Metabolic modelling, Spring 07, Exercise 3, Friday, 13.4.2007

1. Let's revisit the slides of the FBA lecture on 27.3. Explain
   (a) what is odd on slide 31;
   (b) what is odd on slide 34. What does the given objective function actually optimize? (Hint: compare the objective function to the one given on slide 42.)

2. Consider an organism $\mathcal{O}$ with the metabolic network consisting of the following enzymatic reactions: $\rightarrow A, B \rightarrow D, A \rightarrow B, A \rightarrow C, D \rightleftharpoons C, \rightarrow D$ (A and D are external substrates). In addition, the production of biomass (BM) can be modelled as a reaction $A + B + D \rightarrow BM$.
   (a) Draw a graph representation of the network.
   (b) Construct a stoichiometric matrix of the network. Model a bidirectional reaction as two separate reactions. Should the metabolite BM corresponding biomass be balanced?
   (c) Enumerate the enzyme subsets of the network.

3. Enumerate all elementary flux modes of $\mathcal{O}$. Consider all unidirectional reactions as irreversible. Explain the difference between elementary flux modes and simple paths in the metabolic network.

4. Formulate a linear programming problem whose solution is a flux distribution that optimizes for growth, that is, the production of biomass of $\mathcal{O}$. Set capacity constraints stating that all enzymatic reactions will have a flux smaller or equal than 10 units in every feasible solution. Compute the number of variables and constraints in your formulation. Based on these numbers, is the flux balance analysis feasible with genome-size metabolic models?

5. Write a MATLAB function that solves the linear programming problem of the the previous assignment(hint: function *linprog*). Record the rate of optimal growth as well as a flux distribution realizing the optimal growth. Alter your network by removing reaction $A \rightarrow B$ from the network and repeat the analysis. Then, put $A \rightarrow B$ back to the network and remove $C \rightarrow D$ and repeat the analysis. Compare all the results together. How would you interpret them?