Gaussian chain

- Consider a macromolecular chain comprised of “$N$” segments of length “$b$” (the Kuhn length)
- Collection of rigid connected segments is approximated as a random walk with a Gaussian probability distribution
- Valid for $N \gg 1$; $R \ll (Nb)$
- Force-extension curve:
  - not valid in the limit $F \rightarrow \infty$

\[ F = \frac{3k_B T}{Nb^2} R = \frac{3k_B T}{2l_p} \frac{R}{L_c} \]
Freely-jointed chain

- Similar to Gaussian chain, but does not assume a Gaussian probability distribution
- Self avoiding and imposes maximum length

\[
F_{FJC} = \frac{k_B T}{b} \left[ \frac{3R}{L_c} + \frac{9}{5} \left( \frac{R}{L_c} \right)^3 + \frac{297}{115} \left( \frac{R}{L_c} \right)^5 \right]
\]

- Note that this agrees with the Gaussian chain for small forces \((R/L_c \ll 1)\).
Worm-like chain

- Polymer is treated as a flexible rope rather than a collection of freely-jointed rigid rods
- Bending stiffness accounted for directly
- Enthalpic contributions important
- Use Fourier transform methods and equipartition of energy

\[ F_{WLC} = \frac{kT}{l_p} \left[ \frac{1}{4} \left( 1 - \frac{R}{L_c} \right)^{-2} - \frac{1}{4} + \frac{R}{L_c} \right] \]
# Summary of models

<table>
<thead>
<tr>
<th>Model</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gaussian chain</td>
<td>$F_{GC} = \frac{3kT}{Nb^2}$, $R = \frac{3kT}{2l_p} \frac{R}{L_c}$</td>
</tr>
<tr>
<td>Freely-jointed chain</td>
<td>$F_{FJC} = \frac{k_BT}{2l_p} \left[ \frac{3R}{L_c} + \frac{9}{5} \left( \frac{R}{L_c} \right)^3 + \frac{297}{115} \left( \frac{R}{L_c} \right)^5 \right]$</td>
</tr>
<tr>
<td>Worm-like chain (approx.)</td>
<td>$F_{WLC} = \frac{kT}{l_p} \left[ \frac{1}{4} \left( 1 - \frac{R}{L_c} \right)^{-2} - \frac{1}{4} + \frac{R}{L_c} \right]$</td>
</tr>
</tbody>
</table>
How much force is required to stretch a typical strand of DNA by 10% of its contour length?

\[ k_B T = 4 \text{ pN} \cdot \text{nm} \]

\[ l_p = 50 \text{ nm} \]

\[ R/L_c = 0.01 \]

\[ L_c = 15 \mu\text{m} \]

\[ F = \frac{3k_B T}{Nb^2} R = \frac{3k_B T}{2l_p} \frac{R}{L_c} \]

\[ F = ?? \]
DNA extension -- comparison of Gaussian chain (Hooke’s law) FJC and WLC.

Bustamante et al. 2001

DNA extension -- comparison of Gaussian chain (Hooke’s law) FJC and WLC.

Diagram of DNA extension with force and extension axes.


© source unknown. All rights reserved. This content is excluded from our Creative Commons license. For more information, see [http://ocw.mit.edu/help/faq-fair-use/].
But this neglects the effects of internal bonds (H-bonds, ionic or hydrophobic interactions)

Figure 8.23: Force-displacement curve for a variety of different molecules illustrating the sense in which single molecule experiments serve as the basis of force spectroscopy.

Each “jump” represents a transition to a different energetic state. How do we account for this?
Unfolding PrP (prion protein)

Causes transmissible spongiform encephalopathies (prion diseases)

Yu et al., PNAS, 2012
Measured energy landscape for PrP at $F = 9.1$ pN
Reversible Unfolding of Single RNA Molecules by Mechanical Force

Jan Liphardt, Bibiana Ono, Steven B. Smith, Ignacio Tinoco Jr., Carlos Bustamante

SCIENCE VOL 292 27 APRIL 2001

A

P5ab

P5abcΔA

P5abc

Streptavidin bead

B

Antidigoxigenin bead

RNA/DNA handle A

RNA/DNA handle B

20 nm 1 s

220 230 240

Ft

10 12 14 16 18

Extension (nm)

100 150 200 250

15.2 pN

14.6 pN

14.2 pN

14.1 pN

14.0 pN

13.6 pN
Concept of an energy landscape

Linear springs produce a quadratic energy landscape model

Consider the landscape as a surface with local minima

Consider a protein with two local minima in its energy landscape (2 states)

Externally applied forces shift the equilibrium position, and can cause a jump from one “state” to another