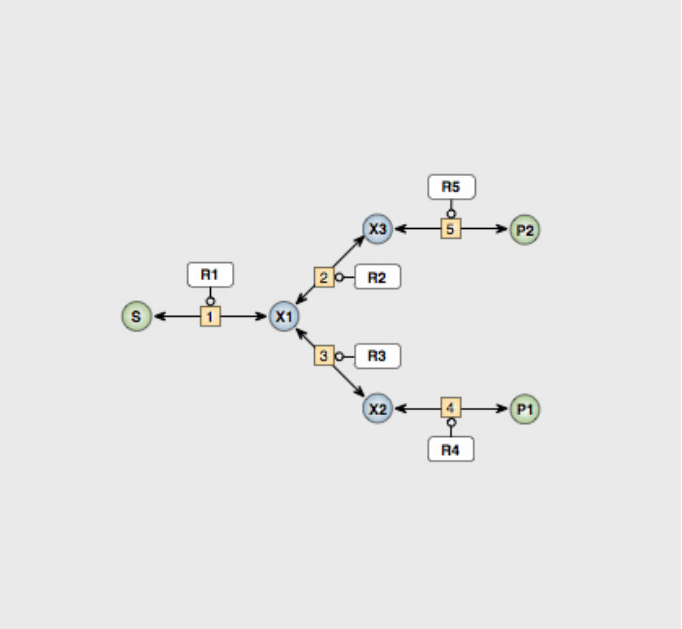
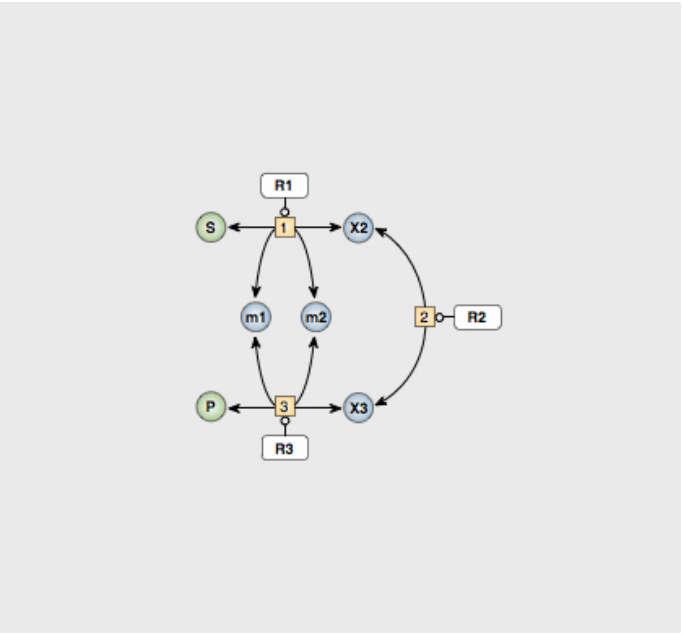
Systems Biology Tutorial 4: Structural analysis of reaction networks

1. Consider the linear branched pathway:



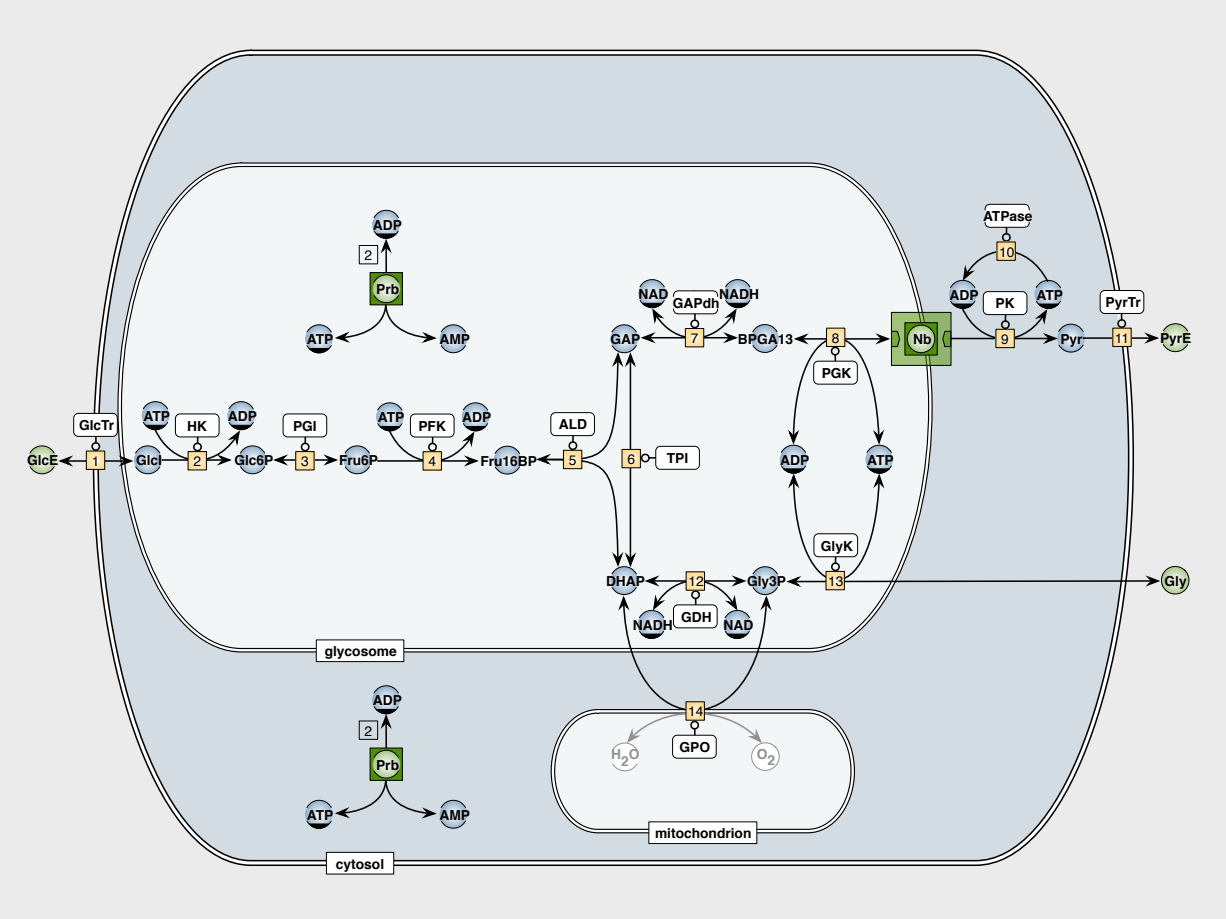
   (a) Construct the stoichiometric matrix **N** by hand.
   (b) Are there any dependent metabolites?
   (c) Derive the steady-state flux relations by hand from **N.v** = **0**. How many independent fluxes are there?
   (d) Check your answers by running the **branch5** model on JWS Online and generating the **N**, **L** and **K** matrices.
   https://jjj.bio.vu.nl/models/branch5/simulate/

2. Consider the linear pathway with a moiety:



   (a) Construct the stiochiometric matrix by hand.
   (b) Are there any dependent metabolites?
   (c) Derive the steady-state flux relations by hand. How many independent fluxes are there?
   (d) Check your answers by running the **lin3moi** model on JWS Online and generating the **N**, **L** and **K** matrices. https://jjj.bio.vu.nl/models/lin3moi/simulate/

3. Consider the following model for glycolysis in *Trypanosoma brucei*:



(a) How many independent fluxes are there?

(b) Assuming anaerobic glycolysis (J14 = 0, i.e. no flux through vGPO):

i. What is the flux relation between

A. J12 and J7,

B. J13 and J1?

ii. What is the ratio of PyrE to Gly produced?

iii. How many moles of ATP are produced per mole of Glc in the glycosome?

iv. How many moles of ATP are produced per mole of Glc in the cytosol?

(c) Assuming aerobic glycolysis (J14 $\neq$ 0):

i. Production of which product will increase?

ii. What is the maximal flux in J7 relative to J1?

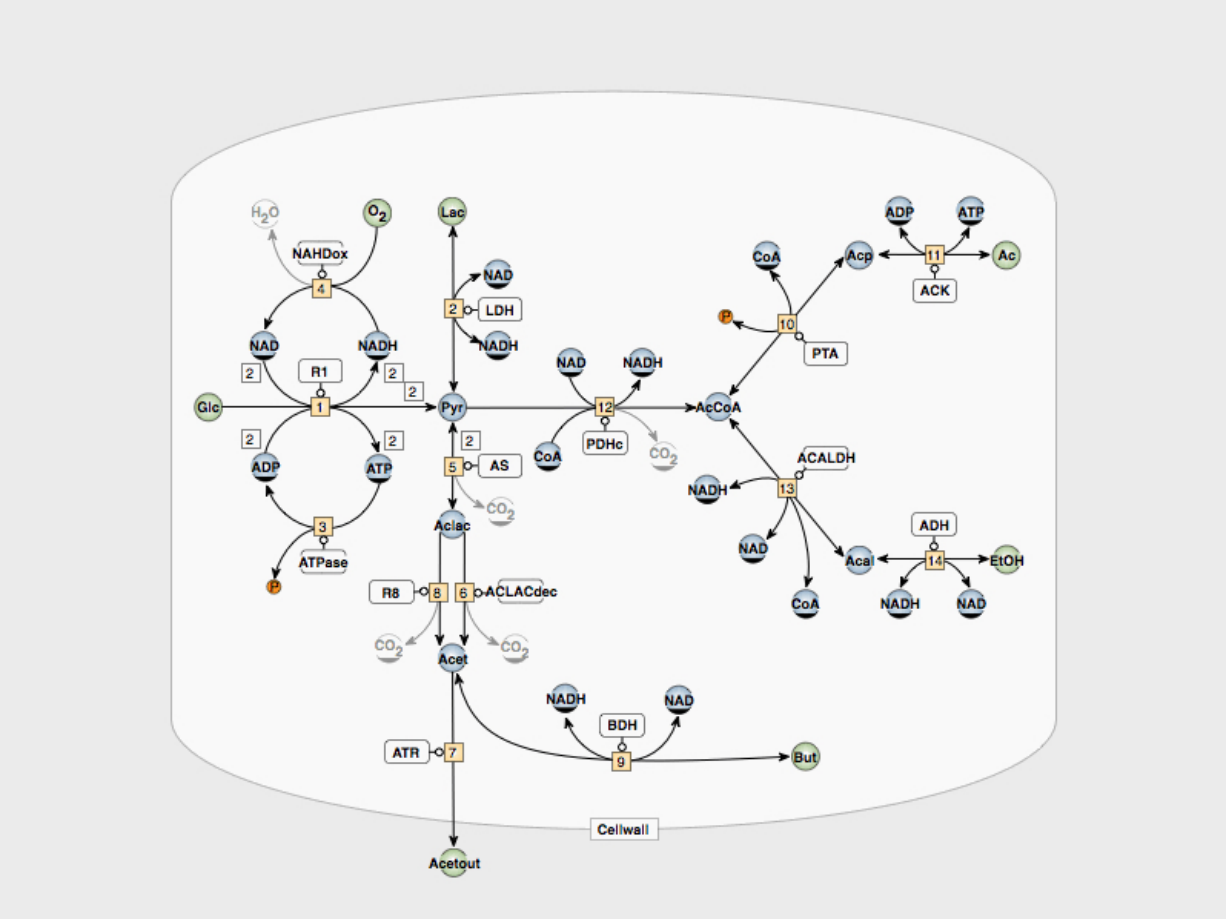
iii. How many moles of ATP are produced per mole of Glc in the glycosome (maximally)?

iv. How many moles of ATP are produced per mole of Glc in the cytosol (maximally)?

(d) Test your answer by running the **kerkhovenA** model on JWS Online. Adjust the kinetic parameters of GPO to simulate anaerobic / aerobic conditions and plot the relevant rates.

(e) Would glycolysis reach a steady state in the absence of the glycerol branch?

4. Consider the following model (**hoefnagel1**) for glycolysis in *Lactococcus lactis*:



(a) Consider anaerobic glycolysis (vNADHox = 0):

i. Would steady-state production of lactate be possible for anaerobic glycolysis? If so, what will be the flux relation bewteen J2 and J1 if all available pyruvate is converted to lactate? How many moles of lactate will be produced per mole of glucose?

ii. How much EtOH will be formed per mole of glucose if all pyruvate were converted to AcCoA?

(b) Consider aerobic glycolysis (vNADHox $\neq$ 0):

i. Which branch would maximize ATP production?

ii. How many moles of product will be formed per mole of glucose if this branch was carrying all the flux?

(c) Is the production of 1 butanol redox neutral (anaerobic) ?

(d) What would be the ratio of Ac to EtOH in the case of anaerobic glycolysis if v12 does not consume NAD under these conditions (special case in *E. coli* where pyruvate formate lyase catalyses this reaction)?