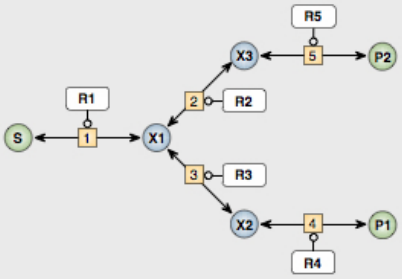
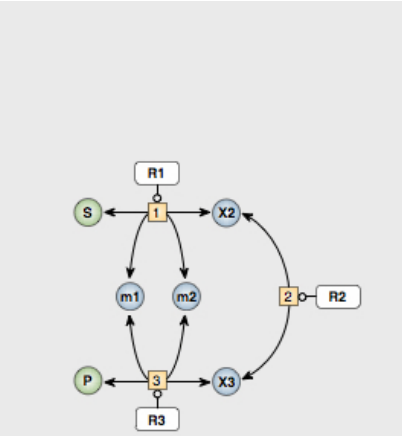
Systems Biology Tutorial 4: Structural analysis of reaction networks

1. Consider the branched pathway below right:



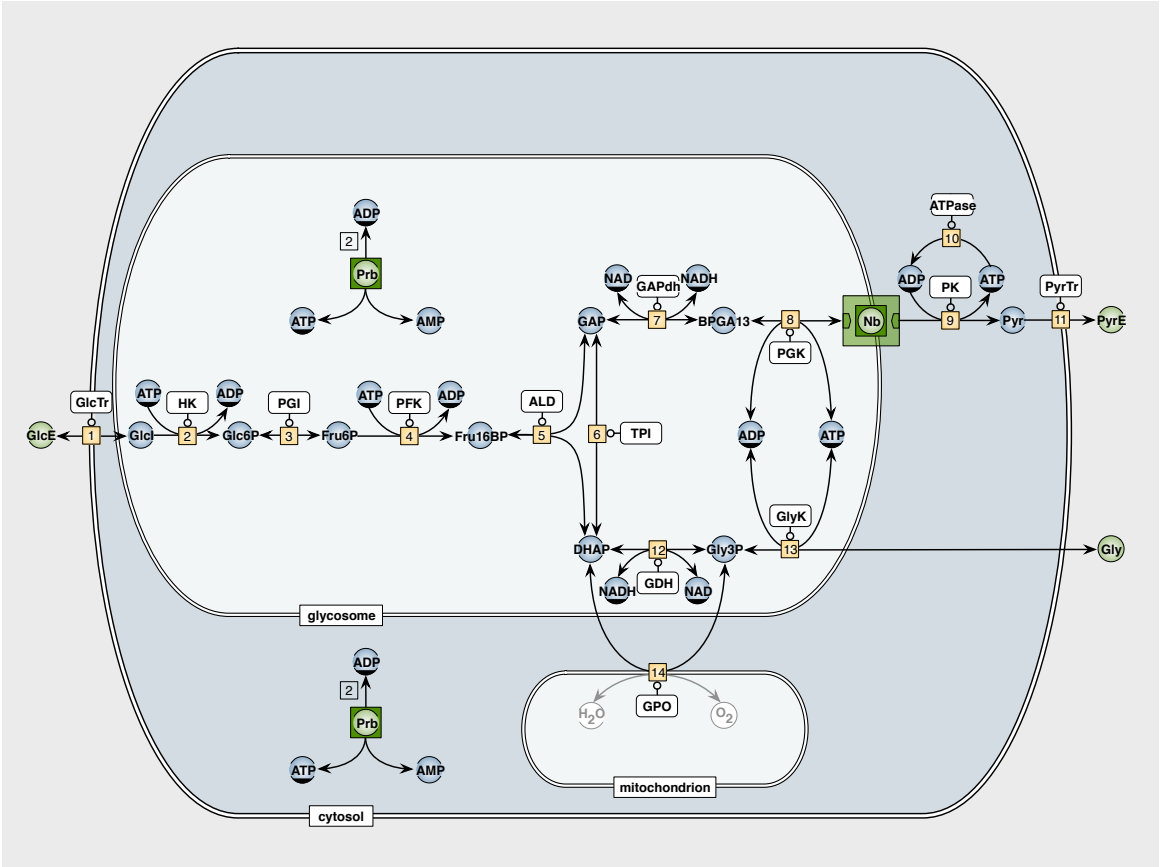
   (a) Construct the stoichiometric matrix **N** by hand.
   (b) Are there any dependent metabolites?
   (c) Derive the steady-state flux relations by hand from **Nv** = **0**. How many independent fluxes are there?
   (d) Load the model `branch5.psc` into PySCeS. Obtain the **N**, **K** and **L** matrices with the commands `mod.showN()`, `mod.showK()` and `mod.showL()`. Show the flux relationships with `mod.showFluxRelationships()`. Show the metabolite conservation relationships with `mod.showConserved()`.
   (e) Check your answers by running the `branch5` model on JWS Online (`http://jjj.biochem.sun.ac.za/models` or `http://jjj.bio.vu.nl/models`) and generating the **N**, **K** and **L** matrices.

2. Consider the linear pathway with a moiety below right:



   (a) Construct the stoichiometric matrix **N** by hand.
   (b) Are there any dependent metabolites?
   (c) Derive the steady-state flux relations by hand from **Nv** = **0**. How many independent fluxes are there?
   (d) Using the PSC file from Question 1 as template, create a new PSC file for this pathway and save it as `lin3moi.psc`. Load this model into PySCeS and obtain the **N**, **K** and **L** matrices as in Question (1d).
   (e) Check your answers by running the `lin3moi` model on JWS Online and generating the **N**, **K** and **L** matrices.

3. Consider the following model for glycolysis in *Trypanosoma brucei*. The PSC file for this model is available for download (`Bakker.psc`), and you can run it on JWS Online (`bakker`).



(a) How many independent fluxes are there?

(b) Assuming anaerobic glycolysis ($J_{14} = 0$, i.e. no flux through v_{GPO}):

i. What is the flux relation between
- J_{12} and J_7,
- J_{13} and J_1?

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 ($J_{14} \neq 0$):

i. Production of which product will increase?

ii. What is the maximal flux through J_7 related to J_1?

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

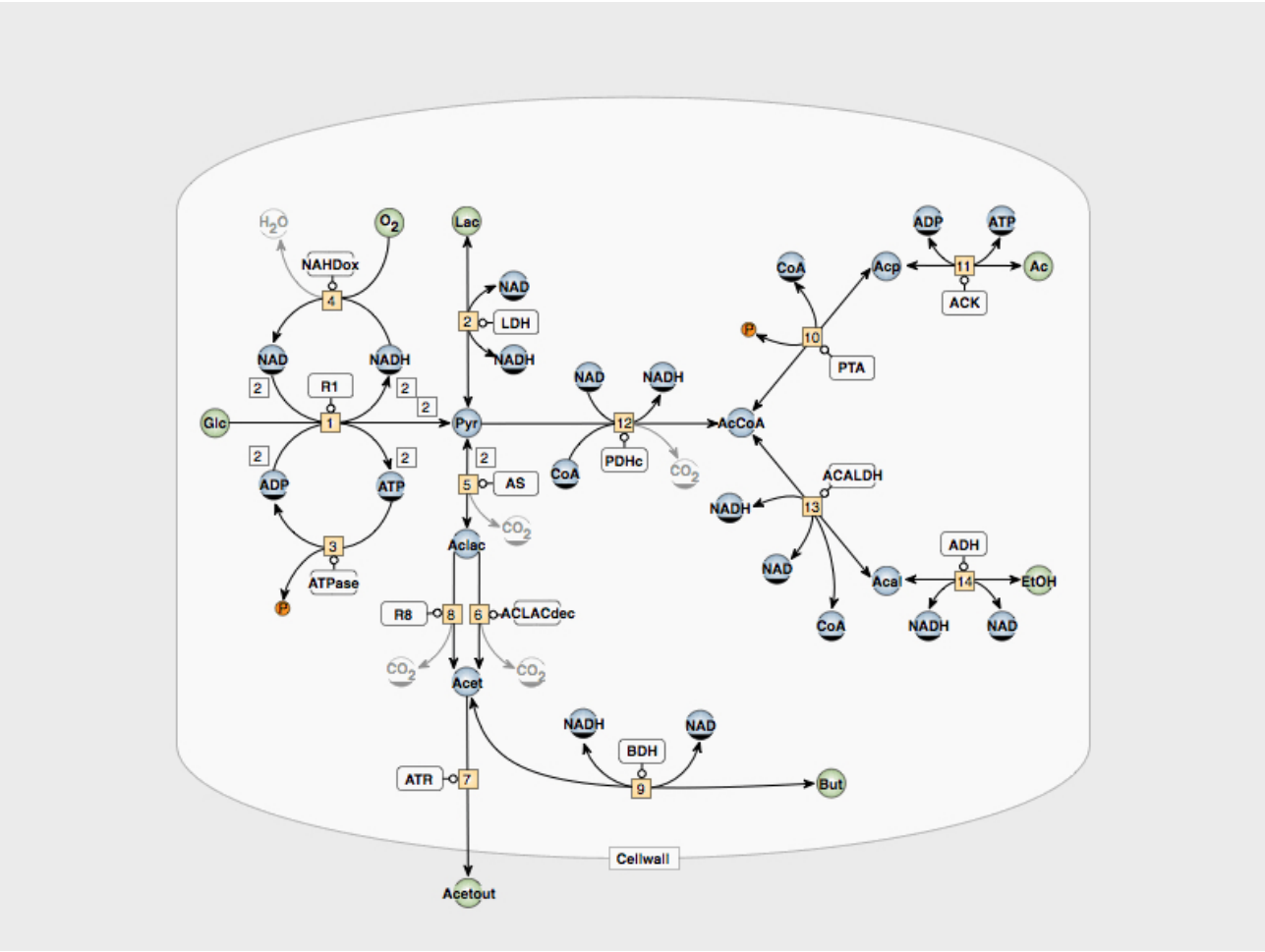
iv. How many moles of ATP are produced per mole of Glc in the cytosol (maximally)?

(d) Test your answer by running the `Bakker.psc` model in PySCeS. Adjust the V_{max} of GPO (`Vm9` in the model) to simulate anaerobic/aerobic conditions, calculate the steady state and display the results with `mod.showState()`.

(e) You can also run the model in JWS Online. Do the results agree?

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

4. Consider the following model for glycolysis in *Lactococcus lactis*. The numbers $\boxed{2}$ are stoichiometric coefficients. Unless indicated in this way, all other stoichiometries are 1. The PSC file for this model is available for download (`Hoefnagel1.psc`), and you can run it on JWS Online (`hoefnagel1`).



(a) Consider anaerobic glycolysis ($v_{NADHox} = 0$):

i. Would the production of lactate be possible for anaerobic glycolysis? If so, what would be the flux relation bewteen J_2 and J_1 if all available pyruvate is converted tot 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 ($v_{NADHox} \neq 0$):

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 butanol redox neutral?

(d) What would be the ratio of Ac to EtOH in the case of anaerobic glycolysis in *E. coli* if v_{12} does not consume NAD under these conditions?