Vorlesung "Modellierung von Zellprozessen"
Aufgabenblatt 1: Modellierung

WS 2009/2010, Dozent: Wolfram Liebermeister

1. **Small network structure**

   Draw the the reaction system

   $P_1 + S_2 \overset{v_1}{\leftrightarrow} S_1 + S_3$
   $S_1 + S_3 \overset{v_2}{\leftrightarrow} P_2 + S_2$

   as a network, write down its stoichiometric matrix, and determine potential fluxes in stationary state. Are there linear conservation relations? (v_i: reaction rate, S_j: internal (variable) compounds, P_k: external (fixed) compounds)

2. **From the ODEs back to the reaction**

   Consider the following system of differential equations. Try to find out a reaction scheme that corresponds to these reactions. Are there cases of activation or inhibition?

$$\begin{aligned}
\frac{dM_1^-}{dt} &= -k_1 \cdot M_1^- \cdot \frac{1}{(1+M_3^+)} + k_2 \cdot M_1^+ \\
\frac{dM_1^+}{dt} &= +k_1 \cdot M_1^- \cdot \frac{1}{(1+M_3^+)} - k_2 \cdot M_1^+ \\
\frac{dM_2^-}{dt} &= -k_3 \cdot M_2^- \cdot M_1^+ + k_4 \cdot M_2^+ \\
\frac{dM_2^+}{dt} &= +k_3 \cdot M_2^- \cdot M_1^+ - k_4 \cdot M_2^+ \\
\frac{dM_3^-}{dt} &= -k_5 \cdot M_3^- \cdot M_2^+ + k_6 \cdot M_3^+ \\
\frac{dM_3^+}{dt} &= +k_5 \cdot M_3^- \cdot M_2^+ - k_6 \cdot M_3^+
\end{aligned}$$

3. **The repressilator** The repressilator (M. Elowitz and S. Leibler, Nature 2000) is a genetic circuit consisting of three proteins, each inhibiting the production of the following protein in a circle. Consider the following kinetic equations for synthesis and degradation of the proteins:

$$\begin{aligned}
v_i^{\mathrm{syn}} &= \frac{\beta}{1 + x_{l(i)}/k} \\
v_i^{\mathrm{degr}} &= \alpha\, x_i
\end{aligned}$$

   with $i = 1, 2, 3$ and $l(1) = 3,\ l(2) = 1,\ l(3) = 2$.
   The reaction rate vector reads $v = (v_1^{\mathrm{syn}}, v_2^{\mathrm{syn}}, v_3^{\mathrm{syn}}, v_1^{\mathrm{degr}}, v_2^{\mathrm{degr}}, v_3^{\mathrm{degr}})^{\mathrm{T}}$.

   (a) Write down the stoichiometric matrix and the differential equations for the protein levels x_i.

   (b) Consider a stationary state with $x_1 = x_2 = x_3 = \bar{x}$. Calculate the elasticity matrix ε^{S}. (Hint: it is not necessary to compute the value of $\bar{x}$.)

   (c) Compute the Jacobian matrix by the formula $M = N\varepsilon^{\mathrm{S}}$.

   (d) How could you decide based on M whether the stationary state is stable?