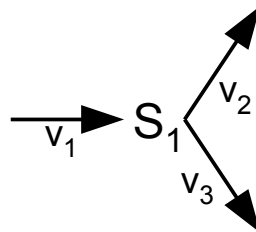


**Worksheet: SENSITIVITIES AND METABOLIC CONTROL
ANALYSIS (12. June 2012)
Lecture "Computational Systems Biology", Dr. Jürgen Pahle**

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 Biomedels.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?