Metabolic Modelling, Spring 2009, Exercises 21.4.2009

These exercises will consist of two parts:

- *five "normal" assignments (below) that will be completed at home and reviewed in the exercise session of 21.4*
- *Writing a summary of the article* Planes F.J, Beasley J.E: A critical examination of stoichiometric and path-finding approaches to metabolic pathways. Brief Bioinform. 2008 Sep;9(5):422-36 `http://www.cs.helsinki.fi/bioinformatiikka/mbi/courses/08-09/memo/private/422.pdf` *(This paper is accessible from computers at the depertment of computer science, not outside, due to copyright issues.)*

  The guidelines for writing the summary and grading (1-5 exercise points) are the same as for the summary wirtten as the first exercise. The deadline for returning the summary is Friday 24.4.

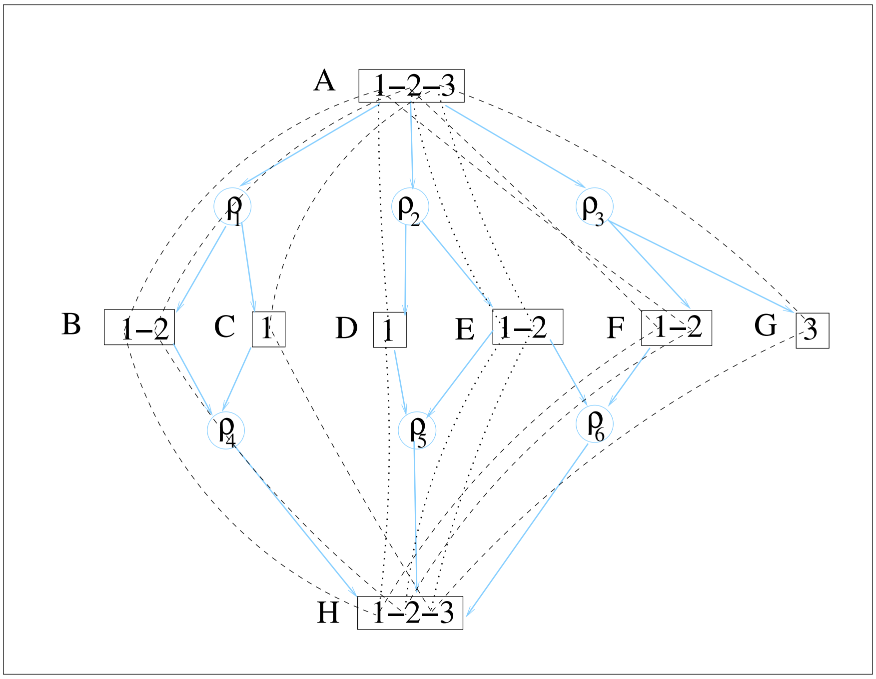

Figure 1: Example metabolic system.

1. On the lecture of April 3rd, an incremental procedure was shown that in a tree-shaped metabolic network topology (i.e. when there is a single path in between any to metabolites) can be used to determine all internal fluxes of the network. Explain rigorously why the procedure is correct, in particular, how it can be quaranteed that the process does not stop before all fluxes have been determined.

2. In figure 1, a metabolic system with six reactions $\rho_1, \ldots, \rho_6$ and eight metabolites $A,\ldots,H$ is depicted, together with the atom mappings between the carbons (dashed lines). Enumerate all equivalence sets of carbon fragments in this system.

3-4. Consider the metabolic system of Figure 1. Assume the isotopomer distribution of metabolite A is the following. $\mathbb{P}\{^{000}A\} = 0.50$, $\mathbb{P}\{^{010}A\} = 0.25$, and $\mathbb{P}\{^{111}A\} = 0.25$.

   - Determine the isotopomer distributions of products $H|\rho_4$, $H|\rho_5$ and $H|\rho_6$ of the reactions ρ_4, ρ_5 and ρ_6.
   - Examine the isotopomer distributions you have generated. Which of the isotopomers of H carry useful information for determining the relative fluxes of the three reactions?

   (Hint: to save manual work, the MATLAB command *kron()* can be used to compute product distributions of two fragment isotopomer distributions.)

5. Assume we have measured the isotopomer distribution D_H of metabolite H to be the following: $\mathbb{P}\{^{000}H\} = 0.3750$, $\mathbb{P}\{^{001}H\} = 0.0938$, $\mathbb{P}\{^{010}H\} = 0.1406$, $\mathbb{P}\{^{011}H\} = 0.0781$, $\mathbb{P}\{^{100}H\} = 0.0781$, $\mathbb{P}\{^{101}H\} = 0.0156$, $\mathbb{P}\{^{110}H\} = 0.0156$, $\mathbb{P}\{^{101}H\} = 0.0625$.

   - Using the isotopomer distributions determined in the previous exercise, write down the matrix A containing the coefficients $\mathbb{P}\{^{xyz}H|\rho_j\}$ of the isotopomeric balance equations of metabolite H.
   - Assume that the exchange flux consuming H has value 1.
   - Form the system of equations $A\mathbf{v} = D_H$ and solve the fluxes v_{ρ_4}, v_{ρ_5} and v_{ρ_6}.