Bioinformatics III

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Tutorial 8
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Submit your solutions on paper, hand-written or printed, 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 and Rate Equations

Exercise 8.1: Theoretical Drill (20 points)

(a) **Name 3 commercial applications of minimum flux models.** (5)

(b) **Elaborate on advantages and disadvantages of the Flux based analysis?** (5)

(c) **Constraint based modeling.**

  (1) Please name the constraints that one can apply on the stoichiometric analysis of the metabolism. (5)

  (2) What are the available constraints-based programming packages in Python for running metabolic analysis? (5)

Exercise 8.2: 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.
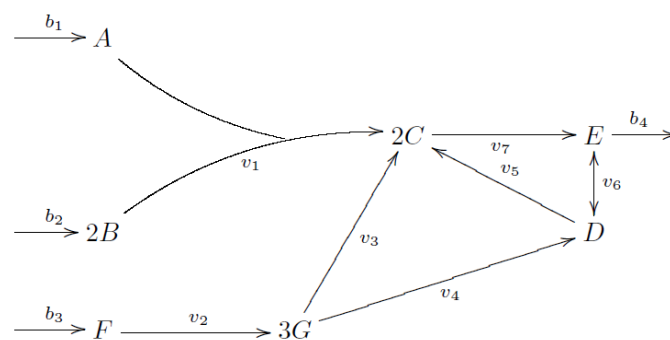

Figure 1: Reaction network to derive extreme pathways from.

Hint: reaction v6 can be split in two.

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

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

(c) **Determine the pathway length matrix. Which informations does it provide?** (5)

(d) **Cut-set.** (5)

The output of our network corresponds to the flux through reaction $b4$. A reaction is essential for the network, when there is no output if this reaction is blocked. List all those reactions. *Hint: can you figure out how to determine this cut-set from the extreme pathways?*

(e) **Fluxes.** (10)

For the following steps we will neglect the internal reactions. Then we can see how the (black box) network transforms input through $b1$, $b2$ and $b3$ into output through $b4$ and $b5$. Complete the table given below, which relates the input through $b1$, $b2$ and $b3$ to the output via $b4$ and contains the fluxes through the reactions $v1$, $v2$ and $v7$.

Hint: If there are multiple possibilities, list one of them and specify the characteristics of the possibilities.

	I	II	III	IV	V	VI
b_1		1		1		1
b_2		1		2		1
b_3		3		1		0
b_4					3	
v_1	0		1		1	
v_2	1		0		2	
v_7			1			

Figure 2: Table for you to fill-in.

Exercise 8.3: Hands-on with COnstraint-Based Reconstruction and Analysis (CO-BRA) in Python. (40 points)

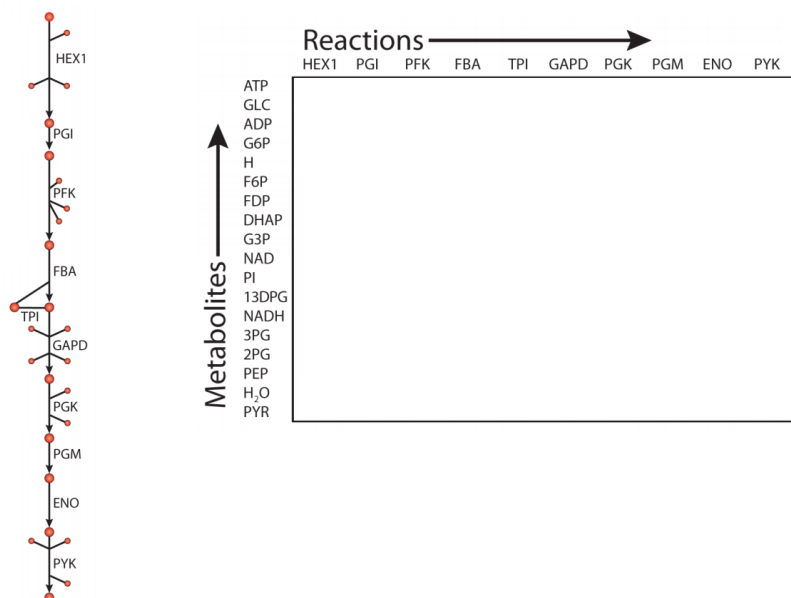Please submit your code via email to get the grade.

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.** (10)

(b) **Fill in the stoichiometry matrix, Figure 3.** (10)

(c) **Create the model for the given chain of reactions. Provide the number of reactions, metabolites and genes in it.** (15)

(d) **Which tool(s) would you use to visualise the results of the COBRA analysis?** (5)

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.

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.