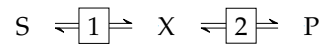

Systems Biology Tutorial 5: MCA

In this tutorial, we will explore MCA with a simple 2-step pathway:



The rate equations for the reactions are given by:

$$v_1 = k_{1f} \left(s - \frac{x}{K_{eq1}} \right)$$
$$v_2 = \frac{\frac{V_{f2}}{K_x} \left(x - \frac{p}{K_{eq2}} \right)}{1 + \frac{x}{K_x} + \frac{p}{K_p}}$$

A Mathematica notebook for this pathway is available as Tut5.nb. Inspect this file, note that it also has values for the kinetic parameters and initial values for the variable concentrations.

1. Perform a time simulation for $0 \leq t \leq 10$. Plot the concentration of x vs. time. Plot the rates of both reactions vs. time. What are the values of the steady-state concentration of x and the flux J ?
2. Calculate C_{v1}^J and C_{v2}^J using perturbation control analysis. To do this, increase k_{1f} (or V_{2f} respectively) by 1% from its original value and note the new flux. Calculate the flux-control coefficient using the formula you learnt in the MCA lecture.
3. Do the flux control coefficients for the model sum to 1? If not, explain the difference.
4. By how many percent would v_2 change upon a 1% increase in K_x ? Calculate the elasticity of the enzyme using the analytical derivative.
5. Increase the K_x by 1% and obtain a new model simulation. Determine the %-change in the rate of v_2 at the new steady state ($R_{K_x}^J$). Did the local behaviour of the reaction match that of the pathway as a whole? If v_2 had complete control of the pathway, what change would you have expected?
6. Give expressions for the flux control coefficient i.t.o. elasticity coefficients using the connectivity and flux summation theorems.
7. Determine the elasticities of e_x^{v1} and e_x^{v2} at steady state using the analytical method. Calculate the flux control coefficients using your answers. Do the flux control coefficients sum to 1? How do they compare to the flux control coefficients that we determined in Question 2?
8. Use the partitioned response $R_x^J = C_{v1}^J e_x^{v1} + C_{v2}^J e_x^{v2}$ to show that a 1% change in the concentration of x will not affect the flux.