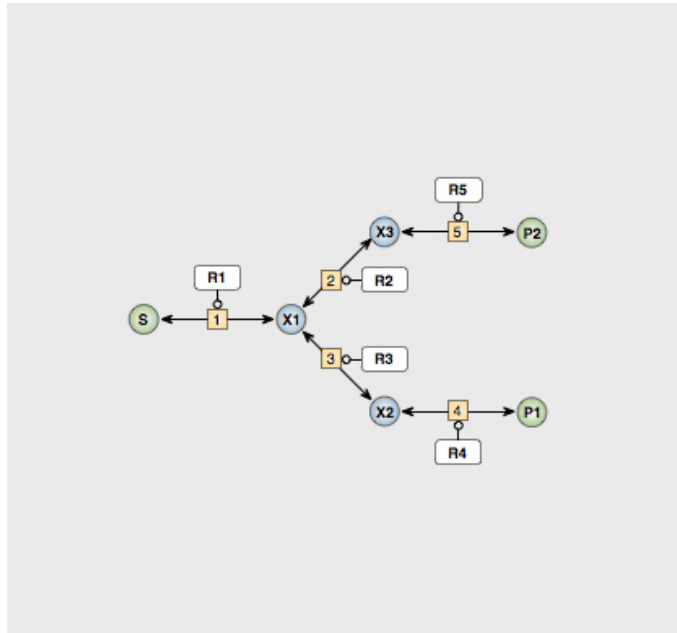


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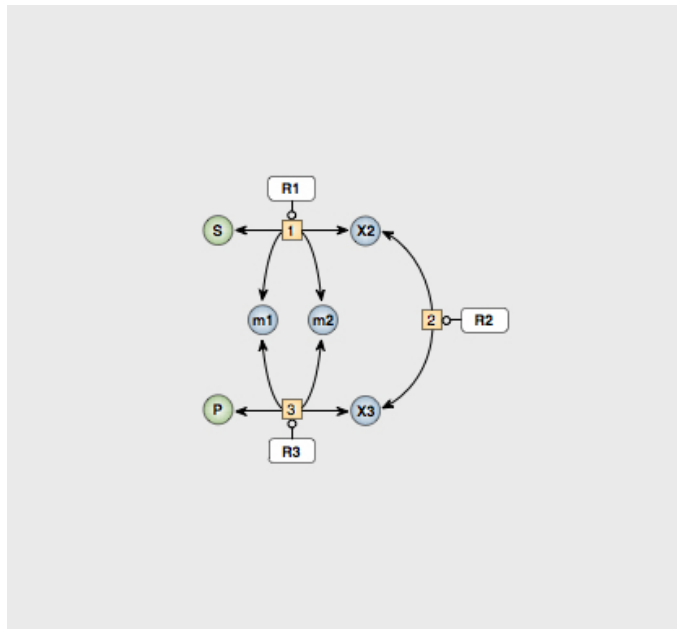
## Systems Biology Tutorial 4: Structural analysis of reaction networks

1. Consider the linear branched pathway:



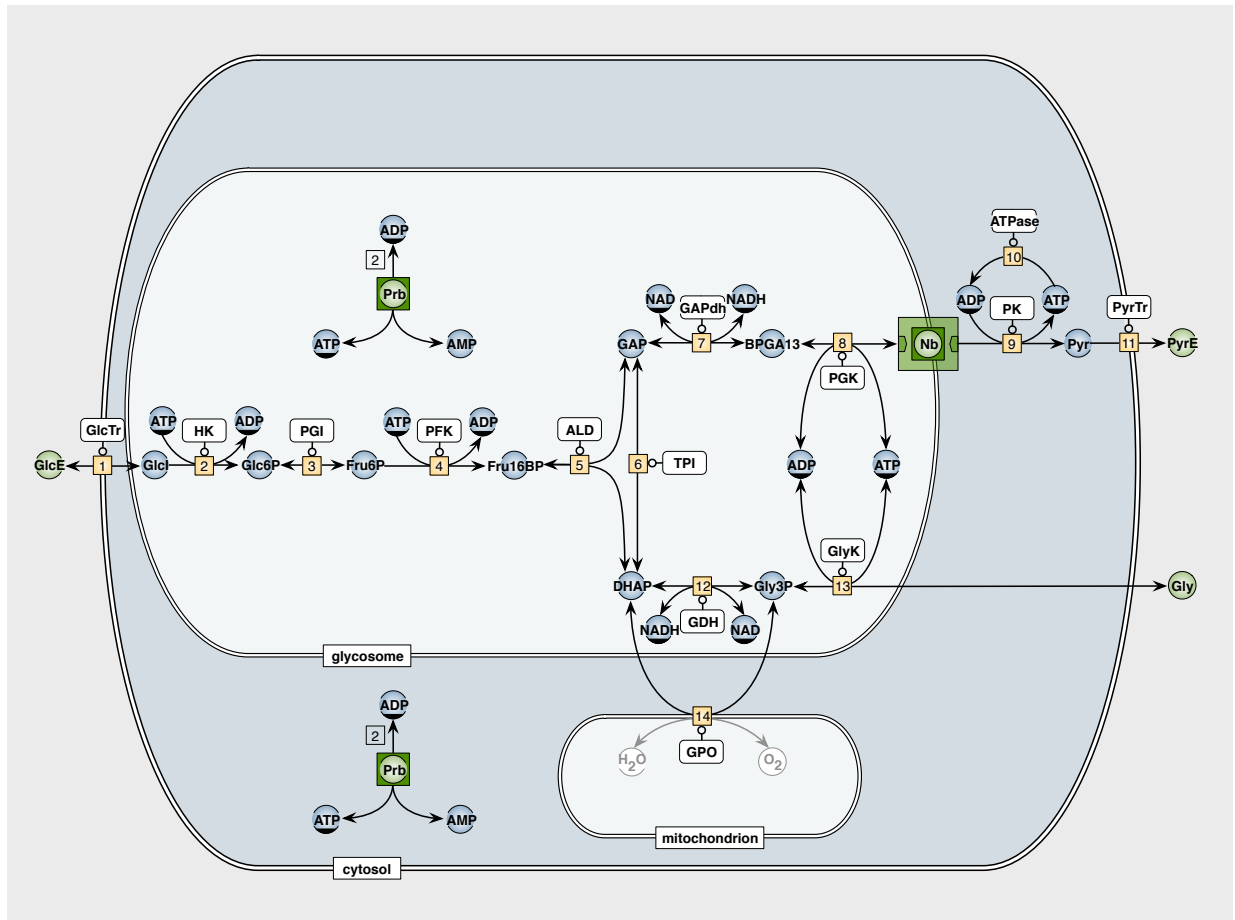
- Construct the stoichiometric matrix  $N$ .
- Are there any dependent metabolites?
- Derive the steady-state flux relations by hand from  $Nv = 0$ . How many independent fluxes are there?
- Check your answers by running the branch5 model on JWS Online ([jjj.bio.vu.nl](http://jjj.bio.vu.nl)) and generating the  $N$ ,  $L$  and  $K$  matrices.

2. Consider the linear pathway with a moiety:



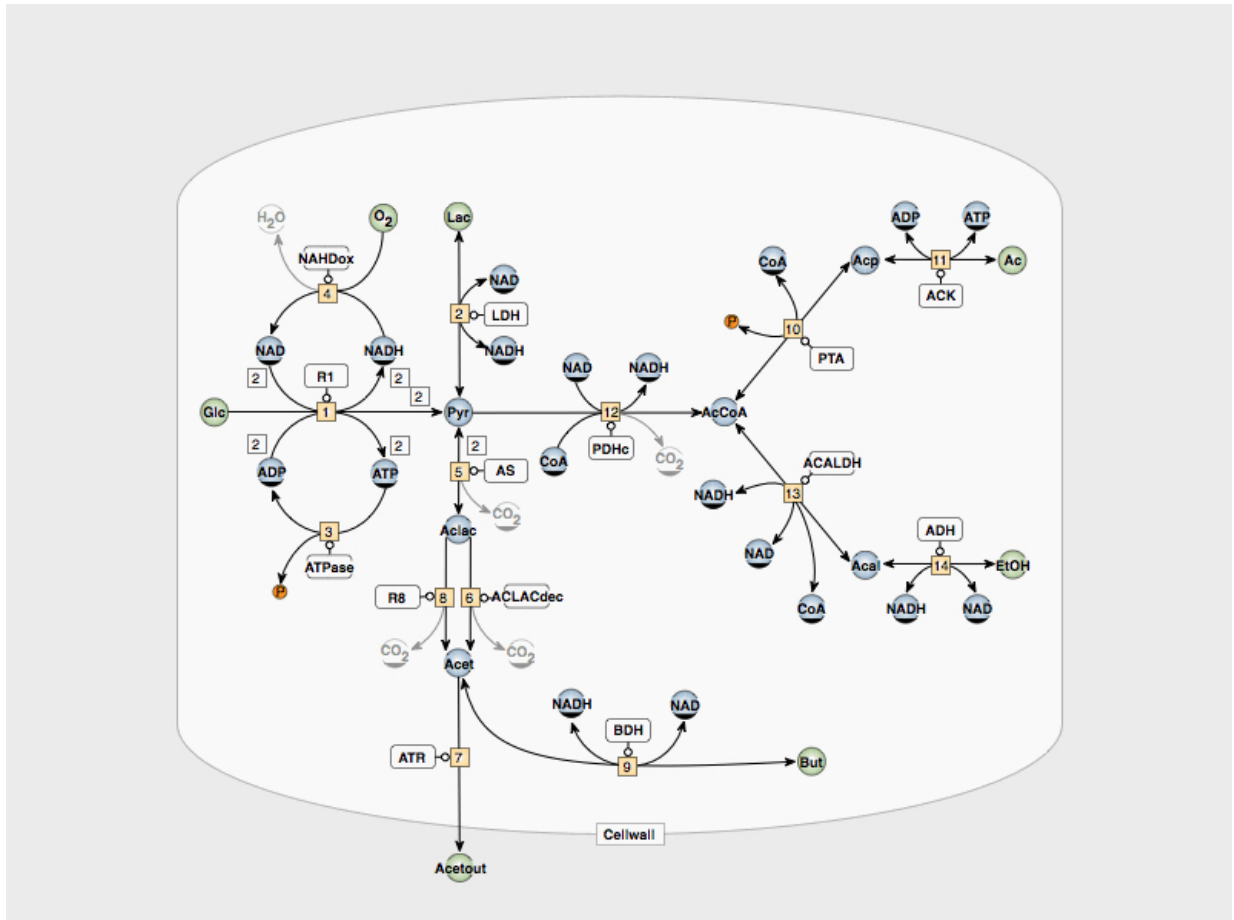
- Construct the stoichiometric matrix.
- Are there any dependent metabolites?
- Derive the steady-state flux relations by hand from  $Nv = 0$ . How many independent fluxes are there?
- Check your answers by running the lin3moi model on JWS Online and generating the  $N$ ,  $L$  and  $K$  matrices.

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



- How many independent fluxes are there?
- Assuming anaerobic glycolysis ( $J_{14} = 0$ , i.e. no flux through vGPO):
  - What is the flux relation between
    - $J_{12}$  and  $J_7$ ,
    - $J_{13}$  and  $J_1$ ?
  - What is the ratio of PyrE to Gly produced?
  - How many moles of ATP are produced per mole of Glc in the glycosome?
  - How many moles of ATP are produced per mole of Glc in the cytosol?
- Assuming aerobic glycolysis ( $J_{14} \neq 0$ ):
  - Production of which product will increase?
  - What is the maximal flux in  $J_7$  related to  $J_1$ ?
  - How many moles of ATP are produced per mole of Glc in the glycosome (maximally)?
  - How many moles of ATP are produced per mole of Glc in the cytosol (maximally)?
- 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.
- Would glycolysis reach a steady state in the absence of the glycerol branch?

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



- (a) Consider anaerobic glycolysis ( $v_{\text{NADHox}} = 0$ ):
- Would the production of lactate be possible for anaerobic glycolysis? If so, what will be the flux relation between  $J_2$  and  $J_1$  if all available pyruvate is converted to lactate? How many moles of lactate will be produced per mole of glucose?
  - How much EtOH will be formed per mole of glucose if all pyruvate were converted to AcCoA?
- (b) Consider aerobic glycolysis ( $v_{\text{NADHox}} \neq 0$ ):
- Which branch would maximize ATP production?
  - 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?
- (d) What would be the ratio of Ac to EtOH in the case of anaerobic glycolysis if  $v_{12}$  does not consume NAD under these conditions?