Faculty of Science

Lecture 6. Part II. Linear Elimination

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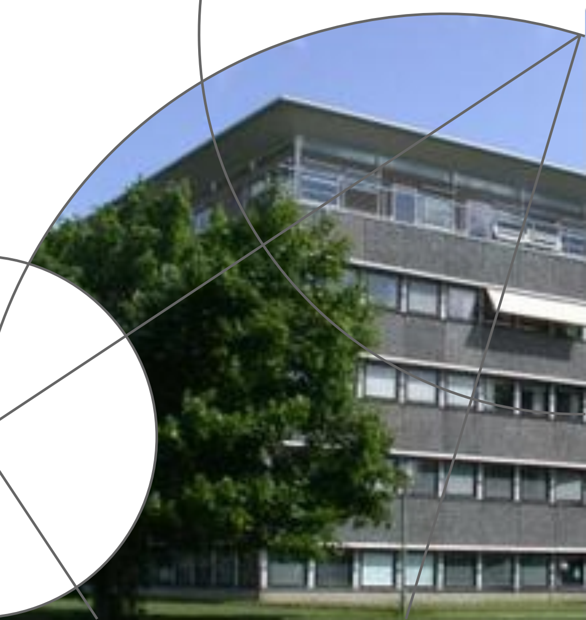


A hybrid histidine kinase

We consider a histidine kinase HK that can be phosphorylated at two sites, and which transfers the phosphate group to an additional protein Htp that has one phosphorylation site.
We have 6 species:

$$X_1 = \mathrm{HK}_{00}, \quad \mathrm{X}_2 = \mathrm{HK}_{\mathrm{p0}}, \quad \mathrm{X}_3 = \mathrm{HK}_{\mathrm{0p}}, \quad \mathrm{X}_4 = \mathrm{HK}_{\mathrm{pp}}$$

$$X_5 = \mathrm{Htp}, \quad X_6 = \mathrm{Htp}_{\mathrm{p}}$$

The reactions of the network are:

$$\mathrm{HK}_{00} \xrightarrow{\kappa_1} \mathrm{HK}_{\mathrm{p0}} \xrightarrow{\kappa_2} \mathrm{HK}_{\mathrm{0p}} \xrightarrow{\kappa_3} \mathrm{HK}_{\mathrm{pp}} \qquad X_1 \xrightarrow{\kappa_1} X_2 \xrightarrow{\kappa_2} X_3 \xrightarrow{\kappa_3} X_4$$

$$\mathrm{HK}_{\mathrm{0p}} + \mathrm{Htp} \xrightarrow{\kappa_4} \mathrm{HK}_{00} + \mathrm{Htp}_{\mathrm{p}} \qquad X_3 + X_5 \xrightarrow{\kappa_4} X_1 + X_6$$

$$\mathrm{HK}_{\mathrm{pp}} + \mathrm{Htp} \xrightarrow{\kappa_5} \mathrm{HK}_{\mathrm{p0}} + \mathrm{Htp}_{\mathrm{p}} \qquad X_4 + X_5 \xrightarrow{\kappa_5} X_2 + X_6$$

$$\mathrm{Htp}_{\mathrm{p}} \xrightarrow{\kappa_6} \mathrm{Htp} \qquad X_6 \xrightarrow{\kappa_6} X_5$$

Finding a Gröbner basis

System of steady states in stoichiometric compatibility classes $(C_{\kappa,T})$:

$$
\begin{aligned}
0 &= \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
0 &= \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 & T_1 &= x_1 + x_2 + x_3 + x_4 \\
0 &= \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 & T_2 &= x_5 + x_6 \\
0 &= \kappa_6 x_6 - \kappa_4 x_3 x_5 - \kappa_5 x_4 x_5
\end{aligned}
$$

$$
\begin{gathered}
X_1 \xrightarrow{\kappa_1} X_2 \xrightarrow{\kappa_2} X_3 \xrightarrow{\kappa_3} X_4 \\
X_3 + X_5 \xrightarrow{\kappa_4} X_1 + X_6 \\
X_4 + X_5 \xrightarrow{\kappa_5} X_2 + X_6 \\
X_6 \xrightarrow{\kappa_6} X_5
\end{gathered}
$$

Finding a Gröbner basis

System of steady states in stoichiometric compatibility classes ($C_{\kappa,T}$):

$$\begin{aligned}
0 &= \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
0 &= \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \\
0 &= \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \\
0 &= \kappa_6 x_6 - \kappa_4 x_3 x_5 - \kappa_5 x_4 x_5
\end{aligned}$$

$$T_1 = x_1 + x_2 + x_3 + x_4 \qquad T_2 = x_5 + x_6$$

$$X_1 \xrightarrow{\kappa_1} X_2 \xrightarrow{\kappa_2} X_3 \xrightarrow{\kappa_3} X_4$$
$$X_3 + X_5 \xrightarrow{\kappa_4} X_1 + X_6$$
$$X_4 + X_5 \xrightarrow{\kappa_5} X_2 + X_6$$
$$X_6 \xrightarrow{\kappa_6} X_5$$

Gröbner basis, lexicographic order in $x_1, x_2, x_3, x_4, x_6, x_5$:

$$\begin{aligned}
p_1(x_5) = {} & (\kappa_1+\kappa_2)\kappa_4\kappa_5\kappa_6 x_5^3 + \big(\kappa_1(T_1\kappa_2\kappa_4 + \kappa_2\kappa_6 + \kappa_3\kappa_6) - T_2(\kappa_1+\kappa_2)\kappa_4\kappa_6\big)\kappa_5 x_5^2 \\
& + \big(\kappa_1\kappa_2\kappa_3(T_1\kappa_5 + \kappa_6) - T_2\kappa_1(\kappa_2+\kappa_3)\kappa_5\kappa_6\big)x_5 - T_2\kappa_1\kappa_2\kappa_3\kappa_6 \\
p_6(x_1, x_5) = {} & \kappa_1\kappa_2\big(\kappa_1(\kappa_4-\kappa_5) + \kappa_3\kappa_5\big)x_1 + (\kappa_1+\kappa_2)\kappa_4\kappa_5\kappa_6 x_5^2 \\
& + \kappa_4\big((T_1\kappa_5+\kappa_6)\kappa_1\kappa_2 - T_2(\kappa_1+\kappa_2)\kappa_5\kappa_6\big)x_5 - T_2\kappa_1\kappa_2\kappa_4\kappa_6
\end{aligned}$$

Finding a Gröbner basis

System of steady states in stoichiometric compatibility classes ($C_{\kappa,T}$):

$$X_1 \xrightarrow{\kappa_1} X_2 \xrightarrow{\kappa_2} X_3 \xrightarrow{\kappa_3} X_4$$
$$X_3 + X_5 \xrightarrow{\kappa_4} X_1 + X_6$$
$$X_4 + X_5 \xrightarrow{\kappa_5} X_2 + X_6$$
$$X_6 \xrightarrow{\kappa_6} X_5$$

$$\begin{aligned} 0 &= \kappa_4 x_3 x_5 - \kappa_1 x_1 \\ 0 &= \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \qquad T_1 = x_1 + x_2 + x_3 + x_4 \\ 0 &= \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \qquad T_2 = x_5 + x_6 \\ 0 &= \kappa_6 x_6 - \kappa_4 x_3 x_5 - \kappa_5 x_4 x_5 \end{aligned}$$

Gröbner basis, lexicographic order in $x_1, x_2, x_3, x_4, x_6, x_5$:

$$\begin{aligned} p_1(x_5) &= (\kappa_1+\kappa_2)\kappa_4\kappa_5\kappa_6 x_5^3 + \big(\kappa_1(T_1\kappa_2\kappa_4 + \kappa_2\kappa_6 + \kappa_3\kappa_6) - T_2(\kappa_1+\kappa_2)\kappa_4\kappa_6\big)\kappa_5 x_5^2 \\ &\quad + \big(\kappa_1\kappa_2\kappa_3(T_1\kappa_5+\kappa_6) - T_2\kappa_1(\kappa_2+\kappa_3)\kappa_5\kappa_6\big)x_5 - T_2\kappa_1\kappa_2\kappa_3\kappa_6 \\ p_6(x_1,x_5) &= \kappa_1\kappa_2\big(\kappa_1(\kappa_4-\kappa_5)+\kappa_3\kappa_5\big)x_1 + (\kappa_1+\kappa_2)\kappa_4\kappa_5\kappa_6 x_5^2 \\ &\quad + \kappa_4\big((T_1\kappa_5+\kappa_6)\kappa_1\kappa_2 - T_2(\kappa_1+\kappa_2)\kappa_5\kappa_6\big)x_5 - T_2\kappa_1\kappa_2\kappa_4\kappa_6 \end{aligned}$$

From p_6 we obtain:

$$x_1 = \frac{(\kappa_1+\kappa_2)\kappa_4\kappa_5\kappa_6 x_5^2 + \kappa_4\big((T_1\kappa_5+\kappa_6)\kappa_1\kappa_2 - T_2(\kappa_1+\kappa_2)\kappa_5\kappa_6\big)x_5 - T_2\kappa_1\kappa_2\kappa_4\kappa_6}{\kappa_1\kappa_2\big(\kappa_1(\kappa_5-\kappa_4)+\kappa_3\kappa_5\big)}$$

When is this positive?

Manual approach

Solving a linear system in x_1, x_2, x_3, x_4, x_6:

$$
\begin{aligned}
x_1 &= \frac{\kappa_2\kappa_4\kappa_5 T_1 x_5^2}{(\kappa_1+\kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2+\kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3} \\
x_2 &= \frac{\kappa_1(\kappa_4 x_5+\kappa_3)\kappa_5 T_1 x_5}{(\kappa_1+\kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2+\kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3} \\
x_3 &= \frac{\kappa_1\kappa_2\kappa_5 T_1 x_5}{(\kappa_1+\kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2+\kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3} \\
x_4 &= \frac{\kappa_1\kappa_2\kappa_3 T_1}{(\kappa_1+\kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2+\kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3} \\
x_6 &= T_2 - x_5.
\end{aligned}
$$

$$
\begin{aligned}
0 &= \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
0 &= \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \\
0 &= \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \\
0 &= \sout{\kappa_6 x_6 - \kappa_4 x_3 x_5 - \kappa_5 x_4 x_5} \\
T_1 &= x_1 + x_2 + x_3 + x_4 \\
T_2 &= x_5 + x_6.
\end{aligned}
$$

Manual approach

Solving a linear system in x_1, x_2, x_3, x_4, x_6:

$$x_1 = \frac{\kappa_2\kappa_4\kappa_5 T_1 x_5^2}{(\kappa_1 + \kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2+\kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3}$$

$$x_2 = \frac{\kappa_1(\kappa_4 x_5 + \kappa_3)\kappa_5 T_1 x_5}{(\kappa_1 + \kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2+\kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3}$$

$$x_3 = \frac{\kappa_1\kappa_2\kappa_5 T_1 x_5}{(\kappa_1 + \kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2+\kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3}$$

$$x_4 = \frac{\kappa_1\kappa_2\kappa_3 T_1}{(\kappa_1 + \kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2+\kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3}$$

$$x_6 = T_2 - x_5.$$

$$0 = \kappa_4 x_3 x_5 - \kappa_1 x_1$$

$$0 = \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2$$

$$0 = \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5$$

$0 =$ ~~$\kappa_6 x_6 - \kappa_4 x_3 x_5 - \kappa_5 x_4 x_5$~~

$$T_1 = x_1 + x_2 + x_3 + x_4$$

$$T_2 = x_5 + x_6.$$

These expressions into the remaining equation give the same polynomial:

$$p_1(x_5) = (\kappa_1+\kappa_2)\kappa_4\kappa_5\kappa_6 x_5^3 + \big(\kappa_1(T_1\kappa_2\kappa_4 + \kappa_2\kappa_6 + \kappa_3\kappa_6) - T_2(\kappa_1+\kappa_2)\kappa_4\kappa_6\big)\kappa_5 x_5^2$$
$$+ \big(\kappa_1\kappa_2\kappa_3(T_1\kappa_5 + \kappa_6) - T_2\kappa_1(\kappa_2+\kappa_3)\kappa_5\kappa_6\big)x_5 - T_2\kappa_1\kappa_2\kappa_3\kappa_6.$$

$\{$Positive roots of p_1 smaller than $T_2\} \leftrightarrow \{$positive steady states$\}$

Linear Elimination

Let's take a look at part of the linear system:

$$
\begin{aligned}
(\dot{x}_1 = 0) \quad 0 &= \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
(\dot{x}_2 = 0) \quad 0 &= \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \\
(\dot{x}_3 = 0) \quad 0 &= \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \\
(\dot{x}_4 = 0) \quad 0 &= \kappa_3 x_3 - \kappa_5 x_4 x_5 \\
T_1 &= x_1 + x_2 + x_3 + x_4
\end{aligned}
$$

$$
\begin{gathered}
X_1 \xrightarrow{\kappa_1} X_2 \xrightarrow{\kappa_2} X_3 \xrightarrow{\kappa_3} X_4 \\
X_3 + X_5 \xrightarrow{\kappa_4} X_1 + X_6 \\
X_4 + X_5 \xrightarrow{\kappa_5} X_2 + X_6 \\
X_6 \xrightarrow{\kappa_6} X_5
\end{gathered}
$$

Can you see why the system is linear?

Linear Elimination

Let's take a look at part of the linear system:

$$
\begin{aligned}
(\dot{x}_1 = 0) \quad 0 &= \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
(\dot{x}_2 = 0) \quad 0 &= \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \\
(\dot{x}_3 = 0) \quad 0 &= \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \\
(\dot{x}_4 = 0) \quad 0 &= \kappa_3 x_3 - \kappa_5 x_4 x_5 \\
T_1 &= x_1 + x_2 + x_3 + x_4
\end{aligned}
$$

$$
\begin{gathered}
X_1 \xrightarrow{\kappa_1} X_2 \xrightarrow{\kappa_2} X_3 \xrightarrow{\kappa_3} X_4 \\
X_3 + X_5 \xrightarrow{\kappa_4} X_1 + X_6 \\
X_4 + X_5 \xrightarrow{\kappa_5} X_2 + X_6 \\
X_6 \xrightarrow{\kappa_6} X_5
\end{gathered}
$$

Can you see why the system is linear?

Consider the steady state equations of the 4 species X_1, X_2, X_3, X_4, which do not interact with each other, and write it as a linear system in x_1, x_2, x_3, x_4:

$$
\begin{pmatrix}
-\kappa_1 & 0 & \kappa_4 x_5 & 0 \\
\kappa_1 & -\kappa_2 & 0 & \kappa_5 x_5 \\
0 & \kappa_2 & -\kappa_3 - \kappa_4 x_5 & 0 \\
0 & 0 & \kappa_3 & -\kappa_5 x_5
\end{pmatrix}
\begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix}
=
\begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}
$$

Linear Elimination

Let's take a look at part of the linear system:

$$\begin{aligned}
(\dot{x}_1 = 0) \quad & 0 = \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
(\dot{x}_2 = 0) \quad & 0 = \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \\
(\dot{x}_3 = 0) \quad & 0 = \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \\
(\dot{x}_4 = 0) \quad & 0 = \kappa_3 x_3 - \kappa_5 x_4 x_5 \\
& T_1 = x_1 + x_2 + x_3 + x_4
\end{aligned}$$

$$\begin{gathered}
X_1 \xrightarrow{\kappa_1} X_2 \xrightarrow{\kappa_2} X_3 \xrightarrow{\kappa_3} X_4 \\
X_3 + X_5 \xrightarrow{\kappa_4} X_1 + X_6 \\
X_4 + X_5 \xrightarrow{\kappa_5} X_2 + X_6 \\
X_6 \xrightarrow{\kappa_6} X_5
\end{gathered}$$

Can you see why the system is linear?

Consider the steady state equations of the 4 species X_1, X_2, X_3, X_4, which do not interact with each other, and write it as a linear system in x_1, x_2, x_3, x_4:

$$\begin{pmatrix} -\kappa_1 & 0 & \kappa_4 x_5 & 0 \\ \kappa_1 & -\kappa_2 & 0 & \kappa_5 x_5 \\ 0 & \kappa_2 & -\kappa_3 - \kappa_4 x_5 & 0 \\ 0 & 0 & \kappa_3 & -\kappa_5 x_5 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

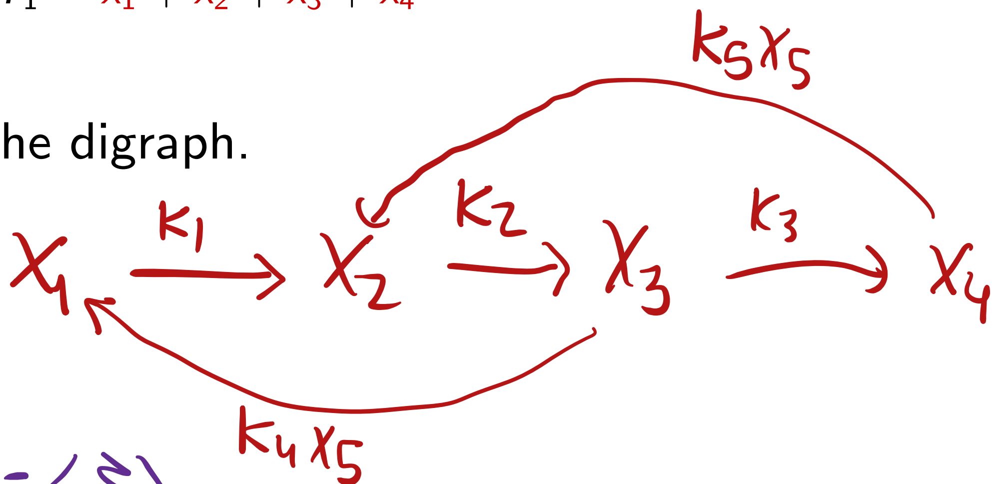
Is this matrix a Laplacian matrix of a labeled digraph with positive labels?

Linear Elimination

$$
\begin{aligned}
(\dot{x}_1 = 0) \quad & 0 = \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
(\dot{x}_2 = 0) \quad & 0 = \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \\
(\dot{x}_3 = 0) \quad & 0 = \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \\
(\dot{x}_4 = 0) \quad & 0 = \kappa_3 x_3 - \kappa_5 x_4 x_5 \\
& T_1 = x_1 + x_2 + x_3 + x_4
\end{aligned}
$$

$$
\begin{pmatrix} -\kappa_1 & 0 & \kappa_4 x_5 & 0 \\ \kappa_1 & -\kappa_2 & 0 & \kappa_5 x_5 \\ 0 & \kappa_2 & -\kappa_3 - \kappa_4 x_5 & 0 \\ 0 & 0 & \kappa_3 & -\kappa_5 x_5 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}
$$

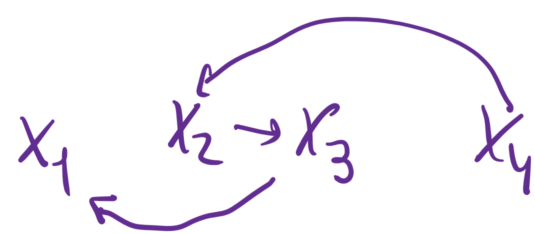
We draw the digraph.



$\ker A_\kappa = \langle \xi \rangle$

$\xi_1 = \kappa_4 x_5 \cdot \kappa_2 \cdot \kappa_5 x_5$

$= \kappa_2 \kappa_4 \kappa_5 x_5^2$



Linear Elimination

$$\begin{aligned}
(\dot{x}_1 = 0) \quad & 0 = \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
(\dot{x}_2 = 0) \quad & 0 = \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \\
(\dot{x}_3 = 0) \quad & 0 = \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \\
(\dot{x}_4 = 0) \quad & 0 = \kappa_3 x_3 - \kappa_5 x_4 x_5 \\
& T_1 = x_1 + x_2 + x_3 + x_4
\end{aligned}$$

$$\begin{pmatrix} -\kappa_1 & 0 & \kappa_4 x_5 & 0 \\ \kappa_1 & -\kappa_2 & 0 & \kappa_5 x_5 \\ 0 & \kappa_2 & -\kappa_3 - \kappa_4 x_5 & 0 \\ 0 & 0 & \kappa_3 & -\kappa_5 x_5 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

Any solution is of the form $\lambda\xi$ with

$$\xi = \left(\kappa_2\kappa_4\kappa_5 x_5^2, \kappa_1\kappa_5 x_5(\kappa_4 x_5 + \kappa_3), \kappa_1\kappa_2\kappa_5 x_5, \kappa_1\kappa_2\kappa_3\right)$$

Linear Elimination

$$
\begin{aligned}
(\dot{x}_1 = 0) \quad & 0 = \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
(\dot{x}_2 = 0) \quad & 0 = \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \\
(\dot{x}_3 = 0) \quad & 0 = \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \\
(\dot{x}_4 = 0) \quad & 0 = \kappa_3 x_3 - \kappa_5 x_4 x_5 \\
& T_1 = x_1 + x_2 + x_3 + x_4
\end{aligned}
$$

$$
\begin{pmatrix} -\kappa_1 & 0 & \kappa_4 x_5 & 0 \\ \kappa_1 & -\kappa_2 & 0 & \kappa_5 x_5 \\ 0 & \kappa_2 & -\kappa_3 - \kappa_4 x_5 & 0 \\ 0 & 0 & \kappa_3 & -\kappa_5 x_5 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}
$$

Any solution is of the form $\lambda\xi$ with

$$
\xi = \big(\kappa_2\kappa_4\kappa_5 x_5^2, \kappa_1\kappa_5 x_5(\kappa_4 x_5 + \kappa_3), \kappa_1\kappa_2\kappa_5 x_5, \kappa_1\kappa_2\kappa_3\big)
$$

But we have the extra equation $T_1 = x_1 + x_2 + x_3 + x_4$:

$$
T_1 = \lambda\big(\kappa_2\kappa_4\kappa_5 x_5^2 + \kappa_1\kappa_5 x_5(\kappa_4 x_5 + \kappa_3) + \kappa_1\kappa_2\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3\big)
$$

so

$$
\lambda = \frac{T_1}{\kappa_2\kappa_4\kappa_5 x_5^2 + \kappa_1\kappa_5 x_5(\kappa_4 x_5 + \kappa_3) + \kappa_1\kappa_2\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3}
$$

Linear Elimination

$$
\begin{aligned}
(\dot{x}_1 = 0) \quad & 0 = \kappa_4 x_3 x_5 - \kappa_1 x_1 \\
(\dot{x}_2 = 0) \quad & 0 = \kappa_5 x_4 x_5 + \kappa_1 x_1 - \kappa_2 x_2 \\
(\dot{x}_3 = 0) \quad & 0 = \kappa_2 x_2 - \kappa_3 x_3 - \kappa_4 x_3 x_5 \\
(\dot{x}_4 = 0) \quad & 0 = \kappa_3 x_3 - \kappa_5 x_4 x_5 \\
& T_1 = x_1 + x_2 + x_3 + x_4
\end{aligned}
$$

$$
\begin{pmatrix} -\kappa_1 & 0 & \kappa_4 x_5 & 0 \\ \kappa_1 & -\kappa_2 & 0 & \kappa_5 x_5 \\ 0 & \kappa_2 & -\kappa_3 - \kappa_4 x_5 & 0 \\ 0 & 0 & \kappa_3 & -\kappa_5 x_5 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}
$$

Any solution is of the form $\lambda\xi$ with

$$\xi = (\kappa_2\kappa_4\kappa_5 x_5^2, \kappa_1\kappa_5 x_5(\kappa_4 x_5 + \kappa_3), \kappa_1\kappa_2\kappa_5 x_5, \kappa_1\kappa_2\kappa_3)$$

But we have the extra equation $T_1 = x_1 + x_2 + x_3 + x_4$:

$$T_1 = \lambda(\kappa_2\kappa_4\kappa_5 x_5^2 + \kappa_1\kappa_5 x_5(\kappa_4 x_5 + \kappa_3) + \kappa_1\kappa_2\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3)$$

so

$$\lambda = \frac{T_1}{\kappa_2\kappa_4\kappa_5 x_5^2 + \kappa_1\kappa_5 x_5(\kappa_4 x_5 + \kappa_3) + \kappa_1\kappa_2\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3}$$

We recover

$$x_1 = \frac{\kappa_2\kappa_4\kappa_5 T_1 x_5^2}{(\kappa_1 + \kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2 + \kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3} \qquad x_2 = \frac{\kappa_1(\kappa_4 x_5 + \kappa_3)\kappa_5 T_1 x_5}{(\kappa_1 + \kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2 + \kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3}$$

$$x_3 = \frac{\kappa_1\kappa_2\kappa_5 T_1 x_5}{(\kappa_1 + \kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2 + \kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3} \qquad x_4 = \frac{\kappa_1\kappa_2\kappa_3 T_1}{(\kappa_1 + \kappa_2\kappa_4)\kappa_5 x_5^2 + \kappa_1(\kappa_2 + \kappa_3)\kappa_5 x_5 + \kappa_1\kappa_2\kappa_3}$$

Another example

$$0 \underset{\kappa_2}{\overset{\kappa_1}{\rightleftharpoons}} X_1 \qquad X_1 + X_3 \xrightarrow{\kappa_3} X_2 \qquad X_2 + X_4 \xrightarrow{\kappa_6} X_1$$

$$0 \xrightarrow{\kappa_7} X_3 \qquad 0 \xrightarrow{\kappa_8} X_4.$$

Non-interacting sets?

Another example

$$0 \underset{\kappa_2}{\overset{\kappa_1}{\rightleftharpoons}} X_1 \qquad X_1 + X_3 \xrightarrow{\kappa_3} X_2 \qquad X_2 + X_4 \xrightarrow{\kappa_6} X_1$$

$$0 \xrightarrow{\kappa_7} X_3 \qquad 0 \xrightarrow{\kappa_8} X_4.$$

Non-interacting sets? For example $\{X_1, X_2\}$:

$$\begin{aligned} \dot{x}_1 &= -\kappa_1 x_1 x_3 + \kappa_2 x_2 x_4 + \kappa_3 - \kappa_4 x_1 \\ \dot{x}_2 &= \kappa_1 x_1 x_3 - \kappa_2 x_2 x_4. \end{aligned}$$

At steady state ($\dot{x}_1 = \dot{x}_2 = 0$):

$$\begin{pmatrix} -\kappa_1 x_3 - \kappa_4 & \kappa_2 x_4 & \kappa_3 \\ \kappa_1 x_3 & -\kappa_2 x_4 & 0 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ 1 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

Is the coefficient matrix a Laplacian matrix of a digraph?

Another example

$$0 \underset{\kappa_2}{\overset{\kappa_1}{\rightleftharpoons}} X_1 \qquad X_1 + X_3 \xrightarrow{\kappa_3} X_2 \qquad X_2 + X_4 \xrightarrow{\kappa_6} X_1$$

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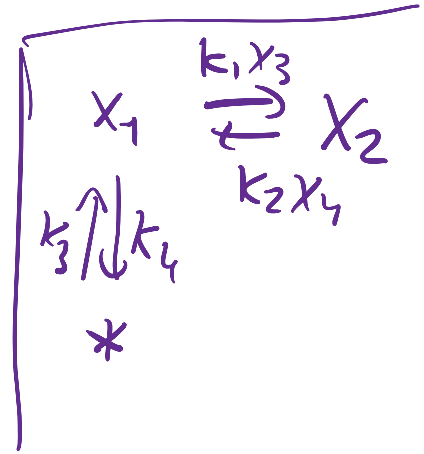

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MT-theorem: any vector in the kernel of A_κ is a multiple of (ξ_1, ξ_2, ξ_3) with ξ_i positive. As we want $\xi_3 = 1$:

$$x_1 = \frac{\xi_1}{\xi_3}, \qquad x_2 = \frac{\xi_2}{\xi_3}$$

at any steady state.

The linear elimination theory

Let G be a reaction network with set of species $\mathcal{X} = \{X_1, \dots, X_n\}$.

Definition: A subset

$$U = \{X_1, \dots, X_p\} \subseteq \mathcal{X}$$

is said to be non-interacting, if no pair of species in U appear on the same side of a reaction and they all appear with stoichiometric coefficient equal to one.

Given a non-interacting set, the system of steady state equations $\dot{x}_1 = 0, \dots, \dot{x}_p = 0$ is linear in $x_1, \dots, x_p$.

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Case 1: $x_1 + \cdots + x_p$ is a conservation law.
The coefficient matrix of the linear system is the Laplacian matrix of the labeled digraph G_U with

- Set of nodes: $\{X_1, \dots, X_p\}$
- An edge $X_i \xrightarrow{\lambda} X_j$, $i \neq j$, for each reaction

$$X_i + \sum_{\ell=p+1}^{n} \alpha_\ell X_\ell \xrightarrow{\kappa} X_j + \sum_{\ell=p+1}^{n} \beta_\ell X_\ell,$$

where $\lambda = \kappa\, x_{p+1}^{\alpha_{p+1}} \cdots x_n^{\alpha_n}$.

The linear elimination theory

Case 2: $x_1 + \cdots + x_p$ is not a conservation law.
The coefficient matrix of the linear system agrees with the first p rows of the Laplacian matrix of the labeled digraph G_U with

- Set of nodes: $\{X_1, \ldots, X_p, \star\}$
- An edge $X_i \xrightarrow{\lambda} X_j$, $i \neq j$, for each reaction

$$X_i + \sum_{\ell=p+1}^{n} \alpha_\ell X_\ell \xrightarrow{\kappa} X_j + \sum_{\ell=p+1}^{n} \beta_\ell X_\ell.$$

- An edge $X_i \xrightarrow{\lambda} \star$, for each reaction

$$X_i + \sum_{\ell=p+1}^{n} \alpha_\ell X_\ell \xrightarrow{\kappa} \sum_{\ell=p+1}^{n} \beta_\ell X_\ell.$$

- An edge $\star \xrightarrow{\lambda} X_i$, for each reaction

$$\sum_{\ell=p+1}^{n} \alpha_\ell X_\ell \xrightarrow{\kappa} X_i + \sum_{\ell=p+1}^{n} \beta_\ell X_\ell.$$

- In all cases, $\lambda = \kappa\, x_{p+1}^{\alpha_{p+1}} \cdots x_n^{\alpha_n}$.

The linear elimination theorem

Theorem: Let G be a reaction network with set of species $\mathcal{X} = \{X_1, \dots, X_n\}$. Let

$$U = \{X_1, \dots, X_p\} \subseteq \mathcal{X}$$

be non-interacting.

If the digraph G_U is strongly connected, then at steady state

$$x_j = \varphi_j(x_{p+1}, \dots, x_n), \qquad j \in \{1, \dots, p\},$$

with φ_j a rational function with all coefficients (depending on κ and T) positive. (T is relevant only when $x_1 + \cdots + x_p = T$ is a conservation law).

The functions φ_j's are found using the Matrix-Tree Theorem on G_U.

Feliu, Wiuf (2012)
Variable elimination in chemical reaction networks with mass action kinetics. SIAM Journal on Applied Mathematics. 72:4 pp 959–981.