Bioinformatics III

Prof. Dr. Volkhard Helms
Nadine Schaadt, Christian Spaniol
Winter Semester 2012/2013

Saarland University
Chair of Computational Biology

Exercise Sheet 6

Due: 21.12.2012 13:15

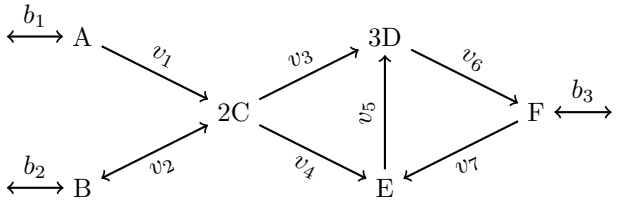
Send your solutions via email with a single PDF attachment. Please include source code listings. Alternatively, you may submit your solutions on paper, hand-written or printed at the beginning of the lecture or in building E2 1, Room 3.03. Additionally, hand in all source code via mail to nschaadt@bioinformatik.uni-saarland.de.

Pathways of Metabolic Networks and Rate Equations

Extreme Pathways

Exercise 6.1: Extreme Pathways and Steady State Flux Distribution (80 points)

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



(a) **Stoichiometric Matrix (6)**
Construct the stoichiometric matrix.

(b) **Extreme Pathways (34)**
Calculate from the stoichiometric matrix the extreme pathways. Give the intermediate steps as well as the pathways as

(1) formulas (i.e., e.g.: $p_{17} = b_{13} + v_7$) and

(2) sketch the pathways in the same layout as in the above network.

(c) **Pathway Length Matrix (8)**
Determine the pathway length matrix. Which informations does it provide?

(d) **Reaction Participation Matrix (8)**

(1) Determine the reaction participation matrix.

(2) Which reactions contribute to the most pathways?

(3) Are there reactions that contribute to all pathways?

(4) Are there reactions that do not contribute at all?

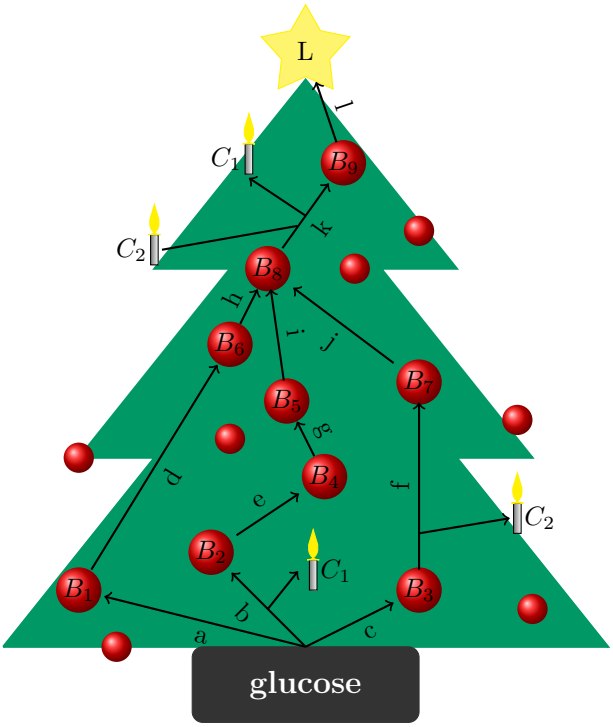
(e) **Cut-set (12)**
Let us assume that the output (biomass production) of our network corresponds to the flux through reaction b_3. Figure out the cut-set (all essential internal reactions) from the extreme pathways.

(f) **Fluxes (12)**
For the following steps, we will neglect the internal reactions. Then, we can see how the (black box) network transforms input into output. For this, consider the formula representation of the pathways.

Complete the following table which relates the input through b_1 and b_2 to the output via b_3. Determine also the fluxes through the internal reactions.

	b_1	b_2	b_3	v_1	v_2	v_3	v_4	v_5	v_6	v_7
I		0	1				1			
II		1		0				0		
III				1	1	1				
IV		1				2	1			

Exercise 6.2: Drug Design: Identifying Targets (20 points)



The Christmas tree shown on the left side produces light (in its star) from glucose. In various intermediate steps, accessory Christmas balls and candles are involved.

(a) **Essential Substrates (6)**
Consider all pathways in the tree. Identify without calculation the important Christmas balls that are essential to light up the star. Explain your findings.

(b) **Inhibition of Biomass Production (10)**
Now assume that this Christmas tree is the central part of the metabolism of a dangerous bacterium and you want to develop an efficient drug.

(1) On which reactions (enzymes) would you concentrate when searching for an inhibitor? Explain your answer.

(2) Would you change your strategy, if you knew that high concentrations of C_1 slow down or even reverse reactions b and k?

(3) Would you change your strategy, if you knew that high concentrations of B_8 were lethal for the host? What would then be a suitable inhibitor?

(c) **Inhibitor = Drug? (4)**
Let us assume that you find a suitable inhibitor for one or several reactions mentioned above. Does it mean you have a potent therapeutic drug or which other problems you might encounter?

Have fun!