In the Name of God

Computational Systems Biology

Final Exam

Fall Semester 1400-01

Department of Computer Engineering

Sharif University of Technology

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Duration: 150 minutes

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1. (4 points) Consider the following metabolic network, with the default bounds ($M = 1000$) and the sink of D as the biomass reaction. Assume that A is the limiting resource allowed to be taken up with a maximum flux of 10, B is an unlimited resource, and F is the exported metabolic product. Find a flux vector for which the biomass flux rate is at maximum in this network. What is wrong with this network?

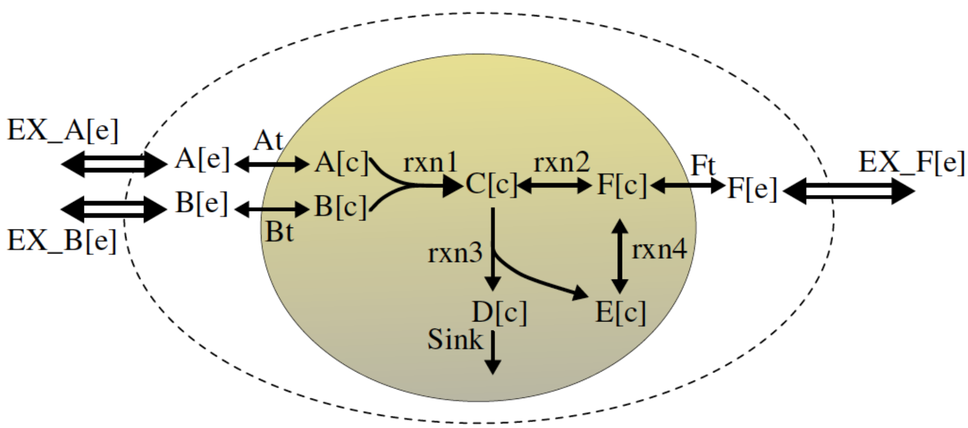

Figure 1: the metabolic network for the question 1

2. (4 points) Consider the metabolic network represented in Figure 2 in which the glucose uptake rate is limited at 10 and the exchange reactions are only EX_Glucose, EX_DHAP, and EX_Biomass (ATP, ADP, CO_2, and P_i are freely exchangeable). After running the FBA, the output flux rates are as follows:

$$v_1 = 10,\ v_2 = 10,\ v_3 = 10,\ v_4 = 10,\ v_5 = 20,\ v_6 = 20,\ v_7 = 20,$$
$$v_8 = 20,\ v_9 = 20,\ v_{10} = 0,\ v_{11} = 0,\ v_{12} = 20,\ v_{13} = 0,$$

in which the assumed direction for the reactions 3, 6, and 7 are downward, and rightward for the reaction 4. By calculating flux variabilities, define the reactions which their fluxes are reliable.

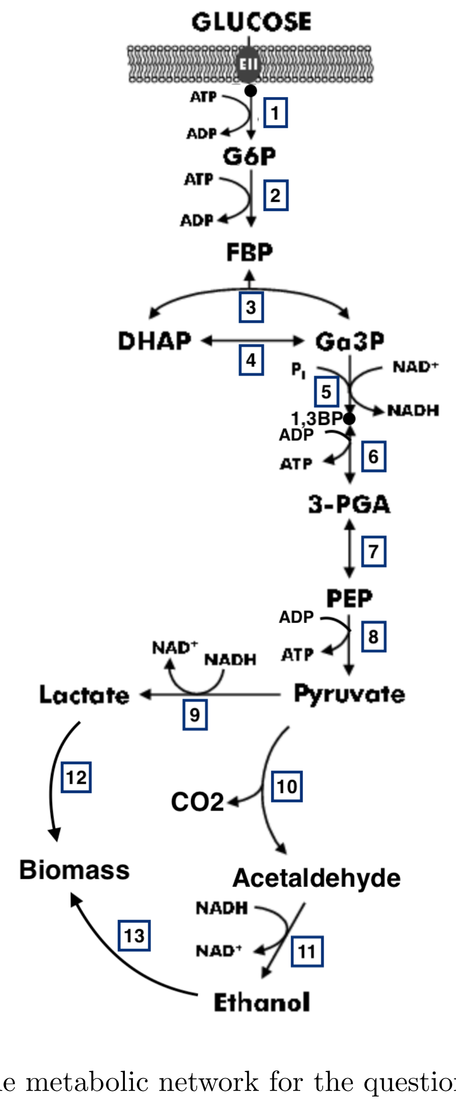

Figure 2: the metabolic network for the questions 2, 3, 4, 5, and 6

3. (4 points) In the metabolic network represented in Figure 2:
   (a) Find all essential reactions (growth percentage: $f = 0.01$).
   (b) Does your answer change for $f = 0.6$?
   (c) From non-essential reactions (based on part a), find all synthetic lethal pairs.

4. (4 points) To manufacture Ethanol in a lab, a researcher is trying to use an organism with the metabolic network represented in Figure 2. To ensure that it is a proper organism for this purpose, he solved the following optimization problem:

$$\begin{aligned} \text{maximize} \quad & v_{13} \\ \text{subject to} \quad & Sv = 0 \\ & l \leq v \leq u \end{aligned}$$

   and received the objective value equal to 20. But when executing the experiment in the lab, he observed no Ethanol production.

   (a) What is the problem? Rewrite the optimization problem that tells us whether the Ethanol production is <u>guaranteed</u> in the lab or not.
   (b) What change(s) can we apply to the organism's metabolic network to guarantee Ethanol production?

5. (4 points) Consider the metabolic network represented in Figure 2.
   (a) Find the reactions directionally coupled to the forward direction of reaction 4 ($R : R_4 \to R$).
   (b) Find the reactions to which the reaction 4 is directionally coupled ($R \to R_4$).
   (c) Find the reactions partially coupled to the reaction 8.
   (d) Find the reactions fully coupled to the reaction 9.

6. (Extra 4 points) To find a quantitative QFCA equation for the reaction 2 in the metabolic network of Figure 2, we ran the following optimization problem:

$$\begin{aligned} \text{maximize} \quad & \sum_{i \in I} \min\{v_i, 1\} \\ \text{subject to} \quad & Sv = 0 \\ & v_i \geq 0 \quad i \in I \\ & v_2 = 0 \end{aligned}$$

that rendered the following dual vector corresponding to equality constraints:

$$\nu = \begin{bmatrix} \nu_{GLC} \\ \nu_{G6P} \\ \nu_{FBP} \\ \nu_{DHAP} \\ \nu_{Ga3P} \\ \nu_{1,3BP} \\ \nu_{3PGA} \\ \nu_{PEP} \\ \nu_{PYR} \\ \nu_{LAC} \\ \nu_{ACET} \\ \nu_{EThOL} \\ \nu_{BIO} \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ -2 \\ -1 \\ -1 \\ -1 \\ -1 \\ -1 \\ -1 \\ 0 \\ -1 \\ 0 \\ 0 \end{bmatrix}.$$

For inequality constraints, we know that dual variables λ satisfy the equation $\lambda = S^T \nu$. Using the results, find a quantitative equation for this reaction in the form of:

$$v_2 = \sum_{i \in I} c_i v_i.$$