

# CHEME 7770/5440 - Problem Set 3

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File "srk-ps3-1.jl" contains the answers to a,b,c. Main points are summarized here. That Julia file references several subfunctions which are included in the repository as separate Julia files. To run, all files must be put in the same folder. To run, run the "srk-ps3-1.jl" file in PowerShell.

## 1. Answer to part a:

Assume everything in the system (the box) is at steady-state, and therefore that the time derivative is 0. "S original" is the stoichiometric matrix below (in srk-ps3-1 ) In part b, the S will be rewritten.

$$\frac{dx}{dt} = \begin{pmatrix} -1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 1 & -1 & 0 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & -1 \\ 0 & 0 & 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 0 & 0 & 1 & 0 & 0 & 0 \\ -1 & 0 & 0 & 1 & -1 & 1 & 0 & 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_{5,1} \\ v_{5,-1} \\ b_1 \\ b_2 \\ b_3 \\ b_4 \end{pmatrix} = 0 \quad (1)$$

$$S_{original} = \begin{pmatrix} -1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 1 & -1 & 0 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & -1 \\ 0 & 0 & 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 0 & 0 & 1 & 0 & 0 & 0 \\ -1 & 0 & 0 & 1 & -1 & 1 & 0 & 0 & 0 & 0 \end{pmatrix} \quad (2)$$

where we have the following k-cat (from KEGG and PS3),

$$k_{cat} \text{ for the following } \begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_{5,1} \\ v_{5,-1} \end{pmatrix} = \begin{pmatrix} 203s^{-1} \\ 34.5s^{-1} \\ 249s^{-1} \\ 88.1s^{-1} \\ 13.7s^{-1} \\ 13.7s^{-1} \end{pmatrix} \quad (3)$$

(Assume that  $v_{5,1}$  is from citruline to arginine, and that  $v_{5,-1}$  is arginine to citruline.)  
and,

$$\mathbf{x} = \begin{pmatrix} \textit{Aspartate} \\ \textit{Argininosuccinate} \\ \textit{Fumarate} \\ \textit{Arginine} \\ \textit{Urea} \\ \textit{Ornithine} \\ \textit{CarbarmoylPhosphate} \\ \textit{Citruline} \end{pmatrix} \quad (4)$$

## 2. Answer to part b:

Each of the different molecules has the following chemical formula:

Aspartate =  $\text{C}_4\text{H}_7\text{NO}_4$

Argininosuccinate =  $\text{C}_{10}\text{H}_{18}\text{N}_4\text{O}_6$

Fumarate =  $\text{C}_4\text{H}_4\text{O}_4$

Arginine =  $\text{C}_6\text{H}_{14}\text{N}_4\text{O}_2$

Urea =  $\text{CH}_4\text{N}_2\text{O}$

Ornithine =  $\text{C}_5\text{H}_{12}\text{N}_2\text{O}_2$

Carbarmoyl Phosphate =  $\text{CH}_4\text{NO}_5\text{P}$

Citruline =  $\text{C}_6\text{H}_{13}\text{N}_3\text{O}_3$

**An Atom Array with these formulas was put in srk-ps3-1, labeled "atom original" to denote the array that does not yet include additional metabolites."**

To check the original balance, calculate E original:

$$E_{original} = S_{original} * atom_{original} = () \quad (5)$$

"E\_original" can be gotten from the command line. The results of the E\_original show non-zero values for all the rates v1 to v5,-1 (represented by the columns) except v2. As a result, research for all of the reactions was done to understand other species that might be involved.

v1 (6.3.4.5): ATP substrate (enters) (rate b5,  $\text{C}_{10}\text{H}_{16}\text{N}_5\text{O}_{13}\text{P}_3$ ), ADP product (leaves) ( $\text{C}_{10}\text{H}_{16}\text{N}_5\text{O}_{13}\text{P}_3$ , rate b6), diphosphate product (leaves) (rate b7,  $\text{H}_4\text{P}_2\text{O}_7$ ); The cleavage of ATP probably added the energy for this reaction to occur, and is how the product got phosphorlyated (energized for future reactions.)

v2 (4.3.2.1): no extra substrates or products

v3 (3.5.3.1):  $\text{H}_2\text{O}$  substrate (enters, rate b8); Arginine was probably cleaved into urea and ornithine through a hydrolysis reaction.

v4 (2.1.3.3): phosphate product (leaves, rate b9,  $\text{H}_3\text{PO}_4$ ); The cleavage of a phosphate group probably provided energy for this reaction)

v5,1 (1.14.13.39, citruline to arginine): nitric oxide substrate (enters, b10, NO), NADP+ substrate (enters b11,  $\text{C}_{21}\text{H}_{29}\text{N}_7\text{O}_{17}\text{P}_3$ ),  $\text{H}_2\text{O}$  substrate (enters, b12,  $\text{H}_2\text{O}$ ), NADPH product (leaves, rate b13,  $\text{C}_{21}\text{H}_{30}\text{N}_7\text{O}_{17}\text{P}_3$ ),  $\text{H}^+$  product (leaves, rate b14, H)  $\text{O}_2$  product (leaves, rate b20,  $\text{O}_2$ )

v5,-1 (1.14.13.39, arginine to citruline): NADPH substrate (enters, rate b15, C21H30N7O17P3), H+ substrate (enters, rate b16, H) O2 substrate (enters, rate b21, O2) nitric oxide product (leaves, rate b17, NO), NADP+ product (leaves, b18, C21H29N7O17P3), H2O product (leaves, b19, H2O)

Changes were made the stoichiometric matrix. Please see "stoichiometric\_matrix\_balanced" for the new values for all reactions and the coefficients of reactants. The "E\_balanced" shows zero values for all reactions v1 - v5. These variables can be printed from the command line.

### 3. Answer to part c:

Assume:

-there is negligible consumption of metabolites for biomass growth

-there is negligible dilution of metabolites during biomass growth

-allosteric control function is 1

**Bounds** Lower Bounds: Since v5 was split into v5,1 and v5,-1 (forwards/backwards respectively as defined in a,) the minimum rate was 0 for all since they were assumed irreversible.

Upper Bounds:

The upper bound was determined with:

$$v_{max} = k_{cat} * \frac{e_j}{e} * \theta * \sum_i^N \frac{x_i}{K_m + x_i} \quad (6)$$

where N is the # of metabolites, E is the steady state concentration

$$E = \frac{e_j}{e} = 0.01(assume)[\mu mol/gDW], \quad (7)$$

and theta is the control element

$$\theta = \theta_{max} = 1. \quad (8)$$

- I could not find the concentrations of Arginosuccitate, Fumarate, Urea, Orinithine, and Carbarmoyl Phosphate. I could also not find Km for all substrates in all reactions. In these cases where Km or concentration could not be found, the saturation terms for those in the upper bound calculation was assumed to be 1 (the max.) This is because if you assume concentration is much greater than Km, ( $x_i \gg K_m$ ), you go from the original saturation term equation:

$$\frac{x_i}{K_m + x_i} \quad (9)$$

to

$$\frac{x_i}{x_i} = 1 \quad (10)$$

4. Use inline equations for simple math  $1 + 1 = 2$ , and centered equations for more involved or important equations

$$a^2 + b^2 = c^2. \quad (11)$$

Some people like to write scalars without boldface  $x + y = 1$  and vectors or matrices in boldface

$$\mathbf{Ax} = \mathbf{b}. \quad (12)$$

An example of a matrix  $\text{\LaTeX}$ :

$$\mathbf{A} = \begin{pmatrix} 3 & -1 & 2 \\ 0 & 1 & 2 \\ 1 & 0 & -1 \end{pmatrix}. \quad (13)$$

With a labeled equation such as the following:

$$\frac{d^2x}{dt^2} = a \quad (14)$$

you can refer to the equation later. In equation 14 we defined acceleration.

5. Answer to question 2