Worksheet: STANDARDS, SOFTWARE, DATABASES and STRUCTURAL ANALYSIS (29. May 2012)
Lecture "Computational Systems Biology", Dr. Jürgen Pahle

1) Navigate to the Biomodels database at http://www.ebi.ac.uk/biomodels-main and download the model that is described in the article Leloup JC, Goldbeter A (1999) Chaos and birhythmicity in a model for circadian oscillations of the PER and TIM proteins in drosophila. *J Theor Biol* **198**(3):445-59.

a) Investigate the SBML code. Which databases do the MIRIAM annotations link the different entities to? What is "RDF"? Does the SBML model contain a "list of rules". What for?

b) Import the model in COPASI, define an appropriate plot and simulate it over 100 s. What does the asymptotic dynamics look like? Does the model also have a steady state with this parameter set? If yes, what is its stability?

2) A canonical view of the upper part of glycolysis starts with glucose and comprises the following reactions (in brackets: possible abbreviations): The enzyme hexokinase (HK, E1) phosphorylates glucose (Gluc, S1) to glucose-6-phosphate (G6P, S2) under consumption of ATP (S5) and production of ADP (S6). The enzyme phosphoglucoisomerase (PGI, E2) converts glucose-6-phosphate to fructose-6-phosphate (F6P, S3). The enzyme phosphofructokinase (PFK, E3) phosphorylates F6P a second time to yield fructose-1,6-bisphosphate (F16BP, S4). The enzyme fructosebisphosphatase (E4) catalyzes the reverse reaction.

a) Sketch the reaction network and formulate a set of differential equations (without specifying the kinetics of the individual reactions).

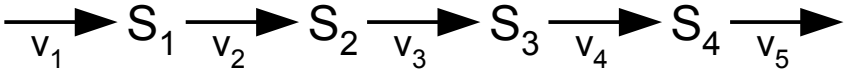
b) Formulate the stoichiometric matrix $\boldsymbol{N}$. What is the rank of $\boldsymbol{N}$?

c) Calculate steady state-fluxes (matrix $\boldsymbol{K}$) and conservation relations (matrix $\boldsymbol{G}$).

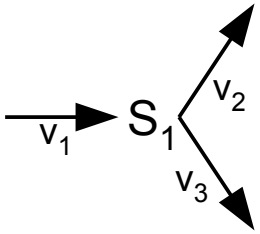
3) Given the following networks:

N1:

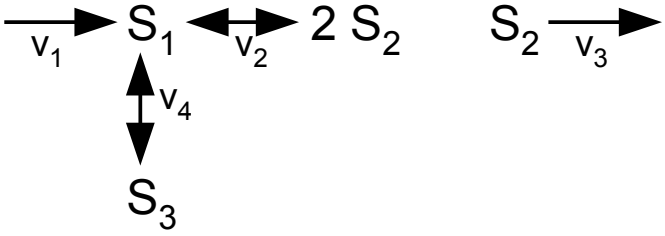
N2:



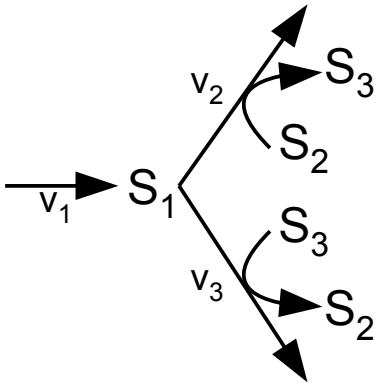
N3:



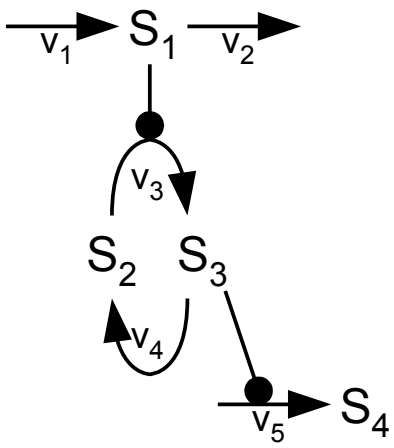
N4:



N5:



N6:



(arrows with filled circles at the end denote activation)

a) Write down the sets of differential equations for the networks N1 - N6 given above without specifying their kinetics.

b) Determine the rank of the stoichiometric matrices, independent steady state-fluxes, and conservation relations.

Do all systems have a (nontrivial) steady state?

4) Inspect networks N3 and N4 given in 3). Can you find elementary flux modes? Use an available tool (COPASI, Metatool, etc.) to check this.