Metabolic Modelling, Spring 2009, Exercises 31.3.2009

In assigments 1-4, we consider a metabolic network consisting of the following enzymatic reactions: $R_1 : B \Rightarrow D$, $R_2 : A \Rightarrow B$, $R_3 : A \Rightarrow C$, $R_4 : C \Rightarrow D$, $R_5 : A_{ext} \Rightarrow A$, $R_6 : D \Rightarrow D_{ext}$. A_{ext} and D_{ext} are external metabolites, the rest are internal metabolites.

Assignments 3-4 require MATLAB to be completed, assignment 2 can be completed either with MATLAB or by pen and paper.

1.

   - Draw the metabolic network of the above system, use metabolites as nodes and reactions as edges connecting the metabolites. Draw the system boundary in the appropriate place.
   - Draw the total stoichiometric metrix S_{tot} of the above system. Indicate the partitioning of the matrix.
   - Draw the exchange stoichiometric matrix $S_{exc}$of the system.

2. The following rate vectors satisfy steady-state condition of the system described by S_{exc} i.e. are valid flux vectors

$$v_1 = [0, 0, 1, 1, 1, 1], v_2 = [1, 1, 0, 0, 1, 1]$$

   Determine which of the following are valid flux vectors and explain why:

   - $v = [0, 0, 0, 0, 0, 0]'$
   - $v = v_1 + v_2$
   - $v = v_1 + 1$
   - $v = v_1 - 2v_2$

3. The MATLAB command $null(S)$ computes the null space of the stoichiometric matrix The result gives the kernel matrix K, where the columns are basis vectors spanning the space of steady state flux vectors.

   - Compute the kernel K_{exc} of the exchange stoichiometric matrix S_{exc}.
   - For each basis vector in the kernel, draw the metabolic network so that the reaction velocities given by the basis vectors are used as the weights of the reaction edges. Illustrate the reaction direction by arrowheads on the graph edges.

- Compute the kernel K_{tot} of the total stoichiomatrix matrix S_{tot}. Repeat the procedure of (2b) using the kernel. What part of the metabolic system can operate in steady state by these results? Explain why the result in different from the one obtained in (2b)

4. Using the kernel matrices K_{exc} and K_{tot} Identify the enzyme subsets of the systems S_{exc} and S_{tot}. Explain for each subset why the particular reactions belong to the subset.

5-6. Read the article *N. Duarte, S.A. Becker, N.Jamshidi, I. Thiele, M.L. Mo, T.D. Vo, R. Sivas and B. Palsson: Global reconstruction of human metabolic network based on genomic and bibliomic data. PNAS vol 104, no. 6, pp. 1777-1782* `http://www.pnas.org/content/104/6/1777.abstract` and prepare to present the main points of the article. The presentation should contain approx. 5 slides.