Metabolic Modeling, Spring 2007, Exercise 5

27.4.2007

1. Consider a reaction with Michaelis-Menten type kinetics $v_k = \frac{V_{max} S_i}{K_m + S_i}$. Give a detailed derivation for the equations

   (a) ϵ_i^k

   (b) $\pi_{K_m}^k$

   (c) $\pi_{V_{max}}^k$

2. A simple rate law for irreversible reaction subject to competitive inhibition is given by

$$v = \frac{V_{max} S}{(K_m + S)(1 + I K_I)},$$

   where I denotes the concentration of the inhibitor and K_I the equilibrium constant for binding/releasing the inhibitor.

   Derive π-elasticity coefficient π_I for inhibitor concentration and interpret the derived coefficient: how do the inhibitor concentration I and the equilibrium constant K_I affect the reaction rate.

3. Give a detailed derivation for the equations given on Lecture 10, slides 28 and 30, for the flux control coefficients FCC_1^J, FCC_2^J and the concentration control coefficients CCC_1^S, CCC_2^S.

4. Consider a metabolic network with three reactions $r_1 : A \to B, r_2 : B \to C, r_3 : B \to D$. Assume that the elasticity coefficients have been determined as $\epsilon_B^1 \approx -0.5, \epsilon_B^2 \approx 0.25, \epsilon_B^3 \approx 0.5$, and the flux control coefficient $FCC_{v_1}^{J_2} \approx 0.25$ for the flux J_2 from B to C.

   Determine the coefficients $FCC_{v_2}^{J_2}$ and $FCC_{v_3}^{J_2}$.

   Hint: use the flux summation ($\sum_{k=1}^r FCC_k^j = 1$) and connectivity ($\sum_{k=1}^r FCC_{v_k}^{J_j} \epsilon_{S_i}^{v_k} = 0$) theorems.

5. Read the article **Cascante et al.: Metabolic control analysis in drug discovery and disease. Nature Biotechnology 20 (2002), pp. 243–249** so that you can explain the main points of the article