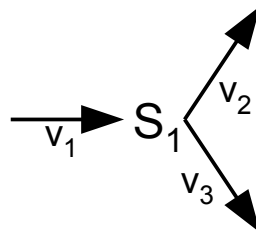


**Worksheet: SENSITIVITIES AND METABOLIC CONTROL
ANALYSIS (12. June 2012)
Lecture "Computational Systems Biology", Dr. Jürgen Pahle**

1) Comprehension questions:

- a) Why is metabolic control analysis (MCA) only locally valid?
- b) What is meant when one says that flux/concentration control coefficients measure global properties of the system?
- c) What is a rate-limiting step/reaction? Why is that concept problematic?
- d) What control coefficients are defined for the following network?



- e) Can control coefficients be negative? If no, prove it. If yes, give examples for both negative flux and negative concentration control coefficients.
- f) If an enzyme E is explicitly included as a species in a model, and this enzyme catalyses a reaction for which a Michaelis-Menten kinetics is assumed. What is the ϵ -elasticity of this reaction with respect to enzyme E?
- g) What are the connectivity theorems? Why are they essential for the practical calculation of coefficients in MCA?

2) Calculate the ϵ -elasticities with respect to substrate and product for

- a) reversible mass action rate law, and
- b) reversible Michaelis-Menten kinetic function.

3) Download model 23 from the [Biomodels.net](http://www.biomodels.net) database (described in Rowher and Botha (2011) Analysis of sucrose accumulation in the sugar cane culm on the basis of in vitro kinetic data. *Biochem. J.* **358**(2):437). The model describes the accumulation of sugar in sugar cane. Sucrose

accumulation in the vacuole is described by reaction *v11* and the hydrolysis (degradation) of sucrose happens in reaction *v9*. To increase the yield of sugar one should therefore increase the flux over reaction *v11* while decreasing the flux over reaction *v9*.

- a) Use the metabolic control analysis task in COPASI to find out which reaction has the most control over sugar accumulation (reaction *v11*).
- b) Which enzyme corresponds to this reaction?
- c) If this enzyme is overexpressed by 20% what increase in flux over reaction *v11* would you expect based on MCA?
- d) Why is this enzyme probably not a good candidate for overexpression when you want to increase the yield in sugar?
- e) What are better candidates?