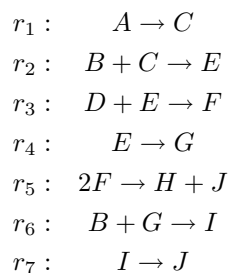


# Metabolic Modelling, Spring 2009, Exercises

## 7.4.2009

1. Consider the metabolic network given by the following reaction equations



Add exchange reactions  $r_8, r_9, r_{10}, r_{11}$  and  $r_{12}$  to metabolites  $A, B, D, H$  and  $J$ , respectively, so that non-zero flux through system becomes possible. Construct the stoichiometric matrix  $S = [S_{II} \ S_{IE}]$  corresponding to reactions  $r_1, \dots, r_7$  and the exchange reactions.

2. From of the above system, list the following (if any):

- Dead ends
- Enzyme subsets
- Conserved pools
- Elementary flux modes

Explain the results.

3. Write down the Flux Balance Analysis problem where you try to maximize the production of metabolite  $J$  assuming that the uptake (exchange) flux  $v_9$  to metabolite  $B$  is constrained,  $0 \leq v_9 \leq 1$ , and other exchange fluxes are unconstrained. You may use MATLAB linprog, or solve the problem by hand.

What is the maximum production of  $J$ ? What flux vector  $\mathbf{v}$  do you obtain from optimization? Is this solution unique? Why/why not?

4. Perform reachability analysis in the network given in the previous assignment.

First, assume that the input set  $\mathcal{A} = \{r_8, r_9\}$ . Find out the maximal set of reactions and metabolites that can be reached. In which order do you

add items to the set of reachable nodes? Hint: apply the rules given on page 27 of the fourth set of lecture slides repeatedly, adding nodes to the set of reachable nodes as you go on.

Second, add  $r_{10}$  to  $\mathcal{A}$  and perform the reachability analysis again assuming the same input set as previously.

Is it possible to produce  $J$  without uptake of  $D$ ? How would you discover this using FBA?

- 5-6. Read 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://bib.oxfordjournals.org/cgi/content/abstract/bbn018> and prepare to present the main points of the article. The presentation should contain approx. 5 slides.