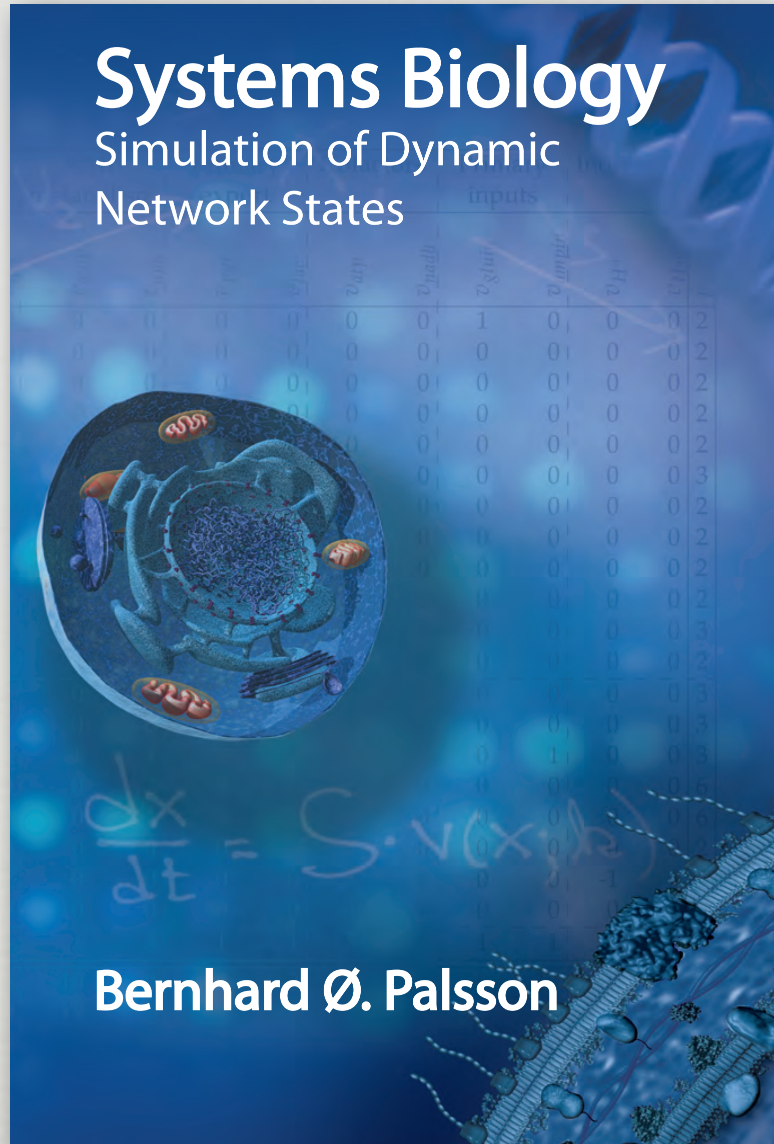


Lecture #4

Chemical Reactions

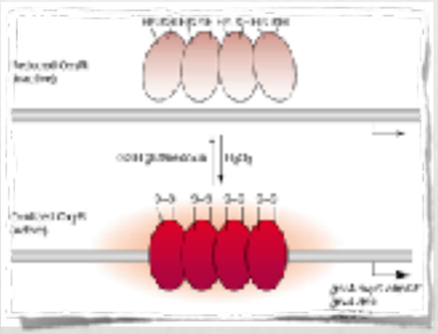
Basic Properties of Chemical Reactions

- Stoichiometry – counting molecules (chemistry)
- Relative rates – thermodynamics;
  - ✓ $K_{eq} = f(P, T)$
- Absolute rates – kinetics $\longrightarrow$ DNA sequence dependent
- Bi-linearity
  - ✓ X + Y <=> X:Y

Example: Hb assembly

$$\left.\begin{array}{l} \alpha+\beta \rightleftarrows \alpha\beta \\ \alpha+\beta \rightleftarrows \alpha\beta \end{array}\right\rangle \longrightarrow \alpha_2\beta_2$$

Example: TF binding



Pomposiello, P.J. and Demple, B. *Tibtech*, **19**: 109-114, (2001).

Cases Studied in Chapter 4

- Reversible linear reaction

$$x_1 \rightleftharpoons x_2$$

- Reversible bi-linear reaction

$$x_1 + x_2 \rightleftharpoons x_3$$

- Connected reversible linear reactions

$$x_1 \rightleftharpoons x_2 \rightarrow x_3 \rightleftharpoons x_4$$

- Connected reversible bi-linear reactions

$$x_1 + x_2 \rightleftharpoons x_3 \rightleftharpoons x_4 + x_5$$

Starting simple $x_1 \rightleftharpoons x_2$

THE REVERSIBLE LINEAR REACTION

The Reversible Reaction:
basic quantities

$$x_1 \underset{v_{-1}}{\overset{v_1}{\rightleftharpoons}} x_2$$

$$v_1 = k_1 x_1$$
$$v_{-1} = k_{-1} x_2$$

$$\mathbf{S} = \begin{array}{c} \\ \\ \end{array}\begin{array}{cc} \boldsymbol{v}_1 & \boldsymbol{v}_{-1} \\ \left(\begin{array}{c} -1 \\ 1 \end{array}\right. & \left.\begin{array}{c} 1 \\ -1 \end{array}\right) \end{array}\begin{array}{c} \\ x_1 \\ x_2 \end{array}, \quad \mathbf{v}(\mathbf{x}) = \begin{pmatrix} v_1(x_1) \\ v_{-1}(x_2) \end{pmatrix} = \begin{pmatrix} k_1 x_1 \\ k_{-1} x_2 \end{pmatrix}$$

$$K_{eq} = \frac{k_1}{k_{-1}} = \frac{x_2}{x_1}$$

$k_1$and $k_{-1}$are dependent

The Reversible Reaction: dynamic mass balances

$$\frac{d\mathbf{x}}{dt} = \mathbf{S}\mathbf{v}(\mathbf{x})$$

dynamic mass balances

$$\frac{d}{dt}\begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix}\begin{pmatrix} k_1 x_1 \\ k_{-1} x_2 \end{pmatrix}$$

for a linear system

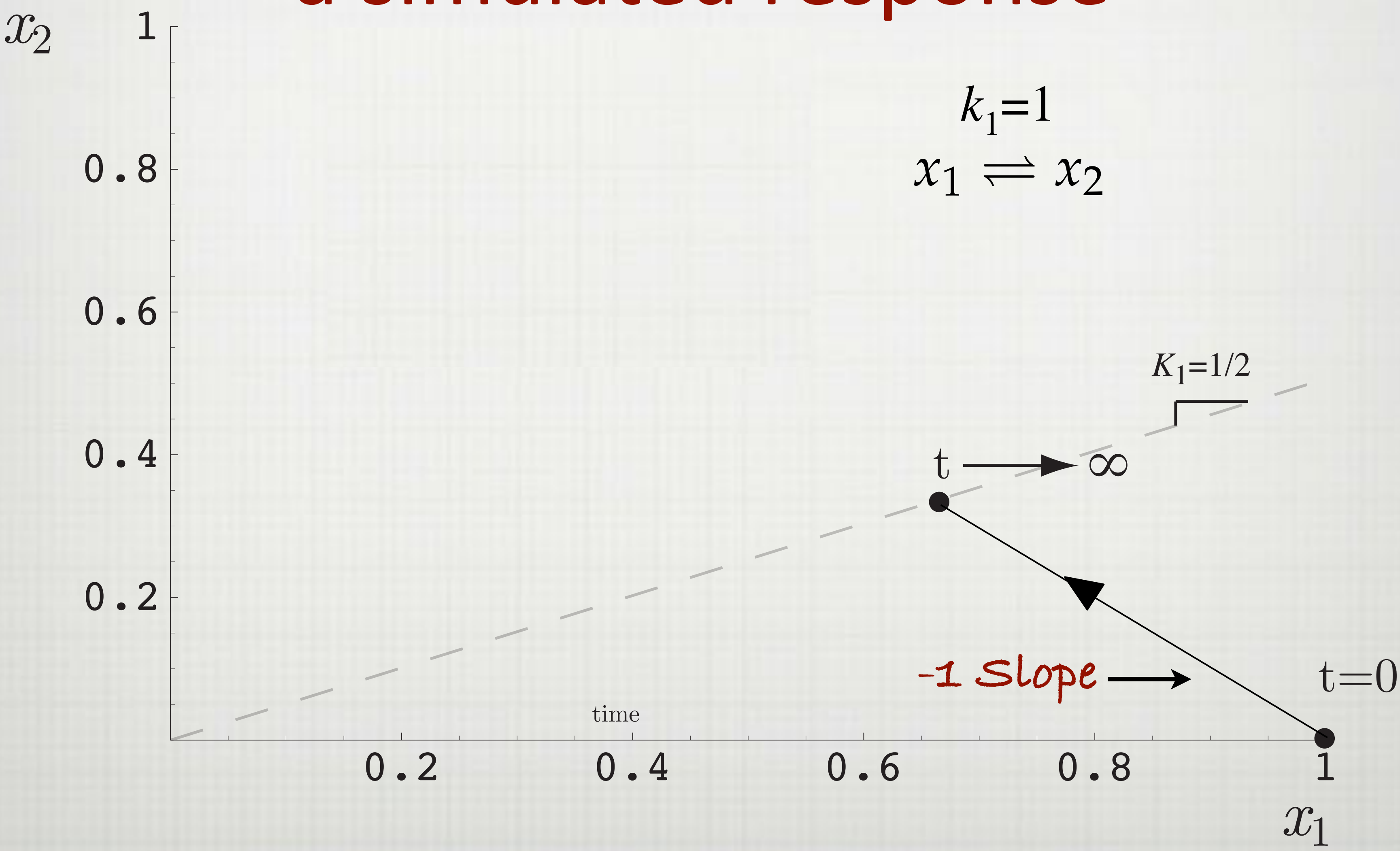
$$= \begin{pmatrix} -k_1 & k_{-1} \\ k_1 & -k_{-1} \end{pmatrix}\begin{pmatrix} x_1 \\ x_2 \end{pmatrix}$$

$$\frac{dx_1}{dt} = -k_1 x_1 + k_{-1} x_2 = -\frac{dx_2}{dt}$$

$$\frac{dx_2}{dt} = k_1 x_1 - k_{-1} x_2$$

$$\frac{d(x_1 + x_2)}{dt} = 0 \Rightarrow x_1 + x_2 = a$$

The Reversible Reaction: a simulated response



The Reversible Reaction:
forming aggregate variables

$$p_1 = (1,\ -1/K_{eq}) \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = x_1 - x_2/K_{eq} \longrightarrow 0 \text{ as } \frac{x_2}{x_1} \to K_{eq}$$

dis-equilibrium variable

$$p_2 = (1,1) \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = x_1 + x_2 = \text{ constant}$$

conservation variable

$$\text{fraction} = \frac{x_1}{x_1 + x_2} = \frac{x_1}{p_2}$$

the fraction of the pool p_2 that is in the form of x_1

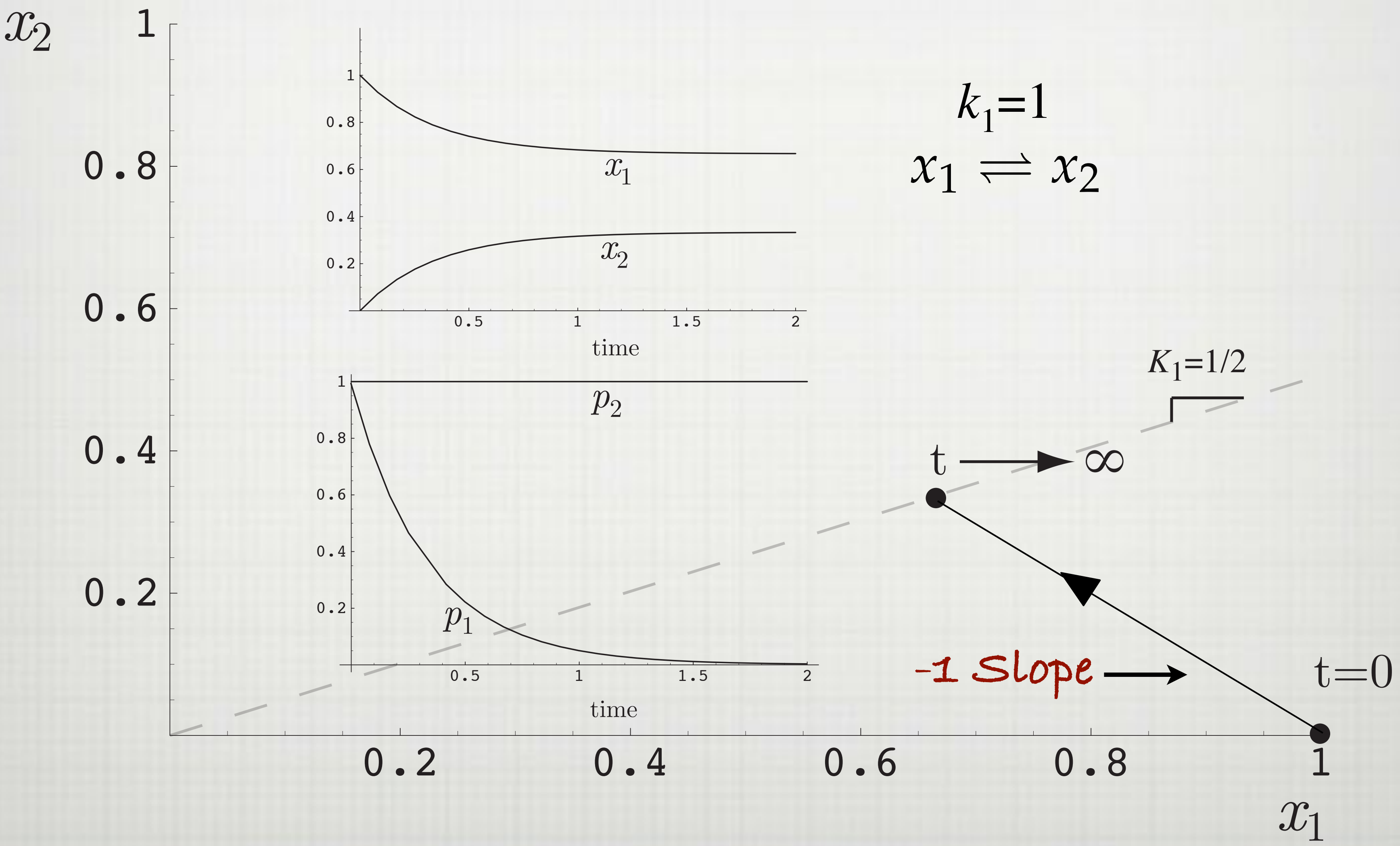
The Reversible Reaction:
basic equations in terms of pools

concentrations, x pooled variables, p

$$\mathbf{p}(t) = \mathbf{P}\mathbf{x}(t)$$

$$\begin{pmatrix} p_1(t) \\ p_2(t) \end{pmatrix} = \begin{pmatrix} 1 & -1/K_{eq} \\ 1 & 1 \end{pmatrix} \begin{pmatrix} x_1(t) \\ x_2(t) \end{pmatrix}$$

The Reversible Reaction: a simulated response



$$x_1 + x_2 \rightleftharpoons x_3$$

THE REVERSIBLE BI-LINEAR REACTION

The Bi-linear Reaction:
basic equations

$$\boxed{x_1 + x_2 \underset{v_{-1} = k_{-1} x_3}{\overset{v_1 = k_1 x_1 x_2}{\rightleftharpoons}} x_3}$$

$$\mathbf{S} = \begin{array}{c} \\ \\ \end{array}\begin{array}{cc} v_1 & v_{-1} \end{array}$$

$$\mathbf{S} = \begin{pmatrix} -1 & 1 \\ -1 & 1 \\ 1 & -1 \end{pmatrix}\begin{array}{c} x_1 \\ x_2 \\ x_3 \end{array} \; ; \quad \mathbf{v}(\mathbf{x}) = \begin{pmatrix} k_1 x_1 x_2 \\ k_{-1} x_3 \end{pmatrix} \quad \boxed{\frac{d\mathbf{x}}{dt} = \mathbf{S}\mathbf{v}(\mathbf{x})}$$

bi-linear term

$$\frac{dx_1}{dt} = -v_1 + v_{-1} = \underbrace{-\overbrace{k_1 x_1 x_2}^{\text{bi-linear term}} + k_{-1} x_3}_{= -v_{1,net}} = -k_1 \left(x_1 x_2 - x_3 / \underbrace{K_{eq}}_{K_{eq} = \frac{k_1}{k_{-1}} = \left.\frac{x_3}{x_1 x_2}\right|_{eq}} \right)$$

$$\frac{dx_2}{dt} = \frac{dx_1}{dt}$$

$$\frac{dx_3}{dt} = -\frac{dx_1}{dt}$$

$$\boxed{\frac{d(x_1 + x_3)}{dt} = \frac{d(x_2 + x_3)}{dt} = 0}$$

conservation variables

The Bi-linear Reaction:
forming aggregate variables

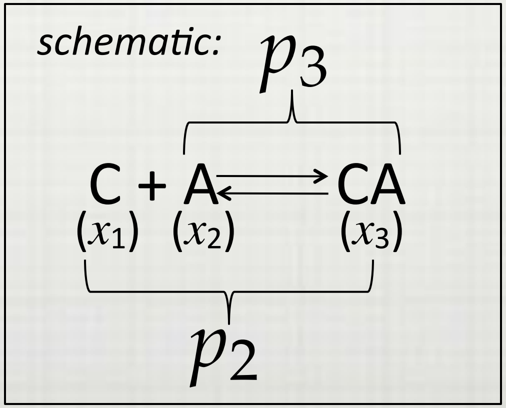
1) dis-equilibrium variable

$$p_1 = x_1 x_2 - x_3/K_{eq} \longrightarrow 0\;;\;\; \frac{x_3}{x_1 x_2} \rightarrow K_{eq}$$

2) conservation variables

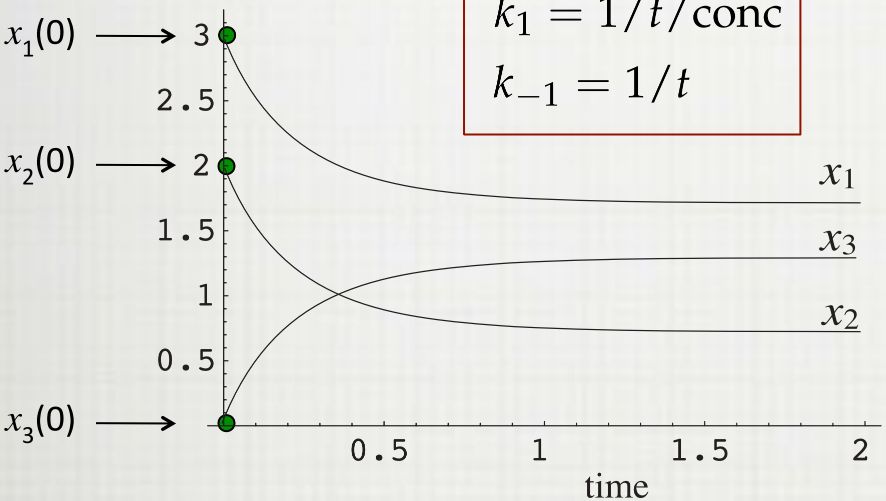
$$p_2 = x_1 + x_3$$

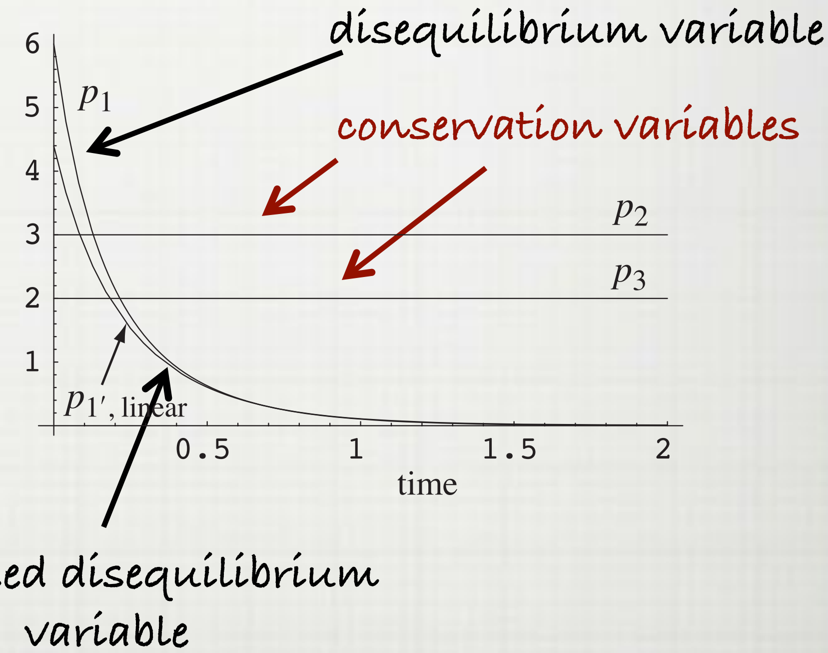
$$p_3 = x_2 + x_3$$



The Bi-linear Reaction:
a simulated response

$$k_1 = 1/t/\text{conc}$$
$$k_{-1} = 1/t$$





$$x_1 + x_2 \underset{v_{-1} = k_{-1}x_3}{\overset{v_1 = k_1 x_1 x_2}{\rightleftharpoons}} x_3$$

$$x_1 \rightleftharpoons x_2 \longrightarrow x_3 \rightleftharpoons x_4$$

THE CONNECTED REVERSIBLE LINEAR REACTIONS

Connected Linear Reactions:

basic equations

$$x_1 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} x_2 \xrightarrow{k_2} x_3 \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} x_4$$

fast *slow* *fast*

$$\mathbf{S} = \begin{array}{c} \\ \end{array}\begin{array}{ccccc} v_1 & v_{-1} & v_2 & v_3 & v_{-3} \\ \end{array}$$

$$\mathbf{S} = \left(\begin{array}{cc:c:cc} -1 & 1 & 0 & 0 & 0 \\ 1 & -1 & -1 & 0 & 0 \\ \hdashline 0 & 0 & 1 & -1 & 1 \\ 0 & 0 & 0 & 1 & -1 \end{array}\right)\begin{array}{c} x_1 \\ x_2 \\ x_3 \\ x_4 \end{array} \qquad \mathbf{v}(\mathbf{x}) = \begin{pmatrix} k_1 x_1 \\ k_{-1} x_2 \\ k_2 x_2 \\ k_3 x_3 \\ k_{-3} x_4 \end{pmatrix}$$

dynamic coupling

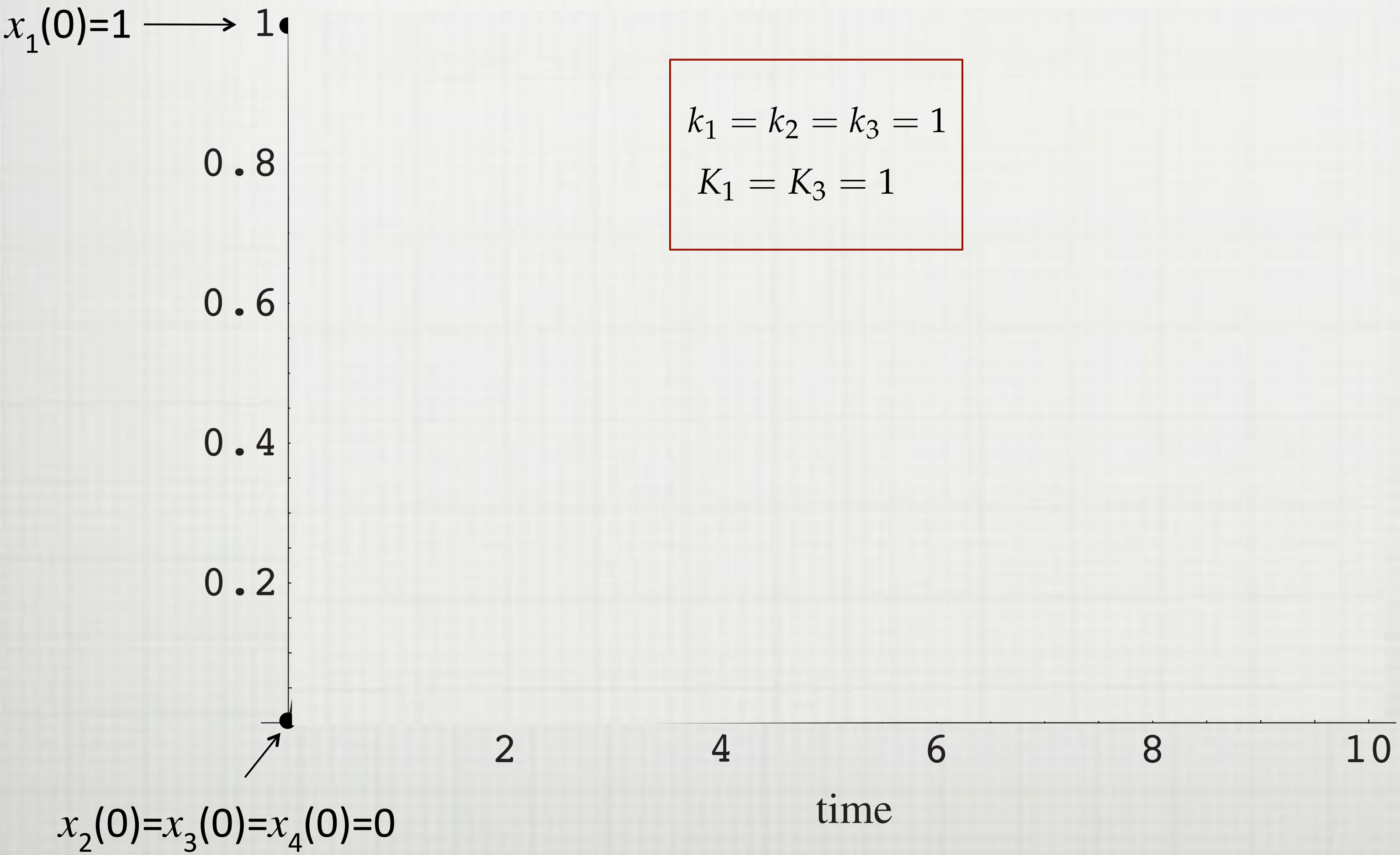
$$\frac{d\mathbf{x}}{dt} = \mathbf{S}\mathbf{v}(\mathbf{x}) = \mathbf{J}\mathbf{x}$$

simulate

Connected Linear Reactions:

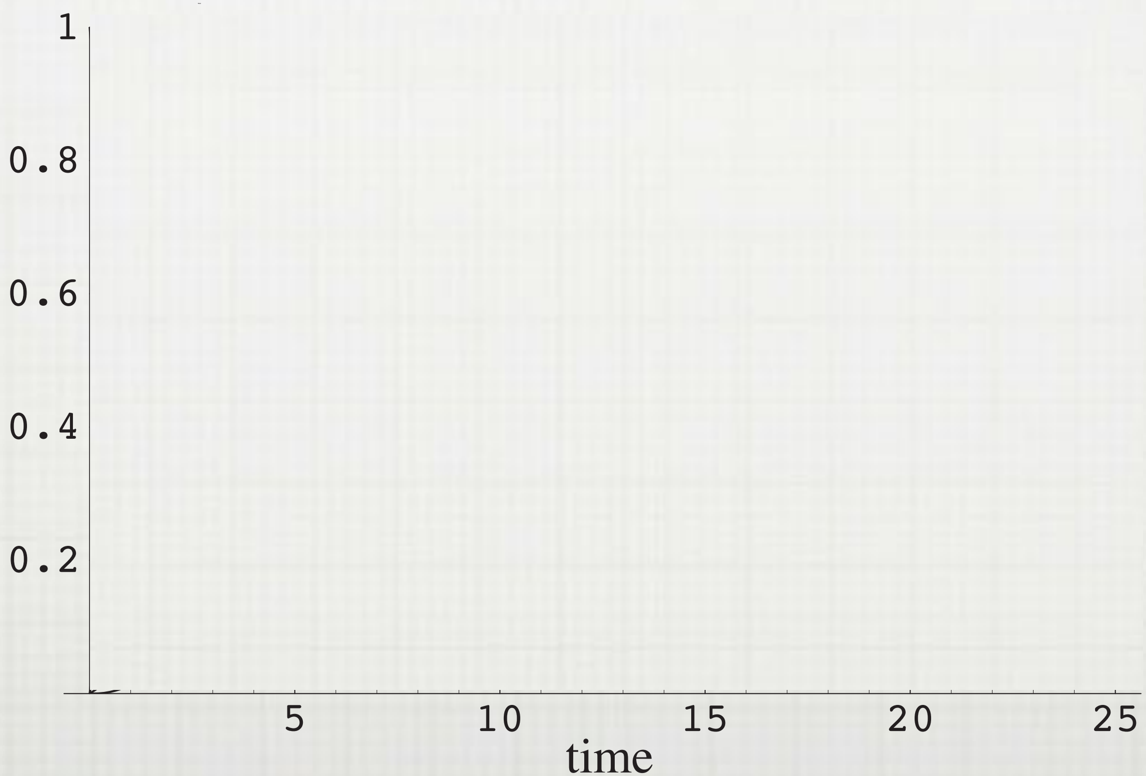
a simulated response

$$x_1 \rightleftharpoons x_2 \longrightarrow x_3 \rightleftharpoons x_4$$



Connected Linear Reactions:
simulated dynamic response

$$x_1 \rightleftharpoons x_2 \longrightarrow x_3 \rightleftharpoons x_4$$



$$K_1 = K_3$$
$$k_1 = 5k_2 = k_3$$

$$x_1 + x_2 \rightleftharpoons x_3 \rightleftharpoons x_4 + x_5$$

THE CONNECTED REVERSIBLE BI-LINEAR REACTION

The Bi-linear Reaction:

basic equations

$$x_1 + x_2 \underset{v_{-1}}{\overset{v_1}{\rightleftharpoons}} x_3 \underset{v_{-2}}{\overset{v_2}{\rightleftharpoons}} x_4 + x_5$$

if $x_2 = x_4$
this is the reversible form of the MM mechanism (Ch 5)

$$\mathbf{S} = \begin{array}{c} \\ \left(\begin{array}{cc|cc} -1 & 1 & 0 & 0 \\ -1 & 1 & 0 & 0 \\ \hline 1 & -1 & -1 & 1 \\ \hline 0 & 0 & 1 & -1 \\ 0 & 0 & 1 & -1 \end{array}\right) \end{array} \begin{array}{c} \\ x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \end{array}$$

(columns: v_1, v_{-1}, v_2, v_{-2})

coupling variable

$$\mathbf{v}(\mathbf{x}) = \begin{pmatrix} k_1 x_1 x_2 \\ k_{-1} x_3 \\ k_2 x_3 \\ k_{-1} x_4 x_5 \end{pmatrix}$$

block diagonal terms

$$\frac{d\mathbf{x}}{dt} = \mathbf{Sv}(\mathbf{x}) \xrightarrow[\textit{simulate}]{}$$

Conservation Pools

$$
\begin{array}{ccccccccc}
AB & + & C & \rightleftharpoons & ABC & \rightleftharpoons & A & + & BC \\
(x_1) & & (x_2) & & (x_3) & & (x_4) & & (x_5)
\end{array}
$$

$$
\begin{array}{cl}
\left(\begin{array}{ccccc}
1 & 0 & 1 & 1 & 0 \\
1 & 0 & 1 & 0 & 1 \\
0 & 1 & 1 & 0 & 1
\end{array}\right) &
\begin{array}{l}
\textit{Conservation of A} \\
\textit{Conservation of B} \\
\textit{Conservation of C}
\end{array}
\end{array}
$$

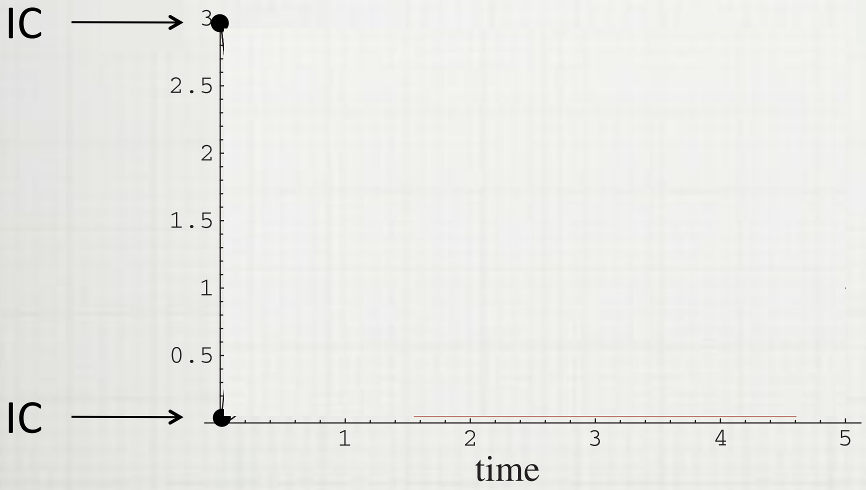
The 3 conservation quantities

Coupled Bi-linear Reactions:

a simulated response

$$x_1 + x_2 \rightleftharpoons x_3 \rightleftharpoons x_4 + x_5$$

Concentrations



$$\boxed{\begin{aligned} K_1 &= K_2 = 1 \\ k_1 &= k_3 = 1 \end{aligned}}$$

@ equilibrium: $x_{1,eq}x_{2,eq} = x_{3,eq} = x_{4,eq}x_{5,eq} \rightarrow x_{i,eq} = 1 \text{ , all } i$

Summary

- Chemical properties associated with chemical reactions are stoichiometry, thermodynamics, and kinetics. The first two are physicochemical properties, while the third can be biologically altered through enzyme action.
- The dynamic mass balances are readily formed for simple chemical reactions.
- Dynamic simulation and graphical representation is simple.
- Dynamics of chemical reactions can be represented in terms of aggregate variables.
- Fast dis-equilibrium pools can be relaxed.
- Removing a dynamic variable reduces the dynamic dimension of the description.
- Dynamic coupling can be through columns or rows in **S**