$$\vec{n} = (n_S, n_E, n_{ES}, n_{S^*}) \qquad E + S \underset{k_u}{\overset{k_b}{\rightleftharpoons}} ES \xrightarrow{k_{cat}} E + S^*$$

$$n_S + n_{ES} + n_{S^*} = M_S$$

$$n_E + n_{ES} = M_E$$

$$M_S = 2, \quad M_E = 2$$

$$\begin{array}{rcccc} & n_S & n_E & n_{ES} & n_{S^*} \\ \vec{n} = & (2 & 2 & 0 & 0) \\ \text{binding} \downarrow & (1 & 1 & 1 & 0) \\ \text{catalysis} \downarrow & (1 & 2 & 0 & 1) \end{array}$$

all possible non-zero off-diag. entries of $\Omega_{\vec{n}\vec{m}}$ for $\vec{n} \neq \vec{m}$ (all ways $\underset{\text{start}}{\vec{m}} \to \underset{\text{end}}{\vec{n}}$)

i) binding

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

$\vec{m} = (m_S, m_E, m_{ES}, m_{S^*})$ start

if
$$n_S = m_S - 1$$
$$n_E = m_E - 1$$
$$n_{ES} = m_{ES} + 1$$
$$n_{S^*} = m_{S^*}$$
is true $\Rightarrow$

b/c there are m_E targets

$$\Omega_{\vec{n},\vec{m}} = \alpha_b K_S \frac{m_S}{V} m_E$$

cell volume

binding reaction (single target) $\sim \alpha_b K_S c$ ← conc. of searcher

$$= \tilde{k}_b m_S m_E$$

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

ii) unbinding

if
$$n_E = m_E + 1$$
$$n_S = m_S + 1$$
$$n_{ES} = m_{ES} - 1$$
$$n_{S^*} = m_{S^*}$$
is true $\Rightarrow \Omega_{\vec{n},\vec{m}} = k_u m_{ES}$

iii) catalysis

if
$$\begin{aligned} n_E &= m_E + 1 \\ n_S &= m_S \\ n_{ES} &= m_{ES} - 1 \\ n_{S*} &= m_{S*} + 1 \end{aligned}$$
is true $\Rightarrow \Omega_{\vec{n},\vec{m}} = k_{cat}\, m_{ES}$

portion of Ω:

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

diag: ~ make sure columns sum to zero

TRICK: recall $\langle i \rangle_t = \sum_i i\, p_i(t)$

derived $\dfrac{d\langle i \rangle_t}{dt} = \sum_{i,j} (j-i)\, \Omega_{ji}\, p_i(t)$

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

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

∘ ∘ ∘ 4 eqn's

plug in Ω : 1) $$\frac{d\langle n_s\rangle_t}{dt} = \sum_{\vec{m}} \Big[-\tilde{k}_b m_s m_E P_{\vec{m}}(t) + k_u m_{ES} P_{\vec{m}}(t) \Big]$$

∘ ∘ ∘

$\Rightarrow$ 4 eqn's : exact eqn's for avg's

1) $$\frac{d\langle n_s\rangle_t}{dt} = -\tilde{k}_b \langle n_s n_E\rangle_t + k_u \langle n_{ES}\rangle_t$$

2) $$\frac{d\langle n_E\rangle_t}{dt} = -\tilde{k}_b \langle n_s n_E\rangle_t + (k_u + k_{cat}) \cdot \langle n_{ES}\rangle_t$$

3) $$\frac{d\langle n_{ES}\rangle_t}{dt} = \tilde{k}_b \langle n_s n_E\rangle_t - (k_u + k_{cat}) \langle n_{ES}\rangle_t$$

4) $$\frac{d\langle n_s^*\rangle_t}{dt} = k_{cat} \langle n_{ES}\rangle_t$$

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

but only 4 equ's

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

note : gives 4 eqns & 4 unknowns $\Rightarrow$ can solve!

Why is this justified?

digression: imagine two variables describing a system, X and Y

joint prob. distribution $\mathcal{P}(X, Y)$
↳ frac. of pop. w/ value (X, Y)

marginal prob.

$$\mathcal{P}(X) = \sum_Y \mathcal{P}(X, Y)$$

$$\mathcal{P}(Y) = \sum_X \mathcal{P}(X, Y)$$

$$\langle X \rangle = \sum_{X,Y} X\, \mathcal{P}(X,Y) = \sum_X X\, \mathcal{P}(X)$$

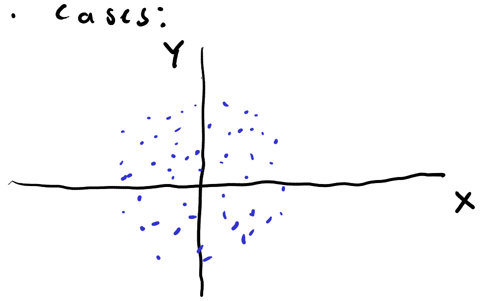
$$\langle Y \rangle = \sum_{X,Y} Y\, \mathcal{P}(X,Y) = \sum_Y Y\, \mathcal{P}(Y)$$

$$\langle XY \rangle = \sum_{X,Y} XY\, \mathcal{P}(X,Y)$$

in general $\langle XY \rangle \neq \langle X \rangle \langle Y \rangle$

when is $\langle XY \rangle \approx \langle X \rangle \langle Y \rangle$

diff. cases:

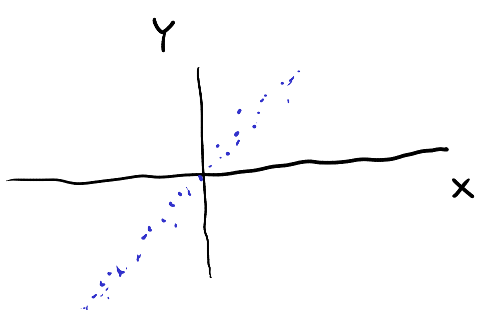


X + Y not strongly correlated

$$\mathcal{P}(X,Y) \approx \mathcal{P}(X)\,\mathcal{P}(Y)$$

$$\langle XY \rangle \approx \langle X \rangle \langle Y \rangle$$

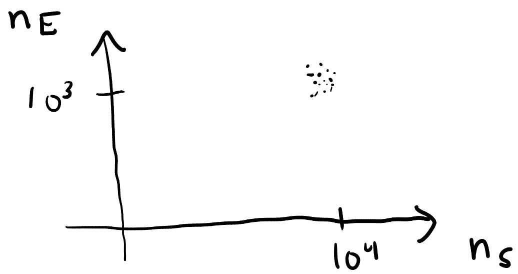
opposite case:



strong correlations

$$\langle XY \rangle \neq \langle X \rangle \langle Y \rangle$$

for chemical systems, mean number of chemical types (# mol's) is quite high ($10^2 - 10^5$ mol/cell) + fluctuations $\ll$ mean #



$\Rightarrow$ shape of cloud is irrelevant

$$\langle n_S n_E \rangle_t \approx \langle n_S \rangle_t \langle n_E \rangle_t$$

define concentrations: $c_S(t) = \dfrac{\langle n_S \rangle_t}{V}$

chemical kinetics

"law of mass action"

$$\begin{cases} \dfrac{dc_S}{dt} = -\tilde{k}_b V c_S c_E + k_u c_{ES} \\[2ex] \dfrac{dc_E}{dt} = -\tilde{k}_b V c_S c_E + (k_u + k_{cat}) c_{ES} \\[2ex] \dfrac{dc_{ES}}{dt} = \tilde{k}_b V c_S c_E - (k_u + k_{cat}) c_{ES} \\[2ex] \dfrac{dc_S^*}{dt} = k_{cat} c_{ES} \end{cases}$$

4 eqn's for c_E, c_S, c_{ES}, c_S^*