

Response Coefficients

Control coefficients measure the response of a pathway to changes in enzyme activities. What about the effect of external factors such as inhibitors, pharmaceutical drugs or boundary species? Such effects are measured by another coefficient called the response coefficient. The flux response coefficient is defined by:

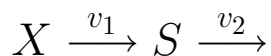
$$R_X^J = \frac{dJ}{dX} \frac{X}{J}$$

and the concentration response coefficient by:

$$R_X^S = \frac{dS}{dX} \frac{X}{S}$$

The response coefficient measures how sensitive a pathway is to changes in external factors other than enzyme activities. What is the relationship of the response coefficients with respect to the control coefficients and elasticities?

Like many proofs in this theory we can carry out a thought experiment as follows. Consider the pathway fragment below:



where X is the pathway boundary species. Let us increase the activity of v_1 by increasing the concentration of E_1 . This will cause the steady state flux and concentration of S and in fact all downstream species to increase. Let us now decrease the concentration of X such that we restore the flux and steady state concentration of S back to its original value. From this thought experiment we can write the operations in terms of the local response equation and a system response equation as follows:

$$\frac{\delta v_1}{v_1} = \varepsilon_X^{v_1} \frac{\delta X}{X} + \varepsilon_{E_1}^{v_1} \frac{\delta E_1}{E_1} = 0$$

$$\frac{\delta J}{J} = R_X^J \frac{\delta X}{X} + C_{E_1}^J \frac{\delta E_1}{E_1} = 0$$

We can eliminate the $\delta E_1/E_1$ term in the system response equation by substituting the term from the local response equation and recalling that $\varepsilon_{E_1}^{v_1} = 1$ we can obtain:

$$0 = R_X^J \frac{\delta X}{X} - C_{E_1}^J \varepsilon_X^{v_1} \frac{\delta X}{X}$$

From this we conclude that:

$$R_X^J = C_{E_1}^J \varepsilon_X^{v_1}$$

This gives us the relationship we seek. It can be generalized for multiple external factors acting simultaneously but summing up individual responses:

$$R_X^J = \sum_{i=1}^n C_{E_i}^J \varepsilon_X^{v_i}$$

Likewise the response of a species, S to an external factor is given by:

$$R_X^S = \sum_{i=1}^n C_{E_i}^S \varepsilon_X^{v_i}$$

The response coefficient carries an important message, which is that the response of some external factor, X , is a function of two things, the effect the factor has on the step it acts upon and the effect that the step itself has on changing the system. This means that an effective external factor, such as a pharmaceutical drug, must not only be able to bind and inhibit the enzyme being targeted, but the step itself must be able to transmit the effect to the rest of the pathway.