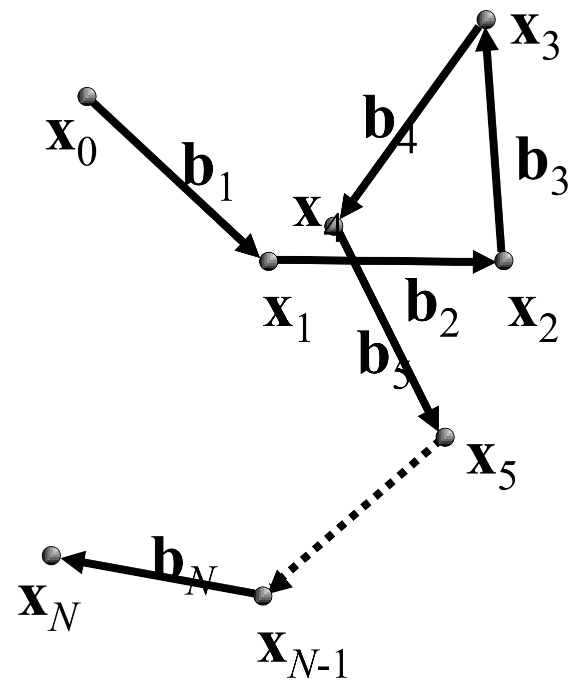
Gaussian chain

- 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 $F \rightarrow$ infinity



$$F = \frac{3k_BT}{Nb^2}R = \frac{3k_BT}{2l_p}\frac{R}{L_c}$$

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 ($R/L_c << 1$).

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

Gaussian chain	$$F_{GC} = \frac{3kT}{Nb^2} R = \frac{3kT}{2l_p} \frac{R}{L_c}$$
Freely-jointed chain (approx.)	$$F_{FJC} = \frac{k_B T}{2l_p} \left[\frac{3R}{L_c} + \frac{9}{5} \left(\frac{R}{L_c} \right)^3 + \frac{297}{115} \left(\frac{R}{L_c} \right)^5 \right]$$
Worm-like chain (approx.)	$$F_{WLC} = \frac{kT}{l_p} \left[\frac{1}{4} \left(1 - \frac{R}{L_c} \right)^{-2} - \frac{1}{4} + \frac{R}{L_c} \right]$$

How much force is required to stretch a typical strand of DNA by 10% of its contour length?

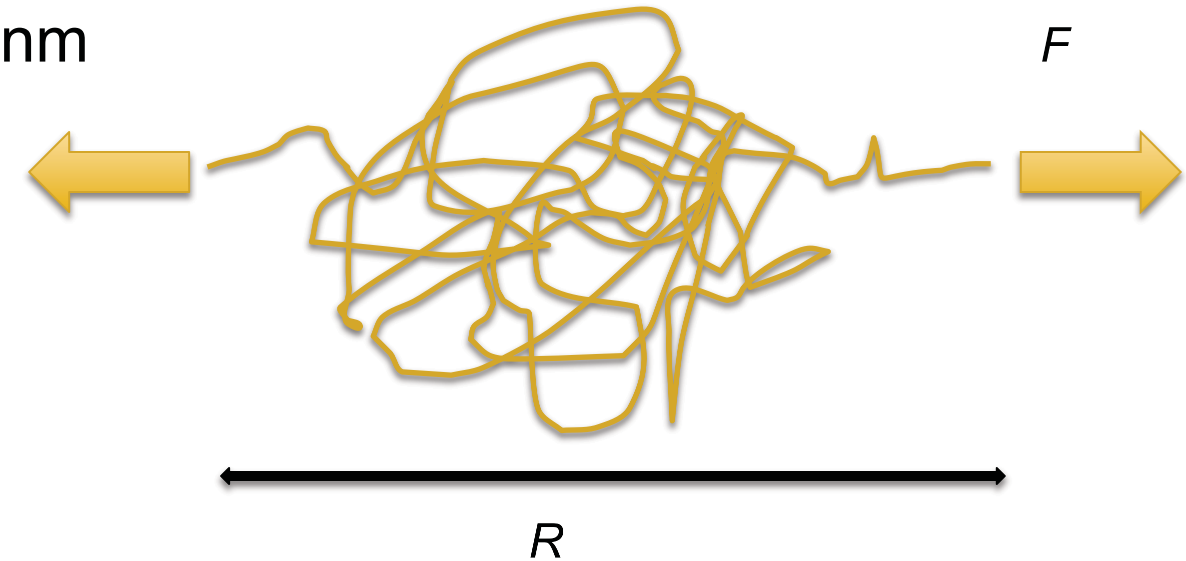
k_BT = 4 pN·nm

l_p = 50 nm

R/L_c = 0.01

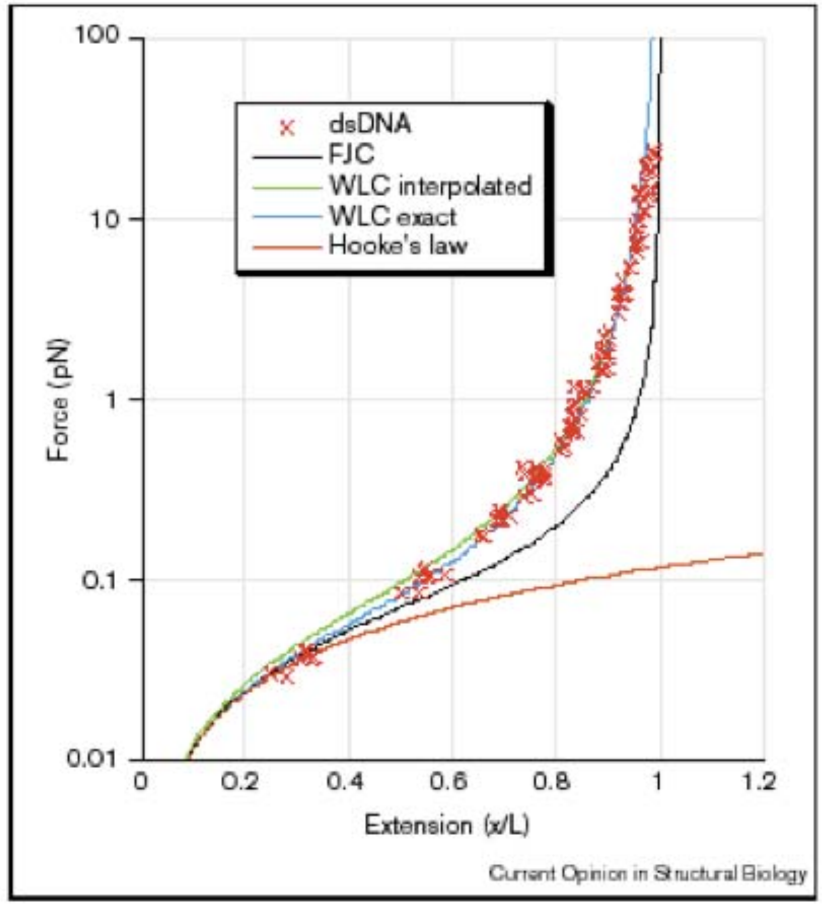
L_c = 15 µm

F = ??



$$F = \frac{3k_BT}{Nb^2}R = \frac{3k_BT}{2l_p}\frac{R}{L_c}$$

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

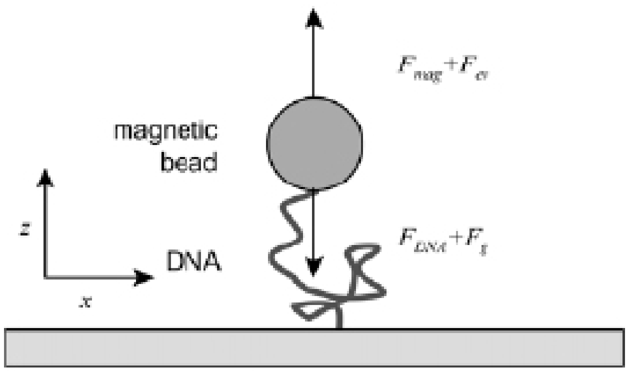


Force versus extension data (red crosses) for λ phage dsDNA (48,502 bp) pulled by magnetic beads in 10 mM Na+ buffer [4]. The data are fit to a WLC model solved numerically (WLC exact) or using Equation 3 (WLC interpolated), both assuming P = 53 nm. The FJC curve assumes b = 2P = 106 nm. The Hooke's law force curve is from Equation 2.

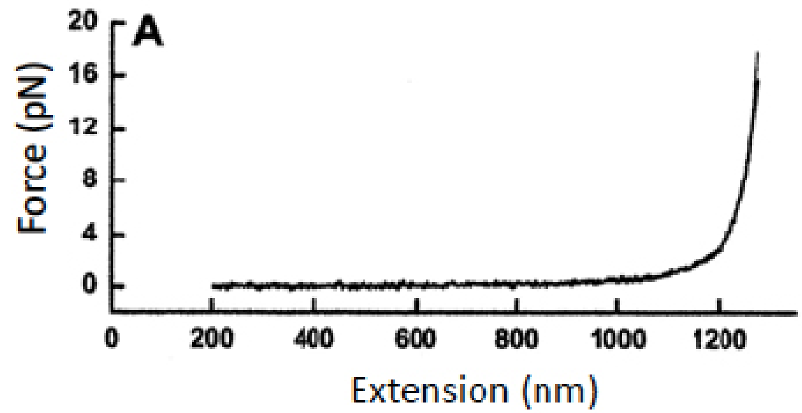
Bustamante et al. 2001

Source: Bustamante, Carlos, Steven B. Smith, et al. "Single-molecule Studies of DNA Mechanics." *Current Opinion in Structural Biology* 10, no. 3 (2000): 279-85.

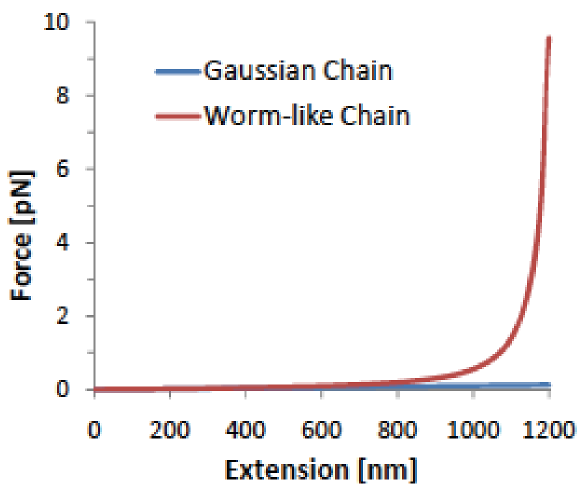
DNA extension -- comparison of Gaussian chain (Hooke's law) FJC and WLC.

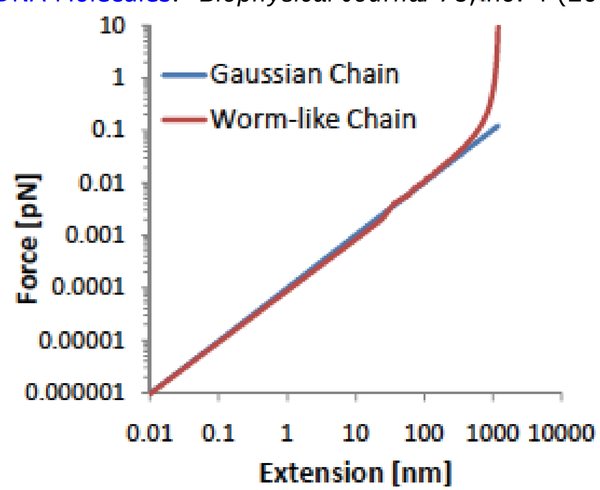


Baumann et al. *Biophys J* 2000



Source: Baumann, Christoph G., et al. "Stretching of Single Collapsed DNA Molecules." *Biophysical Journal* 78, no. 4 (2000): 1965-78.





But this neglects the effects of internal bonds (H-bonds, ionic or hydrophobic interactions)

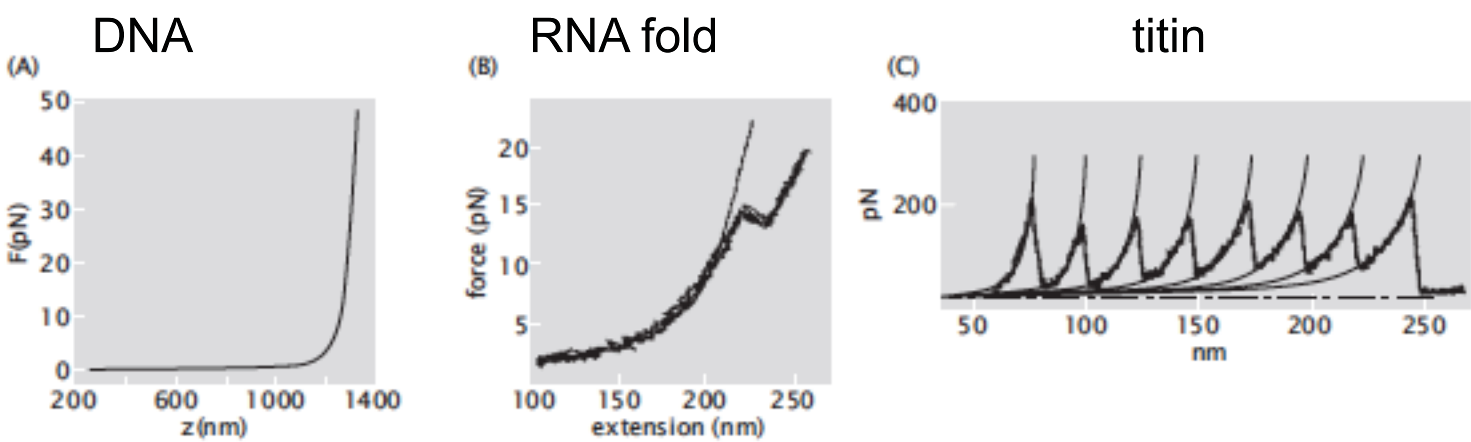
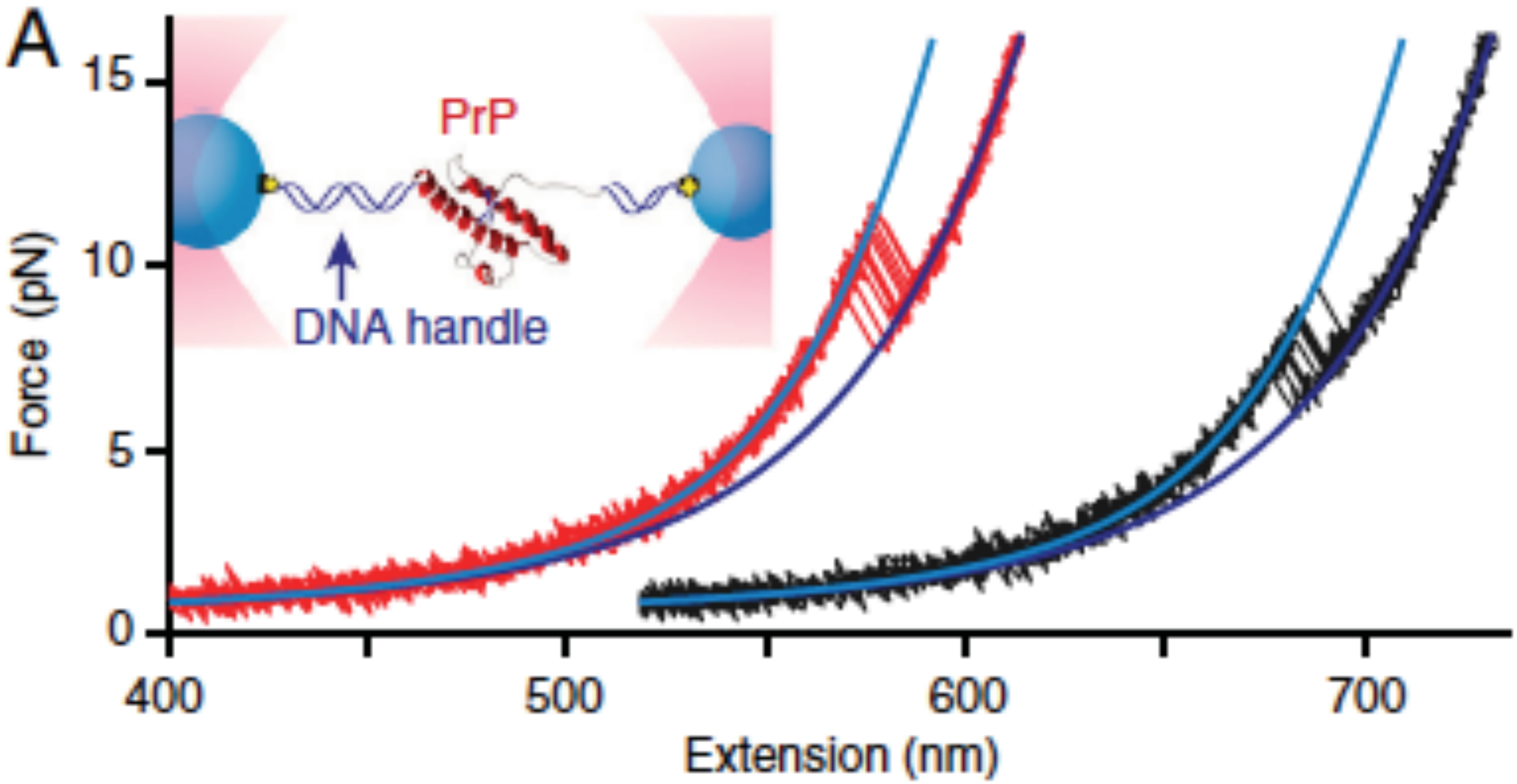


Figure 8.23: Force-displacement curve for a variety of different molecules illustrating the sense in which single molecule experiments serve as the basis of force spectroscopy.

Each “jump” represents a transition to a different energetic state. How do we account for this?

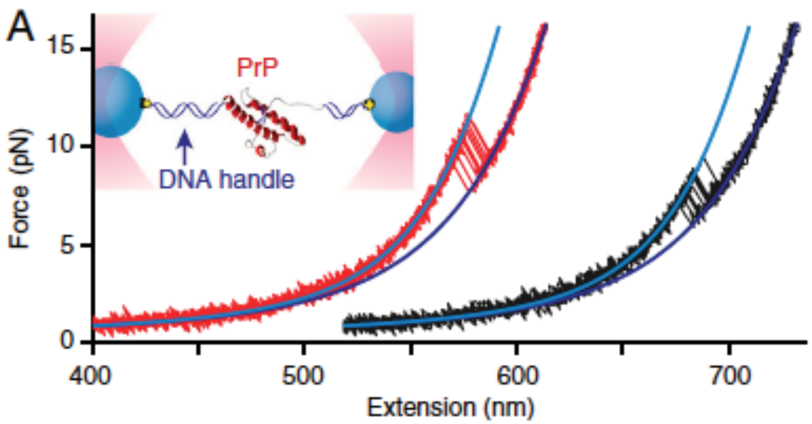
Unfolding PrP (prion protein)

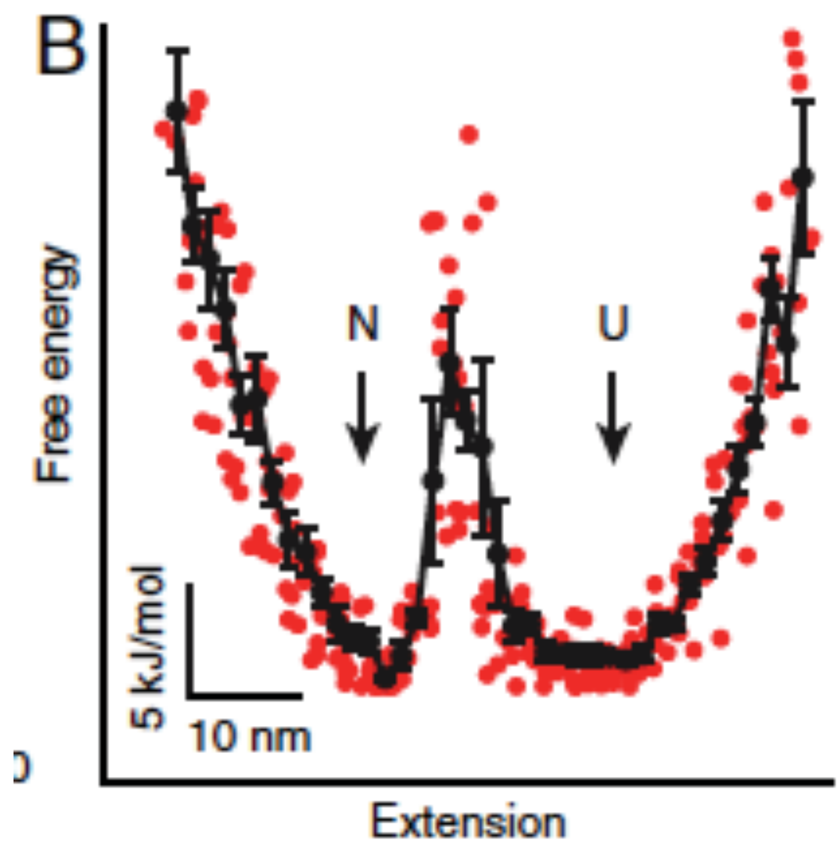
Causes transmissible spongiform encephalopathies (prion diseases)



Yu et al., PNAS, 2012

Measured energy landscape for PrP at F = 9.1 pN

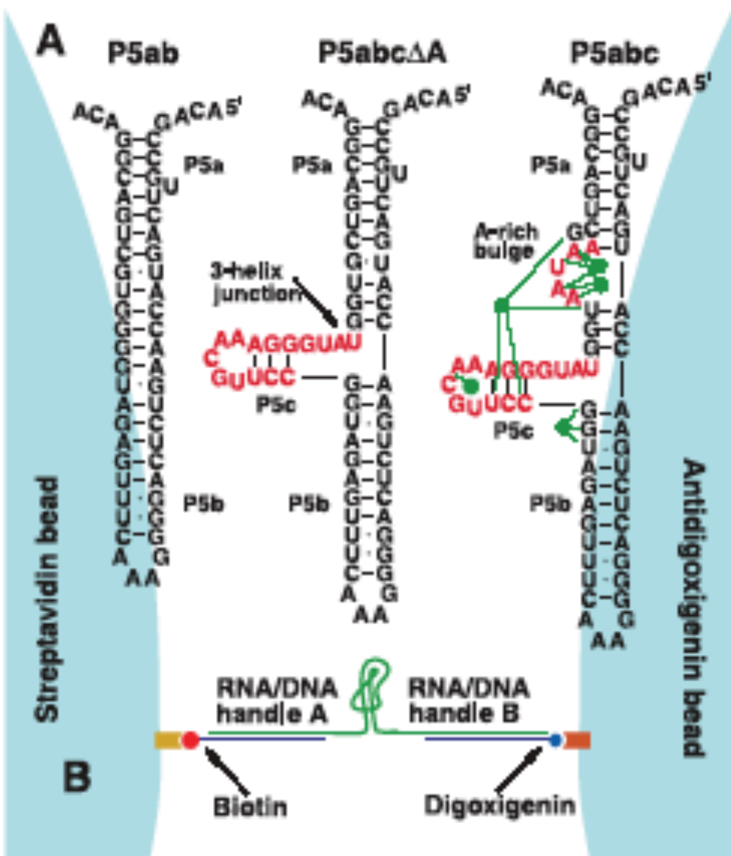


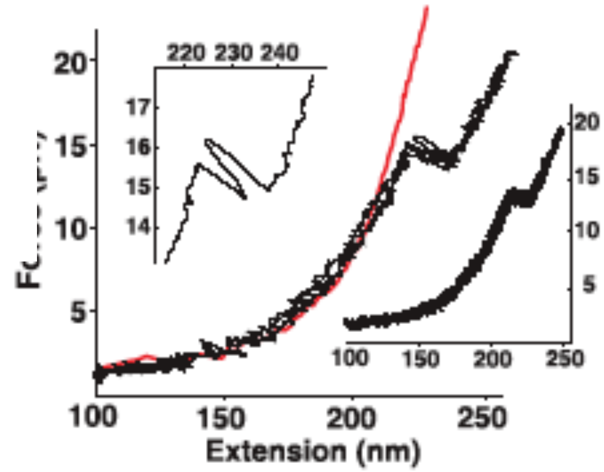


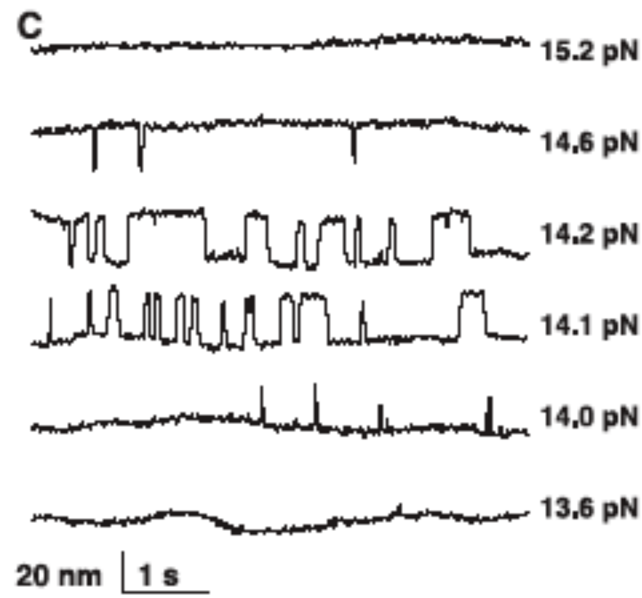
Reversible Unfolding of Single RNA Molecules by Mechanical Force

Jan Liphardt,[1] Bibiana Onoa,[1] Steven B. Smith,[2] Ignacio Tinoco Jr.,[1] Carlos Bustamante[1,2*]

SCIENCE VOL 292 27 APRIL 2001







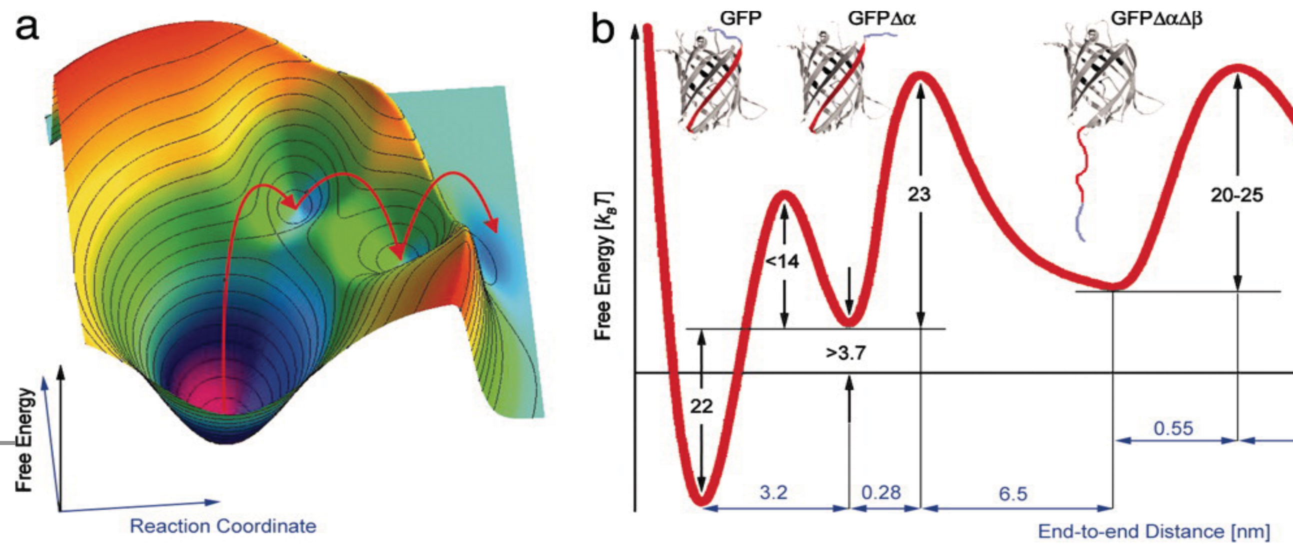
Concept of an energy landscape

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



20.310J / 3.053J / 6.024J / 2.797J Molecular, Cellular, and Tissue Biomechanics
Spring 2015