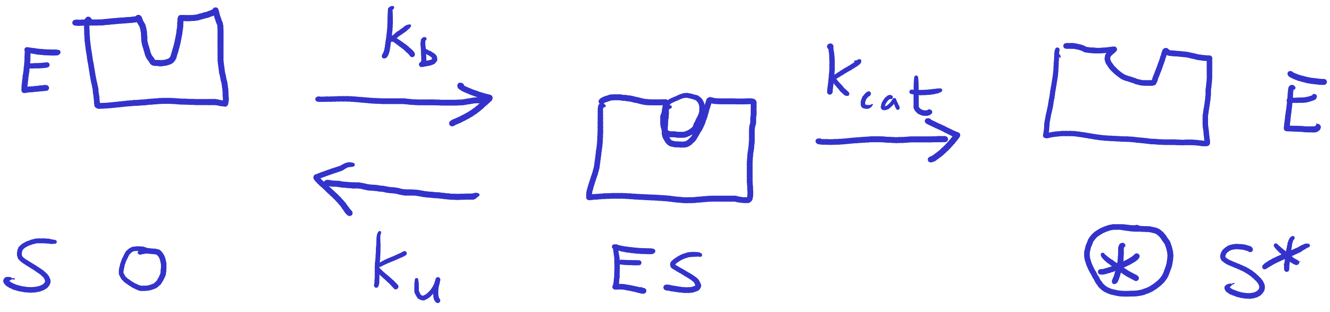
PHYS 320/420 Lecture 14

Doing chemistry "exactly" . . .

a.k.a. "The Horror!"



chemical state:

$$\vec{n} = (n_S, n_E, n_{ES}, n_{S*})$$

Conservation laws: $n_\alpha \geq 0$ for all α

$$\left.\begin{aligned} n_E + n_{ES} &= M_E \\ n_S + n_{ES} + n_{S*} &= M_S \end{aligned}\right\} \text{const.}$$

example: $M_E = 2$, $M_S = 2$

allowed states:

$$\begin{aligned} \vec{n} = &(2, 2, 0, 0) \\ &(1, 1, 1, 0) \\ &(1, 2, 0, 1) \\ &(0, 0, 2, 0) \end{aligned}$$

binding

unbinding

k_{cat}

etc.

lots of possible combos!

probability $p_{\vec{n}}(t)$ to be in $\vec{n}$ at time t

$$\frac{dp_{\vec{n}}(t)}{dt} = \sum_{\vec{m}} \Omega_{\vec{n},\vec{m}}\, p_{\vec{m}}(t)$$

$\Omega_{\vec{n},\vec{m}}$ for $\vec{n} \neq \vec{m}$ is trans. rate $\vec{m} \to \vec{n}$

columns of Ω sum to zero

$$\sum_{\vec{n}} \Omega_{\vec{n},\vec{m}} = 0$$

off-diag. entries of Ω:

categories: $\vec{m} \to \vec{n}$ $(\vec{m} \neq \vec{n})$

(i) binding

$$\text{if} \left(\begin{array}{l} n_S = m_S - 1 \\ n_E = m_E - 1 \\ n_{ES} = m_{ES} + 1 \\ n_{S*} = m_{S*} \end{array} \right) \text{ is true}$$

then entry is:

$$\alpha_b K_s \frac{m_s}{V} m_E \equiv \tilde{k}_b m_s m_E$$

$K_s = 4\pi D R$ — V ↳ vol. of cell — $\tilde{k}_b \equiv \frac{\alpha_b K_s}{V}$

(ii) unbinding

$$\text{if} \begin{pmatrix} n_E = m_E + 1 \\ n_s = m_s + 1 \\ n_{ES} = m_{ES} - 1 \\ n_{s*} = m_{s*} \end{pmatrix} \text{ true}$$

entry: $k_u m_{ES}$ b/c any of the ES complexes can unbind

(iii) catalysis $(S \to S^*)$:

$$\text{if} \begin{pmatrix} n_E = m_E + 1 \\ n_s = m_s \\ n_{ES} = m_{ES} - 1 \\ n_{s*} = m_{s*} + 1 \end{pmatrix} \text{ is true}$$

entry: $k_{cat} m_{ES}$

some portion of Ω matrix:

Ω	$(2,2,0,0)$	$(1,1,1,0)$	$(1,2,0,1)$
$(2,2,0,0)$	$\sim$	k_u	
$(1,1,1,0)$	$4\tilde{k}_b$	$\sim$	
$(1,2,0,1)$		k_{cat}	$\sim$

$\cdots \qquad \ddots$

giant complex mess
(but good if only a
few proteins exist in cell)

How can we make progress?

Let's use our diffusion example
trick of focusing on the
moments (averages):

recall: $$\langle i \rangle_t = {\sum_i}' \, i \, p_i(t)$$

$$\frac{d\langle i \rangle_t}{dt} = {\sum_{i,j}}' (j-i)\,\Omega_{ji}\,p_i(t)$$

general version:

$$\frac{d\langle n_S\rangle}{dt} = \sum_{\vec{m},\vec{n}} (n_S - m_S)\,\Omega_{\vec{n},\vec{m}}\, P_{\vec{m}}$$

$$\frac{d\langle n_E\rangle}{dt} = \sum_{\vec{m},\vec{n}} (n_E - m_E)\,\Omega_{\vec{n},\vec{m}}\, P_{\vec{m}}$$

etc.

to derive:

$$\langle n_S\rangle_t = \sum_{\vec{n}} n_S\, P_{\vec{n}}(t)$$

take deriv. of both sides + plug in master equ.

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next step: plug in our Ω matrix

some algebra:

$$\frac{d\langle n_S\rangle_t}{dt} = \sum_{\vec{m}} \left[-\tilde{k}_b\, m_S\, m_E\, P_{\vec{m}}(t) + k_u\, m_{ES}\, P_{\vec{m}}(t) \right]$$

$$= -\tilde{k}_b \langle n_S n_E\rangle_t + k_u \langle n_{ES}\rangle_t$$

$$\langle n_S n_E \rangle_t = \sum_{\vec{n}} n_S n_E P_{\vec{n}}(t)$$

$$\langle n_{ES} \rangle_t = \sum_{n} n_{ES} P_{\vec{n}}(t)$$

similarly for other equations:

$$\boxed{\begin{aligned} \frac{d\langle n_E \rangle_t}{dt} &= -\tilde{k}_b \langle n_S n_E \rangle_t + k_u \langle n_{ES} \rangle_t \\ &\quad + k_{cat} \langle n_{ES} \rangle_t \\ &\text{etc.} \end{aligned}}$$

Equations are intuitive but not useful in current form:

unknowns on left

$\langle n_S \rangle_t$, $\langle n_E \rangle_t$, $\langle n_{ES} \rangle_t$, $\langle n_{S^*} \rangle_t$

more unknowns on right:

$\langle n_S n_E \rangle_t$, etc.

4 equations for 5 unknowns

$\Rightarrow$ problem!