NATIONAL TAIWAN UNIVERSITY,
GRADUATE INSTITUTE OF BIOMEDICAL ENGINEERING AND BIOINFORMATICS

BEBI5009:
Mathematical Modeling of System Biology
Homework 5

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1 5.6.3 Metabolic Control Analysis: supply and demand

Consider the two-step reaction chain $\xrightarrow{v_0} S \xrightarrow{v_1}$, where the reactions are catalysed by enzymes E_0 and E_1 with concentrations e_0 and e_1. The Summation Theorem (Section 5.2.1) states that

$$C^J_{e_0} + C^J_{e_1} = 1$$

A complementary result, the Connectivity Theorem (Heinrich and Schuster, 1996) states that

$$C^J_{e_0}\epsilon^0_S + C^J_{e_1}\epsilon^1_S = 0$$

a) Use these two statements to determine the flux control coefficients of the two reactions as

$$C^J_{e_0} = \frac{\epsilon^1_S}{\epsilon^1_S - \epsilon^0_S}$$
$$C^J_{e_1} = \frac{-\epsilon^0_S}{\epsilon^1_S - \epsilon^0_S}$$

According to Cramer's Rule, it is easy to solve these two variables equations:

$$C^J_{e_0} = \frac{\begin{vmatrix} 1 & 1 \\ 0 & \epsilon^1_S \end{vmatrix}}{\begin{vmatrix} 1 & 1 \\ \epsilon^0_S & \epsilon^1_S \end{vmatrix}} = \frac{\epsilon^1_S}{\epsilon^1_S - \epsilon^0_S}$$
$$C^J_{e_1} = \frac{\begin{vmatrix} 1 & 1 \\ \epsilon^0_S & 0 \end{vmatrix}}{\begin{vmatrix} 1 & 1 \\ \epsilon^0_S & \epsilon^1_S \end{vmatrix}} = \frac{-\epsilon^0_S}{\epsilon^1_S - \epsilon^0_S}$$

b) In addressing the control of flux through the pathway, we can think of v_0 as the 'supply rate' and v_1 as the 'demand rate'. Given the result in part (a), under what conditions on the elasticities ϵ^0_S and ϵ^1_S will a perturbation in the rate of supply affect pathway flux more than an equivalent perturbation in the rate of demand?

c) Suppose the rate laws are given as $v_0 = e_0(k_0 X - k_{-1}[S])$ and $v_1 = e_1 k_1 [S]$, where X is the constant concentration of the pathway substrate. Verify that the elasticities are

$$\epsilon^0_S = \frac{k_{-1}[S]}{k_0 X - k_{-1}[S]}$$
$$and \quad \epsilon^1_S = 1$$

Determine conditions on the parameters under which perturbation in the supply reaction v_0 will have a more significant effect than perturbation in the demand reaction v_1. Hint: at steady state $k_0 X - k_{-1} s = e_1 k_1 s / e_0$.

2 6.8.18 Frequency response analysis of a two-component signaling pathway

a) Following the procedure in Section 6.6.3, determine the linearization of the two-component signaling pathway model of Section 6.1.1 at an arbitrary nominal input value. Use species conservations to reduce the model before linearizing.

b) example q2