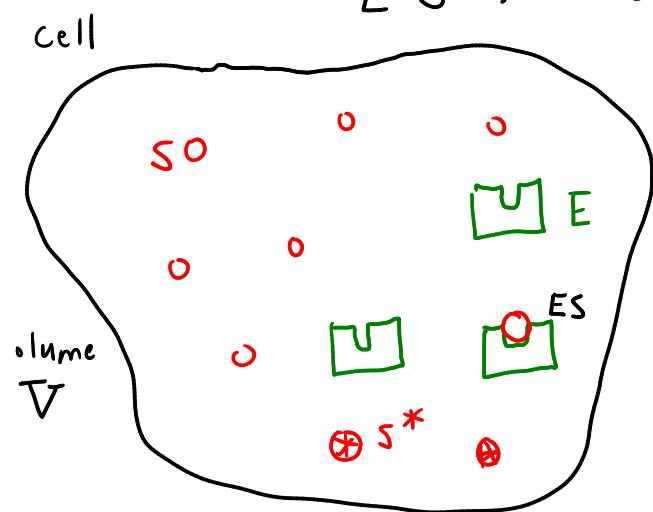


enzyme E (one type of protein)

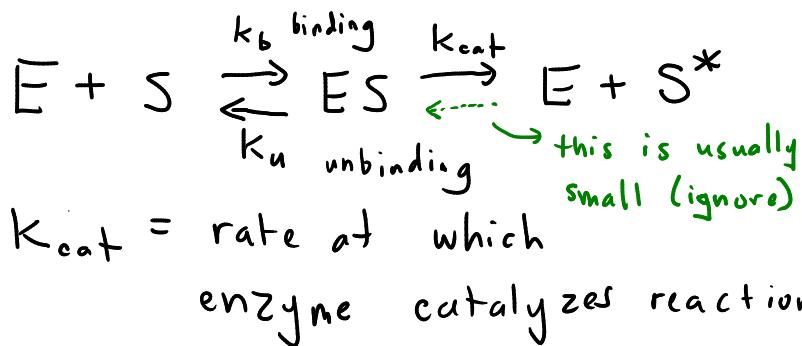
substrate S (another protein or small molecule)

reaction $S \rightarrow S^*$ (modified version of substrate)

ES : enzyme bound to substrate



Reaction scheme:



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

n_α = # of type α molecules

before:

$$\Omega_{nm}$$

 $m \rightarrow n$

\rightsquigarrow
generalize

$\Omega_{\vec{n}\vec{m}}$ = trans. rate from state \vec{m} to \vec{n}
(for $\vec{m} \neq \vec{n}$)

probability $p_{\vec{n}}(+)$ = prob. to observe state \vec{n} at time t

$$\sum_{\vec{n}} p_{\vec{n}}(+) = 1 \Rightarrow \text{columns of } \Omega_{\vec{n}\vec{m}} \text{ sum to zero}$$
$$\sum_{n_S=0}^{\infty} \sum_{n_E=0}^{\infty} \sum_{n_{ES}=0}^{\infty} \sum_{n_{S^*}=0}^{\infty}$$
$$\sum_{\vec{n}} \Omega_{\vec{n}\vec{m}} = 0$$

Conservation laws (stoichiometry)

$$n_s + n_{Es} + n_{s*} = \text{const} \equiv M_s$$

$$n_E + n_{Es} = \text{const.} \equiv M_E$$

$n_\alpha \geq 0$ for all α

example: $M_s = 2$, $M_E = 2$

allowed states

$$\begin{aligned} \vec{n} &= \begin{pmatrix} n_s & n_E & n_{Es} & n_{s*} \\ 2 & 2 & 0 & 0 \end{pmatrix} \xrightarrow{\text{binding}} \\ &= \begin{pmatrix} 1 & 1 & 1 & 0 \end{pmatrix} \\ &= \begin{pmatrix} 1 & 2 & 0 & 1 \end{pmatrix} \xrightarrow{\text{catalysis}} \\ &\quad \text{etc.} \end{aligned}$$

All possible $\overset{\text{nonzero}}{\text{off-diagonal}}$ rates $\Omega_{\vec{n}, \vec{m}}$ ($\vec{m} \neq \vec{n}$):

i) binding:

if $\begin{cases} n_s = m_s - 1 \\ n_E = m_E - 1 \\ n_{Es} = m_{Es} + 1 \\ n_{s*} = m_{s*} \end{cases}$ is true \Rightarrow

$$\Omega_{\vec{n}, \vec{m}} = \alpha_b K_s \frac{M_s}{V} m_E$$

$$= \tilde{k}_b M_s M_E$$

$$\tilde{k}_b = \frac{\alpha_b K_s}{V}$$

(ii) unbinding

if $\begin{cases} n_E = m_E + 1 \\ n_s = m_s + 1 \\ n_{Es} = m_{Es} - 1 \\ n_{s*} = m_{s*} \end{cases}$ is true $\Omega_{\vec{n}, \vec{m}} = k_u M_{Es}$

(iii) catalysis
if $\begin{pmatrix} n_E = m_E + 1 \\ n_s = m_s \\ n_{ES} = m_{ES} - 1 \\ n_{S^*} = m_{S^*} + 1 \end{pmatrix}$ is true $\Rightarrow \sum_{\vec{n}, \vec{m}} = k_{cat} m_{ES}$

a portion of Ω matrix:

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

diag.
entries
are
det.
by col's
summing
to zero

\Rightarrow giant mess! can we make things simpler?

TRICK: recall $\langle i \rangle_t = \sum_i i p_i(t)$
derived $\frac{d\langle i \rangle_t}{dt} = \sum_{i,j} (j-i) \Omega_{ji} p_i(t)$

general version: $\langle n_s \rangle_t = \sum_{\vec{n}} n_s p_{\vec{n}}(t)$
 $\langle n_E \rangle_t = \sum_{\vec{n}} n_E p_{\vec{n}}(t)$ etc.

1) $\frac{d\langle n_s \rangle_t}{dt} = \sum_{\vec{n}, \vec{m}} (n_s - m_s) \sum_{\vec{n}, \vec{m}} p_{\vec{m}}(t)$

2) $\frac{d\langle n_E \rangle_t}{dt} = \sum_{\vec{n}, \vec{m}} (n_E - m_E) \sum_{\vec{n}, \vec{m}} p_{\vec{m}}(t)$

\ddots

plug in Ω : 1) $\frac{d\langle n_s \rangle_t}{dt} = \sum_m \left[-\tilde{k}_b m_s m_E p_m^+(t) + k_u m_{ES} p_m^-(t) \right]$

$\left. \begin{array}{l} 1) \Rightarrow \frac{d\langle n_s \rangle_t}{dt} = -\tilde{k}_b \langle n_s n_E \rangle_t + k_u \langle n_{ES} \rangle_t \\ 2) \quad \frac{d\langle n_E \rangle_t}{dt} = -\tilde{k}_b \langle n_s n_E \rangle_t + (k_u + k_{cat}) \langle n_{ES} \rangle_t \\ 3) \quad \frac{d\langle n_{ES} \rangle_t}{dt} = \tilde{k}_b \langle n_s n_E \rangle_t - (k_u + k_{cat}) \langle n_{ES} \rangle_t \\ 4) \quad \frac{d\langle n_s^+ \rangle_t}{dt} = k_{cat} \langle n_{ES} \rangle_t \end{array} \right\}$
 4 eqn's

5 unknown funcs: $\langle n_s \rangle_t, \langle n_E \rangle_t, \langle n_{ES} \rangle_t,$
 $\langle n_s^+ \rangle_t, \langle n_s n_E \rangle_t$

"dirty" trick: $\langle n_s n_E \rangle_t \approx \langle n_s \rangle_t \langle n_E \rangle_t$

$\Rightarrow 4 \text{ eqns} / 4 \text{ unknowns} \Rightarrow \text{can solve!}$

next time: when does this work?