

□ Boltzmann distribution

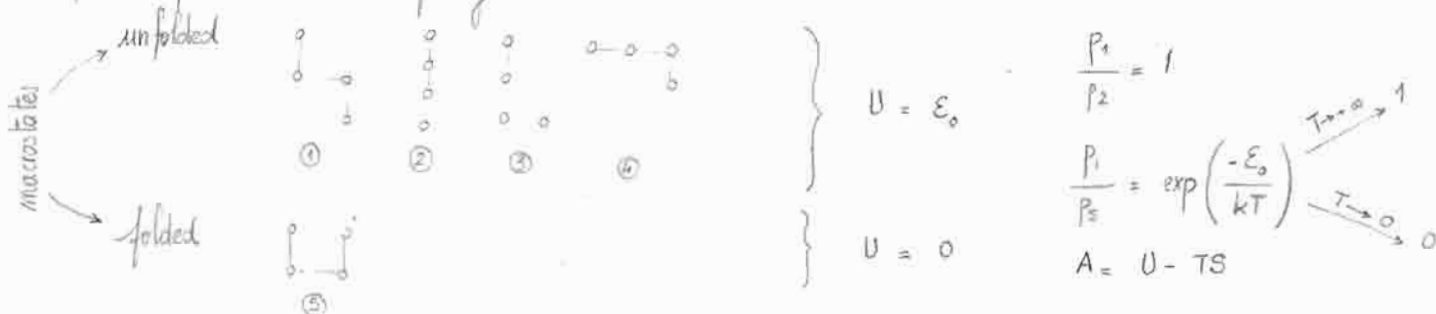
thermodynamic equilibrium of a system with T, V, N held constant \Rightarrow minimize Helmholtz free energy A .
 derivations p. 113 Dill & Bromberg

satisfy $\begin{cases} A = \langle U \rangle - TS \\ S = -k_B \sum_i p_i \ln p_i \\ \text{constraint } \sum_i p_i = 1 \end{cases}$ minimize A subject to constraints (use Lagrange multiplier)

result: probability of being in microstate $i = p_i = \frac{e^{-U_i/k_B T}}{\Omega}$
 partition function $\Omega = \sum_i \exp\left(-\frac{U_i}{k_B T}\right)$
 canonical ensemble

relative populations: $\frac{p_j}{p_k} = \exp\left(-\frac{U_j - U_k}{k_B T}\right)$

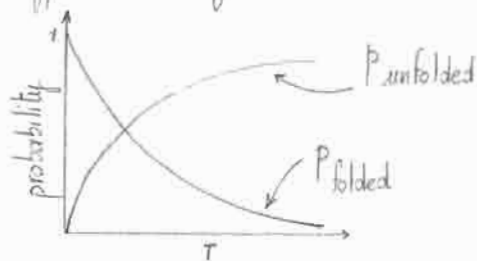
▷ Example: protein / RNA folding



at low T , you don't sample these states, you just end up in the lower energy state.
 if system driven by entropy, the system wants on the contrary to explore all of its states.

more generally $\frac{P_{\text{unfolded}}}{P_{\text{folded}}} = 4 \exp\left(\frac{-\epsilon_0}{k_B T}\right)$
 multiplicity of the unfolded microstates

▷ Typical melting curves



comment: $\frac{U_j}{k_B T}$ measure of accessibility of state j scaled by $k_B T$

□ Free energy & conformation macrostates of molecules

folded macrostate: collection of microstates with various U_i $\sum_i \sum_n \sum_m$
 unfolded macrostate: " " " " $\sum_i \sum_n \sum_m$

relationship $A = -k_B T \ln \Omega$ or $\Omega = \exp\left(-\frac{A}{k_B T}\right)$ - not proven here, just used.

consider macrostates

$$P_{\text{folded}} = \frac{\sum_{\text{folded microstates}} \exp(-U_i/kT)}{\Omega} = \frac{\Omega_{\text{folded}}}{\Omega}$$

$$P_{\text{unfolded}} = \frac{\Omega_{\text{unfolded}}}{\Omega}$$

$$\frac{P_{\text{unfolded}}}{P_{\text{folded}}} = \frac{\Omega_{\text{unfolded}}}{\Omega_{\text{folded}}} = \exp\left(\frac{-\Delta A}{k_B T}\right)$$

generic result

How do applied forces change the distribution?

new thermodynamic system T, V, N, \underline{f} reversible
equilibrium \Rightarrow minimize $A' = A - \underline{r} \cdot \underline{f}_{\text{rev}}$
result = modified Boltzmann distribution:

new free energy, taking force into account

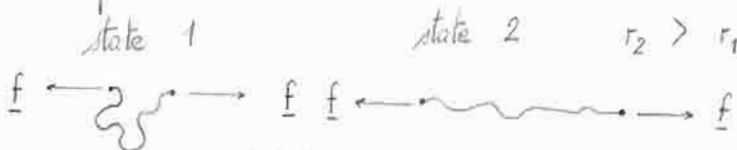
$$P_i = \frac{1}{\Omega'} \exp\left(\frac{-U_i}{k_B T}\right) \exp\left(\frac{\underline{f} \cdot \underline{r}_i}{k_B T}\right)$$



$$\Omega' = \sum_i \exp\left(\frac{-U_i + \underline{f} \cdot \underline{r}_i}{k_B T}\right)$$

(usually \underline{r} and \underline{f} colinear)

constant force



isotension experiment

(not isometric: $r_2 \neq r_1$)

force can change distribution

need our force to be reversible for this analysis to hold.

Example: RNA unfolding - Liphardt et al., 2001

free energy change (between folded & unfolded state) $dA = -p dV + \underline{F} \cdot d\underline{r} - S dT$
assume V, T constant: $\Delta A = A_{\text{unfolded}} - A_{\text{folded}} = \int_{\text{folded}}^{\text{unfolded}} \underline{F} \cdot d\underline{r}$

from the plot "force as a function of extension",

area under the curve $\Delta A = 157 \pm 20 \text{ kJ} \cdot \text{mol}^{-1}$
($kT \approx 2.5 \text{ kJ} \cdot \text{mol}^{-1}$)

second way to get ΔA from data

$$\frac{P_{\text{unfolded}}}{P_{\text{folded}}} = \exp\left(\frac{-\Delta A}{k_B T}\right) \exp\left(\frac{F_z \Delta r_x}{k_B T}\right) \Rightarrow \Delta A = 193 \pm 6 \text{ kJ} \cdot \text{mol}^{-1}$$

equilibrium constant

$$K(F) = \frac{P_{\text{unfolded}}}{P_{\text{folded}}} = \exp\left(\frac{-\Delta A + F_z \Delta r_x}{k_B T}\right) \quad \text{or} \quad \frac{d \ln K(F)}{dF_x} = \frac{\Delta x}{k_B T}$$

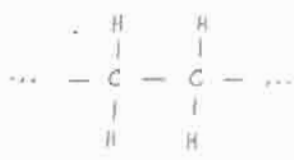
gives them $\Delta x \approx 23 \text{ nm}$

forces favor the more extended state

note: comparable contribution of energy (U due to base pairing) & entropy in this example
($\approx 30 k_B T$ each)

Entropic elasticity & polymers

- polymer = "having many parts"
examples: linear polyethylene (PE)



biological polymers: RNA } repeats of nucleotides (single or double stranded)
DNA }

- actin: actin monomers (G-actin)
- microtubules: tubulin monomers

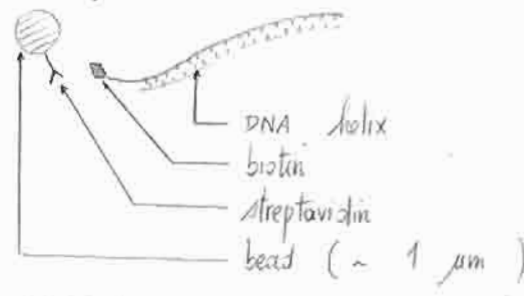
cytoskeleton of cells, they are railroad tracks for molecular motors

- polymer elasticity: freely jointed chain (FJC)

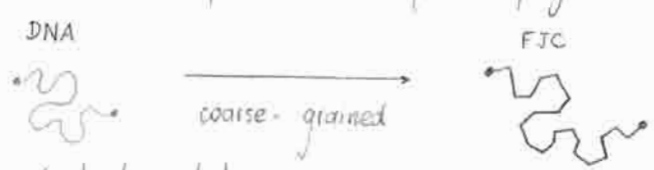
Kuhn & Gr \ddot{u} n 1942

Kramers 1944 => Kramers chain

• note: how you pull on DNA



• Generic statistical representation of a polymer



$N = \text{number of links}$

- FJC:
- phantom links = can cross over
 - rigid links of length $b = \text{Kuhn step (length)}$
 - freely rotating links (not atomic model)
 - fixed contour length = Nb
 - no link-link interactions (electrostatic e.g.)
 - molecular parameters = b, N