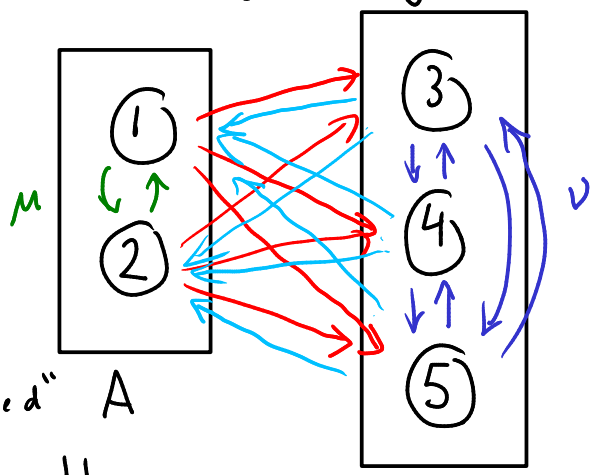
example of coarse-graining:



k_u unfolding

k_f folding

$\mu, \nu >> k_u, k_f$

$\sigma_A = 2$

"folded" A

enthalpy H_A

σ_B = # microstates in B $= 3$

B "unfolded"

H_B

write down master equ. for microstates:

$$\frac{dp_1}{dt} = -3k_u p_1 - \mu p_1 + k_f (p_3 + p_4 + p_5) + \mu p_2$$

$$\frac{dp_2}{dt} = -3k_u p_2 - \mu p_2 + k_f (p_3 + p_4 + p_5) + \mu p_1$$

...

coarse-grained prob: $p_A = p_1 + p_2$

$p_B = p_3 + p_4 + p_5$

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

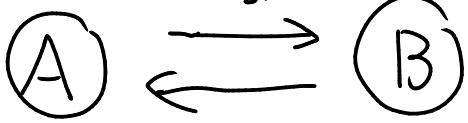
$$\Rightarrow \frac{d}{dt} p_A = -3k_u p_A + 2k_f p_B$$

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

$$\frac{d}{dt}\begin{pmatrix} P_A \\ P_B \end{pmatrix} = \Omega \begin{pmatrix} P_A \\ P_B \end{pmatrix}$$

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

rate from microstate to microstate



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

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

generalize: macrostates

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

microstates obey LDB:

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

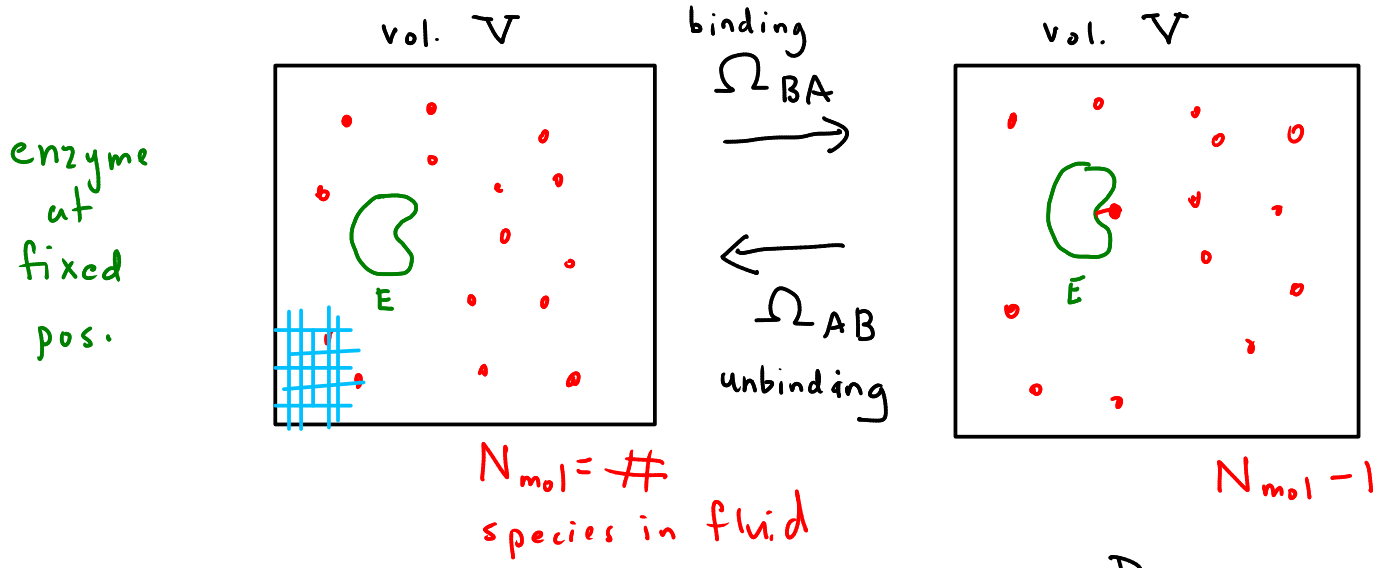
↑ other work

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

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

effective "work" term coming from coarse-graining

example:



macrostate A
= all configs of N_{mol} in fluid

B
= all configs of $N_{mol}-1$ in fluid
+ 1 bound to enzyme

binding / unbinding

$$\frac{\Omega_{BA}}{\Omega_{AB}} = e^{-\beta\left(\underbrace{H_B - H_A}_{<0 \text{ for molecule forming a bond (if binding is thermod. favorable)}} - k_B T \ln \frac{\sigma_B}{\sigma_A}\right)} \qquad W_{BA} = 0 \text{ no other work terms}$$

σ_A = # configs of N_{mol} molecules in a box of volume V (ignore vol. of E $\ll V$)

divide up vol. V into small volumes

V_{mol} = vol. of molecule (big enough to fit one molec.)

$$\#\ \text{boxes} = N_{pos} = \frac{V}{V_{mol}}$$

Ω_A = how many ways to arrange N_{mol} objects into N_{pos} possible positions?

$$\Omega_A = \binom{N_{pos}}{N_{mol}} = \frac{N_{pos}!}{N_{mol}!\,(N_{pos}-N_{mol})!}$$

$$\Omega_B = \binom{N_{pos}}{N_{mol}-1} = \frac{N_{pos}!}{(N_{mol}-1)!\,(N_{pos}-N_{mol}+1)!}$$

$$\frac{\Omega_B}{\Omega_A} = \frac{N_{mol}}{N_{pos}-N_{mol}+1} \approx \frac{N_{mol}}{N_{pos}}$$

$N_{pos} \gg N_{mol}$ (dilute sol'n)

$$k_B T \ln \frac{\Omega_B}{\Omega_A} \approx k_B T \ln \frac{N_{mol}}{N_{pos}}$$

$$= k_B T \ln c V_{mol}$$

$$= \underbrace{k_B T \ln V_{mol}}_{M_0 = \text{const.}} + k_B T \ln c$$

M_0 = const. = "standard" chem. potential

$$N_{pos} = \frac{V}{V_{mol}}$$

$$c = \frac{N_{mol}}{V} = \text{conc.}$$

chemical potential $\equiv \mu = k_B T \ln \frac{G_B}{G_A}$

$= \mu_0 + k_B T \ln C$

$\frac{\text{binding}}{\text{unbinding}}$ $\quad \frac{\Omega_{BA}}{\Omega_{AB}} = e^{-\beta (\underbrace{H_B - H_A}_{<0} - \mu)}$ Eq. 1

makes binding favorable

When $N_{pos} >> N_{mol} \Rightarrow \mu < 0$

increasing $C \Rightarrow \mu$ less negative

$\Rightarrow$ makes Ω_{BA} larger rel. to Ω_{AB}

$\Rightarrow$ larger conc. C favors binding

recall from FAR $\rightleftharpoons$ NEAR $\rightleftharpoons$ BOUND

$0 \leq \alpha_b \leq 1$

Smol. rate

Eq. 2 $\quad \frac{k_b}{k_u} = \frac{\Omega_{BA}}{\Omega_{AB}} = \frac{\alpha_b k_s C}{k_u}$

both Eq. 1 & Eq. 2 are prop. to C

$\Rightarrow$ consistent!

next time: generalize to many types of particles in fluid around our system

type j molec: $\mu_j = \mu_0^j + k_B T \ln c_j$

↳ conc. of type j molec.