Bioinformatics III

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Exercise Sheet 7

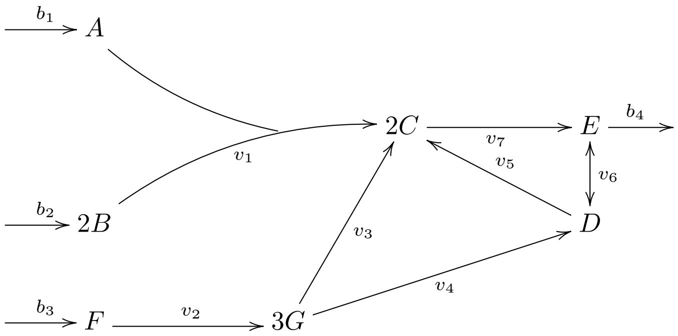
Due: 06.01.2014 14:15

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 3.06. Additionally, hand in all source code via mail to duy.nguyen@bioinformatik.uni-saarland.

Pathways of Metabolic Networks and Rate Equations

Exercise 7.1: Extreme Pathways and Steady State Flux Distribution (70 points)

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



(a) **Stoichiometric Matrix (5)**
Construct the stoichiometric matrix.

(b) **Extreme Pathways (15)**
Calculate from the stoichiometric matrix the extreme pathways. Give the pathways as

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

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

(d) **Reaction Participation Matrix (5)**

  (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 (15)**
The output of our network corresponds to the flux through reaction b_4. A reaction is essential for the network, when there is no output if this reaction is blocked. List all those reactions.

(f) **Fluxes (15)**

For the following steps we will neglect the internal reactions. Then we can see how the (black box) network transforms input through b_1, b_2 and b_3 into output through b_4 and b_5.

Complete the table given on the right, which relates the input through b_1, b_2 and b_3 to the output via b_4 and contains the fluxes through the reactions v_1, v_2 and v_7.

	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			

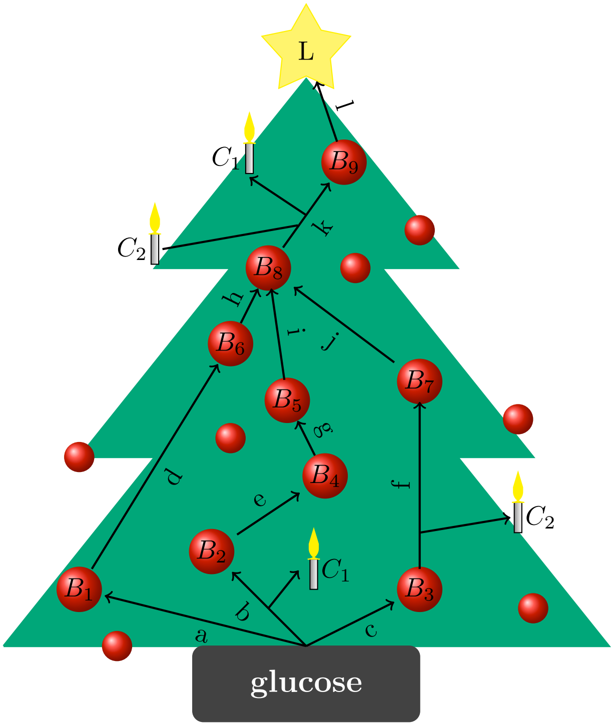
(g) **Biomass Production (10)**
Now assume that the total input into the network through b_1, b_2 and b_3, i.e., the sum of the fluxes through these reactions is limited to 5 units.

(1) How must this input be distributed onto these three reactions to give the highest output through b_4?

(2) What is the contribution of each of the extreme pathways?

(3) What is the flux through reactions v_1 and v_2?

Exercise 7.2: Drug Design: Identifying Targets (30 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 (10)**
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 (15)**
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? (5)**
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?