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

1. (a) Euclidian distance does not translate to linear objective function.
   (b) Adding ratios of different precursor metabolites of biomass to coefficients of objective function does not as such guarantee that in the solution to the linear program precursors are produced in those ratios for biomass. It is better to add an artificial reaction that produces biomass to the network (see V_{growth} in slides 40 – 42). The stoichiometric coefficients of this biomass reaction correspond to ratios of different precuror metabolites needed for the production of biomass.

2. Because of a typo in the specification of the network, no untrivial enzyme subsets exists. "Biomass" metabolite should not be added to the stoichiometric matrix as there does not exist a reaction consuming it. Thus, biomass cannot be balanced in untrivial way.

3. Elementary flux modes:
   (a) $3(\rightarrow A); 2(A \rightarrow B); B \rightarrow D; A + B + D \rightarrow BM$
   (b) $3(\rightarrow A); A \rightarrow B; A \rightarrow C; C \rightarrow D; A + B + D \rightarrow BM$
   (c) $C \rightarrow D; D \rightarrow C$
   (d) $2(\rightarrow A); A \rightarrow B; \rightarrow D; A + B + D \rightarrow BM$

4. Let v_{growth} denote a flux of artifical reaction $A + B + D \rightarrow BM$ producing biomass.

$$\begin{aligned} \min \quad & -v_{growth} \\ \texttt{subject to} \quad & \\ \mathbf{Sv} \quad & = \mathbf{0} \\ v_i \quad & \geq 0 \qquad \forall \texttt{ fluxes } v_i \\ v_i \quad & \leq 10 \qquad \forall \texttt{ fluxes } v_i \end{aligned}$$

5. MATLAB function in a separate text file. Deleting $A \rightarrow B$ from the networks stops the growth of an organsim. Thus, the deletion of gene(s) catalyzing $A \rightarrow B$ are lethal. Deleting $C \rightarrow D$ does not affect to the optimal growth. Thus, the organism is (in some sense) robust againts deletion of gene(s) catalyzing $C \rightarrow D$. On the other, this also shows

that the original network has many alternative flux distributions for optimal growth, as FBA on the original network produced an optimal flux distribution with non-zero flux for $C \rightarrow D$.