7.3.2 Control Coefficients

A control coefficient is a relative measure of how much a perturbation on a parameter affects a system variable (e.g. fluxes or concentrations). It is defined [**?**] as:

$$C_{v_i}^{A} = \frac{\partial A}{\partial v_i}\frac{v_i}{A}$$

where A is the variable, i the step (enzyme) and v the steady-state rate of the perturbed step. The most common control coefficients are those for fluxes and species concentrations, but any variable of the system can be analyzed with MCA and have control coefficients defined by equations analogous to equation 1. In fact, there is no need even for the system to be in a steady state. COPASI only calculates directly the steady-state concentration- and flux-control coefficients, those for other variables can still be estimated by simulating small perturbations.

7.3.3 Summation Theorem

A very important property of steady-state metabolic systems was uncovered with the MCA formalism. This concerns the summation of all the flux control coefficients of a pathway. By various procedures [**?**] it can be demonstrated that for a given reference flux the sum of all flux-control coefficients (of all steps) is equal to unity:

$$\sum_i C_{v_i}^{J} = 1$$

For a given reference species concentration the sum of all concentration-control coefficients is zero:

$$\sum_i C_{v_i}^{[M]} = 0$$

where the summations are over all the steps of the system.

According to the first summation theorem, increases in some of the flux-control coefficients imply decreases in the others so that the total remains unity. As a consequence of the summation theorems, one concludes that the control coefficients are global properties and that in metabolic systems, control is a systemic property, dependent on all of the system's elements (steps).

7.3.4 Enzyme Kinetics and the Elasticity Coefficients

In enzyme kinetics the behavior of isolated enzymes is studied through the dependence of the initial rates of reaction with the concentration of the substrate(s). Enzyme kinetic studies are centered on derivation of rate equations and the determination of their kinetic constants such as Michaelis constants or limiting-rates or even on the elementary rate constants of a specific reaction mechanism.

In metabolic control analysis the properties of each (isolated) enzyme are measured in a way very similar to the flux-control properties: using a sensitivity, known as the elasticity coefficient [**?**]. In this case, one has to consider the effect of perturbations of a reaction parameter on the local reaction rate. By local one means that this sensitivity refers to the isolated reaction which has the same characteristics (effector and enzyme concentrations, temperature, and so on) as in the whole system at the operating point (steady state) of interest. The elasticity coefficients are defined as the ratio of relative change in local rate to the relative change in one parameter (normally the concentration of an effector). Infinitesimally, this is written as:

$$\varepsilon_{p}^{v_i} = \frac{\partial v_i}{\partial p}\frac{p}{v_1}$$

where v is the rate of the enzyme in question and p is the parameter of the perturbation. Each enzyme has as many elasticity coefficients as the number of parameters that affect it. One can immediately recognize the concentration of the reaction substrates, products and modifiers as parameters of the reaction. Unlike control coefficients, elasticity coefficients are not systemic properties but rather measure how isolated enzymes are sensitive to changes in their parameters. The elasticity coefficients can be obtained from the kinetic functions by partial derivation. Again like the control coefficients, the elasticity coefficients are not constants, they are dependent on the value of the relevant parameter and so are different for each Steady-State.