Work coupling LDB : $\frac{\Omega_{nm}}{\Omega_{mn}} = e^{-\beta(E_n - E_m - W_{nm})}$

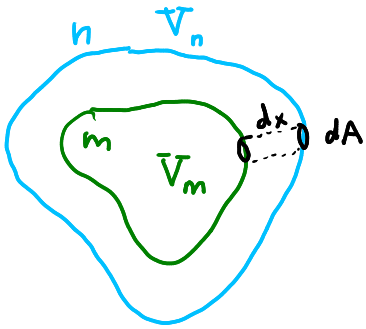
W_{nm}: work by env. on sys

$Q_{nm} = E_n - E_m - W_{nm}$

Explore details of W_{nm}:

- work against pressure
- "chemical" work $\Rightarrow$ chemical potential

pressure: biomolecule



P pressure

(m) volume V_m (n) volume V_n

force $= P\,dA$

work $P\,dA\,dx = P\,dV$

total work in $m \to n$ transition done by sys. on env.

$$\int_{\text{area}} P\,dV = P(V_n - V_m)$$

$$W_{nm} \text{ (by env. on sys)} = -P(V_n - V_m) = -PV_n + PV_m$$

conservative work

plug in:

$$\frac{\Omega_{nm}}{\Omega_{mn}} = e^{-\beta(E_n - E_m + PV_n - PV_m)} = e^{-\beta(H_n - H_m)}$$

new state variable

$$H_n = E_n + PV_n$$

= enthalpy of state n

All the earlier ESS results hold w/ just energy $E_n \rightarrow$ enthalpy H_n

w/ no other work: $p_n(t) \xrightarrow[t\to\infty]{} p_n^S = \frac{e^{-\beta H_n}}{Z}$

modified ESS

$$Z = \sum_n e^{-\beta H_n}$$

in general: $\frac{\Omega_{nm}}{\Omega_{mn}} = e^{-\beta (H_n - H_m - W_{nm})}$

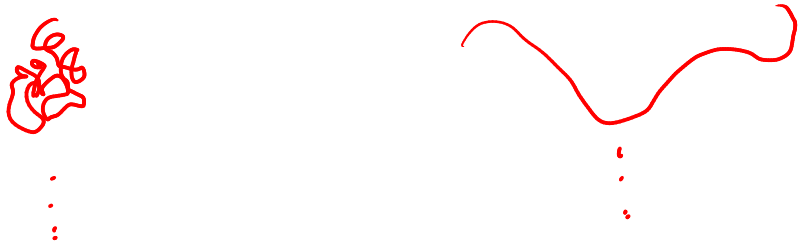
W_{nm}: non-pressure work terms

Observation: most biological "states" in our models are coarse-grained descriptions ("macrostates") corresponding to many possible "microstates" (atomic configurations)

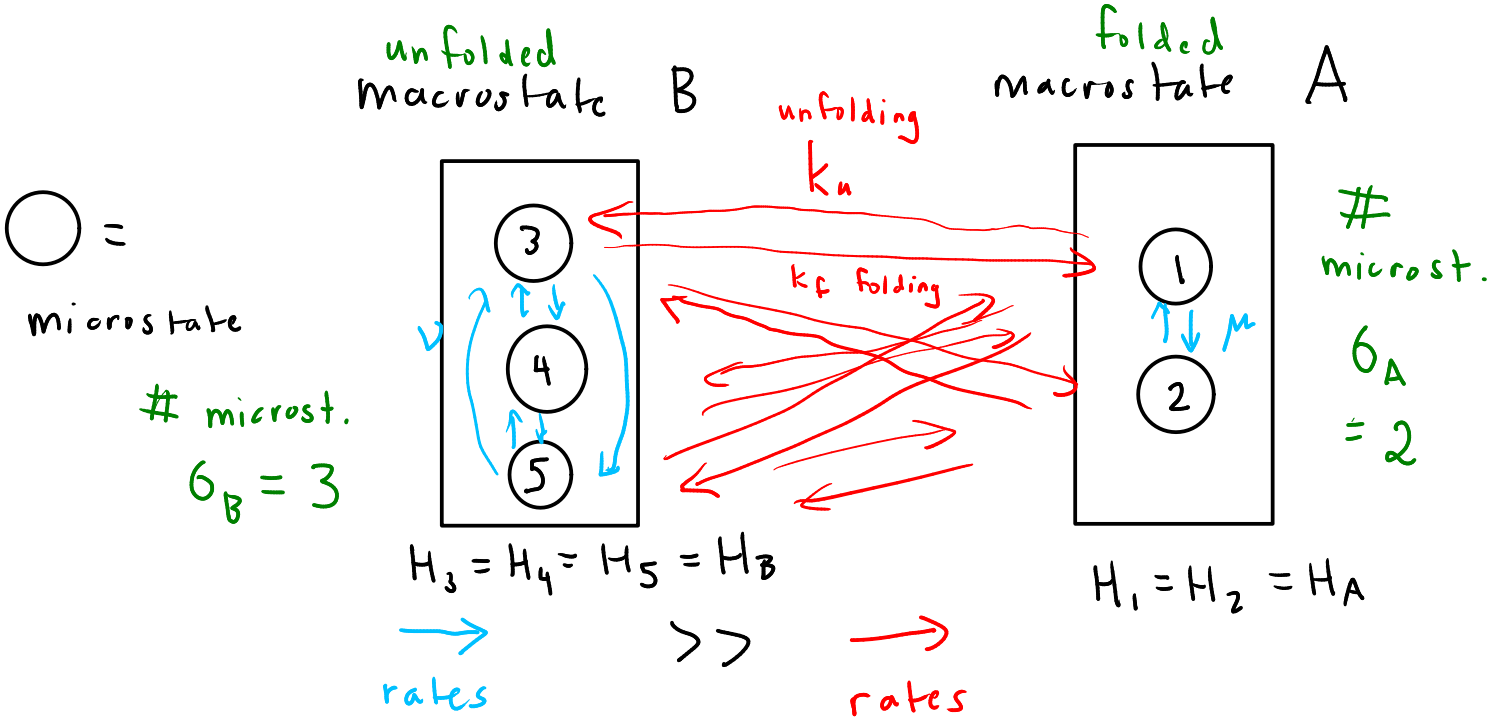
state: folded protein $\rightleftharpoons$ unfolded protein







assumption: "separation of timescales": transitions b/t microstates in same macrostate are much faster than trans. b/t macrostates



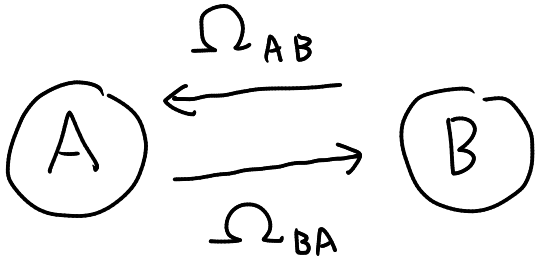
turn this into concrete example

assume folded H_A < unfolded H_B

b/c folded states make internal bonds making energy lower ⇒ enthalpy lower

Goal: create a coarse-grained master eqn. just for macrostates

map our system $\Rightarrow$



can we find Ω_{AB}, Ω_{BA} such that physics is the same as the original?

write down master eqn. for orig system:

$$\frac{dp_1}{dt} = -3k_u p_1 + k_f(p_3+p_4+p_5) - Mp_1 + Mp_2$$

$$\frac{dp_2}{dt} = -3k_u p_2 + k_f(p_3+p_4+p_5) - Mp_2 + Mp_1$$

. . .

Coarse-grained prob:

$$p_A = p_1 + p_2$$

$$p_B = p_3 + p_4 + p_5$$

add $\frac{dp_1}{dt} + \frac{dp_2}{dt}$ eqn's:

$$\frac{d}{dt}(p_1+p_2) = -3k_u(p_1+p_2) + 2k_f(p_3+p_4+p_5)$$

$$\frac{d}{dt}p_A = -3k_u p_A + 2k_f p_B$$

similar steps: $\frac{d}{dt} p_B = 3k_u p_A - 2k_f p_B$

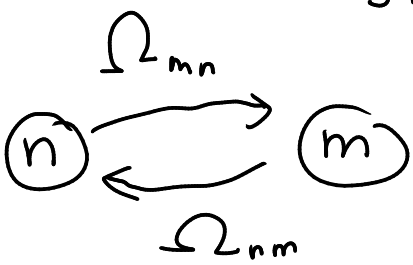
$\Omega_{AB} = 2k_f = 6_A k_f$

general pattern:



$\Omega_{BA} = 3k_u = 6_B k_u$

macrostate



Ω_{mn}

Ω_{nm}

CG (coarse-grained mod.)

$\Omega_{mn} = 6_m k_{mn}$

↑ rate from microst. to microst. (OG model)

$\Omega_{nm} = 6_n k_{nm}$

$$\frac{\Omega_{nm}}{\Omega_{mn}} = \frac{6_n k_{nm}}{6_m k_{mn}} = \frac{6_n}{6_m} e^{-\beta(H_n - H_m - W_{nm})}$$

↑ other work

$$= e^{-\beta(H_n - H_m - k_B T \ln \frac{6_n}{6_m} - W_{nm})}$$

↑ is an effective "chemical" work term due to coarse-grained