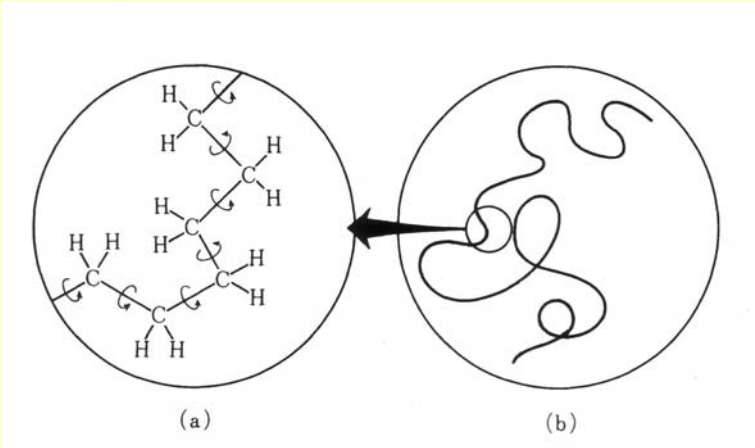
FÍSICA DE POLÍMEROS:

Un polímero es una molécula hecha de unidades repetidas unidas con enlaces covalentes en forma de cadena larga.

Artificiales: plásticos, poliestireno, poliacetileno, etc.
Biológicos: Proteínas, acidos nucleícos (RNA, DNA)

A pesar de la diferencias microscópicas presentan una gran cantidad de propiedades ***universales.***



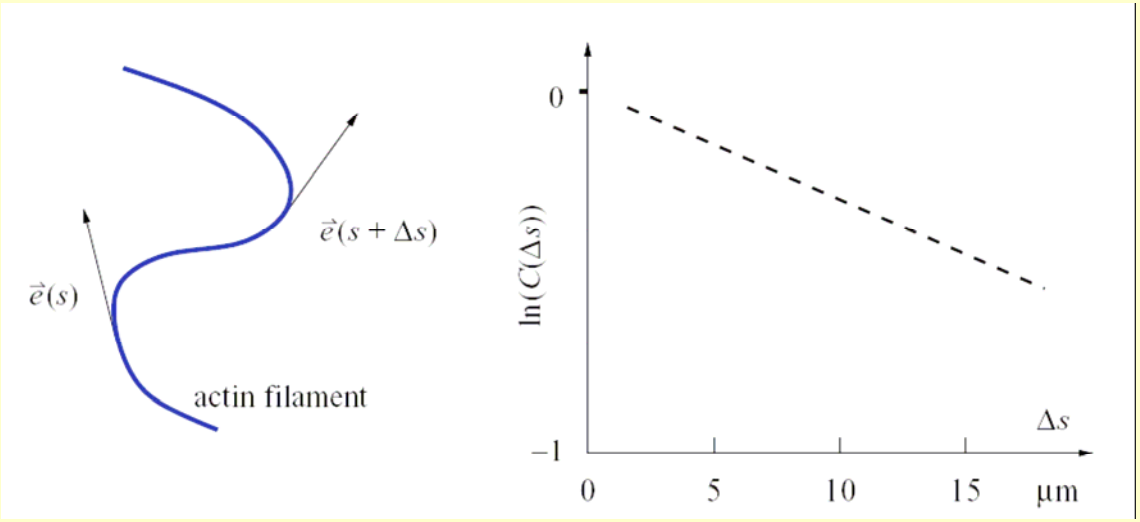
Clasificación:

Composición: Homopolímeros,

Copolímeros (“random”, “block”, “sequenced”)

Estado: líquido, cristalino, vidrio, cristal líquido.

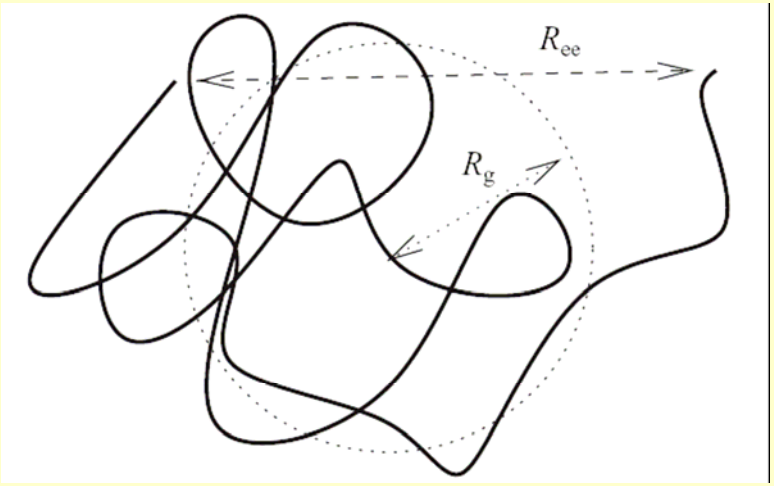
Longitud de persistencia (l_p, ξ) :



$$correlation\ function\ C(x, y) = \langle e(x) \cdot e(y) \rangle.$$

$$C(|x-y|) = \langle e(x) \cdot e(y) \rangle \propto \exp(-|x-y|/l_{\mathrm{p}})$$

Distancias Relevantes:



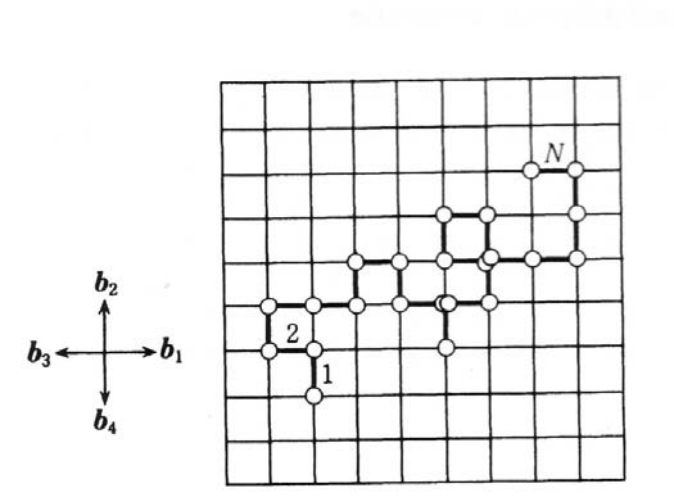
$$\mathbf{R} = \int_0^L \vec{e}(s)\mathrm{d}s$$

$$\begin{aligned}
\langle R^2 \rangle &= \left\langle \int_0^L \vec{e}(t)\mathrm{d}t \cdot \int_0^L \vec{e}(s)\mathrm{d}s \right\rangle \\
&= \int_0^L \int_0^L \langle \vec{e}(t) \cdot \vec{e}(s) \rangle \mathrm{d}t\mathrm{d}s = \int_0^L \int_0^{L-s} \exp(-t/l_\mathrm{p})\mathrm{d}t\mathrm{d}s \\
&= 2l_\mathrm{p}\left(\frac{L}{l_\mathrm{p}} - 1 + \exp(-\frac{L}{l_\mathrm{p}})\right) \approx 2Ll_\mathrm{p} \quad \text{for} \quad L \gg l_\mathrm{p}
\end{aligned}$$

Modelos de Polímeros:

Polímeros ideales: representamos los monómeros con segmentos de longitud *b (longitud de Kuhn l_K)*. Si no interaccionan entre sí, tenemos un "random walk" en una red (bi) o (tri)-dimensional.

La cadena cumple la ecuación de difusión. Sea *P(N,R)* la probabilidad de que la cadena de *N* monómeros tenga tamaño *R* (distancia de extremo a extremo).



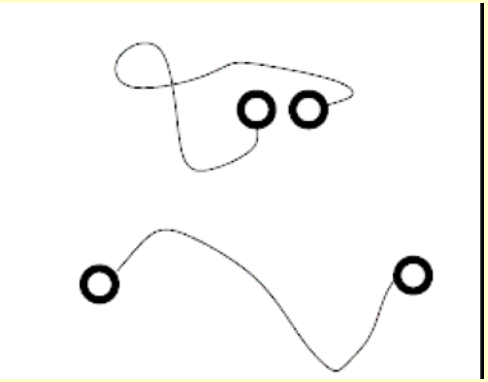
en 3 dimensiones:

$$\frac{\partial}{\partial N} P(N,R) = \frac{b^2}{6} \frac{\partial^2}{\partial R^2} P(N,R)$$

cuya solución es (N=0, R=0):

$$P(N,R) = \left(\frac{3}{2\pi N b^2} \right)^{3/2} \exp\left(-\frac{3R^2}{2Nb^2} \right)$$

“Random walk” en 1d:



$$\mathcal{N}_1 = \frac{N!}{N_+!N_-!}$$

$$N = N_+ + N_-$$

$$x = N_+ - N_-$$

$$\mathcal{N}_1 = \frac{N!}{((N-x)/2)!((N+x)/2)!}$$

$$\mathcal{N}_1 = \frac{2^N}{(1-x/N)^{(N-x)/2}(1+x/N)^{(N+x)/2}}$$

$$n! = (n/\mathrm{e})^n$$

$$\ln(\mathcal{N}_1) = N\left(\ln(2) - \frac{1}{2}(1-x/N)\ln(1-x/N) - \frac{1}{2}(1+x/N)\ln(1+x/N)\right)$$

$$\ln(1+x) = x - x^2/2$$

$$\ln(\mathcal{N}_1) = N(\ln(2) - \frac{1}{2}\,(\frac{x}{N})^2)$$

$$\boxed{\mathcal{N}_1 = 2^N \ \exp(-\frac{x^2}{2N})}$$

Esto es una distribución Gaussiana:

$\langle \boldsymbol{R} \rangle = 0$ (ya que las estructuras se distribuyen homogéneamente alrededor de 0.

$\langle \boldsymbol{R}^2 \rangle = \mathrm{N} b^2$. Esta cantidad da una medida del tamaño del polímero, $b = 2l_p$.

$$R \propto \mathrm{N}^{1/2}.$$

Otra cantidad importante es el llamado "radio de giro":

$$R_G^2 \equiv \frac{1}{N} \sum_{i=1}^{N} \left(R_i - R_{CM} \right)^2$$

Si consideramos que hay interacciones de corto alcance (dentro de la cadena) estos resultados apenas se modifican.

$$\langle \boldsymbol{R}^2 \rangle = \mathrm{N} b_{efectiva}^2 \qquad \text{y} \qquad R \propto \mathrm{N}^{1/2}$$

En los polímeros reales dos segmentos pueden interaccionar aunque estén separados por una distancia larga (dentro de la cadena).

Energía libre de una cadena ideal:

En los modelos anteriores no hay ningún término de energía luego la única contribución viene de la entropía:

$$S(R) = k_B \log \Omega(R) \approx k_B \log P(R) = cte - \frac{3k_B}{2Nb^2} R^2$$

La energía libre es por tanto

$$F(R) = U - TS = -TS = \frac{3k_B T}{2Nb^2} R^2 + cte.$$

La fuerza que ejerce el polímero sobre el extremo *f*(R):

$$f(R) = -\frac{\partial}{\partial R} F(R) = -\frac{3k_B T}{2Nb^2} R$$

Es un muelle “entrópico”. (La presión de un gas ideal también es entrópica !!!)

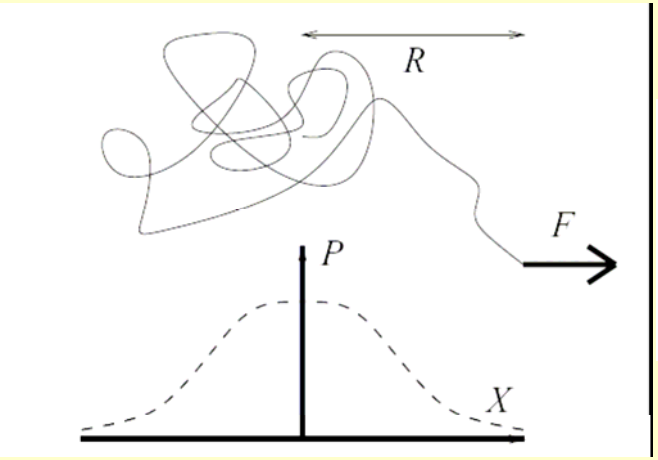


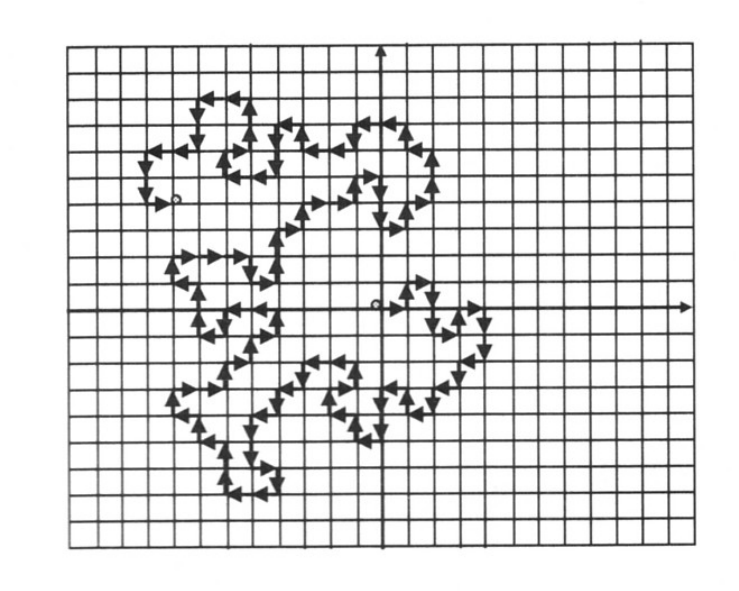
Figure 2.10. Number of confirmations $\mathcal{N}$ of a polymer as function of end-to-end distance X. Note that $\mathcal{N} \propto P(X)$, where P is the probability. When the polymer is stretched to distance X it therefore exerts a force $= -T(\mathrm{d}S/\mathrm{d}X) = T(\mathrm{d}\ln(P)/\mathrm{d}X) \propto -k_\mathrm{B}T \cdot (3X/Nl_\mathrm{k}^2)$ on its surroundings. Thus the polymer acts as a spring with spring constant $k_\mathrm{spring} = 3k_\mathrm{B}T/(Ll_\mathrm{k})$. Typical entropic spring constants are a fraction of a pico Newton per nanometer (pN/nm).

A single polymer molecule makes a very soft spring. Consider, for example, a polystyrene coil with $N \sim 10^3$, $l_\mathrm{k} = 1$ nm; the size of the coil is $\langle R^2 \rangle^{1/2} = l_\mathrm{k}\ N^{1/2} \sim$30 nm and the spring constant is $3k_\mathrm{B}T/(Nl_\mathrm{k}^2) \sim 10^{-2}$ pN/nm, since

$$\frac{k_\mathrm{B}T}{1\ \mathrm{nm}} \approx 4\ \mathrm{pN} \qquad \text{(at room temperature } T = 300\ \mathrm{K}) \tag{2.20}$$

The entropic elasticity of a single coil can be measured directly through micromechanical experiments (Fig. 2.11).

Polímeros reales: Efecto de volumen excluido.
los monómeros no se pueden cruzar. Es lo se denomina un “self-avoiding random walk”. El tamaño del polímero es mayor. Se modifica la ley de escala:

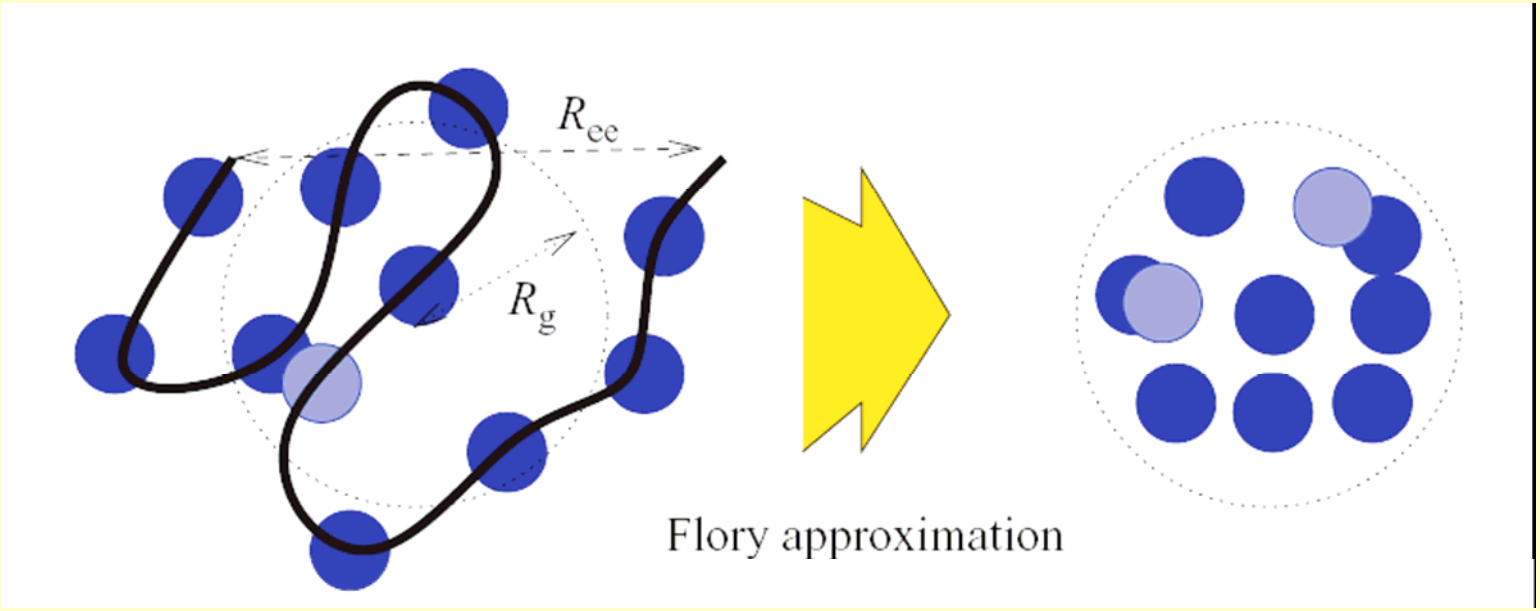


$$\left\langle R^2 \right\rangle^{1/2} \propto N^{\nu} \quad \text{con } \nu \geq 1/2$$

Veamos un argumento sencillo para obtener el exponente (Flory):

¿cómo cambia la entropía de un gas ideal al considerar el volumen de las partículas? (van der Waals)

$$\frac{S_{ideal}}{N} = k_B \log\left(a \frac{V}{N} \right) \quad \Rightarrow \quad \frac{S_{vdW}}{N} = k_B \log\left(a \frac{V - Nv}{N} \right)$$


R_{ee}
R_g
Flory approximation

$$\frac{S_{vdW}}{N} = k_B \log\left(a \frac{V - Nv}{N} \right) = \frac{S_{ideal}}{N} + k_B \log\left(1 - \frac{vN}{V} \right) \approx$$

$$\approx \frac{S_{ideal}}{N} - k_B v \left(\frac{N}{V} \right)$$

El polímero ocupa un volumen R^3, la entropía disminuye y por tanto, la energía libre aumenta (i.e. es equivalente a una interacción repulsiva).

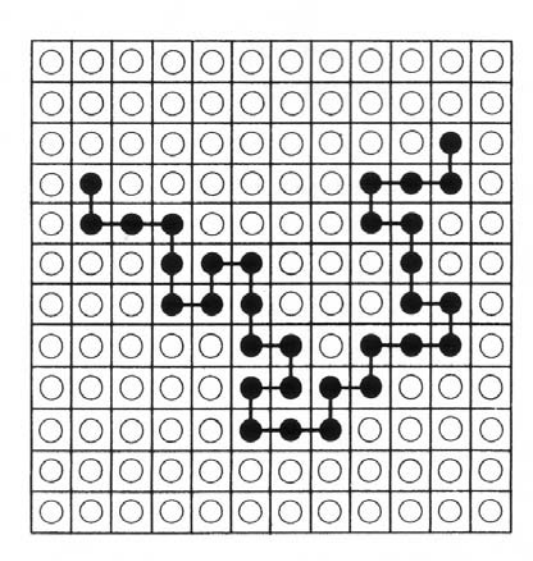
$$F(R) = F_{ideal} + k_B T v \frac{N^2}{R^3} = \frac{3k_B T}{2Nb^2} R^2 + k_B T v \frac{N^2}{R^3}$$

minimizando respecto a R y tomando $v = b^3$.

$$\frac{d}{dR} F(R) = 0 \quad \Rightarrow \quad R^5 \propto b^5 N^3 \Rightarrow R \propto N^{\nu} \text{ con } \nu = \frac{3}{5}$$

Un cálculo más sofisticado (RG) da $\nu = 0.588$ (comparar con 0.6).

Interacción con un solvente: transición globular (“coil-globule”).



Las energías (libres) involucradas:

polymer segment – polymer segment	$-\epsilon_{pp}$
polymer segment – solvent molecule	$-\epsilon_{ps}$
solvent molecule – solvent molecule	$-\epsilon_{ss}$.

La energía de una configuración es por tanto:

$$E_i = -N_{pp}^{(i)}\epsilon_{pp} - N_{ps}^{(i)}\epsilon_{ps} - N_{ss}^{(i)}\epsilon_{ss}.$$

Tomando los valores medios y definiendo $\phi = Nv/R^3$:

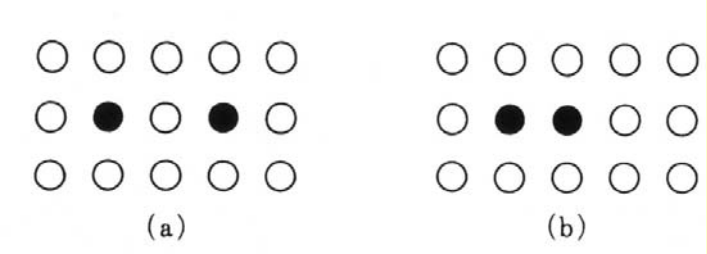
$$\overline{N_{pp}^{(i)}} \simeq \frac{1}{2} zN\phi,$$

$$\overline{N_{ps}^{(i)}} \simeq zN(1-\phi),$$

$$\overline{N_{ss}^{(i)}} \simeq N_{ss}^{0} - [\frac{1}{2} zN\phi + zN(1-\phi)].$$

$$\bar{E}(R) \simeq -\frac{1}{2} z N \phi \left(\epsilon_{\mathrm{pp}} + \epsilon_{\mathrm{ss}} - 2\epsilon_{\mathrm{ps}}\right) + \text{ terms independent of } \phi$$
$$= -\frac{z N^2 v_{\mathrm{c}}}{R^3} \Delta\epsilon + \text{terms independent of } R.$$

donde $$\Delta\varepsilon = \tfrac{1}{2}\left(\varepsilon_{pp} + \varepsilon_{ss}\right) - \varepsilon_{sp}$$



La dependencia con R es igual que la contribución (con signo contrario) de la del volumen excluido. Definimos χ como:

$$\chi = \frac{z\Delta\varepsilon}{k_B T}$$

$$F(R) = \frac{3k_B T}{2Nb^2} R^2 + k_B T v \frac{N^2}{R^3}\left(1 - 2\chi\right)$$

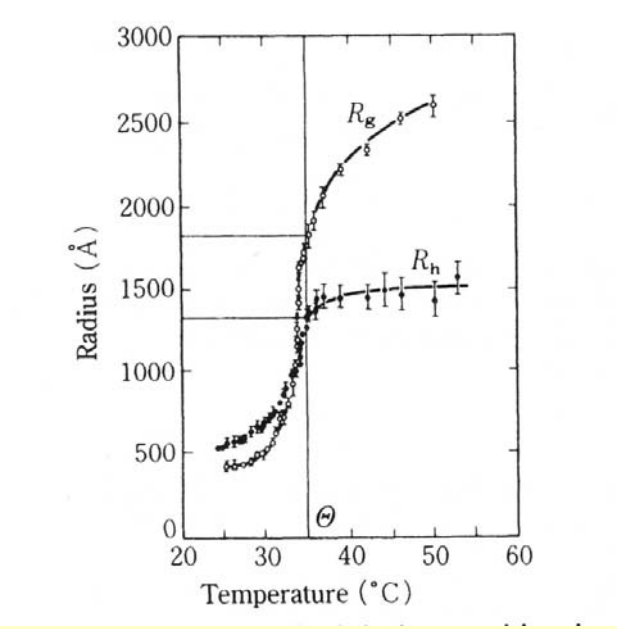
Discusión:

$\Delta\varepsilon$ representa el decrecimiento de energía cuando dos segmentos de polímeros están juntos. Si $\Delta\varepsilon < 0$ se repelen, si $\Delta\varepsilon > 0$ se atraen.

1.- Para $\chi < ½$ tenemos potencial repulsivo y por tanto $R \propto N^{3/5}$. Este se refiere como comportamiento de "buen solvente".

2.- Para $\chi = ½$ (condición Θ). El efecto del solvente compensa el efecto el efecto repulsivo del volumen excluido y $R \propto N^{1/2}$.
Ello ocurre a la temperatura $\Theta = 2z\,\Delta\varepsilon/k_B$.

3.- Para $\chi > ½$ ("mal solvente"). La interacción es atractiva y el polímero colapsa. Es la transición "coil-globule".



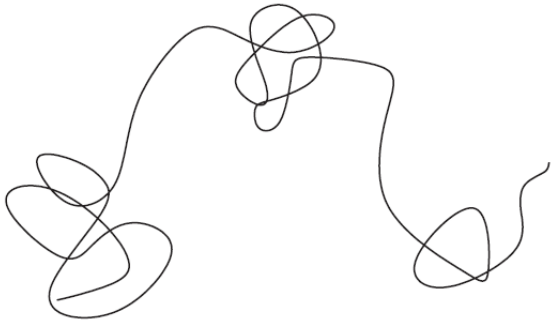
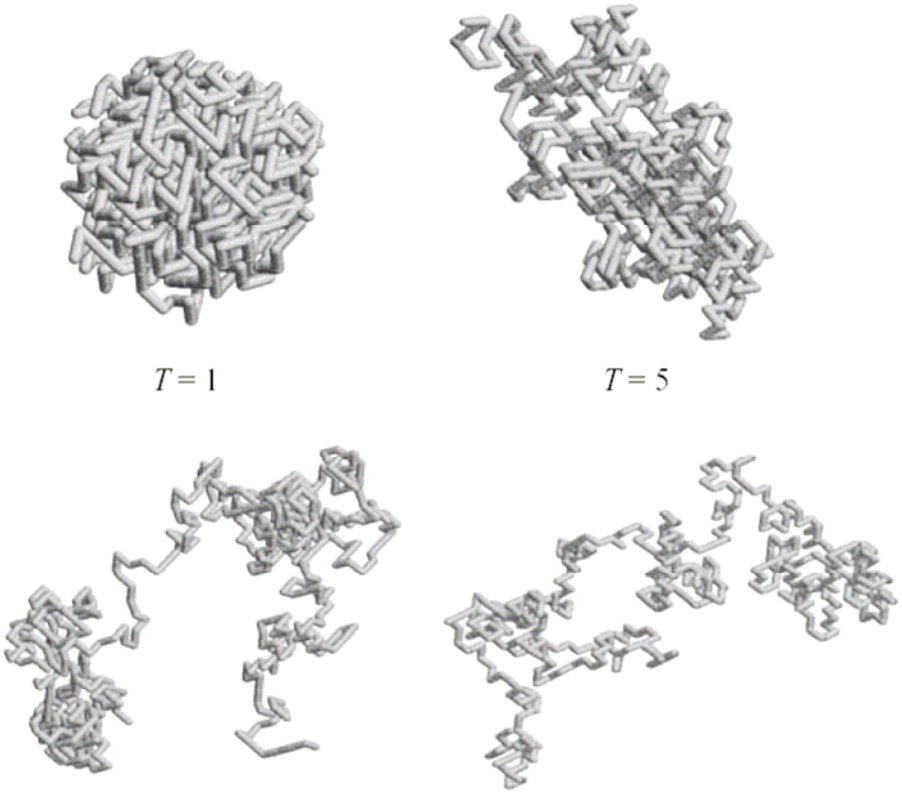
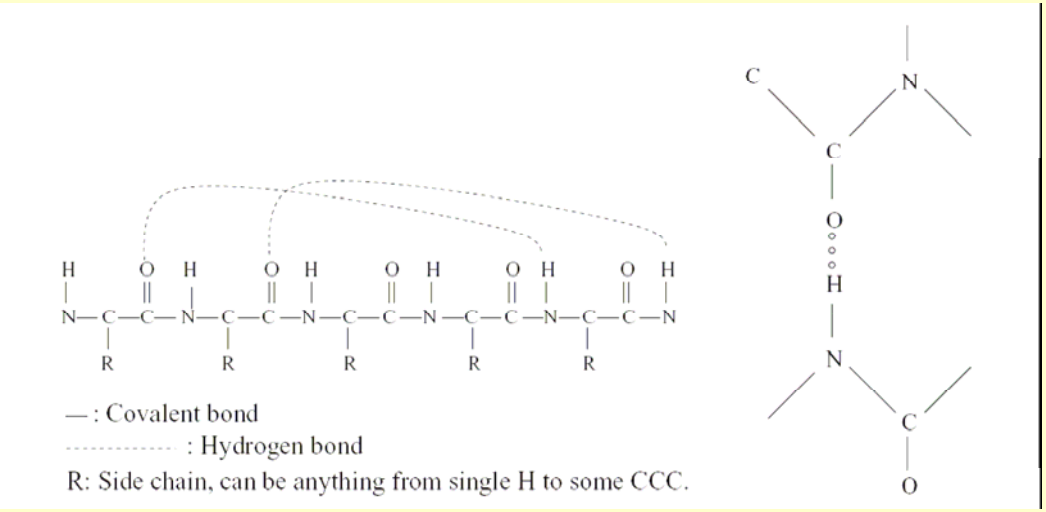
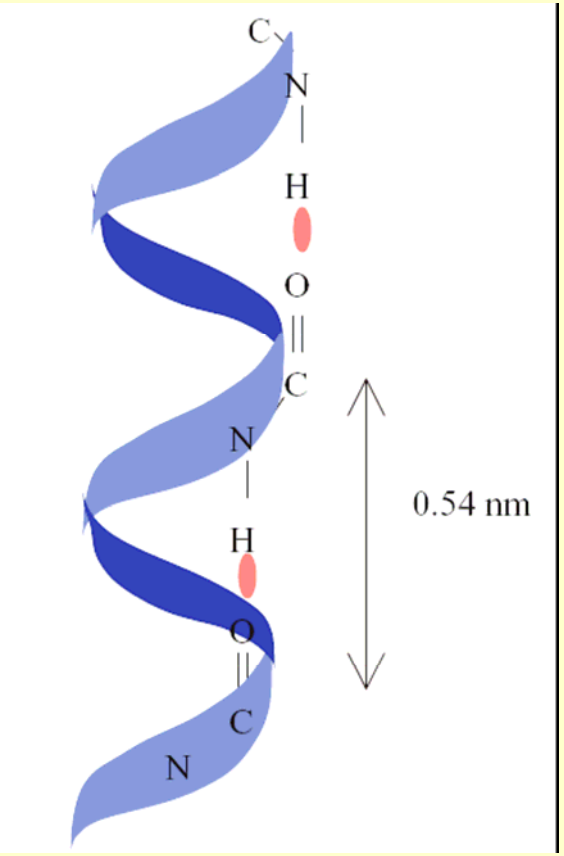


Figure 2.17. Homopolymer close to, but above, the Θ point. Small regions of random coil are separated by longer stretches of polymer that prevents overlap on larger scales.



Transición Hélice-ovillo. (Helix-coil transition).





σs = statistical weight to initiate a helix in the coil region,
s = statistical weight to continue the helix.

$$F_c = 0$$

$$\exp(-F_c/k_B T) = 1$$

$$F_{ch} = F_{hh} - TS_{ch}$$

$$\exp(-F_{ch}/k_B T) = \sigma s$$

$$F_{hh}$$

$$\exp(-F_{hh}/k_B T) = s$$

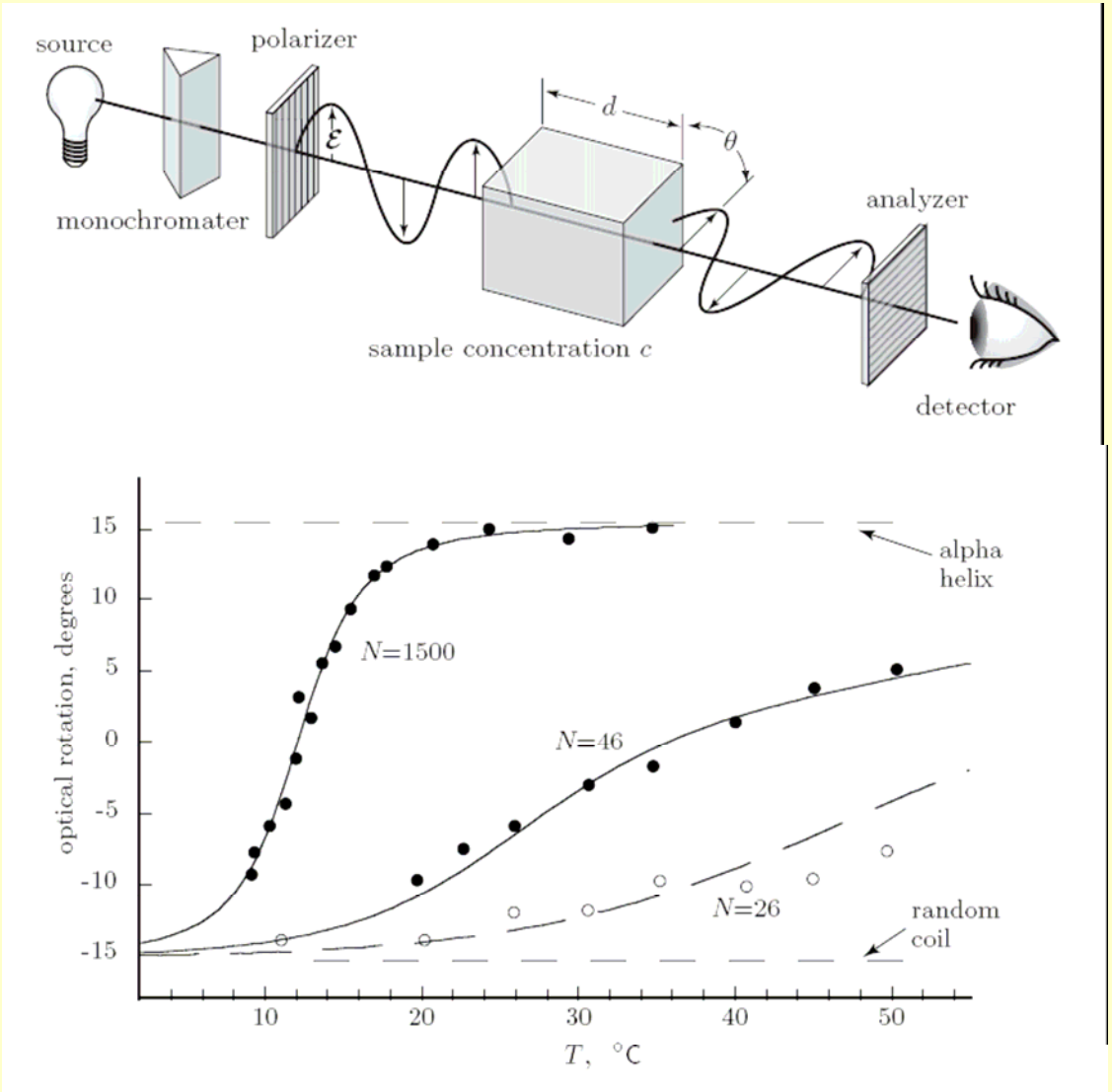


Figure 9.6: (Experimental data with fit.) Alpha-helix formation as a function of temperature for solutions of poly-[γ-benzyl-L-glutamate] (an artificial polypeptide), dissolved in a mixture of dichloroacetic acid and ethylene dichloride. At low temperature all samples displayed an optical rotation similar to that of isolated monomers, whereas at high temperatures the rotation changed, indicating alpha-helix formation. *Top dots:* polymer chains of weight-average length equal to 1500 monomers. *Middle dots:* 46-monomer chains. *Lower circles:* 26-monomer

El peso de cada configuraciónesta dado por

cccccccchhhhhhhhhhccccchhhhhhh

$$\sigma^j s^k = \sigma^2 s^{17}$$

$$\begin{aligned} c &\rightarrow h: \sigma s \\ c &\rightarrow c: 1 \\ h &\rightarrow h: s \\ h &\rightarrow c: 1 \end{aligned}$$

Y la función de partición queda:

$$Z = \sum_{\{\text{sequences } s\}} \exp\left(-\frac{F\{s\}}{k_B T}\right)$$

$$Z(N) = Z_c(N) + Z_h(N)$$

La función de partición se puede calcular teniendo en cuenta la recurrencia:

$$\begin{aligned} Z_c(N+1) &= Z_c(N) + Z_h(N) \\ Z_h(N+1) &= s\sigma\ Z_c(N) + s\ Z_h(N) \end{aligned}$$

$$\begin{pmatrix} Z_c(N+1) \\ Z_h(N+1) \end{pmatrix} = \mathbf{M} \begin{pmatrix} Z_c(N) \\ Z_h(N) \end{pmatrix}$$

$$\mathbf{M} = \begin{pmatrix} 1 & 1 \\ \sigma s & s \end{pmatrix}$$

$$\begin{pmatrix} 1 \\ \sigma s \end{pmatrix} = \mathbf{M} \begin{pmatrix} 1 \\ 0 \end{pmatrix}$$

$$\begin{pmatrix} Z_c(N) \\ Z_h(N) \end{pmatrix} = \mathbf{M}^N \begin{pmatrix} 1 \\ 0 \end{pmatrix}$$

$$Z(N) = Z_c(N) + Z_h(N) \sim \lambda_{\max}^N$$

$$\begin{aligned} F &= -k_B T \ln(Z) = -k_B T N \ln(\lambda_{\max}) \\ &= -k_B T N \ \ln(\frac{1}{2}(1 + s + \sqrt{(1-s)^2 + 4\sigma s})) \end{aligned}$$

¿ Cómo expresar los promedios ?, k es el número de monómeros en hélice.

$$Z = \sum \Omega_{jk} \sigma^j s^k$$

$$\frac{d \ln(Z)}{d \ln(s)} = \frac{s}{Z} \frac{dZ}{ds} = \frac{\sum \Omega_{jk} k \sigma^j s^k}{\sum \Omega_{jk} \sigma^j s^k} = \langle k \rangle$$

Problema: ....

(4) Consider the formal steps that we glossed over in Eqs. (2.68)–(2.72). The total partition sum was

$$Z(N) = Z_c(N) + Z_h(N) = (1,\,1)\begin{pmatrix} Z_c(N) \\ Z_h(N) \end{pmatrix} = (1,\,1)\mathbf{M}^N \begin{pmatrix} 1 \\ 0 \end{pmatrix} \tag{2.82}$$

When diagonalizing $\mathbf{M}$ we apply the transformation $\mathbf{T} : \mathbf{M} \to \mathbf{T}^{-1}\mathbf{M}\mathbf{T} = \mathbf{\Lambda}$ such that

$$\mathbf{\Lambda} = \begin{pmatrix} \lambda_{\max} & 0 \\ 0 & \lambda_{\min} \end{pmatrix} \tag{2.83}$$

Where $\mathbf{M}^N = \mathbf{T}\mathbf{T}^{-1}\mathbf{M}\mathbf{T}\mathbf{T}^{-1} \ldots \mathbf{M}\mathbf{T}\mathbf{T}^{-1} = \mathbf{T}\Lambda^N\mathbf{T}^{-1}$ and thus

$$Z(N) = (1,\ 1)\ \mathbf{T} \begin{pmatrix} \lambda_{\max}^N & 0 \\ 0 & \lambda_{\min}^N \end{pmatrix} \mathbf{T}^{-1} \begin{pmatrix} 1 \\ 0 \end{pmatrix} \tag{2.84}$$

Calculate explicitly $\mathbf{T}$ in the above expression, and examine to what extent $Z(N) \approx \lambda_{\max}^N$.

El porcentaje de hélices es:

$$\Theta = \frac{1}{N}\frac{\mathrm{d}\ln(Z)}{\mathrm{d}\ln(s)} = \frac{s}{2\lambda_{\max}}\left(1 + \frac{s + 2\sigma - 1}{\sqrt{(1-s)^2 + 4\sigma s}}\right)$$

Y el porcentaje de de iniciadores hélices es:

$$\langle j \rangle = \frac{1}{N}\frac{\mathrm{d}\ln(Z)}{\mathrm{d}\ln(\sigma)} = \frac{s\sigma}{\lambda_{\max}\sqrt{(1-s)^2 + 4\sigma s}}$$

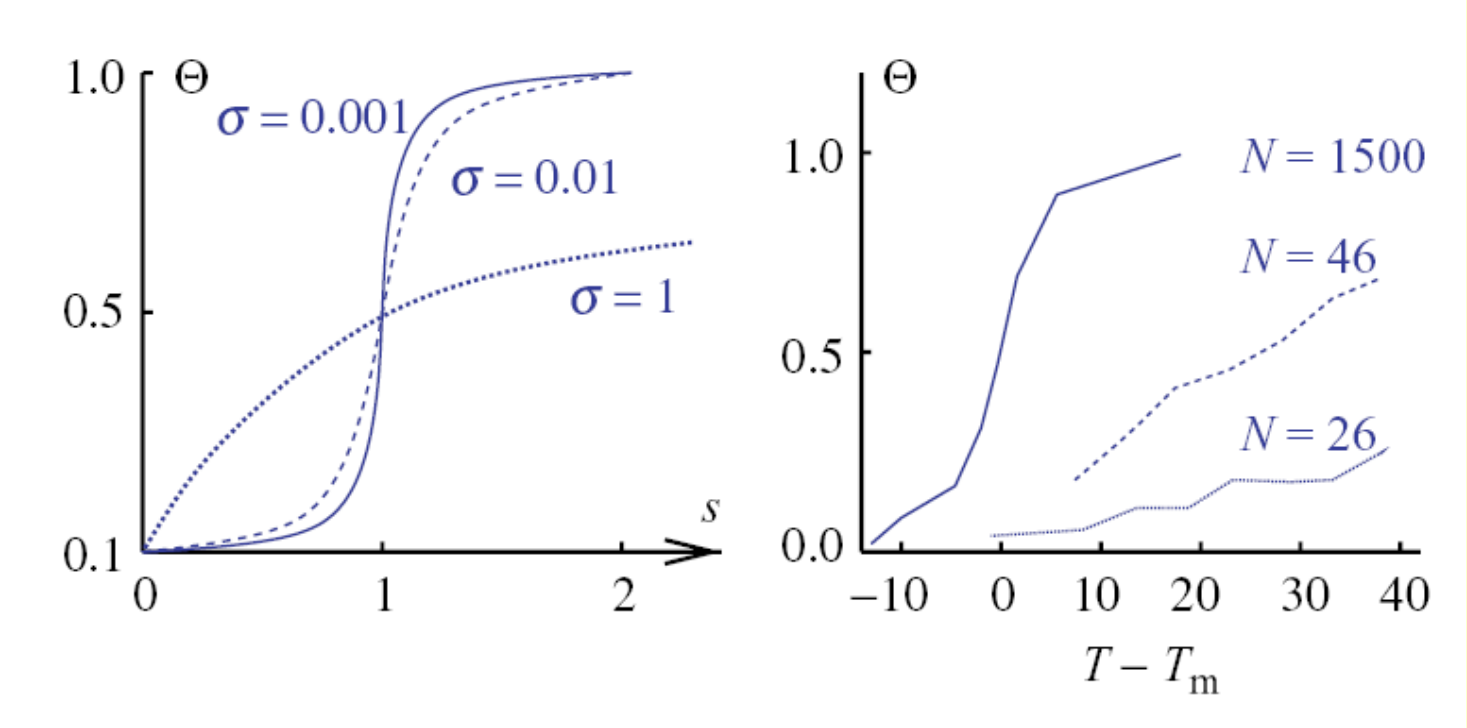
Before discussing the temperature dependence of the parameters, let us stress the operational range for s and σ. Note that s counts the statistical weight of continuing a helix. If $s < 1$ a helix will tend to break up; if $s > 1$ helices tend to grow. In fact from the equations above you can see that for $s \ll 1$ then $\Theta \to 0$, while $s \gg 1$ implies $\Theta \to 1$.

The value of σ is typically $\ll 1$, reflecting a nucleation threshold for initiating helices along the polymer. The smaller the value of σ, the longer the interval between subsequent helix segments, as we can see from $\langle j \rangle \propto \sigma$. In fact the helix–coil transition behaves somewhat as a first-order phase transition as long as $N < 1/\sigma$, where there is at most one helix segment in the system. However, when $N > 1/\sigma$, there will be several nucleation sites along the polymer, and the sharpness of the transition will not increase with further increase in N.

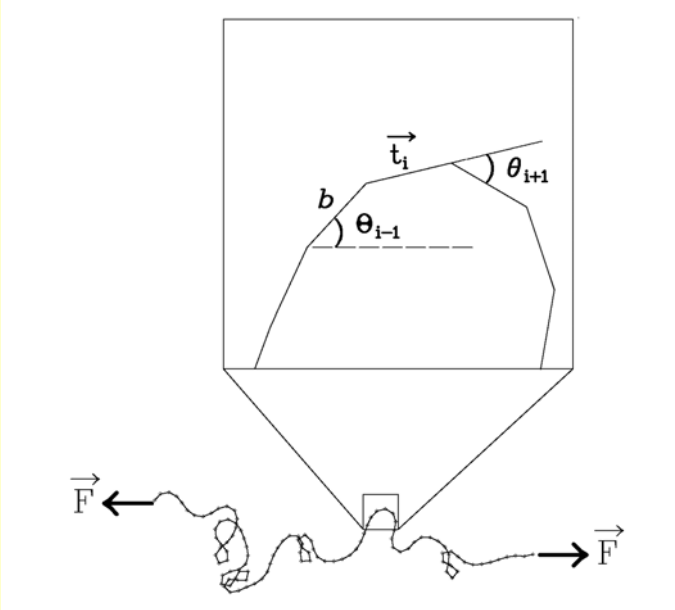
Experimentally the helix–coil transition can be induced by varying temperature. In terms of the parameters in the model, changing temperature changes s, while σ remains fairly constant. Let us investigate the connection between s and T around the transition temperature T_{m}, i.e. for $s \approx 1$; remember that $\sigma \ll 1$, and consider the case $N < 1/\sigma$. Then we have a problem similar to a chemical equilibrium between h and c, and we can consider the corresponding equilibrium constant

$$K = \mathrm{e}^{-\Delta G/k_{\mathrm{B}}T} \tag{2.77}$$

$$s(T) = 1 + \epsilon \quad \text{with} \quad \epsilon \approx \frac{\Delta H_1}{k_B T_m^2}(T - T_m)$$



Comportamiento Mecánico. Efecto de la rigidez en los polímeros (modelo Kratky-Porod o modelo WLC discreto))



Sea B el "bending modulus".

$$\mathcal{E}_{\mathrm{KP}} = -\frac{B}{b}\sum_{i=2}^{N}\vec{t}_i\cdot\vec{t}_{i-1} = -\frac{B}{b}\sum_{i=2}^{N}\cos\theta_i$$

(nota: esto es el modelo Heisenberg clásico en 1d)

$$\langle\vec{t}_i\cdot\vec{t}_j\rangle = \mathrm{e}^{-b|i-j|/\xi}$$

donde ξ es la llamada longitud de persistencia ($\xi = B/k_BT$). Para el ADN ξ = 50 nm.

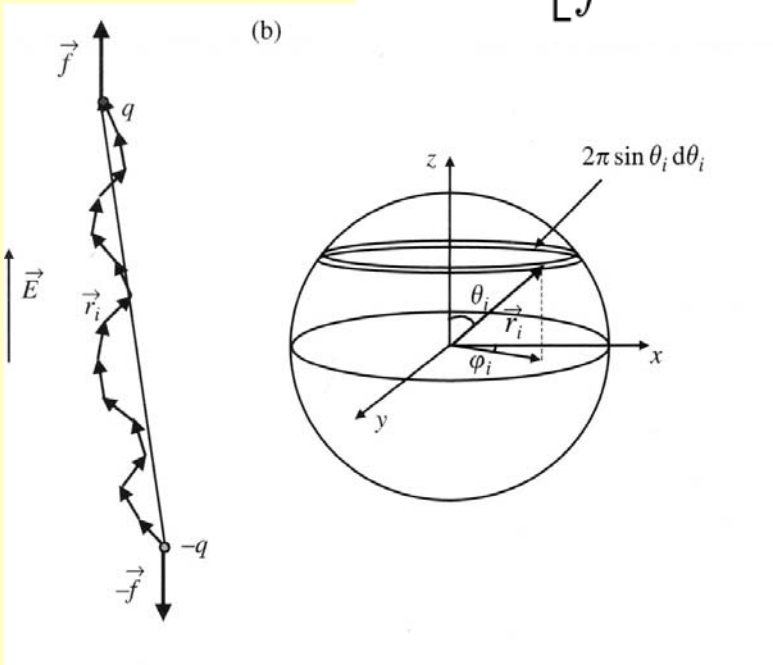
$$R_g^2 \equiv \langle\vec{R}^2\rangle = \left(b\sum_{i=1}^{N}\vec{t}_i\right)^2 \simeq 2Nb\xi = 2l_0\xi$$

Es un polímero ideal. $R \propto N^{1/2}$.

Una variación del modelo: los segmentos pueden apuntar en cualquier dirección libremente (B = 0). “Freely Jointed Chain” (FJC). Equivale a tomar b = 2ξ (longitud de Kuhn). Si aplicamos una fuerza el problema e el mismo que un paramagneto en un campo externo.

$$\mathcal{Z} = \sum_{\vec{t}_i} \mathrm{e}^{-\mathcal{E}_{\mathrm{FJC}}/k_B T} = \sum_{\vec{t}_i} \prod_{i=1}^{N} \mathrm{e}^{Fb\cos\Theta_i/k_B T}$$

$$\mathcal{Z} = \left[\int \mathrm{d}\Omega\, \mathrm{e}^{Fb\cos\Theta/k_B T}\right]^N = \left[\frac{2\pi k_B T}{Fb}\sinh\frac{Fb}{k_B T}\right]^N$$



$$\mathcal{F} = -k_B T \log \mathcal{Z}$$

$$\langle z\rangle = -\frac{\partial\mathcal{F}}{\partial F} = l_0\left(\coth\frac{Fb}{k_B T} - \frac{k_B T}{Fb}\right)$$

Otra variación del modelo: Tomamos el límite continuo. La cadena es una cuerda (algo rígida B ≠ 0). “Worm Like Chain” (WLC).

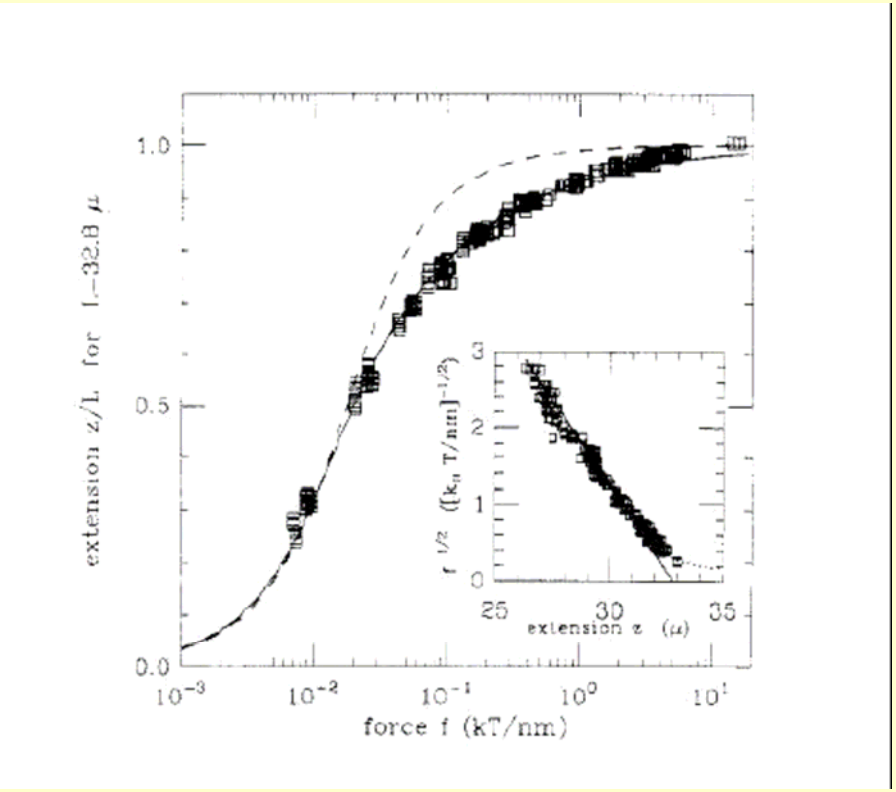
$$\frac{\mathcal{E}_{\mathrm{WLC}}}{k_B T} = \frac{\xi}{2} \int_0^{l_0} \left(\frac{\mathrm{d}\vec{t}}{\mathrm{d}s} \right)^2 \mathrm{d}s - \frac{F}{k_B T} \int_0^{l_0} \cos \Theta(s) \, \mathrm{d}s$$

Es más complicado de resolver (mediante métodos de “matriz de transferencia”), pero ajusta muy bien los datos experimentales y determina con precisión la longitud de persistencia $\xi = 52 \pm 2$ nm (en condiciones fisiológicas). Funcionan bastante bien las llamadas formulas de de interpolación.

$$\beta L_p F(x) = \frac{1}{4(1 - x/L_c)^2} - \frac{1}{4} + \frac{x}{L_c},$$

El comportamiento de ambos modelos es diferente a fuerzas altas

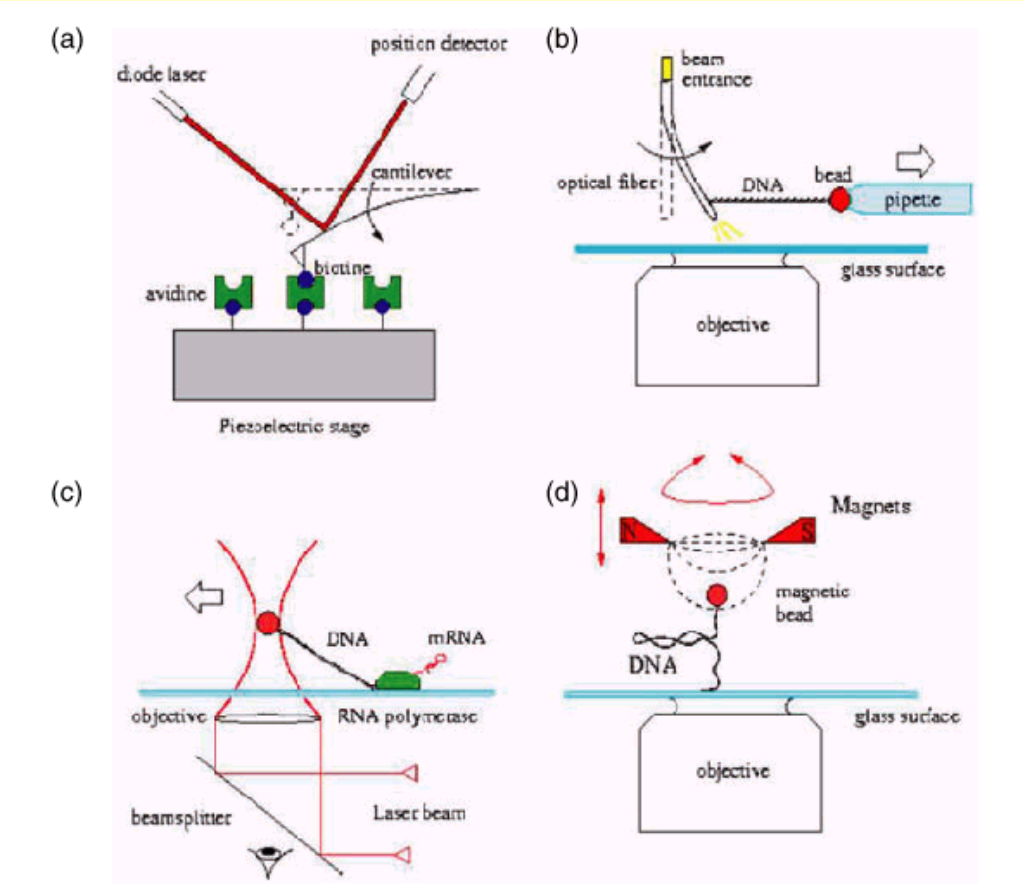
$$1 - \frac{\langle x \rangle}{L_c} \simeq \begin{cases} 1/\sqrt{F} & \text{(WLC)} \\ 1/F & \text{(FJC)} \end{cases}.$$



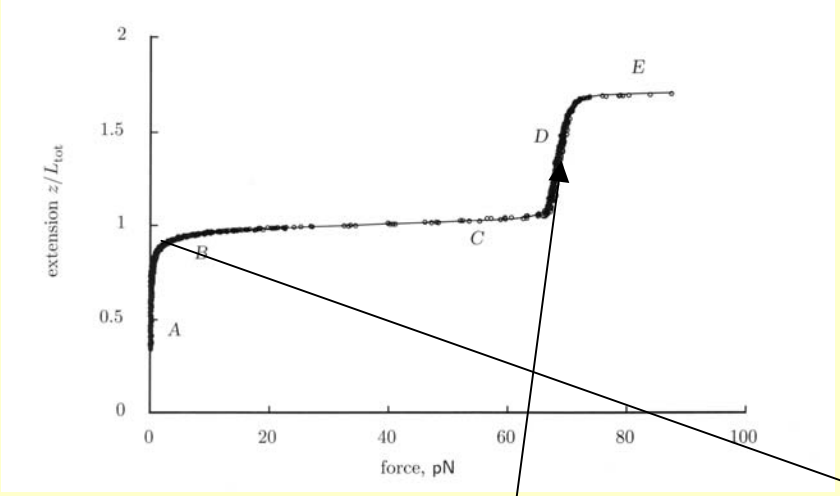
$$L_c = 32.8\ \mu\text{m and } L_p = 53\ \text{nm}.$$

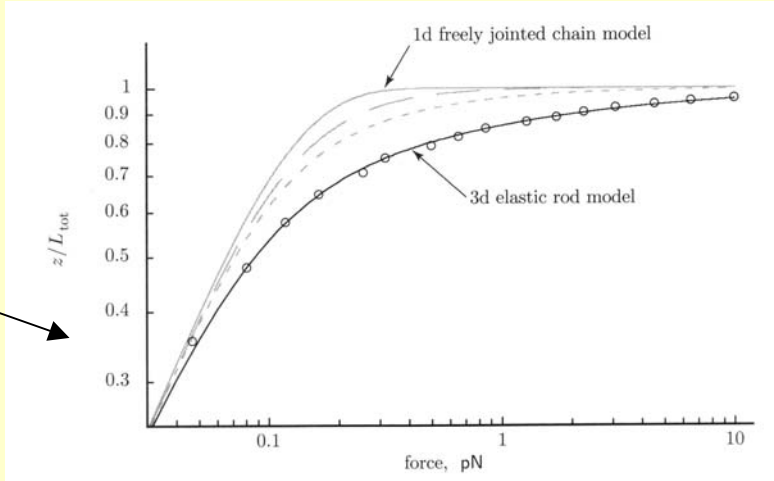
$$b = 2L_p = 100\ \text{nm}$$

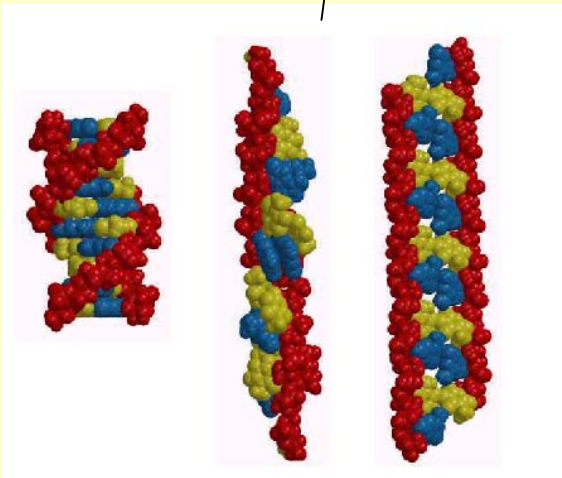
Medidas de “stretching”: sobre ADN y Proteínas.



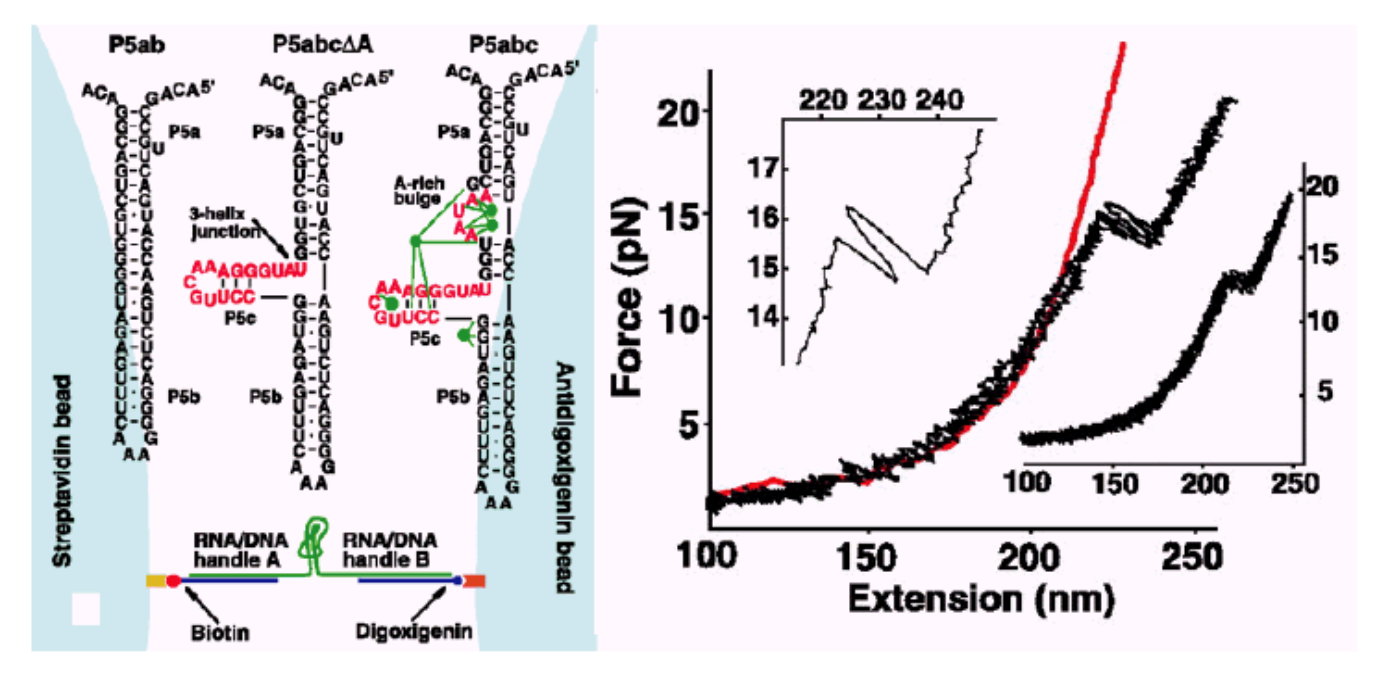
Comportamiento mecánico del ADN:



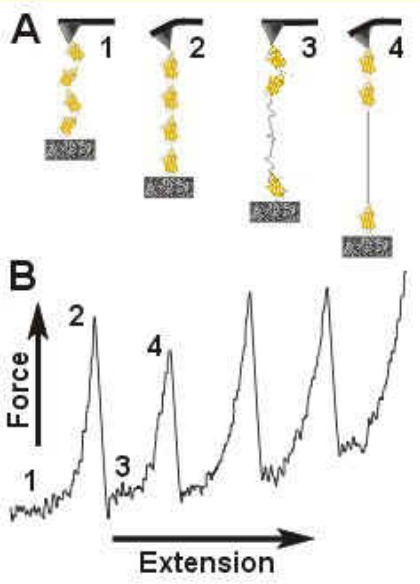


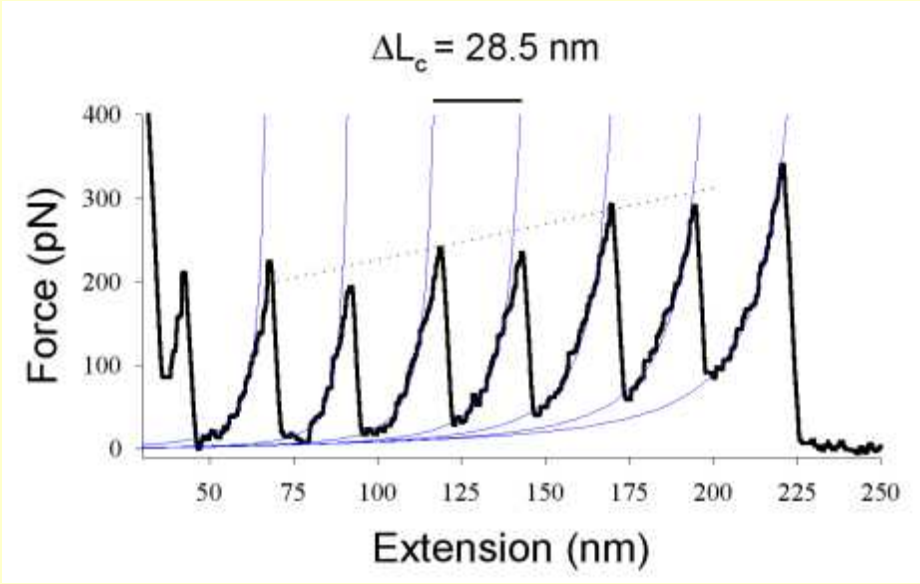


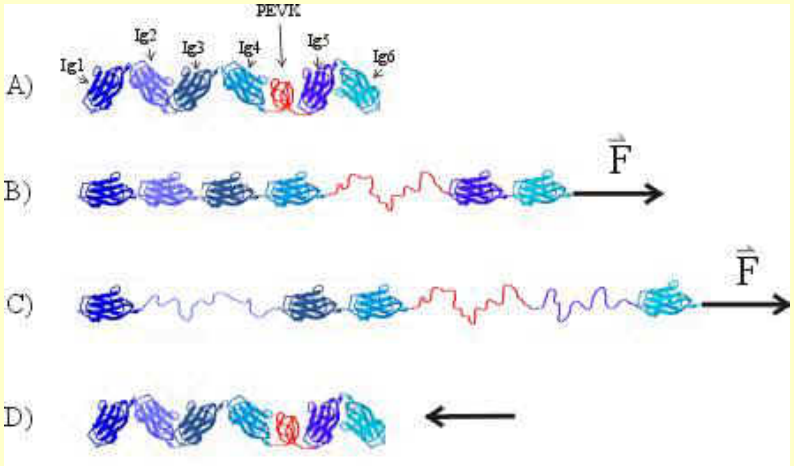
Comportamiento mecánico del ARN:



Comportamiento mecánico de Proteínas:







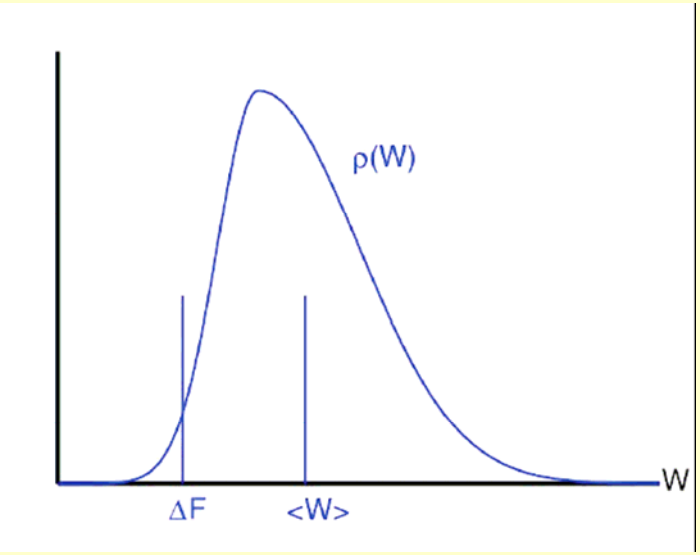
Igualdad de Jarzynski:
Para un procesos reversible, cuasiestático e isotermo:

$W_{rev} = \Delta F$, en caso contrario (fuera del equilibrio) $W_{rev} > \Delta F$.

Sin embargo, Jarzynski (PRL 1997) probó que:

$$\boxed{\left\langle e^{-\beta W} \right\rangle = e^{-\beta \Delta F}}$$

$$\int dW\, \rho(W) e^{-\beta W} \qquad 1/k_B T$$



Teorema de Fluctuación de Crooks (PRE, 1999, 2000)

$$\frac{P_F(W)}{P_R(-W)} = \exp\left(\frac{W - \Delta G}{k_B T}\right)$$

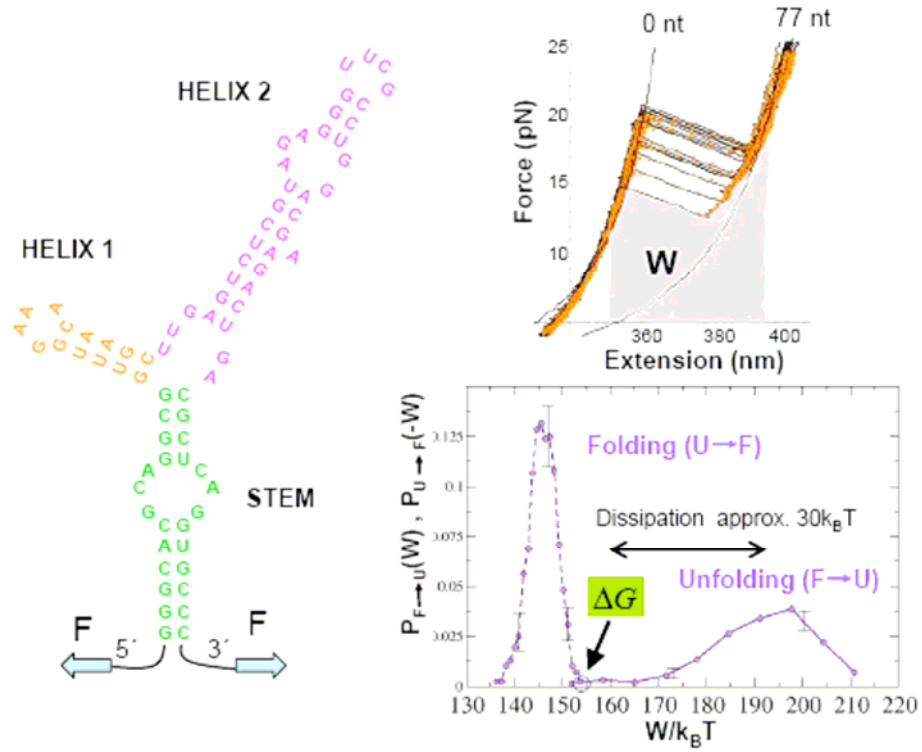


Figure 12. Recovery of folding free energies in a three-helix junction RNA molecule [175]. (A) Secondary structure of the junction containing one stem and two helices. (B) Typical force-extension curves during the unfolding process. The gray area corresponds to the work exerted on the molecule for one of the unfolding curves. (C) Work distributions for the unfolding or forward paths ($F \to U$) and the refolding or reverse ($U \to F$) paths obtained from 1200 pulls. According to the Crooks FT (2) both distributions cross at $W = \Delta G$. After subtracting the free energy contribution coming from stretching the handles and the ssRNA this measurements provide a direct measure of the free energy of the native structure.