Assignment 8

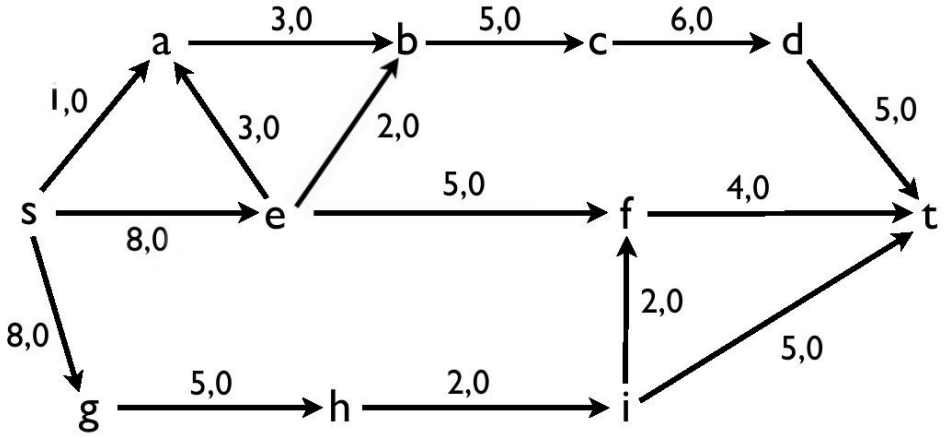
for lecture "Bioinformatics III" WS 08/09

Return by email to p.walter@bioinformatik.uni-saarland.de until **Jan. 25**. This assignment will be discussed in the tutorial on Jan. 26, 2009, room15, building E1 3

ZBI ZENTRUM FÜR BIOINFORMATIK

1. The FFEK algorithm (30 points)

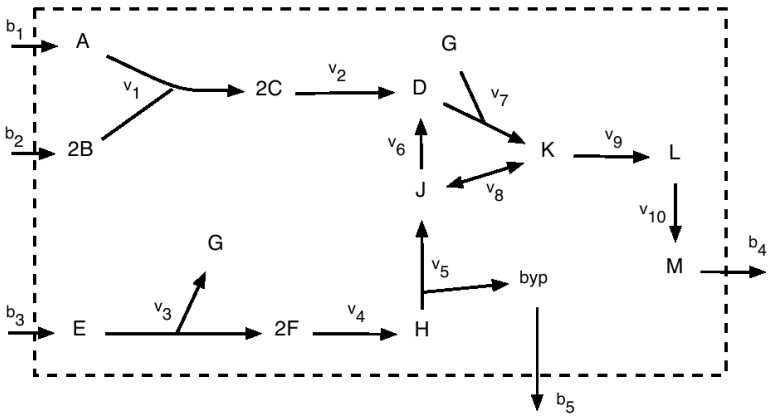
Apply the Ford, Fulkerson, Edmonds and Karp (FFEK) algorithm explained in the lecture to determine the s-t cut and the capacity of the network given to the right.
For each iteration, give the indices of the nodes, the resulting *f*-augmenting path with its capacity, and the updated *val(f)*. Sketch the newly found *f*-augmenting paths. Also update the currents through the arcs.



Hint: If you find multiple possible paths from s to t with the same length, then choose the one with the highest ΔQ

2. Extreme pathways (50 points)

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



(a) As a first step, simplify the given network by eliminating reactions that only convert one metabolite into an other one. You can reduce the network to three internal metabolites.

(b) For the simplified network construct the stoichiometric matrix and calculate the extreme pathways. Give the pathways as formulas (i.e., as $e_1=b_1+b_2+v_1+...$) and sketch the pathways in the topology as in the above network.

(c) Determine both the pathway length matrix and the reaction participation matrix. Which information do they provide? Which reactions contribute to the most pathways. Are

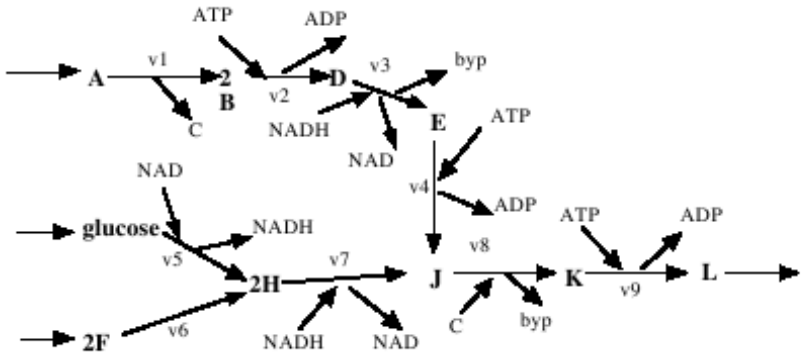
there reactions that do not contribute at all?

(d) The output ("biomass production") of our network correponds 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 reactions of the simplified network. Which reactions would this be in the complete network?

Hint: You can figure out how to determine this cut-set from the extreme pathways?

3. Drug design: Identifying targets (20 points)

The hypothetical metabolic network given to the right produces "biomass" L from the substrates A and F. In various intermediate steps, accessory substances are consumed or produced. Look at the network and identify (without calculation) the important substrates that are essential for the network. Explain your findings.



Now assume that this network is the central part of the metabolism of a dangerous bacterium and you want to develop an efficient drug. On which reactions (enzymes) would you concentrate when searching for an inhibitor? Explain your answer.

Would you change your strategy if you knew that high concentration of byp slow down or even reverse reactions v3 and v8. What would you do, if additionally high concentrations of J were lethal for the host? 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?

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