Exercise for Constraint-based Modeling of Cellular Networks
10 November 2022

Homework should be sent to Anika (ankueken@uni-potsdam.de)

Exercise

Metabolic network representation – Cobra Format

Reaction number	Reaction abbreviation	Reaction formula	Reversible
R1	$RUBISCO_{carboxylation}$	$RUBP \rightarrow 2 \cdot 3PGA$	No
R2	$RUBISCO_{oxygenation}$	$RUBP \rightarrow 3PGA + 2PG$	No
R3	PGP	$2PG \rightarrow$	No
R4	$GAPDH$	$3PGA \leftrightarrow T3P$	Yes
R5	$FBA1$	$2 \cdot T3P \leftrightarrow FBP$	Yes
R6	$FBPase$	$FBP \rightarrow F6P$	No
R7	$TK1$	$F6P + T3P \leftrightarrow E4P + PP$	Yes
R8	$FBA2$	$T3P + E4P \leftrightarrow SBP$	Yes
R9	$SBPase$	$SBP \rightarrow S7P$	No
R10	$TK2$	$S7P + T3P \leftrightarrow R5P + PP$	Yes
R11	PPI	$R5P \leftrightarrow PP$	Yes
R12	PRK	$PP \rightarrow RUBP$	No
R13	PGI	$F6P \leftrightarrow$	Yes

From the list of reactions above, construct a model (struct) called *SampleModel* in Matlab, which contains the following fields:

- stoichiometry matrix (mxn double matrix, SampleModel.S)
- short metabolite names (mx1 cell array, SampleModel.mets)
  - for simplicity use M_1 to M_n
- full metabolite names (mx1 cell array, SampleModel.metNames)
  - use abbreviations from table above
- short reaction names (nx1 cell array, SampleModel.rxns)
  - for simplicity use reaction number
- long reaction names (nx1 cell array, SampleModel.rxnNames)
  - use abbreviations from table above
- lower and upper bounds on reaction flux (nx1 double matrix, SampleModel.lb and nx1 double matrix, SampleModel.ub)
  - use 1000 as upper bound
  - use -1000 as lower bound for reversible reactions, 0 otherwise

We want to solve the LP

$$\max v_{Rubisco\_carboxylation}$$
$$s.t.$$
$$Nv = 0$$
$$lb \leq v \leq ub$$

Add a vector including the right-hand side values to your model (mx1 double matrix, SampleModel.b)

Add a vector including the coefficients in the objective to your model (nx1 double matrix, SampleModel.c)

Save your model in the .mat format.

Use linprog to solve the LP!

Which reactions carry non-zero flux at the particular optimal solution?

COBRA Toolbox

Download and install the COBRA Toolbox following the instructions in their documentation (see link below)

https://opencobra.github.io/cobratoolbox/stable/installation.html

Homework

In case you have problems with the cobra toolbox installation use linprog instead of optimizeCbModel.

From the BIGG database (http://bigg.ucsd.edu/models/e_coli_core) download the *E. coli* core model in .mat format.

Load the model and answer the following questions: (1 point each)

a. How many metabolites and reactions are in the model?
b. How many compartments are in the model?
   The compartment is given as identifier of the form metName_CompartmentAbbreviation in .mets
   Hint: maybe use unique and cellfun to get a list of compartment identifiers in .mets
c. How many metabolites belong to each of the model compartments?
d. What are the substrates and what are the products of citrate synthase reaction?
e. How many reactions are reversible?
f. Which reaction flux is optimized?

The cobra toolbox provides a function to solve LP called *optimizeCbModel. OptimizeCbModel* can use different solver. Here we want to use the solver coming with Matlab, so run the following line

```
>> changeCobraSolver('matlab')
```

- Now use *optimizeCbModel* to calculate the value of maximum flux through the reaction you identified to be optimized in task f. (1 point)

- Is the underlying LP homogeneous, which field in the model struct defines/shows this? (1 point)

As output from optimizeCbModel you not only get the optimal value of $z = c'v$, but also one solution for v.

- What is the flux through fumarase at the optimal solution? (1 point)

The model contains reversible reactions.

- Change the model such that each reversible reaction is splitted into two irreversible reactions, $r = r_{foreward} - r_{backward}$, **without** the use of a function like *convertToIrreversible()*. (3 points)

An exchange reaction (e.g. A -> or -> B) is a reaction that only consumes or only produce a metabolite.

- How many import reactions are in the model? How many export reactions are in the model?
  Hint: you can use the model with splitted reversible reactions from the step before, otherwise be careful that A <-> would be counted as import and export reaction. (3 points)