BMC Systems Biology

Poster presentation

Visualizing regulatory interactions in metabolic networks

Stephan Noack*[1], Aljoscha Wahl[2], Marco Oldiges[1] and Wolfgang Wiechert[3]

Address: [1]Inst. of Biotechn, Research Centre Jülich, Germany, [2]MPI for Complex Technical Systems Magdeburg, Germany and [3]Inst. of Syst. Eng., Dept. of Simulation, University of Siegen, Germany

Email: Stephan Noack* - s.noack@fz-juelich.de

* Corresponding author

from BioSysBio 2007: Systems Biology, Bioinformatics and Synthetic Biology
Manchester, UK. 11–13 January 2007

Published: 2 May 2007

BMC Systems Biology 2007, **1**(Suppl 1):P5 doi:10.1186/1752-0509-1-S1-P5

This article is available from: http://www.biomedcentral.com/1752-0509/1?issue=S1

In the field of System Biology most research projects produce large amounts of data that usually spread over various "omics" domains. In most cases the collected data are dependent on time, specific organisms or physiological conditions. Irrespectively of whether this data is produced in a lab or on a computer, its evaluation requires visualization representing as much information as possible in an intuitive way. Clearly, the direct visualization of data sets in the context of a biochemical network drawing is one of the most appealing approaches in this field. Visualization methods for metabolic networks such as hypergraphs, where the nodes represent metabolite pools and the edges chemical reaction steps or bipartite graphs with directed one-to-one edges are well established and implemented in various software tools.

However, there is still one important information missing that is very helpful to interpret and to understand the function of metabolic networks. It is related to the strength of regulatory interactions between metabolite pools and the reaction steps influenced by these pools. Interestingly, this qualitative regulatory information has never been represented in a quantitative way in available visualization tools. In particular this information would be a valuable information that can complement the already displayed pool size and flux data. If, for example, a flux is downregulated although its substrate pools are at high levels and product pools are at low levels, the reason can only be given by an inhibitory effect of some other metabolite pool. Thus the incorporation of additional edges for inhibitors and activators will help to explain why metabolic fluxes are at their present levels.

In this contribution we present a general definition for the Regulatory Strength (RS) of an effector interaction and its application to a relevant biochemical network model. The basic idea of this RS value is to find a relation on how strongly a reaction step is up- or downregulated compared to the completely non-inhibited or, respectively, non-activated state (see Figure 1). One conceptional difficulty with the introduction of a RS is that the activation or inhibition state of a reaction step in relation to the state where all activators or inhibitors are absent must be quantitated by exactly k numbers, where k is the number of effectors. This immediately indicates the implicit assumption that activators and inhibitors act independently (i.e. multiplicatively) on a reaction. In contrast, it is well known from enzyme kinetics that this is not always the case.

The concept of RS presented here is applicable to any reaction kinetic formula. One numerical RS value is associated to any effector edge contained in the network. Thus it is possible to visualize RS's directly in the network context. Each RS is interpretable as a percentage where 100% means the maximal possible inhibition or activation and 0% means the absence of a regulatory interaction. If many effectors influence certain reaction steps the respective percentages indicate the proportion in which the different effectors contribute to the total regulation of the reaction step.

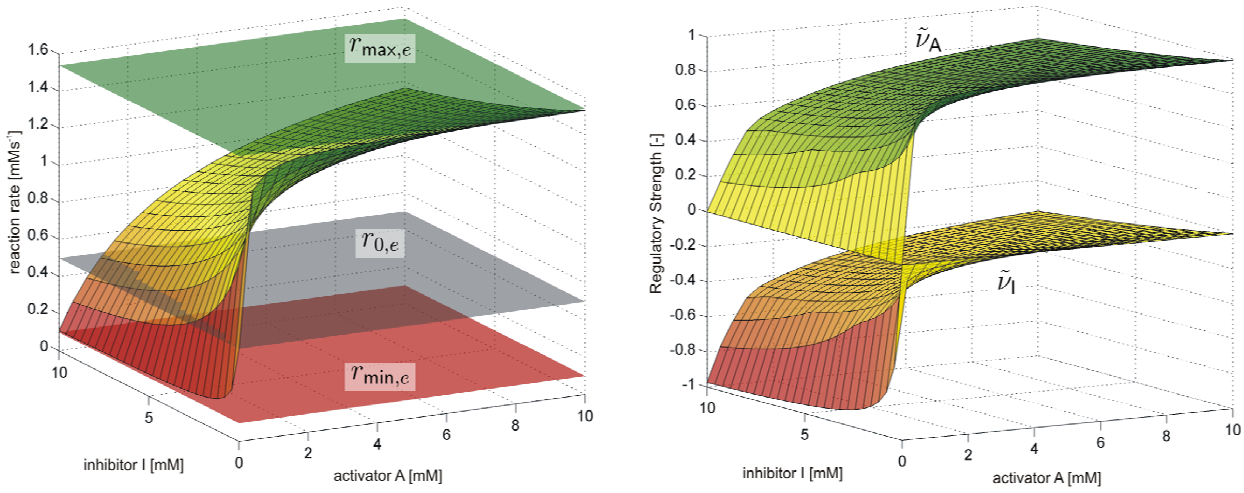

Figure 1

Example kinetic of Michaelis-Menten type comprising one substrate, activator and inhibitor pool. The two effectors are competitive with respect to each other. Left: Determination of the overall regulatory effect (ν_{res}) is done by scaling of the present flux. Right: Using ν_{res} the scaled single effector influences of the activator ($\tilde{\nu}_A$) and the inhibitor ($\tilde{\nu}_I$) can be determined.