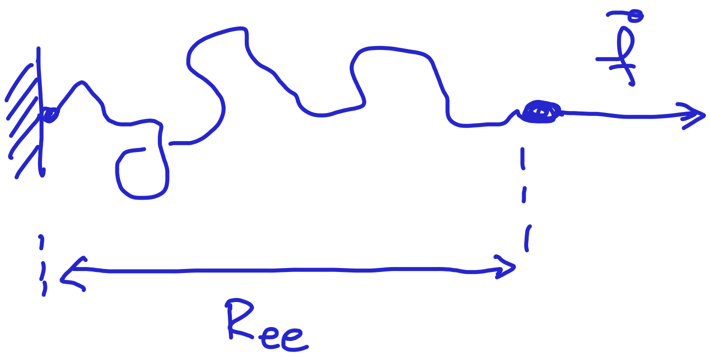
6. Force - extention characteristic of polymers

In the cell, proteins, DNA and RNA are constantly manipulated by protein machines that apply forces on them, to stretch or compactify them. Then, it would be instructive to know with what force a polymer reacts to an applied force.

Experiments

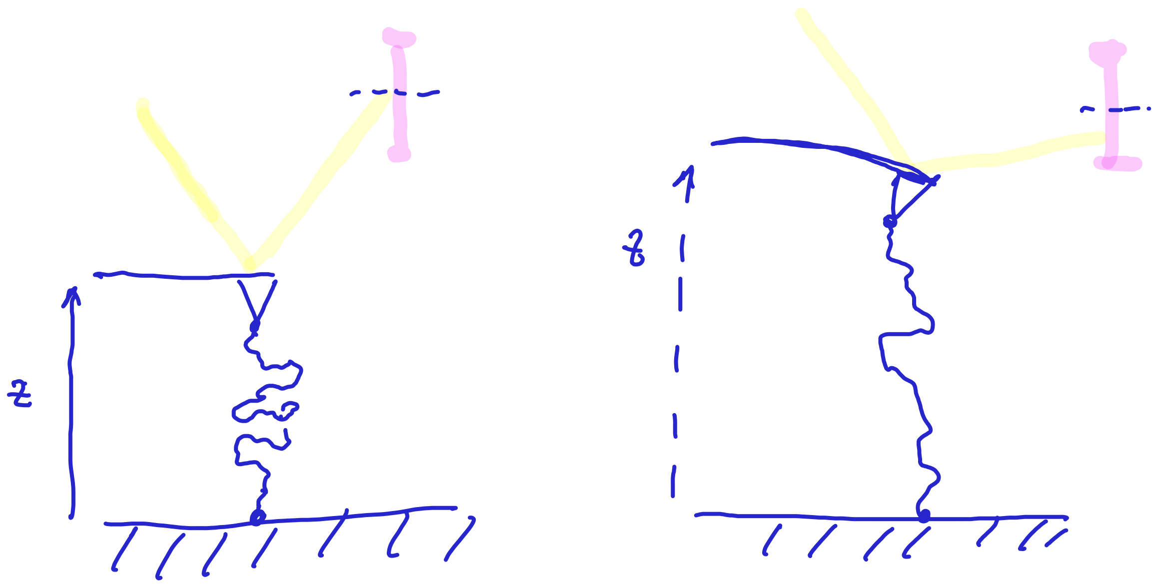


length L
force $\vec{f}$

$R_{ee} = ?$

This idealised experiment can be realized in single-molecule experiments :

AFM (Atomic Force Microscope)



The AFM cantilever is attached to one end of the polymer, while the other end is attached to a surface. The distance z between the tip and the surface is known (very precisely! 1 nm or less, in principle), and the force is measured by the deflection of the laser:

$$\Rightarrow \quad V(\theta) = \frac{1}{2} k \theta^2 = \frac{1}{2} \frac{k}{\ell^2} \delta z^2 = V(\delta z)$$

$$\theta \simeq \frac{\delta z}{\ell}$$

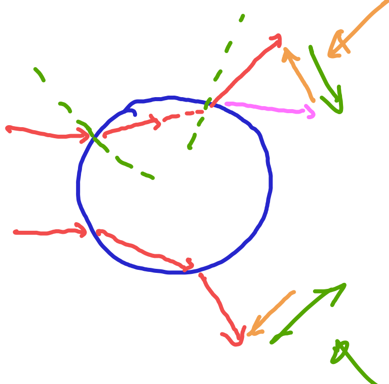
provided by the vendor

$$\Rightarrow \quad f = -\frac{\partial V}{\partial \delta z} = -\boxed{\frac{k}{\ell^2}} \delta z$$

By increasing z, the mecanical equilibrium sets a given δz for each z $\Rightarrow$ f is the force applied by the polymer for a given extension

Optical tweezers

It is possible to capture a latex bead in the focus of a laser beam:



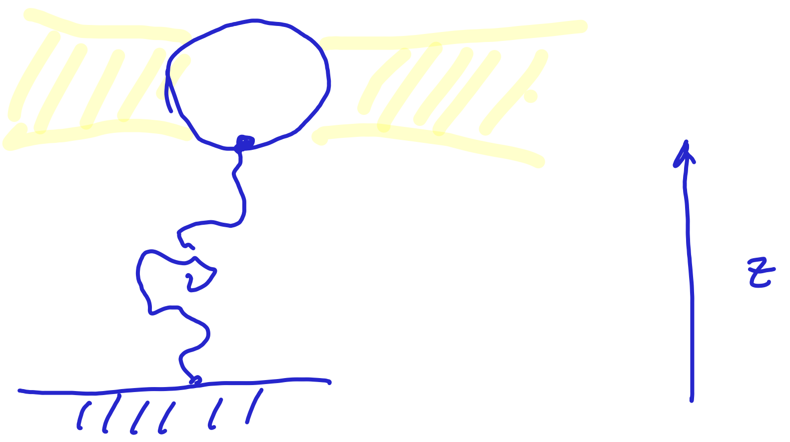
change of momentum of the photons ⇒ 3rd law of Newton

is the momentum applied to the bead, which is thus pushed on the beam

they push forward and toward the middle of the beam.

By carefully shaping the beam, it stays in the focus region

Then it is just as before



can be controlled
by moving the beam.
and the deviation from
the center of the beam
is due to the extra force
exherted by the polymer.

Since the effective potential due to the beam is known, one can measure the force.

Reality is of course way more complex, but by and large this is it. Of course the measurement must be interpreted using models.

The first model we use is the FJC in the Gaussian approximation:

$$P_{FJC}(\vec{R}_{ee}) = \underbrace{\left(\frac{\boxed{3}}{2\pi b^2 N}\right)^{\boxed{3}/2}}_{} e^{-\frac{\boxed{3}}{2b^2N}\vec{R}_{ee}^{\,2}}$$

we consider here only the 3D case

We look here in two ways:

1) We remind that we can write

$$P_{FJC}(\vec{R}_{ee}) = \frac{1}{Z}\, e^{-F(\vec{R}_{ee})/k_BT}$$

and as a consequence

$$F(\vec{R}_{ee}) = k_B T \frac{3}{2b^2N} \vec{R}_{ee}^{\,2}$$

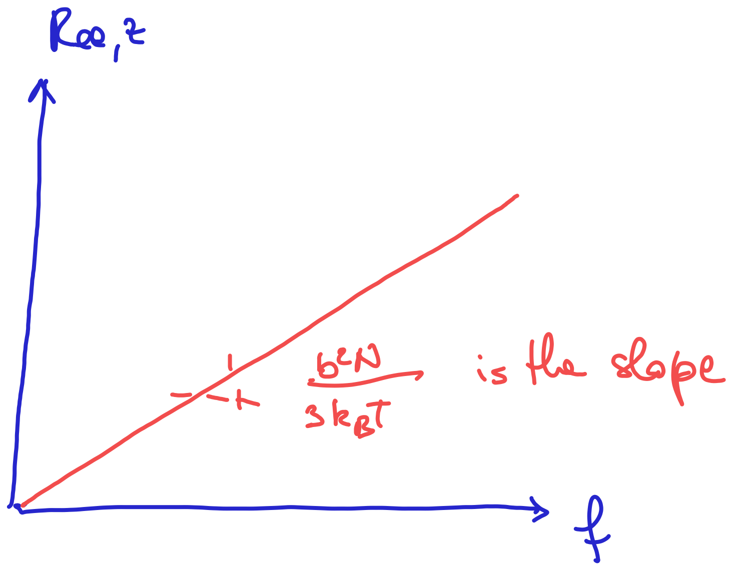
This is the potential (although it is a free-energy) similar to the one of a spring, it is quadratic!

If we apply a pulling force f in a given direction, say $\hat{z}$, then mechanical equilibrium is established if

$$\hat{z}\, f = \vec{\nabla}_{\hat{z}} F(\vec{R}_{ee}) = \frac{3\,k_B T}{b^2 N} R_{ee,z}\, \hat{z}$$

⇒ the extension of the polymer is

$$\boxed{R_{ee,z} = \frac{b^2 N}{3\,k_B T} f}$$



2) More formally:

What is the probability of a certain extension $\vec{R}_{ee}$ given an external force $f\hat{z}$?

We know that an external constant force is obtained by taking the gradient of the potential acting on the polymer end (and thus on $\vec{R}_{ee}$) with respect to $\vec{R}_{ee}$

This means that the force $f\hat{z}$ must come from a potential

$$V(\vec{R}_{ee}) = -f\,\hat{z}\cdot\vec{R}_{ee}$$

$$\Rightarrow \qquad f\hat{z} = -\vec{\nabla}_{\vec{R}_{ee}} V(\vec{R}_{ee})$$

We must then consider this potential in the probability distribution of $\vec{R}_{ee}$:

Boltzmann like

$$P_{FJC}(\vec{R}_{ee}\,;f) = \frac{1}{Z}\, e^{-\frac{3}{2b^2N}\vec{R}_{ee}^{\,2} + \boxed{f\,\hat{z}\cdot\vec{R}_{ee}/k_BT}}$$

and of course

$$Z = \int d\vec{R}_{ee}\; e^{-\frac{3}{2b^2N}\vec{R}_{ee}^{\,2} + f\,\hat{z}\cdot\vec{R}_{ee}/k_BT}$$

We must then take $\langle \vec{R}_{ee}\cdot\hat{z}\rangle$, which is

$$\langle \hat{z}\cdot\vec{R}_{ee}\rangle = \frac{1}{Z}\int d\vec{R}_{ee}\,(\hat{z}\cdot\vec{R}_{ee})\, e^{-\frac{3}{2b^2N}\vec{R}_{ee}^{\,2} + f\,\hat{z}\cdot\vec{R}_{ee}/k_BT} =$$

$$= \frac{1}{Z}\left[k_BT\frac{\partial}{\partial f} Z\right] = k_BT\frac{\partial}{\partial f}\ln Z = -\frac{\partial}{\partial f}\left(-k_BT\ln Z\right) =$$

$$= -\frac{\partial \overset{\text{Gibbs}}{G}}{\partial f}\Big|_T$$

This is very similar to the pressure/volume relation

Indeed, at constant volume we have

$$p = -\frac{\partial \boxed{F}}{\partial V}\Big|_T \longrightarrow \text{Helmholtz free energy}$$

while at constant pressure we have

$$V = -\frac{\partial \boxed{G}}{\partial p}\Big|_T \longrightarrow \text{Gibbs}$$

In our case the force (= pressure · area) is constant and we identify the free-energy as the Gibbs free-energy

We must still perform the calculation:

$$Z = \int d\vec{R}_{ee}\, e^{-\frac{3}{2b^2N}\vec{R}_{ee}^{\,2} + f\,\hat{z}\cdot\vec{R}_{ee}/k_BT} =$$

$$= \underbrace{\int dR_{ee_x}\, dR_{ee_y}\, e^{-\frac{3}{2b^2N}\left(R_{ee_x}^2 + R_{ee_y}^2\right)}} \int dR_{ee_z}\, e^{-\frac{3}{2b^2N}R_{ee_z}^2 + \frac{fR_{ee_z}}{k_BT}} =$$

$$= \overbrace{\left(\frac{3}{2\pi b^2N}\right)} \cdot \left(\frac{3}{2\pi b^2N}\right)^{1/2} e^{\frac{1}{2}\frac{b^2N}{3(k_BT)^2}f^2}$$

$$\Rightarrow \quad G = -k_BT \ln Z = \underbrace{\text{Const}}_{\text{w.r.t. } f} - \frac{1}{2}\frac{b^2N}{3k_BT}f^2$$

and eventually

$$\langle R_{ee,z} \rangle = -\frac{\partial G}{\partial f} = \frac{b^2 N}{3 k_B T} f$$

which is the same result as above.

Several observations are in order:

1) There is a linear relation between elongation and force: this is reminiscent of a spring!

$$E(x) = \frac{1}{2} k x^2 \qquad \underbrace{f = +kx}_{\text{mechanical equilibrium}} \Rightarrow x = \frac{1}{k} f$$

the spring constant is thus here

$$k = \frac{3 k_B T}{b^2 N}$$

This is interesting: it increases with temperature !!!

If we try and slightly bend a metal rod, within the elastic approximation (small deformation), it gets easier to bend it as it gets hotter.

The reason is simple: bending distorts the atoms away from their energetically favorable position. Higher temperatures favor fluctuations away from the optimal positions, and thus help the bending. For a metal we thus expect k to decrease in T.

But the FJC has no energy whatsoever!

The resistance to be stretched is purely entropic: the more it is stretched, the fewer conformations it can take, which runs against thermodynamics:

$$\underset{\substack{\uparrow \\ \text{free energy}}}{F} = \underset{\substack{\uparrow \\ \text{internal energy}}}{U} - TS \leftarrow \text{entropy}$$

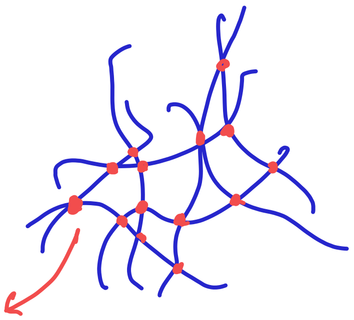
FJC: $U = 0 \Rightarrow F = -TS \Rightarrow$ larger T favor larger S

$\Downarrow$

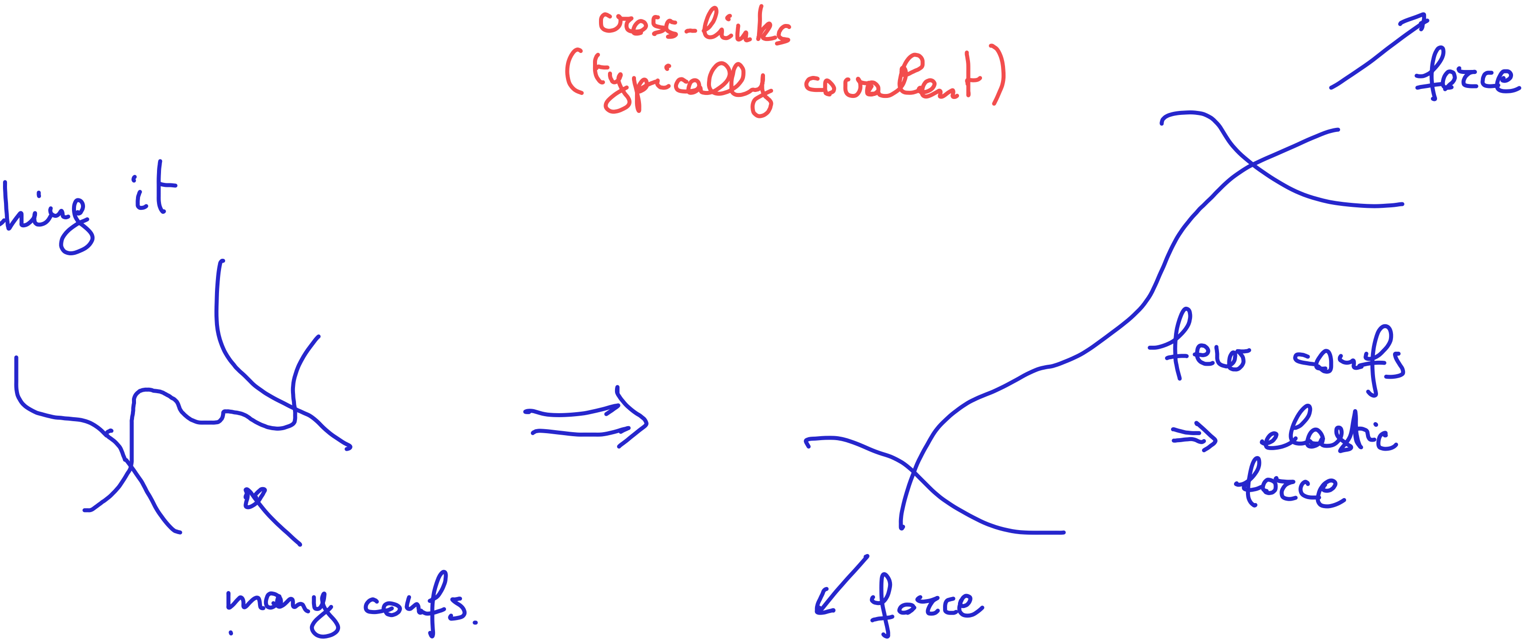
more resistence to stretching.

This result instructs us about the elasticity of rubber:

Rubber is a mesh of cross-linked polymers

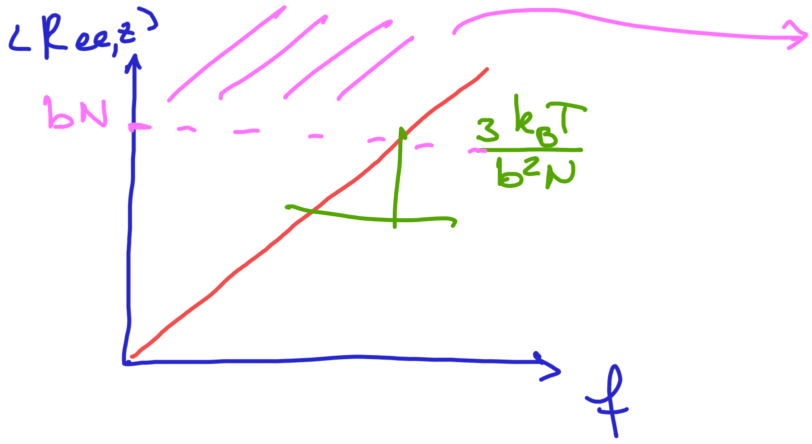


Stretching it



This implies that, in principle, rubber should become stiffer with higher T: indeed this happens (see videos on YouTube). Of course at too-high temperatures even the cross-links fall apart and rubber melts.

2) The solution that we have found has a problem

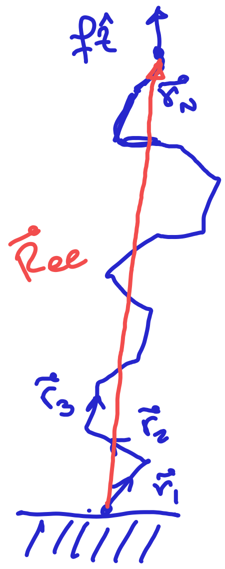


this region should be forbidden!!! Instead our formula remains valid there too.

This follows from the use of the Gaussian P_{FJC}, which is the Central Limit Theorem consequence, which we know badly approximates the tails. The tails are what is physically explored by pulling.

We need thus a better model, where the FJC is explicit.

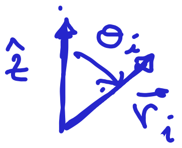
Exact Solution



The energy function is the same we wrote before:

$$E(\vec{R}_{ee}) = -f\,\hat{z}\cdot\vec{R}_{ee} =$$

$$= -f\,\hat{z}\sum_i \vec{r}_i = -fb\sum_i \cos\theta_i$$



$$\langle R_{ee,z}\rangle = \frac{\int d\vec{r}_1\dots d\vec{r}_N \overbrace{\left[b\sum_i \cos\theta_i\right]}^{R_{ee,z}=\vec{R}_{ee}\cdot\hat{z}} p(\vec{r}_1)p(\vec{r}_2)\dots p(\vec{r}_N)\, e^{\frac{fb}{k_BT}\sum_i\cos\theta_i}}{\underbrace{\int d\vec{r}_1\dots d\vec{r}_N\; p(\vec{r}_1)p(\vec{r}_2)\dots p(\vec{r}_N)\, e^{fb/k_BT\sum_i\cos\theta_i}}_{Z}} =$$

$$= \frac{1}{Z}\, k_BT\, \frac{\partial}{\partial f} Z = -\frac{\partial}{\partial f}\left(-k_BT\ln Z\right) = -\frac{\partial G}{\partial f}\Big|_T \qquad \text{as before}$$

We must thus only compute Z

$$Z = \int d\vec{r}_1\dots d\vec{r}_N\; p(\vec{r}_1)\dots p(\vec{r}_N)\prod_i e^{\frac{fb}{k_BT}\cos\theta_i} =$$

$$= \left[\int d\vec{r}\; p(\vec{r})\, e^{\frac{fb}{k_BT}\cos\theta}\right]^N = \left[\int_0^{2\pi} d\phi \int_0^{\pi} d\theta\, \sin\theta\, \overset{\overset{p(\vec{r})}{\downarrow}}{\left(\frac{1}{4\pi}\right)} e^{\frac{fb}{k_B}\cos\theta}\right]^N$$

$$= \left[\frac{1}{4\pi}\, 2\pi \int_0^{\pi} d\theta\, \sin\theta\; e^{\frac{fb}{k_0T}\cos\theta}\right] =$$

$$= \left[\frac{1}{2}\int_0^{\pi} d\theta\, \frac{k_BT}{fb}\, \frac{\partial}{\partial\theta}\left[-e^{fb/k_BT\,\cos\theta}\right]\right]^N =$$

$$= \left[\frac{k_BT}{fb}\right]^N \left[\sinh\left(\frac{fb}{k_BT}\right)\right]^N$$

$$\Rightarrow \qquad G = -k_BT\ln Z = -k_BT N\left\{\ln\left(\frac{k_BT}{fb}\right) + \ln\sinh\left(\frac{fb}{k_BT}\right)\right\}$$

and

$$\langle R_{ee,z}\rangle = -\frac{\partial G}{\partial f} = k_BT N\left\{-\frac{1}{f} + \frac{b}{k_BT}\coth\left(\frac{fb}{k_BT}\right)\right\} =$$

$$= \overset{\text{total length } L}{\boxed{b\,N}} \left\{ \coth\left(\frac{fb}{k_BT}\right) - \frac{k_BT}{fb} \right\} = bN\,\mathcal{L}\left(\frac{fb}{k_BT}\right)$$

where $\mathcal{L}(x) = \coth(x) - \frac{1}{x}$ is the Langevin function.

We can explore the behavior of $\mathcal{L}(x)$ in two limits

1) Weak force : $f \ll \frac{k_BT}{b} \quad \Rightarrow \quad x \ll 1$

$$\mathcal{L}(x) \simeq \frac{1 + \frac{1}{2}x^2}{x} - \frac{1}{x} = \frac{1}{x} + \frac{x}{2} - \frac{1}{x} = \frac{x}{2}$$

$\coth x = \frac{\cosh x}{\sinh x}$

$$\Rightarrow \quad \langle R_{ee,z} \rangle \underset{fb \ll k_BT}{\simeq} \frac{b^2 N}{2\,k_BT} f$$

compare with the result in the Gaussian approx:

$$\langle R_{ee,z} \rangle \simeq \frac{b^2 N}{3\,k_BT} f$$

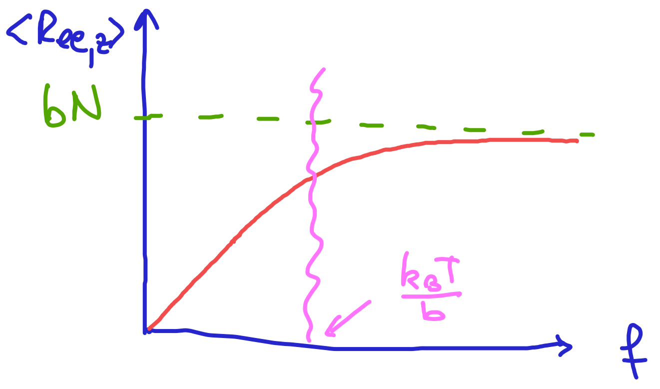
Apart from the numerical factor, the relation is expectedly linear

2) Strong force : $f \gg \frac{k_BT}{b} \quad \Rightarrow \quad x \gg 1$

$$\mathcal{L}(x) = \coth(x) - \frac{1}{x} \simeq \frac{\cosh(x)}{\sinh(x)} - \frac{1}{x} = \frac{1 + e^{-2x}}{1 - e^{-2x}} - \frac{1}{x} \simeq$$

$$\simeq 1 - \frac{1}{x}$$

$$\Rightarrow \quad \langle R_{ee,z} \rangle \simeq bN\left(1 - \frac{k_BT}{bf}\right)$$



Here we find that the relation is linear, expectedly, for small forces, and saturates at bN for strong forces

This is an instructive relation because the argument of the Langevin function is $\frac{fb}{k_BT}$, which is a natural variable for the system:

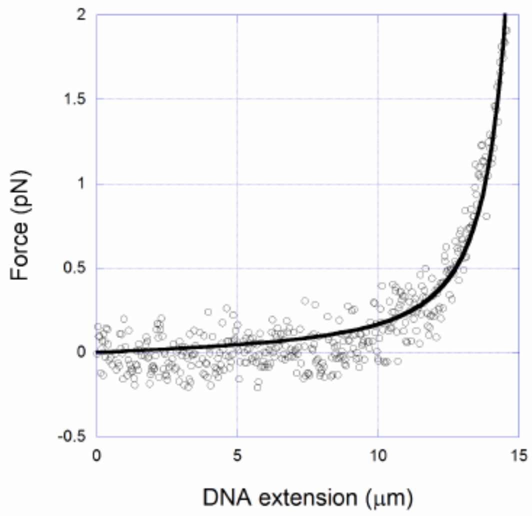
fb is proportional (same order of) to the work done by the force to align one elementary vector in its direction, while

k_BT is the thermal energy associated to one degree of freedom

That ratio, $\frac{fb}{k_BT}$, tells when the force is strong, on the scale of b, compared to thermal agitation.

It is clearly the right scale.

How do these results compare to real experiments?



DNA from λ-phage
(a virus)

The fitting function is similar to ours, although it is obtained, with some more painful calculations, using the Worm-Like-Chain, which is more appropriate for DNA.

The take home message is that for the analysis of forces applied to biopolymers, self-avoidance is not required. This is intuitive, because as the polymer is elongated, it has few chances of folding back on itself and have intersections.

Hence, FJC and/or KP are enough.