Boltzmann distribution

thermodynamic equilibrium of a system with T, V, N held constant = minimize Helmholtz free energy A

derivations p. 113 Bill & Bramberg

satisfy
\[ \begin{align*}
A &= \langle U \rangle - TS \\
S &= -k_B \sum_i p_i \ln p_i \\
\text{constraint} \quad \sum_i p_i &= 1
\end{align*} \]

result: probability of being in microstate \( i \) is
\[ p_i = \frac{\exp \left( \frac{-U_i}{k_B T} \right)}{\sum_j \exp \left( \frac{-U_j}{k_B T} \right)} \]

partition function \( Z = \sum_i \exp \left( \frac{-U_i}{k_B T} \right) \) canonical ensemble

relative populations:
\[ \frac{p_i}{p_k} = \exp \left( \frac{-U_i - U_k}{k_B T} \right) \]

Example: protein/RNA folding

unfolded

folded

more generally
\[ \frac{P_{\text{unfolded}}}{P_{\text{folded}}} = \exp \left( \frac{-E_i}{k_B T} \right) \]

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

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 \( U_i \). \( i = \sum_i U_i \)

unfolded macrostate

relationship \( A = k_B T \ln \mathcal{Q} \) or \( \mathcal{Q} = \exp \left( \frac{-A}{k_B T} \right) \) not proven here, just used.
How do applied forces change the distribution?

New thermo-dynamic system $T, V, N, f_{\text{reversible}}$.

Minimize free energy $A' = A - F \cdot f_{\text{reversible}}$.

Modified Boltzmann distribution:

$$P_x = \frac{1}{Q'} \exp \left( - \frac{U_i}{k_B T} \right) \exp \left( \frac{f \cdot r_i}{k_B T} \right)$$

$$Q' = \sum_x \exp \left( - \frac{U_i + f \cdot r_i}{k_B T} \right)$$

(a) For constant force.

- State 1 $\rightarrow$ state 2 $r_2 > r_1$

(b) Insolation experiment.

- Force can change distribution.

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


Free energy change (between folded & unfolded state):

$$dA = -pdV + E \cdot dr - SDT$$

Assume $V, T$ constant:

$$dA = A_{\text{unfolded}} - A_{\text{folded}} = \int_{\text{unfolded}}^{\text{folded}} E \cdot dr$$

From the plot "force as a function of extension", area under the curve:

$$dA = 134 \pm 20 \text{ kJ mol}^{-1}$$

(kT = 2.3 kJ mol$^{-1}$)

Second way to get $dA$ from data:

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

Equilibrium constant:

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

Given $\Delta x \approx 23 \text{ nm}$.

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)
Polymer elasticity & polymers
- polymer = "having many parts"
  examples: linear polyethylene
  \[
  \text{PE} \quad \cdots \quad \text{C} - \text{C} - \cdots
  \]
  biological polymers: RNA, DNA \{ repeats of nucleotides \ (single or double stranded) \}
  active: actin monomers (G-actin)
  microtubules: tubulin monomers
- cytoskeleton of cells, they are railroad tracks for molecular motors
- polymer elasticity: freely jointed chain (FJC)  Kohn & Grün 1942
- note: how you pull on DNA

- Generic statistical representation of a polymer
  DNA
  \[
  \text{N} \quad \text{number of links}
  \]
  \( FJC \):
  \[
  \begin{align*}
  \text{phantom links:} & \quad \text{can cross over} \\
  \text{rigid links of length} & \quad b = \text{Kuhn step (length)} \\
  \text{freely rotating links} & \quad (\text{not atomic model}) \\
  \text{fixed contour length} & \quad N \cdot b \\
  \text{no link-link interactions} & \quad (\text{electrostatic e.g.)} \\
  \text{molecular parameters} & \quad b, N
  \end{align*}
  \]