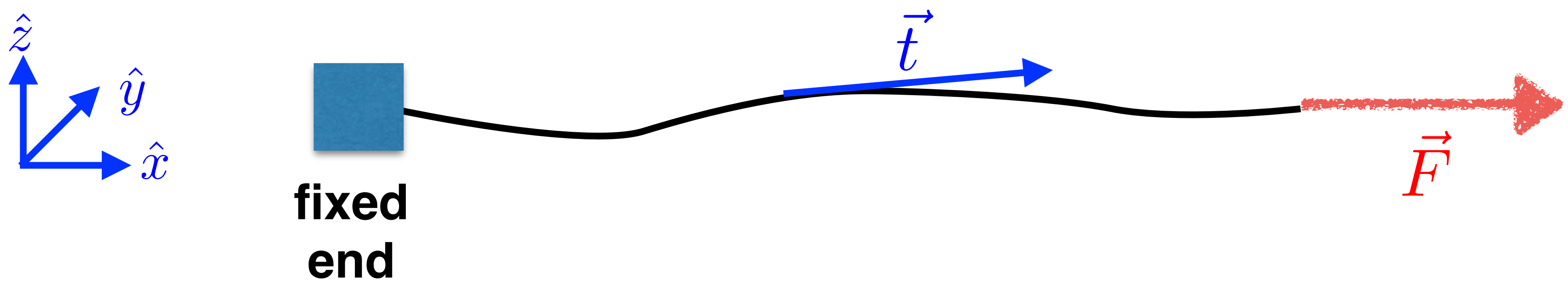
Bending energy to the lowest order in A_y and A_z.

$$E_{\rm bend} = \frac{\kappa}{2}\int_0^L ds \left|\frac{d\vec{t}(s)}{ds}\right| \approx \frac{\kappa}{2}\int_0^L ds \left[\left(\frac{dA_y(s)}{ds}\right)^2 + \left(\frac{dA_z(s)}{ds}\right)^2\right]$$

Work due to external forces to the lowest order in A_y and A_z.

$$W = \vec{F}\cdot\vec{r}(L) = \int_0^L ds\ \vec{F}\cdot\vec{t}(s) \approx FL - \int_0^L ds\ \frac{F}{2}\left[A_y(s)^2 + A_z(s)^2\right]$$

Stretching of worm-like chains at large forces



$F\ell_p \gg k_B T$

Free energy to the lowest order in *A_y* and *A_z*.

$$E = E_{\text{bend}} - W \approx -FL + \frac{1}{2}\int_0^L ds \left(\kappa\left[\left(\frac{dA_y(s)}{ds}\right)^2 + \left(\frac{dA_z(s)}{ds}\right)^2\right] + F\left[A_y(s)^2 + A_z(s)^2\right]\right)$$

Rewrite free energy in terms of Fourier modes

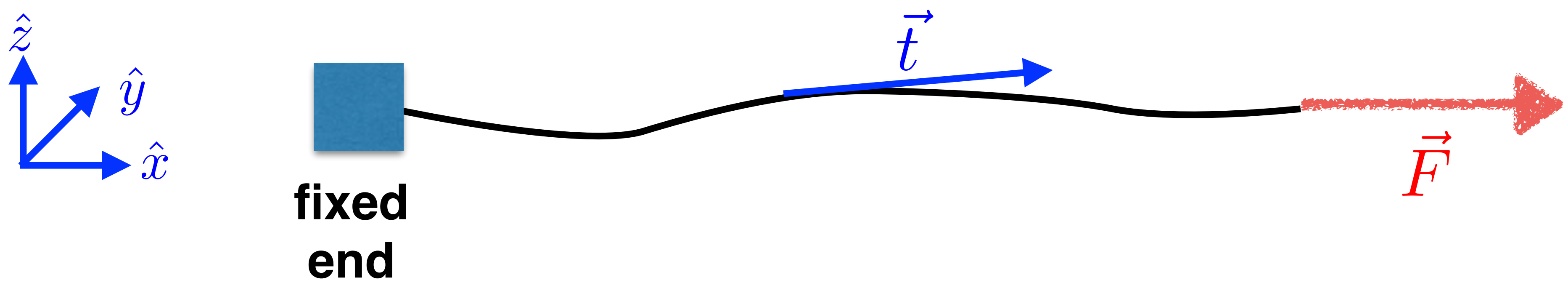
$$A_{y,z}(s) = \sum_q e^{iqs}\tilde{A}_{y,z}(q) \qquad \tilde{A}_{y,z}(q) = \int_0^L \frac{ds}{L} e^{-iqs} A_{y,z}(s) \qquad \begin{array}{l} q = 2\pi m/L \\ m = 1, 2, \cdots \end{array}$$

$$E \approx -FL + \frac{1}{2}\sum_q L(F + \kappa q^2)\left[|\tilde{A}_y(q)|^2 + |\tilde{A}_z(q)|^2\right]$$

From equipartition theorem we can find average fluctuations of *A_y* and *A_z*

$$\left\langle |\tilde{A}_y(q)|^2 \right\rangle = \left\langle |\tilde{A}_z(q)|^2 \right\rangle \approx \frac{k_B T}{L(F + \kappa q^2)}$$

Stretching of worm-like chains at large forces



$F\ell_p \gg k_B T$

At large forces chains are nearly straight and oriented along *x* direction.

$$\vec{t}(s) \approx \left[1 - \frac{A_y(s)^2 + A_z(s)^2}{2}\right]\hat{\mathbf{x}} + A_y(s)\hat{\mathbf{y}} + A_z(s)\hat{\mathbf{z}}$$

From equipartition theorem we can find average fluctuations of A_y and A_z

$$\left\langle |\tilde{A}_y(q)|^2 \right\rangle = \left\langle |\tilde{A}_z(q)|^2 \right\rangle \approx \frac{k_B T}{L(F + \kappa q^2)}$$

Stretching due to large force is

$$\langle x \rangle \approx \left\langle \int_0^L ds \left[1 - \frac{[A_y(s)^2 + A_z(s)^2]}{2}\right] \right\rangle = L - \frac{L}{2}\sum_q \left[\left\langle |\tilde{A}_y(q)|^2 \right\rangle + \left\langle |\tilde{A}_z(q)|^2 \right\rangle\right]$$

$$\langle x \rangle \approx L\left[1 - \frac{k_B T}{2\sqrt{F\kappa}}\right] = L\left[1 - \sqrt{\frac{k_B T}{4F\ell_p}}\right]$$

Stretching of worm-like chains

Small force

$$F\ell_p \ll k_B T$$

$$\langle x \rangle \approx L \, \frac{2F\ell_p}{3k_B T}$$

Large force

$$F\ell_p \gg k_B T$$

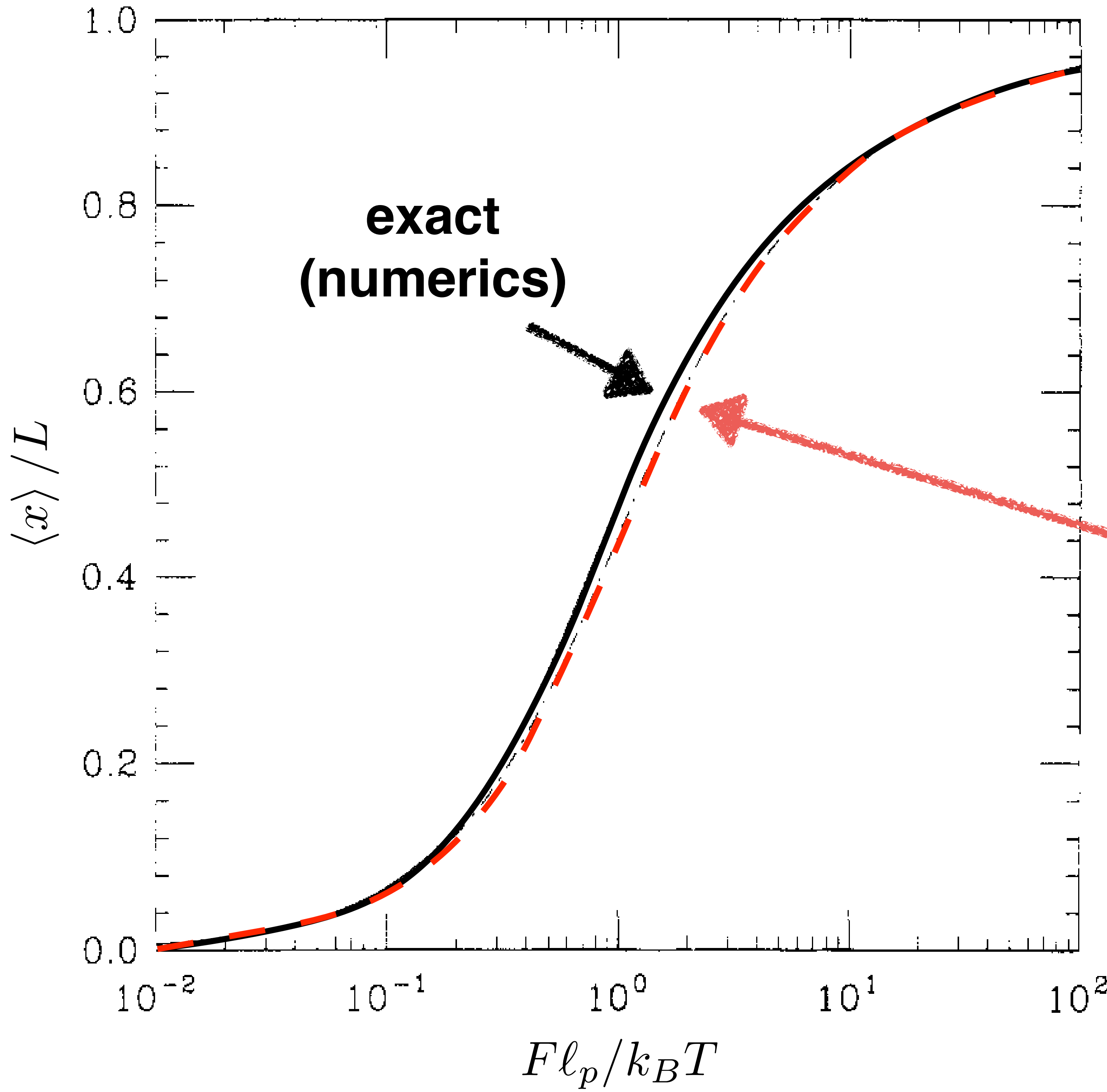
$$\langle x \rangle \approx L \left[1 - \sqrt{\frac{k_B T}{4F\ell_p}} \right]$$

Approximate expression that interpolates between both regimes

$$\frac{F\ell_p}{k_B T} = \frac{1}{4}\left(1 - \frac{\langle x \rangle}{L}\right)^{-2} - \frac{1}{4} + \frac{\langle x \rangle}{L}$$

J.F. Marko and E.D. Siggia, Macromolecules 28, 8759-8770 (1995)

Stretching of worm-like chains



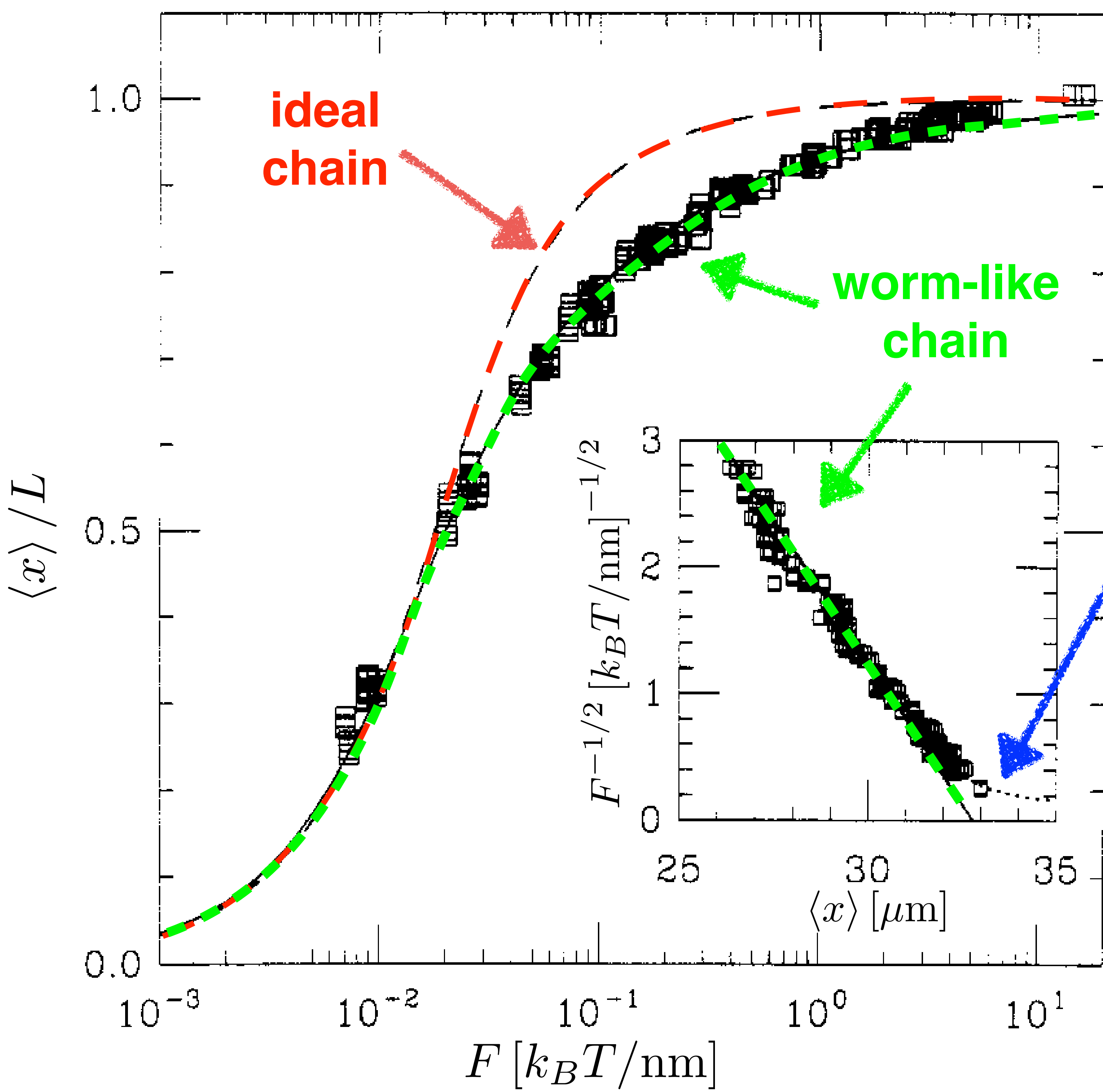
Interpolation formula

$$\frac{F\ell_p}{k_B T} = \frac{1}{4}\left(1 - \frac{\langle x \rangle}{L}\right)^{-2} - \frac{1}{4} + \frac{\langle x \rangle}{L}$$

J.F. Marko and E.D. Siggia,
Macromolecules 28, 8759-8770 (1995)

Experimental results for stretching of DNA

$L = 32.8\mu\text{m}$



$1k_BT/\text{nm} \approx 4\text{pN}$

Stretching of the DNA backbone

$$\langle x \rangle \approx L\left[1 - \sqrt{\frac{k_BT}{4F\ell_p}}\right] + \frac{FL}{\gamma}$$

For DNA

$\ell_p = 50\text{nm}$

$\gamma \approx 500 k_BT/\text{nm} \approx 2\text{nN}$

Improved interpolation formula

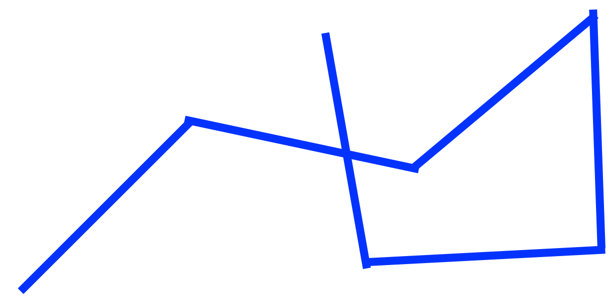
$$\frac{F\ell_p}{k_BT} = \frac{1}{4}\left(1 - \frac{\langle x \rangle}{L} + \frac{F}{\gamma}\right)^{-2} - \frac{1}{4} + \frac{\langle x \rangle}{L} - \frac{F}{\gamma}$$

J.F. Marko and E.D. Siggia, Macromolecules 28, 8759-8770 (1995)

Steric interactions

So far we ignored interactions between different chain segments, but in reality the chain cannot pass through itself due to steric interactions.

Example of forbidden configuration in 2D



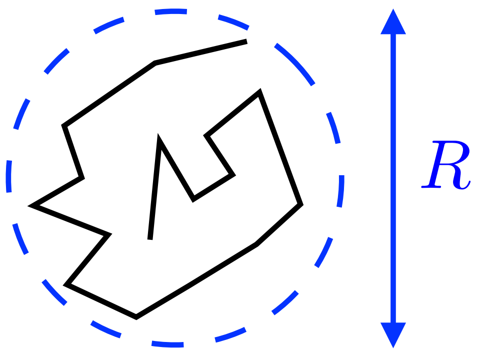
Polymer chains are realizations of self-avoiding random walks!

Steric interactions are important for long polymers in the absence of pulling forces

Steric interactions are not important in the presence of pulling forces.

Mean field estimate for the radius of self-avoiding polymers

Paul Flory



Approximate partition function: estimate number of self-avoiding random walks of *N* steps of size *a* that are restricted to a sphere of radius *R*.

$$Z(R,N) \approx g^N \times \frac{e^{-3R^2/2Na^2}}{[2\pi N a^2/3]^{3/2}} \times \underbrace{\left[1 \cdot \left(1 - \frac{a^3}{R^3}\right) \cdot \left(1 - \frac{2a^3}{R^3}\right) \cdots \left(1 - \frac{(N-1)a^3}{R^3}\right)\right]}_{C_{\text{ev}}}$$

total number of random walks (g^N)

reduction in entropy when constrained to sphere of radius R ($[2\pi N a^2/3]^{3/2}$)

C_{ev}: **reduction in entropy due to excluded volume**

Excluded volume effect

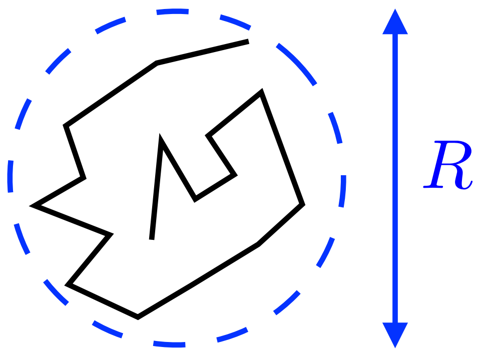
$$\ln C_{\text{ev}} = \sum_{k=1}^{N-1} \ln\left(1 - \frac{ka^3}{R^3}\right) \approx \sum_{k=1}^{N-1}\left(-\frac{ka^3}{R^3} - \frac{k^2a^6}{2R^6} - \cdots\right) \approx -\frac{N^2a^3}{2R^3} - \frac{N^3a^6}{6R^6}$$

Approximate partition function

$$\ln Z(R,N) \approx N \ln g - \frac{3}{2}\ln(2\pi N a^2/3) - \frac{3R^2}{2Na^2} - \frac{N^2a^3}{2R^3} - \frac{N^3a^6}{6R^6}$$

Mean field estimate for the radius of self-avoiding polymers

Paul Flory



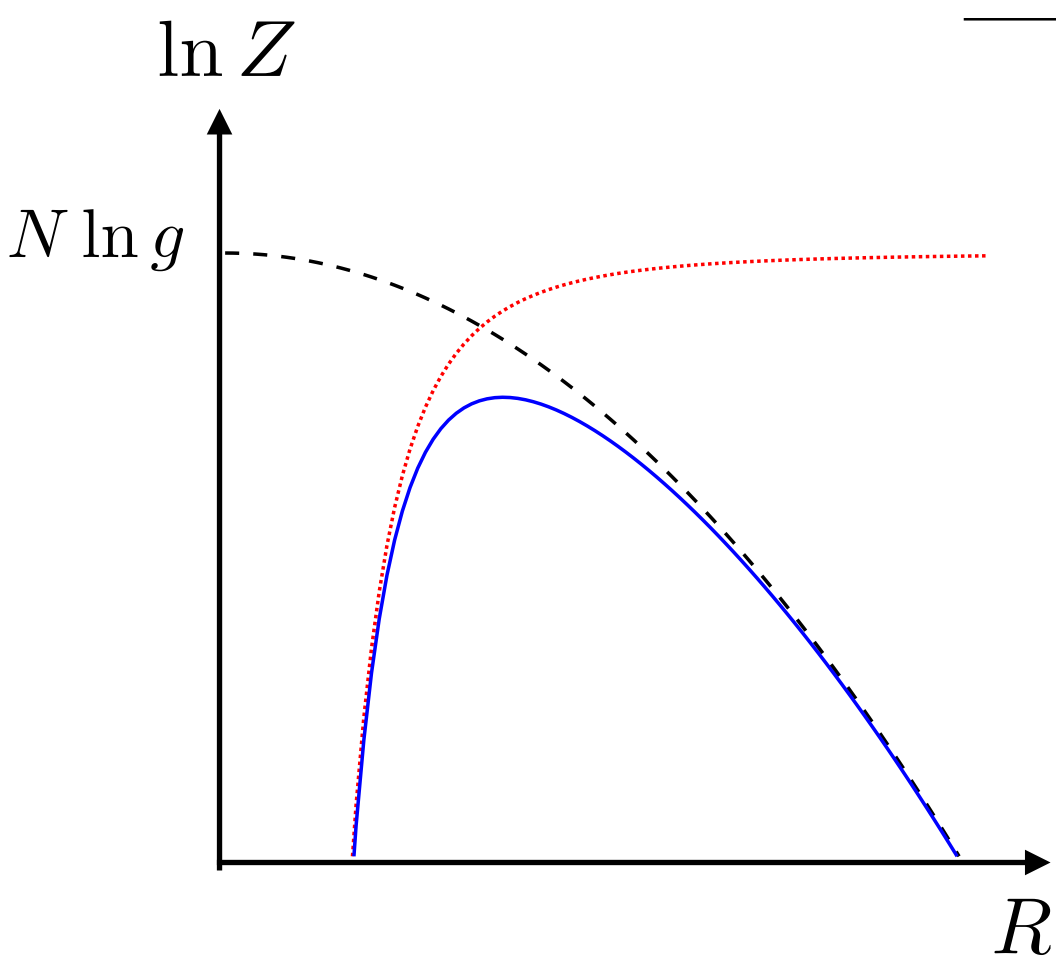
Approximate partition function

$$\ln Z(R,N) \approx N \ln g - \frac{3}{2}\ln(2\pi N a^2/3) - \frac{3R^2}{2Na^2} - \frac{N^2a^3}{2R^3} - \frac{N^3a^6}{6R^6}$$

Estimate polymer radius by maximizing the partition function

$$\frac{\partial \ln Z(R,N)}{\partial R} \approx -\frac{3R}{Na^2} + \frac{3}{2}\frac{N^2a^3}{R^4} + \frac{N^3a^6}{R^7} = 0$$

(higher order term can be ignored)



$$R \sim aN^{\nu} \sim \ell_p \left(\frac{L}{\ell_p}\right)^{\nu}$$

Flory exponent $\nu = 3/5$

Exact result from more sophisticated methods

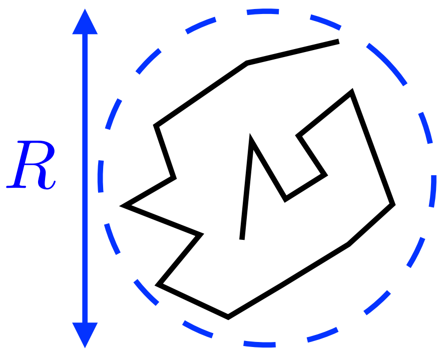
$\nu \approx 0.591$

non-avoiding random walks

$\nu = 1/2$

Self-avoiding walks in *d* dimensions

Paul Flory



Approximate partition function

$$Z(R,N) \approx g^N \times \frac{e^{-dR^2/2Na^2}}{[2\pi N a^2/d]^{d/2}} \times \left[1 \cdot \left(1 - \frac{a^d}{R^d}\right) \cdot \left(1 - \frac{2a^d}{R^d}\right) \cdots \left(1 - \frac{(N-1)a^d}{R^d}\right)\right]$$

$$\ln Z(R,N) \approx N \ln g - \frac{d}{2}\ln(2\pi N a^2/d) - \frac{dR^2}{2Na^2} - \frac{N^2 a^d}{2R^d}$$

Estimate *R* by maximizing the partition function

$$\frac{\partial \ln Z(R,N)}{\partial R} \approx -\frac{dR}{Na^2} + \frac{d}{2}\frac{N^2 a^d}{R^{d+1}} = 0$$

$$R \sim aN^{\nu} \qquad \nu = \frac{3}{d+2}$$

For $d \geq 4$ Flory exponent is $\nu \leq 1/2$, but for non-avoiding walk $\nu = 1/2$.

For $d \geq 4$ excluded volume is irrelevant!

d	1	2	3	≥ 4
ν	1	3/4	3/5	1/2

Note: except for *d*=3 these exponents are exact!