Bioinformatics III

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Summer Semester 2018

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Tutorial 9

June 29 2018 10:15

Submit your solutions on paper, hand-written or printed, by/at the beginning of the lecture or in the building E2.1, Room 3.09. Alternatively you may send an email with a single PDF attachment of the solution paper to daria.gaidar@bioinformatik.uni-saarland.de. If requested in the assignment, please forward your source code via mail, too.

Pathways of Metabolic Networks

Exercise 9.1: Extreme Pathways and Steady State Flux Distribution. Paper-based (40 points)

For the following network, Figure 1, we want to investigate the steady state properties via the extreme pathways.

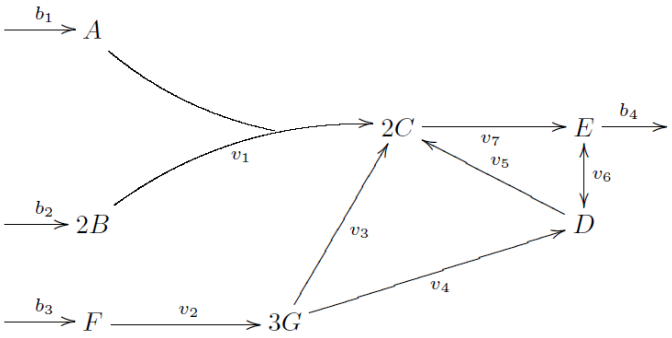


Figure 1: Reaction network to derive extreme pathways from.

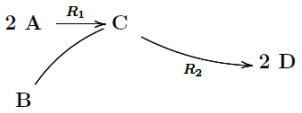
Hints:

- *Reaction v6 can be split in two.*
- *b1-b4 are exchange fluxes.*
- *The activity of these exchange fluxes is constrained to be positive if the metabolite is exiting or being produced by the system, and negative if the metabolite is entering or being consumed by the system.*
- *Check an example network on the Figure 2: two molecules of **A** associate to create one **C**, which is converted into **D**, when it encounters one molecule of **B**.*

(a) **Construct the stoichiometric matrix.** (10)

(b) **Calculate from the stoichiometric matrix the extreme pathways. Give pathways as formulas.** (10)

(c) **Formulate the pathway length matrix. Which information does it provide (diagonal vs off-diagonal entries?** (5)



Set up the stoichiometrix matrix.

	R_1	R_2
A	-2	0
B	-1	0
C	1	-1
D	0	+2

Figure 2: Example of the network and its corresponding stoichiometric matrix.

(d) **Formulate the reaction particiaption matrix. Which information does it provide?** (5)

(e) **Cut-set.** (5)
A reaction oe a set of reactions are essential for the network, when there is no output if this reactions are blocked. List all those reactions.
Hint: can you figure out how to determine this cut-set from the extreme pathways?

(f) **Biomass producation.** (5)
Now assume that the potential input into the network through b1, b2, and b3, i.e., the sum of the fluxes through these reactions is limited to 5 units. How must this input be distributed onto these reactions to give the highest output through b4?

Exercise 9.2: Hands-on with COnstraint-Based Reconstruction and Analysis (COBRA) in Python. (20 points)

Please submit your code via email to get the grade.

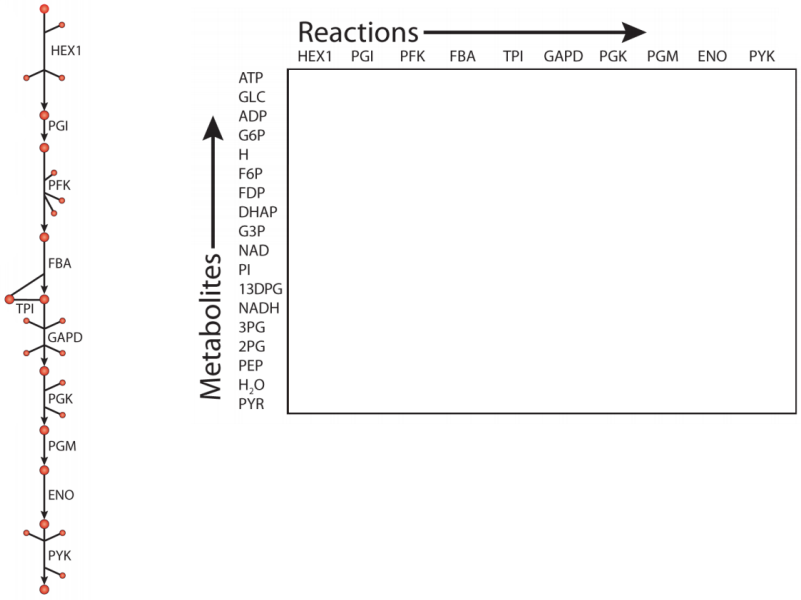


Figure 3: Fragment of the *E.coli* metabolic network (left). The template of the stoichiometry matrix for you to fill-in. Plots are adapted from (1) and (2).

Get yourself comfortable with COBRA package for Python. Go through the docs sections 1 to 4. To get the reactions and their stoichiometry you can query the BiGG Knowledge base. But the docs will teach you a shorter way.

(a) **Provide formulas of the reactions participating in the chain given on the Figure 3.** (5)

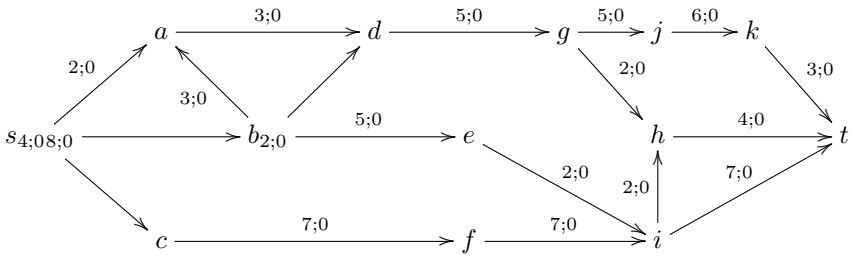
(b) **Fill in the stoichiometry matrix, Figure 3.** (5)

(c) **Create the model for the given chain of reactions. Provide the number of reactions, metabolites and genes in it. (Python)** (10)

As now You got the methodology of Flux Based Analyis, You also got closer to be called a modern alchemist. Have a look on how the modern Alchemy works.

Exercise 9.3: FFEK Algorithm (40 points)

Apply the Ford, Fulkerson, Edmonds, and Karp (FFEK) algorithm explained in the lecture to determine the s-t-cut and the capacity of the network given below.
For each iteration, give the indices of the nodes, the resulting f-augmenting path with its capacity, and the updated $val(f)$. Sketch the newly found f-augmenting paths. Also update the currents through the arcs.
If you find multiple possible paths from s to t with the same length, then choose the one with the highest ΔQ.



References

[1] Reed, Jennifer L., et al. "Towards multidimensional genome annotation." Nature Reviews Genetics 7.2 (2006): 130-141.

[2] Schellenberger, Jan, et al. "Quantitative prediction of cellular metabolism with constraint-based models: the COBRA Toolbox v2. 0." Nature protocols 6.9 (2011): 1290-1307.