Problem Set 3

- You may use your course materials and/or any literature resources (as well as the internet) to formulate your solutions.
- You may work in teams. All model/analysis code must be submitted to GitHub and the link submitted to the teaching staff email. Each student on the team must be a collaborator on the GitHub repository.
- Problem Set 3 is due on **Thursday, March 25, 2021** by **11:59 PM**.

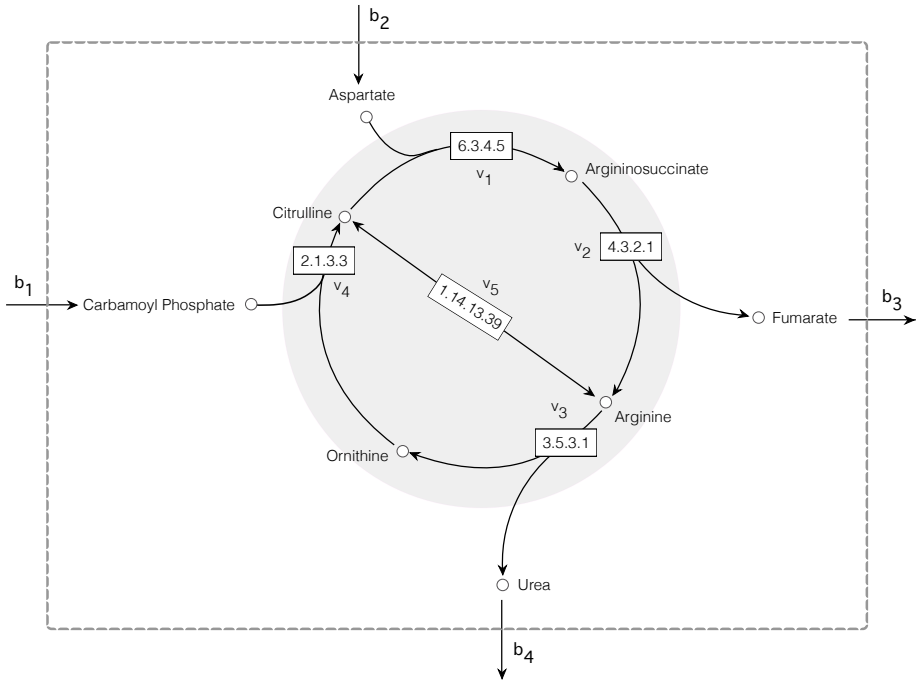

Figure 1: Schematic of the Urea cycle.

1. The urea cycle eliminates excess nitrogen from the cell (Fig. 1). Let's explore this cycle in a growing population of human cells with a doubling time of τ_d = 20 hr using Flux Balance Analysis (FBA). FBA code is available at: `https://github.com/varnerlab/CHEME-5440-7770-PS3-S21.git`.

   Assume: (i) k_{cat}'s for the enzymes in the pathway are: EC:3.5.3.1 = 249s^{-1}; EC:2.1.33 = 88.1s^{-1}; EC:4.3.2.1 = 34.5s^{-1}; EC:6.3.4.5 = 203s^{-1} and EC:1.14.13.39 = 13.7s^{-1};

(ii) the approximate steady-state concentration for enzymes in the pathway (E) is uniform, and given by $E \simeq 0.01$ μmol gDW^{-1}; (iii) ignore dilution due to growth; (iv) all enzymes are maximally active.

a) Use KEGG (Arginine biosynthesis in human) to construct the stoichiometric matrix **S** for the urea cycle shown in Fig. 1. The KEGG link is: `https://www.genome.jp/kegg-bin/show_pathway?hsa00220`. Save your stoichiometric matrix into a file called `Network.dat` and put this file into the `config` directory under `src`.

b) Determine if your urea cycle reconstruction is elementally balanced for C,H,N,O,P and S. If not, how can you correct the balances? (**hint**: write elemental balances around C,H,N,O,P and S).

c) Calculate the maximum rate of urea production (b_4 mmol/gDW-hr) given: 0 $\leq$b$_j$ $\leq$ 10 mmol/gDW-hr $\forall j$ using Flux Balance Analysis (FBA). If additional inputs/output exchanges are required, assume they obey the same bound constraints. To complete this calculation, please fill in the missing items in the `Problem.jl` file in the `src` directory, then include the file `execute_me_for_flux.jl` in the julia REPL.